Université de Montréal

Déconstruire l'hétérogénéité des systèmes neurocognitifs sous-jacents aux comportements antisociaux:

de l'analyse développementale aux corrélats neurobiologiques

Par

Jules Dugré

Thèse présentée en vue de l’obtention du grade de Philosophiae Doctor (Ph.D) en sciences biomédicales, option sciences psychiatriques

Août 2022

Université de Montréal

Département de Psychiatrie et d'Addictologie, Faculté de Médecine

---

Cette thèse intitulée

Déconstruire l'hétérogénéité des systèmes neurocognitifs sous-jacents aux comportements antisociaux:

de l'analyse développementale aux corrélats neurobiologiques

Présenté par

Jules R. Dugré

Anne Crocker, PhD.
Président-rapporteur

Stéphane Potvin, PhD.
Directeur de recherche

Vincent Taschereau-Dumouchel, PhD.
Membre du jury

Gabriella Gobbi, MD., PhD.
Examinateur externe

Résumé

Contexte. L'étiologie des comportements antisociaux est encore mal comprise. La population d'individus commettant ce type de comportements est hautement hétérogène, suggérant ainsi que plusieurs mécanismes biopsychosociaux pourraient augmenter ou réduire le risque de délinquanceau cours du développement humain. Objectif. L'objectif principal de cette thèse est d'identifier cesmécanismes sous-jacents à la délinquance, par l'entremise de quatre méthodes scientifiquesdistinctes, mais complémentaires : les analyses de trajectoires développementales, l'activité cérébrale induite par une tâche, la connectivité cérébrale au repos ainsi que l'étude des lésions cérébrales. Méthodologie. Afin d'atteindre cet objectif, une première étude a été réalisée en réanalysant les données de l'Étude Longitudinale du Développement des Enfants du Québec (n=1309). Par l'entremise de modèles de trajectoires par classes latentes, cette étude visait à identifier des sous-groupes de jeunes présentant des trajectoires développementales de traits psychologiques (c.-à-d., l'insensibilité émotionnelle, les traits anxio-dépressifs, l'irritabilité et les traits d'hyperactivité/impulsivité) à risque de comportements antisociaux à l'enfance et l'adolescence. Par ailleurs, deux méta-analyses portant sur des études d'activation cérébrale (71 et 147 études) ont été réalisées afin d'identifier les principales altérations de l'activité cérébrale sous-jacent à différents domaines neurocognitifs, ainsi que leur similarité avec d'autres problématiques psychiatriques. De plus, une troisième méta-analyse (18 études) a été accomplie afin d'étudier si les individus antisociaux présentaient des déficits lors de la connectivité cérébrale au repos. De manière à combler les limites de la littérature sous-jacente à la connectivité cérébrale au repos des individus antisociaux, une étude transversale a été effectuée sur 1,416 enfants et adolescents issue Healthy Brain Network aux États-Unis. Outre l'objectif de valider les résultats de la méta-analyse précédente, cette étude a été conçue de manière à mieux comprendre le rôle de l'interaction entre des systèmes neurobiologiques dans l'explication des comportements antisociaux. Finalement, une récente revue de la littérature scientifique produite par des chercheurs américains a permis d'identifier 17 cas dans lesquels des lésions au cerveau étaient temporellement liés à l'émergence de comportements antisociaux. Grâce à une reconstruction des images de lesdites lésions, des analyses de coactivation méta- analytique ont

été conduites afin de récréer les réseaux neurobiologiques altérés qui seraient possiblement à l'origine de de gestes délinquants. Résultats. Les résultats ont soutenu l'importance des traits d'insensibilité émotionnelle dans l'explication du risque de délinquance, et aussi montré que l'interaction développementale entre les traits psychologiques augmentait jusqu'à 10 fois le risque de comportements antisociaux à l'enfance. Sur une base neurobiologique, les résultats ont révélé que les personnes ayant commis des gestes délinquants rapporteraient d'importants déficits dans les régions cérébrales impliquées dans le contrôle cognitif, la réponse àune menace et les cognitions sociales. En comparaison avec le trouble du déficit de l'attention avec hyperactivité et les troubles anxieux et dépressifs, le trouble des conduites serait associé à un dysfonctionnement commun de régions cérébrales impliquées dans le contrôle des émotions et dusystème somato-moteur. Par ailleurs, les résultats indiquent que la population étudiée serait principalement caractérisée par une dysconnectivité fonctionnelle entre les réseaux socioaffectifse et attentionnels, mais aussi entre les systèmes somato-moteurs, attentionnels et ceux impliqués dansla détection de stimuli saillants. Finalement, les lésions cérébrales pourraient causer des comportements délinquants par l'entremise de trois mécanismes neurobiologiques, notamment parune défaillance du réseau de la récompense (lobe frontal), du réseau impliqué dans le traitement des émotions négatives (lobe temporal) ainsi que la reconnaissance émotionnelle faciale (amygdale). Conclusions. Les résultats des travaux présentés dans cette thèse soutiennent l'importance de mieux comprendre l'hétérogénéité de domaines neurocognitifs dans l'explicationdes comportements délinquants. D'une part, ceux-ci soulignent l'importance des systèmes neurobiologiques à valence négative (associés à l'anxiété et l'irritabilité), aux systèmes cognitifs (associés à l'hyperactivité/impulsivité et à l'inattention) ainsi qu'aux processus sociaux (associés à l'insensibilité émotionnelle). D'autre part, les résultats suggèrent un rôle limité des systèmes de récompense, mais un rôle prépondérant du système sensorimoteur (associé à l'action et au contrôledes mouvements). La présente thèse offre une perspective novatrice et exhaustive sur l'hétérogénéité neurocognitive sous-jacente à la délinquance. Or, la variabilité interindividuelle dessystèmes neurobiologiques étudiés dans cette thèse reste à être identifiée, de manière à découvrir des cibles thérapeutiques prometteuses pour réduire le risque de délinquance.

Mots-clés : Comportements antisociaux, trajectoires développementales, neuroimagerie, connectivité cérébrale, lésions cérébrales, émotions négatives, psychopathie, impulsivité.

Abstract

Background. The etiology of antisocial behaviors remains largely misunderstood. Antisocial population is characterized as highly heterogeneous, therefore indicating that several biopsychosocial mechanisms may increase or reduce the risk for delinquency during human development. Aim. The principal aim of this thesis is to identify these mechanisms underlying delinquent behaviors through different yet complementary method: developmental trajectories, task-based brain activity, brain connectivity at rest as well as the study of brain lesions. Methodology. To do so, a first study was conducted by reanalyzing cohort data from the *Quebec Longitudinal Study of Child Development* (n=1,309). Latent growth curve models allowed to identify subgroups of children exhibiting developmental trajectories of psychological traits (i.e., callous-unemotional traits, anxio-depressive traits, irritability and hyperactivity/impulsivity) that are at risk for antisocial behaviors during childhood and adolescence. Also, two meta-analyses of neuroimaging studies (71 and 147 studies) were carried out to highlight main deficits in brain activity underlying distinct neurocognitive systems as well as their similarity with other psychiatric disorders. Moreover, a third meta-analysis(18 studies) is presented to better understand whether antisocial subjects may exhibit brain connectivity at rest. In order to overcome limitations of past studies examining resting-state functional connectivity, a cross-sectional study was performed on 1,416 children and adolescents derived from the Healthy Brain Network in the United States. Additionnally to examine reliability of meta-analytic findings, this study was conducted in order to better understand the role of the interaction between neurobiological systems in our understanding of antisocial behaviors. Finally, a recent literature review carried out by American researchers highlighted 17 cases during which focal brain lesions were temporally associated with emergence of antisocial behaviors. By reconstructing images of these brain lesions, meta-analytic coactivation modelling was conducted in order to recreate neurobiological systems which would possibly be the origins of delinquent acts. Results. The results observed in this thesis support the crucial role of callous- unemotional traits in our understanding of the risk for delinquency, but also suggest that the developmental interaction between psychological markers increases up to 10 times this risk. On aneurobiological ground, results revealed that individuals

that have committed antisocial behaviorswere mainly characterized by dysfunctions in brain regions involved in cognitive control, threat detection as well as social cognition. In comparison to attention-deficit/hyperactivity disorder and anxiety and depressive disorders, conduct disorder was similarly associated with dysfunction in regions related to emotion regulation and somatomotor functions. Moreover, the results suggest that antisocial population may be characterized by dysconnectivity between socio-affective and attentional processes and between somatomotor and attentional processes as well as those involvedin salient detection mechanism. Finally, brain lesions may cause antisocial behaviors by three neurobiological mechanisms, notably by disrupting the reward network (frontal lesions), the network involved in negative emotion processing (temporal lesions) and the emotional face processing (amygdala lesions). Conclusions. The results of the work presented in this thesis supportthe importance of studying the heterogeneity in neurocognitive systems for our understanding of antisocial behaviors. On the one hand, these results highlight the role of neurobiological systems of negative valence (related to anxiety and irritability), cognitive systems (related tohyperactivity/impulsivity and inattention) and social cognition (related to callous-unemotional traits). On the other hand, the results underline the limited contribution of positive valence system,but a prominent role of sensorimotor system (related to action and motor control). The current thesis offers a novel and exhaustive perspective on the heterogeneity of neurocognitive systems underlying delinquent behaviors. The interindividual variability of these systems is yet to be unveiled in order to uncover promising targets for treatment in a hopeful aim to reduce risk for delinquency.

Keywords: Antisocial Behaviors, Developmental Trajectories, Neuroimaging, Brain Connectivity, Brain Lesion, Negative Emotions, Psychopathy, Impulsivity.

Table des matières

Liste des tableaux

Liste des figures

À celui qui n'aurait jamais osé,

À ceux qui ne l'ont jamais cru.

Remerciements

Par manque de temps et d'inspiration pour formuler quelque chose d'acceptable, mes remerciements seront brefs. L'aspect concis de ceux ne reflète en rien mes traits psychopathiques.

D'Andràs, Laura et Maria à Jean-Pierre et Jean vous avez été placé sur mon chemin par pure coïncidence. Merci pour tout le plaisir et toute la stimulation intellectuelle que vous m'avez apporté.

À ma famille qui m'a supporté émotionnellement et financièrement (la bière coûte chère), les organismes subventionnaires ont clairement des croûtes à manger. Vous êtes mes piliers, mes sources d'inspirations, mes meilleurs amis, ma vie. Cette thèse est le reflet total des valeurs fondamentales que vous m'avez montré.

Hello Hello Stéphane. Un énorme merci du soutien pendant les bons et moins bons moments. Tu m'as poussé à me dépasser, à donner mon 110%. Tu as une énorme part de responsabilité dans le chercheur que je suis (lecteurs/lectrices, je vous laisse le soin de déteminer si c'est positif ou négatif…) Ce fût un funky périple !! Le ti-gars de crimino qui s'amuse dans le cerveau humain. Ehhh tabouère, qui l'aurait cru.

"*The ultimate measure of a man is not where he stands in moments of comfort and convenience, but where he stands in times of challenge and controversy*" (Martin Luther King, 1963).

CHAPITRE 1 - UN BREF APERÇU DES COMPORTEMENTS ANTISOCIAUX

Les comportements antisociaux sont généralement définis par des gestes violant les droits d'autrui et transgressant les normes sociétales (APA, 2013). Cette définition inclut un large éventail de comportements allant de l'agression physique et sexuelle, aux vols, à la destruction de biens et aux incendies criminels. Il importe de mentionner que la criminalité, tant chez les jeunes que les adultes, est une problématique mondiale ayant des répercussions dévastatrices sur les victimes (Harrendorf,Heiskanen, & Malby, 2010; Mikton, Butchart, Dahlberg, & Krug, 2016). Au Canada, les coûts associés à la victimisation, à la répression policière et au système pénal ont doublé depuis 1998, atteignant aujourd'hui près de 85 milliards par année (Easton, Brantingham, & Furness, 2014). Or, bien qu'on rapporte une diminution du taux de crimes déclarés par la police à travers les dernières décennies, on indique néanmoins une augmentation marquée des taux de crimes à caractères sexuels, de menaces, de fraudes, conduites avec les facultés affaiblies et de crimes associés aux drogues telles que la méthamphétamine et les opioïdes (Moreau, 2020). Depuis 2014, on dénote aussi une tendance à la hausse du taux de crimes violents et de l'indice de gravité de ceux-ci et ce, même chez les jeunes (Moreau, 2020). Il importe aussi de mentionner que le Canada est l'un des pays rapportant des taux les plus élevés d'agression physique et sexuelle au monde (Harrendorf et al., 2010). Cependant, un nombre important de crimes ne sera jamais rapporté à la police, ce dernier étant nommé le « chiffre sombre du crime » (Traduction libre de « dark figure of crime ») (Biderman & Reiss, 1967; van Dijk, 2010). On différenciera ainsi la criminalité des comportements antisociaux par la source des données, soient les documents officiels des autorités ou les comportements auto-rapportés. Ces derniers étant davantage prévalents, on estime qu'environ 1 jeune sur 3 sera impliqué directement dans une bagarre physique (Elgar et al., 2015) et près de 40 % d'adolescents rapporteront avoir commis un geste délinquant dans la dernière année (Enzmann et al., 2010). On différenciera aussi les comportements antisociaux du trouble des conduites (TC) et du trouble de la personnalité antisociale (TPA) par le diagnostic rendu par un psychiatre lorsque l'individu satisfait un certain nombre de critères diagnostiques. En effet, le TC est un trouble psychiatrique caractérisé par une persistance de comportements antisociaux de l'enfance à l'adolescence. Le TC est émis lorsque l'enfant ou l'adolescent rencontre minimalement 3 critères sur 15 tels que des comportements agressifs envers autrui et/ou des animaux, des dommages matériels importants, des vols et des

violations graves de règles (APA, 2013). On estime sa prévalence mondiale entre 3 % et 8 % dans la population générale (Fairchild et al., 2019; Mohammadi, Salmanian, & Keshavarzi, 2021) et entre 45 % et 68 % en détention juvénile (Beaudry, Yu, Långström, & Fazel, 2021; Livanou, Furtado, Winsper, Silvester, & Singh, 2019). Quant à sa version adulte, le TPA est déterminé par un seuil minimal de 3 critères sur 7 incluant : (1) la non-conformitéaux normes sociales (2) la duperie (3) l'impulsivité (4) l'agressivité (5) le mépris inconsidéré pour sa sécurité ou celle d'autrui (6) l'irresponsabilité (7) l'absence de remords (APA, 2013). Dans une étude épidémiologique portant sur plus de 36,000 adultes, on a estimé que plus de 4.3 % des États-Uniens satisferaient les critères de TPA (incluant le TC durant l'enfance) (Goldstein et al., 2017). On observerait, par ailleurs, une surreprésentation du TPA en milieu carcéral, atteignant près de 50 % de cette population (Fazel & Danesh, 2002).

Depuis plus d'une centaine d'années, les chercheurs tentent de mieux comprendre les facteurs biopsychologiques qui seraient à l'origine de l'émergence de ces comportements. En effet, les résultats de deux récentes méta-analyses indiquent une forte contribution des facteurs génétiques liés aux comportements antisociaux (héritabilité estimée entre 56 % et 58 %) (Burt, 2009b; Ferguson, 2010). Or, les comportements antisociaux sont hétérogènes et les mécanismes biopsychosociaux sous-jacents sont multiples. Par conséquent, les chapitres ultérieurs tenteront de mieux comprendrela complexité de la problématique antisociale par l'entremise d'études à la croisée entre la psychologie et la neuroscience.

CHAPITRE 2 - LE CONCEPT FONDAMENTAL D'HÉTÉROGÉNÉITÉ CLINIQUE

Le TC et le TPA que nous connaissons aujourd'hui ont été façonnés par la taxonomie de Terrie Moffitt (1993). En effet, peu de temps avant la publication du DSM-IV (APA, 1994), l'éminente chercheuse proposa l'idée selon laquelle on retrouverait deux principales trajectoires développementales des comportements antisociaux. Ces deux trajectoires dépendraient majoritairement de l'âge à laquelle émergent les premiers comportements, notamment à l'enfance ou à l'adolescence. En effet, il est estimé qu'environ 5 % des enfants persisteront dans leur parcours antisocial jusqu'à l'âge adulte, tandis que d'autres commettront des gestes délinquants seulement durant l'adolescence (Moffitt, 1993). On proposera ainsi que les individus du premier groupe seraient caractérisés par un nombre important de déficits individuels et sociaux tandis quele passage à l'acte du second groupe serait plutôt expliqué par l'association aux pairs déviants et l'âge (Moffitt, 1993). Contrairement à ces propositions, les résultats de travaux actuels suggèrent que ces deux groupes ne se différencieraient pas significativement l'un de l'autre (Bevilacqua, Hale, Barker, & Viner, 2018; Fairchild, van Goozen, Calder, & Goodyer, 2013). Les résultats d'une récente méta-analyse indiquent que les deux groupes seraient significativement associés au risque d'avoir des symptômes dépressifs, des problématiques d'usage de substance ainsi qu'une persistance d'agression et de comportements criminels, mais que ces niveaux de risque seraient plus sévères lorsque la délinquance débuterait tôt durant l'enfance (Bevilacqua et al., 2018). Ces résultats suggèrent ainsi que l'âge du début serait analogue à la sévérité de la pathologie plutôt qu'un facteur discriminant l'hétérogénéité clinique des individus antisociaux. Par conséquent, l'étude de facteurs sous-jacents à l'hétérogénéité de cette population demeure cruciale de manière àmieux comprendre la délinquance.

Durant les derniers 30 ans de recherche scientifique, une forte majorité des auteurs ont considéré les comportements antisociaux comme un construit unidimensionnel (Tremblay, 2010). En effet, un nombre important de résultats indiquent que le TPA, et même la psychopathie, (Bucholz, Hesselbrock, Heath, Kramer, & Schuckit, 2000; Carvalho, Hauck, Pianowski, & Muner,2019; Krueger, Markon, Patrick, & Iacono, 2005; Marcus, Lilienfeld, Edens, & Poythress, 2006; Marcus, Ruscio, Lilienfeld, & Hughes, 2008; Walters, Diamond, Magaletta, Geyer, & Duncan, 2007; Edens, Marcus, Lilienfeld, & Poythress Jr, 2006; Guay, Ruscio, Knight, &

Hare, 2007; Marcus, John, & Edens, 2004; Murrie et al., 2007; Ren, Li, Chen, Wang, & Xia, 2020; Walters, Duncan, & Mitchell-Perez, 2007; Walters, Ermer, Knight, & Kiehl, 2015; Walters, Gray, et al., 2007) étaient mieux caractérisés par une structure dimensionnelle plutôt qu'une catégorie distincte. Or, que le construit soit dimensionnel ou discret, le fait d'étudier les comportements antisociaux comme homogène limite substantiellement notre compréhension des variations interindividuelles associées à ceux-ci. Son utilisation nous permet seulement d'avoir un aperçu global de la sévérité de la pathologie antisociale, rejetant aussitôt la complexité derrière l'étude de la délinquance et du délinquant. Par exemple, dans le TC, on estime théoriquement plus de 32,647 différentes combinaisons de critères qui répondraient au seuil minimal de 3 critères sur 15 afin d'émettre un diagnostic de TC (Nock, Kazdin, Hiripi, & Kessler,2006b; Olbert, Gala, & Tupler, 2014). En d'autres mots, le TC et le TPA représenteraient des populations hautement hétérogènes sur le plan comportemental, et ce, sans compter la variabilité interindividuelle en termes de facteurs psychologiques. De manière à mieux comprendre cette hétérogénéité, les prochaines sections feront l'état des connaissances en ce qui a trait aux principaux facteurs comportementaux et psychologiques pouvant l'expliquer.

L'Hétérogénéité des comportements antisociaux

Lors de la publication de la deuxième version du DSM (APA, 1968), on reconnaissait l'hétérogénéité des comportements sous-jacents au TC, qui était fortement inspiré des travaux de Hewitt et Jenkins (1946) et Quay (1964). En effet, on distinguait 1) la réaction de fugue aux situations menaçantes (voir 308.3, APA, 1968), 2) la réaction agression non socialisée (c.-à-d. désobéissance hostile, colère et agressivité, voir 308.4, APA, 1968), et 3) la réaction délinquante de groupe (c.-à-d. valeurs et aptitudes délinquantes développées en groupe, voir 308.5 APA, 1968).À travers les années, on gagna l'intérêt clinique de distinguer les comportements de manière à mieux comprendre leur(s) mécanisme(s) sous-jacent(s). En effet, les résultats de recherche indiquent que certains types de comportements antisociaux seraient associés à des facteurs étiologiques différents ainsi que des trajectoires développementales distinctes.

L'Agression et la délinquance non agressive

La distinction entre l'agression et la délinquance non agressive est l'une des plus anciennes distinctions rapportées dans la littérature. Bien qu'apparu dans le DSM-II (APA, 1968), ce n'est qu'à la troisième version du DSM qu'on opposera l'agression à la délinquance non-agressive aux extrémités d'une dimension comportementale (voir p.45, APA, 1980). À travers la littérature scientifique, il est aujourd'hui majoritairement accepté que les comportements agressifs englobent les manifestations comportementales violentes dirigées envers autrui (incluant les animaux), tandis que les gestes délinquants non-agressifs sont plutôt observés à l'école et à la maison tels que les vols, le vandalisme, l'absentéisme à l'école et la violation des règles (Burt, Donnellan, Iacono, & McGue, 2011; Frick et al., 1993; Loeber & Stouthamer-Loeber, 1998; Rogers, Duncan, Lynett, & Sewell, 1994; Tackett, Krueger, Iacono, & McGue, 2005; Tackett, Krueger, Sawyer, & Graetz, 2003; Tremblay, 2010). Additionnellement à leurs différences sur le plan comportemental, ces deux grandes classes se différencieraient par leurs facteurs étiologiques ainsi que leur trajectoire développementale.

Premièrement, on estime que ces deux types de comportements se distingueraient par leurs influences génétiques et environnementales, tels qu'observés par l'entremise d'études de jumeaux. En effet, les résultats d'une méta-analyse indiquent un niveau d'héritabilité davantage élevé pour les comportements agressifs vis-à-vis la délinquance non-agressive (Burt, 2009a). On indique que les influences génétiques expliqueraient environ 65 % de la variance pour les manifestations agressives contre 48 % pour la délinquance non-agressive. En revanche, on note un rôle plus important des influences environnementales partagées en ce qui a trait à la délinquance non-violente (18 %) contrairement aux comportements agressifs (5 %). Dans le même ordre d'idées, seulement 38.4 % des influences génétiques et 10.2 % des influences environnementales non partagées chevaucheraient entre ces deux types de comportements, justifiant ainsi leur dissociation (Burt, 2013). Ces résultats méta-analytiques pourraient être expliqués par le fait que les comportements agressifs seraient davantage associés au tempérament, tandis que la délinquance non violente semblerait être plutôt influencée par des facteurs des risques environnementaux. Par exemple, les résultats de deux importantes méta-

analyses indiquent que les gestes agressifs auraient une plus forte relation avec le névrosisme et l'instabilité émotionnelle, contrairement aux comportements délinquants non-violents (Jones, Miller, & Lynam, 2011; Vize, Collison, Miller, & Lynam, 2019). Plus précisément, l'agressivité serait principalement associée à l'excitabilité émotionnelle (Lorber, 2004), aux symptômes d'anxiété et de dépression (Dugré, Dumais, Dellazizzo, & Potvin, 2019; Dugré & Potvin, 2020; Garofalo & Velotti, 2017), aux traits d'impulsivité (Dugré, Dumais, et al., 2019; Dugré & Potvin, 2020; Loeber, 1990; Rey, Sawyer, & Prior, 2005), à la victimisation à l'école (Ttofi, Farrington, & Lösel, 2012). En revanche, la délinquance non-agressive serait plutôt associée à l'affiliation aux pairs déviants, à l'usage de substance (Loeber, 1990; Shader, 2001) et à la recherche d'excitation (Jones et al., 2011; Vize et al., 2019).

Deuxièmement, les recherches démontrent que ces deux types de comportements seraient caractérisés par des trajectoires développementales distinctes. Par exemple, entre la première et deuxième année de vie, on indique une augmentation drastique du nombre d'enfants rapportant avoir poussé, avoir donné des coups de pieds ou frappés (Tremblay et al., 1999). Dès l'âge de 2 ans, près de 80 % des enfants auront eu des comportements dits agressifs (Tremblay et al., 1999). Malgré cette augmentation durant les premières années de vie, ceux-ci déclineraient à partir de l'âge de 3 ans (Côté, Vaillancourt, Barker, Nagin, & Tremblay, 2007; Hay, Tremblay, Hartup, & Archer, 2005; NICHD, 2004). Les résultats de recherche montrent qu'entre 3 % et 17 % (Moyenne : 9.91 %) des jeunes suivront une trajectoire marquée par des niveaux significativement élevés d'agression physique de l'enfance à la fin de l'adolescence (Becht, Prinzie, Deković, van den Akker, & Shiner, 2016; Bongers, Koot, van der Ende, & Verhulst, 2004; Broidy et al., 2003; Fontaine, Lacourse, Vitaro, & Tremblay, 2014; Givens & Reid, 2019; Isen et al., 2022; Martino, Ellickson, Klein, McCaffrey, & Edelen, 2008; Underwood, Beron, & Rosen, 2011; van Lier, Vitaro, Barker, Koot, & Tremblay, 2009; Xie, Drabick, & Chen, 2011). En revanche, entre 1.2 % et 15.6 % (Moyenne de 7.85 %) des enfants seraient caractérisés par une trajectoire élevée de comportements délinquants non agressifs jusqu'à la fin de l'adolescence (Becht et al., 2016; Bongers et al., 2004; Fontaine et al., 2014; Givens & Reid, 2019; Isen et al., 2022; van Lier et al., 2009). Or, tandis que les comportements agressifs déclineraient de l'enfance à l'adolescence (Bongers et al., 2004; Stanger, Achenbach, & Verhulst, 1997; Tremblay et al., 2004),

la délinquance non-agressive augmenterait significativement au cours de l'adolescence (Bongers et al., 2004; Moffitt, 2003). Il est intéressant de constater que la trajectoire développementale de la délinquance non-agressive (Becht et al., 2016; Bongers et al., 2004; Givens & Reid, 2019; Isen et al., 2022; van Lier et al., 2009) semble être davantage similaire à celle « *limitée à l'adolescence* » (Moffitt, 1993).

Bien que les résultats de travaux des dernières décennies nous indiquent que les deux types de comportements antisociaux se différencieraient sur la base de facteurs étiologiques et de trajectoires développementales, ceux-ci ne sont pas mutuellement exclusifs. En d'autres mots, un même enfant peut commettre les deux types de comportements à travers son développement. En effet, on indique qu'entre 50 % et 64 % des enfants ayant commis des gestes agressifs auraient aussi des comportements délinquants non agressifs (Bartels et al., 2003). Par ailleurs, dans certains échantillons, les chercheurs ont trouvé une absence de jeunes ayant seulement des comportements agressifs (Odgers et al., 2007) ou seulement des comportements délinquants non agressifs (Dugré,Potvin, Dellazizzo, & Dumais, 2021; Frick et al., 1991). Par exemple, en réanalysant les données de plus de 62,786 enfants du secondaire, des chercheurs ont trouvé qu'environ 15.5 % auraient seulement des comportements agressifs et 8.25 % seraient caractérisés par les deux types, tandis qu'aucun enfant n'aurait seulement commis de la délinquance non agressive (Dugré et al., 2021). L'aspect dynamique et non mutuellement exclusif des comportements antisociaux démontrent ainsi la complexité d'étudier le comportement humain à travers son développement. La distinction entre les comportements agressifs et la délinquance non-agressive semble être appropriée afin de mieux comprendre l'émergence des comportements antisociaux. Or, à travers la littérature scientifique, l'agression serait un construit hétérogène caractérisé par deux mécanismes distincts.

L'Agression Proactive & Réactive

Les comportements antisociaux se distingueraient principalement par la présence ou non d'agression envers autrui. Cependant, les résultats de certains travaux nous indiquent que

l'agression réactive et proactive se différencieraient par leurs fonctions et leurs facteurs motivationnels (Barratt& Felthous, 2003; Meloy, 2006; Rosell & Siever, 2015; Stahl, 2014). D'une part, la violence réactive, impulsive, affective, hostile ou défensive serait définie comme une réponse comportementale motivée par la présence d'une provocation (Dodge & Coie, 1987; Wrangham, 2018). En revanche, la violence proactive, préméditée, instrumentale ou prédatrice serait plutôt motivée par l'atteinte d'un bénéfice ou d'une récompense en l'absence de provocation ou menace(Dodge & Coie, 1987; Wrangham, 2018).

Il est intéressant de constater que ces comportements pourraient être observés dès les premières années de vie. Par exemple, les résultats de recherche indiquent qu'un nombre important d'enfants âgés d'environ 17 mois s'appropriera un jouet des mains d'un autre enfant (entre 56 % et 80.3 %, Hay,Castle, & Davies, 2000) ou poussera les autres afin d'obtenir ce qu'ils veulent (entre 30 % et 59 %, Tremblay et al., 1999). Par ailleurs, chez les enfants âgés entre 18 et 60 mois, les comportements d'agression réactive les plus fréquemment rapportés sont les coups de pieds (27 %), le fait de frapper (26 %) et de pousser (23 %) (Potegal & Davidson, 2003). Ce début précoce de comportements agressifs pourrait être expliqué par l'importance des influences génétiques dans l'explication de l'agression réactive (entre 26 % et 55 %) et proactive (entre 32 % et 46 %) (Brendgen, Vitaro, Boivin, Dionne, & Pérusse, 2006; Paquin et al., 2014; Tuvblad, Raine, Zheng, & Baker, 2009). L'agression, en général, serait davantage expliquée par les influences génétiques (approximativement 65 %) tandis que les influences environnementales non partagées caractérisaient plutôt le type d'agression, tel que l'agression réactive (entre 45 % et 61 %) et proactive (47 % et 59 %) (Brendgen et al., 2006; Paquin et al., 2014; Tuvblad et al., 2009). Les similarités entre les deux types d'agression s'observeraient aussi par leur trajectoire développementale. En effet, on rapporte des proportions similaires en ce qui a trait aux jeunes suivant une trajectoire développementale caractérisée par de hauts niveaux de violence réactive (entre 6.6 % et 14.6 %) ou proactive (entre 6.7 % et 12 %) jusqu'à l'adolescence (Barker, Tremblay, Nagin, Vitaro, & Lacourse, 2006; Barker et al., 2010; Cui, Colasante, Malti, Ribeaud, & Eisner, 2016). Cependant, on retrouverait entre 6 % et 22 % moins d'individus commettant de la violence proactive comparativement à la violence réactive (Barker et al., 2006; Barker et al., 2010; Cui et al., 2016), indiquant une quelconque normalisation des comportements agressifs en réaction à

une provocation.

La distinction entre la violence proactive et réactive tire son origine dans les travaux d'Albert Bandura et Leonard Berkowitz. En effet, il a été postulé que l'agression pourrait être apprise et renforcée en observant autrui recevoir une récompense à la suite d'un comportement agressif (Bandura, Ross, & Ross, 1963), mais pourrait aussi être la résultante comportementale de l'interaction entre une frustration et des prédispositions individuelles à l'agression, telles que l'irritabilité et la colère (Berkowitz, 1989). Il n'est donc pas surprenant de constater qu'à travers les résultats de plusieurs méta-analyses, la violence proactive serait associée à la recherche de plaisir/d'excitation, tandis que l'agression réactive serait plutôt liée à la labilité émotionnelle ainsi qu'à la victimisation par les pairs (Card & Little, 2006; Vize et al., 2019). Dans le même ordre d'idée, l'agression semble être associée à la fois à l'urgence négative (r=0.24, c.-à-d. la tendance à agir sous l'impulsion d'émotions négatives) et à l'urgence positive (r=0.34, la tendanceà agir sous l'impulsion d'émotions positives), soutenant l'importance de différencier les mécanismes sous-jacents l'agression (Bresin, 2019). Par ailleurs, plusieurs résultats de recherche semblent aussi indiquer que la violence proactive serait associée aux traits psychopathiques et une hypoactivité psychophysiologique (Fite, Raine, Stouthamer-Loeber, Loeber, & Pardini, 2009; Murray-Close, Holterman, Breslend, & Sullivan, 2017; Thomson & Centifanti, 2018; Xu, Raine, Yu, & Krieg, 2014). Par exemple, la réponse galvanique de la peau semble être négativement associée à l'agression proactive, mais positivement avec l'agression réactive (Armstrong et al., 2019; Boccadoro et al., 2021; Hubbard, McAuliffe, Morrow, &Romano, 2010; Moore et al., 2018). Ces résultats de recherche suggèrent donc la proximité entre la violence proactive et les mécanismes associés à la récompense et l'hypoexcitabilité émotionnelle tandis que la violence réactive serait plutôt liée aux émotions négatives.

Bien que ces deux types diffèrent significativement sur le plan clinique, ils sont tout de même interreliés. En effet, on observe une forte relation entre les deux types de violence, représentés par des coefficients de corrélation entre .64 (Polman, Orobio de Castro, Koops, van Boxtel, & Merk, 2007) et .68 (Card & Little, 2006). Cette importante relation demeurerait stable même lorsqu'étudiée par l'entremise de mesures en laboratoire (*r*=.52, Boccadoro et al., 2021). Par

ailleurs, on rapporte qu'entre 4.2 % et 26 % de la population rapporteraient les deux types d'agression (Ang, Huan, Li, & Chan, 2016; Centifanti, Fanti, Thomson, Demetriou, & Anastassiou-Hadjicharalambous, 2015; Colins, 2016; Euler, Steinlin, & Stadler, 2017; Kokkinos, Kirpitsi, Voulgaridou, & Markos, 2022; Marsee et al., 2014; Muñoz, Frick, Kimonis, & Aucoin, 2008; Smeets et al., 2017; Thomson & Centifanti, 2018) et ce taux serait davantage élevé dans les populations cliniques (Colins, 2016; Euler et al., 2017; Marsee et al., 2014; Muñoz et al., 2008). Cependant, il est fort intéressant de constater qu'à travers les études, aucun groupe d'individus rapportant seulement de l'agression proactive n'est répertorié, remettant ainsi en question l'apport de cette distinction comportementale dans notre compréhension de la délinquance.

Résumé

En somme, les différents comportements antisociaux seraient caractérisés par des corrélats psychologiques et physiologiques distincts tels que les émotions négatives (agression réactive), les émotions positives/récompenses (agression proactive et comportements antisociaux non-agressifs) et l'impulsivité (agression réactive). Cependant, la typologie comportementale comporte plusieurs limites. Par exemple, le comportement humain est dynamique dans sa nature, c'est-à-dire qu'il est généré par une interaction entre des facteurs individuels et sociaux dans un contexte donné, dans un temps précis. Bien qu'on observe des différences entre les gestes délinquants, un même individu n'est pas restreint à un seul type de comportements. Ainsi, l'étude du comportement délinquant limite notre capacité à identifier de potentielles cibles thérapeutiques. Dans une perspective de prévention du risque, le fait de se concentrer sur des dispositions individuelles et malléables à l'intervention, tels que des facteurs psychologiques et traits de personnalité est d'une importance particulière. Dans le même ordre d'idée, on postule que l'hétérogénéité des facteurs psychologiques chez les individus antisociaux serait à l'origine d'une incapacité à traiter et réduire le risque de délinquance (Brazil, van Dongen, Maes, Mars, & Baskin-Sommers, 2018).

L'Hétérogénéité des corrélats psychologiques

Dès la première apparition des comportements antisociaux en tant que condition médicale,lors de la publication du DSM-II, on caractériserait principalement le TPA par des facteurs psychologiques et traits de personnalité relatifs aux relations conflictuelles avec autrui (par ex. égoïsme, irresponsabilité, manque de remords, insensibilité à la punition et faible tolérance à la frustration) plutôt qu'à une description comportementale (p.41, APA, 1968). Or, les DSM-I (APA, 1952) et DSM-II (APA, 1968) ne se basaient sur aucun critère opérationnel afin de définir le diagnostic. Les psychiatres devaient ainsi se fier à leur jugement clinique afin d'évaluer la sévérité de symptômes pour émettre un diagnostic (Brunoni, 2017). Il n'est donc pas surprenant de constater le manque de fiabilité interjuge par rapport au diagnostic à poser sur un même individu. De manière à limiter ce manque de fiabilité, la troisième édition du DSM (APA, 1980) fût athéorique et mettait plutôt l'accent sur des critères opérationnels ayant été validés empiriquement (c.-à-d. comportements), au détriment des traits de personnalité et d'hypothèses étiologiques. Ce changement drastique a résulté en la création d'un fossé entre l'anormal et le normal, entre le délinquant et le non-délinquant, dû au faible pourcentage d'individus commettant des comportements antisociaux dans notre société. Contrastant substantiellement à cette doctrine, l'étude des corrélats psychologiques demeure cruciale, car elle permet d'identifier des vulnérabilités en amont, c'est-à-dire des facteurs étiologiques pouvant augmenter ou réduire le risque de comportements antisociaux.

Que ce soit Eysenck et Eysenck (c.-à-d. le psychoticisme et le névrosisme, Eysenck & Eysenck, 1970), Cloninger (c.-à-d. la recherche de nouveauté, l'évitement du danger et la dépendance à la récompense, Cloninger, 1987), Quay (c.-à-d. le système d'activation comportementale, Quay, 1988, 1993) ou Pinatel (c.-à-d. l'égocentrisme, la labilité, l'agressivité et l'indifférence affective, Bouzat & Pinatel, 1963), on postule, depuis des décennies, que le noyau de la personnalité criminelle reposerait sur des traits de personnalité associés aux relations interpersonnelles, à la labilité émotionnelle et au contrôle des impulsions. Ceci concorde avec les résultats de trois récentes méta-analyses comprenant des dizaines de milliers d'individus ayant commis des gestes antisociaux. En effet, les résultats indiquent que les individus antisociaux seraient principalement caractérisés par des niveaux inadéquats d'agréabilité, de conscienciosité, mais aussi d'anxiété (névrosisme), de colère et d'hostilité (névrosisme), d'impulsivité (névrosisme) et

de recherche d'excitation (extraversion) (Decuyper, De Pauw, De Fruyt, De Bolle, & De Clercq, 2009; Jones et al., 2011; Vize et al., 2019). Cette section fera ainsi l'état des connaissances sur les rôles que peuvent jouer certains facteurs psychologiques sur l'émergence de comportements antisociaux, notamment les traits d'insensibilité émotionnelle, la labilité émotionnelle et les traits d'hyperactivité/impulsivité et déficits de l'attention.

Les traits d'Insensibilité émotionnelle

Les traits d'insensibilité émotionnelle sont généralement définis comme des traits caractérisés par « un manque de culpabilité, un manque d'empathie, un manque d'inquiétude face aux mauvaises performances ainsi qu'un affect défaillant et superficiel » ([Traduction libre] (De Brito et al., 2021). Par exemple, les traits seraient caractérisés par un manque d'empathie, de remords et de culpabilité, ainsi que l'absence de comportements prosociaux (Waller et al., 2020). On estime que les influences génétiques associées à ceux-ci expliqueraient entre 67 % et 79 % de la variance chez les enfants et adolescents (Henry, Pingault, Boivin, Rijsdijk, & Viding, 2016; Viding, Blair, Moffitt, & Plomin, 2005; Viding, Jones, Frick, Moffitt, & Plomin, 2008) et diminueraient significativement à la fin de l'adolescence et à l'âge adulte (entre 38 % et 53 %) (Blonigen, Carlson, Krueger, & Patrick, 2003; Blonigen, Hicks, Krueger, Patrick, & Iacono, 2005; Larsson, Andershed,& Lichtenstein, 2006). Les résultats de travaux portant sur les trajectoires développementales des traits d'insensibilité émotionnelle indiquent qu'environ 12.5 % des jeunes suivraient une trajectoire caractérisée par des traits élevés de l'enfance à l'adolescence (Fontaine, Hanscombe, Berg,McCrory, & Viding, 2018; Fontaine, McCrory, Boivin, Moffitt, & Viding, 2011; Fontaine, Rijsdijk, McCrory, & Viding, 2010; Goulter, Kimonis, Hawes, Stepp, & Hipwell, 2017). Plus précisément, l'insensibilité émotionnelle serait caractérisée par deux trajectoires distinctes, notamment la trajectoire élevée et stable (entre 2.6 % et 4.7 %) et la trajectoire augmentant au cours de la puberté (entre 7.3 % et 9.6 %) (Fontaine et al., 2018; Fontaine etal., 2011; Fontaine et al., 2010).

Déjà au 19^{e} siècle on caractérisait les traits d'insensibilité émotionnelle comme un

débalancement des affects et du raisonnement moral (Prichard, 1835, cité dans Berrios,1999; Prichard, 1837, cité dans Gunn, 1998), détectable dès l'enfance et réfractaire au changement (voir « *Gemütlose* », Schneider, 1928, cité dans Wetzell, 2010). En effet, les délinquants juvéniles présenteraient, de manière disproportionnée, une absence de remords et une indifférence aux conséquences, et ce même si la punition renvoie à la peine de mort (Topping, 1941). La proximité entre ces traits et la délinquance est telle, qu'on définira ainsi la « psychopathie » comme entité clinique caractérisée par une sévérité aberrante de ces deux facteurs (c.-à-c. affectif et comportemental, Cleckley, 1941; Hare, 1980, 2021). Bien que la psychopathie représenterait 1 % des individus issus de la population générale, le taux de prévalence serait substantiellement plus élevé en milieu carcéral (entre 16 % et 25 %) (De Brito et al., 2021). Chez les enfants et adolescents, on rapporte une corrélation modérée entre les traits d'insensibilité émotionnelle et la délinquance (entre *r*=.33 et .39) (Frick, Ray, Thornton, & Kahn, 2014b; Geerlings, Asscher, Stams, & Assink,2020; Longman, Hawes, & Kohlhoff, 2016). Par ailleurs, près de 44.5 % des jeunes ayant un TC auraient des traits élevés d'insensibilité émotionnelle (entre 6.1 % et 83.7 %) (Colins, Van Damme, Hendriks, & Georgiou, 2020). Cette association pourrait être expliquée par le fait que les traits d'insensibilité émotionnelle et les comportements antisociaux, de manière générale, partageraient des influences génétiques similaires (Blonigen et al., 2005; Mann et al., 2017). Cependant, certains ont trouvé que les influences génétiques sous-jacentes aux traits d'insensibilité émotionnelle seraient davantage corrélées avec les comportements délinquants non-agressifs (*r*A=.80) qu'avec l'agression (*r*A=.38) (Mann, Tackett, Tucker-Drob, & Harden, 2018).

À travers la littérature scientifique, certains ont postulé que les traits d'insensibilité émotionnelle moduleraient la réactivité émotionnelle face aux stimuli menaçants chez les enfants et adolescents ayant un TC (Viding, Fontaine, & McCrory, 2012b). En effet, ceux rapportant de faibles niveaux d'insensibilité émotionnelle seraient hyperréactifs tandis que ceux ayant de hauts niveaux seraient plutôt hyporéactifs. Ce dernier groupe serait donc caractérisé par des difficultés dans la perception émotionnelle d'autrui, mais aussi dans sa propre réponse au stress. Par exemple, dans une méta-analyse portant sur 26 études, des chercheurs ont trouvé que les traits d'insensibilité émotionnelle étaient significativement associés aux difficultés dans la reconnaissance

émotionnelle faciale et vocale (Dawel, O'Kearney,McKone, & Palermo, 2012), et plus précisément en ce qui a trait aux émotions négatives telles que la peur et la tristesse (Dawel et al., 2012; Wilson, Juodis, & Porter, 2011). Bien que ces résultats semblent soutenir l'hypothèse d'un groupe distinct, certains ont trouvé que ces déficits seraient plutôt associés à la sévérité des comportements antisociaux (Kohls et al., 2020; Marsh & Blair, 2008; Martin-Key, Brown, & Fairchild, 2017). Dans le même ordre d'idées, bien que les traits d'insensibilité émotionnelle seraient négativement associés aux réponses psychophysiologiques (au repos et en réaction à des stresseurs), telles que mesurées par la fréquence cardiaque et la conductance cutanée (Fanti et al., 2019; Lorber, 2004; Portnoy & Farrington, 2015), l'effet pourrait être largement attribuable à la sévérité des comportements antisociaux. En effet, ces marqueurs psychophysiologiques seraient davantage associés à la violence (*d*=-.35) et aux comportements impulsifs et antisociaux (*d*=-.35) comparativement aux traits d'insensibilité émotionnelle (*d*=-.11) et la psychopathie (*d*=-.19) (Portnoy & Farrington, 2015). Par conséquent, il se pourrait donc que les réponses physiologiques perçues dans le groupe caractérisé par des traits d'insensibilité émotionnelle soient artéfactuelles, c'est-à-dire qu'elles soient mieux expliquées par d'autres facteurs psychologiques tels que la recherchede sensation forte (Hammerton et al., 2018; Kavish et al., 2017; Portnoy et al., 2014; Sijtsema et al., 2010).

On mentionne également que les jeunes ayant un TC et les personnes incarcérées ayant des traits élevés de psychopathie feraient significativement plus d'erreurs lors de tâches d'évitement passif (Blair et al., 2004; De Brito, Viding, Kumari, Blackwood, & Hodgins, 2013; Finger et al., 2011; Newman & Kosson, 1986; Newman, Widom, & Nathan, 1985) et ce, indépendamment de la sévérité de la perte (par ex. entre -1 et -2000 points) (Blair et al., 2004; De Brito et al., 2013). Ces résultats suggèrent que les individus antisociaux, avec ou sans traits d'insensibilité émotionnelle, semblent être caractérisés par une incapacité à adapter leur comportement face aux signaux punitifs. Il est donc plausible que ces déficits puissent expliquer, en partie, le faible sentiment de culpabilité et la récidive criminelle, malgré l'utilisation de stratégies punitives (c.-à-d. restriction de liberté).

Il est sans équivoque que les traits d'insensibilité émotionnelle sont associés à l'émergence de

comportements antisociaux. Or, il est à se demander si l'insensibilité émotionnelle ne serait pas intrinsèque au diagnostic de TC/TPA. En effet, 2 critères du TPA sur 7 sont sous-jacents aux traits d'insensibilité émotionnelle, soient le *manque de remords* et le *mépris pour la sécurité d'autrui* (APA, 2013). Par ailleurs, des chercheurs n'ont trouvé aucune différence significative entre les groupes de TC avec et sans traits d'insensibilité émotionnelle en ce qui a trait à la persistance et la stabilité des comportements antisociaux (Colins, Andershed, Salekin, & Fanti, 2018; Colins & Vermeiren, 2013; Déry, Bégin, Toupin, & Temcheff, 2019). Par exemple, malgré un niveau de base (c.-à-d., ordonné à l'origine) plus élevé chez ceux ayant des traits d'insensibilité émotionnelle, ceux-ci n'auraient aucun impact sur la pente de la trajectoire développementale de comportements antisociaux (Déry et al., 2019). En d'autres mots, la présence d'insensibilité émotionnelle aurait un effet sur la précocité et la sévérité des comportements antisociaux au cours du développement, mais ne caractériserait pas une sous-population clinique spécifique.

La labilité émotionnelle

La labilité émotionnelle (Leaberry, Walerius, Rosen, & Fogleman, 2020) est souvent définie comme étant une prédisposition à faire l'expérience d'émotions négatives telles que l'irritabilité, l'anxiété et la dépression. Celle-ci s'accompagne souvent d'instabilité affective et de difficultés dans la régulation des émotions. Bien que l'irritabilité et les traits anxio-dépressifs sont souvent jumelés sous une même échelle (par ex. névrosisme) ces derniers se différencieraient par leur mécanisme évolutif. En effet, lorsqu'on détecte une menace potentielle, l'un peut avoir tendance à combattre celle-ci (c.-à-d. comportements d'approche) tandis que l'autre aurait plutôt tendance à la fuir (c.-à-d. comportements d'évitement)[1] (Gross & Canteras, 2012). Par conséquent, l'irritabilité permettrait d'approcher cette menace afin de la combattre, tandis que les traits anxio-dépressifs seraient davantage associés aux comportements de fuite (Leibenluft,

[1] Il est à noter que la réaction de paralysie active (Roelofs & Dayan, 2022) et passive (Fadok et al., 2017) sont aussi observables.

2017; Vidal-Ribas, Brotman, Valdivieso, Leibenluft, & Stringaris, 2016). Les résultats de travaux de recherches démontrent que ces deux traits seraient significativement associés à la délinquance, par l'entremise de mécanismes distincts.

L'irritabilité

Encore aujourd'hui, il n'existe pas de consensus scientifique par rapport à la définition de l'irritabilité. Cependant, certains définissent l'irritabilité comme étant l'humeur d'une personne facilement agacée et susceptible, caractérisée par des accès de colère (Stringaris, 2011). Dans une méta-analyse portant sur plus de 12,692 paires de frères et sœurs, on a observé que les problèmes d'irritabilité seraient principalement caractérisés par des influences génétiques (59 %), suivi des contributions d'influences environnementales non-partagées (31 %) (Burt, 2009b). Il n'est donc pas surprenant d'observer des symptômes d'irritabilité dès les premières années de vie. En effet, ceux-ci augmenteraient entre 18 et 36 mois (entre 87 % à 91 % des enfants) et diminueraient significativement après la troisième année de vie (approximativement 32 %) (Potegal & Davidson, 2003). L'irritabilité seraient principalement identifiables par des crises qui incluent des pleurs (86 %), des cris (47 %) et des hurlements (39 %) (Potegal & Davidson, 2003). Or, entre 2.6 % et 13.4% des enfants continueront de démontrer une sévérité élevée de traits d'irritabilité jusqu'à l'adolescence (Bongers et al., 2004; Ezpeleta, Granero, de la Osa, Trepat, & Domènech, 2016; Musser, Karalunas, N. Dieckmann, Peris, & Nigg, 2016; Nagin & Tremblay, 1999; Orri et al., 2019; Wiggins, Mitchell, Stringaris, & Leibenluft, 2014). Il est particulièrement intéressant de constater que la trajectoire développementale de l'irritabilité semble similaire à celle caractérisant l'agression, suggérant une proximité entre ces deux construits.

On observe les traits d'irritabilité à travers une variété de troubles psychiatriques. En effet, ces traits seraient intrinsèquement liés au trouble perturbateur de l'humeur (Bruno et al., 2019), au trouble oppositionnel avec provocation (TOP), au trouble explosif intermittent ainsi qu'au TC et TPA (APA, 2013). Par exemple, les adolescents ayant un TC seraient de 12.1 à 89 fois plus à risque d'avoir un TOP (Moyenne=43.3, Écart-type=27.1; Maughan, Rowe, Messer, Goodman, & Meltzer, 2004; Nock et al., 2006b; Simonoff et al., 1997; Wichstrøm et al., 2012), et inversement, les

adolescents ayant un TOP seraient de 12.9 à 64 fois plus à risque de recevoir un diagnostic de TC (Moyenne=46.5, Écart-type=24.6; Rowe, Maughan, Pickles, Costello, & Angold, 2002; Simonoffet al., 1997; Wichstrøm et al., 2012). Chez les enfants ayant un trouble perturbateur de l'humeur (Brotman et al., 2006; Mayes, Waxmonsky, Calhoun, & Bixler, 2016), entre 25.9 % et 29.5 % de ceux-ci rencontreraient les critères diagnostiques de TC, et inversement, 45 % des enfants ayant un TC rapporteraient des symptômes du trouble perturbateur de l'humeur (Mayes et al., 2016). Malgré ces chevauchements importants, les auteurs d'une récente méta-analyse ont trouvé que l'irritabilité n'était pas significativement associée au TC (Vidal-Ribas et al., 2016). Ceci pourrait être expliqué par le fait que l'irritabilité serait davantage associée à des types spécifiques de comportements antisociaux plutôt qu'au diagnostic général de TC. En effet, certains ont trouvé que les traits d'irritabilité prédiraient l'agression physique, mais pas la délinquance non-agressive (Bolhuis et al., 2017). Plus précisément, les individus caractérisés par des hauts traits d'irritabilité commettraient davantage d'agression réactive (*d*=.79-1.17) et continueraient même en l'absence de provocation (*d*=.64-.75 condition neutre) (Bettencourt, Talley, Benjamin, & Valentine, 2006). Ainsi, ces résultats suggèrent que les mécanismes sous-jacents l'irritabilité seraient significativement associé au risque d'agression, mais pas à la délinquance non-agressive.

Les résultats d'études démontrent que les traits d'irritabilité seraient fréquents chez les enfants et adolescents ayant un trouble psychiatrique et augmenteraient spécifiquement le risque d'agression. Depuis près d'une centaine d'années, on postule que les signes d'irritabilité seraient associés à une plus forte propension à commettre des comportements agressifs (APA, 1968; Berkowitz, 1989; Dollard, Miller, Doob, Mowrer, & Sears, 1939b). Cependant, ce lien ne serait pas direct. En effet, l'agression serait observée seulement lorsque la situation produit un affect négatif suffisamment sévère afin d'y produire des penchants agressifs (par ex. irritabilité) (Berkowitz, 1989). En d'autres mots, le lien entre l'irritabilité et l'agression dépendrait de la sévérité de l'affect négatif produit par ladite situation.

Les traits internalisés

Dans une méta-analyse portant sur plus de 13,099 paires de frères et sœurs, on rapporte que plus

de 51 % (entre 47 % et 55 %) de la variance associée aux traits internalisés (c.-à-d. anxiété et dépression) serait attribuable aux influences génétiques, tandis que les influences environnementales partagées et non-partagées représenteraient respectivement 16 % et 33 % (Burt, 2009b). Conséquemment, un bon nombre d'enfants présenteraient des niveaux élevés de traits anxio-dépressifs jusqu'à l'adolescence. En effet, on estime qu'entre 2.2 % à 20.8 % des jeunes suivront une trajectoire élevée et stable de traits anxio-dépressifs de l'enfance à l'adolescence (Allan et al., 2014; Broeren, Muris, Diamantopoulou, & Baker, 2013; Crocetti, Klimstra, Keijsers, Hale, & Meeus, 2009; Duchesne, Larose, Vitaro, & Tremblay, 2010; Dugré, Dumais, et al., 2019; Feng, Shaw, & Silk, 2008; Goulter et al., 2017; Morin et al., 2011). Ces résultats nous pousse ainsi à nous questionner sur le rôle qu'ils peuvent jouer sur le développement de comportements antisociaux.

La présence de traits anxieux et dépressifs chez les individus ayant des comportements antisociaux est bien documentée dans la littérature (Baranyi, Cassidy, Fazel, Priebe, & Mundt, 2018; Bedaso, Ayalew, Mekonnen, & Duko, 2020; Fazel & Seewald, 2012). En effet, on estime que plus du deux tiers des détenus ayant un TPA répondraient aux critères diagnostiques pour un trouble anxieux pendant leur vie (Hodgins, De Brito, Chhabra, & Côté, 2010). On rapporte aussi qu'entre 10.2 et 36.9% de la population carcérale aurait un trouble de dépression majeure (Bedasoet al., 2020; Fazel & Seewald, 2012). Par ailleurs, les adolescents ayant un TC seraient de 1.6 à 18.1 fois plus à risque d'avoir un trouble dépressif (Moyenne=8.6, Écart-type=4.5 Angold, Costello, & Erkanli, 1999; Maughan et al., 2004; Nock et al., 2006b; Simonoff et al., 1997; Wichstrøm et al., 2012) et de 1.4 à 5.8 fois plus à risque de recevoir un diagnostic de trouble anxieux (Moyenne=3.39, Écart-type=1.59; Angold et al., 1999; Maughan et al., 2004; Nock et al., 2006b; Simonoff et al., 1997; Wichstrøm et al., 2012). À l'inverse, les jeunes ayant un trouble dépressif seraient de 1.56 à 22 fois plus à risque de recevoir un diagnostic de TC (Moyenne=11.51, Écart-type=9.94; (Bird et al., 2006; Simonoff et al., 1997; Weller, Blanford, & Butler, 2018), tandis que les jeunes ayant un trouble anxieux seraient 1.4 à 3.6 fois plus à risque de recevoir un TC (Moyenne=2.5, Écart-Type=1.56; Bird et al., 2006; Simonoff et al., 1997).

Depuis les dernières années, on tente de comprendre si la présence de traits anxio-dépressifs chez

les individus antisociaux refléterait la présence d'un groupe distinct. Par exemple, Hodgins et collaborateurs (2010) ont trouvé que les détenus ayant un diagnostic de trouble anxieux rapporteraient plus de comportements antisociaux, de comportements suicidaires, mais aussi un plus grand nombre de condamnations pour des crimes violents (c.-à-d. meurtres, agression physique et sexuelle) comparativement à ceux sans trouble anxieux. Chez les adolescents, le groupe comorbide rapporterait aussi une plus grande sévérité de comportements antisociaux comparativement au groupe sans symptômes internalisés (Polier, Vloet, Herpertz-Dahlmann, Laurens, & Hodgins, 2012a; Roos et al., 2016). Sur la base psychophysiologique, ce groupe serait davantage similaire à celui ayant seulement des traits internalisés que les jeunes ayant seulement un TC (Fanti, 2018). Tandis que les jeunes ayant un TC seraient caractérisés, de manière générale, par une hyporéactivité psychophysiologique, le groupe comorbide montrerait plutôt des réponses opposées. Tel qu'observé dans le cas de l'irritabilité, ces résultats pourraient être expliqués par le fait que les symptômes internalisés seraient davantage associés à l'agression qu'aux comportements délinquants non agressifs (Jones et al., 2011; Vize et al., 2019), et plus précisément à l'agression réactive comparativement à l'agression proactive (Vize et al., 2019). Par conséquent, on peut émettre l'hypothèse que l'hyperréactivité psychophysiologique, fréquemment observée dans la population aux traits internalisés, augmenterait le risque d'agression réactive.

Les traits d'hyperactivité/impulsivité et déficits de l'attention

Les symptômes du trouble de déficit de l'attention/hyperactivité (TDAH) sont généralement caractérisé par deux grands facteurs, notamment les symptômes d'hyperactivité/impulsivité (par ex. *la difficulté à rester assis*, *agir sans réfléchir*, *l'impatience*) et les symptômes d'inattention (par ex. *la difficulté de concentration*, *être facilement distrait*, *la difficulté à finir des tâches*) (APA, 2013; Pillow, Pelham, Hoza, Molina, & Stultz, 1998). On estime que les symptômes d'hyperactivité et d'inattention seraient en grande partie héréditaire, tel que démontré par l'importance des influences génétiques (entre 50 % et 71 %) (Bezdjian, Baker, & Tuvblad, 2011; Nikolas & Burt, 2010). Les résultats de recherche développementale suggèrent qu'entre 5 % et

21.4 % des enfants démontreraient des niveaux élevés etstables de symptômes d'hyperactivité et d'impulsivité jusqu'à l'adolescence (Galéra et al., 2011; Larsson, Dilshad, Lichtenstein, & Barker, 2011; Lee, Park, Jeong, Chae, & Oh, 2017; Musser, Karalunas, Dieckmann, Peris, & Nigg, 2016; Nagin & Tremblay, 1999; Pingault et al., 2013; Salla et al., 2016; Vergunst et al., 2019). Ces taux seraient relativement similaires dans le cas des symptômes d'inattention. En effet, entre 2.5 % et 24.1 % des enfants de la population générale montreront des symptômes élevés d'inattention jusqu'à l'adolescence (Larsson et al., 2011; Lee et al., 2017; Pingault et al., 2013; Salla et al., 2016; Sasser, Beekman, & Bierman, 2015;Vergunst et al., 2019). Ainsi, l'importance des influences génétiques ainsi que la proportion de jeunes ayant des traits élevés au cours de leur passage de l'enfance à l'adolescence nous porte à nous questionner sur le rôle que peux jouer ces symptômes sur l'émergence de comportements antisociaux.

Les traits d'hyperactivité/impulsivité et les déficits de l'attention sont au cœur des mécanismes psychologiques associés à la délinquance, et ce, depuis plus d'une centaine d'années. Déjà au tournant du 20^{e} siècle, on indiquait que les personnes facilement distraites ayant peu de persévérance et une difficulté à contrôler leur tempérament (voir « *Haltlose* » et « *Triebmenschen* ») étaient propices aux comportements délictuels tels que des vols et de l'escroquerie ainsi que de la prostitution (Adler, 1917; Kraepelin, 1909). Malgré l'hétérogénéité du construit, impliquant généralement *la difficulté à inhiber une réponse*, *le manque de persévérance et préméditation*, *la recherche de sensation forte* et *l'incapacité à différer lagratification* (Verbruggen & Logan, 2008; Whiteside & Lynam, 2001), l'impulsivité a été identifiée comme un élément central et étiologique des comportements délictuels (Gottfredson & Hirschi, 1990; Quay, 1988; Rogers et al., 1994). En effet, les études portant sur des instruments neuropsychologiques ont montré que les sujets antisociaux présenteraient principalement des altérations lors de tâches d'inhibition, de planification et d'attention (Hobson, Scott, & Rubia, 2011; Morgan & Lilienfeld, 2000; Ogilvie, Stewart, Chan, & Shum, 2011; Séguin,Sylvers, & Lilienfeld, 2007). Or, les résultats de deux méta-analyses indiquent que les déficits cognitifs seraient davantage associés à la criminalité en générale (d=0.61-0.94) et à la délinquance non-agressive (d=0.41-0.78) comparativement aux autres comportements (Morgan & Lilienfeld, 2000; Ogilvie et al., 2011). Par ailleurs, les jeunes ayant TC/TOP semblent montrer davantage de déficits les adultes ayant un TPA (d=0.54 contre

d=0.19) (Morgan & Lilienfeld, 2000; Ogilvie et al., 2011). Cette association serait donc plus importante durant l'enfance et l'adolescence qu'à l'adolescence, ce qui pourrait être expliqué en partie par le rôle de la puberté sur les processus d'inhibition. Ceci concorderait avec les résultats de recherche indiquant que le TDAH serait davantage répertorié chez les jeunes en détention juvénile (entre 7.8 % et 68 %) (Young, Moss, Sedgwick, Fridman, & Hodgkins, 2015), que chez les détenus adultes (entre 10 % et 29 %) (Konstenius et al., 2015; Moore, Sunjic, Kaye, Archer, & Indig, 2016; Rösler, Retz, Yaqoobi, Burg,& Retz-Junginger, 2009; Westmoreland et al., 2010; Young et al., 2015). En effet, les adolescents ayant un TC seraient de 3.2 à 36.2 fois plus à risque de recevoir un diagnostic de TDAH (Maughanet al., 2004; Nock et al., 2006b; Simonoff et al., 1997; Wichstrøm et al., 2012). À l'inverse, les jeunes ayant un TDAH seraient de 3.2 à 82 fois plus à risque d'avoir un TC (Angold et al., 1999; Bird et al., 2006; Park, Lee, & Kim, 2017; Simonoff et al., 1997; Wichstrøm et al., 2012). Certains ont même postulé que l'association entre le TDAH et le TC serait artéfactuelle dû à un mécanisme commun entre les deux troubles (Lilienfeld & Waldman, 1990). Or, les résultats des travaux de Donald Lynam (1996,1998) indiquent que comparativement à ceux ayant seulement des comportements antisociaux ou seulement des symptômes de TDAH, les enfants issus du sous-groupe comorbide (« *fledgingpsychopaths* »), auraient davantage de comportements antisociaux (Waschbusch, 2002), rapporterait une plus grande variété de délinquance et d'importants déficits lors de tâches d'inhibition, de tâches incluant une récompense (par ex. le délai de gratification) ainsi que des tâches attentionnelles (Lynam, 1996, 1998).

L'Impulsivité motrice

L'impulsivité motrice est souvent définie comme le fait d'agir sans réfléchir (Patton, Stanford, & Barratt, 1995). Bien qu'elle fasse partie intégrante du diagnostic de TDAH, ce type d'impulsivité est principalement associé à la criminalité précoce (Pechorro, Maroco, Ray, & Gonçalves, 2015), à un risque plus élevé de recevoir un diagnostic de TC et TPA (Pechorro et al., 2015; Swann,Lijffijt, Lane, Steinberg, & Moeller, 2009), une plus grande sévérité des crimes (Pechorro et al., 2015), notamment d'agression proactive et réactive (Azevedo, Pais-Ribeiro, Coelho, & Figueiredo-Braga,

2018; Azevedo, Vieira-Coelho, Castelo-Branco, Coelho, & Figueiredo-Braga, 2020; Chen,Yang, & Qian, 2013; Pechorro et al., 2015). Ceci pourrait être expliqué par le fait que le groupe comorbide TC-TDAH aurait davantage de difficulté à inhiber leur réponse. En effet, dans une méta-analyse portant sur 22 études utilisant des tâches neuropsychologiques dont le paradigme stop-signal, Waschbush (2002) a démontré que le groupe comorbide avaient davantage de déficits que les sujets contrôles (d=.50) et que les jeunes ayant seulement un TC (d=.30).

La recherche de récompenses/sensations

L'une des premières théories sur le rôle des déficits cognitifs associés à la récompense et les comportements antisociaux datent de plus d'une trentaine d'années. Appuyé par la théorie biopsychologique de Gray (1970), Herbert Quay (1988, 1993) postulait que les enfants ayant un TC auraient une incapacité à inhiber leurs comportements dirigés vers une récompense. À travers les décennies, un nombre grandissant de résultats ont soutenu l'importance du système d'activation comportementale. Par exemple, les enfants ayant un TDAH comorbide au TC auraient davantage tendance à continuer de répondre à la récompense malgré la présence de punitions, en comparaison à leurs homologues sans TDAH (Matthys, van Goozen, de Vries, Cohen-Kettenis, & van Engeland, 1998). La population antisociale avec des traits élevés de psychopathie ferait plus d'erreurs lors de la présence de récompenses, comparativement à ceux sans trait psychopathique, et aux sujets contrôles (De Brito, Viding, Kumari, Blackwood, & Hodgins, 2013). Ceux-ci auraient donc un intérêt exagéré envers la récompense et, par conséquent, n'apprendraient pas des pertes associées à leur choix risqué (Mitchell, Colledge, Leonard, & Blair, 2002; Newman & Kosson, 1986; Scerbo et al., 1990; White et al., 2013b). Par ailleurs, les enfants ayant des comportements antisociaux (Mann, Paul, Tackett, Tucker-Drob, & Harden, 2018) ainsi que les patients psychiatrisés avec un trouble de la personnalité (Dugré, Giguére, Percie du Sert, Potvin, & Dumais, 2019) auraient des niveaux significativement plus élevés de recherche de sensation. On mentionne également que l'hyporéactivité physiologique augmenterait spécifiquement le risque de délinquance non-agressive par l'entremise de la recherche de sensation (Sijtsema et al., 2010). Ceci pourrait être expliqué par le fait que

les personnes ayant une hyporéactivité émotionnelle auraient davantage tendance à la recherche de sensation forte afin de retrouver un niveau de stimulation adéquat (Eysenck, 1997).

Les déficits de l'attention

À travers la littérature scientifique, une forte majorité de recherches ne distingue pas les différents symptômes de TDAH afin d'étudier leur rôle dans l'explication des mécanismes associés aux comportements antisociaux. Or, tandis que certains rapportent une corrélation modérée à élevée entre l'inattention et la délinquance(*r*=.50 à *r*=65) (Cardoos, Loya, & Hinshaw, 2013; Giannotta & Rydell, 2016a; Pardini, Obradović, & Loeber, 2006), d'autres n'ont observé aucun lien significatif (Babinski, Hartsough, & Lambert, 1999; Giannotta & Rydell, 2016b). Ces résultats conflictuels suggèrent cependant que la relation entre l'inattention et la délinquance pourrait être mieux expliquée par d'autres facteurs (c.-à-d. médiateurs). Par exemple, on mentionne que l'inattention serait significativement associée à l'échec scolaire (Lundervold, Bøe, & Lundervold, 2017; Pingault et al., 2014), au rejet par les pairs (Hoza et al., 2005; Miller-Johnson, Coie, Maumary-Gremaud, & Bierman, 2002; Tseng et al., 2012), mais aussi à la fréquentation de pairs déviants (Cardoos et al., 2013; Marshal & Molina, 2006), ce qui augmenterait significativement le risque de comportements antisociaux à l'adolescence. Quoi qu'il en soit, l'inattention jouerait un rôle crucial dans le développement socioémotionnel qui est intrinsèquement lié aux comportements antisociaux. Par exemple, bien que les individus antisociaux seraient caractérisés par des déficits dans la reconnaissance émotionnelle en général, ils rapporteraient davantage de problèmes dans l'attention portée vers les stimuli menaçants (c.-à-d. le nombre et la durée de fixation vers la région des yeux)(Billeci et al., 2019; Boll & Gamer, 2016; Dadds, El Masry, Wimalaweera, & Guastella, 2008; Dadds, Jambrak, Pasalich, Hawes, & Brennan, 2011; Dargis, Wolf, & Koenigs, 2018; Gillespie, Rotshtein, Wells, Beech, & Mitchell, 2015; Hodsoll, Lavie, & Viding, 2014; Kimonis, Frick, Munoz, & Aucoin, 2008; Kimonis, Graham, & Cauffman, 2018; Loney, Frick, Clements, Ellis, &Kerlin, 2003). Tel que mentionné précédemment, certains ont trouvé que le sous-groupe ayant des niveaux élevés d'insensibilité émotionnelle aurait moins tendance à

poser leur regard au niveau des yeux de visages exprimant des émotions négatives. Cependant, il demeure encore inconnu si ces résultats sont dus à la pathologie antisociale et/ou aux symptômes cooccurrents d'inattention. En effet, certains postulent que la reconnaissance d'émotions en générale serait principalement associée à la sévérité de la pathologie antisociale tandis que les symptômes de TDAH seraient plutôt liés aux déficits sous-jacents la fixation sur la région des yeux (Airdrie, Langley, Thapar, & van Goozen, 2018). Enfin, les recherches indiquent un rôle central des symptômes d'hyperactivité/impulsivité dans l'étude des comportements antisociaux. Il n'en demeure pas moins que les symptômes d'inattention semblent aussi associés à l'antisocialité par l'entremise de difficultés scolaires et relationnels.

L'antisocialité en tant qu'interaction de facteurs psychologiques ?

Les résultats de recherches démontrent sans équivoque que les jeunes ayant des comportements antisociaux proviennent d'une population hautement hétérogène (Fanti, 2018; Hawes, 2014). La section précédente avait donc pour but de présenter les principaux comportements antisociaux ainsi que les différents facteurs psychologiques pouvant expliquer l'hétérogénéité dans cette population. Les traits d'insensibilité émotionnelle, l'irritabilité, les traits internalisés ainsi que l'hyperactivité et l'inattention seraient tous associés à un risque plus élevé de commettre une panoplie de comportements antisociaux. Cependant, le rôle individuel de chacun de ces traits ne peut suffire afin d'expliquer l'hétérogénéité sous-jacents aux comportements antisociaux et la complexité du passage à l'acte.

Dans la quatrième version du DSM, on rapporte que les troubles de la personnalité pourraient être expliqués par des déficits dans plusieurs domaines neurocognitifs. En effet, on mentionne:

> La caractéristique essentielle d'un trouble de la personnalité est d'être une modalité durable de l'expériencevécue et des conduites qui dévie notablement de ce qui est attendu dans la culture de l'individu et qui se manifeste dans au moins deux des domaines suivants: la cognition, l'affectivité, le fonctionnement interpersonnel ou le contrôle des impulsions (p.630, APA, 1994).

Il est intéressant de constater que cette définition renvoie principalement aux facteurs psychologiques décrits dans la section précédente. En effet, le rôle des domaines cognitifs, affectifs et interpersonnels semble essentiel dans la compréhension du TPA (et du même coup du TC). Toutefois, une forte majorité des chercheurs étudie ces facteurs indépendamment les uns des autres, rendant difficile la capacité à mieux comprendre si les comportements antisociaux pourraient être résulté d'une interaction développementale entre ces traits. En effet, l'interaction entre ces facteurs au cours du développement humain pourrait nous offrir des pistes de solution afin de mieux comprendre l'émergence des comportements antisociaux. À travers les dernières décennies, certains chercheurs ont tenté de trouver le nombre optimal ainsi que les regroupements principaux de facteurs psychologiques pouvant discriminer les personnes délinquantes des individus n'en ayant jamais commis. L'une des interactions ayant reçu le plus d'attention en recherche est la typologie de la psychopathie primaire et secondaire. En effet, déjà en 1941, Benjamin Karpman postulait la présence de deux entités cliniques caractérisées par des traits psychopathiques qui se différenciaient par la présence ou non de labilité émotionnelle (c.-à-d. réactivité aux émotions négatives telles que la dépression et l'anxiété) (Karpman, 1941, 1948). En effet, on suggèrera que les individus ayant un niveau élevé de psychopathie, mais bas d'anxiété (c.-à-d. psychopathie primaire) auraient une faible excitabilité émotionnelle et une réponse réduite aux signaux sociaux (Craig, Goulter, & Moretti, 2021; Skeem, Poythress, Edens, Lilienfeld, & Cale, 2003). À l'inverse, la surexcitabilité émotionnelle et la sensibilité aux émotions négatives seraient caractéristiques principales de ceux présentant des sévérités élevées aux deux facteurs psychologiques (c.-à-d. psychopathie secondaire) (Craig et al., 2021; Skeem et al., 2003). Tandis que les deux groupes seraient à risque élevé de comportements antisociaux, certains ont trouvé que le deuxième variant démontrerait davantage de comportements agressifs (Docherty, Boxer, Huesmann, O'Brien, & Bushman, 2016; Kahn et al., 2013; Kimonis, Skeem, Cauffman, & Dmitrieva, 2011; Vaughn, Edens, Howard, & Smith, 2009), notamment de violence réactive (Goulter et al., 2017; Kimonis et al., 2011), et serait plus à risque de recevoir le diagnostic de TC (Goulter et al., 2017; Meehan, Maughan, Cecil, & Barker, 2017). Par ailleurs, le deuxième variant serait associé à une sévérité plus élevée de symptômes d'hyperactivité/impulsivité, de traits internalisés, d'irritabilité, d'usage de substance et de comportements suicidaires (Cecil, McCrory,

Barker, Guiney, & Viding,2018; Fanti, Demetriou, & Kimonis, 2013; Goulter et al., 2017; Huang, Fan, Lin, & Wang, 2020; Kahn et al., 2013; Kimonis et al., 2011; Meehan et al., 2017). Ces résultats suggèrent cependant un manque de spécificité entre les deux groupes. Autrement dit, ces deux groupes se différencieraient davantage par la sévérité plutôt que par la spécificité des corrélats psychologiques et comportementaux. Ainsi, ces résultats justifient la nécessité de mieux caractériser l'hétérogénéité des facteurs psychologiques sous-jacents aux comportements antisociaux.

À travers la littérature, on rapporte d'autres tentatives d'expliquer l'hétérogénéité des individus antisociaux à l'aide de combinaisons à 2 et à 3 facteurs psychologiques. Celles-ci étant majoritairement fondées sur des études transversales (Cloninger, 1987; Eysenck & Eysenck, 1970), seul un petit nombre étudie l'interaction entre les trajectoires développementales de facteurs psychologiques. Par exemple, Tremblay et collaborateurs (Tremblay, Pihl, Vitaro, & Dobkin, 1994) ont trouvé que 28 % des enfants en garderie ayant un niveau élevé d'impulsivité (mais bas d'anxiété et de sensibilité sociale) présenteraient des comportements antisociaux au début de l'adolescence. Dans le même ordre d'idées, Côté et collaborateurs (2002) ont observé que les jeunes de 6 ans présentant des niveaux élevés d'hyperactivité jusqu'à 12 ans (mais de bas niveaux d'indifférence affective et d'insensibilité à la peur (OR=4.27), et ceux ayant des niveaux élevés aux trois traits (OR=3.93) seraient tous significativement plus à risque de recevoir le diagnostic de TC. Ces résultats semblent concorder avec l'idée d'équifinalité, c'est-à-dire que des sous-groupes seraient à risque d'un même comportement (antisocial). Il est intéressant de constater que l'interaction entre différents traits pourraient expliquer la spécificité de comportements antisociaux. Par exemple, certains ont trouvé que les niveaux élevés d'hyperactivité/impulsivité et d'irritabilité (entre 6 et 12 ans) seraient associés à l'agression et à la délinquance non-agressive, tandis que les trajectoires seulement élevées d'hyperactivité/impulsivité expliqueraient plutôt la délinquance non-agressive (Galera et al., 2020). Ces résultats probants suggèrent que l'interaction entre des traits spécifiques augmenteraient le risque de comportements distincts. Par exemple, la co-occurrence de l'irritabilité et l'anxiété durant l'enfance augmenterait significativement le risque d'agression physique à la fin de l'adolescence (Dugré, Dumais, et al., 2019). Par ailleurs, en réanalysant les données longitudinales de plus de 4800 enfants, des

chercheurs ont montré que ceux caractérisés par une trajectoire élevée d'irritabilité (et bas en anxiété et en hyperactivité, OR=3.1) ou d'hyperactivité (et bas en irritabilité et en anxiété OR=3.7) présentaient une propension similaire à l'agression physique à l'âge de 15 (Dugré & Potvin, 2020). Or, la cooccurrence de ces traits, à savoir que l'appartenance à des trajectoires élevées d'irritabilité, d'anxiété et d'hyperactivité doublait le risque d'agression physique (OR=7.7) (Dugré & Potvin, 2020). Ces résultats de recherche indiquent l'importance d'étudier l'interaction développementale entre ces traits afin de mieux comprendre l'émergence et la spécificité des comportements antisociaux. Il importe néanmoins de mentionner qu'à ce jour, aucune étude ne tentespécifiquement d'étudier, de manière exhaustive, l'interaction développementale entre les traits psychologiques et des comportements antisociaux spécifiques, tels que l'agression et la délinquance non-violente.

Résumé

En somme, les recherches semblent montrer que les traits d'insensibilité émotionnelle, la labilité émotionnelle ainsi que les traits d'hyperactivité/impulsivité et déficits de l'attention seraient majoritairement héréditaire, identifiables dès l'enfance, mais seraient caractérisés par des trajectoires développementales différentes. Leur rôle individuel dans l'explication des mécanismes sous-jacents aux comportements antisociaux semble toutefois limité. Les résultats de recherche suggèrent plutôt l'effet additif de ces facteurs psychologiques sur l'émergence de comportements antisociaux. Plus précisément, on note que l'interaction entre certains facteurs pourrait expliquer différents comportements tels que l'agression et la délinquance non-violente. Cependant, on cherche toujours à savoir quel est le regroupement optimal de facteurs et quel(s) rôle(s) ces facteursjouent-ils dans l'émergence de comportements antisociaux (**Objectifs de l'Article 1**). L'avancement des nouvelles techniques d'imagerie par résonance magnétique fonctionnelle pourrait nous offrir une meilleure compréhension des mécanismes neurobiologiques pouvant expliquer l'hétérogénéité clinique dans la population antisociale.

CHAPITRE 3 – LA CARTOGRAPHIE CÉRÉBRALE DES COMPORTEMENTS ANTISOCIAUX

À travers les dernières décennies, la psychologie et la sociologie ont eu un apport considérable dans notre compréhension des comportements antisociaux. Or, la recherche de facteurs biologiques demeure complémentaire et fondamentale. Depuis l'arrivée des techniques d'imagerie cérébrale vers la fin des années 1990, notre compréhension des fonctions cérébrales fondamentales à l'être humain suit une trajectoire exponentielle. Les théories biologiques modernes sont majoritairement influencées par le postulat selon lequel les facultés mentales seraient contrôlées par des systèmes neurobiologiques qui interagiraient les uns avec les autres (Cloninger, 1987). Par exemple, Panksepp décrit sept circuits émotionnels de base caractérisés par des régions cérébrales sous-corticales présentes chez tous les mammifères, notamment le système de rage (colère),de peur (anxiété), de recherche (désire), de désire (sexualité), de prise en charge (soins maternels), de deuil (anxiété de séparation), de jeu (engagement social et physique) (Panksepp, 1998, 2010). Et si les comportements antisociaux pouvaient être expliqués par un débalancement des fonctions cérébrales fondamentales à l'être humain ? Afin d'y répondre, les prochaines sections feront l'état des connaissances du lien entre les processus mentaux et les comportements antisociaux grâce à diverses techniques d'imagerie par résonance magnétique fonctionnelles telles que l'activité cérébrale lors de tâches cognitives spécifiques ainsi que la connectivité fonctionnelle au repos.

Les principaux processus mentaux et leurs corrélats neurobiologiques

Encore aujourd'hui, les chercheurs tentent de définir et mieux caractériser les principaux processus neurobiologiques sous-jacents aux facultés mentales. En réponse aux limites substantielles de la catégorisation des troubles mentaux, tels que l'augmentation exponentielle du nombre de diagnostics, la réduction du seuil des critères diagnostique, l'inflation de la prévalence des diagnostics, l'hétérogénéité intra-diagnostique ainsi que l'importante comorbidités psychiatriques entre les troubles (Andreasen, 2007; Frances, 2013; Jones, 2012; Olbert et al., 2014; Regier et al., 2013), l'Institut National de la Santé Mentale des États-Unis (NIMH) a récemment développé une des classifications des processus mentaux les plus

exhaustives jusqu'à présent. Le *Research Domain Criteria* (RDoC) tente de décrire les systèmes neurocognitifs sous-jacents aux troubles mentaux par l'entremise de données génétiques, moléculaires, physiologiques et d'imagerie cérébrale (Cuthbert, 2015; Insel et al., 2010; Ross & Margolis, 2018). Les principaux domaines neurocognitifs étudiés sont notamment les systèmes à valence négative, les systèmes à valence positive, les systèmes cognitifs, les systèmes de processus sociaux et les systèmes d'éveil/régulatoires (Cuthbert & Insel, 2013; Morris & Cuthbert, 2012). Ce cadre théorique est donc pertinent afin de mieux comprendre les mécanismes neurobiologiques responsables de l'importante hétérogénéité dans la population antisociale individus antisociaux et plus particulièrement grâce aux données d'imagerie par résonance magnétique fonctionnelle (IRMf). Plus précisément, l'activité cérébrale, telle qu'étudiée par le taux d'oxygénation du sang dans le cerveau (réponse BOLD), nous permet d'identifier les régions cérébrales impliquées dans certaines fonctions mentales induites par une tâche spécifique. La fluctuation de la réponse hémodynamique de certaines régions cérébrales pourrait donc être associée à la variabilité de comportements antisociaux. Dans cette section, quatre des cinq domaines du RDoC seront détaillés, dû à leur proximité avec les facteurs psychologiques présentés antérieurement, mais aussi du fait que la quasi-totalité des études en IRMf portant sur l'antisocialité renvoie à l'un de ces quatre domaines.

Les Systèmes à Valence Négative

Les systèmes à Valence négative, de manière générale, est définie comme des systèmes caractérisés par de réponses à des situations ou contextes aversifs tels que la peur, la frustration et la perte (Morris & Cuthbert, 2012). On postule que ce domaine serait associé aux traits de personnalité sous-jacents à la labilité émotionnelle tels que la propension à la colère, la peur et la vulnérabilité à l'anxiété et la dépression (Hasratian, Meuret, Chmielewski, & Ritz, 2022; Watson, Stanton, & Clark, 2017). Sur le plan neurobiologique, la labilité émotionnelle implique majoritairement l'amygdale, le cortex préfrontal ventromédian, l'insula et la partie antérieure du cortex cingulaire (Calder, Ewbank, & Passamonti, 2011; Deyoung & Gray, 2009; Kennis, Rademaker, & Geuze, 2013).

Tel que mentionné dans la section précédente, les individus ayant des comportements antisociaux présentent une importante labilité émotionnelle, telle qu'observée par la sévérité des traits d'irritabilité et d'anxiété. On mentionne également que la population antisociale aurait une importante difficulté à modifier leur comportement même à la suite d'une punition (par ex. restriction de liberté). En neuroimagerie, les recherches indiquent que les individus ayant comportements antisociaux présenteraient des déficits spécifiquement dans 3 des 5 systèmes neurocognitifs à Valence négative, soient la réponse à la détection de menaces imminentes, la frustration (ou l'omission imprévue de récompenses) ainsi que le système de perte (Blair, Veroude, & Buitelaar, 2018b; Matthys, Vanderschuren, & Schutter,2013a). Cette section fera l'état, en premier lieu, des processus neurobiologiques sous-jacents chaque système et, en second lieu, leur(s) rôle(s) dans notre compréhension des comportements antisociaux.

La réponse à la détection de menaces imminentes

Selon le RDoC (p.290, Kozak & Cuthbert, 2016), la réponse à la détection de menaces imminentes est définie comme suit : « Response to acute threat involves a defensive motivation system that drives behavior to protect against imminent harm, either exteroceptive or interoceptive.» (Réponse à une menace imminente qui implique un système de motivation défensive qui pousse le comportement à se protéger contre un danger imminent, soit extéroceptif ou intéroceptif [Traduction Libre]). L'un des modèles les plus influents afin d'expliquer la réponse à la détection de menace imminente est celui de Joseph LeDoux qui postule que la perception de la peur serait seulement déterminée que lorsqu'on devient conscient que notre cerveau (et plus largement notre corps), a déjà détecté la présence d'une menace, inconsciemment (LeDoux & Pine, 2016). En effet, le modèle à deux systèmes (LeDoux & Pine, 2016; Taschereau-Dumouchel, Michel, Lau, Hofmann, & LeDoux, 2022) suggère qu'à la suite de la détection d'une menace par notre système sensoriel, un premier circuit sous-cortical incluant l'amygdale, le cortex préfrontal ventromédian et l'hippocampe activerait un nombre important de systèmes physiologiques (par ex. la dilatation des pupilles, augmentation du rythme cardiaque, etc.) et comportementaux (par ex. approche/évitement/paralysie) et ce, de manière égosyntone à la perception et l'évaluation de

l'imminence du danger (LeDoux, 2015). Parallèlement, un second circuit, dît fronto-pariétal, traiterait alors l'information afin de construire une représentation consciente du danger et de son contexte. C'est principalement ce dernier, en interagissant avec le premier circuit, qui serait responsable de l'expérience subjective de la peur (LeDoux & Pine, 2016). En effet, plusieurs résultats de recherche semblent supporter cette théorie (Taschereau-Dumouchel, Kawato, & Lau, 2020), suggérant d'importantes différences dans les mécanismes associés à l'évaluation subjective de la peur (Servaas et al., 2013) et ceux associés à la conductance cutanée (voir méta-analyse Beissner, Meissner, Bär, & Napadow, 2013).

Afin d'étudier la réponse au danger, les principales modalités en neuroimagerie sont : 1) la présentation de stimuli élicitant des émotions négatives et (2) le conditionnement de peur. D'une part, la présentation visuelle de stimuli menaçants est souvent associée à l'activation de l'amygdale, de l'hippocampe, du thalamus, du cortex cingulaire antérieur, du cortex fronto-insulaire et du gyrus fusiforme (voir Figure 1). D'autre part, les résultats de méta-analyses portant sur le conditionnement de peur indiquent l'implication des mêmes structures, mais suggèrent aussi l'apport important du striatum dorsal, du précuneus, du cortex préfrontal dorsolatéral, du cortex somatosensoriel secondaire, et de la substance grise périaqueducale (Voir Figure 1). Bien que le rôle de l'amygdale dans le conditionnement de peur fasse encore l'objet de vifs débats (Fullana etal., 2019; Morriss, Hoare, & van Reekum, 2018), cette structure fait partie d'un système complexe impliquant une variété de mécanismes régulatoires chez l'humain.

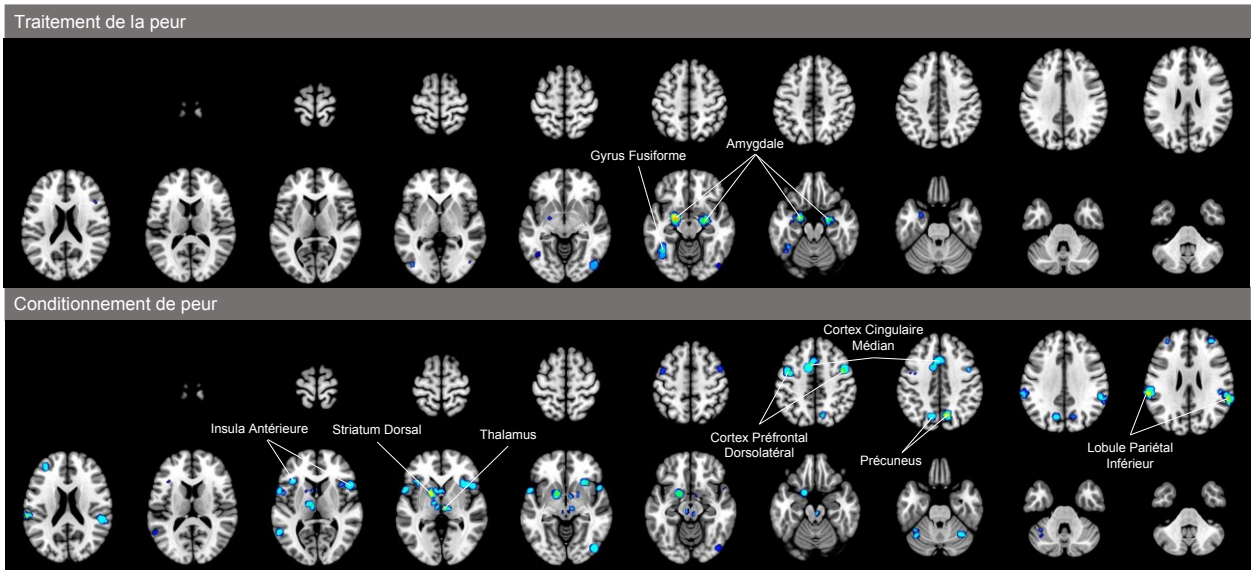

Figure 1. Les régions cérébrales impliquées dans la réponse à la menace imminente

Ces images représentent le chevauchement spatial entre les résultats de méta-analyses portant sur le traitement de la peur (Pozzi, Vijayakumar, Rakesh, & Whittle, 2021; Ran, Cao, & Chen, 2018; Tao, He, Lin, Liu, & Tao, 2021; Vytal & Hamann, 2010) et le conditionnement de la peur (Biggs et al., 2020; Fullana et al., 2018; Fullana et al., 2016; Mechias, Etkin, & Kalisch, 2010). Les coordonnées de chaque méta-analyse ont été extraites des articles et modélisées par une sphère de 8.41mm largeur à mi-hauteur. Les images méta-analytiques ont ensuite été juxtaposées pour évaluer le chevauchement spatial.

Tel que mentionné dans le chapitre précédent, on rapporte que les individus ayant des comportements antisociaux auraient de niveaux d'anxiété élevé mais des réponses psychophysiologiques déficientes. En effet, les individus antisociaux démontreraient un fonctionnement sous-optimal de l'axe hypothalamo-pituitaire-adrénalien en réponse à une menace (Fairchild, Baker, & Eaton, 2018). Ceci pourrait être reflété par une activité déficiente des régions impliquées dans la détection d'une menace (par ex. l'amygdale, cortex préfrontal ventromédian, substance grise périaqueducale et l'hypothalamus) (Blair, 2016; Blair et al., 2018b; Crowe & Blair, 2008). On mentionne également que les sujets avec des traits d'insensibilité émotionnelle seraient principalement caractérisés par une hyporéactivité de l'amygdale (Blair, Leibenluft, & Pine, 2014; Hyde, Shaw, & Hariri, 2013; Viding, Fontaine, & McCrory, 2012a). En effet, dans les premières études en neuroimagerie fonctionnelle portant sur la psychopathie, des chercheurs ont montré que ceux ayant des traits élevés de psychopathie se distingueraient des sujets contrôles par l'hypoactivation de l'amygdale, de l'insula et du cortex cingulaire antérieur lors d'acquisition du conditionnement de peur (Birbaumer et al., 2005). Certains ont donc postulé que ces déficits refléteraient leur déficit à détecter une menace d'un point de vue physiologique (Blair et al., 2014; Hyde et al.,2013; Viding, Fontaine, et al., 2012a). Or, tel que mentionné dans le chapitre précédent, les réponses psychophysiologiques seraient davantage associées aux comportements violents qu'à la psychopathie. Certains ont même noté que l'hypoactivité de l'amygdale serait associée au facteur comportemental de la psychopathie (c.-à-d. comportements impulsifs et irresponsables plutôt qu'aux traits d'insensibilité émotionnelle (Cohn et al., 2013).

Il a aussi été postulé que l'agression réactive serait caractérisée par une dysrégulation du circuit amygdale-hypothalamus-substance grise périaqueducale et par une altération des mécanismes pouvant le régulé (c.-à-d. cortex frontaux orbital, médial et inférieur) (Bertsch, Florange, & Herpertz, 2020; Crowe & Blair, 2008; Panksepp, 2004; Panksepp & Zellner, 2004). Bien que les individus antisociaux semblent rapporter une hyporéactivité émotionnelle, ces individus seraient aussi à risque d'agression réactive (r=.19 à .40, Blais, Solodukhin, & Forth, 2014). Ces résultats paradoxaux témoignent de la complexité des processus sous-jacents l'antisocialité. Toutefois,

tandis que les individus antisociaux seraient caractérisés par une hyporéactivité générale face aux stimuli menaçants, certains contextes, tels qu'une omission imprévue de récompenses, pourraient engendrer une hyperréactivité neurobiologique afin de préparer l'individu à la confrontation.

La frustration ou l'omission imprévue de récompenses

Selon le RDoC (p.290, Kozak & Cuthbert, 2016), « Frustration occurs in response to prevention or withdrawal of a reward, especially after repeated or sustained effort. » (La frustration survient en réponse à la prévention ou au retrait d'une récompense, en particulier après un effort répété ou soutenu [Traduction Libre]). Bien que le RDoC caractérise la frustration comme une résultante affective, d'autres ont précédemment défini la frustration comme une *situation* durant laquel une récompense est bloquée ou retirée, menant ainsi à une surcharge émotionnelle qui est souvent associée à l'irritabilité, la colère, la rancune, ainsi qu'à la vengeance (Berkowitz, 1989; Dollard, Miller, Doob, Mowrer, & Sears, 1939a). Dans une perspective évolutionniste, cette réactivité émotionnelle face à la frustration serait nécessaire à la survie des espèces afin de protéger les ressources de base, et particulièrement lorsqu'elles se font rares. Ces manifestations ont été rapportées dans une variété d'espèces telles que chez les chiens (Mohan-Gibbons, Weiss, & Slater, 2012), les rats (Burokas, Gutiérrez-Cuesta, Martín-García, & Maldonado, 2012; de Almeida & Miczek, 2002; Gallup, 1965), les cochons (Arnone & Dantzer, 1980; Dantzer, Arnone, & Mormede, 1980), les poissons (Vindas et al., 2012;Vindas et al., 2014) ainsi que chez les oiseaux (Azrin, Hutchinson, & Hake, 1966; Duncan & Wood-Gush, 1971).

Chez les animaux, les mécanismes neurobiologiques sous-jacents à ce système impliquent majoritairement l'amygdale, l'hypothalamus et la partie dorsolatérale de la substance grise périaqueducale (Crowe & Blair, 2008; Lischinsky & Lin, 2020; Nelson & Trainor, 2007; Panksepp & Zellner, 2004). Or, chez l'humain, les mécanismes neurobiologiques entourant la réponse à l'omission de récompense sont complexes. De manière à mieux comprendre cette complexité, Dugré et Potvin (Preprint) ont synthétisé les résultats d'une soixantaine d'études et ont trouvé que la frustration reposerait sur deux systèmes interdépendants : les systèmes de désactivation

et d'activation cérébrale (voir Figure 2). Plus précisément, le système de désactivation inclurait principalement le striatum ventral et le cortex préfrontal ventromédian et orbitofrontal qui concorderaient avec de récentes découvertes indiquant une dépression de la libération de dopamine lors de l'omission de récompense (Schultz, 2016; Sosa, Mata-Luévanos, & Buenrostro-Jáuregui, 2021; Tian & Uchida, 2015). Par ailleurs, le système d'activation impliquerait le cortex fronto-insulaire (bilatéral) ainsi que la partie antérieure du cortex cingulaire médian/l'aire motrice présupplémentaire. Or, ces deux régions sont des structures importantes dans la détection de stimuli saillants dans l'environnement, la régulation (Buhle et al., 2014; Morawetz, Bode, Derntl, & Heekeren, 2017) et la conscience émotionnelle (Gu, Hof, Friston, & Fan, 2013) telle que l'expérience de colère (Sorella, Grecucci, Piretti, & Job, 2021). Contrairement aux animaux, on différencie l'irritabilité de l'agressivité, notamment grâce aux manifestations émotionnelles de colère et d'irritabilité en l'absence de comportements violents (Bettencourt et al., 2006). Cette distinction entre l'état et le comportement pourrait en partie expliquer les différences entre les modèles neurobiologiques de la frustration chez les animaux et chez l'être humain.

La frustration est importante dans notre compréhension des comportements antisociaux, due au fait que ce système est un facteur important dans l'émergence d'agression réactive. En effet, durant l'omission de récompenses, les individus ayant des traits externalisés semblent montrer une plus grande désactivation du striatum ventral en comparaison aux sujets contrôles (Bjork, Chen, Smith, & Hommer, 2010; Bjork, Smith, & Hommer, 2008). On rapporte aussi une plus importante désactivation du cortex préfrontal ventromédian chez les enfants ayant un TC/TOP (White et al., 2013b) et chez les adultes avec des traits élevés de psychopathie (Bjork, Chen, & Hommer, 2012), en comparaison au groupe contrôle. Il est aussi intéressant de constater que des lésions et l'inactivation du cortex préfrontal ventromédian et orbitofrontal semblent être associées à une réactivité émotionnelle exagérée et à des comportements d'agression réactive (Agustín-Pavón et al., 2012; Berlin, Rolls, & Iversen, 2005; Berlin, Rolls, & Kischka, 2004; Grupe, Wielgosz, Davidson, & Nitschke, 2016; Izquierdo, Suda, & Murray, 2005; Kuniishi et al., 2017; Milad et al., 2009; Shiba, Kim, Santangelo,& Roberts, 2015; VanElzakker, Staples-Bradley, & Shin, 2018). Ces réactions pourraient être dû à son effet désinhibiteur sur l'amygdale (Motzkin, Philippi, Wolf,

Baskaya, & Koenigs, 2015). Spécifiquement durant l'omission de récompenses, les jeunes ayant de hauts niveaux d'irritabilité semblent montrer des déficits dans l'activité de la partie antérieure du cortex cingulaire, de l'aire motrice (pré)-supplémentaire, du cortex fronto-insulaire (Hodgdon et al., 2021), mais aussi du cortex préfrontal dorsolatéral et dorsomédian (Tseng et al., 2019). Par ailleurs, certains ont trouvé une dysconnectivité entre les régions principales des deux systèmes (c.-à-d. le cortex préfrontal ventromédian et le cortex ventrolatéral) chez les jeunes atteints de trouble bipolaire ayant des hauts niveaux d'irritabilité (Ross et al., 2020).

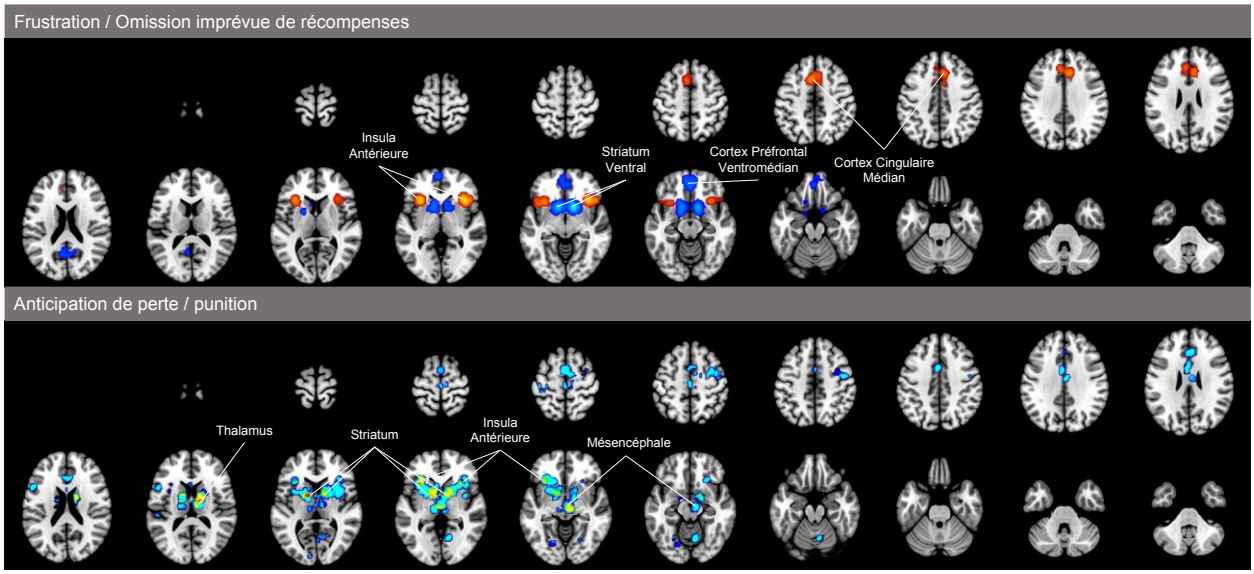

Figure 2. Les régions cérébrales impliquées dans la réponse à frustration et à l'anticipation de perte

Ces images représentent les résultats de la méta-analyse portant sur la frustration (Dugré et Potvin, en révision), et le chevauchement spatial entre les résultats de méta-analyses portant sur l'anticipationde perte/punition (Dugré, Dumais, Bitar, & Potvin, 2018; Wilson et al., 2018). Les coordonnées de chaque méta-analyse ont été extraites des articles et modélisées par une sphère de 8.41mm largeur à mi-hauteur. Les images méta-analytiques ont ensuite été juxtaposées pour évaluer le chevauchement spatial.

Le système de perte/punition

Le système de perte est principalement associé au sentiment de culpabilité et à la honte. En effet, selon le RDoC (p.290, Kozak & Cuthbert, 2016), on mentionne que : « Loss is deprivation of a desired object or situation, social or nonsocial, episodic or sustained. » (La perte est la privation d'un objet ou d'une situation désirée, sociale ou non sociale, épisodique ou durable [Traduction Libre]). En neuroimagerie fonctionnelle, l'une des tâches les plus utilisées afin de mieux comprendre les mécanismes neurobiologiques sous-jacents au système de perte est le « Monetary Incentive Delay Task » (Knutson, Westdorp, Kaiser, & Hommer, 2000). Durant cette tâche, les participants doivent répondre à un stimulus cible suivant un signal incitatif indiquant un potentiel gain ou perte monétaire. Les chercheurs peuvent donc étudier les réponses cérébrales lors de l'anticipation d'une perte potentielle et de la réception d'un stimulus punitif. Les résultats de deux récentes méta-analyses montrent que l'anticipation et la réception d'une perte monétaire reposeraient principalement sur l'activité du cortex cingulaire antérieur, de l'aire motrice (pré)-supplémentaire, du cortex fronto-insulaire, du striatum, de l'amygdale, du diencéphale et du mésencéphale (Dugré et al., 2018; Wilson et al., 2018) (Voir Figure 2).

En neuroimagerie, très peu d'études ont tenté de mieux comprendre l'activité cérébrale des personnes ayant des comportements antisociaux lors de tâches punitives (Byrd, Loeber, & Pardini, 2014; Murray, Waller, & Hyde, 2018). Certains ont trouvé que les enfants ayant un TC/TOP et des traits élevés d'insensibilité émotionnelle seraient caractérisés par des altérations dans l'activité de cortex préfrontal latéral et du noyau caudé (Finger et al., 2011; Finger et al., 2008). Or, d'autres ont montré que les jeunes ayant un TC/TOP ne se différencieraient pas significativement des sujets contrôles en ce qui a trait à l'activité cérébrale lors de l'anticipation et la réception de perte et ces résultats ne sembleraient pas être médié par les traits d'insensibilité émotionnelle (Byrd et al., 2021). Malgré leur très grand échantillon d'enfants âgés d'environ 10 ans (n>10,000), l'utilisation de régions d'intérêts (contrairement à l'utilisation de l'ensemble du cerveau) limite grandement la portée des résultats. D'autres études suggèrent que lors de tâches punitives, les adultes ayant un TPA se distingueraient des sujets contrôles dans l'activité du cortex cingulaire antérieur, du cortex fronto-insulaire, du cortex préfrontal dorsolatéral ainsi que du précuneus

(Gregory et al., 2015; Völlm etal., 2007). Ces déficits semblent notamment corrélés avec la sévérité des comportements antisociaux et des traits d'insensibilité émotionnelle chez les adolescents (Murray, Lopez-Duran, Mitchell, Monk, & Hyde, 2022). Les déficits de l'activité cérébrale lors de tâches punitives pourraient ainsi refléter l'indifférence aux conséquences qui caractérisent fréquemment les individus antisociaux. Par conséquent, on pourrait postuler que leur insensibilité physiologique et neurobiologique à la détection d'une menace pourrait avoir des répercussions sur la capacité à percevoir et intégrer une punition comme renforçateur négatif à travers leur développement, augmentant ainsi le risque de comportements antisociaux.

Les recherches portant sur le fonctionnement cérébral des individus ayant des comportements antisociaux lors de tâches associées aux systèmes à valence négative indiquent d'importantes altérations des régions limbiques. Il est intéressant de constater que ces systèmes impliquent en grande partie le réseau sérotoninergique (Fisher & Hariri, 2013). Les dysfonctions cérébrales rapportées chez les individus antisociaux concorderaient ainsi avec les résultats d'études indiquant qu'un fonctionnement sous-optimal du réseau sérotoninergique prédisposerait les individus à l'agression réactive (da Cunha-Bang & Knudsen, 2021; Duke, Bègue, Bell, & Eisenlohr-Moul, 2013; Seo, Patrick, & Kennealy, 2008). En somme, il est sans équivoque que les individus antisociaux sont caractérisés par d'important déficits du fonctionnement cérébral sous-jacents aux systèmes à valence négative.

Les Systèmes de Processus Sociaux

Bien que les individus antisociaux puissent montrer des altérations neurobiologiques sous-jacentes aux systèmes à valence négative, ceux-ci montreraient aussi d'importants déficits interpersonnels tels que des problèmes dans la communication sociale (par ex. reconnaissance émotionnelle faciale) ainsi que dans la perception et la compréhension d'autrui (par ex. empathie,prise de perspective et raisonnement moral).

La Communication Sociale

Tel que mentionné par le RDoC (p.291, Kozak & Cuthbert, 2016), la communication sociale est définie comme « Is a dynamic process that includes receptive and productive exchange of socially relevant information. » ([La communication sociale] est un processus dynamique qui comprend un échange entre la réception et la production d'informations socialement pertinentes. [Traduction Libre]). L'un des piliers de la communication sociale est sans aucun doute la reconnaissance émotionnelle faciale. En effet, l'évaluation des expressions émotionnelles d'autrui est indispensable afin de percevoir et interpréter adéquatement notre environnement de manière à y faire face. Dans une récente méta-analyse de plus de 385 études en neuroimagerie, des chercheurs ont observé que la communication sociale impliquerait l'activité cérébrale de l'aire motrice supplémentaire, du cortex fronto-insulaire, du gyrus fusiforme et de la partie postérieure du sillon temporal supérieur (Lobo et al., 2022). Cependant, la reconnaissance des expressions faciales inclurait aussi l'amygdale, la partie antérieure du cortex cingulaire médian ainsi que le cortex préfrontal dorsolatéral (Voir Figure 3). On rapporte que la reconnaissance d'expressions faciales serait caractérisée par une séquence temporelle particulière de ces régions cérébrales (Guillory & Bujarski, 2014). En effet, ce mécanisme neurobiologique serait représenté par une activation précoce du gyrus fusiforme et de l'amygdale (inférieure à 200 millisecondes), suivi de la partie antérieure du cortex cingulaire médian et du cortex temporal latéral (supérieur à 500 millisecondes)et finalement l'activité du cortex préfrontal (orbitofrontal) latéral (entre 600 et 1300 millisecondes).

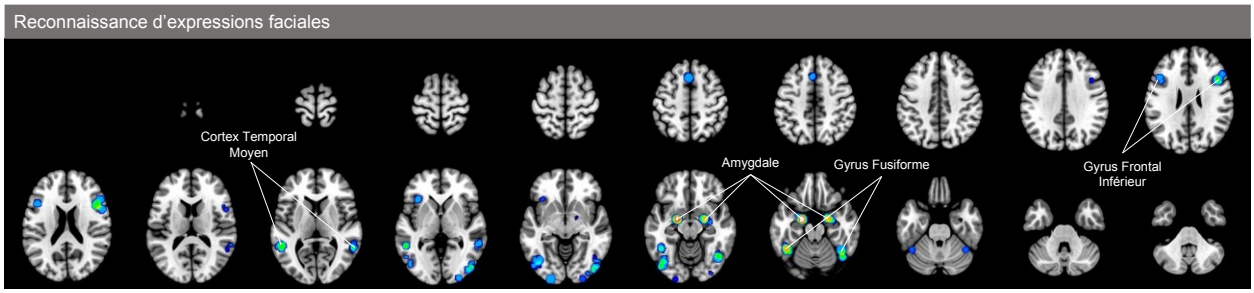

Figure 3. Les régions cérébrales impliquées dans la Communication Sociale

Ces images représentent le chevauchement spatial entre les résultats de méta-analyses portant sur la *reconnaissance d'expressions faciales* (Dricu & Frühholz, 2016; Liu, Liu, Zheng, Zhao, & Fu, 2021; Mende-Siedlecki, Said, & Todorov, 2013; Müller, Höhner, & Eickhoff, 2018; Zinchenko, Yaple, & Arsalidou, 2018). Les coordonnées de chaque méta-analyse ont été extraites des articles et modélisées par une sphère de 8.41mm largeur à mi-hauteur. Les images méta-analytiques ont ensuite été juxtaposées pour évaluer le chevauchement spatial.

Tel que mentionné précédemment, les individus antisociaux semblent montrer un nombre important de déficits lors de la reconnaissance des expressions émotionnelles d'autrui. En neuroimagerie, plusieurs chercheurs ont trouvé que les jeunes ayant un TC montraient des déficits au niveau de l'activité de l'insula, de la partie antérieure du cortex cingulaire médian, du cortex préfrontal ventromédian, ainsi que dans plusieurs régions temporales telles que le gyrus fusiforme (Fairchild et al., 2014; Menks et al., 2021; Passamonti et al., 2010). Par ailleurs, certains chercheurs ont trouvé que les jeunes ayant un TC avec des traits élevés d'insensibilité émotionnelle seraient caractérisés par à une hypoactivation de l'amygdale lors de la perception d'expression faciale (de peur et colère), en comparaison à des sujets sains (Ewbank et al., 2018; Jones, Laurens, Herba, Barker, &Viding, 2009; Klapwijk et al., 2016; Marsh et al., 2008). D'autres ont cependant montré que l'amygdale serait négativement associée à la sévérité des symptômes de TC lors de la présentation de stimuli émotionnels faciaux (Fairchild et al., 2014). Finalement, tandis qu'on observerait une hyperactivité de cette structure chez les TC sans traits d'insensibilité émotionnelle, ceux avec des traits élevés d'insensibilité auraient des réponses similaires que les sujets contrôles (Sebastian et al., 2014; Viding, Sebastian, et al., 2012).

Ces résultats suggèrent que la reconnaissance d'expression faciale pourrait être lié à divers mécanismes pouvant expliquer les comportements antisociaux. D'une part, la sévérité des comportements antisociaux serait associée à des scores élevés de névrosisme et une hyperactivité de l'amygdale tandis que les traits d'insensibilité émotionnelle seraient plutôt associés à des scores significativement plus bas de névrosismes et une hyporéactivité de l'amygdale (Hyde, Byrd, Votruba-Drzal, Hariri, & Manuck, 2014). D'autre part, Lozier et collaborateurs (2014) ont cependant trouvé que les traits d'insensibilité corrélaient négativement avec l'activité de l'amygdale lors de la reconnaissance émotionnelle faciale de peur et que celle-ci médiait la relation entre les traits d'insensibilité émotionnelle et l'agression proactive. Ces résultats contradictoires reflètent la complexité d'étudier une population aussi hétérogène que les individus antisociaux. Or, l'activité de l'amygdale pourrait bel et bien être aussi médié par d'autres facteurs qui ne sont pas pris en compte dans les études en neuroimagerie. Tel que mentionné dans le chapitre précédent, on pourrait présumer que l'hyporéactivité psychophysiologique (et

neurobiologique) serait associée à la recherche de sensation forte et aux traits d'insensibilité émotionnelle, ce qui augmenterait le risque de violence proactive et de délinquance non-agressive.

La Perception et Compréhension d'autrui

Selon le RDoC (p.291, Kozak & Cuthbert, 2016), la perception et la compréhension d'autrui est défini comme « involves representations of other animate entities, including their cognitive or emotional states or traits. » (Impliquant des représentations d'autres entités animées, y compris leurs états ou traits cognitifs ou émotionnels [Traduction Libre]). En effet, ce système serait principalement caractérisé par l'empathie, la prise de perspective d'autrui ainsi que le raisonnement moral. On indique que celui-ci serait caractérisé par l'activité du cortex préfrontal médial (ventral à dorsal), de la partie antérieure du cortex cingulaire moyen, de l'aire motrice présupplémentaire, du cortex fronto-insulaire, du cortex cingulare postérieur, du gyrus fusiforme, du cortex temporal moyen ainsi que de la jonction temporo-pariétale (Lobo et al., 2022). Bien qu'ils semblent être caractérisés par des structures cérébrales similaires, les sous-systèmes de la perception et compréhension d'autrui comportent de subtiles différences.

Premièrement, l'empathie est définie comme étant une tentative de représentation ou de simulation des expériences subjectives d'autrui (c.-à-d. sensoriels, affectives ou cognitives) (Marsh, 2022). Ce sous-système inclurait majoritairement le cortex cingulaire antérieur (dorsal), l'aire motrice présupplémentaire, le cortex fronto-insulaire, le cortex préfrontal dorsomédial et dorsolatéral, le thalamus et le mésencéphale (voir Figure 4). Les individus antisociaux, étant principalement caractérisés par un manque de remords et d'empathie (APA, 2013), il n'est donc pas surprenant de constater un fonctionnement cérébral aberrant lors de tâches impliquant l'empathie. En effet, certains ont trouvé des déficits dans l'activité de l'amygdale (Decety, Michalska, Akitsuki, & Lahey, 2009; Marsh et al., 2013; Sebastian et al., 2012; von Polier et al., 2020) ainsi que d'autres structures corticales tels que le cortex fronto-insulaire, le cortex cingulaire antérieur (dorsal), la partie antérieure du cortex cingulaire médian et l'aire motrice présupplémentaire et le cortex préfrontal dorsolatéral (Decety et al., 2009; Lockwood et al.,

2013;Marsh et al., 2013; Meffert, Gazzola, Den Boer, Bartels, & Keysers, 2013). Par exemple, dans leur échantillon de 18 détenus ayant de hauts traits psychopathiques, des chercheurs ont trouvé que ceux-ci montraient une activité cérébrale significativement plus élevée du cortex préfrontal médial, du cortex préfrontal dorsolatéral ainsi que du gyrus angulaire, comparativement aux sujets sains (Meffert et al., 2013). Par ailleurs, certains ont postulé que les altérations dans l'activité cérébrale sous-jacentes à l'empathie seraient associées au risque d'agression proactive (Blair, 2018; Gillespie, Kongerslev, Sharp, Bo, & Abu-Akel, 2018).

Deuxièmement, la prise de perspective d'autrui (ou la théorie de l'esprit) est souvent définie comme étant le raisonnement à propos des intentions, des buts et des motivations d'autrui (Frith &Frith, 2005). En effet, le fait de pouvoir inférer et représenter les expériences d'autrui est crucial afin de reconnaître nos différences, mais aussi afin de mieux comprendre et expliquer leurs actions (Baker, Jara-Ettinger, Saxe, & Tenenbaum, 2017). On rapporte que le circuit neurobiologique sous-jacent à la prise de perspective serait similaire à celui de l'empathie, mais inclurait davantage le cortex préfrontal médial (ventral et dorsal), le cortex préfrontal ventrolatéral, le précuneus et cortex cingulaire postérieur ainsi que la jonction temporo-pariétale et le cortex temporal moyen (Figure 4). Lors de tâches de prise de perspective d'autrui, les individus ayant des comportements antisociaux semblent montrer très peu de déficits dans l'activité cérébrale, et les traits d'insensibilité émotionnelle ne semblent avoir aucun impact sur ceux-ci (Gao et al., 2019; O'Nions et al.,2014). Néanmoins, certains ont trouvé que les individus ayant un TPA avec et sans schizophrénie seraient caractérisés par une hyperactivité de la partie antérieure du cortex cingulaire médian et de l'aire motrice présupplémentaire, du cortex préfrontal dorso- et ventrolatéral ainsi que la jonction temporo-pariétale (Schiffer et al., 2017).

Finalement, le raisonnement moral relèverait plutôt de la capacité à comprendre et à distinguer le bien du mal et l'application des normes morales. Le système neurobiologique sous-jacent au raisonnement moral inclurait principalement le cortex préfrontal médian (ventral et dorsal), le précuneus et cortex cingulaire postérieur ainsi que la jonction temporo-pariétale, le cortex temporal moyen et l'amygdale (Voir Figure 4). Bien que ce système soit moins étudié que les deux autres, deux exhaustives revues de la littérature indiquent que les individus antisociaux

seraient caractérisés par une activité cérébrale anormalement élevée du gyrus angulaire, du cortex préfrontal médian et ventromédian ainsi que de l'amygdale et du gyrus temporal supérieur (Raine, 2019; Raine & Yang, 2006). Ces déficits seraient par ailleurs davantage rapportés dans la psychopathie primaire et seraient principalement associée à l'agression proactive (Raine, 2019).

Les individus antisociaux semblent montrer d'importants déficits dans le fonctionnement cérébral lors de la présentation de stimuli sociaux. Ceci pourrait refléter leur manque d'empathie envers leur victime et le manque de remords et de sentiment de culpabilité à la suite de la perpétration de délits. Il est intéressant de constater que l'ocytocine, un neuropeptide, serait associée aux processus sociaux tels que la reconnaissance émotionnelle faciale et l'empathie (Gong et al., 2017; Jones, Barrera, Brothers, Ring, & Wahlestedt, 2017; Leppanen, Ng, Tchanturia, & Treasure, 2017; Shahrestani, Kemp, & Guastella,2013; Van IJzendoorn & Bakermans-Kranenburg, 2012), par l'entremise de l'amygdale, le cortex fusiforme et le cortex temporal supérieur (Grace, Rossell, Heinrichs, Kordsachia, & Labuschagne,2018; Tully, Gabay, Brown, Murphy, & Blackwood, 2018). On rapporte des altérations du niveau d'ocytocine dans la population antisociale (Mitchell et al., 2013) et la prise intranasale de celle-ci semble agir sur la partie antérieure du cortex cingulaire médian et de l'insula des individus antisociaux (Tully et al., 2022). En somme, les résultats rapportés à travers la littérature scientifique suggèrent que les individus antisociaux semblent montrer un nombre important d'altérations dans l'activité cérébrales lors de tâches associées aux processus sociaux, et plus particulièrement lors de la reconnaissance émotionnelle d'autrui

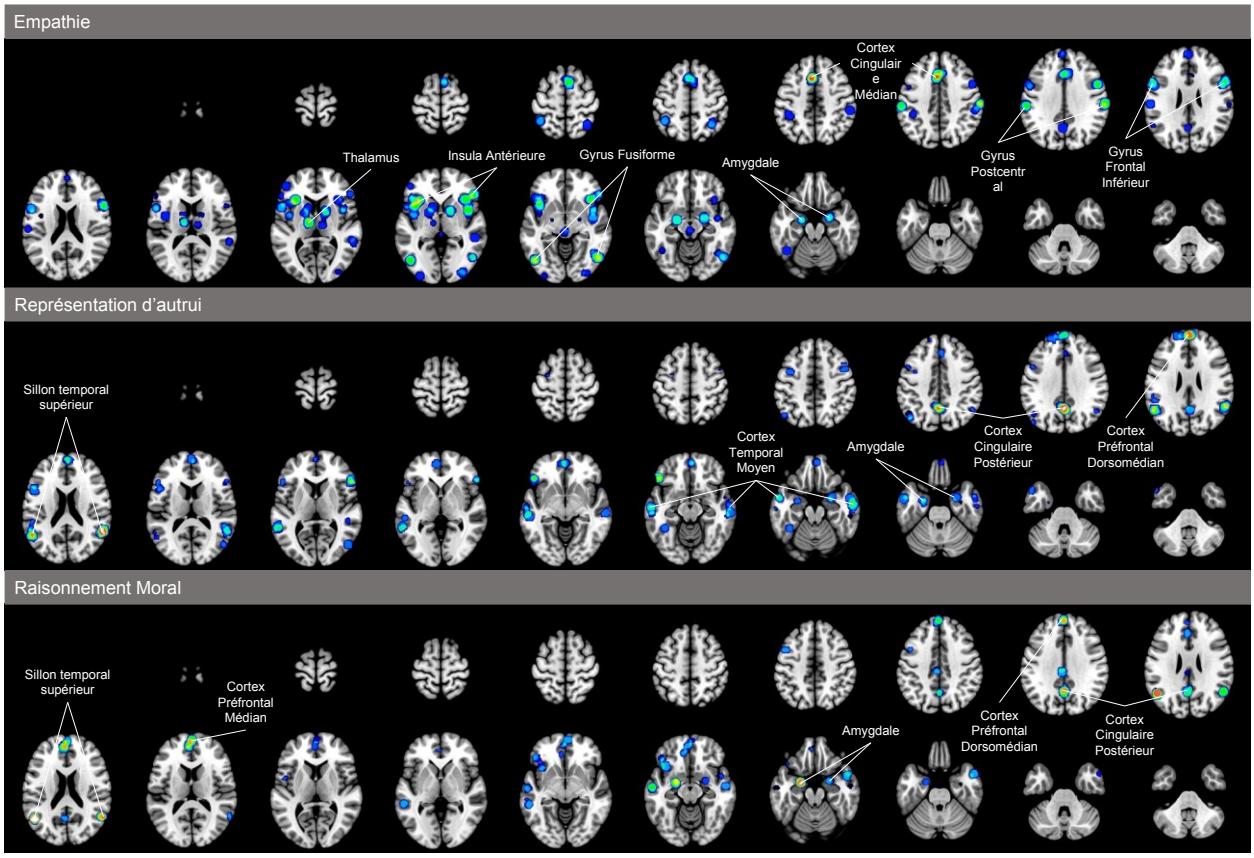

Figure 4. Les régions cérébrales impliquées dans la Perception et Compréhension d'Autrui

Ces images représentent le chevauchement spatial entre les résultats de méta-analyses portant sur *l'empathie* (Arioli, Cattaneo, Ricciardi, & Canessa, 2021; Bzdok et al., 2012; Ding et al., 2020;Fallon, Roberts, & Stancak, 2020; Fan, Duncan, de Greck, & Northoff, 2011; Jauniaux, Khatibi, Rainville, & Jackson, 2019; Kogler, Müller, Werminghausen, Eickhoff, & Derntl, 2020; Lamm, Decety, & Singer, 2011; Schurz et al., 2021; Timmers et al., 2018), sur *la représentation d'autrui* (Arioli & Canessa, 2019; Arioli et al., 2021; Bzdok et al., 2012; Mar, 2011; Schurz, Aichhorn,Martin, & Perner, 2013; Schurz et al., 2021; Spreng, Mar, & Kim, 2009), ainsi que sur *le raisonnement moral* (Boccia et al., 2017; Bzdok et al., 2012; Eres, Louis, & Molenberghs, 2018; Fede & Kiehl, 2020; Han, 2017). Les coordonnées de chaque méta-analyse ont été extraites des articles et modélisées par une sphère de 8.41mm largeur à mi-hauteur. Les images méta-analytiques ont ensuite été juxtaposées pour évaluer le chevauchement spatial.

Les Systèmes à Valence Positive

Les résultats d'études indiquent que les traits de personnalité du système à valence positive (incluant l'extraversion, la dépendance à la récompense, la recherche de sensation forte et le système d'approche comportemental) seraient associés à l'activité du striatum ventral et dorsal, du cortex orbitofrontal et du cortex préfrontal ventromédian et dorsolatéral (Deyoung & Gray, 2009; Kennis, Rademaker, & Geuze, 2013). Or, on rapporte majoritairement deux grands systèmes associés à la valence positive tels que la réactivité à la récompense et la valorisation de récompenses.

La réactivité à la récompense

Selon le RDoC (p.290, Kozak & Cuthbert, 2016), on définit la motivation à la récompense comme étant « the computation of probability and benefit of a potential outcome, involving external information, biases, and deprivation states. » (Le calcul de la probabilité et des avantagesd'un résultat potentiel, impliquant des informations externes, des biais et des états de privation. [Traduction Libre]). En neuroimagerie fonctionnelle, on peut étudier ce système par l'entremise d'un large éventail de tâches afin d'éliciter un gain, notamment grâce au « Monetary Incentive Delay Task » décrit précédemment. D'une part, l'anticipation d'une récompense serait majoritairement associée à l'activité cérébrale du striatum ventral et dorsal, du cortex fronto-insulaire, de la partie antérieure du cortex cingulaire médian et de l'aire motrice présupplémentaire, du thalamus et du mésencéphale (Voir Figure 5), tandis que la réception de récompense recruterait plutôt le cortex préfrontal, le cortex cingulaire postérieur et le striatum ventral et dorsal (Voir Figure 5).

Deux récentes revues de la littérature indiquent que les individus antisociaux seraient caractérisés par une hyperactivité du striatum (ventral et dorsal) et d'une hypoactivation du cortex préfrontal ventromédian, du cortex préfrontal ventrolatéral et de la partie antérieure du cortex cingulaire médian (Byrd et al., 2014; Murray et al., 2018). On soulève cependant que les traits d'insensibilité émotionnelle pourraient jouer un rôle dans la modulation de certaines régions cérébrales lors de l'anticipation et la réception de récompenses (Bjork, Chen, Smith, &

Hommer, 2010; Cohn, Veltman, et al., 2015; Pujara, Motzkin, Newman, Kiehl, & Koenigs, 2014). Or, certains chercheurs ont trouvé que les effets liés à l'activité du striatum ventral seraient plutôt attribuables aux traits impulsifs-antisociaux (Carré, Hyde, Neumann, Viding, & Hariri, 2013; Geurts et al., 2016; Korponay et al., 2017; Murray, Shaw, Forbes, & Hyde, 2017a, 2017b), tandis que d'autres n'ont trouvé aucun lien avec l'activité de cette même région (Hoskinget al., 2017; Murray et al., 2022; Pujara et al., 2014). Malgré le peu de recherches, ces résultats semblent néanmoins suggérer que les individus antisociaux pourraient être caractérisés par des dysfonctions cérébrales lors de l'anticipation de récompense (Murray et al., 2018).

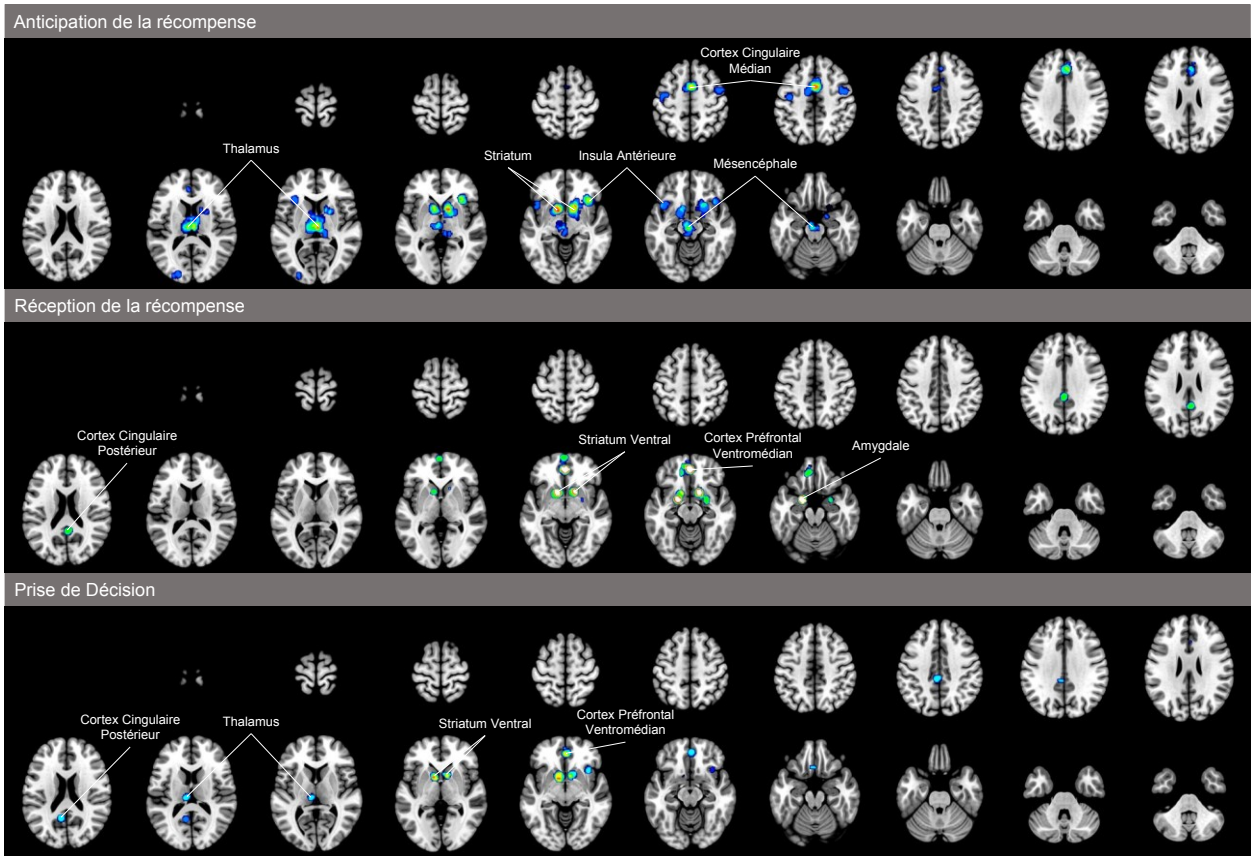

Figure 5. Les régions cérébrales impliquées dans les Systèmes à Valence Positive

Ces images représentent le chevauchement spatial entre les résultats de méta-analyses portant sur *l'anticipation d'une récompense* (Diekhof, Kaps, Falkai, & Gruber, 2012; Knutson & Greer, 2008;Liu, Hairston, Schrier, & Fan, 2011; Oldham et al., 2018; Wilson et al., 2018), *la réception d'unerécompense* (Diekhof et al., 2012; Knutson & Greer, 2008; Liu et al., 2011; Oldham et al., 2018; Wilson et al., 2018) et *la prise de décision* (Bartra, McGuire, & Kable, 2013; Clithero & Rangel, 2014; Kühn & Gallinat, 2012; Schüller, Kuhn, Jessen, & Hu, 2019). Les coordonnées de chaque méta-analyse ont été extraites des articles et modélisées par une sphère de 8.41mm largeur à mi-hauteur. Les images méta-analytiques ont ensuite été juxtaposées pour évaluer le chevauchement spatial.

La prise de décision

La prise de décision lors de la présence de récompenses définie ce système comme étant (p.290-291, Kozak & Cuthbert, 2016), « The computation of the cost of obtaining a potential outcome » (La computation des coûts afin d'obtenir un potentiel gain [Traduction Libre]). Dans la présente thèse, une définition plus large sera utilisée afin de s'accorder aux études en neuroimagerie : l'attribution d'une saillance incitative à un stimulus telle que l'évaluation subjective de plaisance d'un stimulus. On rapporte que le mécanisme neurobiologique sous-jacent à ce système impliquerait la partie périgenual du cortex cingulaire antérieur, le cortex orbitofrontal médian, le cortex préfrontal ventromédian, l'insula, le striatum ventral et le thalamus (Voir Figure 5).

Seule une très faible proportion d'études en neuroimagerie portant sur le système à valence positive chez les individus antisociaux inclue une tâche sous-jacente à la prise de décision. On note néanmoins que les jeunes ayant un TC présenteraient des déficits dans le cortex préfrontal ventromédian lorsqu'ils choisissent des stimuli, ainsi que des altérations dans le striatum dorsal lorsqu'ils font des erreurs dans la prédiction de récompense (White et al., 2013a). Ceci pourrait être reflété par le fait que ces enfants opteraient pour de plus petites récompenses mais immédiates contrairement à de grandes récompenses futures (Blair et al., 2020; White et al., 2014). Par ailleurs, on note que la présence de symptômes d'hyperactivité/impulsivité, mais pas les traits d'insensibilité émotionnelle, pourrait jouer médier cette prise de décision (Blair et al., 2020; White et al., 2014). Considérant le très peu d'étude, l'apport de ce système dans l'explication des comportements antisociaux demeure encore méconnu. Cependant, des déficits dans la prise de décision semblent aussi caractériser la population ayant des problèmes d'usage de substance (Bjork & Pardini, 2015). On pourrait ainsi émettre l'hypothèse que les déficits dans la prise de décision seraient davantage associés aux comportements externalisés en général, c'est-à-dire aux problèmes d'usage de substances et à la délinquance non-agressive.

Les systèmes à valence positive impliquent généralement le fonctionnement dopaminergique par l'entremise des réseaux mésolimbique et mésocorticolimbique (Kujawa, Klein, Pegg, & Weinberg, 2020; Olino, 2016). Malgré qu'un nombre considérable d'études ont trouvé une certaine association entre des marqueurs génétiques du réseau dopaminergique et l'émergence

de comportements antisociaux (Veroude et al., 2016), les résultats d'une méta-analyse indiquent un rôle limité de ceux-ci sur l'émergence de comportements antisociaux (Vassos, Collier, & Fazel, 2014). Similairement rapporté en neuroimagerie, on suggère de *potentielles* altérations des régions cérébrales impliquées dans les systèmes à valence positive. Cependant, les petits échantillons et les différences méthodologiques limiteraient notre compréhension du rôle de ces systèmes dans l'explication des comportements antisociaux.

Les Systèmes Cognitifs

Les systèmes attentionnels

Le RDoC défini les systèmes attentionnels comme étant (p.291, Kozak & Cuthbert, 2016): « Processes that regulate access to capacity-limited systems, such as awareness, higher perceptual processes, and motor action. » (Processus qui régulent l'accès aux systèmes à capacité limitée, telsque la conscience, les processus perceptifs supérieurs et l'action motrice [Traduction Libre]). Les méta-analyses portant sur les études en neuroimagerie fonctionnelle incluant des tâches attentionnelles ont montré que l'attention impliquerait l'activité du cortex fronto-insulaire, du cortex préfrontal dorsolatéral, de la partie antérieure du cortex cingulaire médian, de l'aire motrice présupplémentaire, du gyrus précentral et du lobule pariétal inférieur (Voir Figure 6).

À travers la littérature, on note que les individus ayant des comportements délinquants présenteraient certaines altérations dans les régions impliquées dans les systèmes attentionnels. Par exemple, White et collaborateurs (2012) ont trouvé que les jeunes ayant un TC et des traits d'insensibilité émotionnelle rapporteraient une hypoactivation des régions associées au réseau attentionnel dorsal (c.-à-d. le lobule pariétal supérieur et le sillon pariétal inférieur) lors d'une tâche cognitive incluant des visages de peur. Lorsque la charge attentionnelle est élevée, les jeunes ayant un TC hypoactiveraient l'insula (Hwang et al., 2016). Ces déficits attentionnels pourraient être expliqués par la difficulté à filtrer l'information pertinente afin de moduler les comportements orientés vers un but (Baskin-Sommers & Brazil, 2022). En effet, on rapporte que les individus ayant des traits élevés de psychopathie montreraient une hyperactivité du cortex

préfrontal latéral et d'une hyporéactivité de l'amygdale lors d'une tâche attentionnelle impliquant des stimuli négatifs (Larson et al., 2013). Cependant, d'autres n'ont trouvé aucune différence entre des jeunes ayant un TC avec des traits d'insensibilité émotionnelle et les sujets contrôles lorsque la charge attentionnelle était élevée (White, Marsh, et al., 2012). Bien que les études portant sur les systèmes attentionnels semblent limitées, un certain nombre indiquent néanmoins que ces systèmes pourraient potentiellement expliquer l'hyporéactivité émotionnelle observée dans la population antisociale (Baskin-Sommers & Brazil, 2022). Davantage de recherche est nécessaire afin de mieux comprendre son rôle dans l'explication des comportements antisociaux.

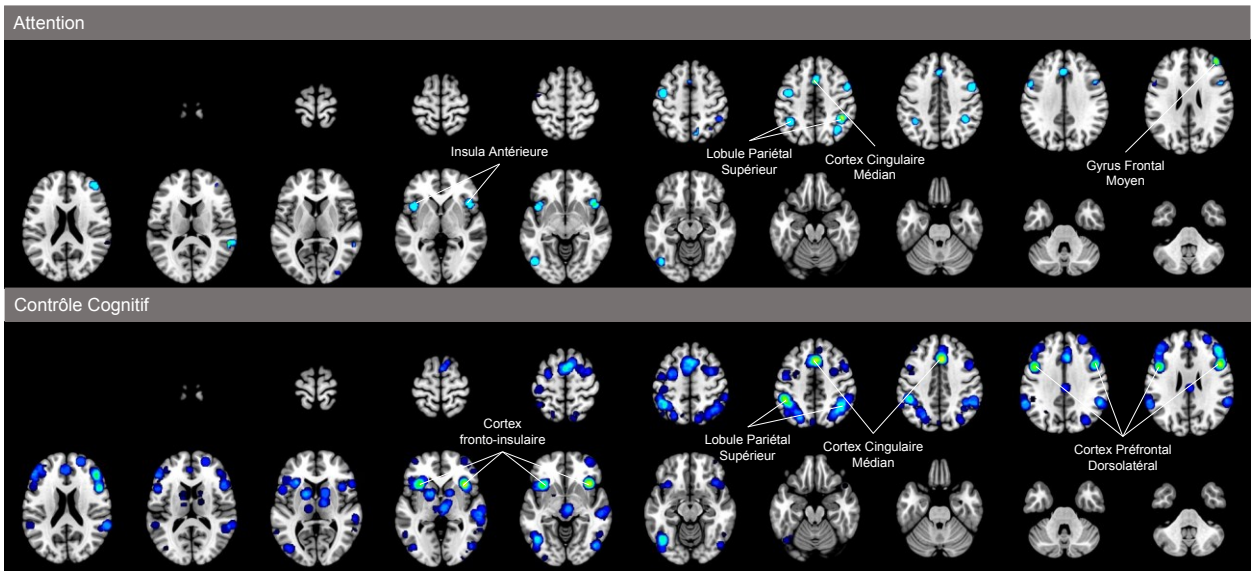

Figure 6. Les régions cérébrales impliquées dans les Systèmes Cognitifs

Ces images représentent le chevauchement spatial entre les résultats de méta-analyses portant sur *l'attention* (Krall et al., 2015; Langner & Eickhoff, 2013; Morandini et al., 2020; Wallis, Stokes, Cousijn, Woolrich, & Nobre, 2015) et *le contrôle cognitif* (Buchsbaum, Greer, Chang, & Berman,2005; W. Cai et al., 2019; Cieslik, Mueller, Eickhoff, Langner, & Eickhoff, 2015; Criaud & Boulinguez, 2013; Derrfuss, Brass, Neumann, & von Cramon, 2005; Hung, Gaillard, Yarmak, & Arsalidou, 2018; Kim, Cilles, Johnson, & Gold, 2012; Laird et al., 2005; Neumann, Lohmann, Derrfuss, & von Cramon, 2005; Puiu et al., 2020; Rae, Hughes, Weaver, Anderson, & Rowe, 2014;Simmonds, Pekar, & Mostofsky, 2008; Song et al., 2017; Swick, Ashley, & Turken, 2011; Tao, Wang, Zhu, & Cai, 2021; Wesley & Bickel, 2014; Worringer et al., 2019; Zhang et al., 2021). Les coordonnées de chaque méta-analyse ont été extraites des articles et modélisées par une sphère de 8.41mm largeur à mi-hauteur. Les images méta-analytiques ont ensuite été juxtaposées pour évaluer le chevauchement spatial.

Le contrôle cognitif

Finalement, le RDoC défini le contrôle cognitif comme étant (p.291, Kozak & Cuthbert, 2016): « the modulation of other cognitive and emotion systems in the service of goal-directed behavior... » (la modulation d'autres systèmes cognitifs et émotionnels au service d'un comportement orienté vers un but [Traduction Libre]). Plus précisément, ce système est un domaine neurocognitif impliquant les fonctions exécutives qui servent fréquemment à freiner une réponse (Miller & Cohen, 2001). En neuroimagerie, les résultats de méta-analyses semblent montrer que ce système impliquerait majoritairement la partie antérieure du cortex cingulaire médian, de l'aire motrice supplémentaire, du cortex fronto-insulaire, du cortex préfrontal dorsolatéral, du gyrus supramarginal et du lobule pariétal inférieur et du striatum dorsal (voir Figure 6).

Les revues de la littérature portant sur les études en neuroimagerie fonctionnelle utilisant des tâches de contrôles cognitifs indiquent que les personnes commettant des gestes délinquants seraient caractérisées par une hypoactivation du cortex fronto-insulaire, du lobe temporal, de la partie antérieure du cortex cingulaire médian et de l'aire motrice supplémentaire (Alegria, Radua, & Rubia, 2016; Blair et al., 2018b; Matthys, Vanderschuren, & Schutter, 2013b; Noordermeer, Luman, & Oosterlaan, 2016). Par exemple, Alegria et collaborateurs (2016) ont montré que les jeunes ayant un TC hypoactiveraient les gyrus temporaux médian et supérieurs, le putamen ainsi que l'insula postérieure lors de tâches exécutives. On pourrait ainsi émettre l'hypothèse selon laquelle les altérations observées chez les individus antisociaux seraient le reflet de l'impulsivité motrice qui semble être un facteur important dans notre compréhension du passage à l'acte délinquant.

Tel que mentionné dans le chapitre précédent, il est d'une importance capitale de mieux comprendre les mécanismes impliqués dans l'émergence de comportements antisociaux. De manière générale, les recherches indiquent que les individus antisociaux présenteraient un nombre important de déficits dans l'activité cérébrale lors de tâches associées aux systèmes à valence négative, à valence positive, aux systèmes de processus sociaux ainsi que les systèmes cognitifs. Par ailleurs, on note que certains systèmes seraient particulièrement associés à certains

types de comportements tels que les systèmes à valence négative à l'agression réactive et les systèmes à valence positive à l'agression proactive et la délinquance non-agressive. Cependant, les petits échantillons et les différences méthodologiques limitent la fiabilité des résultats en en neuroimagerie et, par conséquent, notre compréhension des altérations cérébrales associées aux comportements antisociaux. Par conséquent, il est nécessaire de synthétiser les résultats d'études en neuroimagerie en utilisant une méthodologie méta-analytique (**Objectifs de l'Article 2**). Aussi, on ne sait toujours pas si les altérations rapportées à travers les études sont spécifiques aux individus antisociaux. En effet, tel que mentionné précédemment, on retrouve un chevauchement important entre le TC et d'autres troubles psychiatriques à l'enfance tels que le TDAH et les troubles internalisés, suggérant ainsi que certains déficits neurobiologiques pourraient être partagés entre les différents troubles (**Objectifs de l'Article 3**). Finalement, les individus antisociaux pourraient aussi être caractérisés par des altérations dans l'interaction entre les différents systèmes neurocognitifs. En effet, depuis quelques années, les chercheurs s'intéressent au rôle que peut jouer la connectivité cérébrale dans l'explication de certains troubles psychiatriques.

L'avènement de la connectivité fonctionnelle au repos

L'avancement des connaissances dans le domaine de la neuroimagerie nous permet aujourd'hui de mieux caractériser les divers processus mentaux. Complémentaire aux analyses d'IRMf basées sur l'activation induite par une tâche expérimentale, la connectivité fonctionnelle nous permet d'explorer le degré de dépendance ou de corrélation du signal BOLD entre deux régions ou groupes de voxels (Friston, 2011). La connectivité au repos n'est pas contingente de la performance à une tâche donnée, suscitant ainsi un engouement dans le monde scientifique. Il n'est donc pas surprenant de constater que le nombre d'études portant sur cette technique a explosé depuis plusieurs années et surpasserait même le nombre d'études sur l'activité cérébrale (Friston, 2011). Plus précisément, des chercheurs ont trouvé que les fluctuations du signal BOLD à basse fréquence (généralement entre 0.01 et 0.1 Hertz) des différentes structures cérébrales étaient fortement corrélées lors d'un état de repos (Biswal, Yetkin, Haughton, & Hyde, 1995;

Hampson, Olson, Leung, Skudlarski, & Gore, 2004). On découvrait ainsi la présence de réseaux moteurs (Biswal et al., 1995) et visuels (Hampson et al., 2004). Quelques années plus tard, le nombre de réseaux de connectivité au repos s'estimait entre 5 (De Luca, Beckmann, De Stefano, Matthews, & Smith, 2006) et 10 (Damoiseaux et al., 2006), notamment les réseaux visuels, auditifs, exécutifs, moteurs ainsi que le réseau du mode par défaut (traduction libre de *default mode network* [DMN]). Par exemple, les régions sous-jacentes au DMN ont la particularité d'être fortement corrélées lors de l'état au repos et correspondent aux régions dont l'activité diminue lors de tâches cognitives (par ex. mémoire de travail) afin de laisser place aux réseaux cognitifs (Greicius, Krasnow, Reiss, & Menon, 2003). À ce jour, on compte plus de 6 réseaux robustes et réplicables, notamment le 1) réseau occipital (c.-à-d. le système visuel médian et latéral, impliqué dans la détection et l'interprétation de stimuli), 2) le réseau péricentral (ou somatomoteur [SomMot], impliqué dans la coordination et la préparation lors de tâches motrices) ; 3) le réseau frontopariétal dorsal (ou le réseau attentionnel dorsal [DorsAttn], impliqué dans le contrôle de l'attentionvisuospatiale); 4) le réseau frontopariétal latéral (ou control [CON], impliqué dans le contrôle cognitif); 5) le réseau cingulo-insulaire (ou saillance [SAL], attentionnel ventral [VentAttn], cingulo-operculaire [CingOperc], impliqué dans la détection de stimuli saillants) et finalement 6) le réseau frontopariétal médian (ou DMN, impliqué dans les processus mentaux internes tels que la mentalisation)(Gordon et al., 2016; Schaefer et al., 2018; Uddin, Yeo, & Spreng, 2019; Yeo et al., 2011). Par ailleurs, certains rapportent un réseau limbique, incluant le cortex préfrontal ventromédian et le cortex orbitofrontal, analogue aux réseaux mésolimbiques et mésocorticolimbiques (Gordon et al., 2016; Schaefer et al., 2018; Uddin et al., 2019; Yeo et al., 2011).

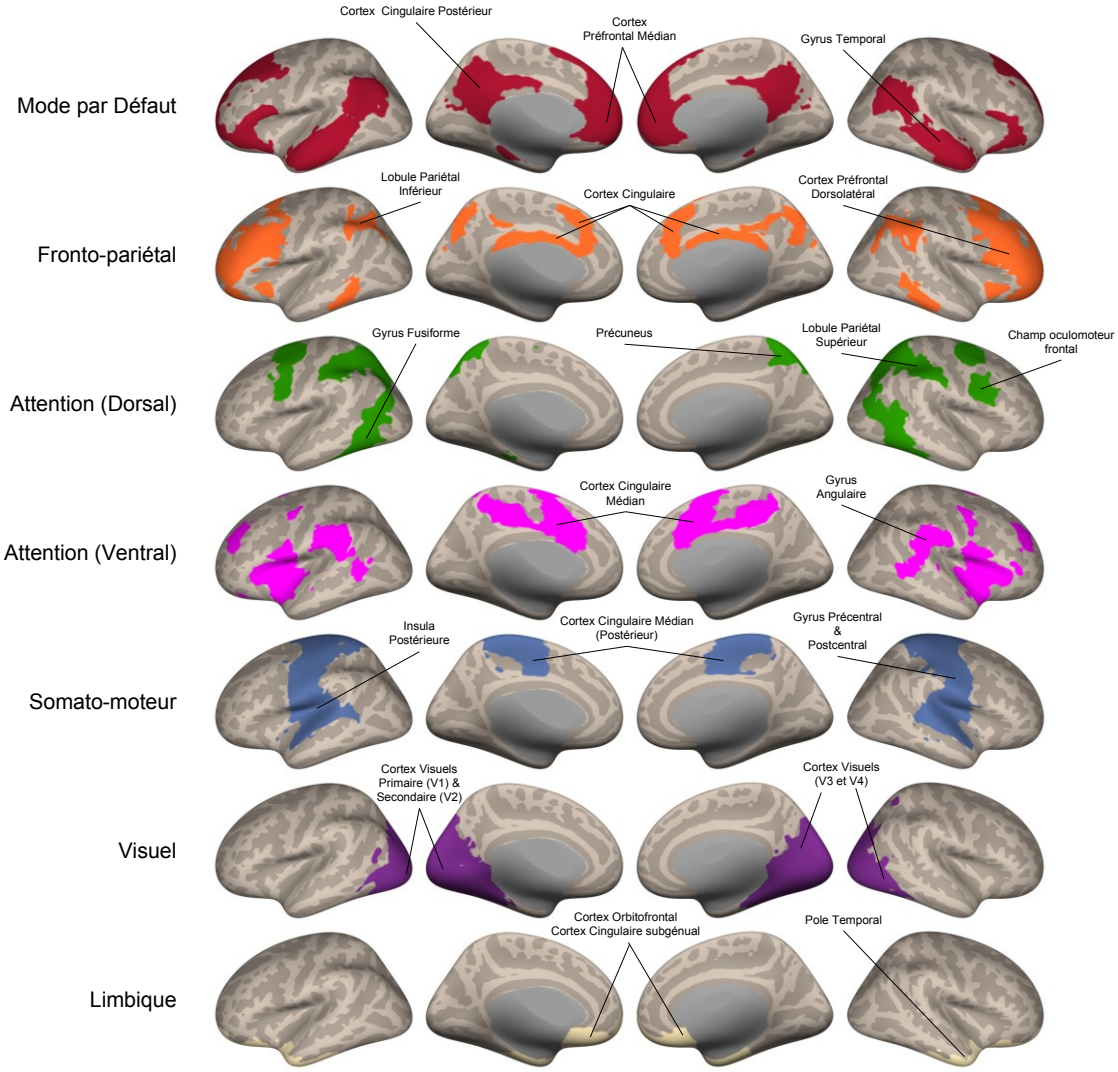

Figure 7. Exemple des réseaux de connectivité cérébrale

Cette figure représente l'atlas de Yeo et collaborateurs (Yeo et al., 2011) montrant 7 principaux réseaux de connectivité cérébrale au repos.

Récemment, l'étude de la connectivité cérébrale au repos a connu un essor considérable dans la littérature sur la délinquance. Par exemple, des chercheurs ont trouvé que la sévérité des comportements antisociaux était associée à la connectivité à l'intérieur du réseau DorsAttn, tandis que les traits d'insensibilité émotionnelle étaient plutôt associés à un dysfonctionnement du DMN (Umbach & Tottenham, 2020). On estime aussi que les comportements antisociaux seraient caractérisés par une dysconnectivité entre l'amygdale et des régions impliquées dans le réseau DMN (Kärgel et al., 2015; Motzkin, Newman, Kiehl, & Koenigs, 2011; Siep et al., 2019; Sukhodolsky et al., 2022), tandis que la colère et l'agressivité seraient principalement caractérisées par des dysconnectivités des régions du DMN avec ceux du SomMot, du VentAttn et du FP (Weathersby, King, Fox, Loret,& Anderson, 2019). À travers la littérature, certains ont trouvé que les comportements antisociaux seraient associés à des dysconnectivité du VentAttn avec le DMN (Pujol et al., 2012) et le réseau FP (Cohn, Pape, et al., 2015a), tandis que d'autres semblent plutôt montrer l'importance de la dysconnectivité entre le réseau DorsAttn et le DMN et VentAttn (Shannon et al., 2011).

Considérant ces résultats, on note que la majorité des altérations dans la connectivité fonctionnelle au repos des individus commettant des gestes délinquants se retrouve dans le réseauDMN, DorsAttn, VentAttn et SomMot. En d'autres mots, les résultats semblent suggérer que la délinquance pourrait être associée à des altérations de l'interaction entre les processus internes, les systèmes sensorimoteurs et attentionnels. Cependant, un nombre considérable d'études utilisent des régions (par ex. l'amygdale) ou des réseaux d'intérêts (par ex. le DMN) ce qui peut augmenterle risque de biais. Ainsi, l'utilisation de méthodes méta-analytiques afin de synthétiser les résultats **(Objectif de l'Article 4**) ainsi que l'étude du connectome (c.-à-d. sans restreindre les analyses à certaines régions ou réseaux) (**Objectif de l'Article 5**) nous permettraient de mieux comprendre les dysconnectivités cérébrales associées aux comportements antisociaux. Bien que la connectivitéfonctionnelle puisse nous aider à mieux comprendre les interactions entre certaines régionscérébrales, il est difficile de conclure que les corrélats neurobiologiques observés sont spécifiquesaux comportements antisociaux. L'aspect corrélationnel de ces études suggère un manque flagrantde connaissances sur l'apport ***causal*** des

altérations cérébrales dans l'émergence de délinquance. Par conséquent, l'étude des lésions cérébrales pourrait nous permettre de mieux comprendre l'émergence de comportements antisociaux.

L'apport des lésions cérébrales dans l'émergence des comportements antisociaux

Depuis plusieurs années, l'intérêt pour le lien entre les traumatismes craniocérébraux et les comportements antisociaux est en constante augmentation. En effet, les comportements antisociaux et les gestes agressifs ont été associés aux lésions cérébrales traumatiques (Bellesi, Barker, Brown, & Valmaggia, 2019; Buckley, Kaye, Stork, Heinze, & Eckner, 2017) ainsi qu'aux commotions cérébrales répétées (par ex., Encéphalopathie traumatique chronique, McKee et al., 2013; Omalu,Hamilton, Kamboh, DeKosky, & Bailes, 2010). Par exemple, on estime qu'environ 1 délinquant sur 2 rapporterait avoir déjà subi un traumatisme crânien (Durand et al., 2017). Les résultats de méta-analyses indiquent un taux de prévalence d'environ 30 % pour les délinquants juvéniles (Farrer, Frost, & Hedges, 2013) et plus de 60 % pour les adultes incarcérés (Shiroma, Ferguson, & Pickelsimer, 2012). Par ailleurs, il est intéressant de constater que les causes principales de ces traumatismes chez les jeunes délinquants sont les batailles ainsi que les chutes, les accidents de laroute ainsi que les blessures reliées au sport (Gordon, Spielman, Hahn-Ketter, & Sy, 2017; Williams, Cordan, Mewse, Tonks, & Burgess, 2010). Une des explications possibles du rôle des traumatismes craniocérébraux dans l'émergence des comportements antisociaux pourrait être l'impulsivité. En effet, les commotions cérébrales dans les sports portent fréquemment atteinte auxlobes frontaux et temporaux (Greenwald, Gwin, Chu, & Crisco, 2008) et celles-ci augmenteraient significativement le risque d'impulsivité (Kerr et al., 2014). Ceci concorderait avec les résultats de recherche clinique montrant l'importance des déficits des fonctions exécutives dans la compréhension des comportements antisociaux. Cependant, un bon nombre d'études est transversal, laissant ainsi la séquence temporelle entre le traumatisme et l'émergence des comportements largement méconnue (Bellesi et al., 2019; Buckley et al., 2017). Par ailleurs, à travers ces études, on ne peut identifier les régions cérébrales spécifiquement atteintes lors de ces traumatismes. L'application de nouvelles techniques de neuroimagerie à

l'étude des lésions cérébrales nous permettrait ainsi de mieux comprendre cette relation complexe.

Localisation des causes cérébrales de la délinquance

Le lien entre les lésions cérébrales et l'émergence des comportements antisociaux date depuis près de 150 ans. En effet, l'un des cas de lésions cérébrales les plus connus du monde médical est celui de Phinéas Gage qui a survécu après avoir été empalé par une barre de fer d'environ 3 centimètres de largeur. Certains chercheurs ont été en mesure de reconstruire la trajectoire de la barre de fer et ont observé que cette dernière avait transpercé le cerveau de Gage allant du cortex préfrontal dorsomédian au cortex orbitofrontal latéral (Damasio, Grabowski, Frank, Galaburda, & Damasio, 1994; Ratiu, Talos, Haker, Lieberman, & Everett, 2004). Suivant cet accident, son médecin traitant nota d'importants changements dans le comportement de son patient. En effet, ceux-ci se rapprochaient des critères diagnostiques d'un trouble de la personnalitéantisociale (APA, 2013) telle qu'un défaut de se conformer aux normes sociales (critère 1), une irresponsabilité et une incapacité à conserver un emploi stable (critère 6), une impulsivité et un défaut de prévoir à l'avance (critère 3) (voir p.14, Harlow, 1869).

Ce cas fascinant demeure encore aujourd'hui l'une des principales bases empiriques afin demieux comprendre les changements comportementaux à la suite de lésions cérébrales, nous rappelant par le fait même la complexité derrière le débat entre l'inné et l'acquis afin d'expliquer le comportement humain. L'absence de comportements agressifs chez Gage malgré la lésion au lobe frontal nous pousse à nous questionner si les lésions à différentes structures cérébrales peuventrésulter en des comportements distincts, notamment en des comportements agressifs et de la délinquance non-agressive. Par exemple, au début du 20^{e} siècle, des chercheurs ont été capables de produire une agressivité prononcée en décérébrant des chats, c'est-à-dire en séparant le néocortex (Bazett & Penfield, 1922; Cannon & Britton, 1925; Woodworth & Sherrington, 1904). La production de cette rage a été répliquée, plus précisément, en sectionnant le néocortex du diencéphale (hypothalamus et thalamus) et du mésencéphale (incluant la substance grise périaqueducale) (Bard, 1928, 1934), supportant ainsi l'importance de l'hypothalamus et de la substance grise périaqueducale dans la réponse agressive.

Il est intéressant de constater que la littérature portant sur les lésions cérébrales chez les humains indique que les régions associées à l'émergence de comportements délinquants seraient principalement l'amygdale et le cortex préfrontal ventromédian. Ces observations concordent aussi avec les récents résultats de recherche démontrant l'importance des systèmes sérotoninergiques et dopaminergiques dans notre compréhension des comportements antisociaux (Ficks & Waldman, 2014; Gard, Dotterer, & Hyde, 2019; Rafiei & Kolla, 2021; Veroude et al., 2016). En effet, ces systèmes sont connus pour intégrer l'amygdale et le cortex préfrontal médian (Haber & Knutson, 2010; Kaller et al., 2017). Bien que Gage ne semblait pas avoir développé de comportements agressifs, certains ont néanmoins suggéré que les lésions du lobe frontal (incluant le cortex préfrontal ventromédian et le cortex orbitofrontal) seraient principalement associées à l'agression (Brower & Price, 2001; Grafman et al., 1996; Séguin, 2004; 2009), tandis que les lésions à l'amygdale seraient plutôt associées aux traits d'insensibilité émotionnelle (Lilienfeld et al., 2018). Or, d'autres ont trouvé que les lésions à l'amygdale sembleraient perturber le système associé à la détection d'une menace (Adolphs et al., 2005; Adolphs, Tranel, Damasio, & Damasio, 1995; Adolphs et al., 1999; Graham, Devinsky, & Labar, 2007; Taubert et al., 2018; Tippett et al., 2018), tandis que les lésions du lobe frontal seraient plutôt associées à des altérations dans la prise de décision lors de la présence d'une potentielle récompense (Hiser & Koenigs, 2018; Koenigs, Kruepke, & Newman, 2010; Mok et al., 2021; Yu, Kan, & Kable, 2020). Par conséquent, l'altération du cortex préfrontal médian et de l'amygdale seraient particulièrement importante dans notre compréhension de l'émergence de la délinquance. Il importe néanmoins de mentionner que les lésions cérébrales ne peuvent expliquer à elles seules l'émergence de comportements antisociaux (Séguin, 2009). En effet, elles font partie d'un réseau complexe impliquant un nombre considérable de régions cérébrales. Par conséquent, la lésion pourrait ainsi perturber la connectivité cérébrale à d'autres régions spécifiques, ce qui pourrait augmenter le risque de comportements antisociaux.

Mieux comprendre l'impact des lésions à l'aide de la connectivité cérébrale

En 2015, des chercheurs ont développé une nouvelle méthode afin de recréer le réseau de

connectivité cérébral associé à un comportement causé par des lésions au cerveau (Fox, 2018; Joutsa, Corp, & Fox, 2022; Siddiqi, Kording, Parvizi, & Fox, 2022). En retraçant manuellement les lésions répertoriées dans les études de cas clinique, des chercheurs ont été en mesure d'évaluer le réseau de connectivité cérébral spécifique à chaque lésion, et ce, même si les lésions associées àun même comportement étaient différentes en termes de grosseurs et d'emplacement. En effet, le chevauchement spatial entre les images de connectivité nous permettrait de trouver un réseau commun entre les différentes lésions pour une problématique donnée (Joutsa, Corp, et al., 2022). Par l'entremise d'étude de cas, on augmente notre certitude face à la séquence temporelle entre le traumatisme et l'émergence des comportements. Outre la proximité causale entre la lésion et le comportement, l'identification d'un réseau commun de connectivité est d'une importance capitale, car elle nous permettrait de trouver de potentielles cibles thérapeutiques pour la stimulation transcrânienne (Joutsa, Shih, et al., 2018).

Aujourd'hui, on dénote plus de 40 symptômes et comportements ayant fait l'objet de la méthode « Lesion Network Mapping » (Fox, 2018; Siddiqi et al., 2022), notamment les hallucinations (Kim et al., 2021), le délire de capgras (Darby, Laganiere, Pascual-Leone, Prasad, & Fox, 2017), les symptômes parkinsoniens (Fasano, Laganiere, Lam, & Fox, 2017; Joutsa, Horn,Hsu, & Fox, 2018), les troubles neurodégénératifs (Darby, Joutsa, & Fox, 2019), l'amnésie (Ferguson et al., 2019), le libre arbitre (Darby, Joutsa, Burke, & Fox, 2018), la prosopagnosie (Cohen et al., 2019), l'évasion mentale (Philippi et al., 2021) et la dépendance (Joutsa, Moussawi,et al., 2022). Récemment, Darby et collaborateurs (Darby, Horn, Cushman, & Fox, 2018) ont étudié le réseau de connectivité cérébral de 17 lésions qui étaient temporellement associées avec les comportements antisociaux. En estimant le réseau de connectivité au repos de chacune des 17 lésions à l'aide de données de 1,000 sujets sains, ces chercheurs ont observé que les lésions étaient principalement connectées aux régions du réseau du DMN et négativement corrélé aux régions dusystème visuel médian et des réseaux attentionnels VentAttn et DorsAttn. Finalement, il a aussi démontré que ce réseau partageait d'importantes similarités avec les régions cérébrales associées àprise de décision morale (Darby, Horn, et al., 2018).

Cette étude contient d'importantes limites qui doivent être discutées afin de permettre

l'avancement des connaissances. Premièrement, la taille de l'échantillon de lésions ainsi que la sélection d'un seuil statistique arbitraire sont vivement critiquées dû à leur impact substantiel sur les résultats (Boes, 2020; Sperber & Dadashi, 2020). En effet, un petit échantillon ainsi qu'un seuil statistique libéral augmentent généralement les erreurs de type II ou faux négatifs, c'est-à-dire de faussement accepter l'hypothèse nulle (Lieberman & Cunningham,2009). Outre les limites sur le plan statistique, certaines inquiétudes doivent être soulevées par rapport à l'interprétabilité des réseaux de connectivité au repos estimé chez les sujets sains. Comme démontré dans les sections précédentes, les individus antisociaux semblent rapportés des déficits neurobiologiques dépendant de certains contextes. En d'autres mots, une lésion à une région particulière (ex. l'amygdale) occasionnerait des symptômes plus importants (ex. comportements agressifs) lorsqu'en présence d'un contexte particulier (ex. frustration) comparativement à un autre (ex. récompense). De manière à mieux étudier les processus mentaux altérés par les lésions cérébrales, l'utilisation de tâches d'imagerie cérébrale devient d'une importance capitale. Par ailleurs, on ne sait toujours pas si les lésions cérébrales causent une réorganisation cérébrale compensatoire (Adolphs, Gläscher, & Tranel, 2018). L'utilisation de données cérébrales chez les sujets sains devient donc problématique. En effet, si les lésions cérébrales causent bel et bien une réorganisation cérébrale, l'utilisation de données chez les personnes présentant des comportements antisociaux pourrait nous permettre d'identifier le réseau de connectivité *causal* à l'émergence deces gestes délinquants (**Objectifs de l'Article 6**).

Problématique et Objectifs de la thèse

Depuis les dernières décennies, un nombre substantiel d'études a mis à l'évidence que la population ayant des comportements délinquants serait hétérogène. En effet, les recherches en psychocriminologie ont effectivement montré que les traits d'insensibilité émotionnelle, la labilitéémotionnelle ainsi que les traits d'impulsivité et des déficits de l'attention seraient tous liés au passage à l'acte. Par ailleurs, ceux-ci seraient associés à différents types de comportements antisociaux tels que l'agression réactive, proactive et la délinquance non agressive. Dans le même ordre d'idées, la psychopathie, le trouble perturbateur de l'humeur, le

TOP, les troubles anxieux etdépressifs ainsi que le TDAH seraient tous autant associés au TC et TPA. Additionnellement, les altérations du fonctionnement cérébral des personnes ayant des comportements antisociaux sont majoritairement perceptibles lors de tâches impliquant les systèmes à valence négative, à valence positive, aux systèmes de sociaux et systèmes cognitifs. Finalement, les études en connectivité cérébrale fonctionnelle au repos semblent montrer des déficits importants dans la connectivité du DMN, des réseaux attentionnels (VentAttn et DorsAttn) et du SomMot. Ces résultats suggèrent donc que les individus antisociaux se distingueraient potentiellement les uns des autres par leurs trajectoires développementales ainsi que par leurs facteurs étiologiques neurobiologiques. Bien qu'une variété de traits ait été associée à l'antisocialité, l'interaction développementale entre ces facteurs psychologiques et son lien avec certains types de comportements demeurent encore méconnus. Dans une perspective étiologique neurobiologique, les recherches portant sur l'étude des corrélats neurobiologiques (c.-à-d. l'activité cérébrale et la connectivité fonctionnelle) contiennent de petits échantillons, utilisent des méthodologies distinctes et incluent un large éventail de tâches distinctes. La synthèse de celles-ci étant difficile, on ne rapporte aucune étude tentant de synthétiser, de manière méta-analytique, les altérations de l'activité cérébrale et de la connectivité fonctionnelle en lien avec les comportements antisociaux. Par ailleurs, on ne sait toujours pas si le TC se distingue réellement des autres troubles psychiatriques chez l'enfant tel que le TDAH et les troubles anxieux et dépressifs, en ce qui a trait aux déficits du fonctionnement cérébral et de la connectivité fonctionnelle. Finalement, bien que certains ont mis en lumière le rôle de lésions cérébrales dans l'émergence de comportements antisociaux, les processus mentaux altérés par les celles-ci demeurent largement méconnus. Par conséquent, les articles suggérés dans la présente thèse ont des objectifs distincts, mais complémentaires afin de mieux comprendre l'hétérogénéité des mécanismes sous-jacents l'émergence de comportements antisociaux.

Objectifs de l'Article 1 (Chapitre 4)

En réaction à la revue de la littérature indiquant le rôle important des traits d'insensibilité

émotionnelle, de la labilité émotionnelle et des traits d'hyperactivité/impulsivité et de l'inattentiondans notre compréhension de l'agir délinquant, l'**Article #1** de cette thèse (c.-à-d. *Multiple Developmental Pathways underlying Conduct Problems: A Multi-Trajectory Framework*) avait pour but de mieux comprendre les rôles que ceux-ci pourraient jouer dans notre compréhension de l'hétérogénéité dans la population antisociale. Par l'entremise d'analyses multitrajectoires développementales, cet article a permis de mieux comprendre l'interaction de trajectoires développementales de ces traits de l'enfance à l'adolescence. D'autre part, cette étude a permis demettre en lumière le rôle que les groupes de trajectoires développementales exerçaient sur le risque de comportements. Plus précisément à savoir si certains groupes de trajectoires développementales étaient associés à différents types de comportements antisociaux, c'est-à-dire l'agression et la délinquance non-agressive.

Objectifs des Articles #2 et #3 (Chapitre 5)

Un second objectif général de cette thèse était de mieux comprendre les déficits dans l'activité cérébrale associés aux comportements antisociaux. Ainsi, deux articles scientifiques sont présentés afin de répondre à cet objectif. En effet, l'**Article #2** (c.-à-d. *Neurofunctional Abnormalities in Antisocial Spectrum: A Meta-analysis of fMRI studies on Five distinct Neurocognitive Research Domains* visait à synthétiser, de manière méta-analytique, l'état des connaissances sur les déficits de l'activité cérébrale des individus ayant des comportements antisociaux. Plus précisément, plusieurs méta-analyses ont été conduites en suivant le cadre théorique du RDoC, c'est-à-dire en séparant les études par domaines de tâches en neuroimagerie tels que le domaine à valence négative, à valence positive, le domaine cognitif et les cognitions sociales. L'**Article #3** (c.-à-d. *Meta-analytical Transdiagnostic Neural Correlates in common Pediatric Psychiatric Disorders*) est présenté afin de mieux comprendre la spécificité et la similarité des altérations du fonctionnement cérébral des jeunes ayant un TC en comparaison avecceux trouvés dans d'autres troubles psychiatriques de l'enfant et l'adolescence, tels que le TDAH et les troubles anxieux et dépressifs. Par l'entremise d'une méta-analyse novatrice et axée sur les données d'imagerie cérébrale, cette étude a permis de mettre en lumière les similitudes

etdifférences entre les altérations dans l'activité cérébrale des troubles psychiatriques chez l'enfant et l'adolescent. Par conséquent, celle-ci nous permet de mieux comprendre hétérogénéité des systèmes neurocognitifs associés à l'antisocialité.

Objectifs des Articles #4 et #5 (Chapitre 6)

Bien qu'une forte majorité des études en neuroimagerie focalise sur l'activité cérébrale des individus antisociaux, ces personnes pourraient bel et bien être aussi caractérisées par des déficitsdans la connectivité cérébrale entre certains systèmes neurocognitifs. Or, les recherches publiées jusqu'à présent comportent de petits échantillons et utilisent des méthodes différentes pour l'étudede la connectivité cérébrale au repos. Afin d'identifier ces altérations, deux études sont présentées. D'une part, l'**Article #4** (c.-à-d. *Impaired attentional and socio-affective networks in subjects withantisocial behaviors: A meta-analysis of resting-state functional connectivity studies*) vise à synthétiser les résultats d'études portant sur la connectivité cérébrale au repos des individus ayantdes comportements antisociaux et ce, par l'entremise d'une méta-analyse en neuroimagerie. Or, les études publiées jusqu'à présent mettent fréquemment l'emphase sur des régions d'intérêts au détriment de la compréhension globale de la connectivité cérébrale au repos. En réponse à ces limites, l'**Article #5** (c.-à-d. *Clarifying the role of Cortico-Cortical and Amygdalo-Cortical braindysconnectivity associated with Conduct Problems*) est présenté. Celui-ci vise principalement à mieux comprendre le lien entre la connectivité cérébrale au repos et la sévérité des comportements antisociaux, en prenant en considération toutes les connexions possibles du cerveau humain (c.-à-d. le connectome). Ce cinquième article vise, par ailleurs, à évaluer si les altérations de la connectivité cérébrale associée aux comportements délinquants sont aussi reliés à d'autres psychopathologies notamment l'irritabilité, les symptômes de TDAH et les traits d'insensibilité émotionnelle.

Objectifs de l'Article #6 (Chapitre 7)

Finalement, l'**Article #6** (c.-à-d. *The origins of evil: from lesions to functional architectureof the antisocial brain*) est présenté afin d'offrir une perspective plutôt causale que corrélationnelle sur

l’émergence de comportements antisociaux. En effet, cette étude vise à mieux comprendre les réseaux de co-activation sous-jacents aux lésions cérébrales qui ont été associés à l’émergence de comportements antisociaux. En d’autres mots, cet article tente de mieux comprendre les systèmesneurobiologiques pouvant être altérés par des lésions cérébrales, augmentant le risque de comportements antisociaux.

CHAPITRE 4 - L'INTÉRACTION DÉVELOPPEMENTALE DE LA DÉLINQUANCE

PREMIER ARTICLE

Multiple Developmental Pathways underlying Conduct Problems: A Multi-Trajectory Framework.

Jules R. Dugré, MSc [1,2] & Stéphane Potvin, PhD [1,2]

[1] Research Center of the Institut Universitaire en Santé Mentale de Montréal, Montreal, Canada[2] Department of psychiatry and addictology, Faculty of medicine, University of Montreal, Montreal, Canada

Déclaration de l'étudiant

Je déclare être l'auteur principal de cet article. J'ai été impliqué dans la conception de l'étude, conduit les analyses statistiques, interprétés les résultats et écrit la première version et la version finale de l'article. Mon directeur de thèse, Stéphane Potvin, conseillé mon travail de recherche, suggéré des corrections et a approuvé la version finale de l'article.

Abstract

In the past decades, there has been an overemphasis of a descriptive/behavioral approach to study conduct disorder. In an equifinal perspective, we aimed to examine the developmental multi-trajectory groups of psychological features (irritability, interpersonal callousness, hyperactivity/impulsivity & depressive-anxiety symptoms) and their associations with conduct problems. In a population-based cohort (n=1309 participants followed from 5 months to 17 years old), latent-class growth analysis was performed for each psychological feature to identify a 2-trajectory model (from ages 6 to 12). Based on parameters estimates of the 2-trajectory models foreach of the four psychological features, a parallel process growth mixture model identified 8 significant developmental patterns that were subsequently compared to typically developing children. Furthermore, we observed that while interpersonal callousness conferred an increased risk for childhood and adolescence conduct problems, its co-occurrence with hyperactivity/impulsivity, irritability and/or depressive-anxiety symptoms heightened the general risk, but also predicted distinct subtypes of conduct problems (i.e. aggressive and rule-breaking behaviors). Thus, by studying complex developmental combinations of psychological features, weobserved qualitatively distinct pathways towards CP. A multi-trajectory framework of psychological features should be considered as a significant step towards unveiling the multiple aetiological pathways leading to conduct disorder and its substantial clinical heterogeneity.

Introduction

Conduct disorder (CD) is generally defined by serious and persistent patterns of behavior that violate the rights of others (i.e., aggressive and rule-breaking behaviors) (APA, 2013). Recently, the DSM-5 introduced the Limited Prosocial Emotions (LPE) as specifier to CD (APA, 2013), given the extensive work on Callous-Unemotional (CU) traits suggesting that the latter feature is associated with a distinct developmental pathway and more severe and persistent antisocial outcomes (Frick et al., 2014b). However, a growing body of evidence highlights the factthat children with conduct problems (CP) are a highly heterogeneous population (Fanti, 2018; Hawes, 2014). This further emphasizes the importance of recognizing early manifestations of psychopathologies that may be developmental roots of heterogeneity underlying CP.

Heterogeneity in clinical presentation

The operationalization of clinical criteria for CD itself may be itself a source of developmental heterogeneity. In fact, CP usually include aggressive behaviors (AGG) (i.e.,Physical fights, cruelty, sexual assault) and non-aggressive delinquent behaviors or rule-breaking behaviors (RB) (ie. Property, theft, violations of rules) (Burt, Donnellan, Iacono, & McGue, 2011;Frick et al., 1993; Loeber & Stouthamer-Loeber, 1998; Tackett, Krueger, Iacono, & McGue, 2005;Tackett, Krueger, Sawyer, & Graetz, 2003; Tremblay, 2000, 2010). However, although the past 25years of research has considered AGG and RB behaviors on a single CP scale (Tremblay, 2010), ithas been argued that these features should not be aggregated together due to substantial differencesin terms of developmental trajectories and risk factors between AGG and RB behaviors (Tremblay,2010; Burt et al., 2011; Fairchild, Van Goozen, Calder, & Goodyer, 2013). While the AGG syndrome seems to be more stable across adolescence and tend to decrease from early childhood to adulthood (Stanger, Achenbach, & Verhulst, 1997; Tremblay et al., 2004), the RB syndrome appears to increase sharply over the course of adolescence (Moffitt, 2003). Moreover, RB is moreoften associated with environmental risk factors (e.g. low parental education, deviant peers, substance use) (Derzon, 2010; Loeber, 1990), while the AGG component of CD seems to be moreclosely related to temperamental characteristics (e.g. emotional arousability, depressive and anxiety

symptoms [DAS], hyperactive/impulsive traits [H/I]) (Dugré, Dumais, Dellazizzo, & Potvin, 2019; Dugré & Potvin, 2020; Garofalo & Velotti, 2017; Loeber, 1990; Lorber, 2004; Rey,Sawyer, & Prior, 2005). Therefore, the distinction between these two core components of CD needsto be taken into account in developmental research in order to tackle the substantial heterogeneity in this population.

Comorbities and Subgroups

The heterogeneity in CD may also be observed through manifestations of transdiagnostic features or comorbid disorders. For instance, early signs may include temper tantrum tendencies, impulsivity, and headstrong, which encompass attention deficit–hyperactivity disorder (ADHD) and oppositional-defiant disorder (ODD) (Blair, Leibenluft, & Pine, 2014). Thus, the heterogeneity in CD is likely to arise from multiple pathways involving distinct features from several psychopathological dimensions. In fact, the most prevalent co-occurring features of CD is CU (in 20 to 50% of cases) (Frick, Ray, Thornton, & Kahn, 2014). However, previous studies have also shown that there are elevated rates of comorbidity between CD and other psychopathologies. More precisely, children with CD are at moderate to high risk for being also diagnosed with anxiety disorders (i.e. Odds Ratios [OR] 95% Confidence Interval [CI]=1.3-5.9), mood disorders (OR 95%CI=2.1-50.5), ADHD (ADHD; OR 95%CI=3.7-121.9), and ODD (OR 95% CI=5.3-17.3) (Angold et al., 1999; Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; P. J. Frick, J. V. Ray, L. C. Thornton, & R. E. Kahn, 2014; Nock et al., 2006b). This further suggests that the heterogeneity inCD may arise from comorbities involving four main psychopathological dimensions (i.e., CU traits,anxiety and mood disorders, ADHD and ODD) (Blair, Leibenluft, & Pine, 2014; Fanti, 2018).

In the past decades, two main developmental pathways underlying the heterogeneity of CDwere identified: the CD+CU and the CD+Internalizing subtypes (Frick, Ray, Thornton, & Kahn, 2014; Fanti, 2018; Herpers, Rommelse, Bons, Buitelaar, & Scheepers, 2012). While the former isthe most prevalent subgroup and is characterized by more severe and persistent antisocial outcomes and impairment in response/recognition of cues to fear (Frick, Ray, Thornton, & Kahn, 2014), the CD+Internalizing subgroup is associated with more reactive aggression and antisocial/delinquent behaviors as well as physiological over-arousal in negative situations (e.g. threat-related

situations), compared to the CD-only group (Fanti, 2018; Fanti & Henrich, 2010; Polier, Vloet, Herpertz-Dahlmann, Laurens, & Hodgins, 2012). However, to further complicate matters, these two pathways are not mutually exclusive. In fact, compared to children with IC-only (i.e. First variant of psychopathy), those characterized by the co-occurrence of interpersonal callousness (i.e.including affective and interpersonal facets of psychopathic traits [IC]) and anxiety (IC+ANX, i.e.secondary variant of psychopathy) showed also ADHD symptoms, DAS, irritability and anger problems and were more likely to exhibit drug use, risky behaviors and suicidal ideation and attempts (Cecil, McCrory, Barker, Guiney, & Viding, 2018; Fanti, Demetriou, & Kimonis, 2013; Goulter, Kimonis, Hawes, Stepp, & Hipwell, 2017; Huang, Fan, Lin, & Wang, 2019; Kahn et al., 2013; Kimonis, Frick, Cauffman, Goldweber, & Skeem, 2012; Kimonis, Skeem, Cauffman, & Dmitrieva, 2011; Meehan, Maughan, Cecil, & Barker, 2017; Vaughn, Edens, Howard, & Smith, 2009). Furthermore, although some evidence suggest that IC+ANX may exhibit higher levels of AGG behaviors (Kahn et al., 2013; Kimonis et al., 2011) and CD (Goulter et al., 2017; Huang et al., 2019; Meehan et al., 2017), others did not find significant differences between both subgroups (Cecil et al., 2018).

While these subgroups of children at risk for CD have been relatively well-defined in literature, more complex combinations of psychopathological features (resulting in more homogeneous groups of children at risk for CP) have yet to be elucidated. Considering the complexity of the heterogeneity in CD population, more advanced methodologies such as longitudinal person-centered approaches may help disentangle the developmental co-occurrence of psychological factors leading to CD.

Developmental Joint- & Multi-Trajectory

Recent advances in statistical analyses on longitudinal data allows to examinedevelopmental joint- and multi-trajectories within a person-centered approach. In fact, multi- trajectory analysis (Nagin, Jones, Passos, & Tremblay, 2018) or Parallel processes growth mixturemodel (Muthén & Muthén, 2009) are multivariate extensions of univariate growth mixture modelling (i.e. identification of trajectories for a single indicator of interest), permitting to identify the interrelationship of multiple processes over time (Muthén & Muthén, 2009; Nagin et al., 2018;

Nagin & NAGIN, 2005). For instance, this technique enables to study the substantial co-occurrence of child psychological factors in a developmental manner. Past longitudinal research has thus demonstrated that the developmental joint contribution of CU and CP (Fontaine, McCrory, M. Boivin, Moffitt, & Viding, 2011), DAS and irritability/anger proneness (Dugré, Dumais, Dellazizzo, & Potvin, 2019), internalizing and externalizing traits (Fanti & Henrich, 2010) and hyperactivity/Impulsivity symptoms (H/I) and physical aggression (Fontaine et al., 2008) significantly increased the risk of developing a variety of CP. While these studies observed statistical associations between psychological features (e.g. internalizing traits, IC, H/I symptoms) and behaviors (e.g. physical aggression, CP, externalizing behaviors), there is still very limited literature about how developmental combinations of psychological factors (i.e. IC, H/I, ANX, Irritability) – *independently from CD* – may interact withrisk for developing CP symptoms. In other words, is identifying homogeneous developmental combinations of psychological factors sufficient to predict emergence of CP.

To our knowledge, three longitudinal studies has attempted to examine developmental multi-trajectory profiles (i.e. multi-trajectory based on more than 2 indicators of interest) in relationwith CP. Such method may help address the heterogeneity in CD by studying more complex developmental combination of psychological features. For instance, in a population-based cohort, researchers observed that children with H/I only and H/I+IC traits (i.e. low prosocial behaviors and fearlessness) were significantly associated with CD in adolescence even after controlling for earlyantisocial problems (Côté, Tremblay, Nagin, Zoccolillo, & Vitaro, 2002). In another study of 622children from 3 to 7 years old, Ezpeleta, Granero, de la Osa, & Domènech, (2017) found that the groups characterized by co-occurrence of CU+ODD showed higher levels of CP and AGGbehaviors than typically developing children at 7 years old. Finally, based on 3569 children assessed from 5 to 15 years old, we have observed that children following a developmental trajectory characterized by H/I+ Irritable and H/I+Irritable+ANX were respectively 6.47 & 7.68 times more likely than their typically developing counterparts to also exhibit childhood aggression (Dugré & Potvin, 2020). These studies show an additive effect of psychological features on risk for CP, that is, the more problematic psychological features, the greater risk children are for exhibiting CP. However, while these studies showed promising results

for clarifying the heterogeneity underlying CD, to our knowledge, no study has assessed the developmental profilesbased on the four core components that are related to CD (i.e. IC, H/I, ANX, Irritability).Furthermore, considering the heterogeneous clinical presentation of CD (i.e. AGG and RBsyndromes), there is very limited studies exploring the associations between multi-trajectory of psychological patterns and distinct CP symptoms. Overcoming these limitations is therefore crucialfor disentangling the clinical heterogeneous developmental pathways of CD and identifying groupsof children at most risk for CP and its specific syndromes

In the current study, we thus aimed to 1) identify developmental combinations of psychological factors of interest (i.e. H/I, DAS, irritability and IC) from 6 to 12 years old, and 2) assess their longitudinal associations with childhood CP (i.e. AGG and RB syndrome) and adolescence CP (i.e. 15 and 17 years old). Based on previous literature, we argue that multiple combinations of these psychological factors will be differently related to CP. More precisely, multi-trajectory groups characterized by high DAS and Irritability (i.e. more internalizing traits) would be more likely to exhibit AGG behaviors than their counterparts, while those with problematic levels of H/I (i.e. more externalizing traits) would be associated with more RB behaviors. Furthermore, considering the role of IC in CD (Frick et al., 2014), the observed developmental childhood profiles characterized by those with high-IC will predict both AGG and RB in childhood, and general CP in adolescence even after controlling for early CP. Finally, we argued that an additive effect wouldbe observed, that is, children following more complex multi-trajectory (i.e. problematic levels on 3 & 4 psychological factors) would predict CP, compared to those following more simpler ones.

Method

Participants

Participants were drawn from the widely known Québec Longitudinal Study of Child Development (QLSCD) (Orri et al., 2018; Pagani, Fitzpatrick, Barnett, & Dubow, 2010; Simard, Nielsen, Tremblay, Boivin, & Montplaisir, 2008). Briefly, the QLSCD consists of a representative sample of 2120 infants born in the province of Quebec (Canada) in 1997-1998 whomwere followed

up to 17 years of age. More detailed information concerning the methodology behind data collection can be found elsewhere (Jetté & Des Groseilliers, 2000). Data was collectedevery year during childhood (5 months to 8 years of age) and biannually during adolescence (from10 to 17 years of age) by the Québec Statistics Institute. The QLSCD protocol was approved by the Québec Statistics Institute and the St-Justine Hospital Research Center ethics committees. Allprimary caregivers provided written informed consent and assented for child participation at each interview. Participants were included if the school teachers completed assessments at least at 2 time points, in order to adequately estimate the intercept and a linear slope in trajectory analyses, as similarly done in other researches on developmental trajectories (Dugré et al., 2019; Dugré & Potvin, 2020). Of the 2120 infants, school teachers from 1309 participants completed the behaviorquestionnaire at least 2 time periods when children were 6 (Y6), 8 (Y8), 10 (Y10) and/or 12 (Y12)years of age. While deletion may reduce the representativeness of the sample and/or reduce statistical power, subsequent analyses on excluded participants revealed small differences with theoriginal sample in terms of children's sex (effect size= -0.11), socioeconomic status (effect size= -0.19) and children's verbal IQ (effect size -0.09) (M. Orri et al., 2018).

Measures

Teacher ratings of child psychological factors

School teachers rated child behaviors at Y6, Y8, Y10 and Y12 years. The Behavior Questionnaire is a well-validated questionnaire that was created in 1994, for the Canadian NationalLongitudinal Study of Children and Youth (Canada, 2007), and includes items from the Child Behavior Checklist (Achenbach & Edelbrock, 1983) and the Preschool Behavior Questionnaire (Behar, 1977). Each item was assessed relatively to the past 6 months and rated on a 3-point Likertscale (0=Never to 2 =Often occurring).

H/I symptoms were assessed using 6 items (e.g. [CHILD] "*could not sit still, was restless and hyperactive*" and "*was impulsive, acted without thinking*"). Irritability symptoms were assessed with 4 items (e.g. "*had temper tantrums or hot temper" and "reacted in an aggressive manner when teased*") (M. Orri et al., 2018). IC symptoms were assessed with 8 items that included

affective and interpersonal callousness (Gorin et al., 2019) (e.g. "*was unconcerned about the feelings of others*" and "*didn't seem to feel guilty after misbehaving*"). DAS symptoms were assessed with 9 items based on past literature (M. Orri et al., 2018) (e.g. "*was too fearful or anxious*", "*seemed to be unhappy or sad*". Cronbach alphas showed excellent internal consistenciesfor all psychological factor (α values ranging between .85 to .91).

Teacher ratings of child conduct problems

School teachers also rated child CP based on 8 items at Y6, Y8, Y10 and Y12 from the Behavior Questionnaire (see above): including a total score of AGG (3 items, e.g. "*physically attacked people*" and "*hit, bit or kicked other children*") and RB behaviors (5 items, e.g. "*stole things*" and "*damaged or broke things belonging to others*"). Cronbach alphas showed good to excellent internal consistencies for CP total score, AGG and RB behaviors (α values ranging between .76 to .89).

Self-reported Adolescent Conduct Problems

Adolescence CP were assessed using 28 self-reported items derived from the Mental Health and Social Inadaptation Assessment for Adolescents (MIA), spanning DSM-V CD criteria (S. M. Côté et al., 2017). Each item was answered on a 3-point Likert-scale (0=Never True to 2=AlwaysTrue). Cronbach alpha's showed good internal consistency at 15 and 17 years of age (i.e. .87 & .94, respectively).

Statistical procedure

Multi-Trajectory Modelling

Latent class growth analysis (LCGA) was used to identify classes of individuals who have a homogeneous developmental trajectory (e.g. normative *versus* problematic) from childhood to adolescence (Muthén & Muthén, 2000). Briefly, LCGA is a specific type of growth mixture model (GMM) which assumes that all individual growth trajectories within a class are homogeneous in order to identify distinct classes (Jung & Wickrama, 2008). Thus, LCGA does not allow between-subject variability within a class and thus fewer parameters need to be estimated (compared to

GMMs). Since the complexity of the statistical models to be estimated as well as the limited sample size in this study, the LCGA was preferred over the GMMs to avoid overfitting (van der Nest, Passos, Candel, & van Breukelen, 2020).

The current study first aimed to use a data-driven technique to distinguish between children following an atypical developmental trajectory from those typically developing (TD) on each psychological factor. Consequently, we estimated a 2-trajectory LCGA model for each of the 4 psychological factors, separately. The goodness of fit was assessed based on several criteria (Nylund, Asparouhov, & Muthén, 2007), such as the smallest class size (>1%)(Jung & Wickrama, 2008), the Vuong-Lo-Mendell-Rubin Likelihood Ratio Test (VLMR-LRT) as well as the Lo- Mendell-Rubin Adjusted Likelihood Ratio Test (LMR-LRT; $p > 0.05$)(Lo, Mendell, & Rubin, 2001; Vuong, 1989), the entropy (Closest to 1.0)(Celeux & Soromenho, 1996), the average posterior class probabilities (AvePP>0.70) and the odds of correct classification (OCC>5.0)(Nagin& NAGIN, 2005).

Second, the resulting parameters (e.g. number of classes, growth factors) were entered in a parallel process growth mixture model (GMM)(Muthén & Muthén, 2009). Briefly, the latter model estimates the probability of individuals being in a class for each of the processes resulting in a cross-classification of the sets of growth mixtures. Children would thus fall into one of 16 multi-trajectory classes (2^4) based on the maximum posterior class probability. The resulting multi-trajectories were then kept in further statistical analyses if: A) the AvePP≥.70 and the OCC≥5.0, indicating a good latent class separation and high assignment accuracy and B) The multi-trajectory class comprised a total count larger than 1% of the total sample size. For both LCGA and parallel process analyses, we used a full-information maximum likelihood (FIML) estimator with robust standard errors (MLR) under the missing at random assumption, used in Mplus statistical software (Muthén & Muthén, 1998–2011).

Associations between multi-trajectories and childhood conduct problems

Group memberships were then extracted as a categorical variable to further explore the link between groups and longitudinal levels for childhood CP. Generalized Estimating Equations (GEE) (Liang & Zeger, 1986) model with a negative binomial distribution and an unstructured

working correlation matrix was used to examine the longitudinal associations between multi-trajectory classes group membership and teachers ratings of child CP at Y6, Y8, Y10 and Y12. Since Parallel Process GMM assumes that trajectory-group membership is homogeneous across time (i.e. one cannot switch trajectory over time), multi-trajectory group membership was enteredas a fixed effect variable. Children's sex and parental socioeconomic status were included as covariates. The multi-trajectory model having the lowest levels of symptoms was used as the reference group. As post hoc testing, we analyzed the specific associations between multi-trajectories and AGG and RB behaviors separately, since both behaviors are known to have distinct developmental courses (Tremblay, 2010).

Prospective predictions of conduct problems in adolescence from childhood multi-trajectories

Longitudinal predictions of self-reported CP in adolescence (Y15 and Y17) from childhoodmulti-trajectories were also tested using GEE models with a negative binomial distribution and an unstructured working correlation matrix. Estimates were first provided adjusting for children's sex and parental socioeconomic status. Moreover, to examine whether the childhood multi-trajectoriespredicted adolescent CP over and above early CP (Cote et al., 2002), we adjusted the model's estimates for teachers' ratings of CP at Y6 as an indicator of an early onset of antisocial behaviors.

Results

Multi-trajectory modelling

First, 2-trajectory LCGA models were estimated for each of the psychological factors, independently. Models showed good to excellent fit indices for DAS (Entropy=.76, smallest class size=20.88%, smallest AvePP=.87, smallest OCC=5.01, VLMR=p< 0.0001, LMR- LRT=p<0.0001), H/I symptoms (Entropy=.90, smallest class size=18.44%, smallest AvePP=.93, smallest OCC=11.67, VLMR=p<0.0001, LMR-LRT=p< 0.0001), irritability (Entropy=.93, smallest class size=13.43%, smallest AvePP=.94, smallest OCC=10.90, VLMR=p< 0.05, LMR- LRT=p< 0.05) and IC traits

(Entropy=.91, smallest class size=15.95%, smallest AvePP=.92, smallest OCC=13.37, VLMR=p<0.0001, LMR-LRT=p < 0.0001).

Second, by using the parameters of each of the 2-trajectory LCGA models, parallel processGMM was estimated in order to extract every possible developmental combination of psychological factors. Therefore, the Parallel process GMM, resulting in 16 possible combinationsof multi-trajectories (2^4), showed an excellent classification quality (entropy =.89). From these combinations, 9 multi-trajectory groups met the criteria for high quality trajectory classes (see Method Section) (Figure 1): **G0 - Typically Developing (TD)** (67.23% of the total sample, 62.0%of girls); **G1 – DAS only** (7.79%, 50.0%), **G2 – IC only** (1.83%, 41.7%); **G3 – H/I only** (2.6%, 23.5%); **G4 – IC & H/I** (2.14%, 21.4%), **G5 – DAS & H/I** (3.29%, 20.9%), **G6 – Irritable & IC** (1.15%, 60.0%) and **G7 – Irritable, IC & H/I** (2.83%, 29.7%) and **G8 – Irritable, IC, H/I & DAS** (8.10%, 26.4%). Moreover, these 9 groups showed minimal AvePP value higher than 0.70 aswell as OCC higher than 5 (Nagin, 2005), suggesting good to excellent within-class cohesion (seeSupplementary Table 1). The resulting 7 groups of multi-trajectories that did not meet the selection criteria constituted only 3.04% of the total sample was excluded from subsequent analyses (see Supplementary Table 1).

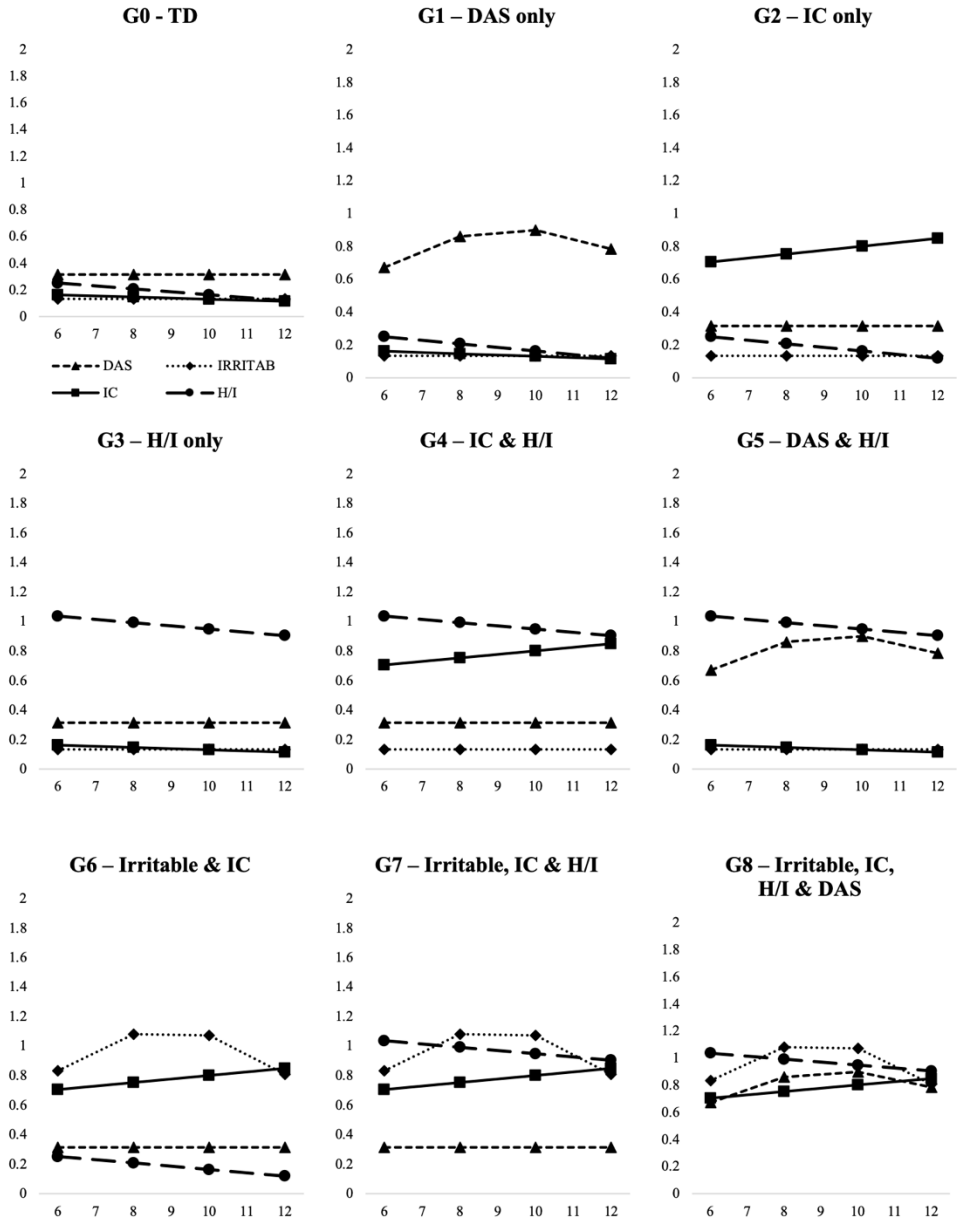

Figure 1. Multi-trajectory classes defined by developmental trajectories of depressive and anxiety symptoms (DAS), irritability, hyperactivity/impulsivity (H/I), and Interpersonal Callousness (IC), at 6, 8, 10, and 12 years of age. TD = Typically Developing. **G0** : AvePP = 0.94 & OCC = 7.92; **G1** : AvePP = 0.79 & OCC = 43.99; **G2** : AvePP = 0.74 &OCC = 150.08; **G3** : AvePP = 0.70 & OCC = 85.46; **G4** : AvePP = 0.78 & OCC = 164.12; **G5** : AvePP = 0.72 & OCC = 76.85; **G6** : AvePP = 0.76 & OCC = 279.25; **G7** : AvePP = 0.73 & OCC = 90.62; **G8** : AvePP = 0.85 & OCC = 66.38.

Associations between multi-trajectories and childhood conduct problems

Results from the GEE models suggest that children in every multi-trajectory class were significantly more likely to exhibit CP in childhood in comparison to their counterparts in the TD group (Table 1). In fact, G1 – DAS only class showed a significant association with CP, whilst being weaker (OR=1.63, 95% CI:1.28-2.09, p< 0.001). G2 – IC only showed a 4.90-fold association with CP. Moreover, G4 – IC and H/I conferred a risk of 5.15 times higher to display CP than the TD group, with a slight tendency to exhibit more RB behaviors than AGG behaviors (OR=7.2 & 5.8, respectively) (See Figure 2). Finally, compared to TD, G6 – Irritable and IC, G7 – Irritable, IC & H/I, G8 – Irritable, IC, H/I and DAS were considered the groups at greatest risk of exhibiting CP during childhood (OR=8.71, 9.30 & 9.62, respectively). Post-hoc analyses on specific CP suggested that while G6, G7 and G8 were significantly more likely to display AGG behaviors than other groups, G4 – IC and H/I, G7 and G8 groups were at higher risk for exhibiting RB behaviors, compared to other groups, but did not differ between each other (See Figure 2 & Supplementary Material).

Table 1. Associations between multi-trajectories and childhood conduct problems (n = 1309).

Group	Psychological patterns				Statistics	
	DAS	Irritability	IC	H/I	OR (95% CI)[A]	p-value
G0	-	-	-	-	-[B]	-[B]
G1	+	-	-	-	1.63 (1.28-2.09)	<0.001
G2	-	-	+	-	4.90 (3.60-6.68)	<0.001
G3	-	-	-	+	3.72 (2.72-5.09)	<0.001
G4	-	-	+	+	5.15 (3.90-6.80)	<0.001
G5	+	-	-	+	3.53 (2.78-4.49)	<0.001
G6	-	+	+	-	8.71 (6.51-11.65)	<0.001
G7	-	+	+	+	9.30 (7.50-11.52)	<0.001
G8	+	+	+	+	9.62 (8.23-11.25)	<0.001

Note. DAS = Depressive and Anxiety Symptoms; IC = Interpersonal Callousness; H/I = Hyperactivity/impulsivity symptoms. [A] Adjusted for the effects of time, children's sex and socioeconomic status; [B] G0 was used as the reference group.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

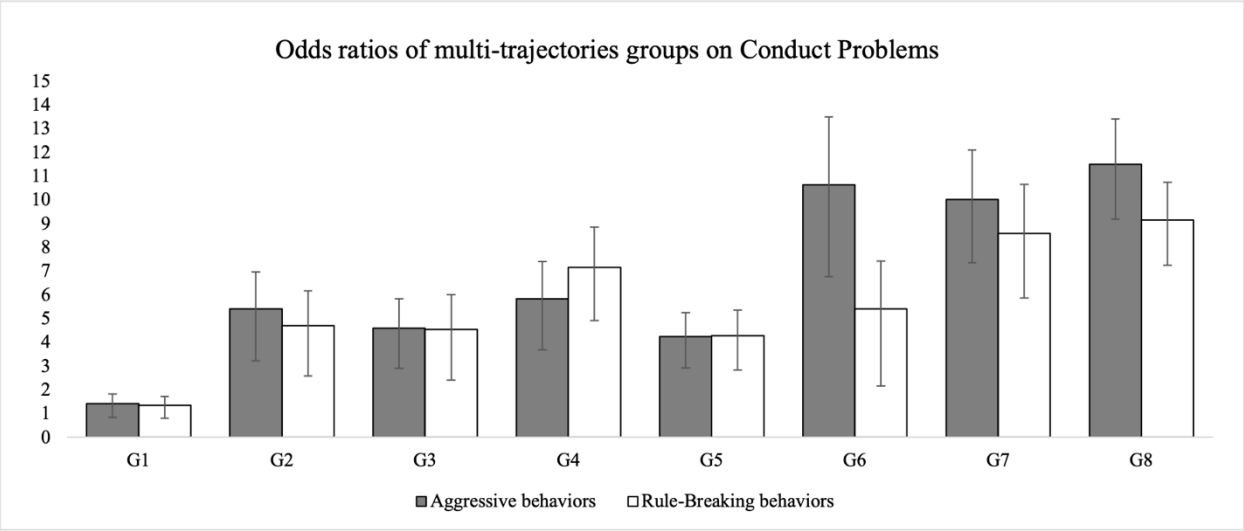

Figure 2. Estimates (Odds ratios) are adjusted for the effects of time, child's sex and socioeconomic status. Error Bars represent 95% confidence interval. **G0 = Typically Developing** (Reference Group); **G1 = Anxious-Depressive only** (Aggressive behaviors: OR = 1.42 & Rule-Breaking Behaviors: OR = 1.34), **G2 = Interpersonal Callousness only** (5.41 & 4.71, respectively); **G3 = Hyperactivity/Impulsivity only** (4.59 & 4.55, respectively); **G4 = Interpersonal Callousness & Hyperactivity/Impulsivity** (5.83 & 7.15, respectively), **G5 = Anxious-Depressive and Hyperactivity/Impulsivity** (4.24 & 4.27, respectively), **G6 = Irritable & Interpersonal Callousness** (10.64 & 5.40, respectively) and **G7 = Irritable, Interpersonal Callousness & Hyperactivity/Impulsivity** (10.01 & 8.59, respectively) and **G8 = Irritable, Interpersonal Callousness, Hyperactivity/Impulsivity & Anxious-Depressive symptoms** (11.49 & 9.15, respectively). Post-Hoc Analyses for Aggressive Behaviors (at $p<0.005$): G8 > G1, G2, G3, G4, G5, G6; G7 > G1, G2, G3, G4, G5; G6 > G1, G2, G3, G5; G5 > G1; G4 > G1; G3 > G1; G2 > G1. Post-Hoc Analyses for Rule-Breaking behaviors (at $p<0.005$): G8 > G1, G2, G3, G5, G6; G7 > G1, G2, G3, G5, G6; G6 > G1; G5 > G1; G4 > G1, G2, G3, G5, G6; G3 > G1; G2 > G1.

Prospective predictions of conduct problems in adolescence from childhood multi-trajectories

GEE models were conducted to evaluate if the multi-trajectory groups predicted adolescence CP longitudinally (i.e. at Y15 and Y17). Of the 8 groups compared to the TD, only 4 remained statistically significant after adjusting for early-onset CP, children's sex and their socioeconomic status: G2 – IC Only (OR=1.92, 95% CI:1.41-2.16, p<0.001), G4 – IC and H/I (OR=1.41, 95% CI:1.04-1.90, p<0.001), G6 – Irritable and IC (OR=1.48, 95% CI: 1.01-2.16, p<0.001), G8 – Irritable, IC, H/I and DAS (OR 1.40, 95% CI: 1.12-1.74, p<0.001).

Table 2. Prospective prediction of conduct problems in adolescence from childhood multi-trajectories (n=1309)

Group	Psychological patterns				Adjusted OR (95% CI)	
	DAS	Irritability	IC	H/I	Model 1	Model 2
G0	-	-	-	-	-[A]	-[A]
G1	+	-	-	-	0.95 (.77-1.16)	1.01 (.77-1.32)
G2	-	-	+	-	1.75 (1.35-2.26)***	1.92 (1.41-2.61)***
G3	-	-	-	+	1.31 (.98-1.77)	1.33 (.93-1.91)
G4	-	-	+	+	1.75 (1.24-2.47)**	1.41 (1.04-1.90)*
G5	+	-	-	+	0.98 (.77-1.24)	0.98 (.74-1.30)
G6	-	+	+	-	1.38 (1.02-1.87)*	1.48 (1.01-2.16)*
G7	-	+	+	+	1.50 (1.15-1.96)**	1.37 (.96-1.96)
G8	+	+	+	+	1.37 (1.17-1.60)***	1.40 (1.12-1.74)**

Note. DAS = Depressive and Anxiety Symptoms; IC = Interpersonal Callousness; H/I = Hyperactivity/impulsivity symptoms [A] = Group used as reference. Model 1 = adjusted for the effects of time, children's sex & parental socioeconomic status; Model 2 = adjusted for the effects of time, children's sex, parental socioeconomic status and conduct problems at 6 years old.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Discussion

In the current study, we aimed to disentangle the heterogeneity in CD population by using a longitudinal person-centered approach in relation with specific subtypes of behaviors underlying CP. To our knowledge, this is the most extensive population-based longitudinal study to examine the developmental combinations of 4 psychological factors that are known to be involved in childhood CP, namely irritability, IC, DAS and H/I symptoms. We observed that children from all multi-trajectory classes were significantly more likely to also exhibit CP in childhood when compared to their *typically developing* counterparts, with ORs ranging between 1.63 and 9.62. Forinstance, being part of a multi-trajectory characterized by *at least* a combination of IC and irritability, with or without H/I and/or DAS, increased drastically the risk for exhibiting CP during childhood. After adjustments for several important factors including early CP, four childhood multi-trajectory groups (those with IC) prospectively predicted CP in adolescence. These results further demonstrate the importance of studying the developmental co-occurrence of these four factors in relationship with CP.

Investigating the relationship between multi-trajectory and subtypes of CP in childhood has revealed significant results. Following past research suggesting a non-negligible overlap in etiological influences between AGG and RB behaviors (S. Burt, 2013), we observed that our multi-trajectory classes were, in general, at somewhat similar risk for exhibiting AGG and RB behaviors, compared to TD. Our results suggested that the co-occurrence of IC and H/I dimensions was mostly associated with an increased risk for RB behaviors, while the co-occurrence of IC and irritability heightened the likelihood of AGG behaviors. First, these results are in line with past researches suggesting that elevated IC are associated with increased risk for more severe general CP (Frick et al., 2014). More precisely, our findings indicated that an additive effect of psychological factors (i.e. Irritability and H/I) may direct children with high IC towards more precise antisocial behaviors (i.e. AGG and RB). For instance, it is known that risky behaviors in children with ADHD could arise from disrupted ability to suppress prepotent behavior (i.e. response inhibition) and/or impaired decision making (e.g. *immediate over delayed rewards*) (Sonuga-Barke, Cortese, Fairchild, & Stringaris, 2016). While it was postulated that H/I symptoms increase the risk for CPin children

already at risk (e.g. those with high IC) (Donald R Lynam, 1996), their co-occurrence with IC traits (e.g. callousness, lack of guilt, manipulative) may enhance the risk for goal-oriented or instrumental behaviors such as RB. As for irritability, this psychological feature may often results in AGG behaviors through aberrant threat-detection and/or frustrative non-reward mechanisms (Argyris Stringaris, Vidal-Ribas, Brotman, & Leibenluft, 2018). Thus, in combinationwith IC traits (e.g. lack of empathy, lack of guilt) irritability could yield AGG behaviors in order to relieve intense negative emotional arousal. Hence, we showed that complex developmental combinations of multiple psychological factors were associated with specific CP subtypes.

Interestingly, although all multi-trajectory classes were significantly associated with childhood CP, only those characterized by IC still remained statistically significant predictor of adolescence CP. As commonly observed in literature on childhood IC, this psychological factor isa crucial predictor of later antisocial behaviors (P. J. Frick et al., 2014; P. J. Frick & S. F. White, 2008). More importantly, evidence has further highlighted the stability of IC traits from childhood to adolescence, above and beyond puberty (Burke, Loeber, & Lahey, 2007; Donald R Lynam et al., 2009; Salekin, Rosenbaum, & Lee, 2008). As for the other psychological factors, their influencemust be considered in light of the strong effects of puberty onset (mean age of 12) on child development. Indeed, past results indicated that from childhood to late-adolescence, children would usually show a moderate decreases in H/I symptoms (Döpfner et al., 2015; Faraone, Biederman, & Mick, 2006; Larsson, Dilshad, Lichtenstein, & Barker, 2011; Nagin& Tremblay, 1999) and a significant increases in DAS (Angold & Costello, 2006; Angold, Costello, & Worthman, 1998; Bongers, Koot, Van der Ende, & Verhulst, 2003). Thus, these opposite shifts in H/I and DAS may likely alter their influence on the propensity towards CP in adolescence, while IC would remain an important and stable predictor of CP throughout adolescence. Researches between DAS and CP have yielded in inconsistent findings (Bubier & Drabick, 2009; Cunningham & Ollendick, 2010; Wolff & Ollendick, 2006). Furthermore, some studies on developmental trajectories have suggested that DAS alone may not sufficient for predicting risky behaviors including CP (Dugré & Potvin, 2020; Ezpeleta et al., 2017; Fanti & Henrich, 2010). Instead, these studies have suggested that the risk for CP would be significantly enhanced through an additive effect of DAS with other factors (e.g. irritability, H/I and IC), similarly to what we observed in the current study.

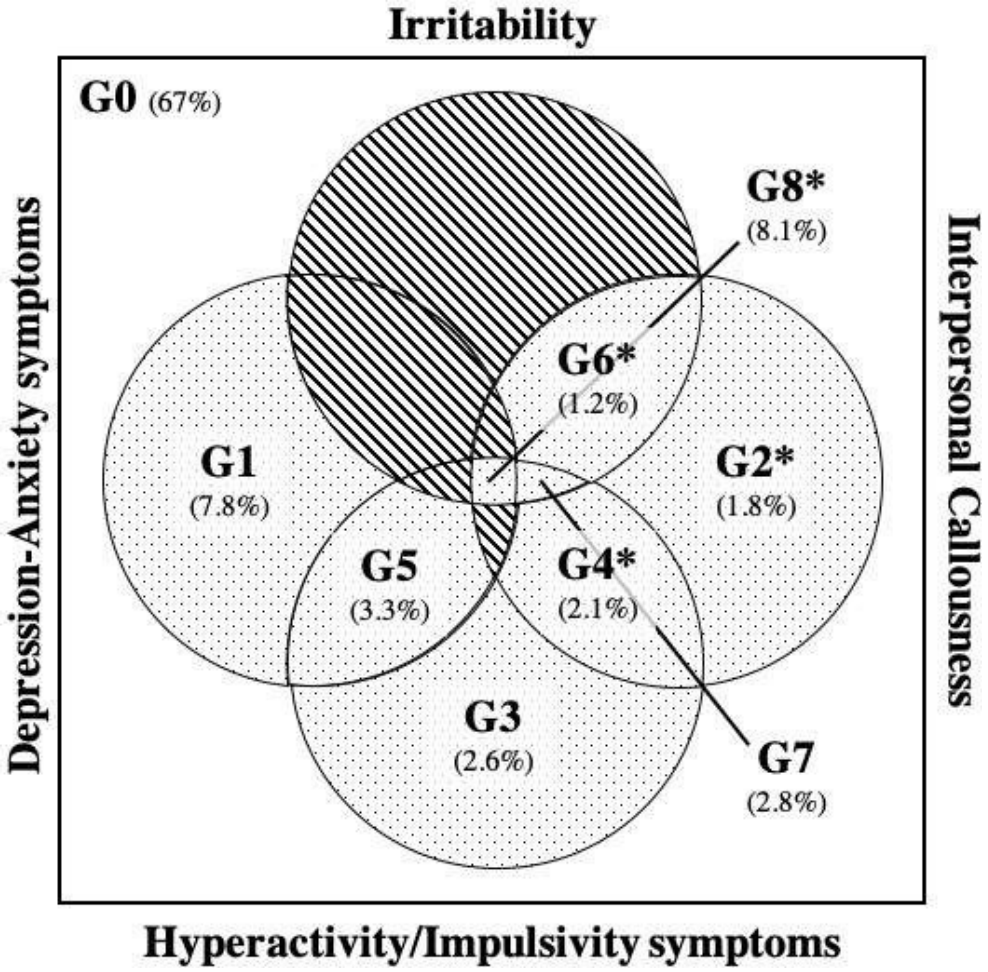

Figure 3. Overlaps between the four psychological features observed in the multi-trajectory analysis. **G0** = Typically Developing; **G1** = Anxious-Depressive only, **G2** = Interpersonal Callousness only; **G3** = Hyperactivity/Impulsivity only; **G4** = Interpersonal Callousness & Hyperactivity/Impulsivity, **G5** = Anxious-Depressive and Hyperactivity/Impulsivity, **G6** = Irritable & Interpersonal Callousness and **G7** = Irritable, Interpersonal Callousness &Hyperactivity/Impulsivity and **G8** = Irritable, Interpersonal Callousness, Hyperactivity/Impulsivity& Anxious-Depressive symptoms. Overlap not observed in the current study is indicated in a hatched figure.

In the past decades, research on CD has been largely influenced by descriptive and behavioral perspectives (Association, 2013; Crick & Dodge, 1996; Moffitt, 1993; R. E. Tremblay,2010). One major drawback of this approach is the substantial behavioral heterogeneity in CD. Infact, while current classifications are usually based on the assumption that subjects within the sameclass (disorder or behavior) are likely to be homogeneous, it appears that over 32,000 different cross-sectional combinations of behaviors would lead to a CD diagnosis (Nock et al., 2006b). Alternatively, very few studies hypothesized that CP could result from multiple combinations of *psychological* factors (Cote et al., 2002; Sigvardsson, Bohman, & Cloninger, 1987; Tremblay, Pihl, Vitaro, & Dobkin, 1994). In that regard, our multi-trajectory framework appearspromising as it offers evidence that furthers our understanding of the heterogeneous developmentalpathways leading to CP. One novel contribution of the current study is that we observed that specific combinations of psychological factors were associated with distinct pathways towards subtypes of CP (i.e., AGG and RB). Second, children following more complex multi-trajectory (i.e. with problematic levels on more than 2 features) on the psychological factors of interest were significantly more likely to exhibit CP which support evidence on the developmental heterogeneity in CD population. Finally, we showed that specific groups identified based on psychological features (independently of CP) significantly predicted adolescence CP even after adjusting for early CP. This current study shows encouraging results for studying CP through a multi-dimensional psychological framework. More importantly, contrarily to the behavioral approach, tailoring preventive strategies for CD, based on psychological patterns, may be more effective when they are adjusted to the needs of specific subgroups (e.g. emotion-regulation; positive reinforcement) (Pardini & Frick, 2013).

Limitations

Despite the fact that some of our multi-trajectory groups remained statistically significant after adjustments for several important indicators including early CP, the strength of the associations between multi-trajectories and CP decreased in adolescence. One explanation is the use of self-report questionnaire for assessing CP in adolescence. Hence, social desirability responsebias (e.g. under-reporting severity/frequency) may have partially altered the associations between

psychological features and CP. Another possibility could be that since CP usually peaks during adolescence (15-17 years old)(Moffitt, 1993), the presence of transient CP during adolescence (i.e. Adolescent-Limited) in "*typically developing*" children could have reduced the magnitude of the effects between groups. Second, the 2-trajectory model for DAS showed acceptable yet relatively low entropy suggesting that latent classes are not highly discriminating. However, it is unlikely that this may have influenced the findings since the entropy value was close to 0.80 (Nagin, 2005) and that other metrics, such as AvePP and OCC suggested good to excellent within-class cohesion. By using more complex models (i.e. higher than a 2-trajectory model) would have helped us identify trajectories that are highly discriminating. Moreover, considering the sample size in the current study, a 2-trajectory model for each psychological factor was chosen since increasing the number of trajectories would have substantially complexified the models, resulting in overfitted models. Consequently, future research should attempt to replicate our results with much larger datasets and more complex trajectory models. Third, while none of the items qualitatively overlapped between psychological features for trajectory groups (e.g. irritability, H/I symptoms) and CP, some constructs are known to be more closely related to CP than others (e.g. irritability versus DAS). It remains thus important to acknowledge that some degree of overlap may have inflated some of the observed associations. Finally, we used the same questionnaire to assess psychological features and childhood CP. Therefore, the common method-variance bias may have affected some results observed in our study.

Conclusion

The current study aimed to investigate the developmental heterogeneity in CD population. Our results clearly suggest that children at risk for CP are a heterogeneous population. More precisely, we showed the importance of studying the developmental co-occurrence of four crucial psychological dimensions (irritability, IC, DAS and H/I symptoms) in relation with subtypes of CP (e.g. AGG and RB), to tackle the substantial heterogeneity associated with the disorder. While the current conceptual framework of heterogeneity in CD is mostly driven by psychopathic traits (and ANX to a lesser extent), we suggest that Irritability and H/I symptoms are also fundamental

characteristics required to identify more homogeneous groups at risk for CD, and its sub-syndromes. Researches on the equifinality (i.e. diversity of pathways leading to the same outcome) and/or multifinality (i.e. one component/experience leading to a variety of developmental outcome) (Cicchetti et Rogosch, 1996) of CD should take into account this heterogeneity in order to be confident about the findings. Furthermore, we argue that adopting a multi-dimensional specifier approach for CD seems promising for for stimulating research on treatment and clinical management of children at risk for CD. Therefore, we encourage researchers to examine the multiple developmental pathways of psychological features over the current behavioral classification, as it should enable incremental progress towards unveiling the numerous aetiologiesunderlying CDs. More precisely, we encourage researchers to replicate our findings with differentsamples (i.e. population-based, clinical) in order to better describe data-driven subgroups at risk for CP. As these homogeneous subgroups may show differential response to treatment, research on data-driven subgroups remains essential as it opens the possibility for targeted prevention strategies and personalized clinical practice for a better case management plan.

CHAPITRE 5 – ACTIVITÉ CÉRÉBRALE ET COMPORTEMENTS ANTISOCIAUX

DEUXIÈME ARTICLE

Neurofunctional Abnormalities in Antisocial Spectrum: A Meta-analysis of fMRI studies on Five distinct Neurocognitive Research Domains

Jules R. Dugré, M.Sc. [1,2]; Joaquim Radua, M.D., Ph.D [3,4,5] ; Matthieu Carignan-Allard, B.Sc. [6];Alexandre Dumais, M.D., Ph.D[1-2-7] ; Katya Rubia, Ph.D[8] & Stéphane Potvin, Ph.D[1,2];

[1] Centre de recherche de l'Institut Universitaire en Santé Mentale de Montréal; Montreal, Canada;
[2] Department of Psychiatry and Addictology, Faculty of medicine, University of Montreal; Montreal, Canada;
[3] Institut d'Investigacions Biomèdiques August Pi i Sunyer, CIBERSAM, Barcelona, Spain
[4] Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience, King'sCollege London, London, England
[5] Centre for Psychiatry Research, Department of Clinical Neuroscience, Karolinska Institutet,Stockholm, Sweden
[6] Department of psychology, Faculty of Arts and Science, University of Montreal, Montreal,Canada
[7] Institut National de Psychiatrie Légal Philippe-Pinel, Montreal, Canada
[8] Department of Child and Adolescent Psychiatry, Institute of Psychiatry, Psychology andNeuroscience, King's College London, London, United Kingdom

Déclaration de l'étudiant

Je déclare être l'auteur principal de cet article. J'ai été impliqué dans la conception de l'étude, mené la revue systématique, conduit les analyses statistiques, interprétés les résultats et écrit lapremière version et la version finale de l'article. Mon directeur de thèse, Stéphane Potvin ainsique les coauteurs, ont conseillé mon travail de recherche, suggérés des corrections et ont approuvé la version finale de l'article.

Abstract

Past functional magnetic resonance imaging on antisocial subjects have shown important inconsistencies and methodological problems (e.g., heterogeneity in fMRI tasks domain, small sample sizes, analyses on regions-of-interest). We aimed to conduct a meta-analysis of whole-brainfMRI studies on antisocial individuals based on distinct neurocognitive domains. A voxel-based meta-analysis via permutation of subject images (SDM-PSI) was performed on studies using fMRI tasks in the domains of acute threat response, cognitive control, social cognition, punishment and reward processing. Overall, 83 studies were retrieved. Using a liberal statistical threshold, several key regions were identified in the meta-analysis, principally during acute threat response, social cognition and cognitive control tasks. Additionally, we observed that the right amygdala was negatively associated with both callous-unemotional traits and severity of antisocial behaviors, in meta-analyses on region-of-interest and on dimensional studies, respectively. The findings show that the most prominent functional brain deficits arise during acute threat response, social cognitions and cognitive control neurocognitive domains. These results provide substantial insightsfor our understanding of aberrant neural processing across specific contexts.

Keywords Antisocial behaviors; conduct disorder; amygdala; acute threat response; empathy; cognitive control

Introduction

Conduct problems (CP) and its adult form, adult antisocial behaviors are usually defined as behaviors that frequently violate the rights of others (i.e. aggressive and rule-breaking behaviors).Developmental research suggests approximately 5% of children would display severe and persistent CP, thus meeting the criteria for conduct disorder (CD) (L. Bevilacqua, D. Hale, E. D. Barker, & R. Viner, 2018). The presence of CP at an early age has been associated with poor adultoutcomes such as antisocial behaviors, high rates of criminality, incarcerations, substance misuse and poor general health (Moffitt, 2018). By studying antisocial problems as a dimensional construct(i.e. problems to antisocial personality disorder (CP/ASPD)), evidence from literature reviews suggests that individuals on the antisocial spectrum show several deficits in brain functioning across various distinct neurocognitive domains (Blair, K. Veroude, & J. Buitelaar, 2018; Blair, 2010; Byrd, Loeber, & Pardini, 2014; Crowe & Blair, 2008; Antonio Del Casale et al., 2015; Glenn & Raine, 2008; Herpers, Scheepers, Bons, Buitelaar, & Rommelse, 2014; Seara-Cardoso & Viding, 2015; Wahlund & Kristiansson, 2009). Nevertheless, consensual evidence about the nature and severity of neural dysfunctions during cognitive and emotional tasksare still lacking. It is thus crucial to better understand the neurobiological impairments in antisocial subjects, across different contexts (i.e. specific neurocognitive research domains), in order to facilitate early prevention research.

Acute Threat Response

The acute threat response system or the defensive survival circuit involves physiological reactions (i.e. autonomic nervous and endocrine systems) and adaptive behaviors (i.e. fight, flightor freeze response) when facing a threatening stimulus (J. LeDoux, 2015). Concerning CP/ASPD subjects, it has been proposed that brain regions involved in response to threat (i.e. amygdala, ventromedial prefrontal cortex (PFC), dorsal anterior cingulate cortex, insular cortex, hypothalamus and periaqueductal gray) may be largely implicated in aggression (R. Blair et al., 2018; R. J. Blair, 2016; Crowe & Blair, 2008). A recent literature review suggests that CP/ASPD individuals show reduced Hypothalamic-Pituitary-Adrenal axis function in response to threat compared to healthy controls

(HC) (G. Fairchild, E. Baker, & S. Eaton, 2018). Furthermore, a meta-analysis on fMRI studies of CP/ASPD subjects found significant underactivation in dorsolateral PFC and temporal pole during emotion processing (Alegria et al., 2016). Additionally,a meta-analysis that focused specifically on psychopathic individuals but pooled studies using fMRI tasks belonging to heterogeneous neurocognitive domains, showed that psychopathic subjects exhibited reduced activation in the right laterobasal amygdala, bilateral lateral PFC and dorsomedial PFC and an increased activation in bilateral fronto-insular cortex compared to HC (Poeppl et al., 2019). Thus, it was hypothesized that callous-unemotional traits (CU) may moderateneural functioning in response to acute threat in antisocial individuals (i.e. hypo- and hyper- reactivity to threat may be associated with CP/ASPD with and without CU traits, respectively, see Blair, Leibenluft, & Pine, 2014; Hyde, Shaw, & Hariri, 2013; Viding, Fontaine, & McCrory, 2012). Evidence for this assertion remains however limited.

Cognitive Control

Cognitive control refers to the neurocognitive domain of executive functions that require the overriding of interfering responses (i.e. motor and interference inhibition, cognitive flexibility,and performance monitoring) (Miller & Cohen, 2001). Neuropsychological studies show thatCP/ASPD subjects exhibit poorer executive functioning, particularly in motor and interference inhibition and response selection tasks compared to HC (Hobson et al., 2011; Morgan & Lilienfeld,2000; Ogilvie et al., 2011; J. R. Séguin et al., 2007). Literature reviews on fMRI studies of cognitivecontrol tasks show that these deficits in CP/ASPD subjects are underpinned by decreased activationin the inferior frontal gyrus, insula, temporal lobe and supplementary motor area (R. Blair et al., 2018; W. Matthys, L. J. Vanderschuren, & D. J. Schutter, 2013; S. D. Noordermeer, Luman, & Oosterlaan, 2016), and to a lesser extent, the precuneus and cingulate cortex (i.e. from anterior to posterior) (Noordermeer et al., 2016). Furthermore, Alegria et al.'s (2016) meta-analysis on cool executive function tasks revealed decreased activations in the right superiorand middle temporal gyrus, posterior insula and putamen. However, their meta-analysis was underpowered (k=8); more evidence is needed to support such neural impairments during cognitive control tasks.

Social Cognitions

In the previous decades, researchers have observed important deficits in social cognition (i.e. lack of empathy and remorse) in subjects on the CP/ASPD spectrum. These researchers found a significant deficiency in recognizing/experiencing others' pain/distress (i.e. cognitive/affective empathy) (Blair et al., 2014; Dawel, O'Kearney, McKone, & Palermo, 2012; Marsh & Blair, 2008; Martin-Key, Graf, Adams, & Fairchild, 2018). It was proposed thatthese deficits may be principally exacerbated by the co-occurrence of psychopathic traits, particularly the CU dimension of psychopathy (Blair, 2013; Blair et al., 2014). However, although an earlier meta-analysis on facial affect recognition found robust evidence between deficits in recognizing fearful expressions in individuals with antisocial behaviors,psychopathy did not moderate the results (Marsh & Blair, 2008). Furthermore, whilesome found no significant differences between individuals with and without CU traits in empathicaccuracy, emotion recognition and affective empathy (Martin-Key et al., 2017), others observed that emotion recognition problems were associated with CU traits (A. Dawel et al., 2012). That said, deficits in social cognitions in CP/ASPD individuals may therefore arise from reduced activations in the amygdala, anterior insula, cingulate cortex and temporo-parietal junction (Blair et al., 2018). Though, since these preliminary findings were based on a limited number of studies, a meta-analysis is necessary to examine these earlier indications of neural dysfunctions during social cognitions tasks.

Reinforcement learning

Finally, punishment and reward processing are key components in human motivation. An insensitivity to punishment (e.g. incapacity to learn from aversive stimuli) has been associated with antisocial problems, while hypersensitivity to reward-seeking has been associated with predatory/instrumental subtype of aggression (Xu, Farver, & Zhang, 2009). Most CP/ASPD individuals appear insensitive to punishment cues, whereas some display a high propensity for reward-seeking ((A. L. Byrd et al., 2014) for a review of behavioral studies). Both components are related to a similar brain network (i.e. ventral striatum, amygdala, anterior insula, medial orbitofrontal cortex, ventromedial PFC and ventrolateral PFC, anterior cingulate cortex, however the medial orbitofrontal cortex seems to be more often elicited during reward processing, while

punishment processing may recruit the middle cingulate cortex (J. R. Dugré, A. Dumais, N. Bitar, & S. Potvin, 2018; B. Knutson & S. M. Greer, 2008; Liu, Hairston, Schrier, & Fan, 2011; Oldham et al., 2018). Although literature reviews suggest alterations in the striatum and ventromedial PFC in response to reward and punishment in CP/ASPD individuals (Blair et al.,2018; Byrd et al., 2014; Matthys et al., 2013), results suggest discrepancies on the directionality of such activations (i.e., hyper- and hypo-activations) (Blair et al., 2018; Murray, Shaw, Forbes, & Hyde, 2017).

Limitations of past neuroimaging studies on individuals with CP/ASPD

Our understanding of neural processing in CP/ASPD individuals is limited in currentliterature due to several weaknesses. In fact, discrepancies in fMRI results may derive from smallsample sizes, comorbid CU traits, distinct methodology (i.e., whole-brain [WB], region-of-interest[ROI] or regression analyses) as well as the use of different statistical thresholds. For instance, literature reviews of fMRI studies (Blair et al., 2018; Blair, 2010; A. L. Byrd et al.,2014; Crowe & Blair, 2008; Antonio Del Casale et al., 2015; Glenn & Raine, 2008; Herpers et al.,2014; Seara-Cardoso & Viding, 2015; Wahlund & Kristiansson, 2009) report some results frombrain regions that were statistically significant in ROI analyses (e.ge.g.,ygdala/PFC), but not inWB analyses. This is critical as ROI analyses substantially reduce the severity of correction formultiple tests (i.e. correcting for a few regions instead of the whole brain) and limit the anatomicalinference to selected ROIs (Poldrack, 2007). Therefore, including ROI results in the interpretationof neural functioning of CP/ASPD subjects across the whole brain may increase the rate of falsepositives and type 1 errors. However, it remains crucial to perform a ROI-based meta-analysis inorder to better understand the relationship between amygdala activity and the antisocial spectrum.

Additionally, previous meta-analyses did not take into consideration the heterogeneity of fMRI tasks used in studies included, even though different neurocognitive domains are known to be associated with distinct underlying brain networks. For example, while some authors performeda meta-analysis independently of task domains (Poeppl et al., 2019; Y. Yang & Raine, 2009), others focused on a specific neurocognitive domain (e.g., executive function) but used heterogeneous tasksand conditions, some being unrelated to the investigated neurocognitive domain (e.g.

reward and punishment tasks included in the executive domain) (S. D. Noordermeer et al., 2016). This heterogeneity limits the generalizability of results across different neurocognitive domains. Studying neural correlates of distinct and well-defined neurocognitive domains will result in a more precise understanding of the underlying neuropathological processes of CP/ASPD individuals. Moreover, although Peoppl et al. (2019) performed a meta-analysis treating psychopathy as a unitary construct, it remains largely unknown whether their results are driven by factor 1 (i.e. affective/interpersonal facets) or factor 2 (i.e. impulsive/antisocial facets) of psychopathy (Latzman, Patrick, & Lilienfeld, 2019). Considering that a large number of psychometric tests includes antisocial behaviors (i.e., Factor 2), studying the specific correlates of brain functioning (i.e., callous-unemotional traits & severity of antisocial behaviors) is therefore crucial to better understand the heterogeneity in CP/ASPD individuals.

Aims of the current study

In all, the primary goal of this meta-analysis was to examine the neural processes of CP/ASPD individuals using only WB studies from five distinct neurocognitive domains based on the Research Domain Criteria (B. N. Cuthbert & T. R. Insel, 2013) and the classification made byBlair, Veroude et Buitelaar (R. Blair et al., 2018): Cognitive Control, Punishment and Reward Processing, Social Cognition and the Acute Threat Response. Main hypotheses are that CP/ASPDsubjects would show a) reduced reactivity to threat (in comparison to HC), primarily in limbic andPFC regions, b) decreased activations in the inferior frontal gyrus/ventro-lateral PFC, insula, supplementary motor area during cognitive control tasks, c) deficits in regions implicated in self-reflection/consciousness such as posterior cingulate cortex/precuneus, medial PFC, the temporo-parietal junction as well as in limbic regions (i.e. amygdala, insula) during social cognitions tasks and d) deficit in valuation system, particularly in the striatum and the ventromedial PFC during reward processing and punishment processing. The current meta-analysis will thus shed light on task-domain dependent neural processing of CP/ASPD individuals. Establishing task-domain dependent neurocognitive deficits may enhance our capacity to target neurocognitive domains in early prevention to reduce the likelihood of problematic outcome associated with CP/ASPD. Additionally, a specific ROI-based meta-analysis on the amygdala was executed to better

disentangle the role of this brain region in CP/ASPD subjects. Following current neurobiological models of CP/ASPD, a negative association between amygdala reactivity and callous-unemotional traits would be observed. Finally, meta-analytic evidence of relationships between brain responsesand antisocial problems and CU traits was also executed based on dimensional studies.

Method

Selection procedures

Search strategies

A systematic search strategy, using three search engines (Google Scholar, PubMed and EMBASE), was performed independently by two researchers (MCA & JRD) up to February 2019 to identify relevant studies. The following search terms were used: ("*conduct problems*" or "*conduct disorder*" or "*disruptive behaviors*" or "*Antisocial personality disorder*" or "*psychopathy*" or "*sociopathy*" or "*dissocial personality disorder*") AND ("*functional magnetic resonance imaging*" ("*fMRI*")). Additional articles were searched by cross-referencing the reference lists of the included articles.

Selection criteria

Flow-chart and reasons of study exclusion can be retrieved in Supplementary Material. Articles were included if they met the following criteria: (1) original paper from a peer-reviewed journal, (2) inclusion of individuals with conduct/antisocial problems to disorder (CP/ASPD) without a comorbid major mental illness or organic impairment (i.e. forensic samples, schizophrenia) (3) use of functional magnetic resonance imaging; (4) use of a fMRI task related to a) cognitive control; b) social cognition (e.g. empathic decision-making, theory of mind); c) rewardprocessing (e.g. monetary incentive delay task, passive avoidance tasks); d) punishment processing (e.g. monetary incentive delay task, Passive Avoidance tasks) or e) responses to threatening stimuli(e.g. negative images/faces); 5) description of results from group comparisons (CP/ASPD versus HC) and/or dimensional associations with antisocial problems and/or callous-unemotional traits; 6) use of WB methodology and/or amygdala predefined ROIs analyses. When studies reported only

ROI analyses, authors were contacted to provide WB results (at $p < 0.001$ uncorrected threshold) (see Table 1 for authors that were contacted). The flow-chart and the reasons of studies' exclusion can be retrieved in Supplementary Material. PRISMA guidelines were followed to achieve a high reporting standard (Moher, Liberati, Tetzlaff, & Altman, 2009) (Supplementary Material). Finally, we examined the moderation effectof CU traits. Since studies used different scales to measure CU traits, mean CU scores were converted using the well-established method *Percent of Maximum Possible scores* (POMP) that allows comparisons between different measures and populations (Cohen, Cohen, Aiken, & West,1999; Fischer & Milfont, 2010), as used in previous meta-analyses (Rogers & De Brito, 2016).

Coordinate-based Meta-analysis

The current voxel-wise meta-analysis was performed using the Seed-based d Mapping with Permutation of Subject Images (SDM-PSI version 6.11) (Albajes-Eizagirre, Solanes, Vieta, & Radua, 2019). Briefly, the SDM-PSI is a voxel-based meta-analysis software using peak coordinates and their t-values as reported from the original studies, to impute, for each study, multiple effect-size maps (Hedges' effect size) of contrast results (increased and decreased activations). Maps are then combined in a standard random-effects model considering sample size,intra-study variability and between-study heterogeneity (J Radua et al., 2012), and multipleimputations are pooled using Rubin's rules (Albajes-Eizagirre et al., 2019). The familywise error rate (FWER) of the results is calculated using a subject-based permutation test (Eklund, Nichols, & Knutsson, 2016). SDM-PSI uses MetaNSUE (Albajes-Eizagirre, Solanes, & Radua, 2018) to estimate the maximum likely effect size within the lower and upper bounds of possible effects sizesfor each study separately and then adds realistic noise (Albajes-Eizagirre et al., 2019).

Meta-analysis procedure

To evaluate the strength of the evidence, a number of criteria were followed including the ten rules for neuroimaging meta-analyses (Müller et al., 2018). These criteria suggested that strong quality evidence would result from the included samples across the five neurocognitive domains (Supplementary Material).

First, whole-brain case-control main meta-analyses were performed to assess neural differences between CP/ASPD and HC on each neurocognitive domain. A binary covariate was included in the main analyses to adjust for studies having used a correction for multiple comparisons. Residual heterogeneity (I^2 statistic) of included studies was examined to assess robustness of results (I^2>50% commonly indicates serious heterogeneity). Funnel plots were created to visually examine if findings had been driven by a small subset of studies or by studies with small sample sizes. Potential publication bias was assessed via a meta-regression of the effect size by its standard error (Egger, Smith, Schneider, & Minder, 1997; Sterne et al., 2011). We reported results using an uncorrected p<0.005 threshold with a cluster extent=10 voxels, since it was found to be optimally balance sensitivity and specificity (Lieberman & W. A. Cunningham, 2009; Joaquim Radua et al., 2012; J Radua et al., 2012). as well as using FWER- corrected p<0.05 with the threshold-free cluster enhancement approach (TFCE) and 5,000 permutations (Smith & Nichols, 2009). Moreover, in order to assess the reliability of our results, we have performed several subanalyses. In fact, meta-regression analyses were performedto assess the moderation effect of CU traits, age (i.e. potential changes from childhood toadulthood), percentage of participants from each sample that have received a comorbid Attention- Deficit/Hyperactivity Disorder (ADHD), percentage of participants being diagnosed with CD/ASPD diagnosis, percentage of participants from each sample that have received medication, repetition time of functional volumes and full width at half maximum of the smoothing kernel. For each subanalysis, alpha level was set at $\alpha = 0.005$ to reduce the risk of type 1 error associated withmultiple testing.

For the amygdala ROI meta-analysis, we examined neural differences between CP/ASPD subjects and HC on left and right amygdala separately. ROIs were defined based on the Automated Anatomical Labeling atlas (Tzourio-Mazoyer et al., 2002). Meta-analyses on dimensional associations between brain response (whole-brain and the amygdala ROIs) and antisocial problemsand callous-unemotional traits, separately, were also performed to better understand the relationships between brain response and severity of antisocial problems/callous-unemotional traits.

Table 1. Included samples and studies across meta-analyses on Case-Control studies (n=65, k=81)

	Case-Control Studies					
First Author, Year	Cognitive Control (k=16)	Acute Threat Response (k=26)	Reward Processing (k=17)	Punishment Processing (k=17)	Social Cognitions (k=22)	Amyg. ROIs (k=35)
Banich, 2007	X	-	-	-	-	-
Birbaumer, 2005*	-	-	-	X	-	X
Bjork, 2010	-	-	X	X	-	-
Bubenzer-Busch, 2016	-	X	X	X	-	-
Byrd, 2018 (A)	-	-	-	-	-	X
Byrd, 2018 (B)	-	-	-	-	-	X
Cardinale et al., 2018	-	-	-	-	X	-
Cohn, 2013 (A)	-	-	-	-	-	X
Cohn, 2013 (B)	-	-	-	-	-	X
Cohn, 2015 (A)	-	-	-	-	-	X
Cohn, 2015 (B)	-	-	-	-	-	X
Contreras-Rodríguez, 2013	-	X	-	-	-	-
Crowley, 2010	-	-	X	X	-	-
Decety, 2009	-	-	-	-	X	-
Deeley, 2006	-	X	-	-	-	-
Dong, 2017	-	-	-	-	X	-
Ewbank, 2018 (A)	-	X	-	-	-	X
Ewbank, 2018 (B)	-	X	-	-	-	X
Fairchild, 2014	-	X	-	-	-	X
Fanti, 2019 (A)	-	-	-	-	-	X
Fanti, 2019 (B)	-	-	-	-	-	X
Fehlbaum, 2018	X	-	-	-	-	-
Finger, 2011	-	-	X	X	-	-
Gatzke-Kopp, 2009	-	-	X	X	-	-
Geurts, 2016*	-	-	X	-	-	-
Gregory, 2015 (A)	-	-	X	X	-	-
Gregory, 2015 (B)	-	-	X	X	-	-
Herpertz, 2008	-	X	-	-	-	X
Hwang, 2016 (A)	X	X	-	-	-	X
Hwang, 2016 (B)	X	X	-	-	-	X
Hwang, 2018*	-	-	X	-	-	-
Jones, 2009	-	X	-	-	-	X
Kalnin, 2011	X	-	-	-	-	-
Klapwijk, 2016a	-	X	-	-	X	-
Klapwijk, 2016b	-	-	-	-	X	-
Kumari, 2009	-	X	-	-	-	-
Lockwood, 2013	-	-	-	-	X	-
Lozier, 2014 (A)	-	-	-	-	-	X
Lozier, 2014 (B)	-	-	-	-	-	X
Marsh, 2008	-	X	-	-	-	-
Marsh, 2011	X	-	-	-	X	X
Marsh, 2013	-	X	-	-	X	-
Meffert, 2013	-	-	-	-	X	-
Mier, 2014	-	-	-	-	X	X
O'Nions, 2014	-	-	-	-	X	-
Passamonti, 2010* (A)	-	X	-	-	-	X
Passamonti, 2010* (B)	-	X	-	-	-	X
Prehn, 2013a	-	X	-	-	-	X
Prehn, 2013b (A)	-	-	X	X	-	-
Prehn, 2013b (B)	-	-	X	X	-	-
Pujol, 2011	X	-	-	-	X	-
Rubia, 2008	X	-	-	-	-	-
Rubia, 2009a	X	-	-	-	-	-
Rubia, 2009	-	-	X	X	-	-
Rubia, 2010	X	-	-	-	-	-

Sakai, 2017 (A)	-	-	-	-	X	-
Sakai, 2017 (B)	-	-	-	-	X	-
Schiffer, 2014	X	-	-	-	-	-
Schiffer, 2017	-	-	-	-	X	X
Schwenck, 2017	-	-	X	X	X	-
Sebastian, 2012	-	-	-	-	X	X
Sebastian, 2014 (A)	-	X	-	-	-	X
Sebastian, 2014 (B)	-	X	-	-	-	X
Sethi, 2018* (A)	-	X	-	-	X	-
Sethi, 2018* (B)	-	X	-	-	X	-
Thornton, 2017	X	X	-	-	-	X
van den Bos, 2014	-	-	-	-	X	-
van Lith, 2018 (A)	-	-	-	X	-	X
van Lith, 2018 (B)	-	-	-	X	-	X
Viding, 2012 (A)	-	X	-	-	-	X
Viding, 2012 (B)	-	X	-	-	-	X
Völlm, 2007	-	-	X	X	-	-
Völlm, 2010	X	-	X	-	-	-
White, 2012a	X	X	-	-	-	-
White, 2012b	X	X	-	-	-	-
White, 2013	-	-	X	X	-	-
White, 2014	-	-	X	X	-	-
White, 2016* (A)	-	-	-	-	X	X
White, 2016* (B)	-	-	-	-	X	X
White, 2018*	-	X	-	-	-	X
Zhang, 2015	X	-	-	-	-	-

Note. (A-B) refers to independent samples derived from the same studies; (1-2) refers to independent fMRI task derived from the same studies; Asterix (*) refer to authors that were contacted and provided results p>0.001 uncorrected threshold

Results

Characteristics of Included Studies for the Whole-Brain Case-Control Meta-Analyses

Sixty-one studies met the whole-brain inclusion criteria for the current meta-analysis. Of these studies, ten studies included two samples (Ewbank et al., 2018; Gregory et al., 2015; Hwanget al., 2016; Prehn et al., 2013; Sakai et al., 2017; Sebastian et al., 2014; Sethi, O'Nions, McCrory, Bird, & Viding, 2018; van Lith et al., 2018; E. Viding, C. L. Sebastian, et al., 2012; White et al., 2015), resulting in a total of 71 samples. This represented a total of 1227 HC and 1328 CP/ASPD individuals (mean age = 20.15, range = 10.9-44.6 years old; 90% males). CU traits were assessed for 54 samples with a mean POMP score of 58.95% (range 22.9-84.4%). We thus performed whole-brain case-control meta-analyses on studies based on five distinct neurocognitive domains: (A) Acute threat response (k = 26 samples of which a majority used tasks involving facial expressions of negative emotions); (B) Punishment Processing (k=17 samples which included passive avoidance, MID or probabilistic response reversal tasks with monetary reward and loss); (C) Reward Processing (k=17 samples, with most employing the same tasks as in punishment processing); (D) Social cognition (k=22 samples with most using tasks involving evaluation of others' pain, ToM and empathic decision-making); (E) Cognitive Control (k=16 samples, in which the majority used Stroop and Go-NoGo tasks). Only one contrast per fMRI task was selected to reduce bias associated with the inflation of study results. More detailed informations about the samples included and excluded as well as contrasts used are available in Supplementary Material.

Whole Brain Case-Control meta-analyses

Meta-analysis on Acute threat response

Twenty-six samples derived from 21 studies were included in the meta-analysis on acute threat response comprising a total of 450 HC and 517 CP/ASPD subjects (See Table 1). The meanage of CP/ASPD subjects was 17.95 (SD=7.40), and 86% of the total sample were males. Presenceof medication was assessed for 19 samples with a mean percentage of 15.71% for CP/ASPD subjects (ranging from 0 to 85.19%). Presence of comorbid ADHD was assessed for 14 samples with a

mean percentage of 50.83%. Finally, percentage of samples diagnosed with a clinical diagnosis of CD/ASPD were provided for 15 samples which revealed that in average 81.1% of individuals from these samples received a CD/ASPD diagnosis. In only 8 samples, all participantshad received a clinical diagnosis of CD/ASPD.

During acute threat response tasks, CP/ASPD subjects showed no significant increased activations relative to HC. However, they revealed statistically significant decreased activations in the bilateral dorsal anterior cingulate gyrus, supplementary motor area (including median cingulate cortex), anterior insula (including the triangular part of the inferior frontal gyrus), bilateral middleoccipital gyri, dorsolateral PFC, inferior parietal gyri and inferior temporal gyrus. (Table 1A; Figure 1). These results did not survive the FWER correction ($p<0.05$). Low between-study heterogeneity for each significant peak (I^2=0.7%-17.64%). Funnel plots suggested that none of theresults were driven by small or noisy studies, and the test for potential publication bias was not statistically significant (p=0.665-0.717).

CU traits were available for 22 samples (84.6%) with a mean CU-POMP score of 61.64% (range 22.9-78.1%). However, no significant association with CU traits in CP/ASPD subjects wasobserved. Concerning percentage of samples under medication, we observed that the dorsal anterior cingulate cortex hypoactivity was negatively associated with medication level (B = -0.011, p = 0.003). Other subanalyses such as repetition time of functional volumes, full width at half maximum, age, comorbid ADHD and percentage of CD/ASPD diagnosis per sample were all statistically non-significant.

Punishment Processing

Seventeen samples of individuals with CP/ASPD (from 14 studies) met the inclusion criteria for the meta-analysis on punishment processing (see Table 1). The meta-analysis compriseda total of 276 CP/ASPD subjects compared to 234 HC. The mean age of CP/ASPD subjects was 21.16 (SD=9.95) and 95% of the total sample were males. CU traits were available for 10 samples(58.8%) with a mean CU-POMP score of 55.31% (range 22.9-76.2%). Sample's percentage under medication was assessed for 15 samples and suggest a mean percentage of 30.97% (ranging from

0% to 100%). ADHD diagnosis comorbidity was assessed for 10 samples, with a mean percentage of 46.2% individuals with comorbid ADHD. Finally, percentage of participants from each sample that received a CD/ASPD was provided for 16 samples which revealed that in average 72% of individuals from these samples received a CD/ASPD diagnosis. In only 5 samples, all participants had received a clinical diagnosis of CD/ASPD.

Results revealed statistically significant increased activations in the left hemispheric Lobule IV (cerebellum) and the midbrain tegmentum in CP/ASPD subjects compared to HC. CP/ASPD subjects showed significant decreased activations in a cluster including the left premotor cortex BA6 (Table 1B; Figure 1). These results did not survive the FWER correction ($p<0.05$). Low between-study heterogeneity for each significant peak (I^2=1.94% - 17.18%). Funnel plots suggested that none of the results were driven by small or noisy studies, and the test for potential publication bias was not statistically significant (p = 0.862-0.976). Meta-regression analysis resulted in no significant association with CU traits in CP/ASPD subjects. Furthermore, no significant effect was observed between our results and moderators.

Table 2. Included samples and studies across meta-analysis on dimensional studies (n=40, k=52)

First Author, Year	Dimensional Studies				Main Neurocognitive domain				
	Antisocial Behaviors		Callous-Unemotional						
	WB (k=10)	Amyg. ROIs (k=23)	WB (k=12)	Amyg. ROIs (k=31)	Cogn. Control	Acute Threat Response	Punishment Processing	Reward Processing	Social Cognitions
Byrd, 2018 (A)	-	X	-	X	-	-	X	-	-
Byrd, 2018 (B)									
Carré, 2013	-	X	-	X	-	X	-	-	-
Cohn, 2013 (A)	-	-	X	X	-	-	X	-	-
Cohn, 2013 (B)									
Cohn, 2015 (A)	-	-	-	X	-	-	X	-	-
Cohn, 2015 (B)									
Cohn, 2016 (A)	-	-	X	X	-	-	X	-	-
Cohn, 2016 (B)									
Contreras-Rodríguez, 2013	X	-	X	-	-	X	-	-	-
Cope, 2014	X	-	X	-	-	-	-	X	-
Decety, 2009	-	X	-	-	-	-	-	-	X
Decety, 2013a (1)	-	X	-	X	-	X	-	-	-
Decety, 2013a (2)	-	X	-	X	-	-	-	-	X
Decety, 2013b (1)	-	X	-	X	-	X	-	-	-
Decety, 2013b (2)	-	X	-	X	-	-	-	-	X
Decety, 2014	-	X	-	X	-	-	-	-	X
Dotterer, 2017	-	X	-	X	-	X	-	-	-
Ewbank, 2018 (A)	-	X	-	X	-	X	-	-	-
Ewbank, 2018 (B)									
Fairchild, 2014	X	X	-	-	-	X	-	-	-
Harenski, 2010	-	X	-	X	-	-	-	-	X
Harenski, 2014a	X	X	X	X	-	-	-	-	X
Harenski, 2014b	X	X	X	X	-	X	-	-	-
Hwang, 2016 (A)	-	-	-	X	-	X	-	-	-
Hwang, 2016 (B)									
Hwang, 2018*	-	-	-	X	-	-	-	X	-
Hyde, 2014	-	X	-	X	-	X	-	-	-
Hyde, 2016	-	X	-	X	-	X	-	-	-
Lozier, 2014 (A)	X	X	X	X	-	X	-	-	-
Lozier, 2014 (B)									
Marsh, 2014	-	X	-	X	-	-	-	-	X
Michalska, 2016	X	-	X	-	-	X	-	-	-
Passamonti, 2010* (A)	-	X	-	X	-	X	-	-	-
Passamonti, 2010* (B)									
Rilling, 2007	-	X	-	X	-	-	-	-	X
Sadeh, 2011a	X	X	X	X	-	X	-	-	-
Sakai, 2017 (A)	-	-	X	-	-	-	-	-	X
Sakai, 2017 (B)									
Schiffer, 2017	-	-	-	X	-	-	-	-	X
Schwenck, 2017	-	-	-	X	-	-	X	-	-
Sebastian, 2012	-	X	-	X	-	-	-	-	X
Sterzer, 2005	-	X	-	-	-	X	-	-	-
van Lith, 2018 (A)	-	-	-	X	-	-	X	-	-
van Lith, 2018 (B)							-		
Viding, 2012 (A)	-	-	-	X	-	X	-	-	-
Viding, 2012 (B)									
White, 2012b	-	-	-	X	-	X	-	-	-
White, 2016* (A)	-	-	-	X	-	-	-	-	X
White, 2016* (B)									
Yoder, 2015 (1)	X	-	X	-	-	-	-	-	X
Yoder, 2015 (2)	X	-	X	-	-	-	-	-	X

Note. (A-B) refers to independent samples derived from the same studies; (1-2) refers to independent fMRI task derived from the same studies; Asterix (*) refer to authors that were contacted and provided results p>0.001 uncorrected threshold

Reward Processing

Seventeen samples from 15 studies met the inclusion criteria on reward processing (see Table 1) which comprised a total of 267 HC and 282 CP/ASPD subjects. The mean age of individuals with CP/ASPD was 22.93 years old (SD=11.48) and 93% were males. CU traits were available for only 8 samples (47.1%) with a mean CU-POMP score of 50.4% (range 22.9-74.4%). Sample's percentage under medication was assessed for 14 samples and suggest a mean percentageof 27.17% (ranging from 0% to 85.19%). ADHD diagnosis comorbidity was assessed for 9 samples, with a mean percentage of 44% across samples. Finally, percentage of samples diagnosedwith a clinical diagnosis of CD/ASPD were provided for 16 samples which revealed that in average,69% of individuals from these samples received a CD/ASPD diagnosis. In only 6 samples, all participants had received a clinical diagnosis of CD/ASPD. During reward processing fMRI tasks, CP/ASPD subjects showed no statistically significant differences in comparison to HC. Meta-regression analysis resulted in no significant association with CU traits in CP/ASPD subjects. Furthermore, no significant effect was observed between our results and moderators.

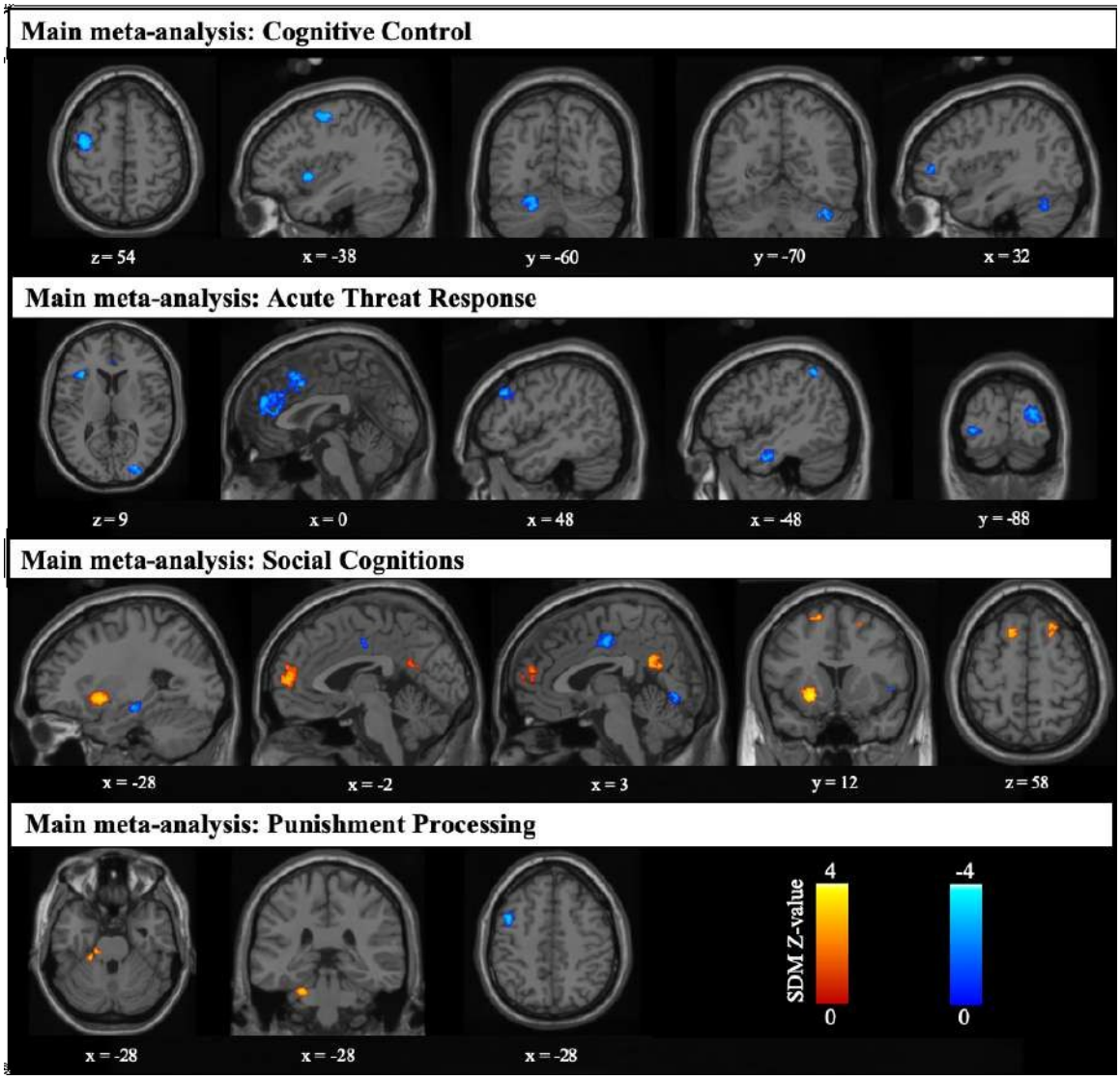

Figure 1. Overlay of brain areas significantly impaired in CP/ASPD individuals compared tohealthy subjects. These blobs were generated using the SDM p-value threshold of p = 0.005 uncorrected derived from the main analyses in Table 1. SDM = Seed-Based d Mapping.

Social Cognition Domain

Twenty-two samples derived from 19 studies were included on social cognition comprising461 CP/ASPD subjects compared to 419 HC. The mean age of CP/ASPD subjects was 19.86 yearsold (SD=9.75) and 94% of the total sample were males. Twenty samples provided CU traits (90.91%) having a mean CU-POMP score of 57.25% (range 28.8-84.4%). Sample's percentage under medication was assessed for 17 samples and suggest a mean percentage of 15% (ranging from 0% to 42.80%). Comorbid ADHD diagnosis was assessed for 8 samples, with a mean percentage of 37% individuals across these samples. Finally, percentage of samples diagnosed witha clinical diagnosis of CD/ASPD were provided for 11 samples which revealed that in average, 80% of individuals from these samples received a CD/ASPD diagnosis. In only 5 samples, all participants had received a clinical diagnosis of CD/ASPD.

During Social Cognition tasks, CP/ASPD subjects showed statistically significant increased activations (as compared to HC) in the putamen, precuneus, medial PFC, bilateral dorsolateral PFC, fusiform gyrus, Crus I and Rolandic operculum. Furthermore, they showed reduced activations in the middle cingulate cortex, hippocampus, lingual and middle occipital gyri, inferior frontal gyrus and fusiform gyrus (Table 2D; Figure 1). These results did not survive the FWER correction ($p<0.05$). These peaks showed low between-study heterogeneity (I^2=0.88%-13.6%). Funnel plots suggested that none of the results were driven by small or noisy studies, and the test for potential publication bias was not statistically significant (p=0.674-0.830). Meta-regression analysis resulted in no significant association with CU traits in CP/ASPD subjects. Furthermore, other subanalyses were all statistically non-significant.

Cognitive Control Domain

Sixteen samples from 15 studies met the inclusion criteria on cognitive control domain (SeeTable 1). These studies included a total of 320 individuals with CP/ASPD and 341 HC. The meanage of CP/ASPD subjects was 19.23 years old (SD=9.97) and 84% of these individuals were males.Ten out of 16 samples reported levels of CU traits (62.5%), having a mean CU-POMP score of 58.1% (range 24.96-78.13%). Presence of medication was assessed for 14 samples with a mean percentage of

19.3% for CP/ASPD subjects (ranging from 0 to 89.7%). Presence of comorbid ADHD was assessed for 11 samples with a mean percentage of 35.9% (ranging from 0 to 70.59). Finally, information about CD/ASPD clinical diagnosis were provided for 14 samples which revealed that in average 88% of individuals received a CD/ASPD. In only 8 samples, all participants had received a clinical diagnosis of CD/ASPD.

During cognitive tasks, individuals with CP/ASPD showed no statistically significant increased activations in comparisons to HC. However, they showed decreased activations in severalregions including the premotor cortex, anterior insula, middle temporal and middle frontal gyri aswell as the hemispheric part of the Lobule VI and Crus I of the cerebellum (Table 2E; Figure 1). These results did not survive the FWER correction ($p<0.05$). These peaks showed low between- study heterogeneity (I^2=1.67%-16.3%). Funnel plots suggested that none of the results were drivenby small or noisy studies, and the test for potential publication bias was not statistically significant (p=0.773-0.879). Meta-regression analysis resulted in no significant association with CU traits in CP/ASPD subjects. Furthermore, no significant effect was observed between our results and moderators.

Meta-analysis based on Amygdala Region-of-Interest

Twenty-three studies that comprised 35 samples, were included in the amygdala ROI meta-analysis. More precisely, 503 healthy controls were compared to 701 CP/ASPD subjects. The mean age across CP/ASPD subjects was 17.72 (SD = 7.34) and the mean POMP score for CU was 60.93% (k = 30). Presence of medication was assessed for 16 samples with a mean percentage of 18.5% for CP/ASPD subjects (ranging from 0 to 100%). Presence of comorbid ADHD was assessed for 18 samples with a mean percentage of 47.92% (ranging from 15% to 73%). Finally, information about CD/ASPD clinical diagnosis were provided for 16 samples which revealed thatin average 81% of individuals received a CD/ASPD. In only 8 samples, all participants had received a clinical diagnosis of CD/ASPD.

No significant results were observed between CP/ASPD and HC subjects for both amygdalaROIs at a $p < 0.005$ uncorrected threshold. The left and right amygdala ROIs showed small to moderate

between-study heterogeneity (I^2 = 37.95 & I^2 = 27.43, respectively). However, meta- regression across task-domains revealed a statistically significant negative relationship between CU traits and the right amygdala that survived a FWER correction for TFCE ($p < 0.05$) with 5,000 permutations (i.e. x=30, y=-2, z=-18; SDM-Z=-3.17, p = 0.005). This relationship was also observed when restricting studies to the acute threat detection domain (SDM-Z=-3.11, p=0.0009) and social cognition domain (SDM-Z=-3.14, p=0.0008) but not punishment processing. Moreover,the relationship between the right amygdala and CU traits across task domains remained significant when restricting to studies with children/adolescent (B = -1.87, $p < 0.001$). Although no significant relationship between the left amygdala and CU traits was observed across task domains, within-task domains subanalyses revealed significant negative association between the left amygdala and CU traits in the acute threat detection domains only (x=-24, y=-2, z=-14, SDM-Z=-2.70, p=0.0035).No other significant effect was observed between the amygdala and moderators.

<u>Meta-analyses based on dimensional associations between brain responses and severity of antisocial problems and callous-unemotional traits.</u>

Voxelwise relationship with antisocial problems

Ten samples from 9 studies were included in this meta-analysis (see Table 2). Therelationship between brain response (at a whole-brain level) and severity of antisocial problems was assessed for 857 subjects from 6 samples related to the acute threat response domain, 3 to social cognitions, 1 to reward processing. The mean age was 25 years old (ranging from 10-39.8),with majority of samples being represented by adults (k=6). Approximately 57% of individuals in samples were males (ranging from 0-100%).

The main meta-analysis was performed across task domains due to the small sample size per task domains. Meta-analysis on dimensional studies assessing whole-brain correlates ofantisocial problems revealed significant negative relationships with the anterior thalamic nuclei/mammillary body (x=0, y=-10, z=-4; SDM-Z = -3.13; Cluster size = 39; p=0.0008) and the right amygdala/parahippocampal gyrus (x=24, y=-2, z=-28; SDM-Z = -3.01; Cluster size = 27;

p=0.0013). These results did not survive the FWER correction (p<0.05). Main peaks showed low between-study heterogeneity (I^2= 1.91-3.26). Funnel plots suggested that none of the results were driven by small or noisy studies, and the test for potential publication bias was not statistically significant (p= 0.543-0.924). Furthermore, the anterior thalamic nuclei (p=0.001) and the right amygdala (p=0.0007) remained statistically significant adjusting for CU traits. Due to the small sample size, no other subanalysis were performed.

Table 3. Results of the meta-analyses of whole-brain fMRI studies on neural correlates of the antisocial spectrum.

Contrast Results	L/R	*MNI* Coordinates	*Z value (a)*	*P Value (b)*	No. of voxels (c)	Breakdown (No. of voxels) (c)
A. Acute Threat Response (k=26)						
Healthy Controls > CP/ASPD						
dACC	R	8, 40, 20	-3.27	0.0005	277	R ACC (80); L mSFG (54); L ACC (108)
SMA	L	-4, 18, 46	-3.18	0.0007	136	L SMA (69); L MCC (21); R MCC (20)
MOG	R	24, -88, 10	-3.38	0.0003	120	R MOG (72); R SOG (20)
aInsula	L	-36, 22, 8	-3.28	0.0005	101	L Insula (60); L IFG triang (34)
ITG	L	-48. -10, -28	-3.12	0.0009	53	L ITG (46)
MOG	L	-32, -88, -2	-3.21	0.0006	40	L MOG (30)
dlPFC	R	48, 30, 34	-3.28	0.0005	36	R dlPFC (36)
IPG	L	-48, -50, 52	-3.06	0.0011	31	L IPG (31)
SMA	R	60, -46, 28	-2.96	0.0015	12	R SMA (12)
B. Punishment Processing (k=17)						
CP/ASPD > Healthy Controls						
Lobule IV (Hemispheric)	L	-24, -34, -30	3.12	0.0009	31	Lobule IV (23)
Midbrain Tegmentum	L	-18, -28, -28	2.74	0.0031	11	Midbrain Tegmentum (11)
Healthy Controls > CP/ASPD						
Premotor Cortex (BA 6)	L	-44, 6, 46	-3.44	0.0002	54	Premotor Cortox (50)
C. Reward Processing (k=17)						
No significant results	-	-	-	-	-	-
D. Social Cognition (k=22)						
CP/ASPD > Healthy Controls						
Putamen	L	-22, 12, -8	3.93	0.00004	176	L Putamen (85); BA 48 (37)
Precuneus	R	4, -60, 20	2.95	0.0016	103	R Precuneus (49); L Precuneus (24)
mPFC	L	-2, 52, 8	2.82	0.0024	90	L mPFC (72)
dlPFC	L	-16, 14, 60	3.12	0.00091	61	L dlPFC (42); L SMA (11)
dlPFC	R	24, 22, 54	3.01	0.0013	56	R dlPFC (47)
FF Gyrus	R	28, -86, -8	2.93	0.0017	18	R Fusiform Gyrus (18)
Rolandic Operculum	R	42, -18, 16	2.75	0.0031	14	Rolandic Operculum (10)
Crus I	R	26, -68, -32	2.66	0.0039	13	Crus 1 (10)
Healthy Controls > CP/ASPD						
MCC	R	8, -16, 46	-2.93	0.0017	90	R MCC (65); L MCC (18)
Lingual Gyrus	R	6, -76, -12	-2.93	0.0017	34	R Lingual Gyrus (17)
Hippocampus	L	-28, -22, -16	-2.9	0.0019	32	L Hippocampus (25)
MOG	L	-42, -78, 4	-2.96	0.0015	20	L MOG (17)
IFG triang.	R	48, 20, 0	-2.8	0.0025	18	R IFG (10)
FF Gyrus	L	-42, -56, -20	-2.73	0.0032	12	L FF Gyrus (11)
E. Cognitive Control (k=16)						
Healthy Controls > CP/ASPD						
Premotor cortex BA 6	L	-42, -4, 54	-3.31	0.00048	131	Premotor cortex BA 6 (131)
Lobule IV (Hemispheric)	L	-26, -72, -24	-2.85	0.0022	80	L Lobule VI (61); L Crus 1 (19)
aInsula	L	-38, 10, -4	-3.14	0.00084	40	L aInsula (37)
MTG	R	60, -14, -10	-2.91	0.0018	40	R MTG (31)
Crus 1	R	36, -60, -30	-2.84	0.0023	30	R Crus 1 (19); R Lobule VI (Hemisph.)(11)
vlPFC	R	38, 48, 0	-2.83	0.0023	27	R vlPFC (19)
SMG	L	-58, -40, 26	-2.79	0.0026	12	SMG (10)
Dimensional studies - Severity of Antisocial problems (k=13)						
Negative Association						
aThal./Mamm.	-	0, -10, -4	-3.13	0.00089	39	Anterior thalamic nuclei; Mammillary Bodies (32)
Amyg./Parahipp.	R	24, -2, -28	-3.01	0.00131	27	Parahippocampal gyrus; Amygdala (19)
Dimensional studies - Severity of Callous-unemotional traits (k=15)						
Negative Association						
Superior Temporal Gyrus	R	40, 10, -26	-3.77	0.00008	190	STG (117); MTG (62)

Note.k = number of samples; ; L = Left; R = Right; ACC = Anterior Cingulate Cortex; AG = Angular Gyrus; SFG = Superior Frontal Gyrus; mSFG = Medial Superior Frontal Gyrus; mPFC = Medial Prefrontal Cortex; SMG = Supramarginal Gyrus; IPL = Inferior Parietal Lobule; MOG = Middle Occipital Gyrus; SOG = Superior Occipital Gyrus; aInsula = Anterior Insula; pInsula = Posterior Insula; IFG Triang = Triangular part of the Inferior Frontal Gyrus; ITG = Inferior Temporal Gyrus; MTG = Middle Temporal Gyrus; SMA = Supplementary Motor Area; MCC = Median Cingulate Cortex; MFG = Middle Frontal Gyrus; IPG = Inferior Parietal Gyris; PreC = Precentral Gyrus; PCC = Posterior Cingulate Cortex; MCC = Median Cingulate Gyrus; Rolandic Operc = Rolandic Operculum; vlPFC = ventro-lateral PFC; LG = Lingual Gyrus; FF Gyrus = Fusiform Gyrus;aThal/Mamm. = anterior thalamic nuclei/Mammillary Bodies; Amyg./Parahipp. = Amygdala/Parahippocampal gyrus; STG = Superior Temporal Gyrus.

(a) Voxel probability threshold: p = 0.005 uncorrected; (c) Cluster extent threshold: 10 voxels. Regions with less than 10 voxels are not reported in the cluster breakdown.

* Remained statistically significant after correcting threshold (TFCE) of p<0.05

Voxelwise relationship with callous-unemotional traits

Twelve samples from 11 studies were included in this meta-analysis (see Table 3). The relationship between brain response and severity of CU traits was assessed for 1009 subjects from 5 samples with fMRI task related to acute threat response domain, 2 to punishment processing, 1 to reward processing and 4 to social cognitions. The mean age was 24.75 years old (ranging from 10.05-39.8), with half of samples being represented by adults (k=6). Approximately 69% of individuals in samples were males (ranging from 0-100%).

The main meta-analysis was performed across task domains due to the small sample size per task domains. Meta-analysis on dimensional studies assessing voxelwise association with CU traits revealed significant negative association with the right superior temporal gyrus (x=40, y=8, z=-26, SDM-Z=-3.77, p=0.00008). This peak did not survive the FWER correction ($p<0.05$). The relationship between superior temporal gyrus and CU traits showed small between study heterogeneity (I^2=4.94%), funnel plot suggest that this is not driven by small or noisy study and egger's test was statistically non-significant (p=0.813). Due to the small sample size, no subanalysis were performed.

Relationship between Amygdala and antisocial problems

Twenty-three samples from 21 studies were included in this meta-analysis (see Table 3). Overall, the relationship between amygdala and severity of antisocial problems was assessed for 1807 subjects from 13 samples with a fMRI task related to the acute threat response domain, 1 to the punishment processing and 9 to social cognitions. The mean age was 21.18 years old (ranging from 10.8-44.6), with majority of samples being represented by adults (k=13). Approximately 74% of individuals in samples were males (ranging from 0-100%).

Main meta-analysis (across domains) and domain-specific meta-analyses (i.e. acute threat response and social cognitions) revealed no significant relationship between severity of antisocial behaviors and left/right amygdala reactivity. The left and right amygdala ROIs showed small to moderate between-study heterogeneity (I^2=30.15 & I^2=15.84, respectively). Subanalyses revealed no significant effects of moderators.

Relationship between the Amygdala and callous unemotional traits

Thirty-one samples from 29 studies were included in this meta-analysis (see Table 3). Overall, the relationship between the severity of CU traits and amygdala reactivity was assessed for 2264 subjects from 14 samples with a task related to the acute threat response domain, 6 to the punishment processing, 10 to social cognitions and 1 to reward processing. The mean age was 20.32 years old (ranging from 10.8-44.6), with majority of samples being represented by children/adolescent (k=17). Approximately 79% of individuals in samples were males (ranging from 0-100%).

Main meta-analysis (across domains) and domain-specific meta-analyses (i.e. acute threat response and social cognitions) revealed no significant associations between CU traits and amygdala reactivity. The left and right amygdala ROIs showed small between-study heterogeneity (I^2=1.71 & I^2=2.77, respectively). Subanalyses revealed no significant effects of moderators.

Discussion

The current study aimed to better identify the neural deficits of CP/ASPD subjects. First, inorder to better describe brain differences between healthy subjects and CP/ASPD, we have performed coordinate-based case-control meta-analyses on whole brain studies according to five main neurocognitive pillars (i.e. acute threat response [k=26, n=517], reward processing [k=17, n=282], punishment processing[k=17, n=276], social cognitions [k=22, n=461] and cognitive control [k=16, n=320]) as well as a case-control meta-analysis on amygdala region-of-interest [k=23, n=701]. Second, to better describe the dimensional relationships between brain-behaviors underlying CP/ASPD subjects (i.e. Callous/unemotional traits/Factor 1 and antisocial problems/Factor 2), we have executed meta-analyses on dimensional studies assessing the relationship between whole-brain response and severity of antisocial problems (k=10, n=857) andseverity of callous-unemotional traits (k=12, n=1009) as well as dimensional meta-analyses on amygdala region-of-interest and severity of antisocial problems (k=23, n=1807) and callous/unemotional traits (k=31, n=2264). To our knowledge, this is the largest study to date, andthe first to investigate deficits in neural functioning of CP/ASPD subjects by considering these

five neurocognitive domains. Our meta-analysis revealed that individuals on the *antisocial pathology* spectrum manifested significant neurofunctional deficits across four of the five domains when using a liberal statistical threshold (i.e. p>0.005 uncorrected, minimal cluster size > 10 voxels), but none when using a conservative one (i.e. p>0.05 FWE-corrected). That being said, the most prominent deficits observed were found in acute threat response, social cognitions and cognitive control, reflecting the importance of these neurocognitive domains as features of CP/ASPD individuals. We found no evidence of the moderation effect of CU traits on limbic system in response to threat, (Blair et al., 2014; L. W. Hyde et al., 2013; E. Viding, N. M. Fontaine, et al., 2012), and no significant differences between CP/ASPD and HC during reward processing were detected. However, we did observe limbic hypo-reactivity in response to threatening stimuli, hyper-reactivity of brain regions involved in self-other differentiation and hypo-activations duringcognitive control tasks. Finally, contrarily to the widely held assumption in research on CP/ASPDsubjects (R. J. R. Blair et al., 2014; L. W. Hyde et al., 2013; E. Viding, N. M. Fontaine, et al., 2012), we did not observe amygdala deficits in these individuals, though a negative relationship was observed with callous/unemotional traits (in the case-control ROI meta-analysis), and with severity of antisocial problems (in dimensional voxelwise meta-analysis).

During social cognition tasks, individuals with CP/ASPD exhibited important alterations inneural functioning in several regions such as the medial PFC and dorsolateral PFC, Precuneus, inferior frontal gyrus, middle cingulate cortex, hippocampus, insula and inferior frontal gyrus, putamen and cerebellar regions, which supports clinical observations suggesting significant socio-emotional impairments in CP/ASPD individuals (Chapman, Gillespie, & Mitchell, 2018; Marsh & Blair, 2008; Oliver, Barker, Mandy, Skuse, & Maughan, 2011). Also, CU traits did not moderate these results. Deficits in several of these regions follow previous meta-analyses on regional grey matter volume in antisocial populations (putamen, insula, fusiform gyrus, medialPFC extending to the anterior and middle portion of the cingulate cortex) (Aoki, Inokuchi, Nakao,& Yamasue, 2013; Rogers & De Brito, 2016) and overlap with brain regions underlying the neural model of morality and antisocial behaviors proposed by Raine & Yang (A. Raine & Y. Yang, 2006). While the medial PFC, and precuneus are largely involved in processes implicated inself-reflection and

theory of mind (Molenberghs, Johnson, Henry, & Mattingley, 2016; M. Schurz,Radua, Aichhorn, Richlan, & Perner, 2014), the hippocampus and the dorsolateral PFC play a major role in episodic memory (i.e. autobiographical) (Spreng & Mar, 2012; Tulving & Markowitsch, 1998; Vargha-Khadem et al., 1997) and executive functions (Barbey, Koenigs, & Grafman, 2013), respectively. It is well known that CP/ASPD individuals show important deficitsin social cognition, specifically regarding the recognition and representation of emotional states ofothers (Chapman et al., 2018; Marsh & R. J. R. Blair, 2008; Mellentin, Dervisevic, Stenager,Pilegaard, & Kirk, 2015). As such, our results suggest that the impairments of CP/ASPD subjects regarding social cognition may arise from inefficient functioning of brain regions involved in the mediation between self/other perspectives (i.e., medial PFC & Precuneus) and in emotional episodic memory (i.e. hippocampus). Although the putamen is frequently considered as a motor structure (G. E. Alexander, DeLong, & Strick, 1986), recent findings suggest that this region may also be involved in the interaction between memory, action and reward (Guo, Schmitz, Mur, Ferreira, & Anderson, 2018; Koster, Guitart-Masip, Dolan, & Düzel, 2015; Sadeh, Shohamy, Levy, Reggev, & Maril, 2011). It can be argued that the alterations observed in the putamen underlie impairmentsin making prosocial decisions during social interactions (e.g., proneness to selfish/self-benefiting decisions at the cost of losses of others) in CD/ASPD individuals (Eimontaite et al., 2019; Schreuders, Klapwijk, Will, & Güroğlu, 2018). See Figure 2 for functional characterization of our results, based on meta-analytical evidence.

During acute threat response tasks, CP/ASPD subjects manifested decreased activations inthe anterior and middle cingulate cortex, anterior insula, and dorsolateral PFC. These brain regionsare known to be largely implicated in emotional processing (Fan, Duncan, de Greck,& Northoff, 2011; Fusar-Poli et al., 2009; Kurth, Zilles, Fox, Laird, & Eickhoff, 2010; Lamm, Decety, & Singer, 2011). More specifically, whereas the dorsal portion of the anterior cingulate cortex and the dorsolateral PFC have been associated with learned emotional responses to threat stimuli and (re-)appraisal of threat (Etkin, Büchel, & Gross, 2015; Hartley & Phelps, 2010; Mechias, A. Etkin, & Kalisch, 2010), the insula is known to be involved in the integration of the interoceptive state, but also in predicting aversiveness of stimuli (Aupperle Robin & Martin,2010) (See Figure 2 for functional characterization of our results, based on meta-analytical evidence). The alterations observed in

the anterior insula are consistent with results of previous (structural and functional) neuroimaging meta-analyses of people with disruptive behaviour disorders which all reported alterations in this brain region (Alegria et al., 2016; Aoki et al., 2013; Noordermeer et al., 2016; Poeppl et al., 2019; Rogers & De Brito, 2016). Contrarily to our observations, Poeppl et al.'s (Poeppl et al., 2019) meta-analysis showed a hyperactivation of the anterior insula in psychopaths. However, this was mostly associated with functional characterization of cognitive rather than emotional subdomains. As such, these results suggest that the anterior insula alterations could be a potential neural marker of abnormal emotional processing in CP/ASPD individuals, specifically in response to acute threat stimuli. As previously suggested,individuals with high propensity for aggression (i.e., CP/ASPD subjects) are thought to exhibit increased acute threat responsiveness (Blair et al., 2018; Blair, 2016). Though, during acutethreat response tasks, we observed no significant limbic hyperactivations in CP/ASPD individualsin comparison to HC. In fact, we rather observed significant hypoactivations in several regions thatwere not moderated by CU traits, contrasting with the dual pathway hypothesis (Blair et al., 2014; Hyde et al., 2013; Viding, Fontaine, et al., 2012). It is worth mentioningthat no direct between-group difference in amygdala activation was detected in the current case- control fMRI meta-analyses, although functional deficits were observed in a previous meta- analysis across neurocognitive domains in psychopathic individuals (Poeppl et al., 2019). Though,no amygdala abnormalities were observed in Alegria et al.'s (Alegria et al., 2016) meta-analysis on hot executive function and on emotional tasks. Likewise, discrepant results have been observedin structural imaging studies examining amygdala volumes in antisocial populations (Aoki et al., 2013; Noordermeer et al., 2016; Rogers & De Brito, 2016). Furthermore, in our ROI meta-analysis, CP/ASPD and HC did not statistically differ on amygdala reactivity. However, a meta-regression revealed significant negative associations between levels of callous-unemotional traits and the right amygdala activity. Albeit only observed in the ROI meta-analysis, this result isconsistent with past theories indicating that the amygdala hypoactivity represents a biomarker of CU traits in children with CP (Blair et al., 2014; Hyde et al., 2013; Viding et al., 2012).

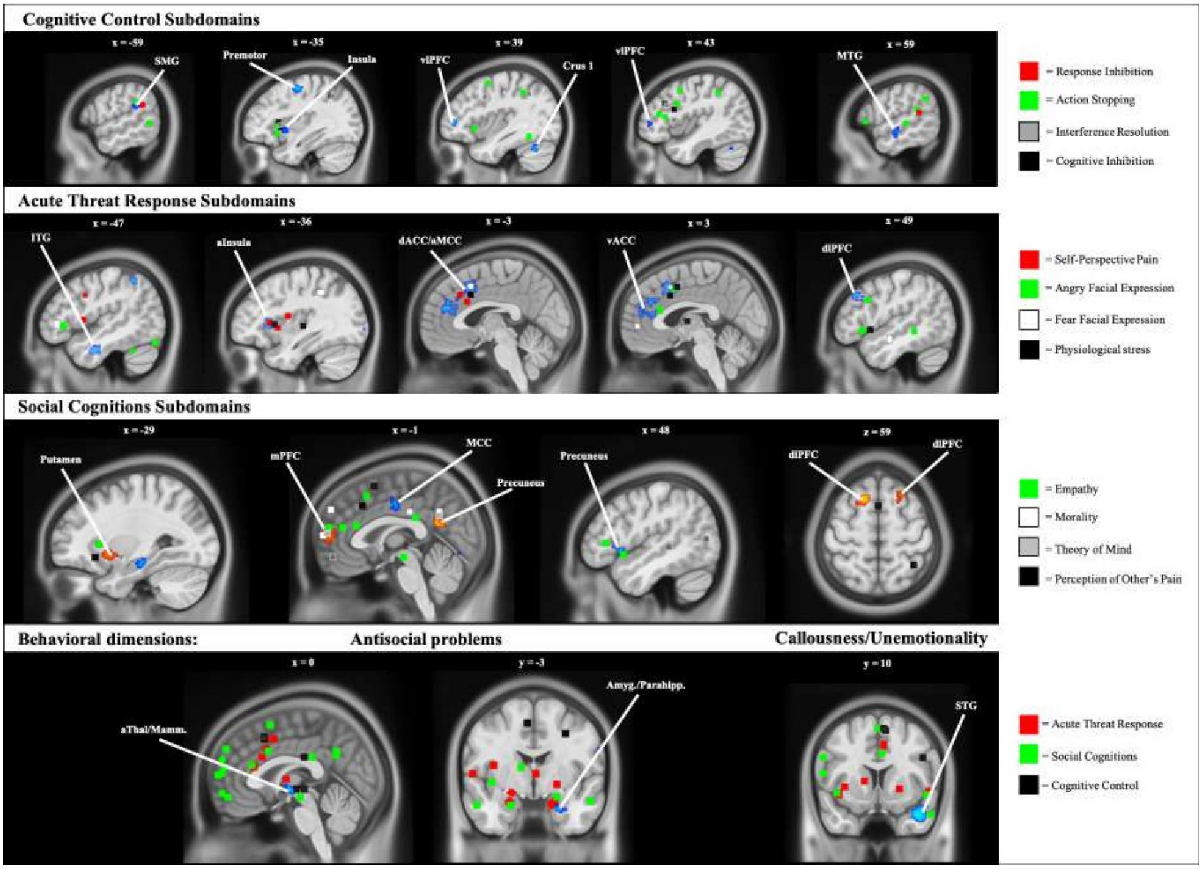

Figure 2. Meta-analytical evidence of functional brain correlates of the antisocial spectrum with spatial functional characterization of the 3 main domains (i.e. Acute Threat Response, Social Cognition and Cognitive Control) and 12 subdomains based on nonexhaustive meta-analytical findings: **Cognitive Control Subdomains:** Response Inhibition (Red: Hung, Gaillard, Yarmak, & Arsalidou, 2018), Action Stopping (Green: Rae, Hughes, Weaver, Anderson, & Rowe, 2014)), Interference Resolution (Grey: (Nee, Wager, & Jonides, 2007)), Cognitive Control (Black: (Hung et al., 2018)); **Acute Threat Response Subdomains:** Self-perspective Pain (Red:(Jauniaux, Khatibi, Rainville, & Jackson, 2019)), Angry Facial Expression (Green: (Fusar-Poli et al., 2009)), Fear Facial Expression (White: (Fusar-Poli et al., 2009)), Physiological Stress (Black, (L. Kogler et al., 2015)).**Social Cognitions Subdomains:** Empathy (Green: (Bzdok et al., 2012)), Morality (White: (Bzdok et al., 2012)); Theory of Mind (Grey: (Bzdok et al., 2012)), Perception of Other's Pain (Black: (J. Jauniaux et al., 2019)). **Antisocial problems and Callousness/unemotionality dimensions:** Acute Threat Response (Red), Social Cognition (Green), Cognitive Control (Black). SMG = Suparamarginal Gyrus; vlPFC = Ventrolateral Prefrontal Cortex; MTG = Middle Temporal Gyrus; ITG = Inferior Temporal Gyrus; aInsula = Anterior Insula; dACC/aMCC = Dorsal Anterior CingulateCortex/Anterior Middle Cingulate Cortex; vACC = ventral ACC; dlPFC = Dorsolateral PFC; mPFC = median PFC; aThal/Mamm. = anterior thalamic nuclei/Mammillary Body; Amyg./Parahipp. = Amygdala/Parahippocampal gyrus; STG = Superior Temporal Gyrus.

The meta-analysis on cognitive control revealed that CP/ASPD subjects, in comparison to HC exhibited reduced activation in premotor cortex, anterior insula, ventrolateral PFC and cerebellar regions. These brain regions are key areas of cognitive control (Aron, Robbins, & Poldrack, 2014; Weidong Cai, Ryali, Chen, Li, & Menon, 2014; Nee et al., 2007; C. L. Rae et al.,2014) . In fact, it has been found that the right ventrolateral PFC plays a critical role in motor inhibition in healthy individuals, while the anterior insula is involved in the processing of the significance (i.e. motivational and affective) of inhibitory failure (Hester, Fassbender, & Garavan,2004; C.-S. R. Li, Yan, Sinha, & Lee, 2008; Padmala & Pessoa, 2010; Ramautar, Slagter, Kok, &Ridderinkhof, 2006). Alegria et al.'s (Alegria et al., 2016) prior meta-analysis also observed reduced activation in the insula together with temporal and striatal regions. The findings furthermore resonate with previous structural meta-analyses on grey matter volume in CP/ASPD that showed volumetric deficits in the insula (Aoki et al., 2013; Noordermeer et al., 2016; Rogers & De Brito, 2016) and ventrolateral PFC (Noordermeer et al., 2016; Rogers & De Brito, 2016), which suggest potential neurobiological markers of cognitive control deficits. Importantly, considering that CP/ASPD subjects display more errors in prepotent response inhibition tasks (i.e. incongruent trials of the Stroop task and No-Go trials of the Stop-Signal task)(Chamberlain, Derbyshire, Leppink, & Grant, 2016; Zeier, Baskin-Sommers, Hiatt Racer, & Newman, 2012), our results not only suggest that CP/ASPD individuals display deficits in motor inhibition (right ventrolateral PFC), but the inhibitory failures are also not processed as being affectively and motivationally significant (anterior insula), which results in difficulties in learningfrom response-inhibition mistakes.

Furthermore, it has been suggested that reinforcement-based decision-making (i.e. punishment and reward processing) is deficient in CP/ASPD subjects (Blair et al., 2018; Byrd et al., 2014). The meta-analysis on punishment processing tasks, revealed small but nevertheless significant differences. CP/ASPD subjects showed increased activations in the hemispheric lobule IV and midbrain tegmentum, and decreased activations in the premotor cortexBA6, in comparison to HC. However, it should be noted that previous meta-analyses on punishment processing in healthy subjects did not observe activation abnormalities in regions detected in our meta-analysis (Dugré et al., 2018; Knutson & Greer, 2008; Liu etal., 2011; Oldham et al., 2018). In view

of the small number of studies on punishment processing, results should be interpreted cautiously. Nonetheless, there is a clear need for future studies on punishment processing in this specific population to support literature reviews suggesting punishment processing deficits in CP/ASPD subjects (Blair et al., 2018; Byrd et al., 2014).Regarding reward processing, we found no significant difference between CP/ASPD subjects. Asindicated by a recent literature review on neuropsychological and fMRI studies, primary deficits inreward processing are inconclusive as studies have produced conflicting results (Byrd et al., 2014). Since it is largely known that dysfunction in reward processing is associated with substancemisuse (Luijten, Schellekens, Kühn, Machielse, & Sescousse, 2017), it is plausible that hyposensivity to reward characterize only particular subgroups of CP/ASPD individuals (i.e. thosewith a comorbid substance use problems). Future studies are thus needed to clarify the role of reward processing in CP/ASPD subjects.

Finally, through voxelwise meta-analyses on dimensional studies assessing brain-behavior relationships, we observed that the amygdala was negatively associated with severity of antisocialbehaviors but not severity of callous-unemotional traits. Furthermore, this relationship remained statistically significant adjusting for CU traits, suggesting that CU traits did not suppress the relationship between antisocial behaviors and the amygdala reactivity. The current neurobiologicalmodels of CP/ASPD posit that the amygdala hypo-reactivity is closely related to high callous-unemotional traits (Blair et al., 2014; Hyde et al., 2013; Viding, Fontaine, et al., 2012). Through arecent systematic review, some authors have suggested that the relationship between CU traits andemotional hyporeactivity is more complex than previously thought, as some subjects with low CUmay also show reduced emotional responsiveness (Northam & Dadds, 2020). That said, future studies should investigate the mediation effect of several factors that could alter the CU-amygdala reactivity including the attentional load, severity of antisocial behaviors, stimuli type (e.g. facial/non-facial stimuli), tasks instructions (e.g. implicit/explicit), the socio-emotional context (e.g. self/other tasks). However, it should be noted that in our meta-analysis on dimensional studies,the severity of antisocial problems was principally assessed by the Factor 2 – impulsivity/antisocialof psychometric scales measuring psychopathy (e.g. PCL-R). This could have led in inflating results from antisocial- yet psychopathic traits, rather than antisocial problems specifically.

The current meta-analysis showed that subjects on the antisocial spectrum had several neurofunctional deficits within four distinct neurocognitive domains. In fact, these findings provide critical insights on the neural functioning of antisocial subjects in different cognitive and emotional contexts. Moreover, our results were not influenced by CU traits, age and fMRI characteristics; no potential publication bias was observed. Notwithstanding the significant results of this meta-analysis, there are limitations that need to be acknowledged. First, the methodology used is basedon peak coordinates and their effect size rather than raw statistical brain maps, thus reducing the results accuracy (J Radua et al., 2012). Second, we used an uncorrected threshold of $p<0.005$. Although previous studies have shown that this threshold adequately controls the false positive rate(J Radua et al., 2012), it remains an approximation of corrected results. Following this, when usinga more conservative statistical threshold ($p<0.05$ FWE-corrected), the meta-analyses yielded no significant results. This could be due to several reasons: a) case-control studies generally includeda small number of cases (mean size per study of 19 *versus* 101 in dimensional studies) and b) the heterogeneity that was not captured in this meta-analysis (e.g. subgroups), could have reduced ourability to observe results surviving conservative statistical thresholding. Although our liberal statistical threshold is generally used in fMRI literature (Lieberman et Cunningham, 2009) and in meta-analyses on neuroimaging studies (Radua et al., 2012a), we have reported results from both statistical thresholding to reduce the bias toward studying large rather than small effects in fMRI results and move beyond the *p-value* (Lieberman et Cunningham, 2009). The results reported in this meta-analysis are general trends from a heterogeneous population, therefore future studies should seek to replicate our results within well-defined homogeneous groups of antisocial subjects rather than developing theoretical framework solely based on p-value. Third, we included the whole spectrum of antisociality ranging from those with antisocial problems to those meeting the criteria for CD/ASPD. Since there are too few studies that included only participants meeting clinical diagnosis of CD/ASPD, it was not possible to examine directly the potential specific task-related neural functioning within those meeting clinical criteria of CD/ASPD only. We didnonetheless perform a subanalysis to investigate whether our results were associated with percentage of samples with CD/ASPD. Future studies should aim to include more systematically the percentage of their

participants that meet clinical criteria of CD/ASPD. Fourth, it would have been optimal to examine the potential moderation effect of other important psychopathological factors such as substance use, psychiatric comorbidities (e.g. anxiety/depression), as well as specific subtypes of antisocial problems (e.g. aggression/rule-breaking behaviors, (R. E. Tremblay,2010) or reactive/proactive aggression, (A. Raine et al., 2006)). However, this was not feasible due to differences in psychometric scales across studies or due to the low quality of reporting of clinicaldata. Fifth, the number of samples in the reward and punishment processing meta-analyses was relatively small. Consequently, the results of these analyses should be interpreted with restraint. As anticipation and outcome of punishment processing are two distinct temporal phases with similar yet different networks (J. R. Dugré et al., 2018; Oldham et al., 2018), it was not possible to distinguish both phases in the present meta-analysis due to the small number of studies. Hence, more studies are necessary to test the hypothesis of deficits in encoding unexpected punishment and integrating cue-stimulus association in CP/ASPD individuals, with confidence (R. Blair et al.,2018; A. L. Byrd et al., 2014). Finally, while the use of a POMP score has permit us to study linear relationship between phenotypes (e.g. antisocial behaviors and CU traits) and neurobiological markers, it is worth noting that there may be discrepancies between psychometric scales made forclinical *versus* community sample. Next meta-analyses should be aware of this and seek to performsubanalyses on scale-specific POMP scores.

Conclusion

To our knowledge, this is the first and largest meta-analysis of fMRI studies on the neural processes of CP/ASPD individuals in clearly distinct neurocognitive domains. The meta-analysis shows that the most prominent deficits were observed during Acute threat response (e.g. dorsal portion of the anterior cingulate cortex, inferior parietal lobule, anterior insula and dorsolateral PFC) and Social cognition subdomains (e.g. Putamen, middle to posterior cingulate cortex/precuneus, medial PFC, hippocampus). Moreover, the present meta-analysis offers potentialneural markers of CP/ASPD, which do not appear to be moderated by CU. Growing evidence shows large heterogeneity among CP/ASPD individuals (Fanti, 2018; Raine et al., 2006; Tremblay, 2010). Although emphasis has been placed on CU traits as being crucial for

distinguishing between subgroups, the neural alterations in other subgroups of CP/ASPD such as those with aggressive *versus* non-aggressive rule breaking profiles (Tremblay, 2010), reactive *versus* proactive aggressive behavior (Raine et al., 2006) or those with high levels of anxiety and depressive traits (Dugré et al., 2019; Fanti, 2018) remains understudied.

TROISIÈME ARTICLE

Meta-analytical Transdiagnostic Neural Correlates in common Pediatric PsychiatricDisorders

Jules R. Dugré*, MSc [1,2], Simon B. Eickhoff [3,4] & Stéphane Potvin*, PhD [1,2]

[1] Research Center of the Institut Universitaire en Santé Mentale de Montréal, Montreal, Canada[2] Department of Psychiatry and Addictology, Faculty of medicine, University of Montreal, Montreal, Canada
[3] Institute of Neuroscience and Medicine (INM-7), Jülich, Germany.
[4] Institute for Systems Neuroscience, Heinrich Heine University, Düsseldorf, Germany.

Déclaration de l'étudiant

Je déclare être l'auteur principal de cet article. J'ai été impliqué dans la conception de l'étude, mené la revue systématique, conduit les analyses statistiques, interprétés les résultats et écrit la premièreversion et la version finale de l'article. Mon directeur de thèse, Stéphane Potvin ainsi que Dr. Simon Eickhoff, ont conseillé mon travail de recherche, suggérés des corrections et ont approuvé la version finale de l'article.

Abstract

In the last decades, neuroimaging studies have attempted to unveil the neurobiological markers underlying pediatric psychiatric disorders. Yet, the vast majority of neuroimaging studies still focus on a single nosological category, which limit our understanding of the shared/specific neural correlates between these disorders. Therefore, we aimed to investigate the transdiagnostic neural correlates through a novel and data-driven meta-analytical method. A data-driven meta-analysis was carried out which grouped similar experiments' topographic map together, irrespectively of nosological categories and task-characteristics. Then, activation likelihood estimation meta- analysis was performed on each group of experiments to extract spatially convergent brain regions. One hundred forty-seven experiments were retrieved (3124 cases compared to 3100 controls): 79 attention-deficit/hyperactivity disorder, 32 conduct/oppositional defiant disorder, 14 anxiety disorders, 22 major depressive disorders. Four significant groups of experiments were observed. Functional characterization suggested that these groups of aberrant brain regions may be implicatedinternally/externally directed processes, attentional control of affect, somato-motor and visual processes. Furthermore, despite that some differences in rates of studies involving major depressivedisorders were noticed, nosological categories were evenly distributed between these four sets of regions. Our results may reflect transdiagnostic neural correlates of pediatric psychiatric disorders, but also underscore the importance of studying pediatric psychiatric disorders simultaneously rather than independently to examine differences between disorders.

Introduction

Common child psychiatric disorders generally include Attention-deficit/hyperactivity disorder (ADHD), Conduct/Oppositional Defiant Disorder (CD/ODD), anxiety disorders (ANX) and depressive disorders (DEP), which affect approximately 3.4%, 5.7%, 6.5% and 2.6% of children and adolescents in the world, respectively (Polanczyk, Salum, Sugaya, Caye, & Rohde, 2015). Indeed, these are the most prevalent disorders in childhood, with age of onset being earlier than other disorders such obsessive compulsive disorder, substance use disorder and schizophrenia (Solmi et al., 2021). Importantly, evidence suggests that comorbidity between thesefour pediatric psychiatric disorders is the norm rather than the exception. In fact, about half of children with ADHD, CD/ODD, ANX or DEP will receive an additional psychiatric disorder (comorbid condition) in the following years (Angold et al., 1999; Bird et al., 2006; Boylan, Vaillancourt, Boyle, & Szatmari, 2007; Costello et al., 2003; Nock, Kazdin, Hiripi, & Kessler, 2006a; Park et al., 2017; Weller, Blanford, & Butler, 2018; Wichstrøm et al.,2012). Although these four diagnostic entities show large comorbidities in children and adolescent,theoretical pathophysiological models taking into account this high level of comorbidity remain largely limited (Rhee, Lahey, & Waldman, 2015).

Recently, there has been a growing body of literature suggesting that several genetic (Cerdá, Sagdeo, Johnson, & Galea, 2010; Consortium, 2013; Network et al., 2015; Sullivan, Daly, & O'donovan, 2012; Walters et al., 2018) and environmental risk factors (Cerdá et al., 2010; Keyes et al., 2012; Tackett et al., 2013) may be non-specific given that they increase the riskfor a plurality of psychiatric disorders. Likewise, meta-analyses of structural and functional magnetic resonance imaging studies have shown that adult with psychiatric disorders may share several neurobiological deficits (Gong et al., 2019; Goodkind et al., 2015; Janiri et al., 2020; McTeague et al., 2017; McTeague et al., 2020). For instance, during cognitive control tasks, transdiagnostic neural signatures in adults with psychiatric disorders (e.g., schizophrenia, bipolar, unipolar depression, anxiety and substance use) may involve the fronto-insular cortex (FIC), the dorsolateral prefrontal cortex and the dorsal anterior cingulate cortex (dACC) to anterior midcingulate/pre-supplementary motor area (aMCC/pre-SMA) and inferior parietal lobule

(McTeague et al., 2017). Similarly, during emotion processing, transdiagnostic features may include deficits in the FIC, amygdala, thalamus and dorso- and ventro-medial PFC (McTeague et al., 2020). Although some differences have been noticed between patients with and without psychotic disorders (McTeague et al., 2017; McTeague et al., 2020), the search for shared/specific neurobiological markers is of great interest for our understanding of the psychophysiological mechanisms underlying psychiatric disorders.

In functional neuroimaging literature in childhood/adolescents, studies that aimed to uncover the specific/transdiagnostic neurobiological markers have been scarce. Indeed, a large majority oftask-based fMRI studies has focused on a single psychiatric disorder, therefore limiting our abilityto identify common/specific neurobiological markers. Additionally, recent transdiagnostic fMRI meta-analyses have excluded disorders which predominantly emerge in childhood/adolescence such as ADHD and CD/ODD (McTeague et al., 2017; McTeague et al., 2020). Nevertheless, pastmeta-analyses and reviews on ADHD (Cortese et al., 2012; Dickstein, Bannon, Xavier Castellanos,& Milham, 2006; Hart, Radua, Mataix-Cols, & Rubia, 2012; Hart, Radua, Nakao, Mataix-Cols, &Rubia, 2013; Lei et al., 2015; Samea et al., 2019), CD/ODD (Alegria et al., 2016; Philip Deming & Michael Koenigs, 2020; Jules R Dugré et al., 2020; S. D. Noordermeer et al., 2016; Poeppl et al., 2019). ANX (Blackford & Pine, 2012; Etkin & Wager, 2007; Kolesar, Bilevicius, Wilson, & Kornelsen, 2019; Madonna, Delvecchio, Soares, & Brambilla, 2019; Milani, Hoffmann, Fossaluza, Jackowski, & Mello, 2017; Pine, Guyer, & Leibenluft, 2008) and DEP (Delvecchio et al., 2012; Fitzgerald, Laird, Maller, & Daskalakis, 2008; J. Graham et al., 2013; Hamilton et al., 2012; Hulvershorn, Cullen, & Anand, 2011; Lai, 2014; Miller, Hamilton, Sacchet, & Gotlib, 2015; Palmer, Crewther, & Carey, 2015) seem to indicate qualitatively similar deficits in the anterior insula, medial and lateral prefrontal cortex, the amygdala and anterior to midcingulate cortex. Yet,there is a clear need for meta-analytical evidence of transdiagnostic neural correlates in children and adolescents. Although these results may provide substantial insight for our understanding of transdiagnostic brain alterations, classical meta-analytical approaches are prone to important biases. Indeed, authors' categorization of groups of interest, categorization of fMRI tasks and the choice of task contrast may significantly alter results. In comparison to the classical meta-analyticapproach which seeks to identify dysfunctional brain

regions in predefined groups of interest, reverse inference meta-analytical method rather aims to discover main dysfunctional brain regions in which some particular groups may be over/underrepresented. The latter approach may address the limitations of the classic approach by searching for common/specific neural correlates irrespective of the task-characteristics or nosological categories. To our knowledge, only one study has investigated transdiagnostic features across adult samples through a region-of-interest (ROI) reverse-inference meta-analytical method (Sprooten et al., 2017). Given that a single region may be implicated in a wide range of cognitive processes and that co-activation patterns are important in inferring mental processes, the use of a data-driven method (rather than a ROI approach) is crucial to examine transdiagnostic features. Here, we carried out a meta-analysis that primarily aimed to identify groups of aberrant brain regions across pediatric psychiatric disorders using a data-driven meta-analytical method. Results from past meta-analyses on adult samples (McTeagueet al., 2017; McTeague et al., 2020) and disorder-specific meta-analyses and reviews (Alegria et al., 2016; Blackford & Pine, 2012; Cortese et al., 2012; Philip Deming & Michael Koenigs, 2020; Dickstein et al., 2006; Dugré et al., 2020; Etkin & Wager, 2007; Hart et al., 2012; Hart et al., 2013; Hulvershorn et al., 2011; Kolesar et al., 2019; Lei et al., 2015; Madonna et al., 2019; Milani et al., 2017; Miller et al., 2015; Noordermeer et al., 2016; Pine et al., 2008; Poeppl et al., 2019; Samea et al., 2019) suggest that transdiagnostic features may be expected in FIC (anterior insula/vlPFC), medial and lateral prefrontal and the dorsal anterior and anterior midcingulate cortices. However, considering that deficits in the amygdala is systematically observed in past meta-analyses on adult ANX (Etkin & Wager, 2007; Kolesar et al., 2019) and DEP (Delvecchio et al., 2012; Fitzgerald et al., 2008; Graham et al., 2013; Hamilton et al.,2012; Hulvershorn et al., 2011; Lai, 2014; Miller et al., 2015; Palmer et al., 2015), but less extensively in CD/ODD (Alegria et al., 2016; Philip Deming & Michael Koenigs, 2020; Dugré et al., 2020; Noordermeer et al., 2016; Poeppl et al., 2019) and not found in ADHD (Cortese et al., 2012; Dickstein et al., 2006; Hart et al., 2012; Hart et al., 2013; Lei et al., 2015; Samea et al., 2019), we hypothesized that the former region would be more closely linked to ANXand DEP than the latter disorders.

Methods

Identification of included studies

Our search focused specifically on four diagnostic categories (i.e., ADHD, CD/ODD, ANX,DEP) since they are the most common psychiatric disorders in childhood and they show substantial comorbidity with each other (Angold et al., 1999; H. R. Bird et al., 2006; Boylan et al., 2007; Costello et al., 2003; Nock et al., 2006a; Park et al., 2017; Solmi et al., 2021; Weller et al., 2018; Wichstrøm et al., 2012). Given that meta-analyses and literature reviews on these disorders have been published recently, we extracted data from their reference lists of ANX (Kolesar et al., 2019; Madonna et al., 2019; Milani et al., 2017), DEP (Hulvershorn et al., 2011; Miller et al., 2015; Schmaal et al., 2020), CD/ODD (Dugré et al., 2020), ADHD (Samea et al., 2019). Inclusion criteria were: (1) original manuscript from a peer-reviewed journal, (2) task-based functional MRI studies, (3) use of a whole-brain methodology (i.e., studies using ROIs wereexcluded) irrespectively of the task constructs, (4) <18 years old participants meeting criteria for at least one of the following pediatric psychiatric disorder: (a) ADHD; (b) Disruptive disorder (CD/ODD); (c) ANX (i.e., Posttraumatic Stress Disorder, Generalized Anxiety Disorder, Social Anxiety Disorder) and/or (d) Unipolar Major Depressive Disorder. These inclusion criteria were followed to preserve an acceptable level of homogeneity within nosological categories. Effect of the disorder were extracted from fMRI studies, irrespectively of the direction (hypo/hyper activation) of the contrast, to create an aberrant activation map. Two experiments from the same study were considered as distinct if they included two different samples or two different fMRI tasks. Each experiment and sample's characteristics were manually annoted and categorized. Coordinates of experiments that were reported originally in Talairach stereotaxic space were converted into MNI (Montreal Neurologic Institute) space.

Neurobiologically-driven Meta-analytical procedure

Modeled Activation & Cross-Correlation Matrix (Step 1 & 2)

Modeled activation (MA) map was created for each experiment (2mm^3 resolution) (Figure1, Step 1). Each resulting MA map was converted into a 1D feature vector of voxel values (i.e. 2mm^3 grey

matter mask in MNI space) and concatenated together to form an experiment (*e*) by voxel matrix (*v*) (147 experiments x 226,654 voxels). Pairwise Spearman's rank correlation was performed between the 1D feature vector of each experiments to obtain spatial similarity betweenmaps (*e* by *e* symmetric correlation matrix) (Figure 1, Step 2).

Correlation-Matrix-Based Hierarchical Clustering (Step 3)

In order to extract data-driven groups of experiments that showed similar brain topographicmap, we performed a Correlation-Matrix-Based Hierarchical Clustering (CMHC) analysis, as previously used on meta-analytic data (Laird et al., 2015; Riedel et al., 2018). The CMHCwas carried out using correlation distance (1–*r*) (Figure 1. Step 2) and average linkage method. Weexamined the most optimal number of clusters using the silhouette and calinski-harabasz indices, variation of information & adjusted rand index for a range of 2 to 15 clusters (Eickhoff, Thirion, Varoquaux, & Bzdok, 2015) (See Supplementary Material). After having found the final number of meta-analytical grouping (MAGs), solutions with less than 10 experiments were considered as outliers and excluded from further analyses, given that analyses involving <10 experimentsdrastically increases the risk that a single experiment drives the results (Eickhoff, Nichols, et al., 2016). All these analyses were performed using Scikit-learn (version 0.21.3) in Python (version 3.7.4) (Pedregosa et al., 2011).

Meta-Analytical Groupings (Step 4)

Experiments (*e*) within each MAG were then meta-analytically processed (Step 4), using the activation likelihood estimate (ALE) algorithm (GingerALE version 3.0.2) (Eickhoff, Bzdok, Laird, Kurth, & Fox, 2012; Eickhoff et al., 2009). Voxel-wise ALE scores were computed as the union of MA maps, which provide a quantitative assessment of spatial convergence across experiments. These voxel-wise maps were cut off by a cluster-forming threshold. In fact, the size of the supra-threshold clusters was compared against a null distribution of cluster sizes derived from artificially created datasets in which foci were shuffled across experiments, but the other properties of original experiments (e.g., number of foci, uncertainty) were kept (Eickhoff et al., 2012). In the current study, we used the following statistical threshold: a voxel-level cluster

forming threshold of p<0.001 and a cluster-level family-wise correction (pFWE<0.05), with 5,000 permutations (Eickhoff, Nichols, et al., 2016).

To examine under- and overrepresentations of nosological categories, task and sample characteristics within each MAG, we carried out one-tailed binomial tests comparing their prevalence with their base rate (across all experiments). Main effects of diagnosis, task and samplecharacteristics between MAGs were investigated through chi-squares (X^2) and Kruskal-Wallis (H)tests. Literature bias was also assessed to compare differences between nosological categories in terms of task and sample characteristics (See Supplementary Material). Finally, for each MAG, weextracted functional characterization using the *Behavioral Analysis plugin* of the Multi-Image Analysis GUI (Lancaster et al., 2012). A z-score higher or equal to 3 is considered significant (i.e.,p<0.05 Bonferroni corrected for multiple comparisons).

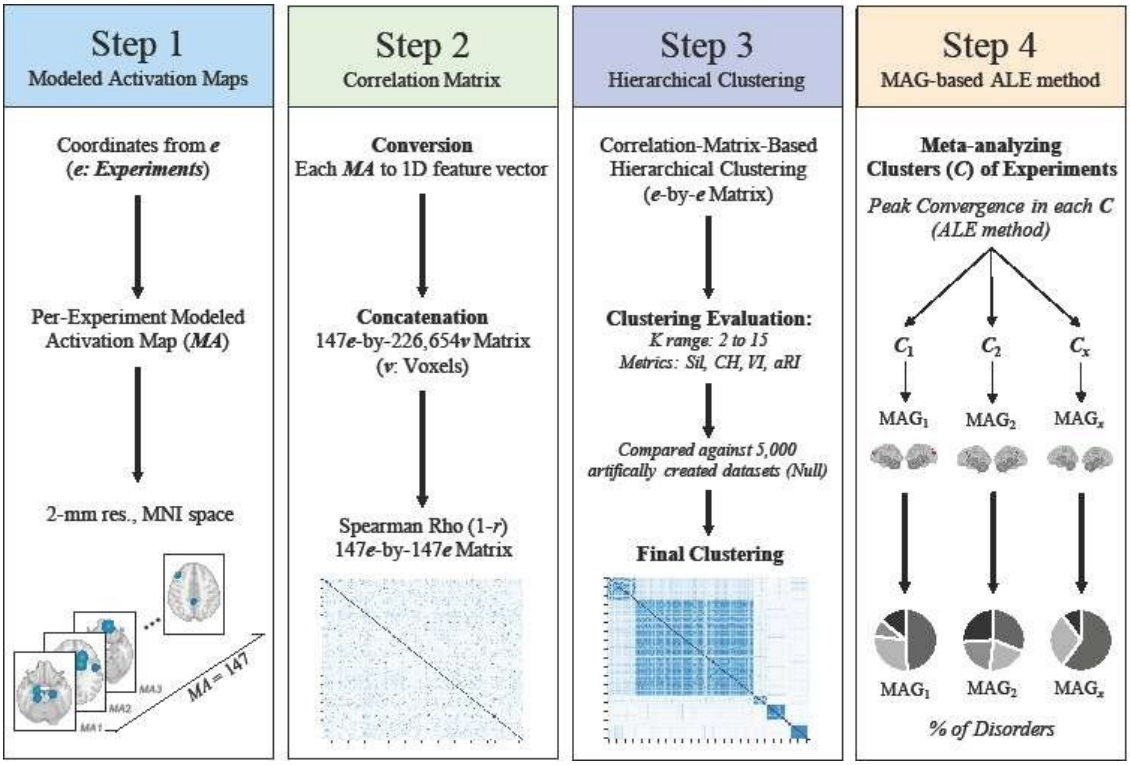

Figure 1. Workflow of the current study. **Step 1:** Creation of a MA map for each experiment, weighted by sample size. **Step 2:** Pairwise Spearman Rho correlation was performed between every MA map. **Step 3:** Clustering analysis was performed on the correlation matrix to extract groups of experiments sharing similar MA map. **Step 4:** ALE meta-analysis was conducted on experiments within each group. Phenotype assessment was then carried out to investigate under/over-representativeness of disorders, sample and task characteristics across identified groups.

Results

Identified studies and characteristics

A total of 124 original studies met the inclusion criteria for the meta-analysis, of which 11involved more than one sample and 8 comprised two or more distinct fMRI task contrasts. This resulted in 147 experiments (1030 foci) involving 3199 cases that were compared to 3024 healthycontrols. Mean age of cases was 13.8 years old (SD=2.25) and the average rate of boys across samples was 71.67%. (see Supplementary Material). Disorder-specific studies showed significantliterature bias regarding the choice of neurocognitive task domains, average of sex ratio, and the average of prescribed medication per samples (See Supplementary Table).

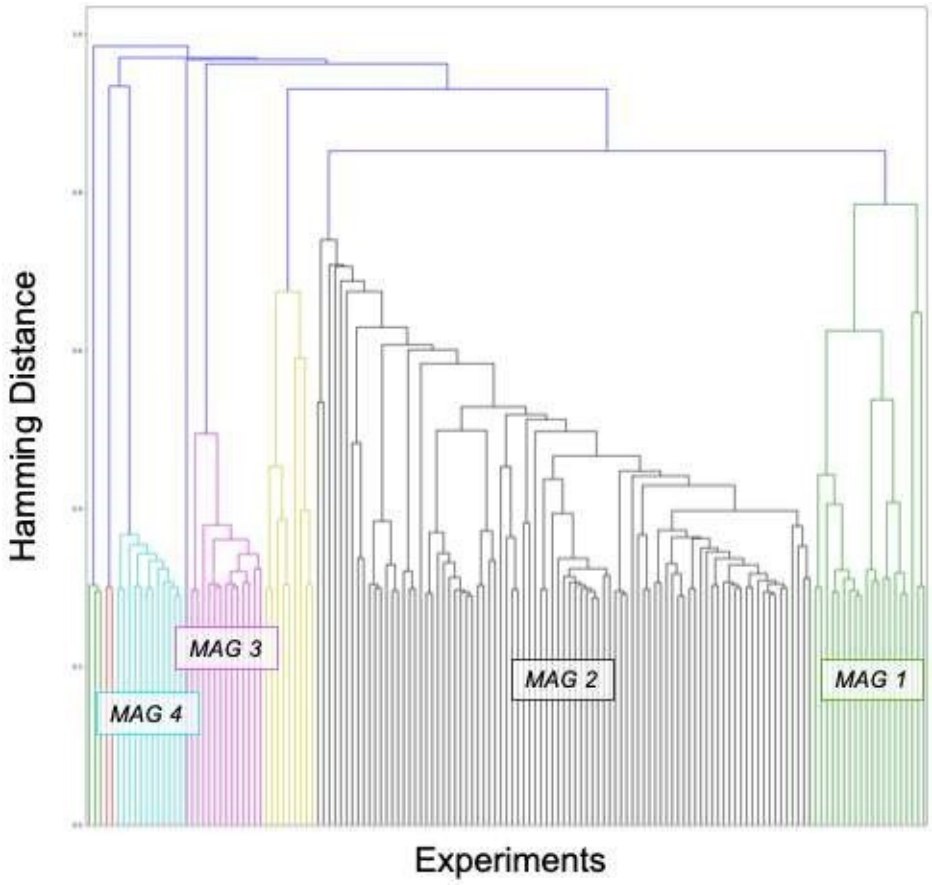

Figure 2. Hierarchical clustering of aberrant activation maps. This dendrogram represents the final hierarchical clustering model which grouped experiment showing similar aberrant activation maps. The 4 significant meta-analytical groupings (MAGs) represented 90.58% of total sample of experiments: MAG1 (green) = 21 experiments and 577 subjects; MAG2 (black) = 87 experiments (1848 subjects); MAG3 = 13 experiments (197 subjects) & MAG4 (cyan) = 12 experiments (278 subjects).

Neurobiologically-driven meta-analysis

Clustering Solution

Clustering solutions were investigated for a range of *K*=2-15 MAGs with resampling method (90% subsamples and 5,000 iterations). Average of the 5,000 iterations metric values for each *K* were plotted. Despite the fact that Calinski-Harabasz exhibited a monotonic behavior (constantly increasing), results from the silhouette index (K=8), aRI (K=3 & K=8) and variation ofinformation (from K=2-3, from K=6-7 & K=7-8) indicated that the solution with 8 MAGs was themost optimal (See Supplementary Figure 1).

Of the 8 MAGs, 4 comprised less than 10 experiments (n=8, 3, 2 & 1, respectively). Thesewere excluded from further analyses. The remaining 4 MAGs represented 90.58% of total sampleof experiments (133 experiments out of 147): MAG1 (577 subjects, 21 experiments and 120 foci), MAG2 (1848 subjects, 87 experiments, 708 foci), MAG3 (197 subjects, 13 experiments, 52 foci), MAG

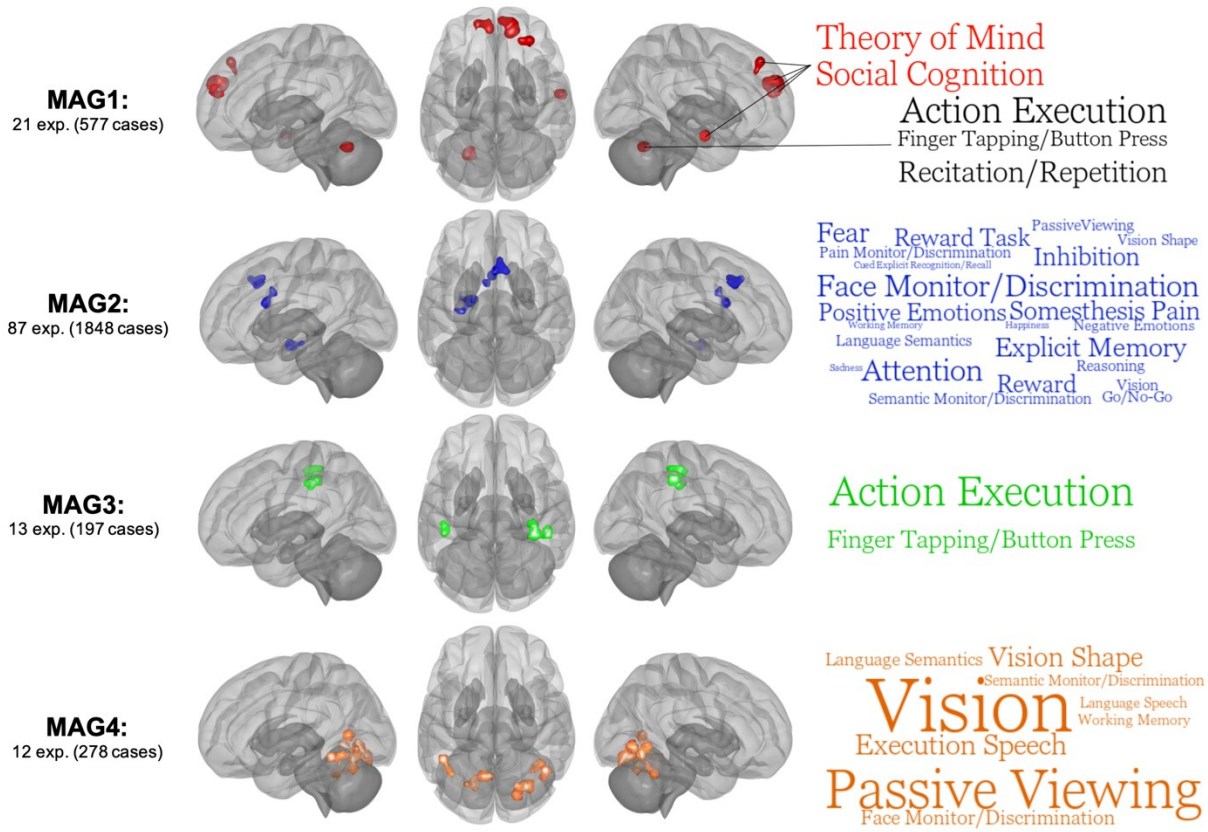

Figure 3. ALE meta-analysis on each significant meta-analytical grouping (MAGs). Images are shown for left hemisphere (lateral), superior view and right hemisphere (lateral) respectively. ALE images were thresholded at $p<0.001$ at the voxel-level and $pFWE > 0.05$. Word clouds were generated using BrainMap database terms (Behavioral Subdomains & Paradigm). Font size represents Z-score associated with the whole MAG (all words are significant $p=0.05$ with Bonferroni correction).

ALE Meta-analysis

As shown in Table 1 and Figure 3, experiments of the MAG-1 had convergent peaks in theright rostrodorsal dorsomedial PFC (dmPFC) and the left caudal dmPFC (see (Eickhoff, Laird, Fox, Bzdok, & Hensel, 2016)), the left cerebellum (Lobule VI), the right dorsolateral prefrontal cortex (dlPFC, Brodmann area [BA] 9/46d, Sallet et al., 2013) and the middle temporal gyrus (MTG). MAG2 included the right anterior MCC (BA32, Palomero-Gallagher, Vogt, Schleicher, Mayberg, & Zilles, 2009; Vogt, et al., 2004), the left amygdala and the left aMCC (BA24 a'-b', Palomero-Gallagher et al., 2009; Vogt et al., 2004). Regarding the MAG3, spatial convergence was found in the right posterior precentral (BA4p) to postcentral gyri (BA2-3), the right supramarginal gyrus and the left postcentral gyrus (BA2) (IntraParietal area 2, Caspers et al.,2006). Finally, spatial map of MAG-4 included occipital/cerebellar regions such as bilateral ventral extrastriate cortex (Rottschy et al., 2007), bilateral fusiform gyrus, bilateral Lobule VI, left calcarine gyrus and right posterior middle/inferior temporal gyrus.

Table 1. ALE meta-analysis results of each significant groups of experiments

MAGs	Clusters	Size (mm^3)	MNI Coordinates			ALE	Cluster Breakdown
			X	Y	Z		
MAG1	1	2456	14	46	28	0.0175	R dmPFC (rostrodorsal)
	2	1152	-16	56	22	0.0154	L dmPFC (caudal)
	3	1096	-24	-60	-28	0.0177	L Cerebellum (Lobule VI)
	4	1048	30	40	46	0.0164	R dlPFC
	5	848	58	-8	-18	0.0216	R MTG/STG
MAG2	1	1352	8	18	40	0.0243	R aMCC (Area 32')/pre-SMA
	2	1296	-20	-10	-16	0.0272	L Amygdala
	3	1040	-2	12	22	0.0321	L dACC (Area 24a'-b')
MAG3	1	976	34	-26	52	0.0125	R Pre-/Postcentral gyri (Area 2-3 & 4p)
	2	800	46	-34	44	0.0133	R Supramarginal gyrus (Area 2, PFt)
	3	720	-42	-32	42	0.0112	L Postcentral gyrus (Area 2, PFt)
MAG4	1	2336	20	-78	-12	0.0172	R Lingual (h0c3v)
	2	1224	-18	-66	-24	0.0159	L Cerebellum (Lobule V1)
	3	968	44	-58	-4	0.0168	R pMTG
	4	912	-44	-48	-14	0.0151	L pITG
	5	736	-8	-62	6	0.0186	L Calcarine Cortex
	6	728	40	-52	-26	0.0155	R Cerebellum (Lobule VI)

Note. MAG = Meta-analytical Grouping; PFC = Prefrontal Cortex; dmPFC = dorsomedial PFC; dlPFC = dorsolateral PFC; MTG = Middle Temporal Gyrus; STG = Superior Temporal Gyrus; aMCC = anterior MidCingulate Cortex; pre-SMA = pre-supplementary motor area; dACC = dorsal anterior cingulate cortex; IPL = Inferior Parietal Lobule; SPL = Superior Parietal Lobule; pMTG = posterior MTG; pITG = posterior ITG.

Functional characterization of MAGs

Functional characterization of MAGs (i.e., MAG-wide & cluster-specific) was performed to examine their relationships with behavioral domains and paradigms of the BrainMap database (see Figure 3, Supplementary Material):

MAG1: Experiments mainly included response inhibition (7) and reward decision-makingtasks (5, e.g., Monetary incentive delay task). Functional characterization using the BrainMap database yielded no significant behavioral/paradigm classes. However, bilateral dmPFC and anterior MTG/STG were positively associated (Z>3.0) with social cognition/theory of mind, and negatively related (Z<-3.0) with action execution. Interestingly the left Lobule VI show positive association with action execution and negative relationship with social cognition, whereas dlPFC was related to action inhibition. In sum, this MAG may be characterized by deficits of brain regionssubserving social cognition during cognitive & reward decision-making tasks.

MAG2: Experiments within this MAG primarily included task contrasts comprising an emotional component (k=42) of which 24 used negative emotional stimuli (e.g., facial expression).MAG2 was characterized by a wide range of behavioral subdomains from the BrainMap Databaseincluding attention, face monitoring & discrimination and explicit episodic memory. Furthermore,the right aMCC/pre-SMA (Attention) shared similar cognitive domains with left amygdala (Face Monitoring/Discrimination) such as explicit memory, semantic monitoring and positive emotions/reward. Also, the right aMCC/pre-SMA and the left dACC were both associated with the somesthesis pain (monitoring and discrimination) domain. Given these findings, the co-occurrenceof the dACC, aMCC/pre-SMA and the amygdala may be involved in stimulus-driven attentional control.

MAG3: Experiments within this MAG included a variety of cognitive and sensorimotor tasks (e.g., finger sequencing, anti-saccade, mental rotation, nback). Using the BrainMap Database, we observed that MAG3 was significantly associated with action execution and finger tapping. Region-specific analyses revealed that the three regions, the right posterior precentral/postcentral, the right SMG and left postcentral , shared action execution, finger

tapping and somesthesis behavioral domains. In sum, brain regions of this MAG may encompass sensorimotor/action execution processes.

MAG4: Experiments from the MAG4 mainly included various cognitive tasks (10). Functional characterization using the BrainMap database revealed significant associations with vision, passive viewing and speech execution. Region-specific analyses revealed that all but the calcarine were significantly related to vision. Furthermore, the right pMTG/ITG, the left pITG/FFand the right lobule VI shared face monitoring/discrimination, passive viewing, vision shape and covert naming domains. In short, MAG4 may reflect co-occurrent deficits in brain regions involvedin visual processing during cognitive tasks.

Table 2. Characteristics of Experiments across meta-analytical groupings

	Total (n=147)		MAG1 (k=21)		MAG2 (k=87)		MAG3 (k=13)		MAG4 (k=12)	
Characteristics	n	%	n	%	n	%	n	%	n	%
Nosological Categories										
ADHD	79	53.7%	14	66.7%	43	49.4%	8	61.5%	8	66.7%
CD	32	21.8%	4	19.0%	17	19.5%	4	30.8%	3	25.0%
ANX	14	9.5%	3	14.3%	9	10.3%	0	0.0%	1	8.3%
DEP	22	15.0%	0*†	0.0%	18†	20.7%	1	7.7%	0	0.0%
Task-contrast Domain										
Cognitive	88	59.9%	10	47.6%	53	60.9%	9	69.2%	10	83.3%
Response Inhibition	44	29.9%	7	33.3%	29	33.3%	3	23.1%	4	33.3%
Attention	23	15.6%	1	4.8%	13	14.9%	3	23.1%	3	25.0%
Emotion	71	48.3%	12	57.1%	42	48.3%	3*	23.1%	5	41.7%
Positive	17	11.6%	6*†	28.6%	7*	8.0%	0	0.0%	1	8.3%
Negative	37	25.2%	4	19.0%	24	27.6%	1	7.7%	2	16.7%
Both	16	10.9%	2	9.5%	10	11.5%	2	15.4%	2	16.7%
Sample Characteristics										
Medication-Naïve	61	41.5%	14†	66.7%	40	46.0%	6	46.2%	5	41.7%
Average Med per sample	-	26.7%	-	35.2%	-	26.3%	-	19.4%	-	20.9%
Mixed Sex Sample	95	64.6%	12	57.1%	60	69.0%	7	53.8%	8	66.7%
Average Boys per Sample	-	71.7%	-	77.6%	-	71.4%	-	76.1%	-	61.1%

Note. * Represents significant difference compared to its base rate (one-tailed $p<0.05$). † Represents significant differences between MAGs ($p<0.05$)

Phenotype Assessment 1: Nosological Categories

MAG1 was less likely to include DEP samples (X^2=4.16, p=0.041), compared to all the other MAGs (Table 2). Indeed, proportions of DEP samples in MAG1 was significantly lower thanits base rate (0% versus 15.00%, one-tailed p=0.028). Taking into account the between-disorder literature bias revealed that the lower rates of DEP samples in MAG1 were replicated when restricting experiments to those using an emotional task contrast and mixed sex samples (Supplementary Material).

Additionally, MAG2 had more DEP samples than other MAGs (X^2 = 8.43, p=0.004). However, compared to its base rate, proportion of DEP samples was not significantly overrepresented in MAG2 (20.7% versus 15.0%, one-tailed p=0.123). After taking into account thebetween-disorder literature bias, we observed that the higher rates of DEP samples in MAG2 wasreplicated when restricting experiments to those using a cognitive task contrast or an emotional task contrast but also in experiments with only medication naïve sample and mixed sex samples (Supplementary Material). Graphical representation of probabilities of aberrant MAG per disorderclass can be found in Supplementary Figure 2.

3.3.5. Phenotype Assessment 2: Task & Sample Characteristics

We observed that the rate of experiments within the MAG1 that included a positive emotional stimulus was higher than other MAGs (X^2=8.62, p=0.003) (Table 2), and significantly overrepresented compared to its base rate (28.6% versus 11.6%, one-tailed p=0.028). Additionally, experiments in MAG2 were less likely to include positive emotional task contrast (X^2=3.97, p=0.046) and marginally associated with greater experiments with negative emotion task contrast (X^2=3.31, p=0.069), compared to other MAGs (Table 2). However, proportions of these task domains were not statistically different than their base rates.

MAG3 had significantly lower rate of general emotional stimuli compared to other MAGs (X^2=4.20, p=0.040), which was marginally lower compared to its base rate (37.5% versus 48.3%,

one-tailed p=0.059). Other characteristics did not reach statistical significance, compared to their base rates.

Although MAG1 had a significantly higher rate of medication-naïve subjects, compared toits base rate (one-tailed p=0.018), MAGs did not differ in rates of experiments with medication- naïve samples (X^2=2.25, p=0.522) and average rate of prescribed medication (Kruskal-WallH=2.74, p=0.433). No differences were observed concerning the rate of mixed sex samples (X^2=1.90, p=0.594) and the average rate of boys in samples (Kruskal-Wall H=2.40, p=0.493).

Discussion

The current meta-analysis was carried out to examine the shared and/or specific neural correlates of pediatric psychiatric disorders (ADHD, CD/ODD, ANX & DEP). To do so, we useda novel data-driven meta-analytical method that aimed to extract groups of experiments which show similar brain topographic maps. We identified 4 significant MAGs, which comprised co-occurrent deficits in brain regions that may share features with (1) internally/externally directed processes; (2) attentional control of emotions, (3) action execution and (4) visual processes. More importantly, compared to their base rate, we found underrepresentation of DEP samples in MAG1and overrepresentation in MAG2. However, no other significant differences were found in nosological categories between MAGs nor by considering their base rates, suggesting potential transdiagnostic correlates. MAG1 included bilateral dmPFC, dlPFC, MTG/STG and Lobule VI. More precisely, we observed that dmPFC-MTG/STG were involved in social cognitions, whereas dlPFC and Lobule VI were characterized as action inhibition and execution, respectively. We also found main task- effect of the utilization of a positive emotional stimulus. Interestingly, findings suggest that duringcognitively demanding tasks, brain regions involved in internally directed processes (e.g., dmPFC& anterior MTG/STG) flexibly shifts their activity to enable goal-directed processes (e.g., dlPFC & Lobule VI) (M. D. Fox et al., 2005; H. Kim, Daselaar, & Cabeza, 2010; Shulman et al., 1997). Given these data, deficits in brain regions involved in MAG1 may reflect a failure to disengage internal processes at the cost of goal-directed processes (Anticevic et al., 2012).

Interestingly, ourresults suggest that these co-occurrent deficits (i.e., dmPFC, dlPFC, Lobule VI and MTG/STG) areless likely to be reported in that DEP samples. However, some studies have shown deficits in fronto-parietal and DMN regions in internalizing disorders (Kaiser, Andrews-Hanna, Wager, & Pizzagalli, 2015; Romer et al., 2020). Given that these findings were observed in adult samples andthat anticorrelation between these processes varies from childhood from adulthood (DeSerisy et al., 2021), it is possible that these deficits may be observed in adulthood but not childhood DEP. Also, the DEP samples did not frequently report using positive emotional stimuli (k=3 out of 22),which was found to be the main task-characteristic of MAG1. This may suggest that the lack of relationship between MAG1 and DEP may be explained by task differences. Considering the smallsample size involved, we cannot completely rule out the possibility of MAG1 deficits in children with DEP.

The largest MAG (MAG2, k=87) was constituted of the aMCC/pre-SMA, amygdala and dACC. This MAG was mainly characterized by attention, face monitoring and explicit episodic memory, using the BrainMap database. We found higher rates of DEP samples, compared to otherMAGs, which concur with past meta-analytical evidence consistently showing aberrant activation in these particular regions during negative emotional tasks in adults with major depression(Delvecchio et al., 2012; Fitzgerald et al., 2008; J. Graham et al., 2013; J. P. Hamilton et al., 2012;Lai, 2014; Palmer et al., 2015). However, no effect was observed in ANX samples, potentially dueto the limited sample size. Nonetheless, deficits in these regions were also observed across adult ANX & DEP samples, during negative emotion processing (Janiri et al., 2020; McTeague et al., 2020; Zilverstand, Parvaz, & Goldstein, 2017). Additionally, we observed a marginally significant association between this MAG and negative emotional stimuli, indicating a possible task-effect. Although rates of ADHD (□50%), CD/ODD (□20%) did not differ between other MAGs, evidence suggests that these disorders may also show deficits in MAG2 regions, particularly during emotion processing tasks (Jules R Dugré et al., 2020; Rubia, 2018) which correlates with general psychopathology score (Kaczkurkin et al., 2018; Romer et al., 2020; Shanmugan et al., 2016). In sum, this MAG may reflect general deficits in emotional lability, inherent to DEP, yet frequently observed in children/adolescent with ADHD (Sobanski et al., 2010) and/or CD (G. Kohls et al., 2020).

We also found deficits in brain regions (e.g., pre- and postcentral gyrus) subserving action execution/finger tapping tasks (MAG3). This MAG was less likely to comprise emotional tasks, which is consistent with the fact that emotional tasks usually require less motor execution. Interestingly, deficits in similar regions (i.e., somato-motor network) were also observed in a recent study showing significant transdiagnostic association with general maladaptive functionality (VanDam et al., 2017). Although deficits in these regions are currently not well understood, sensory deficits such as tactile perception and body awareness are often reported in children with pediatricpsychiatric disorders (C. Fox, Snow, & Holland, 2014; Ghanizadeh, 2011; Gourley, Wind,Henninger, & Chinitz, 2013; He et al., 2021; Puts et al., 2017). It is thus possible that abnormalities in MAG3 may reflect deficits in tactile perception, crucial for accurate performance of purposefulmovements (Borich, Brodie, Gray, Ionta, & Boyd, 2015) such as in cognitive tasks.

Finally, we found evidence of early processing deficits across disorders (MAG4). Recent studies have shown replicable structural alterations in brain regions spanning this MAG. In fact, the authors demonstrated, through two different samples comprising 1246 (Romer et al., 2018) and 875 (Romer et al., 2019) subjects, that the general psychopathology factor score was associated with deficits in occipital and cerebellum regions. These regions are implicated in variety of visual functions such as detecting relevant changes in the environment (e.g., visual oddball) (Downar, Crawley, Mikulis, & Davis, 2000; H. Kim, 2014). Thus, MAG4 may mirror several dysfunctional processes in early visual processing, including gazing at task-irrelevant stimuli. For example, during face-emotion tasks, the number and duration of fixation to the eye regions have been reported to be significantly lower in ADHD with and without CD (J. N. Airdrie, K. Langley, A. Thapar, & S. H. van Goozen, 2018), in childhood psychopathic traits (Dadds et al., 2008), in ODD/CD (Bours et al., 2018; Martin-Key et al., 2018; W. M. Menks et al., 2020), anxiety disorders (Horley, Williams, Gonsalvez, & Gordon, 2003; Horley, Williams, Gonsalvez, & Gordon, 2004; Michalska et al., 2017; Weeks, Howell, & Goldin, 2013)) and depression (T. Armstrong & Olatunji, 2012; Noiret et al., 2015). Likewise, deficits in the ability to filter out irrelevant stimuli are also observed in continuous performance test (Lev, Braw, Elbaum, Wagner, & Rassovsky, 2020) and visual search tasks (T. Armstrong & Olatunji, 2012) in these populations.

Examining transdiagnostic features using the classical meta-analytic approach yielded aberrant activation in the aMCC/pre-SMA (see Supplementary Material). Furthermore, we found that externalizing disorders (i.e., ADHD, CD/ODD) were associated with deficits in the pre-SMA, whereas internalizing disorders (i.e., ANX, DEP) yielded aberrant activity in the dorsal/perigenual ACC. Interestingly, deficits in these regions were also found to be transdiagnostic neurobiological features in adult samples (dACC & aMCC (McTeague et al., 2017)). It nonetheless remains unknown whether these transdiagnostic features may be due to a common vulnerability (e.g., shared risk factors) or the presence of cross-cutting criteria (e.g., impulsivity, neuroticism), which should be tackled in the future. Also, we observed no significant peak convergence across each ofthe disorder-specific meta-analysis. This lack of convergence concurs with results from recent meta-analyses which revealed similar results in CD/ODD, ADHD and DEP, using a somewhat conservative threshold ($p<0.001$, $cFWE<0.05$) (Jules R Dugré et al., 2020; V. I. Müller et al., 2017; Samea et al., 2019). Despite that this lack of convergence might have been attributable to between-study differences (e.g., stimulus, sex effect, statistical threshold, sample size), one possibility that deserves careful attention is the within-disorder heterogeneity. Indeed, it is generally well acceptedthat DSM-derived categories comprise subfactors that are characterized by different psychologicalprocesses (Burns, Boe, Walsh, Sommers-Flanagan, & Teegarden, 2001; Ghanizadeh, 2012; Janson& Kjelsberg, 2006; Y. Li et al., 2014; M. W. Miller et al., 2013; Tackett et al., 2005). Thus, this heterogeneity in criteria substantially increases the risk of finding distinct set of symptoms while still meeting the diagnostic threshold (from 42 [GAD] to 116,200 [ADHD] theoretical set of criteria, (Nock et al., 2006b; Olbert et al., 2014). Therefore, we could not rule out the possibility that increasing the sample size in meta-analyses, which also increase the between-sample heterogeneity, may reduce the ability to detect robust findings.

Limitations

First, included studies were extracted from previous and recent published meta-analyses and literature reviews. Despite that several references were used for each disorder, a systematic search following the PRISMA protocol may have allowed us to identify other studies. Also, we performed cluster analysis across pediatric psychiatric disorders and fMRI paradigms. Since there

were limited data available to perform domain-specific analyses, it is possible that our results may have been altered by literature bias (see Supplementary Material) concerning the use of particular neurocognitive task domains per diagnosis category. However, subanalyses were carried out to examine these confounding effects. Second, the limited sample size in the meta-analysis, such as in the ANX sample (k=14) may have explained the null findings in *classical* disorder-specific meta-analysis and the lack of over/underrepresentation across MAGs and neurocognitive domains. Hence, increasing the number of studies may permit us to detect such differences and unveil more precise aberrant co-activation maps, crucial for understanding transdiagnostic correlates across pediatric psychiatric disorders. Furthermore, we did not provide additional subanalyses on hypo- versushyper-activations across disorders, as the goal of this study was to identify aberrant co- activation maps across disorders and due to the limited number of studies in the case of anxiety disorders. As doing so would have been more optimal, future studies are encouraged to use these maps to examine whether disorders may differ in terms of hypo/hyper-activations. In this meta- analysis, we focused on four main nosological categories to identify shared neural correlates that may reflect their high comorbidities in childhood/adolescence. Future meta-analysis may consider including other disorders such as autism, bipolar depression and phobias to examine differences inneural markers. Finally, we used hierarchical clustering with spearman correlation as distance measure and average linkage algorithm. Although these parameters are frequently utilized in studies using similar meta-analytical approaches, it is possible that the most optimal set of parameters would have been specific to our study.

Conclusion

We observed transdiagnostic neural correlates across common pediatric psychiatric disorders. The identified groups of co-occurrent deficits shared features with internally/externally directed processes, emotional lability, somato-motor & visual processes. We found that DEP samples were less likely to display aberrant co-activation map involving internally/externally directed processes, but more likely to exhibit deficits in brain regions implicated in attentional control of emotions. Also, these MAGs did not specifically fit particular neurocognitive domains,but rather

involved multiple subprocesses (e.g., Self-reflective & Execution/Inhibition; Threat system & Attentional Control). Our results underscore the need for including several psychiatric samples in fMRI studies rather than a single nosological category. As our results indicate shared deficits that could underlie the high rates of comorbidity among children with psychiatric disorders,meta-analyzing between-disorder contrasts, at a study-level, is of great importance to unveil disorder-specific neurobiological markers. Future studies are encouraged to examine how dysfunctions in MAGs may predict worsened outcomes in adulthood, as well as tackling the heterogeneity within psychiatric disorders.

CHAPITRE 6 – LA DYSCONNECTIVITÉ FONCTIONNELLE DE LA DÉLINQUANCE

QUATRIÈME ARTICLE

Impaired attentional and socio-affective networks in subjects with antisocial behaviors:A meta-analysis of resting-state functional connectivity studies.

Jules R. Dugré, MSc [1,2], & Stéphane Potvin, PhD [1,2]

[1] Research Center of the Institut Universitaire en Santé Mentale de Montréal, Montreal, Canada
[2] Department of Psychiatry and Addictology, Faculty of medicine, University of Montreal, Montreal, Canada

Déclaration de l'étudiant

Je déclare être l'auteur principal de cet article. J'ai été impliqué dans la conception de l'étude, menéla revue systématique, conduit les analyses statistiques, interprétés les résultats et écrit la premièreversion et la version finale de l'article. Mon directeur de thèse, Stéphane Potvin a conseillé mon travail de recherche, suggérés des corrections et ont approuvé la version finale de l'article.

Abstract

In the past decade, there has been a growing interest for examining resting-state functional connectivity deficits in subjects with conduct and antisocial personality disorder. Through meta-analyses and literature reviews, extensive work has been done to characterize their abnormalities in brain activation during a wide range of fMRI tasks. However, there is currently no meta- analytical evidence regarding neural connectivity patterns during resting state fMRI. Therefore, we conducted a coordinate-based meta-analysis of resting state fMRI studies on individuals exhibiting antisocial behaviors. Of the retrieved studies, 18 used a seed-based connectivity approach (513 cases versus 488 controls), 20 employed a non-seed-based approach (453 cases versus 460controls) and 20 included a correlational analysis between severity of antisocial behaviors and connectivity patterns (3462 subjects). Meta-analysis on seed-based studies revealed significant connectivity deficits in the amygdala, middle cingulate cortex, ventral posterior cingulate cortex- precuneus, ventromedial and dorsomedial prefrontal cortex, premotor cortex and superior parietal lobule. Additionally, non-seed-based meta-analysis showed increased connectivity in the ventral posterior cingulate cortex and decreased connectivity in the parietal operculum, calcarine cortex and cuneus. Finally, we found meta-analytical evidence for negative relationship between severity of antisocial behaviors and connectivity with the ventromedial prefrontal cortex. Functional characterization and meta-analytical connectivity modelling indicated that these findings overlapped with socio-affective and attentional processes. This further underscore the importance of these functions in the pathophysiology of conduct and antisocial personality disorders.

Introduction

Antisocial personality disorder (ASPD) is temporally contiguous with severe and persistent delinquent behaviors from childhood through adulthood. Estimates suggest prevalence rates beingapproximatively 5% at a population level but up to 50% in prison settings (Black, Gunter, Loveless,Allen, & Sieleni, 2010; Fazel & Danesh, 2002; Pondé, Freire, & Mendonça, 2011). Thus, it isnot surprising to observe that early conduct disorder (CD) is an inherent criterion for adult ASPD and is an important risk factors for criminal conviction, incarceration and a wide range of health and psychosocial problems (Bevilacqua, Hale, Barker, & Viner, 2018; Colman et al., 2009; Erskine et al., 2016; Moffitt, 2003; Moffitt, 2006). Although social science research has substantially increased our understanding of risk factors and outcomes regarding antisocial behaviors, the pathophysiological mechanisms underlying the antisocial spectrum have yet to be elucidated.

In the last decades, researchers have attempted to unveil the neurobiological correlates underlying the antisocial spectrum (i.e., conduct problems-to-antisocial personality disorder spectrum [CP/ASPD]) by using a variety of magnetic resonance imaging (MRI) methods. For instance, studies have mainly focused on structural deficits in CP/ASPD individuals (Aoki et al., 2013; Rogers & De Brito, 2016) and task-based functional abnormalities (Philip Deming & Michael Koenigs, 2020; Dugré et al., 2020; Poeppl et al., 2019). More precisely, results from two voxel-based morphometry meta-analyses (most studies controlling for total intracranial/grey matter volume) revealed that CP/ASPD subjects showed grey matter volume abnormalities in the anterior insula, the amygdala, the ventrolateral (vlPFC) and dorsomedial prefrontal cortex (dmPFC) and the fusiform gyrus (Aoki et al., 2013; Rogers & De Brito, 2016). Likewise, two recent meta-analyses of task-based functional MRI studies indicated that across tasks, psychopathic individuals exhibit significant alterations in the dmPFC, lateral PFC and amygdala (Deming & Koenigs, 2020; Poeppl et al., 2019) ACC, PCC-Precuneus (Deming & Koenigs, 2020) and fronto-insular cortex (Poeppl et al., 2019).Furthermore, Dugré and colleagues (2020) have recently observed, through alarge meta-analysis of task-based fMRI studies, that the antisocial spectrum (i.e., conduct problemsto antisocial personality disorder [CP/ASPD]) is mainly characterized by brain alterations during acute threat response tasks, but also across social cognition and cognitive

control neurocognitive domains. More precisely, during social cognition tasks (e.g., theory of mind, empathic decision making), CP/ASPD individuals exhibited aberrant activation in the putamen, precuneus, medial and dorsolateral PFC, fusiform gyrus, midcingulate cortex (MCC) and the hippocampus. Moreover, in response to threatening stimuli (e.g., negative emotional faces), the authors observeddecreased activation in CP/ASPD in the pregenual anterior cingulate cortex, lateral PFC, anterior insula and inferior parietal lobule, whereas decreased activations in the premotor, anterior insula and vlPFC were mainly observed during cognitive control tasks (e.g., Stroop, Go-No/Go) (Dugré et al., 2020). Despite that evidence suggests task-based and structural abnormalities, the disrupted functional connectivity patterns that may characterize CP/ASPD subjects remains largely unknown.

Recently, resting-state fMRI (rs-fMRI) has gained considerable attention in research on the neurobiological correlates of CP/ASPD. Rs-fMRI modality permits us to examine brain activity *at rest* without an explicit fMRI task, but also to characterize brain regions that communicates with each other (i.e., functional connectivity) during low-frequency spontaneous brain fluctuations. To examine resting-state connectivity, several methods have been developed spanning the network- level, seed-based and non-seed-based approaches. The former method reduce brain features to a macroscopic organization of voxels showing strong temporal coherence. These usually include themedial fronto-parietal (e.g., default-mode network), occipital (e.g., medial and lateral visual), pericentral network (e.g., sensorimotor, somatomotor), dorsal fronto-parietal (e.g., dorsal attention), lateral fronto-parietal (e.g., cognitive control), Midcingulo-insular (e.g., salience, ventral attention, cingulo-opercular) (E. M. Gordon et al., 2016; Schaefer et al., 2018; Uddin et al.,2019; Yeo et al., 2011). Recently, several studies have adopted a large-scale network meta- analytical approach (i.e., inferring large-scale networks from studies' peak coordinates) (Dong, Wang, Chang, Luo, & Yao, 2018; Li et al., 2019; Sutcubasi et al., 2020; Xu et al., 2019). However, this method inherently reduces the spatial preciseness when investigating deficits of a particular disorder. Thus, other techniques such as seed-based approaches have the advantage of the straightforward interpretability of results, but the limitations of being influenced by spatial confounds and noises (Cole, Smith, & Beckmann, 2010). Therefore, examining the spatial convergence across studies (Cortese, Aoki, Itahashi, Castellanos, & Eickhoff, 2020) is one meta-

analytical approach that addresses such limitations.

Concerning individuals from the antisocial spectrum, early evidence by Motzkin, Newman,Kiehl et Koenigs (2011) showed that psychopathic criminals exhibited a reduced amygdala-vmPFC connectivity during resting-state. Although this may be in line with affective deficits observed in psychopathy, the two groups (psychopathic and non-psychopathic offenders) substantially differed on both Factor 1 (i.e. affective/interpersonal factor) and Factor 2 (lifestyle/antisocial behaviors) of the psychopathy checklist (PCL-R, Hare, 2003a), Thus it remains unclear whether this dysconnectivity was driven by severity of antisocial behaviors. Thisreduced connectivity was also observed in pedophilia with child sexual offending (Kärgel et al., 2015), whereas increased connectivity characterized violent offenders and positively correlated with severity of reactive and proactive aggression (Siep et al., 2019). Furthermore, task-based connectivity studies also reported a reduced amygdala-vmPFC connectivity when using fearful facial expressions (Marsh et al., 2008) and moral judgments (Marsh et al., 2011; Yoder, Harenski, Kiehl, & Decety, 2015) stimuli in CP/ASPD. Additionally, using non-seed-based approaches (e.g. amplitude of low frequency fluctuations [ALFF], regional homogeneity [ReHo]), decreased connectivity in the precuneus was associated with both early-onset and late-onset CD (Cao et al., 2019) and adolescent violent offenders (Chen et al., 2015), whereas school bullies with severe delinquent behaviors exhibit a significant increased connectivity in this (Kim et al., 2018). Given the current state of literature which suggests that subjects with antisocialbehaviors may be associated with socio-affective deficits, results on rs-fMRI vary significantly, particularly in the use of seed versus non-seed-based approaches as well as in the selection of seedregions. Therefore, brain regions and underlying the disconnected networks remain to be determined. Meta-analytical findings are thus crucial for a better understanding of the connectivitypatterns characterizing this population.

The current study aims to investigate functional connectivity alterations in CP/ASPD through a spatial convergence meta-analysis of rs-fMRI studies. More specifically we meta- analyzed studies employing a seed-based connectivity (SBC) approach, studies using non-SBC method and studies which reported an association between functional connectivity and dimensionalconstructs

related to the antisocial spectrum. According to previous structural and task-based MRImeta-analyses, we hypothesized that CP/ASPD subjects would show disrupted functional connectivity in brain regions such as the amygdala, anterior insula, medial PFC and the PCC/precuneus.

Method

Selection Procedures

Search Strategies

A systematic search strategy, using three search engines (Google Scholar, PubMed and EMBASE), was performed independently by two researchers (JRD & SP) up to October 2020 to identify relevant studies. The following search terms were used: ("*conduct problems*" or "*conduct disorder*" or "*disruptive behaviors*" or "*antisocial personality disorder*" or "*antisocial behaviors*" or "*psychopathy*" or "*sociopathy*" or "*aggression*" or "*delinquency*" or "*inmates*") AND ("*functional connectivity*" or "*resting state")* AND "*neuroimaging*"). Additional search was executed by cross-referencing the reference lists of the included articles.

Selection criteria

Flow-chart and reasons for study exclusion can be retrieved in Supplementary Figure 1. Articles were included if they met the following criteria: (1) original paper from a peer-reviewed journal, (2) inclusion of individuals with antisocial behaviors without a comorbid major mental illness or organic impairment, (3) use of resting state functional MRI method, (4) employed a case-control SBC, a case-control non-SBC or a dimensional analysis (case-control or one-sample) between rsFC results and constructs closely related to this population: impulsivity/hyperactivity dimension (e.g. ADHD symptoms), affective/interpersonal factor (e.g. F1 score, callousness) and/or lifestyle/antisocial behaviors (e.g. CP or ASPD symptoms, F2 score). Furthermore, when papers did not report peak coordinates for seed or targets, authors were contacted. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)(Liberati et al., 2009) andthe ten rules for neuroimaging meta-analysis (V. I. Müller et al., 2018) were followed across the meta-analysis steps.

Activation Likelihood Estimate method

We used the ALE approach for coordinate-based meta-analysis to extract significantspatially convergent peaks that differ between our population of interest and controls (GingerALEversion 3.0.2, http://www.brainmap.org/ale/). Experiments reporting Talairach coordinates were further converted into MNI (Montreal Neurologic Institute) space before using them in analyses. Briefly, for each experiment, a modeled activation map (MA) was created by modeling coordinatefoci with a spherical Gaussian probability distribution, weighted by the number of subjects in each experiment. This is performed in order to account for spatial uncertainty due to template and between-subject variance (Eickhoff et al., 2009), and ensure that multiple coordinates from a singleexperiment does not jointly influence the modeled activation value of a single voxel. Voxel-wise ALE scores were then computed as the union of modeled activation maps, which provide a quantitative assessment of convergence between brain activation across experiments. the size of the supra-threshold clusters was compared against a null distribution of cluster sizes derived fromartificially created datasets in which foci were shuffled across experiments, but the other propertiesof original experiment (e.g., number of foci, uncertainty) were kept. We used the following statistical threshold: $p<0.001$ at voxel-level and FWE-$p<0.05$ at a cluster-level with 5000 permutations.

Seed-Based Connectivity

In this meta-analysis, we focused on spatial convergence rather than a large-scale network approach. Indeed, we used the ALE method to examine voxels that show spatial convergence across studies, irrespective of the connections between voxels, as used recently (Cortese et al., 2020). Since the main results are presented as peaks that show spatial convergence across connectivity studies (and not dysconnectivity between two brain regions), further analyses were carried out which specifically aimed to examine the connections between a seed-of-Interest (SOI) and voxels regions (target). SOIs were defined as the results of the main seed-based meta-analysis (peaks where there was significant spatial convergence across studies). Next, we assumed that functional connectivity analyses should be reciprocal (i.e., seed A is connected to target B to the same extent that B should also be connected to A). Concretely, we extracted connectivity

experiments from studies that have reported at least 1 coordinate within the SOI. Independent connectivity experiments were defined as the following: In each connectivity result for every original study, A) if the peak coordinate falling within the SOI was a *seed* in the original study, every target was included as *connecting* together in an experiment; B) if the peak coordinate wasa *target*, only the target with its respective seed were entered in the experiment. This method addressed the between-study variability regarding seed selection since the functional connectivitybetween seeds and targets should be reciprocal. For each SOI, significant results therefore suggestthat clusters are *coactivating* (i.e., functionally connected) with their respective SOI across studies. For each SOI, a SBC coactivation meta-analysis was executed on independent connectivityexperiments that meet the inclusion criteria. Meta-analyses were done separately for increased (CP/ASPD > HC) and decreased (HC > CP/ASPD) connectivity since ALE method does not inherently use effect sizes.

*Non-Seed-Based Connectivit*y

We also meta-analyzed non-SBC studies. These included every other rsFC method (than SBC) such as regional homogeneity (ReHo), fractional- and amplitude of low-frequency fluctuations (fALFF & ALFF), Short/Long Range Functional Connectivity Density (FCD) and voxel-mirrored homotopic connectivity (VMHC). Despite that ReHo and ALFF are both voxelwisedata-driven methods to examine rsFC in local brain regions, ReHo measures the synchronisation between the time series of a given voxel and its neighbors (Zang, Jiang, Lu, He, & Tian, 2004), whereas the ALFF estimates the amplitude of fluctuations of individuals voxels (Yu-Feng et al., 2007).Also, studies using large-scale networks analyses (e.g., independent component analysis) were excluded. This was done to avoid contaminating our results with studies using a different approach (peak convergence *versus* large-scale network) than the one used in this meta-analysis. However, these studies were added only in cases where studies reported voxel-wise group effects within specific networks (e.g., within-DMN), since these studies report significant peak coordinates rather than large-scale network statistics.

Subanalyses

Several sensitivity analyses were performed to assess potential moderators of our results. First, since SBC results may have been driven by preference in seed selection (e.g., the amygdala),we ran the meta-analysis by removing every seed from seed-to-voxel studies (i.e., correlation between the time-series of a seed with the time-series of every voxel across the brain) and kept only the target cluster coordinates. Similarly, to address the potential effect of studies investigatingonly a small number of connections, we have performed a second subanalysis by setting a minimumthreshold of 5 seeds in seed-to-voxels studies and 10 seeds in studies using seed-to-ROI (i.e., correlation between time-series of two ROIs), (i.e., resulting in a minimum of 45 connections pairs). In meta-analyses with less than 10 experiments, we carried out jack-knife analyses (i.e., recomputing ALE while leaving one experiment out of the dataset), to examine whether the results may be driven by a single experiment. However, it should be noted that this method is very conservative in small datasets and is unnecessary when meta-analyzing a considerable number of experiments since it is unlikely that results may have been driven by a single experiment (Eickhoff,Nichols, et al., 2016). Also, given the body of research showing that callous-unemotional traits andage-of-onset may be sources of clinical heterogeneity, further subanalyses were carried out(Supplementary Material).

Dimensional associations with psychopathologies

Meta-analyses were also performed to investigate relationships between connectivityresults and psychopathological dimensions associated with CP/ASPD subjects, namely the Hyperactivity/Impulsivity, Affective/Interpersonal of psychopathic traits and Antisocial Behaviors/Lifestyle dimensions. These meta-analyses were performed across SBC and non-SBC studies, for positive and negative rsFC-dimensions relationships, separately.

Exploratory analyses

To better interpret results, meta-analytical connectivity modelling (MACM) and functional characterization analyses were realized. First, we assessed which paradigm and task domains significantly characterize our results, using the BrainMap Database. More precisely, we examined

large scale and brain-wide co-activation profile for each brain region disrupted (ROI) in CP/ASPD subjects. This was done to investigate whether our results mutually co-activate across tasks (BrainMap Database). Thus, we first examined how strongly the ROI-based MACM maps correlated with each other as an indication being part of similar network. Following this, these maps were correlated with well-defined 7 canonical networks for interpretability purpose concerning large-scale networks (Schaefer et al., 2018).

Results

Case-Control Meta-analyses

Seed-Based Connectivity

A total of 19 samples derived from 18 studies (see Supplementary Table 1) were included for the SBC meta-analysis. A total of 513 cases was compared to 488 control subjects (mean age=28.34, 7 samples reporting that all participants met diagnostic criteria for CD/ASPD).

Only 7 studies have reported increased connectivity results in CP/ASPD subjects (42 foci including seeds). We observed significant spatial convergence in the anterior MCC (extending to the pre-supplementary motor area [pre-SMA]) and the left amygdala. Jackknife analyses replicatedresults in 5 out of 7 iterations, indicating that the spatial convergence between both regions mighthave been driven by 2 studies. Additionally, removing seeds coordinates from studies yielded no significant results, suggesting that results may have been driven by seed selection. Finally, no additional analyses were performed since they comprised too few experiments to achieve acceptable statistical power (<=8 experiments).

Meta-analysis on 15 experiments reporting decreased connectivity was performed (13 studies, 110 foci including seeds), revealing spatial convergence in 6 clusters: left ventral PCC/Precuneus (vPCC/PCUN), left vmPFC, left premotor cortex overlapping on the frontal eye field, left amygdala, left and right dmPFC. The left vPCC/PCUN, left amygdala and left premotorcortex remained statistically significant after excluding children' samples from the main analysis (k=11, 99 foci). When adopting a more restricting inclusion approach (i.e., minimum of 5 seed-to-voxels

maps, 10 Seed-to-ROI) (k=8, 64 foci), only the vPCC/PCUN and the right dmPFC were replicated, suggesting that these clusters were not driven by focused studies. Finally, removing seeds coordinates from seed-to-voxel experiments (k=15, 96 foci) revealed that the left premotor cortex and both left and right dmPFC were not driven by seed selection.

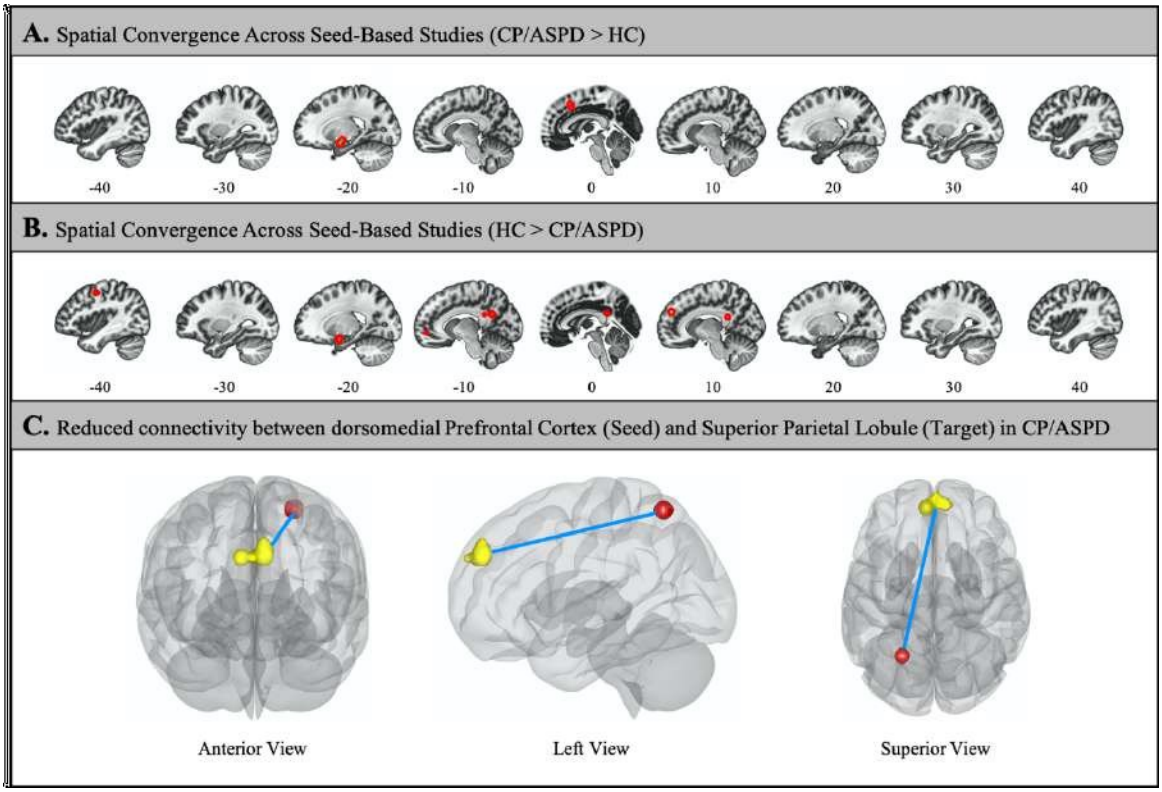

Figure 1. Seed-based connectivity results: A) Convergent peaks across increased SBC studies: Left MidCingulate Cortex & Left Amygdala; B) Convergent peaks across decreased SBC studies: Left Amygdala, Left-Right dorsomedial Prefrontal Cortex, Left Posterior Cingulate Cortex/Precuneus, Left vmPFC & Left Premotor Cortex. C) Significant reduced connectivity (blue edge) between bilateral dorsomedial Prefrontal Cortex (Yellow: Seed) and Superior Parietal Lobule (Red: Target). CP/ASPD = Conduct Problems-to-Antisocial Personality Disorder spectrum. HC = Healthy Controls.

After having identified the convergent peaks across experiments (SOI), we were interested in examining their connectivity targets. Indeed, we meta-analyzed experiments reporting at least 1 peak coordinate located within the SOI, to extract brain regions that significantly coactivate with the SOI. For the left vPCC/PCUN, 11 independent connectivity experiments were included, comprising 32 foci. However, no significant dysconnectivity target was found, even when removing adolescent samples (9 experiments, 28 foci). When examining nodes that were dysconnected with bilateral dmPFC cluster (8 experiments, 19 foci), we observed significant decreased connectivity with the left superior parietal lobule (x=-23, y=-60, z=59, ALE=0.026, 136 voxels) (See Figure 1C). Jackknife analyses replicated results in 6 out of 8 iterations, suggesting that the reduced dmPFC-SPL connectivity might have been driven by 2 studies out of 8. No additional subanalysis was performed on the dmPFC due to insufficient number of experiments. Since the other SOIs (i.e., left vmPFC, left premotor cortex, left amygdala and bilateral dmPFC) comprised too few experiments to achieve acceptable statistical power (< 8 experiments), we did not perform SBC meta-analyses.

Table 1. Main results of the meta-analyses

Main Peaks	MNI Coordinates X	Y	Z	ALE	Voxels
Seed-Based Connectivity					
CP/ASPD > HC					
aMCC/pre-SMA	-2	18	40	0.0103	110
Amygdala	-22	-6	-18	0.0129	90
HC > CP/ASPD					
vPCC/PCUN	-4	-44	24	0.0229	227
vmPFC	-6	54	-6	0.0210	91
PMC	-36	-4	48	0.0162	78
Amygdala	-20	-2	-16	0.0158	77
dmPFC	-4	50	32	0.0165	77
-	8	52	32	0.0180	71
Non-Seed-Based Connectivity					
CP/ASPD > HC					
vPCC	4	-44	20	0.019	148
HC > CP/ASPD					
CAL	10	-74	16	0.0209	129
OP4	54	-6	16	0.0174	123
CUN	-24	-80	40	0.0146	111
Dimensional Association with rsFC					
Severity of Antisocial Behaviors (Negative Association)					
vmPFC	6	50	-5	0.0158	78

Note. CP/ASPD = Conduct Problems to Antisocial Personality Disorder Spectrum; HC = Healthy Controls; aMCC = anterior MidCingulate Cortex; pre-SMA = pre-Supplementary Motor Area; vPCC = ventral Posterior Cingulate Cortex; PCUN = Precuneus; vmPFC = ventromedial Prefrontal Cortex; PMC = Premotor Cortex; dmPFC = dorsomedial Prefrontal Cortex; CAL = Calcarine cortex; OP4 = operculum parietale (area 4); CUN = Cuneus.

Non-Seed-Based Connectivity

Twenty studies were included in the Non-SBC meta-analyses (see Supplementary Table 2). However, one study was removed since the authors failed to provide us their peak coordinates. A total of 453 cases were compared to 460 control subjects (mean age= 19.61, 15 samples reportingthat all participants met diagnostic criteria for CD/ASPD).

Non-SBC meta-analyses were performed for both increased (CP/ASPD > HC: 14 experiments, 42 foci) and decreased rsFC contrasts (HC > CP/ASPD: 18 experiments, 88 foci) (Table 2). ALE meta-analyses revealed significant peak convergence in the right vPCC/PCUN (in studies reporting increased connectivity) as well as in the parietal operculum encompassing the posterior insula, in the right intracalcarine and the left cuneus (in studies reporting decreased connectivity). When removing experiments using adult samples, meta-analysis on increased rsFCstudies replicated the vPCC/PCUN (k=10, 29 foci), while meta-analysis on decreased rsFC studies(k=14, 71 foci) replicated results in the intracalcarine and cuneus.

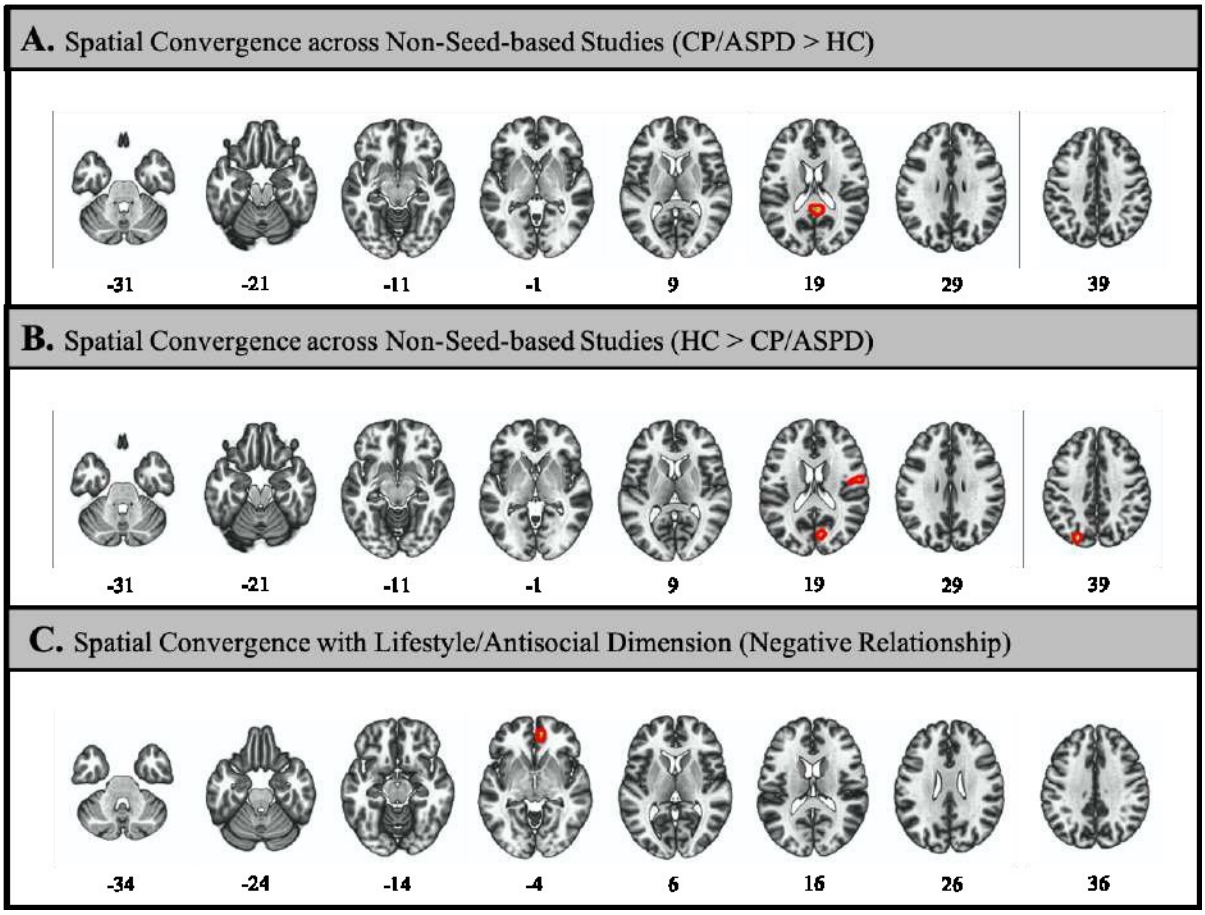

Figure 2. Significant peak convergence across: A. Non-Seed-Based Connectivity studies reporting increased connectivity (i.e., ventral Posterior Cingulate Cortex/Precuneus), B. Non-Seed-Based Connectivity studies reporting decreased connectivity (i.e., parietal operculum, cuneus, intracalcarine), C. Negative relationship between resting state connectivity of the ventromedial prefrontal cortex and severity of lifestyle/antisocial behaviors. CP/ASPD = Conduct Problems-to-Antisocial Personality Disorder spectrum. HC = Healthy Controls.

Dimensional Meta-analyses

A total of 32 studies were included in dimensional meta-analyses (n=3787, mean age=22.87), of which 10 included a measure related to Hyperactivity/Impulsivity dimension (n=263, mean age=19.15, 4 SBC studies), 15 to Affective/Interpersonal psychopathic traits (n=2863, mean age=23.77, 9 SBC studies) and 20 to Lifestyle/Antisocial behaviors dimension (n=3462, mean age=25.25, 14 SBC studies) (See Supplementary Table 3).

Concerning the Lifestyle/Antisocial dimension (k=20), 11 studies found positive rsFC associations (62 foci), 10 observed negative rsFC correlations (45 foci) and 4 yield no significant result. ALE meta-analyses revealed that the Lifestyle/Antisocial dimension was not positively associated with any rsFC but showed a significant peak convergence in the right vmPFC across studies (negative relationship). This result was replicated when removing seeds coordinates from SBC experiments, indicating that the result was not driven by seed selection. No additional subanalyses were performed due to the insufficient number of experiments (< 8 experiments). No analyses were performed on the Affective/Interpersonal component of psychopathic traits, nor on Hyperactivity/Impulsivity dimension since they comprised too few experiments for positive (k=6, k=5 respectively) and negative (k=6 and k=3, respectively) relationships.

Additional analyses

Of the 12 studies that have reported the severity of callous-unemotional traits, only 6 showed severe levels (See Supplementary Material). Thus, we did not perform any meta-analysis.Also, 21 experiments (485 cases, 186 foci) reported a sample comprising at least 50% of early- onset disordered subjects (average 93%, SD=16.8%), whereas 9 experiments (296 subjects, 55 foci) reported other samples (adolescent-onset disorder or less than 50% of subjects with early- onset disorder). Meta-analysis on early-onset disorder replicated results found in the vPCC, the right parietal operculum/posterior insula and right dmPFC. A more detailed description of the results can be found in Supplementary Material.

Exploratory analyses

To better interpret our results, we extracted significant region-of-interest and performed functional characterization and MACM analyses. Pairwise spearman rho was carried out between the MACM map for each ROI. Then overlaps between MACM maps of our ROIs were examined using a dendrogram plot (Figure 3). Further analyses were made to examine MACM correspondence with canonical networks. By investigating brain-wide coactivation map of each ROI, we observed shared similarities in MACM maps between the PCC, vmPFC, dmPFC and amygdala, which were mainly associated with the DMN. Furthermore, we showed that the MACM maps of the aMCC/pre-SMA, SPL, PMC and CUN were closely related altogether, spanning both the ventral and dorsal attention networks. Summary of the MACM analyses is displayed in Figure 3. See Supplementary Figure 2A-H and Table S2 for detailed information.

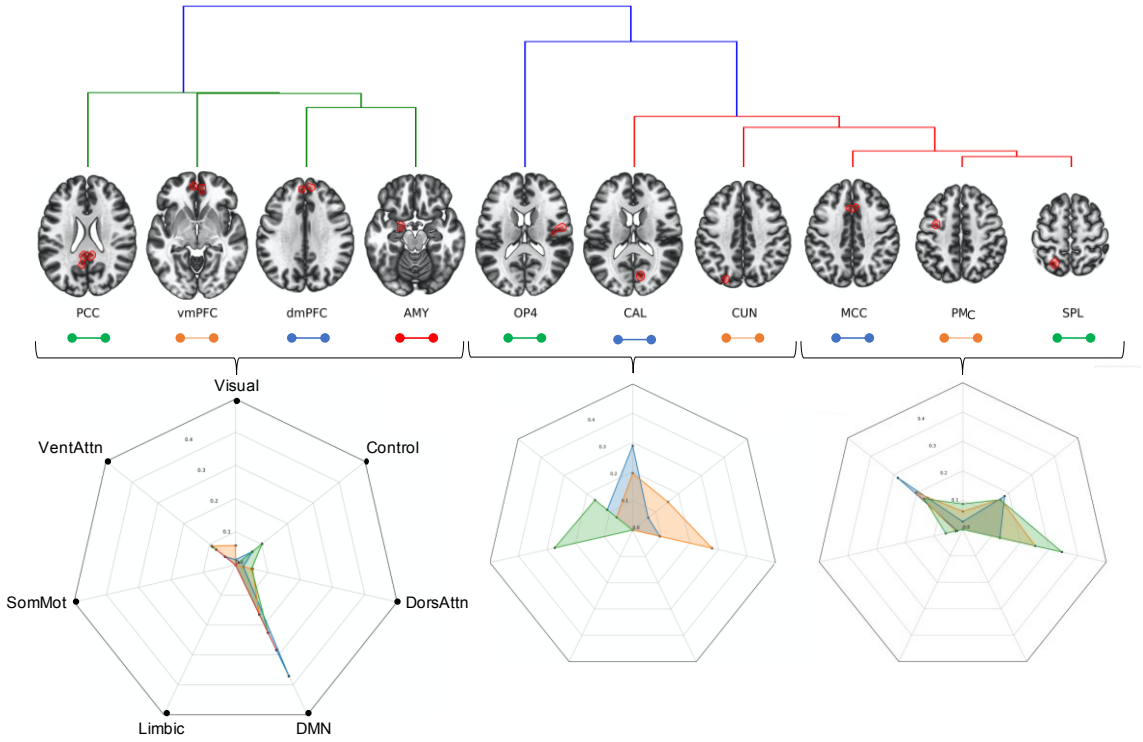

Figure 3. Hierarchical representation of spatial correlations between ROI-based MACM maps and their relationship with Schaefer's 7 intrinsic functional networks. Dendrogram revealed that the ROI-based MACM maps were distributed in 3 groups: Group 1 (DMN: PCC, vmPFC, dmPFC, AMY), Group 2 (SomMot: OP4) and Group 3 (VentAttn, DorsAttn & Visual: MCC, PMC, SPL, CUN, CAL). The CAL & CUN are shown in a different radar chart (than the MCC, PMC and SPL) for display purpose. PCC = Posterior Cingulate Cortex; vmPFC = ventromedial Prefrontal Cortex; dmPFC = dorsomedial Prefrontal Cortex; AMY = Amydgala; OP4 = Operculum Parietale (area 4);CAL = Calcarine Cortex; CUN = Cuneus; MCC = MidCingulate Cortex; PMC = Premotor Cortex; SPL = Superior Parietal Lobule. VentAttn = Ventral Attention; SomMot = Somato-Motor; DMN = Default Mode Network; DorsAttn = Dorsal Attention.

Discussion

In this systematic review and meta-analysis of rsFC studies, we aimed to investigate SBC and non-SBC deficits in individuals with CP/ASPD, as well as connectivity correlates of psychopathological dimensions characterizing CP/ASPD. To our knowledge, this is the first meta- analysis to investigate resting state functional connectivity patterns in this population. In the SBC meta-analysis, comprising 513 cases (18 studies), spatial convergence was observed in amygdala,the MCC, the vPCC/precuneus, the vmPFC and dmPFC and the premotor cortex. Further analyseswere carried out to examine dysconnectivity between two nodes. We observed that CP/ASPD subjects showed significant reduced dmPFC-SPL connectivity. Additionally, the meta-analysis on20 Non-SBC studies revealed aberrant peaks in the vPCC/Precuneus (increased connectivity), the parietal operculum, intracalcarine, and the cuneus (decreased connectivity) in cases compared to controls. Finally, in studies investigating the association between severity of lifestyle/antisocial behavior dimension and connectivity patterns (3462 subjects), significant peak convergence across studies was observed in the vmPFC (negative correlations).

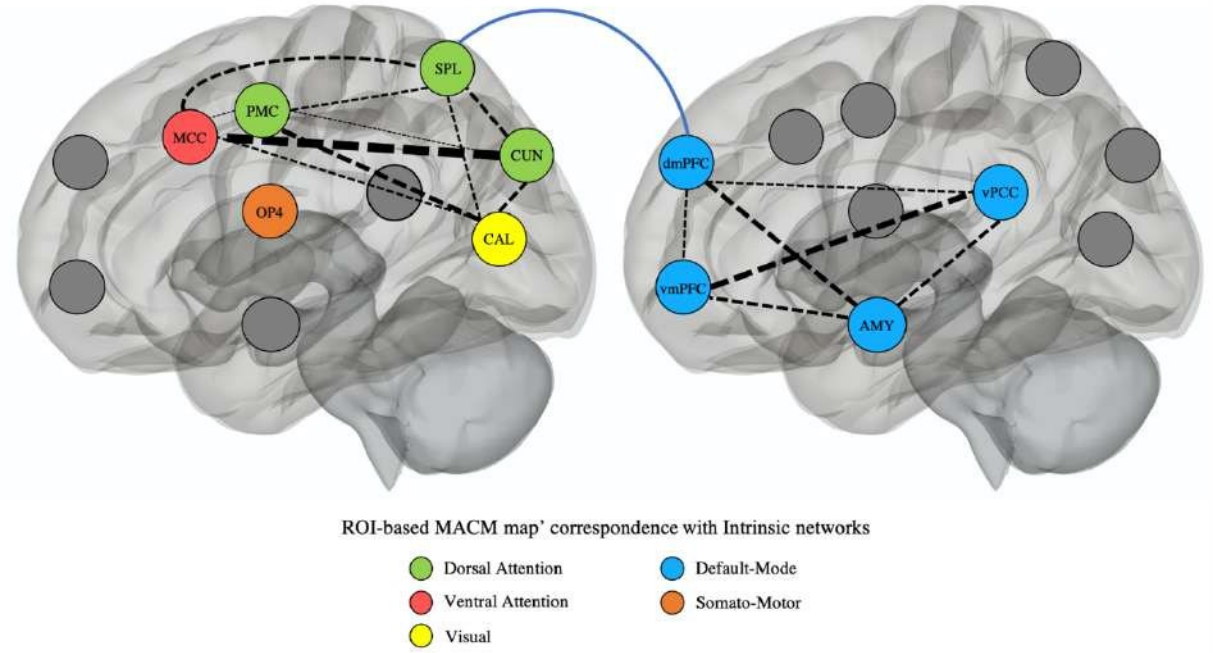

Figure 4. Summary of the results identified in the current meta-analysis in CP/ASPD subjects. Dashed Arrows represent correlation between ROI-based MACM maps (Weighted by correlation coefficient: thickness [pt] from 1pt [*r* = .10-.19] to 7pt [*r* = .70-.79]). Higher values reflect closer spatial correlation. Solid Arrow represent the reduced dmPFC-SPL connectivity observed in the meta-analysis on Seed-Based Connectivity studies. Colours in Nodes represent the intrinsic functional networks that showed the highest correlation coefficient with each ROI-based MACM map. Intrinsic Networks were defined by Schaefer et al. (2018)'s 7-Networks. AMY = Amygdala; MCC = Middle Cingulate Cortex; vmPFC = ventromedial Prefrontal Cortex; dmPFC = dorsomedial Prefrontal Cortex; vPCC = Posterior Cingulate Cortex that includes also the precuneus; PMC = Premotor cortex; OP4 = Operculum Parietal (area4); SPL = Superior Parietal Lobule; CUN = Cuneus; CAL = Calcarine Cortex. ROI = Region-of-Interest; MACM = Meta-Analytical Connectivity Modelling.

Here, we used reverse-inference method to examine the relationship between the disconnected nodes found in the current meta-analysis and large-scale canonical networks. More precisely, the co-activation profiles of our findings, provided by the meta-analytical connectivity modelling analyses, suggested that our results were mainly characterized by networks spanning theDMN and ventral/dorsal attentional networks (see Figure 3-4). Interestingly, this concurs with results of recent studies showing deficits in large-scale networks (not included in this meta- analysis). Indeed, data from the ABCD study (n=9636) indicated that CU traits were negatively associated with within-network connectivity in the DMN, whereas the severity of aggressive and delinquent behaviors were rather associated with connectivity within the Dorsal Attention Network(Umbach & Tottenham, 2020). Likewise, results from a recent study revealed negative relationships between physical aggression and within-network connectivity in the DMN and the Dorsal Attention Network (Weathersby et al., 2019). This concurs with our exploratory analyses (ROI-based MACM) indicating that the clusters observed in the main meta-analysis showed prominent associations with the DMN and attentional networks. Furthermore, we found reduced dmPFC-SPL connectivity suggesting that CP/ASPD may display disrupted connectivity between these networks. Indeed, reduced anti-correlation between the DMN and the Fronto-Parietal Network (which spanned both dorsal & ventral attentional networks) has been observed in CD andwas significantly associated with severity of CU traits (Pu et al., 2017). Past results also demonstrated that physical aggression was negatively associated with a DMN-Ventral Attention anticorrelation (Weathersby et al., 2019). Finally, altered connectivity between DMN and brain regions involved in dorsal attention network (i.e., SPL) was also identified in pedophilic offenders(Cantor et al., 2016) and correlated with severity of psychopathic traits (Dotterer et al., 2020). Hence, through a complementary perspective to our meta-analysis, these studies also highlighted the crucial role of brain regions involved in DMN and attentional canonical networks in the connectivity deficits characterizing CP/ASPD subjects (R. K. Hamilton, Hiatt Racer, & Newman,2015).

In addition, we found spatial convergence in the amygdala across both increased and decreased connectivity experiments, indicating that this particular region may be a crucial node insubjects with CP/ASPD. Despite that the amygdala is not directly involved in canonical networks,some

evidence suggests its association with brain regions subserving the DMN such as the vmPFC,PCC, dmPFC and the temporo-parietal junction during resting-state (Amft et al., 2015; Sylvester et al., 2020). These observations concur with our MACM exploratory analyses indicating overlapsin co-activating network (DMN) across the dmPFC, vmPFC, vPCC and the amygdala. Moreover,the amygdala and DMN regions are frequently co-activated in fMRI tasks eliciting empathy and morality processes (Bzdok et al., 2012). Interestingly, in such tasks, subjects with CP/ASPD exhibit numerous disconnectivities between the amygdala and DMN regions. Indeed, when viewing facial expressions of negative emotions (e.g., fear), Marsh et al. (A. A. Marsh et al., 2008) observed that youths with disruptive behaviors and high psychopathic traits exhibited reduced connectivity between the amygdala and the vmPFC and PCC. Likewise, reduced connectivity between the amygdala and regions subserving the DMN were also noticed in moral judgments tasks (Marsh etal., 2011: vmPFC; Yoder et al., 2015: vmPFC, dmPFC, PCC) as well as in passive viewing of painful situations caused by others (dmPFC: Decety et al., 2009). Hence, these results highlight coupling between the amygdala and DMN regions as a crucial socio-affective network in the understanding of connectivity functioning in CP/ASPD subjects.

In our meta-analysis, we also found spatial convergence in the aMCC/pre-SMA, SPL, premotor (frontal eye field) and the cuneus. These brain regions were further characterized as belonging to attention canonical networks (ventral/dorsal) in our MACM analyses. Indeed, the aMCC/pre-SMA mostly corresponded to the ventral network, whereas the SPL and premotor cortex were associated with the dorsal network. Their relationships are unsurprising given that theaMCC/pre-SMA, SPL and the premotor cortex (frontal eye field) are frequently co-activated in tasks requiring attentional processes (e.g., Meta-analytical finding: shifting: (Wager, Jonides, & Reading, 2004); sustained: (Langner & Eickhoff, 2013); oddball: (H. Kim, 2014); workingmemory: (Rottschy et al., 2012). More precisely, evidence suggests that ventral network regions (e.g., aMCC/pre-SMA) may correspond to a stimulus-driven attentional system, whereas regions subserving the dorsal attentional network (e.g., SPL, premotor cortex) may play a crucial role in top-down or goal-driven attentional control (Corbetta, Patel, & Shulman, 2008; H. Kim, 2014; Vossel, Geng, & Fink, 2014). Despite the overutilization of the amygdala as a seed of interest in CP/ASPD subjects, task-based connectivity studies nonetheless revealed relevant dysconnectivitywith the aMCC and the

SPL. Indeed, past research has shown increased amygdala-aMCC connectivity when CP/ASPD subjects were confronted to negative emotional stimuli such as in moral judgments tasks (Yoder et al., 2015), facial expressions of negative emotions (e.g., fear) (Marsh et al., 2008) or painful situations caused by others (Decety et al., 2009). Researchers have also observed a reduced amygdala-SPL connectivity in antisocial subjects with psychopathic traits during moral judgments tasks (Marsh et al., 2011; Yoder et al., 2015). Hence, these results also highlighted deficits in brain regions involved in attentional processes, which deserve extensive research.

Recently, researchers have shown that some dysconnectivities within and between large- scale networks may be transdiagnostic features. For instance, results from meta-analyses suggest that DMN dysconnectivity is found in patients with schizophrenia (Dong et al., 2018), MDD (Kaiser et al., 2015); obsessive-compulsive disorder (Gürsel, Avram, Sorg, Brandl, & Koch, 2018) and attention-deficits/hyperactivity disorder (Sutcubasi et al., 2020). However, psychiatric disorders may actually differ when examining these abnormalities at a seed level (Gaelle E Doucet et al., 2020). Indeed, in a recent transdiagnostic meta-analysis of resting-state connectivity in the DMN, researchers have found that deficits in the dmPFC was mainly characterized by hyperconnectivity in MDD, whereas deficits in precuneus was mostly associated with hypoconnectivity in schizophrenia (Gaelle E Doucet et al., 2020). In our meta-analysis, we found that CP/ASPD subjects rather exhibited hypoconnectivity in the dmPFC, in a most ventral part of the PCC (compared to the precuneus transdiagnostic cluster) but also in the vmPFC which negatively correlated with severity of antisocial behaviors. Given that most meta-analyses on resting-state connectivity used large-scale network approaches, which reduces spatial preciseness, the comparison of deficits in connectivity found in our study and other mental illnesses remain challenging. Nonetheless, several differences are perceivable when comparing deficits in fMRI co-activation patterns between CP/ASPD subjects (Dugré et al., 2020) and transdiagnostic maps (Janiri et al., 2020; McTeague et al., 2017; McTeague et al., 2020; Sprooten et al., 2017). For instance, across emotion processing tasks, transdiagnostic features mainly involved hyperactivations of subcortical regions (i.e., amygdala, hippocampus, parahippocampal gyrus) as well as hypoactivation of vlPFC (McTeague et al., 2020), whereas CP/ASPD subjects were rather characterized by reduced activation of the anterior insula and dlPFC (Dugré et al., 2020). Dugré

and colleagues (2020) also showed that the activity in the amygdala was negatively associated with severity of antisocial behaviors and callous-unemotional traits. Concerning cognitive control tasks, despite that CP/ASPD subjects and major mental disorders both similarly show hypoactivation in the vlPFC (Jules R Dugré et al., 2020; McTeague et al., 2017), antisocial subjects also display co-occurrent decreased activity within the premotor cortex and the inferior parietal lobule, which were not reported as transdiagnostic features (McTeague et al., 2017). Considering these results, although CP/ASPD subjects may exhibit differences in neural processing compared to other mentalillnesses, more research is needed to better understand their specific or shared deficits.

In sum, various evidence including our functional characterization analyses and ourexploratory MACM but also past meta-analyses of fMRI tasks in healthy subjects and task-based connectivity studies in CP/ASPD subjects showed the involvement of the amygdala, the dmPFC, vPCC and vmPFC in socio-affective processes, whereas the aMCC/pre-SMA, SPL, premotor cortex (frontal eye field), in attention-related processes. Furthermore, the reduced dmPFC-SPL connectivity found in our meta-analysis, alongside studies examining between-network (Pu et al., 2017; Weathersby et al., 2019; Cantor et al., 2016; Dotterer et al., 2020) or task-based connectivity (Yoder et al., 2015; Marsh et al., 2008; Decety et al., 2009; Marsh et al., 2011), indicated that CP/ASPD may potentially show deficits in the interaction between both processes. It is unequivocal that the interaction between socio-affective and attentional processes in CP/ASPD subjects needs to be tackled in future studies. It would also be crucial to examine their specific association with specific subtypes of behaviors (i.e., reactive/proactive aggression versus rule-breaking behaviors)but also with callous-unemotional traits. Nonetheless, these findings support the view that both processes may be crucial to our understanding of rs-fMRI deficits in individuals at risk for antisocial behaviors (Hamilton et al., 2015).

Limitations

First, we performed a coordinate-based meta-analysis rather than a meta-analysis oforiginal

statistical brain maps. Although ALE method yields relatively similar results to image- based meta-analysis (Salimi-Khorshidi, Smith, Keltner, Wager, & Nichols, 2009), this could havereduced results accuracy. Second, to achieve 80% power to detect effects that are present in approximately 1/3 of the population, a sample size of 17 experiments are required when using cluster-level FWE (Eickhoff, Nichols, et al., 2016). Second, in analyses with less than 10 experiments, we performed jackknife reliability analyses. However, these analyses yield very conservative results in small datasets (Eickhoff, Nichols, et al., 2016). Indeed, when spatial convergence is detected in two studies out of 7-8 (such as in this meta-analysis), removing one ofthe contributing studies undoubtedly yield non-significant findings. Third, there is currently no software nor gold standard to meta-analyze functional connectivity studies. Thus, current meta-analytical methods are not designed to explicitly examine dysconnectivity between two nodes. Despite our attempt to carry out such analyses (i.e., vPCC and dmPFC), larger datasets are required to specifically meta-analyze dysconnectivity between two nodes. Fourth, the meta-analysis on Non-SBC connectivity studies included several different methods such as ReHo, ALFF & voxel-wise group effects within ICA-derived networks. Given that there were too few studies per Non-SBC methods, we could not perform a subanalysis on this issue. Fifth, no subanalysis was performed to investigate high versus low callous-unemotional traits due to the small number of studies that have used (or reported) psychometric scales measuring this feature. Likewise, there was only a very limited number of studies that specifically aimed to examine early vs. late-onset disorders (or even reported such distinction). Additionally, in adults with ASPD, no study reported the mean age-of-onset of their sample. More importantly, the CD criterion in ASPD diagnosis suggests occurrence of CD < 15 years old, while early-onset CD is generally defined by appearance of CD prior to 10 years old (APA, 2013). We encourage researchers to report the mean age of onset and levels of callous-unemotional traits in the future. Finally, since studies used different psychometric scales to assess dimensional associations with rsFC results, we had to merge them based on three dimensions.

Conclusion

Results from SBC, Non-SBC and dimensional studies indicate resting state dysconnectivityindicate resting state dysconnectivity in CD/ASPD in several brain regions such as vPCC/Precuneus, vmPFC, dmPFC, premotor cortex, superior parietal lobule, amygdala, MCC, parietal operculum, cuneus and intracalcarine cortex. Further examining these regions by functional characterization and MACM analyses underscores the importance of socio-affective andattentional processes in characterizing CP/ASPD population. This meta-analysis offers a complementary perspective to the emotion-cognition interaction deficits underlying individuals onthe antisocial spectrum. In view of the results obtained in this meta-analysis, there is a crucial needto investigate neural signalling directionality between socio-affective and attentional networks, through effective connectivity methods, to better understand the interaction between both processes in this population. Future studies may seek to examine the specificity of functional connectivity alterations in CP/ASPD subjects compared with patients with major mental disorders.

CINQUIÈME ARTICLE

Clarifying the role of Cortico-Cortical and Amygdalo-Cortical brain dysconnectivityassociated with Conduct Problems

Jules R. Dugré, MSc [1,2], & Stéphane Potvin, PhD [1,2]

[1] Research Center of the Institut Universitaire en Santé Mentale de Montréal, Montreal, Canada

[2] Department of Psychiatry and Addictology, Faculty of medicine, University of Montreal, Montreal, Canada

Déclaration de l'étudiant

Je déclare être l'auteur principal de cet article. J'ai été impliqué dans la conception de l'étude, conduit les analyses statistiques, interprétés les résultats et écrit la première version et la version finale de l'article. Mon directeur de thèse, Stéphane Potvin a conseillé mon travail de recherche, suggérés des corrections et ont approuvé la version finale de l'article.

Abstract

A recent meta-analysis of resting-state functional connectivity studies revealed that individuals exhibiting antisocial behaviors or conduct problems may show disrupted brain connectivity in networks underpinning socio-affective and attentional processes. However, studies included in the meta-analysis generally rely on small sample sizes and substantially differ in terms of psychometric scales and neuroimaging methodologies. Therefore, we aimed to identify reliable functional brain connectivity alterations associated with severity of conduct problems using a large sample of adolescents and two measures of conduct problems. In a sample of 1416 children and adolescents, mass-univariate analyses of connectivity measures between 333 cortical parcels were conducted to examine the relationship between resting-state functional cortical-cortical connectome and the severity of conduct problems using the Child Behavior Checklist (CBCL) and the Strengths and Difficulties Questionnaire (SDQ). At a liberal threshold, results showed that the functional brain connectivity associated with conduct problems assessed by both scales largely differ as only 21 brain connectivity were shared. Permutation feature importance revealed that brain connectivity between precentral/postcentral gyri and lateral prefrontal cortex (both ventral and dorsal) were the most important features in explaining variance in CP. The current study highlights that psychometric measures may yield distinct functional connectivity results. Moreover, severity of conduct problems in children and adolescents are associated with deficient functional connectivity between somatomotor and ventral attention networks which suggests potential alterations in motor, cognitive and reward processes.

Introduction

Conduct disorder (CD) is defined by serious and persistent patterns of behavior that violate the rights of others (i.e., aggressive, and rule-breaking behaviors) (APA, 2013). It has been suggested that approximately 5% of children will display severe and persistent conduct problems (CP) and meet the criteria for CD (Bevilacqua et al., 2018; Fairchild et al., 2019). These children are known to display high levels of comorbid psychopathologies such as callous-unemotional traits (Frick et al., 2014), but also attention-deficit/hyperactivity (ADHD) symptoms (Bird et al., 2006; Boylan et al., 2007; Costello et al., 2003; Nock et al., 2006; Wichstrøm et al., 2012). Past studies have shown that individuals with CP may demonstrate a variety of neurobiological impairments. Indeed, in a recent meta-analysis of functional neuroimaging studies, our research team observed that adolescents and adults exhibiting antisocial behaviors may be characterized by abnormal brain activity during fMRI tasks involving negative emotions processing, social cognition and cognitive control (Dugré et al., 2020). For example, scientific literature has extensively supported the role of the amygdala, medial and lateral prefrontal cortex, insula and cingulate cortex in our understanding of the neural correlates of CP during functional magnetic resonance imaging (fMRI) tasks (Alegria et al., 2016; Dugré et al., 2020; Noordermeer et al., 2016; Raschle et al., 2015; Wong et al., 2019). However, in comparison to other neuroimaging modalities, the functional brain connectivity underpinning CP remains largely understudied.

In the last decade, researchers have aimed to identify intrinsic functional networks which regroup reliable temporally correlated brain regions at rest. Indeed, these large-scale networks usually include the medial fronto-parietal (e.g. default-mode network [DMN]), occipital (e.g. medial and lateral visual), pericentral (e.g. sensorimotor, somatomotor [SomMot]), dorsal fronto-parietal (e.g. dorsal attention [DorsAttn]), lateral fronto-parietal (e.g. cognitive control), midcingulo-insular (e.g. salience [SAL], ventral attention [VentAttn], cingulo-opercular [CingOperc]) networks (Gordon et al., 2016; Schaefer et al., 2018; Uddin et al., 2019; Yeo et al., 2011). Resting-state functional connectivity has recently gained considerable attention in the investigation of the neurobiological mechanisms involved in antisocial behaviors. In a recent meta-analysis of resting-state functional connectivity studies, we found that antisocial subjects exhibited prominent

alterations in functional connectivity in nodes of the DMN (i.e., ventro- and dorso-medial PFC and posterior cingulate cortex), DorsAttn (i.e., Frontal eye field) and VentAttn regions (i.e., anterior midcingulate cortex/pre-supplementary motor area) as well as in the amygdala (Dugré and Potvin, 2021). Using data from the ABCD study (n=9636), authors have recently showed that the severity of CP was significantly associated with average within-connectivity in the DorsAttn, whereas reduced connectivity within the DMN was rather associated with callous-unemotional traits (Umbach and Tottenham, 2020). Similarly, reduced PCC-vmPFC connectivity (within-DMN) was found when comparing inmates with and without psychopathic traits (Motzkin et al., 2011). However, some recent meta-analytic evidence suggests that dysconnectivity of the DMN may not be specific to CP or callous-unemotional traits but may rather act as a transdiagnostic neurobiological markers (Doucet et al., 2020). These results justify the need to search for specific neurobiological markers of CP.

Growing evidence suggests that antisocial behaviors may be mostly associated with impairments of between- rather than within-network connectivity. In a large sample of adults (n=1003), some researchers have found that anger-aggression was mainly correlated with connectivity between the PCC (DMN) and visual, SomMot and VentAttn as well as between the FP and SomMot (Weathersby et al., 2019). Antisocial behaviors appear to be also associated with deficient functional connectivity between VentAttn regions and DMN (Pujol et al., 2012) and FP (Cohn et al., 2015) as well as between the DorsAttn and DMN and VentAttn (Shannon et al., 2011). An increasing number of studies also indicate that antisocial behaviors (e.g., aggression) may also be related with altered resting-state connectivity between the amygdala and brain regions involved in the DMN (Motzkin et al., 2011; Sukhodolsky et al., 2022), FP and VentAttn networks (Sukhodolsky et al., 2022). Overall, these results indicate that most of the resting-state connectivity alterations are found between the DMN, DorsAttn, VentAttn and SomMot. In comparison with other pediatric psychiatric disorders, several brain connectivity (e.g., DMN) associated with CP are also reported in ADHD (Sutcubasi et al., 2020), anxiety (Xu et al., 2019) and depressive (Kaiser et al., 2015) disorders. Once again, these highlight the importance of clarifying the deficits in resting-state connectivity that may be specifically associated with antisocial behaviors, compared to other psychopathologies.

Despite the relevance of the above-mentioned findings, there are several limitations that tamper scientific progress in the field. First, there are discrepancies in results across studies which may be explained by different methodologies such as restricting analyses to *a priori* defined seeds (e.g., amygdala) or a limited number of large-scale networks (e.g., DMN). Likewise, the diversity of psychometric scales used to assess antisocial behaviors and CP may contribute to discrepant results. Studies on resting-state functional connectivity usually include small sample sizes (median: 22 subjects, see Dugré and Potvin, 2021), which may increase the false positive rate. Recently, some have argued that in resting-state functional connectivity investigations, stability and reproducibility in brain-behavior relationships may require thousands of individuals (Marek et al., 2022), thus highlighting the need for larger sample size to investigate the neural correlates of CP.

Therefore, the purpose of the study was twofold. First, we aimed to address these issues by investigating the cortico-cortical and amygdala-cortical functional connectivity at rest associated with two distinct measures of CP, using a large sample of 1416 children and adolescents. We hypothesized that CP will be associated with disrupted functional connectivity within-DMN regions, and between DMN and DorsAttn, VentAttn, SomMot networks, as well as between the amygdala and these networks. Then, as exploratory analyses, we examined whether the significant brain connectivity associated with CP may also be related to other psychopathologies such as irritability, ADHD symptoms and callous-unemotional traits.

Methods

Participants and Neuroimaging Acquisition Parameters

Data from 2200 participants were obtained from the Healthy Brain Network (HBN), an ongoing initiative in New York area (USA) that aims to investigate heterogeneity and impairment in developmental psychopathology (5-21 years old) (Alexander et al., 2017). The HBN adopted a community-referred recruitment model in which advertisements was provided to community members, educators, parents. Exclusion criteria were impairments that prevents full participation in the study (e.g., serious neurological disorders, hearing or visual impairments),

neurodegenerative disorder, acute encephalopathy, acute intoxication, and serious psychiatric disorders (recent diagnosis of schizophrenia and/or manic episode). Supplemental information is provided elsewhere (Alexander et al., 2017).

From the 2200 participants included in the Data Release 7.0, 1583 participants contained available functional neuroimaging data. Written assent was obtained from participants younger than 18 years old, and written consent was obtained from their legal guardians. Written informed consent was obtained from participants aged 18 or older prior to enrolling in the study. The original HBN study was approved by the Chesapeake Institutional Review Board (https://www.chesapeakeirb.com/). The current study was approved by the local ethics committee.

MRI acquisition took place at three different sites: mobile 1.5T Siemens Avanto in Staten Island, 3T Siemens Tim Trio at Rutgers University Brain Imaging Center (RUBIC), and 3T Siemens Prisma at the CitiGroup Cornell Brain Imaging Center (CBIC) (acquisition protocols and parameters can be found in Table S1, in (Alexander et al., 2017) as well as http://fcon_1000.projects.nitrc.org/indi/cmi_healthy_brain_network/). Data at the CBIC were obtained using the same data acquisition protocol implemented at RUBIC. The acquisition of the two resting-state scans lasted 5 min each, during which participants viewed a fixation cross located at the center of the computer screen. Data for the Siemens Avanto were acquired in a single run lasting 10 minutes.

Main Assessments

Conduct problems were assessed using the Child Behavior Checklist (CP-CBCL, Achenbach and Rescorla, 2001), which comprised 33 items from Aggressive (20 items) and Rule-Breaking (11 items) syndromes scales. Parents rated each item using a 3-point scale (0=not true to 2=very true)(α=.93). We also used the 5-item CP scale (2 items on aggressive and 3 on non-aggressive rule-breaking behaviors) of the Strength and Difficulties Questionnaire (CP-SDQ, Goodman, 2001), which showed acceptable internal consistency (α=.72). Pearson's correlation between these two scales of CP revealed moderate-strong association (*r*=.788).

Exploratory analyses were conducted to investigate the association between brain connectivity and irritability, ADHD symptoms and callous-unemotional traits. Irritability was measured using the Parent-report form of the Affective Reactivity Index (Stringaris et al., 2012). This 6-item scale (0=Not True to 2=Certainly True) showed excellent internal consistency (α=.90). ADHD symptoms were measured using the total score of the parent-report form of the Strengths and Weakness of ADHD-symptoms and Normal-behavior (Swanson et al., 2012). This scale, which contains 18 items (+3 = Far Below Average to -3 = Far Above average), also showed excellent internal consistency (α=.95). Finally, callous-unemotional traits were measured using the parent-report form of the Inventory of Callous-Unemotional Traits (Essau, Sasagawa et Frick, 2006). In our study, we examined the relationship between brain connectivity and the three subscales of this 24-item questionnaire (i.e., Callousness, Uncaring, and Unemotional traits), separately, given that they are differently associated with CP and externalizing behaviors. Indeed, a recent meta-analysis showed that the unemotional subscale was weakly related with externalizing problems, compared to the two other subscales (Cardinale and Marsh, 2020). The Callousness (e.g., '*Shows no remorse'*, α=.74), Uncaring (e.g., reversed '*Tries not to hurt others' feelings'*, α=.84) and Unemotional (e.g., '*Does not show emotions'*, α=.79) subscales demonstrated good internal consistency.

fMRI data preprocessing

Functional images were realigned, corrected for motion artifacts with the Artifact Detection Tool (Power et al., 2014)(ART, setting a threshold of 0.9 mm subject ART's composite motion and a global signal threshold of Z = 5) with the implemented in CONN Toolbox (Whitfield-Gabrieli and Nieto-Castanon, 2012), bandpass filtered (0.01 Hz < f < 0.10 Hz) and co-registered to the corresponding anatomical image. The anatomical images were segmented (into GM, white matter, and cerebrospinal fluid) and normalized to the Montreal Neurological Institute (MNI) stereotaxic space. Functional images were then normalized based on structural data, spatially smoothed with a 6 mm full-width-at-half-maximum (FWHM) 3D isotropic Gaussian kernel and resampled to 2 mm^3 voxels. For the preprocessing, the anatomical component-based noise correction method (aCompCor strategy, Behzadi et al., 2007), was employed to remove

confounding effects from the BOLD time series, such as the physiological noise originating from the white matter and cerebrospinal fluid. This method was found to increase the validity and sensitivity of analyses (Chai et al., 2012). In the current study, pre-processing issues due to the poor quality of images were found in 108 participants (n=1475), and 59 adolescents exhibited high movements (exceeding 3mm). Moreover, given that the CBCL measures children and adolescent psychopathologies (< 18 years old), 56 adults subjects were excluded, leaving a final sample size of 1360 adolescents.

Cortico-cortical and Amygdalo-cortical functional connectivity

To examine the cortico-cortical connectivity, we extracted functional connectivity between cortical parcels derived from the Gordon's parcellation (i.e., 333 cortical parcels) covering the whole cortex (Gordon et al., 2016), as used in the ABCD study (Marek et al., 2019). These 333 cortical parcels are grouped into 13 intrinsic networks, namely Auditory, Cingulo-Opercular, Cingulo-Parietal, DMN, DorsAttn, FP, VentAttn, SomMot-Hand, SomMot-Mouth, Retrosplenial-Temporal, Salience, Visual, and Unassigned (None). We additionally included left and right amygdala from the FSL Harvard-Oxford Atlas, provided in the CONN Toolbox. Physiological noise, realignment parameters, and movement artifacts were regressed out as confounding effects from the BOLD time-series for each parcel.

Statistical Analyses

Mass-Univariate analysis

In the first-level analysis, Pearson's correlation coefficients between the residual BOLD time course from each parcel and the time course of all other 332 parcels, for each subject. The same was done for amygdala regions and all Gordon 333 parcels. Coefficients were converted to normally distributed z-scores using a Fisher Z-Transformation. Second-level analyses were conducted using mass-univariate linear regression to examine relationships with CP derived from the CBCL and the SDQ, removing the effect of age, sites, sex, percentage of valid scans and framewise displacement. To identify brain connectivity that were reliably associated with CP, we conducted mass-univariate linear regression analyses on 5,000 random subsamples using 90% of

the total sample at each iteration. Brain connectivity were then considered as statistically associated with CP if the average p-value across the 5,000 iterations met the uncorrected threshold of $p<0.005$. This somewhat liberal threshold was used to keep brain connectivity that has acceptable association with CP. After having selected the most correlated brain connectivity across CBCL and the SDQ ($p<0.005$), we kept only those overlapping between the two scales which may characterize the core features underpinning. These steps were conducted to adequately control for type II errors (i.e., false negative due to stringent thresholding) as well as decreasing type I errors by limiting spurious and scale-specific results. Indeed, selecting the most stable brain connectivity measures across the 5,000 subsampling iterations and those overlapping between scales measuring the same construct may reduce the risk for falsely accepting the null hypothesis on spurious brain connectivity.

Permutation Feature Importance

After having identified brain connectivity associated with CP across scales, we investigated whether brain connectivity results differed between scales regarding their importance in explaining variance of the CBCL and SDQ. We calculated feature importance by conducting a multivariate linear regression which included the resulting brain connectivity measures (independent variables) in association with CP severity (dependent variable), respectively. We permutated each brain connectivity measure 100 times on a test set (20% of the data) and compared R_2 scores between the baseline model on the train set (80% of the data without permutations). Given that results may vary depending on the selected test set, we ran permutation importance on 1,000 randomly selected test set and averaged estimates. Compared to the base model, changes in R_2 score would therefore indicate the relative importance of a particular feature. Finally, we examined differences in feature importance of each brain connectivity between the CBCL and SDQ with Fisher r-to-z transformation ($p<0.05$, two-tailed). Subanalyses were performed using the same statiscal procedure to examine whether results may have been driven by developmental period (i.e., childhood, adolescence) and scanner strength (i.e., 3 Tesla, 1.5 Tesla).

Exploratory analyses

As exploratory analyses, we sought to examine whether the brain connectivity associated with severity of CP were also related to other psychopathologies, namely irritability, ADHD symptoms and callous-unemotional traits. To do so, we conducted partial correlations between brain connectivity and psychopathologies, adjusting for the effect of age, sites, sex, percentage of valid scans and framewise displacement.

Functional Decoding

Functional decoding was conducted to examine the neurocognitive domains (i.e., task fMRI) underlying functional connectivity between two ROIs that are associated with CP, using the BrainMap environment. The BrainMap environment include a repository of neuroimaging studies which contain brain coordinates and metadata (e.g., sample size, behavioral categories) for more than 21,083 experiments. Brain coordinates (foci) and metadata (e.g., behavioral categories, sample size, contrasts) of papers included in the repository are coded by their research team, as well as authors of original papers via Scribe (http://brainmap.org/scribe/) and then verified by BrainMap staff. BrainMap ontology rely on 60 behavioral categories grouped into 5 domains: cognition, emotion, perception, action, interoception. The Behavioral Analysis plugin for Multi-image Analysis GUI (Lancaster et al., 2012) (ric.uthscsa.edu/mango) relies on the binomial "success" probabilities of activation foci within a ROI than expected for random spatial distribution for a behavioral subdomain. Z-score of 3.0 or more represent $p<0.05$ Bonferroni corrected for multiple comparisons.

In the current study, 49 categories from 4 different neurocognitive domains were included (i.e., Action, Emotion, Cognition, Perception) given that none of the parcel was significantly associated with Interoception subcategories. Then, each parcel of a given brain connectivity (parcel A & parcel B) was characterized by a binary set of 49 behavioral categories (0 [$Z < 3$] and 1 [$Z \geq 3$]). We created an adjacency matrix (49 categories-by-49 categories) representing the connected categories between parcel A and parcel B. Then, we summed adjacency matrices for all brain connectivity measure significantly associated with CP, separately for positive and negative

correlations. Finally, behavioral categories at a node-level were ranked based on their number of edges (degree centrality) and influence across the network (betweenness centrality). We also examined what behavioral domains were the most frequently reported across brain connectivity. These analyses were conducted with python's NetworkX package (Hagberg et al., 2008).

Results

Cortico-cortical and Amygdalo-cortical functional connectivity

Mass univariate analysis revealed significant functional brain connectivity associated with CP-CBCL (231 connections at a $p<0.005$ uncorrected threshold) and CP-SDQ (269 connections at a $p<0.005$ uncorrected threshold). From these results, only 21 brain connections were shared across both scales (i.e., 10 positively and 11 negatively associated with CP, see Figure 1A-C and supplementary material). Overall, brain connectivity measures of CP were mainly driven by nodes of the SomMot (6 out of 21 connections) and vAttn networks (4 out of 10 positive connections), but also with unassigned parcels from the Gordon Atlas (None: 4 connections). More precisely, severity of CP was positively associated with functional connectivity within-SomMot (2 connections), between FP and unassigned parcels (i.e., bilateral posterior hippocampus – Frontal Eye Fields) but also between VentAttn and DMN, DorsAttn, FP and SomMot. Furthermore, CP was negatively associated with functional connectivity between cingulo-opercular & visual (2 connections), SomMot & Salience network (2 precentral-dACC), auditory & cingulo-opercular & DMN as well as within-DMN.

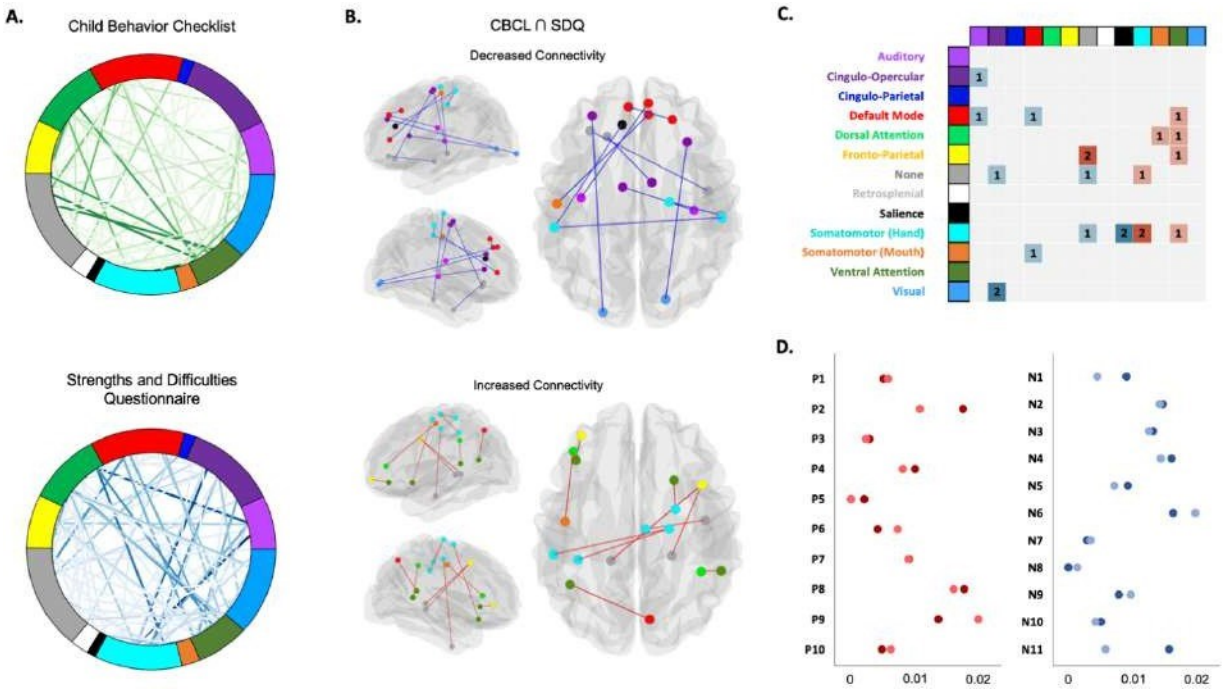

Fig. 1. Associations between cortico-cortical connectivity and Conduct Problems across different scales. **A.** Weight (F-value) of each significant ($p<0.005$) cortico-cortical connectivity across 13 networksof the Gordon (333 parcels, Gordon et al., 2015) after 5,000 random subsampling using 90% of thesample in association with Conduct Problems scales derived from the Child Behavior Checklist (CP-CBCL) and the Strengths and Difficulties Questionnaire (CP-SDQ). **B.** Connectivity positively and negatively associated with Conduct Problems that intersected between the CBCL and SDQ (Red edges = positive associations; Blue edges = negative associations). **C.** Adjacency matrix showing significant within- and between-network connectivity results associated (Red=Positively; Blue=Negatively) with CP. **A.-B.-C.** Resting-state connectivity networks are represented by the following colors: Magenta = Auditory; Purple = Cingulo-Opercular; Blue = Cingulo-Parietal; Red = Default Mode; Green = Dorsal Attention; Yellow = Fronto-Parietal; Grey = None; White = Retrosplenial; Black = Salience; Cyan = Somatomotor (Hand); Orange = Somatomotor (mouth); Dark Green = Ventral Attention; Light Blue = Visual. **D.** Feature importance (R^2 score with Standard Deviation) in association with severity of ConductProblems for the Child Behavior Checklist (CP-CBCL) and the Strengths and Difficulties Questionnaire (CP-SDQ). Permutation importance was conducted by permutating each of the 21 cortico-cortical brain connectivity in a multivariate linear regression 100 times on a test set (20% of the data) repeated 1,000 using Monte-Carlo cross-validation. Red dots=brain connectivity positively associated with CP; Blue dots=brain connectivity negatively associated with CP. Darkercolors=CBCL & Lighter colors=SDQ. Please refer to Table 1. for more detailed information aboutbrain connectivity.

When examining feature importance of the 21 connections in a multivariate linear regression, we observed that between CBCL and SDQ, brain connectivity measures had roughly similar importance (see Table 1), except for P5 (CBCL > SDQ), N8 (SDQ > CBCL) and N11 (CBCL > SDQ). The top 5 most important features were (please refer to Table 1): 1) **P8 connection**: Premotor-Lateral OFC (R_2 change .016-.018); 2) **N6 connection**: Lateral OFC-SMA (R_2 change .016-.020); 3) **P9 connection:** Precentral-dlPFC (R_2 change .014-.020); 4) **P2 connection:** Lateral PFC-vlPFC (R_2 change .011-.018) and 5) **N4 connection**: dmPFC-Lateral PFC (R_2 change .014-.016). The least important feature was N8 connection: dACC-Postcentral (R_2 change 0-.001).

Regarding amygdalo-cortical functional brain connectivity, analyses revealed that the CP-CBCL was negatively associated with functional connectivity between the right amygdala and the left ($F= 10.38$, $p= 0.002$) and right ($F= 9.16$, $p= 0.004$) ventral PCC (BA 23). Additionally, the CP-SDQ only showed negative association between the right amygdala and the pMTG (FP) ($F=12.57$, $p<0.001$ uncorrected). Thus, no significant connectivity intersected between the two scales, which suggest low reliability in amygdala connectivity across CP scales.

Table 1. Multivariate Feature Importance (resting-state brain connectivity) associated with Conduct Problems across assessments tools

Names	Parcel 1 (Network)	Parcel 2 (Network)	Assessments		Comparisons	
			r (CP-CBCL)	*r* (CP-SDQ)	Z	*p*
Positive Associations						
P1	pSMG (DA)	TPJ (VA)	0.070	0.075	0.290	0.772
P2	**lPFC (FP)**	**vlPFC (VA)**	**0.132**	**0.104**	**1.630**	**0.103**
P3	pHipp (None)	FEF (FP)	0.052	0.046	0.350	0.728
P4	pHipp (None)	FEF (FP)	0.100	0.089	0.640	0.523
P5	PoCG (SH)	PrCG (SH)	0.043	0.000	2.480	0.013
P6	PoCG (SH)	PrCG (SH)	0.063	0.085	1.270	0.203
P7	PrCG(SH)	pITG (None)	0.095	0.094	0.060	0.954
P8	**PMC (SH)**	**lOFC (VA)**	**0.133**	**0.127**	**0.350**	**0.727**
P9	**PrCG(SM)**	**dlPFC (DA)**	**0.117**	**0.141**	**1.400**	**0.162**
P10	AG (VA)	PCUN (DMN)	0.068	0.078	0.580	0.563
Negative Associations						
N1	pINS (A)	dmPFC (D)	0.095	0.066	1.680	0.093
N2	aINS (CO)	LG (V)	0.121	0.119	0.120	0.907
N3	SMA (CO)	Heschl (A)	0.115	0.112	0.170	0.861
N4	**dmPFC (D)**	**lPFC (D)**	**0.127**	**0.120**	**0.410**	**0.684**
N5	lOFC (None)	ITG (None)	0.096	0.084	0.700	0.487
N6	**lOFC (None)**	**SMA (CO)**	**0.128**	**0.141**	**0.760**	**0.448**
N7	dACC (S)	PoCG (SH)	0.052	0.057	0.290	0.772
N8	dACC (S)	PoCG (SH)	0.000	0.034	1.960	0.050
N9	PrCg (SH)	pMTG (None)	0.088	0.098	0.580	0.562
N10	PoCg(SM)	pgACC (D)	0.070	0.063	0.410	0.685
N11	V2 (V)	lPFC (CO)	0.125	0.075	2.900	0.004

Note. R^2 scores were converted to correlation coefficient (square root) to allow statistical comparisons. Names of the brain regions were derived from the center coordinates of each parcel using the Anatomy Toolbox (44). Top 5 most important features are in **BOLD.**

Testing for effects of developmental stage and scanning sites

Testing for differences in features importance across developmental periods yielded significant differences when examining- the features' relationships with CP-CBCL. Indeed, importance of N2 (aINS-Lingual, Z=4.44) and N3 (SMA-Heschl, Z=2.4) significantly increased in adolescence, whereas importance of P3 (pHipp-FEF, Z=3.13), P10 (AG-PCUN, Z=2.6), N4 (dmPFC-lPFC, Z=2.45), N5 (lOFC-ITG, Z=3.64), and N10 (Z=3.1) decreased in adolescence. However, when examining feature importance between developmental stages using the CP-SDQ, no significant differences were observed (see supplementary material for complete results).

Moreover, when comparing features importance between scanner strengths (i.e., 3-tesla versus 1.5-tesla), importance of N4 (dmPFC-lPFC) and N6 (lOFC-SMA) were significantly stronger in the 3T subsample for both CBCL and SDQ. Also, P4 (pHipp-FEF), N1 (pINS-dmPFC) and N9 (PrCG-pMTG) showed stronger importance in the 3T subsample compared to the 1.5T subsample when using the CP-CBCL, whereas N10 (PoCG-pgACC) showed stronger importance in the 1.5T compared to the 3T when using the CP-SDQ (see supplementary material).

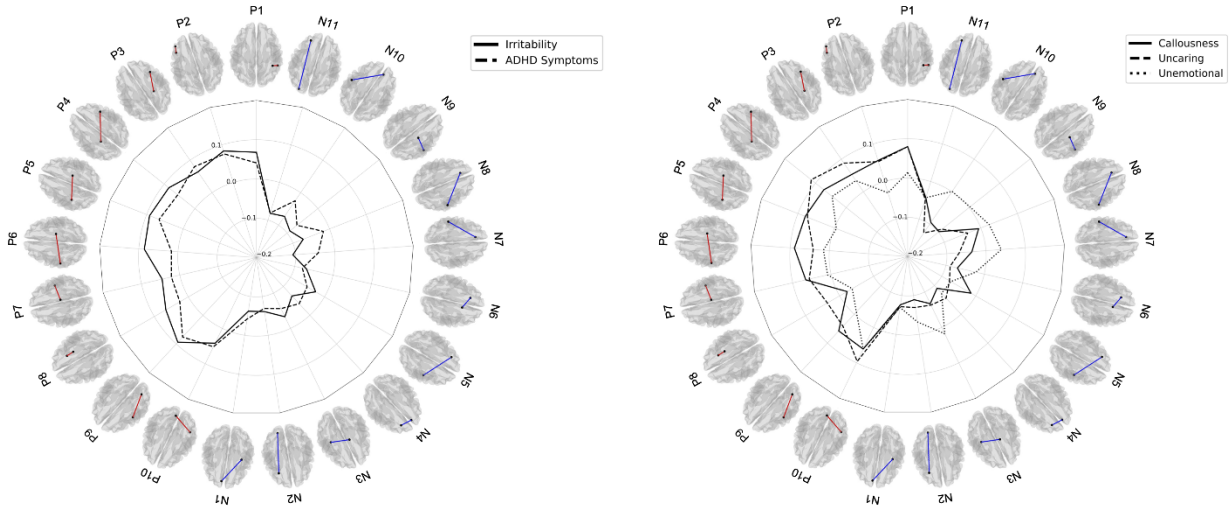

Figure 2. Relationship between functional brain connectivity associated with Conduct Problems and other psychopathologies. Please refer to Table 1 for complete list of brain connectivity measure. Red lines = Positive associations with conduct problems; Blue lines = Negative associations with conduct problems.

Exploratory Analyses

Partial correlations revealed that irritability, ADHD symptoms, callousness, uncaring but not unemotional traits were associated with brain connectivity (see Figure 2 & Table 2). Indeed, after applying FDR correction for multiple comparisons (pFDR<0.05), irritability showed statistically significant associations with 17 out of 21 brain connectivity measures such as (top 3): N7 (dACC-PoCG, *r*=-.107), P9 (PrCG-dlPFC, *r*=.094), and P5 (PoCG-PrCG, *r*=.092). ADHD symptoms were significantly related with 8 brain connectivity measures including N11 (V2-lPFC, *r*=-.081), N6 (lOFC-SMA, *r*=-.08), and P3 (pHipp-FEF, *r*=.08).

Regarding CU traits, severity of uncaring traits was associated with 8 functional connectivity measure such as N10 (PoCG-pgACC, *r*=-.127), P4 (pHipp-FEF, *r*=.114), and P10 (AG-PCUN, *r*=.096), whereas callousness was correlated with 7 brain connectivity including N9 (PrCG-pMTG, *r*=-.098), N10 (PoCG, *r*=-.095), and N4 (dmPFC-lPFC, *r*=-.09).

Table 2. Relationship between resting-state brain connectivity associated with Conduct Problems and other psychopathologies

Names	Brain Connectivity		Psychopathologies				
	Parcel 1 (Network)	Parcel 2 (Network)	Irrit. *r*	ADHD Sx *r*	Callous *r*	Uncaring *r*	Unemot. *r*
Positive Associations							
P1	pSMG (DA)	TPJ (VA)	**0.068**	0.041	**0.080**	**0.080**	0.014
P2	lPFC (FP)	vlPFC (VA)	**0.084**	**0.076**	0.056	0.053	-0.030
P3	pHipp (None)	FEF (FP)	**0.064**	**0.08**	0.053	**0.088**	0.034
P4	pHipp (None)	FEF (FP)	**0.085**	0.056	0.073	**0.114**	0.046
P5	PoCG (SH)	PrCG (SH)	**0.092**	**0.066**	**0.080**	0.074	-0.005
P6	PoCG (SH)	PrCG (SH)	**0.086**	0.017	**0.089**	0.041	0.015
P7	PrCG(SH)	pITG (None)	0.046	0.022	0.066	0.057	0.009
P8	PMC (SH)	lOFC (VA)	**0.066**	0.025	-0.022	0.036	-0.037
P9	PrCG(SM)	dlPFC (DA)	**0.094**	**0.076**	0.058	0.042	-0.008
P10	AG (VA)	PCUN (DMN)	0.042	0.052	0.061	**0.096**	0.061
Negative Associations							
N1	pINS (A)	dmPFC (D)	**-0.062**	-0.042	-0.076	-0.071	-0.069
N2	aINS (CO)	LG (V)	**-0.061**	**-0.069**	**-0.089**	-0.069	-0.032
N3	SMA (CO)	Heschl (A)	-0.033	-0.056	-0.067	-0.063	0.018
N4	dmPFC (D)	lPFC (D)	**-0.067**	-0.04	**-0.09**	-0.056	-0.073
N5	lOFC (None)	ITG (None)	-0.026	-0.051	-0.014	**-0.077**	-0.073
N6	lOFC (None)	SMA (CO)	**-0.069**	**-0.08**	-0.07	**-0.089**	-0.022
N7	dACC (S)	PoCG (SH)	**-0.107**	-0.042	-0.036	-0.068	0.039
N8	dACC (S)	PoCG (SH)	**-0.072**	-0.017	-0.006	-0.036	0.023
N9	PrCg (SH)	pMTG (None)	**-0.091**	**-0.068**	**-0.098**	**-0.088**	0.003
N10	PoCg(SM)	pgACC (D)	**-0.073**	-0.025	**-0.095**	**-0.127**	0.001
N11	V2 (V)	lPFC (CO)	**-0.082**	**-0.081**	-0.043	-0.048	-0.043

Note. Names of the brain regions were derived from the center coordinates of each parcel using the Anatomy Toolbox (44). Correlation strength in **BOLD** represent statistically significant association after correcting for multiple comparisons (pFDR<0.05).

Functional Decoding

As shown in Figure 2., the functional brain connectivity measures associated with CP were characterized by a variety of behavioral categories. First, positive brain connectivity measures were mainly related to interaction between Action and Cognition as well as within-Cognition domains. Indeed, the most frequent connection of behavioral domains was between Speech Execution (Action) and Working Memory (Cognition) with 4 out of 11 pairs of parcels. Also, the top 5 categories with the largest number of connections (node centrality) included: Unspecified (Action), Speech Execution (Action), Working Memory (Cognition), Attention (Cognition) and Semantics (Cognition). The top 5 categories that had the most influence (betweenness centrality) on the network were: Working Memory (Cognition), Unspecified (Action), Speech Execution (Action), Explicit Memory (Cognition) and Semantics (Cognition).

Second, negative brain connectivity measures rather showed a widespread relationship between the four behavioral domains. Indeed, the most frequent connections were 1) Action Execution (Unspecified) & Reward, 2) Attention & Reward, 3) Attention & Somesthesis (Unspecified), and 4) Reward & Somesthesis (Unspecified) with each 3 out of 10 pairs of parcels (Figure 2). Moreover, the top 5 categories with the largest number of connections (node centrality) were: Orthography (Cognition), Shape (Visual), Unspecified (Visual), Speech Execution (Action) and Attention (Cognition). Finally, the top 5 categories that had the most influence on the network were: Orthography (Cognition), Shape (Visual), Unspecified (Visual), Speech Execution (Action) but also Reward (Emotions).

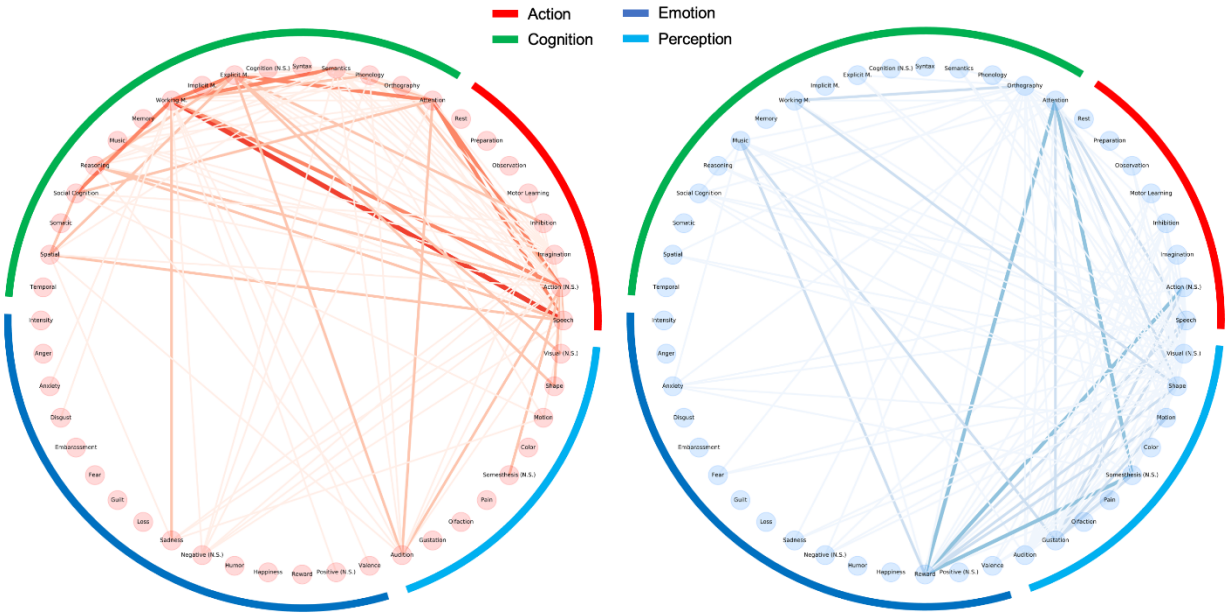

Figure 3. Circular layout displaying the relationship between the behavioral domains significantlyassociated with functional brain connectivity. Red graph = brain connectivity positively related toCP. Blue Graph = brain connectivity negatively related to CP. Thicker line represents larger number of connected behavioral categories across pairs of brain connectivity.

Discussion

Using a large sample of adolescents, we aimed to clarify the role of cortico-cortical and amygdalo-cortical functional brain connectivity associated with CP. More precisely, we investigated the reliability of the relationship between resting-state brain connectivity measures and severity CP using two different psychometric scales (CBCL and SDQ). We observed that both scales show distinctive association with brain connectivity measures. Indeed, using a liberal statistical threshold ($p<0.005$ uncorrected), only 21 cortico-cortical resting-state connectivity measures associated with CP significantly overlapped between the two scales. These mainly included regions involved in the SomMot, VentAttn and FP networks (positive associations) as well as Cingulo-Opercular, Salience and DMN regions (negative associations). Additional analyses revealed that these regions were characterized by interactions between Action & Cognition (i.e., Positive association with CP) as well as between Reward and Cognition, Perception and Action (i.e., Negative associations with CP). Finally, exploratory analyses revealed most brain connectivity were also associated with other psychopathologies such as irritability, ADHD symptoms, callousness, uncaring but not unemotional traits.

In our recent meta-analysis of resting-state connectivity studies, we showed that antisocial subjects exhibited hyperconnectivity with ventral attention network (ie., aMCC/pre-SMA) and amygdala, and hypoconnectivity regions of the DMN (i.e., mPFC and PCC/Precuneus) and Dorsal attention network (i.e., PMC, SPL), compared to healthy controls (Dugré, 2021). In line with these results, we found that CP was positively associated with 4 brain connectivity including regions of the ventral attention network and negatively associated with 2 brain connectivity that involved parcels of the DMN. However, contrasting with results from the meta-analysis, we found that CP was rather prominently associated with disrupted connectivity from the SomMot network (7 connections), from brain regions unassigned to any of the Gordon Networks such as posterior hippocampus and inferior/middle temporal gyri (6 connections), FP (3 connections) as well as cingulo-opercular networks (3 connections). Moreover, we found no reliable evidence of amygdala-cortical connectivity across scales. It is noteworthy to mention that studies included in our prior meta-analysis restricted their analyses on *a priori* seeds and did not investigate the

whole connectome, and this may largely explain the discrepancies between results. Second, the functional connectivity alterations associated with CP may differ between a case-control design versus a study examining severity of CP, dimensionally. In our recent meta-analysis using case-control analysis, we found that antisocial population was characterized by disrupted socio-affective and attentional processes (Dugré and Potvin, 2021). Here, we rather found that CP was dimensionally related to somatomotor and ventral attention, salience and cingulo-opercular networks. While the the results of the former meta-analysis may help understanding the shared features across subjects, the results of the latter may represent brain connectivity associated with severity of the pathology. Discrepant results between our meta-analysis and the current study could also been driven by distinct developmental periods. However, subanalyses revealed that importance of most brain connectivity associated with CP were relatively robust across developmental periods (i.e., childhood and adolescence). Indeed, the top 5 brain connectivity that were the most strongly associated with CP (i.e., P8, N6, P9, P2, and N4) show no significant change across developmental stages (except N4 using the CBCL). Furthermore, the few differences between developmental periods were observed using the CBCL but not with the SDQ. It is noteworthy to mention that the two scales differ in the included items. Indeed, the SDQ comprises 5 broad items characterizing CP (i.e., *tantrum*, *obeys*, *fights*, *lies* & *steals*), whereas the CP-CBCL is composed by 2 subscales namely aggression and rule-breaking behaviors. From childhood to adolescence, aggressive behaviors show a general decline, whereas rule-breaking behaviors are quasi inexistant in childhood but exhibit a sharp increase at the beginning of adolescence (Bongers et al., 2004; Stanger, Achenbach, & Verhulst, 1997; Tremblay et al., 2004). It could thus be hypothesized that the CBCL, items corresponding to aggressive behaviors may be more important in characterizing CP during childhood, whereas the rule-breaking subscale alone shows clinical utility in predicting CD in adolescence (AUC=.90) (Yule et al., 2021).

Interestingly, we provided evidence that brain connectivity measures that were positively associated with CP were mainly characterized by interaction between Action Execution & Cognition behavioral domains. First, brain connectivity measures that were positively associated with CP included lateral PFC regions (i.e., ventro and dorsolateral) and the postcentral/precentral gyri. According to a recent meta-analysis, both the lateral PFC and precentral gyrus co-activate

during n-back working memory tasks (Wang et al., 2019). Indeed, it has been shown that the lateral PFC (ventral and dorsal parts) plays a major role in the reception, maintenance and monitoring of sensory inputs and sending outputs to the motor system (Müller et al., 2002; Passingham and Sakai, 2004), whereas the precentral gyrus may rather be involved in action preparation and the processing of motor movements (Yang, 2015) . As such, these results are in line with a recent meta-analysis of task-based fMRI studies showing that antisocial subjects exhibit aberrant co-activation of these particular brain regions (i.e., precentral and ventrolateral prefrontal cortex) during cognitive control tasks (Dugré et al., 2020). This also concurs with past evidence indicating that deficient activity in somatomotor regions may confer an increased risk for general externalizing behavior (Castellanos-Ryan et al., 2014). Moreover, there is an increasing number of results indicating that deficient activity and connectivity of the somatomotor network might be a transdiagnostic neurobiological marker of general psychopathology in children and adolescent (Dugré, Eickhoff et Potvin, 2022; Schwarzlose et al., 2023) as well as in adults (Van Dam et al., 2017). Interestingly, past results suggests that from 10 to 26 years old, changes in functional connectivity of the somatomotor and cingulo-opercular/salience networks may reflect development of cognitive control (Grayson et Fair, 2017; Marek et al., 2015). This is also supported by our results showing that brain connectivity of somatomotor regions, both within- and between-network, were also associated with irritability, ADHD symptoms and callousness. Developmental trajectories underpinning these psychopathologies is known to significantly predict the risk for CP in childhood and adolescence (Dugré et Potvin, 2022). Even though it may not be specific to CP, future studies should seek to investigate the role of somatomotor network in the development of antisocial behaviors.

Second, brain connectivity measures that were negatively associated with CP mainly included the pg- & dACC, the SMA and the aINS and lateral PFC, which were mainly represented by interactions between Reward and Action Execution, Attention & Somesthesis. In contrast with the functional decoding suggesting their implications in reward processing tasks, we recently found that antisocial subjects exhibited reduced response in these regions (i.e., pg- & dACC extending to the aMCC/pre-SMA as well as the aINS) during acute threat response (Dugré et al., 2020). Indeed, while they are systematically observed across meta-analyses on reward tasks (Diekhof et al.,

2012; Liu et al., 2011; Oldham et al., 2018; Sescousse et al., 2013; Silverman et al., 2015), the ACC and aINS are not specific to any particular neurocognitive domain (Shackman et al., 2011; Yarkoni et al., 2011) and are known to be involved in detecting behaviorally relevant stimuli in the environment (Uddin et al., 2019), in general, and may play an interacting role between internally (i.e., DMN) and externally directed actions (i.e., frontoparietal network) (Uddin, 2015). Dysconnectivity of salience and cingulo-opercular networks were found to be associated with the broad dimension of externalizing pathology in two recent studies (Afzali et al., 2020; Lees et al., 2021). In our study, we also found that reduced connectivity between the dACC (Salience) and the postcentral gyrus (Somatomotor) network were associated with irritability but not the other psychopathologies. Of interest for symptoms of irritability, activity of the dACC is frequently thought to be a core brain region during frustrative non-reward (Bertsch et al., 2020, Dugré et Potvin, Preprint; Leibenluft, 2017), whereas activity of the postcentral gyrus is observed when initiating aggressive and retaliatory behaviors (Dugré et Potvin, Preprint; Wong et al., 2019). It could be hypothesized that a weaker dACC-postcentral gyrus connectivity may increase the proneneness for CP (i.e., aggressive behaviors) by disinhibiting action initiation processes. It is unequivocal that future studies should seek to investigate this relationship more specifically.

Limitations

In our study, we aimed to address several limitations of current literature on resting-state functional connectivity such as the usually low sample size and the variability in the psychometric scales used across studies. Despite the strengths of our study, few limitations need to be acknowledged. Indeed, the sample contains a relatively wide age range spanning from childhood to late adolescence. This could have introduced biases in our results. However, we took additional measures to minimize the effects of age and conducted subanalyses that examined the effect of age on the reliability of our results. Indeed, developmental period only altered a few results, and these were only reported for CBCL, whereas the SDQ showed no significant differences. Secondly, neuroimaging data was collected in 3 different sites (two with identical scanning parameter) that may have altered results. We also tested whether differences in

scanner strengths may have altered our results. We found that importance of some brain connectivity was significantly stronger when using 3T scanner compared to 1.5T. Third, the proximity of Gordon's parcels and the amygdala (Harvard Oxford Atlas) may have caused autocorrelation issues which could explain lack of significant relationship between CP and functional connectivity between the amygdala and other structures such as the anterior medial temporal lobe. Fourth, the HBN adopted a community-referred recruitment model. Therefore, careful interpretations should be made when comparing study results with population-based cohorts. Although the sample size was relatively large in our study, further examination with other samples is needed to validate the generalizability of our results.

Conclusion

In conclusion, we found that brain connectivity associated with CP largely depends on the measure used. In fact, only 21 connections were shared between the CBCL and SDQ even if both scales show relatively strong phenotypic correlation (r=.79). Nonetheless, these 21 connections mainly spanned the SomMot, VentAttn and FP (positive) and Cingulo-Opercular, Salience and DMN (negative) networks. Results of this study indicate that severity CP may principally be associated brain connectivity underpinning cognitive control (positive) and emotional inhibition (negative association). Finally, the brain connectivity associated with CP were also related to other psychopathologies, suggesting that irritability, ADHD symptoms, callousness and uncaring may play a central role in neural features underpinning CP. This concurs with recent research showing that from 6 to 12 years old, the developmental co-occurrence of irritability, hyperactivity and CU traits plays an additive role in the risk for CP (Dugré et Potvin, 2020).

CHAPITRE 7 – LÉSIONS ET RÉSEAUX CÉRÉBRAUX ABERRANTS

SIXIÈME ARTICLE

The origins of evil: from lesions to functional architecture of the antisocial brain

Jules R. Dugré, MSc [1,2] & Stéphane Potvin, PhD [1,2]

[1] Research Center of the Institut Universitaire en Santé Mentale de Montréal, Montreal, Canada

[2] Department of Psychiatry and Addictology, Faculty of medicine, University of Montreal, Montreal, Canada

Déclaration de l'étudiant

Je déclare être l'auteur principal de cet article. J'ai été impliqué dans la conception de l'étude, menéla revue systématique, conduit les analyses statistiques, interprétés les résultats et écrit la premièreversion et la version finale de l'article. Mon directeur de thèse, Stéphane Potvin a conseillé mon travail de recherche, suggérés des corrections et ont approuvé la version finale de l'article.

Abstract

In the past decades, a growing body of evidence has suggested that some individuals may exhibit antisocial behaviors following brain lesions. Recently, some authors have shown that lesions underpinning antisocial behaviors may disrupt a particular brain network during resting-state. However, it remains unknown whether these brain lesions may alter specific mental processes during tasks. Therefore, we conducted meta-analytic coactivation analyses on lesion masks of 17 individuals who acquired antisocial behaviors following their brain lesions. Each lesion mask was used as a seed-of-interest to examine their aberrant coactivation network using a database of 143 whole-brain neuroimaging studies on antisocial behaviors (n=5913 subjects). We aimed to map thelesion specific network that show deficient activity in antisocial population against a null distribution derived from 655 control lesions. We further characterized the lesion-based meta-analytic network using term-based decoding (Neurosynth) as well as receptor/transporter density maps (JuSpace). We found that the lesion meta-analytic network included the amygdala, orbitofrontal cortex, ventro- and dorso-medial prefrontal cortex, fusiform face area, supplementary motor area, which correlated mainly with emotional face processing and serotoninergic system (5-HT1A & 5-HTT). We also investigated the heterogeneity in co-activation networks through data- driven methods and found that lesions could be grouped in four main networks, encompassing emotional face processing, general emotion processing and reward processing. Our study shows that the heterogeneous brain lesions underpinning antisocial behaviors may disrupt specific mentalprocesses, which further increase the risk for distinct antisocial symptoms. It also highlights the importance and complexity of studying brain lesions in relationship with antisocial behaviors.

Introduction

In the past decades, a growing body of evidence has linked traumatic brain injuries (Bellesiet al., 2019; Buckley et al., 2017), repeated concussions (e.g., Chronic traumatic Encephalopathy: (McKee et al., 2013; Omalu et al., 2010) and resection of brain tumors (Anderson, Bechara, Damasio, Tranel, & Damasio, 1999; Nakaji, Meltzer, Singel, & Alksne, 2003; Tonkonogy, 1991) to the emergence of antisocial behaviors and aggressive tendencies. Indeed, it has been shown that sport-related concussions may increase the risk for impulsivity and aggressive behaviors (Kerr et al., 2014) which is potentially due to sport-related impacts to frontal and temporal areas (Greenwaldet al., 2008). These results indicate that medial prefrontal cortex (mPFC) and anterior temporal lobe (ATL) may be particularly relevant for the emergence of antisocial behaviors. For instance, ina recent meta-analysis of task-based functional neuroimaging studies, we found that individuals with antisocial behaviors exhibited deficient activity of the mPFC during social cognition tasks, whereas amygdala activity negatively correlated with severity of antisocial behaviors across neurocognitive domains (Jules R Dugré et al., 2020). Through a meta-analysis of resting-state connectivity studies in antisocial population, we also shown evidence that both amygdala and mPFC (i.e., ventral and dorsal) exhibited disrupted connectivity (J. R. Dugré, Potvin, S., 2021). Moreover, there is a growing body of evidence suggesting the importance of serotoninergic (mainly serotonin transporter [5-HTT] and 5-HTR$_{1B}$ & $_{2A}$ receptors) and dopaminergic systems (mainly Dopamine transporter [DAT] and D_2 & D_4 receptors) in our comprehension of antisocial behaviors (Ficks & Waldman, 2014; Gard et al., 2019; Rafiei & Kolla, 2021; Veroude et al., 2016). Indeed, these systems are known to encompass the amygdala/ATL and mPFC (e.g., mesolimbic/mesocortical dopaminergic pathways) (Haber & Knutson, 2010; Kaller et al., 2017). Although such convergent results underscore the importance of the amygdala/ATL and mPFC, the neurobiological pathways linking brain lesions to antisocial behaviors remain largely unknown. Furthermore, characterizing these neurobiological pathways using receptor/transporter density maps (Dukart et al., 2021) may inform us on potential treatments for reducing antisocial behaviorsfollowing brain lesions.

Most of the current knowledge about neurobiological markers of antisocial behaviors relieson

correlative methods. Lesion studies are therefore crucial as they offer a more causal association between lesion and the emergence of symptoms. Recently, Darby and colleagues (Darby, Horn, etal., 2018) examined the common brain network across 17 lesion cases that were temporally associated with aggression and antisocial behaviors (i.e., using lesion-to-voxel analysis on n=1,000 healthy subjects during resting-state). The authors observed that the lesions were positively connected with brain regions implicated in the DMN but negatively connected with brain regions spanning the medial visual (lingual/calcarine), ventral (aINS, dACC/aMCC and pre-SMA) & dorsal attention (SPL, FEF) networks during resting-state. Moreover, they showed that the criminallesion network was functionally characterized by moral decision making, in comparison to *control*lesion network (i.e., associated with other syndromes) (Darby, Horn, et al., 2018). However, lesion network mapping employing resting-state data in healthy subjects does have several limitations. First, using resting-state data limits our ability to understand what mental processes are specificallydisrupted by the lesion. Indeed, lesion to a particular region (e.g., amygdala) may exhibit more pronounce symptoms (e.g., aggressive behaviors) when faced to a particular context (e.g., threatening stimulus) compared to another (e.g., language processing). Despite that Darby et al. (Darby, Horn, et al., 2018) found that the lesion network was associated with moral decision making, antisocial subjects show prominent neural dysfunctions during fMRI tasks involving threat detection and cognitive control (Dugré et al., 2020). The use of task-based fMRI studies istherefore of utmost importance as it offers the possibility to examine the heterogeneity of mentalprocesses disrupted by lesions. A second limitation of the lesion network mapping using healthysubjects is that it remains unknown whether lesions lead to reorganization and/or compensation ofneural processes which may be responsible for the emergence of a symptom (Adolphs et al., 2018).If this holds true, the neural reorganization and/or compensation should closely resemble thefunctional architecture observed in subjects exhibiting the same symptom. Therefore, using datafrom subjects exhibiting antisocial behaviors would enhance our ability to map brain coactivation(between lesion and whole-brain voxels) that are specifically associated with antisocial behaviors. The current study aims to overcome these limitations to better characterize the lesion-based networks associated with the emergence of antisocial behaviors. In our study, the lesion networkmapping was conducted through meta-analytic connectivity

modelling (MACM) using 143 whole-brain fMRI studies comprising 5913 subjects exhibiting antisocial behaviors. We examined the task-based lesion network at a group-level (across the 17 lesions) compared to 655 control lesionsand identified its corresponding mental function and associated receptor/transporter density maps. Moreover, we investigated whether specific antisocial behaviors may increase the heterogeneity across lesions and conducted additional analyses to group homogeneous lesion-based networks and identify reliable lesion brain networks associated with antisocial behaviors.

Methods

Antisocial and Control Lesions

Lesioned patients were identified through a literature review. Inclusion criteria included: 1)case description of antisocial behaviors; 2) brain lesion; 3) published image of the brain lesion of adequate quality to conduct manual tracing onto a standardized template (MNI space). Darby andcolleagues (Darby, Horn, et al., 2018) retrieved 40 cases but 17 had explicitly described that lesionpreceded the antisocial behaviors. In the current study, we only used these 17 binary masks. Moredetailed information about the method can be found elsewhere (Darby, Horn, et al., 2018). Based on each of the lesioned patient's case study, we manually coded their antisocial symptoms, following the Structured Clinical Interview for DSM-IV-TR (SCID-II; (First, Spitzer, Gibbon, & Williams, 1995)). Symptoms included: deceitfulness (i.e., repeated lying, use of aliases, conning others for personal profit), irritability/aggressivity (i.e., initiation of physical fights, assaults), irresponsibility (i.e., failure to sustain consistent work behavior, failure to honor monetary obligations) and limited prosocial emotions (LPE) (i.e., lack of remorse or guilt, callous-unemotional or lack of empathy, deficient affect). For each symptom, we coded the absence (0) orpresence (1) if the patients exhibited *at least* one of the associated behaviors. Across the 17 cases, 5 lesioned patients exhibited deceitfulness, 12 behaved aggressively, 9 showed irresponsibility and 10 reported limited prosocial emotions.

Control lesions were also used to extract lesion network that are specific to antisocial behaviors. The control lesions were 655 manually segmented lesion masks from the Anatomical Tracings of

Lesions After Stroke (ATLAS) dataset (Liew, Lo, et al., 2022), which were gathered from 44 research cohorts across 11 countries involved in the ENIGMA Stroke Recovery working group (Liew, Zavaliangos-Petropulu, et al., 2022). Lesions were mainly distributed in subcortical regions but also spanned cortical (25.5%) and other areas such as the brainstem (14.8%).

Antisocial Brain Database

Meta-analytic connectivity modelling (i.e., MACM; (A. R. Laird et al., 2013; Robert Langner & Camilleri, 2021; Robinson, Laird, Glahn, Lovallo, & Fox, 2010) is often used to examine which brain regions are co-activated with a defined seed region (i.e., lesion mask) in healthy subjects. This approach identifies all experiments that reported at least one peak coordinates within a seed region and meta-analyse them via a coordinate-based algorithm (e.g., activation likelihood estimation [ALE]). Convergent results would thus indicate significant co- activated brain regions. However, given that we aimed to examine the altered coactivation in antisocial subjects here we used data from the Antisocial Brain Database (https://github.com/JulDugre/AntisocialBrainDatabase), an initiative to collect neuroimaging data(similarly as the BrainMap database) to better characterize brain dysfunctions in subjects exhibitingantisocial behaviors. The database comprises 143 original studies (5913 subjects) which included a total of 323 contrasts of aberrant coactivation observed in antisocial subjects (across hyper- and hypoactivation) (see supplementary material for complete list of studies). Most experiments focused on negative stimuli (48.3%), social cognition (33.7%), positive stimuli (18.3%) and cognitive control (14.2%). Studies were retrieved from recent systematic review and meta-analyseson task-based activation (Blair, Veroude, & Buitelaar, 2018a; A. L. Byrd et al., 2014; A. Del Casaleet al., 2015; P. Deming & M. Koenigs, 2020; J. R. Dugré, Potvin, S., 2021; Jules R Dugré et al., 2020; Herpers et al., 2014; Johanson, Vaurio, Tiihonen, & Lähteenvuo, 2019; Murray et al., 2018;Poeppl et al., 2019; Seara-Cardoso & Viding, 2015; Y. Yang & Raine, 2009). Articles were included if they met the following criteria: (1) original paper from a peer-reviewed journal, (2) using a sample without any comorbid major mental illness or organic impairment, (3) employed avoxelwise (whole-brain) case-control and/or dimensional analysis (see supplementary material for complete list of included studies).

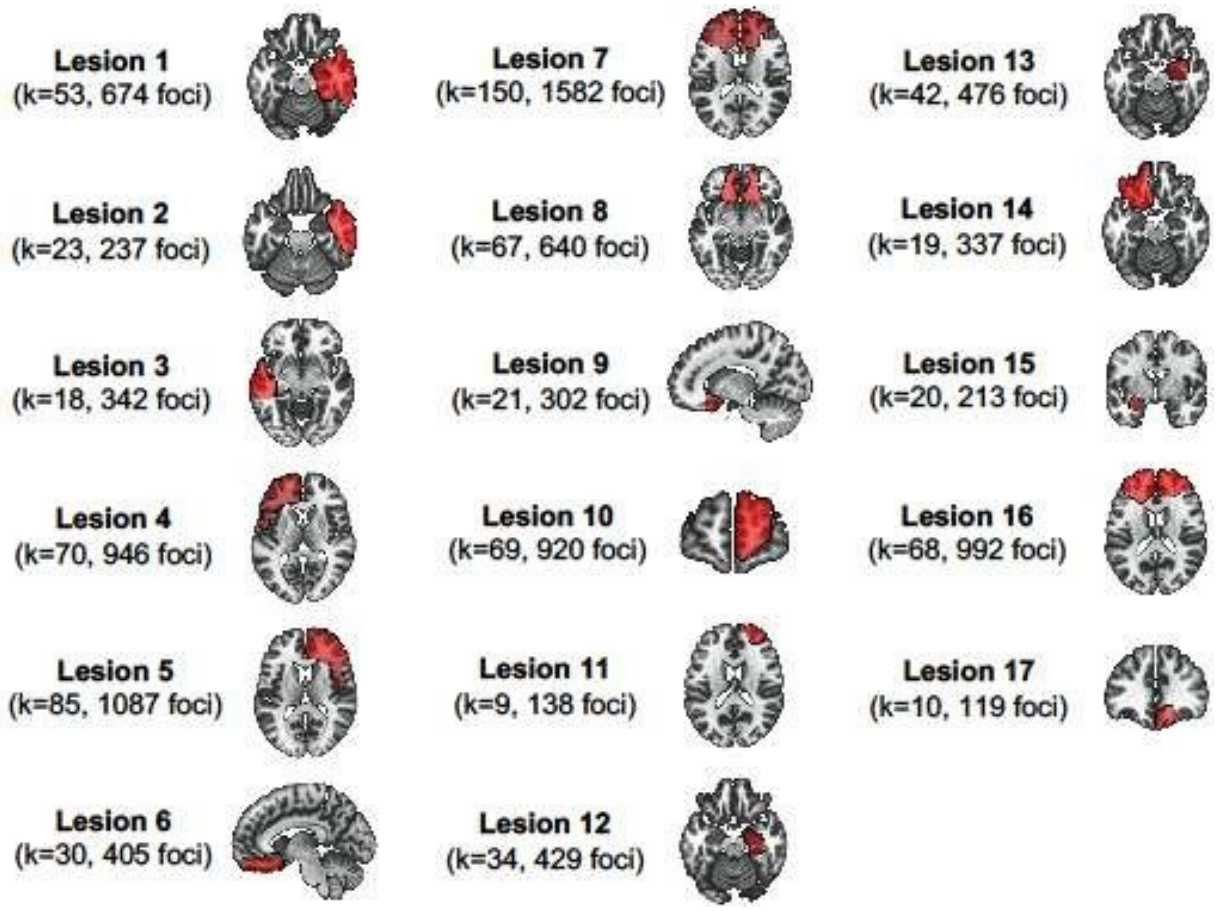

Figure 1. The 17 lesions associated with antisocial behaviors. This figure shows lesion masks (seeds) as well as their respective meta-analytic informations derived from the Antisocial Brain DataBase.

Lesion Network Mapping: Meta-analytic connectivity modelling

Here, we performed MACM using the specific co-activation likelihood estimation (SCALE) algorithm to extract spatially convergent peaks coactivating with each of the 17 lesion masks with the Neuroimaging Meta-Analysis Research Environment package for python (NiMARE; (Salo et al., 2018). Standard MACM procedure includes to extract experiments that reported activation in a particular seed region, then conducting a meta-analysis using the revised version of the ALE algorithm (Eickhoff et al., 2012). For each experiment, a modeled activation (MA) map is created by modeling coordinate foci with a spherical Gaussian probability distribution, weighted by the number of subjects to account for spatial uncertainty due to template and between-subject variance (Eickhoff et al., 2009). It also ensures that multiple coordinates froma single experiment do not jointly influence the MA value of a single voxel. Voxel-wise ALE scoreswere then computed as the union of MA maps, which provide a quantitative assessment of convergence between brain activation across experiments. However, one limitation of this standardapproach is that the base rate of activated voxels, in the whole database, may bias results when running standard MACM on the selected experiments. Therefore, Langner et al., (R. Langner, Rottschy, Laird, Fox, & Eickhoff, 2014) developed a new method that consider the *a priori* probability of finding activation across voxels, namely the specific co-activation likelihoodestimation (SCALE). A voxel-specific null-distribution is thus computed through a Monte-Carlo simulation which included shuffling coordinates from the original database. After 10,000 iterations, a null-distribution of expected convergence is generated given the base rate in the database. In our study, we extracted antisocial experiments that reported at least one peakcoordinate within each of the lesion mask. Moreover, rather than computing a null-distribution from the Antisocial Brain Database, we rather extracted the coordinates underlying control lesions MACM maps to compute the null-distribution. This yield lesion-MACM maps that are specific to antisocial behaviors in comparison to control lesions. Voxelwise z-score map was then extracted for each of the 17 lesion-specific MACM maps. Additionally, usual lesion network mapping utilizestatistical thresholding ranging from $p<0.05$ uncorrected (Fasano et al., 2017) to $pFWE<10^{-11}$ (Cohen et al., 2019), using one-sample t-test in healthy subjects. Given the complexity of our analyses (i.e., 1)

using database of aberrant brain activity [compared to normal functioning]; 2) using coordinates of control lesions [as opposed to base rate of activations] to compute the null- distribution) we decided to use a more lenient threshold ($p<0.05$ uncorrected). After the thresholding, the voxelwise z-score maps were binarized and summed to examine the overlap between lesions at a group-level, namely the task-based lesion network. Additionally, we examinedhow strong the coactivation observed in antisocial subjects deviate from normal functioning by comparing lesion specific MACM map in antisocial subjects with their respective map in healthy subjects (BrainMap database).

Lesion Network Mapping: Investigating its heterogeneity

Given that results at a group-level may be driven by some lesions, we conducted additional analyses to examine the heterogeneity in between lesion networks. First, we aimed to unveil whether antisocial symptoms showed distinct associations with Neurosynth terms. To do so, we computed spatial similarity between the 17 lesion-based MACM maps and Neurosynth meta-analytic terms such as fear, faces, reward & gain. Then, through point-biserial correlation we examined whether spatial similarity coefficient was associated with the presence of specific antisocial symptoms (i.e., Deceitfulness, Irresponsibility, irritability/aggressivity & LPE symptoms). This allowed us to examine whether MACM resemble a term neural map, the stronger or weaker the association with specific antisocial behaviors.

To examine the neural heterogeneity across MACM maps (Please refer to Figure 2 for the workflow), we first computed distance between lesions. To do so, we converted the lesion images (Voxelwise z-score maps) into 17 one-dimensional vectors representing subjects-by-voxels (17 lesions by 902,629 voxels). Then, we computed pairwise Euclidean distance between subjects as well as Spearman Rank Correlation distance ($1 – r$) and ran 3 different clustering algorithms: 1) Agglomerative clustering using the Spearman Rank correlation distance and average linkage, 2) Agglomerative clustering using Euclidean distance and Ward linkage, and 3) kMeans using Euclidean distance. To extract the most optimal number of clusters, we examined silhouette, calinski-harabasz, adjusted rand index as well as variation of information for 2 to 5 cluster solutions, as done recently (Jules R. Dugré, Eickhoff, & Potvin, 2022). When the most optimal

number of clusters was found, we summed lesions MACM maps that defined each cluster to identify convergent brain regions. Finally, we applied dendrogram on similarity between all clusters of the 3 algorithms for interpretability purpose.

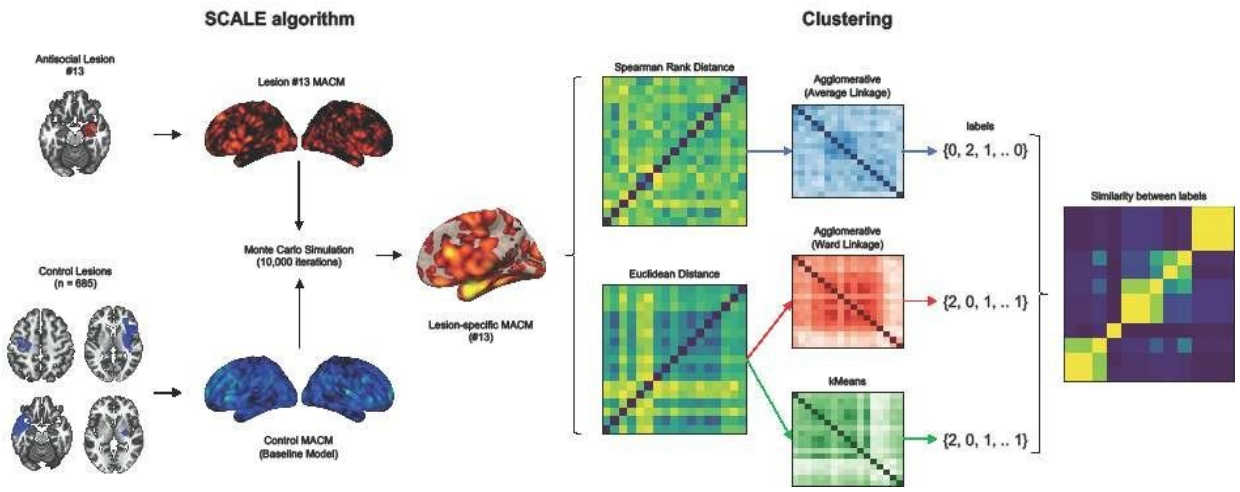

Figure 2. Workflow of the analyses to examine the heterogeneity in lesion network associated with antisocial behaviors. Investigating Disentangling the heterogeneity of meta-analytic networks across lesion underpinning antisocial behaviors. Experiments that reported activation foci within each of the antisocial lesion were identified and compared 10,000 times to a null distribution of control lesion (stroke dataset). Pairwise distances (Spearman Rank and Euclidean) were computedbetween the resulting voxelwise z-score maps. Agglomerative and kMeans clustering methods were runned to extract homogenous subgroups of network.

Functional Characterization

We functionally characterized the MACM networks using Neurosynth term-based decoding (i.e., only the top 10 terms; (Yarkoni et al., 2011) as well as whole-brain receptor/transporter density maps (Dukart et al., 2021) (see list in supplementary material). Briefly,we assessed similarity (Spearman correlation) with 28 receptor/transporter density maps distributed across 8 neurotransmitter systems including dopamine, noradrenaline, serotonin, acetylcholine, glutamate, GABA, cannabinoid, and opioid (see JuSpace v1.4: https://github.com/juryxy/JuSpace). Exact permutation-based p-values (with 1,000 permutations) were computed and then corrected using alse discovery rate (FDR) for the number of tests.

Results

Lesion Network Mapping: Lesion-based Meta-analytic CoactivationModelling

To examine whether lesions may lead to reorganization and/or compensation in neural processes underlying antisocial behaviors, we assess spatial similarity between lesion-specific coactivation in antisocial subjects and their normal coactivation (BrainMap). Results indicated small spatial similarity between lesion-specific coactivation in antisocial and healthy subjects (mean *r*=.21, S.D=.06), the correlation strength between antisocial and normal functions ranged from *r*=.07 (#7) to *r*=.29 (#2).

At a group-level, overlapping the 17 MACM maps (thresholded and binarized) revealed deficient task-based co-activation between bilateral amygdala, medial and lateral OFC, supplementary motor area (SMA), ventro and dorso medial PFC, fusiform area and visual V4 area(see Table 1, Figure 3). However, the overlap between lesion-based meta-analytic maps was only weak ($\cap \leq 7$ out of 17 maps, ≈ 29.41%).

Table 1. Results from the lesion-based meta-analytic connectivity modelling

Regions	MNI coordinates			Lesion Contribution (%)
	x	y	z	
AMY	18	-8	-22	29.41
AMY	-26	2	-26	29.41
mOFC	-18	20	-16	29.41
lOFC	-32	50	-8	29.41
SMA	8	-4	62	29.41
Fusiform Face Area	-38	-42	-24	23.53
vmPFC	14	54	-4	23.53
dmPFC	-14	42	44	23.53
aHIP	-34	-18	-12	23.53
hOc4la	-38	-78	4	23.53
Temporal Pole	-42	10	-42	23.53

Note. The overlap between task based MACM images was performed by overlapping thresholded and binarized images. Only regions showing equal, or more than 4 peaks are reported.

Functional characterization using Neurosynth revealed that the overlap between lesion- based MACM maps was mainly associated with emotional (i.e., neutral, emotional, fear, fearful, happy) and facial terms (e.g., neutral faces, expression, facial) with coefficients r > .24. Also, the task-based lesion network spatially correlated with 5-HT$_{1A}$ (*r*=.34, [^{11}C] CUMI-101 radioligand) as well as serotonin transporters 5-HTT (*rs*=.27-38, [^{11}C]MADAM & [^{11}C]DASB radioligands), after applying the FDR correction.

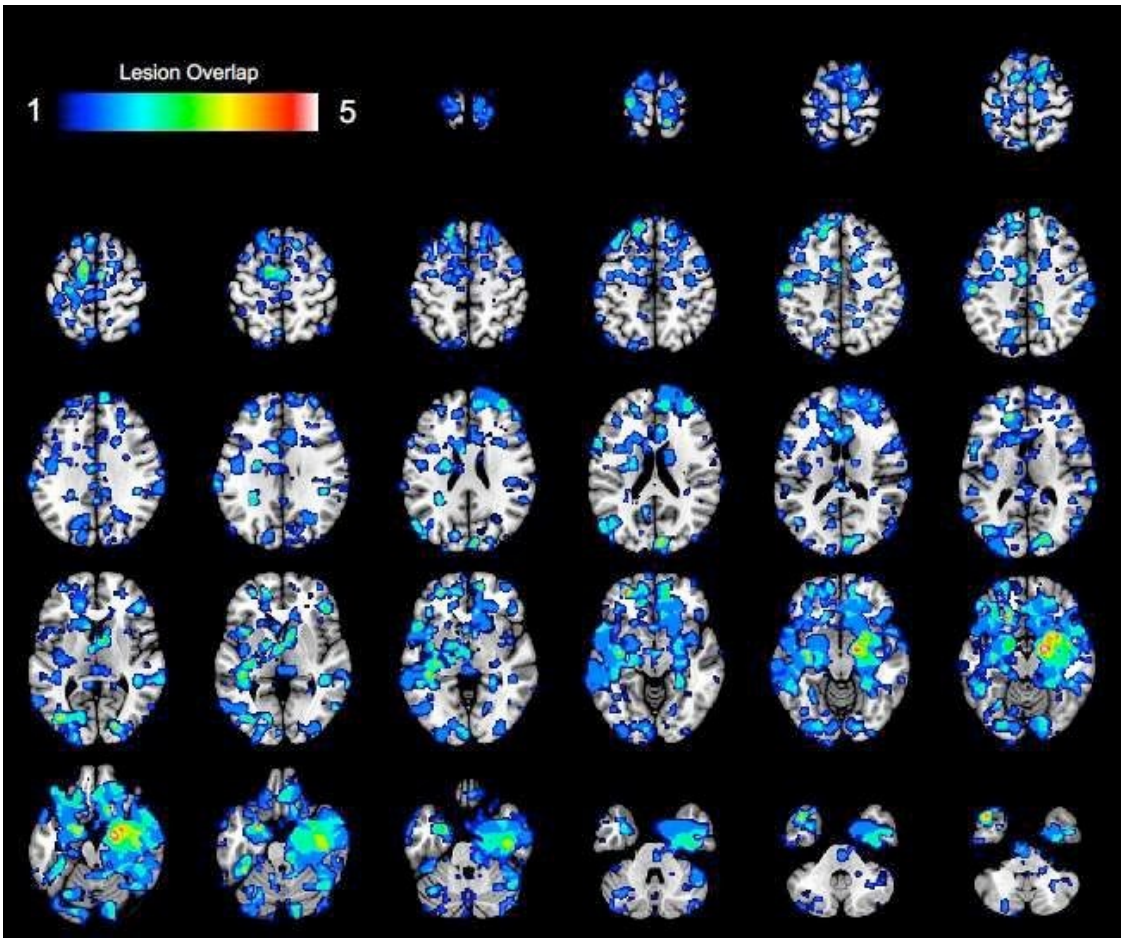

Figure 3. Results of the task-based Lesion Network Mapping. The figure represents the spatialoverlap between binarized lesion-based meta-analytic maps.

Disentangling the clinical heterogeneity

We carried out subsequent analyses to investigate whether spatial similarity between lesion-specific meta-analytic network and Neurosynth meta-analytic terms may be associated with distinct antisocial symptoms. We found that both Deceitfulness and LPE symptoms were positively associated with Neurosynth meta-analytic term *Gain* (i.e., Ventral Striatum, frontopolar cortex, pgACC) (*r*s=.63-76) and negatively with faces (e.g., Amygdala, Fusiform gyrus, MCC). Furthermore, LPE symptoms were positively associated with *Reward* (i.e., Ventral Striatum, vmPFC, frontopolar cortex & pgACC). Also, **aggressivity** and **irresponsibility** symptoms showedno significant association with Neurosynth terms.

Examining the heterogeneity between lesion-based meta-analytic networks

Given that lesions are spatially distributed across ATL and mPFC regions, we sought to examine their heterogeneity in terms of coactivation mapping across fMRI tasks. As expected, analyses unveiled that lesion-based meta-analytic networks were spatially diverse and differed regarding their associated meta-analytic terms and receptor/transporter density maps. The differentmetrics used to assess the clustering solutions revealed that the 4-cluster solution was the most optimal (See Supplementary Material).

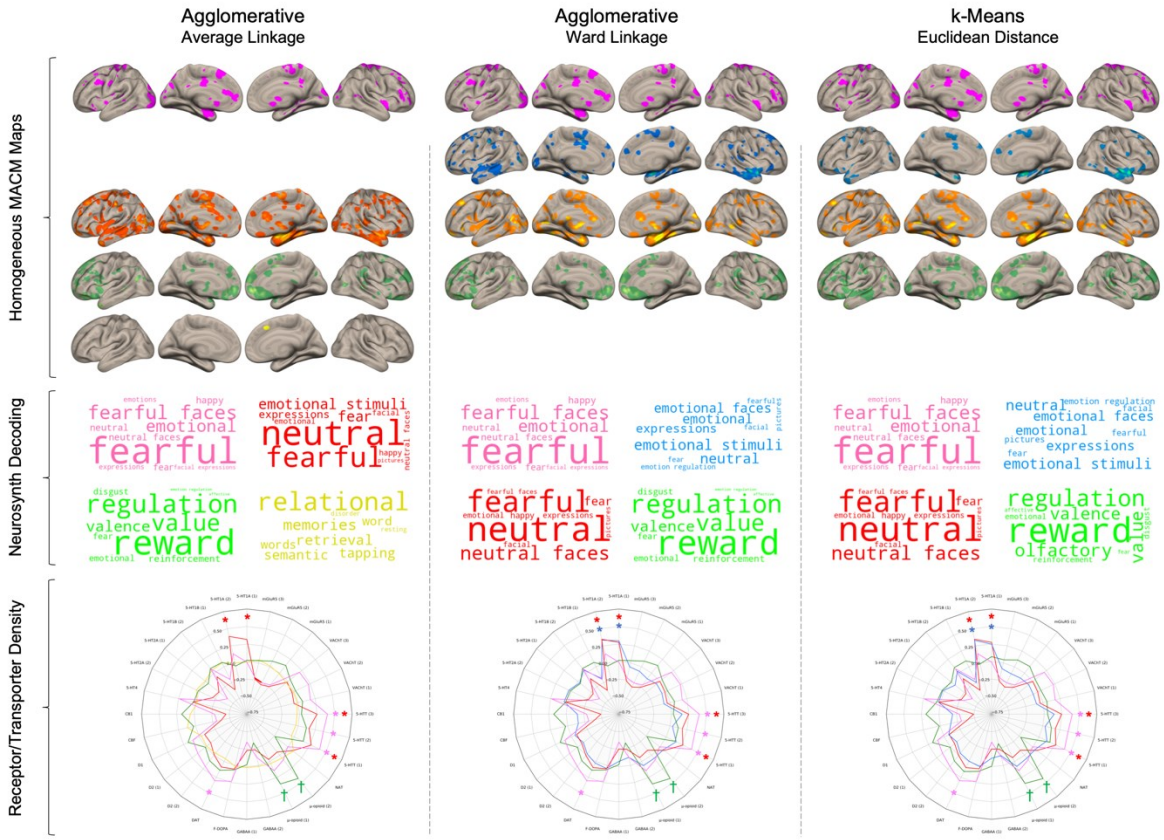

Figure 4. Results from the 3 different clustering algorithms. Rows represent cluster for each of the3 algorithms. For each cluster, its respective brain network was produced by summing thethresholded and binarized lesion-specific networks that were assigned to the cluster. Wordclouds were generated by Neurosynth meta-analytic terms. Larger font represents stronger correlation. InRadar charts, Daggers (†) represent p<0.001 uncorrected and asteri (*) represent pFDR<0.05.

Lesion-based Co-activation Group 1

This network only included lesion to the left amygdala (#15) and was reliably found by thethree clustering algorithms (see Figure 4). It was principally characterized by deficient co-activityin the postcentral, thalamus, inferior frontal gyrus, right amygdala, caudate and visual regions (Supplementary Material). Functional decoding suggested that these maps were closely associated with emotion processing (i.e., fearful, emotional, happy, neutral) as well as face evaluation (i.e., fearful faces, neutral faces, expressions, facial expressions). Furthermore, this meta-analyticnetwork was significantly associated with dopamine (*r*=.30) and serotonin (*rs*=.37-.40) transportermaps.

Lesion-based Co-activation Group 2

The second network was driven by temporal regions (#1 & #2) and was observed across the agglomerative clustering with euclidean distances (#1, #2, #3) and kMeans (#1, #2) but not the agglomerative clustering with spearman rank correlation. This network included the STG, insular cortex, fusiform face area, lateral PFC and lateral OFC (see Supplementary Material for complete results). Functional decoding suggested close associations with Neurosynth terms related to emotion processing in general (e.g., emotional stimuli, emotional faces, emotion regulation). This network was also only associated with 5-HT_{1A} receptor density maps (*rs*=.29-.35).

Lesion-based Co-activation Group 3

This network was mainly formed by lesion to the right amygdala (#12, #13) and was foundby the three clustering algorithms. The agglomerative clustering using the spearman rank correlation found a broader network of lesions to temporal regions (#1, #2, #3, #12, #13) whereasthe two others found only amygdala lesions (#12, #13). This network was mainly characterized bydeficient co-activity in the bilateral amygdala, insular cortex, SMA, Fusiform face area and midbrain, thalamus to a lesser extent (Supplementary Material). This network showed prominent similarity with Neurosynth terms associated with emotional face processing (e.g., neutral, fearful, neutral faces, expressions). Furthermore, it was significantly associated with 5-HT_{1A} receptor density

(*rs*=29-.37) as well as serotonin transporter (only the [^{11}C]DASB radioligands *rs*=.25-.27) maps.

Lesion-based Co-activation Group 4

The fourth network included the remaining lesions which were mostly frontal (#6, #8, #9, #11, #14, #17). However, the included lesions in this group vary between the three method as the agglomerative clustering with spearman rank included 6 lesions (#6, #8, #9, #11, #14, #17), the one with ward linkage included 11 lesions (#4, #5, #6, #7, #8, #9, #10, #11, #14, #16, #17) and the kmeans included 12 lesions (#3, #4, #5, #6, #7, #8, #9, #10, #11, #14, #16, #17). Main aberrant co-activation was found in medial and lateral OFC, ventral to dorsal mPFC as well as posterior temporal gyrus. Neurosynth meta-analytic maps revealed association with reward processing (e.g.,reward, value, valence, reinforcement). This network was significantly associated with μ-opioid (*rs*=.36-.43) and D1 ([^{11}C]SCH23390 radioligand, *r*=.18) at an uncorrected threshold but did not survive FDR correction.

Lesion-based Co-activation Group (other)

The Agglomerative clustering with spearman rank distance revealed a cluster that was not observed by the other two cluster methods, which involved lesions to more dorsal PFC brain regions (#4, #5, #7, #10, #16). The associated network only included the pre-supplementary motor area. It showed similarity with various meta-analytic terms associated with memory and word processing and was not significantly associated with any receptor/transport density maps.

Discussion

Recently, Darby and colleagues (Darby, Horn, et al., 2018) used lesion-to-voxel approach in healthy subjects at rest to examine the lesion brain network underpinning criminal behaviors. They observed that this network principally overlapped with brain structures involved in moral decision-making. In complementarity, we sought to examine the neural architecture of criminal lesions during fMRI tasks. Indeed, we used images of brain lesions from 17 individuals (Darby, Horn, et al., 2018), whom were known to have committed antisocial behaviors after lesions (e.g., trauma, tumors) and conducted MACM using a database of 143 whole-brain fMRI experiments

comprising more than 5900 subjects exhibiting antisocial behaviors. Furthermore, we identified lesion networks that were specific to antisocial behaviors compared to 655 control lesions. First, we found weak to moderate similarity in lesion-specific coactivation between antisocial and healthy subjects, indicating that compensation mechanisms may be linked with antisocial behaviors after lesions. The task-based lesion network associated with antisocial behaviors involved bilateralamygdala, medial and lateral OFC, supplementary motor area (SMA), ventro and dorso medial PFC and fusiform area, which mainly correlated mainly with emotion face processing and serotonin receptor (5-HT_{1A}) and transporter (5-HTT) maps. However, we found only weak overlap between the lesion MACM maps ($\cap \leq 29.4\%$), suggesting substantial heterogeneity between lesions. We therefore examined whether specific antisocial behaviors may explain this heterogeneity. First, we found evidence that specific antisocial symptoms were associated with distinct Neurosynth meta-analytic terms. Second, by using three different clustering algorithms, we observed that the 17 maps could be mainly separated into 4 homogenous groups: 1) lesion to the left amygdala which was associated with emotional face processing; 2) temporal lesions whichwere associated with general emotion processing, 3) right amygdala lesions which were associatedwith emotional face processing, and 4) frontal lesions which were correlated with reward processing. These groups exhibit different association patterns with serotoninergic, dopaminergicand opioid systems.

As highlighted by Adolph and colleagues (Adolphs et al., 2018), individual differences are at utmost importance to understand lesion brain networks underlying criminal behaviors. Indeed, we found that the lesion-based MACM maps minimally overlapped at a group-level (≤ 5 out of 17 lesions). This indicates a non-negligible level of heterogeneity between lesion-specific network, but also questions the usefulness of studying lesion brain networks at a group-level, as this approach is justified only by a broad phenotype that is *shared* between them (e.g., antisocial behavior). We thus performed additional analyses to better understand the interindividual variability concerning specific antisocial symptoms. We observed that antisocial symptoms were significantly associated with distinct Neurosynth meta-analytic terms. For instance, LPE and Deceitfulness were both positively associated with *Gain*. Deceitfulness and LPE are often co-occurring, both representing the interpersonal and affective facets underlying the Factor 1 of

psychopathy (Hare, 2003b). Thus, lesions that alter neural networks associated with *Gain* (e.g., ventral & dorsal Striatum, frontopolar cortex, pgACC, middle frontal gyrus) may increase the risk for deceitfulness and LPE symptoms (e.g., conning others for personal profit, lying, lack of empathy and remorse). Traits associated with factor 1 of psychopathy are often difficult to treat, but evidence nonetheless suggests that they might be more responsive to positive reinforcement strategies than punishment (Hawes, Price, & Dadds, 2014), potentially due to vulnerability towards gain and reward processes. Finally, although it was not statistically significant aggressivity/irritability symptoms showed opposite direction with meta-analytic terms gain (*r*=-.18) and reward (*r*=-.32) and positive association with faces (r=.21) and angry (r=.18). This opposite effect between antisocial behaviors is somewhat unsurprising given that aggressivity is more likely to be associated with negative emotional arousal than reward processes (Siegel & Victoroff, 2009). These also concur with past evidence suggesting that aggressivity and other rule-breaking behaviors are distinct behavioral entities which are characterized by different etiological influences (S. Burt, 2013), developmental risk factors (J. R. Dugré & S. Potvin, 2020) and trajectories (R. E. Tremblay, 2010). Our results therefore highlight the importance of studying specific antisocial behaviors in relationship with neurobiological markers.

In our study, we found that criminal lesions were mainly located in the mPFC and amygdala. Interestingly, past meta-analyses on healthy subjects found that both regions are frequently coactivating when performing various fMRI tasks such as morality (Bzdok et al., 2012), emotion processing (M. Yang, Tsai, & Li, 2020), reward processing (Flannery et al., 2020) and subjective value (Acikalin, Gorgolewski, & Poldrack, 2017). However, we found that in antisocial subjects, lesions to these brain regions may alter distinct brain networks rather than a single common coactivation network. Indeed, by using a data-driven method, we observed four main homogeneous groups of lesion-based MACM maps which encompassed emotion face processing (Group 1 & Group 3: Amygdala, fusiform face area, thalamus and visual regions), general emotion processing (Group 2: Superior Temporal Gyrus, Lateral PFC, Insula, MCC/SMA, Fusiform) and reward processing (Group 4: medial & lateral OFC, dorsal & ventral mPFC, and middle temporal gyrus). The four groups may largely depend on the location of brain lesions, namely the amygdala, temporal and frontal. Indeed, these results concur with past lesion studies indicating that lesions

to the amygdala may be selective to impairments in emotional face processing (Adolphs et al., 2005; Adolphs et al., 1995; Adolphs et al., 1999; Graham et al., 2007; Taubert et al., 2018; Tippett et al.,2018), whereas lesions to mOFC/vmPFC increase deficits in valuation & reward-guided decision-making (Hiser & Koenigs, 2018; Koenigs et al., 2010; Mok et al., 2021; Yu et al., 2020). Interestingly, the four groups also differ in their spatial similarity with receptor maps. For instance, the task based MACM maps of Group 1 (Left Amygdala) and Group 3 (Right Amygdala) was associated with serotonin transporter maps. This concurs with evidence supporting the role of 5-HTT in negative emotionality, neural reactivity of the amygdala (Homberg & Lesch, 2011) but also fearful face processing (Hariri et al., 2002). We also found that the Group 2 (Temporal) was associated with 5-HT_{1A} receptors, which support its role aggressive and hostile behaviors (Caramaschi, de Boer, & Koolhaas, 2007; Clotfelter, O'Hare, McNitt, Carpenter, & Summers, 2007; de Boer & Koolhaas, 2005; Keltikangas-Järvinen et al., 2008), but also emotional lability ingeneral (Popova & Naumenko, 2013). Finally, the Group #4 (frontal lesions) rather showed stronger association with μ-opioid receptors map. Indeed, μ-opioid receptors (Turtonen et al., 2021)are mainly located across the striatum (i.e., nucleus accumbens, globus pallidus, putamen, caudate) but also in vmPFC and medial OFC, supporting the role of reward processing in antisocial behaviors. Interestingly, endogenous opioid system has recently been linked to several reward-related antisocial behaviors (e.g., manipulativeness), substance use and sensation-seeking (Bandelow & Wedekind, 2015; Tiihonen et al., 2020), which supports our results regard Deceitfulness and LPE symptoms. Overall, our results provide evidence of how different neurotransmitter systems may play prominent roles in the emergence of antisocial behaviors (Gard et al., 2019; Rafiei & Kolla, 2021; Veroude et al., 2016). Despite that the emphasis in literature ismainly placed on dopaminergic and serotoninergic systems, the relationship between the opioid system and antisocial behaviors warrants further investigation. Taking together, our results indicate that lesions to distinct brain regions may alter differentbrain networks underlying distinct neurocognitive processes which may increase the risk for distinct antisocial behaviors. Overall, we found that the brain lesions associated with antisocial behaviors were mainly located in frontal and temporal lobes. Interestingly, these complex and heterogeneous interactions between brain regions and behaviors have also been reported infrontotemporal dementias, a

clinical syndrome characterized by degeneration of prefrontal and/or temporal cortices. For instance, up to 57% of patients with frontotemporal dementias have reportedantisocial behaviors (Average percentage across studies=34%; (Mendez, 2022)). More precisely, patients with the frontal variant may exhibit lack of empathy and emotional coldness, disinhibition, significant reduction in agreeableness (i.e., callousness and distrustfulness), but also an increase inpositive emotions (e.g., euphoric mood, exaggerated self-esteem) (Boxer & Miller, 2005; Weder, Aziz, Wilkins, & Tampi, 2007). Moreover, some researchers have found that impairments in working memory is the most common deficit in the frontal variant (Boxer & Miller, 2005). On the other hand, working memory tend to be preserved in temporal lobe variant (Semantic variant: Weder et al., 2007), but patients may show impairments in object recognition, prosopagnosia, and deficits in emotional processing (Boxer & Miller, 2005; Weder et al., 2007). While brain- behavior relationships are complex, our findings tend to demonstrate that antisocial behaviors mayemerge from four different brain mechanisms, largely depending on the location of the brain lesion.In the following years, future studies may seek to investigate the heterogeneity in neural processes associated with lesions as well as the interindividual variability in terms of clinical presentation.

Limitations

There are a few limitations that need to be acknowledged. First, although we haveconducted meta-analyses of aberrant coactivation using data from a large database of more than 5900 antisocial subjects, only 17 lesion masks were used as seeds. Despite the small sample size involved, the clear advantage of this approach is that it allows to establish a clear temporal association between these 17 lesions and the subsequent emergence of antisocial behaviors. Second, we could not perform analyses specifically for each specific neurocognitive domain (i.e., positive valence, negative valence, social cognition, cognitive control), therefore we had to combine them and by doing so, it increased the heterogeneity in the coactivation network of a givenseed. Nonetheless, this is a valid approach given that the standard MACM approach using the BrainMap database (Laird et al., 2013; Langner & Camilleri, 2021; Robinson et al., 2010) is to meta-analyze all available experiments, regardless of the tasks. Also, our control lesionswere stroke lesions. Although the sample size was large, we did not have any information whethersome

patients developed aggressive behaviors or delinquency. As between 15 and 35% ofpoststroke patients may exhibit anger and agitation (Kim, 2016), comparing the antisocial lesions to it may have reduced the ability to find significant differences. As raised by one of the reviewers, it would have been optimal to carefully match the 17 antisocial lesions with control lesions, antisocial subjects (without lesion) and healthy subjects (without lesion). In order to betterunderstand the brain networks associated with antisocial behaviors, future studies should seek to investigate this explicitly. Finally, we conducted clustering analyses using 3 different clustering methods to reduce biases due to the selection of clustering technique. However, as there are numerous clustering methods and distance metrics, it is possible that our results may vary depending on the choice of other clustering methods (e.g., Affinity propagation, DBScan, etc) ordistance metrics (e.g., Manhattan, Minkowski, Jaccard, etc.).

Conclusion

In sum, these results are of crucial importance given that it allows to understand individual variations in the emergence of antisocial behaviors after brain lesion. In other words, despite that all lesioned patients exhibited at least one antisocial behavior, they were all characterized by a different set of antisocial symptoms and a unique brain coactivation network. To reduce the heterogeneity between lesions, we first examined the clinical heterogeneity and found that Deceitfulness and LPE symptoms may be associated with neural maps related to Gain and Reward. Furthermore, we found homogeneous groups of lesion networks which may be associated with increased risk for antisocial behaviors. These were dependent of the lesion's location and mainly encompassed emotional face processing, general emotion processing, and reward processing. Moreover, they show association with distinct receptor/transport maps which may inform us on potential pharmacological treatments to reduce the risk for antisocial behaviors based on the lesion location. Given that the interaction between brain lesions and antisocial behaviors is complex (Hodgins & Guberman, 2022), prospective studies are needed to support our results.

CHAPITRE 8 – DISCUSSION

L'Hétérogénéité des systèmes neurocognitifs associée l'Antisocialité

En réaction au nombre grandissant de résultats de recherche suggérant que les individus antisociaux proviennent d'une population hétérogène, la présente thèse avait comme objectif principal d'identifier les différents systèmes neurocognitifs pouvant expliquer cette hétérogénéité. Par l'entremise de six articles, passant de l'analyses de trajectoires développementales aux analyses d'activité, de connectivité et de lésions cérébrales, plusieurs constats peuvent en être tirés.

À travers les dernières décennies, les mécanismes sous-jacents l'émergence de comportements antisociaux se font de mieux en mieux comprendre. On sait, jusqu'à présent, qu'un nombre important de facteurs psychologiques y sont associés et que les individus ayant un TC ou un TPA rapportent aussi une variété d'autres troubles psychiatriques tels qu'un TDAH, un trouble anxieux et/ou dépressif. Cependant, une forte majorité des chercheurs étudient le rôle individuel de ces facteurs en lien avec l'émergence de la délinquance, ce qui nuit grandement à notre compréhension de la complexité de ces comportements. Par conséquent, le premier article inclus dans cette thèse avait pour but de mieux comprendre si les interactions développementales entre l'irritabilité, les traits anxio-dépressifs, les traits d'insensibilité émotionnelle et les traits d'hyperactivité/impulsivité pouvaient être associées à un risque plus élevé de comportements, mais aussi à des types de comportements différents. Les jeunes suivant une trajectoire développementale caractérisée par une sévérité élevée d'au moins une des 4 psychopathologies étaient significativement plus à risque de montrer des comportements antisociaux à l'enfance. Plus précisément, les groupes caractérisés par la cooccurrence de 3 ou 4 psychopathologies au cours de l'enfance étaient près de 10 fois plus à risque d'avoir aussi des comportements délinquants, signifiant le rôle additif des psychopathologies à l'enfance. Or, seulement 4 groupes furent significativement associés à une persistance de ces comportements jusqu'à l'adolescence. Une des caractéristiques communes entre ceux-ci est la présence de traits d'insensibilité émotionnelle, suggérant le rôle crucial de ces traits dans l'explication de l'émergence de comportements antisociaux. Ces résultats concordent avec l'idée selon laquelle les traits d'insensibilité émotionnelle seraient significativement associés à un début précoce de

comportements (Déry et al., 2019) et augmenteraient significativement le risque de future délinquance (Frick et al., 2014a, 2014b; Frick & White, 2008).

Tableau 1. Résumé des principaux résultats obtenus et évaluation du niveau de preuves scientifiques

Domaines Neurocognitifs	Article #1 Trajectoires	Article #2 IRMf	Article #3 Transdx	Article #4 Connectivité	Article #5 Connectivité	Article #6 Lésions	Niveau De Preuves
Valence Négative	X	X	X	X	X	X	Élevé
Valence Positive	-	-	-	-	X	X	Faible
Processus Sociaux	X	X	X	X	X	X	Élevé
Systèmes Cognitifs	X	X	X	X	X	-	Élevé

Note. IRMf = Imagerie par résonance magnétique fonctionnelle.

Tel qu'observé dans le tableau 1, les résultats obtenus dans les articles présentés dans cette thèse démontrent l'importance des systèmes à Valence Négative, les Processus Sociaux et les systèmes Cognitifs dans notre compréhension des corrélats sous-jacents aux comportements antisociaux. Ces résultats concordent avec les résultats de plusieurs revues de la littérature indiquant le rôle prépondérant de ces systèmes dans l'explication des comportements antisociaux (Blair et al., 2018a; Matthys et al., 2013b). Par ailleurs, les résultats obtenus dans les articles de cette thèse soutiennent le rôle de la connectivité cérébrale entre les systèmes socio-affectifs et attentionnels, ainsi qu'entre les systèmes somato-moteurs, attentionnels et ceux impliqués dans la détection de stimuli saillants. En effet, ces mécanismes pourraient expliquer les symptômes fréquemment observés chez les individus antisociaux tels que l'hyporéactivité à la peur (ou « fearlessness »), le manque de remords et d'empathie ainsi que l'impulsivité (APA, 2013). Finalement, les résultats obtenus dans cette thèse concordent, en partie, à l'hypothèse soutenu par plusieurs chercheurs (Blair et al., 2014; Hyde et al., 2013; Viding, Fontaine, et al., 2012a) selon laquelle l'amygdale jouerait un rôle prépondérant dans l'explication de la délinquance. En effet, des altérations dans cette structure sont répertoriés dans l'Article #2, #3, #4 et #6. Les résultats indiquent que cette structure semble être associé aux comportements antisociaux ainsi qu'aux traits d'insensibilité émotionnelle. Malgré qu'il y ait encore de vifs débats entourant le rôle que pourrait jouer cette structure dans notre compréhension des comportements antisociaux et de la psychopathie (Deming, Heilicher, Koenig, 2022), davantage de recherches est nécessaire afin de mieux comprendre la relation complexe entre cette structure est certains types de comportements antisociaux tels que l'agression proactive, réactive et la délinquance non-agressive. Les résultats obtenus dans cette thèse indiquent par ailleurs que plusieurs autres structures, autant frontales (c.-à-d. le cortex préfrontal dorsomédian, la partie dorsale du cortex cingulaire antérieur, le cortex préfrontal dorsolatéral, le cortex précentral, la partie antérieure du cortex cingulaire moyen), pariétales (c.-à-d. cortex cingulaire postérieur, précuneus, lobule pariétal inférieur), temporales (c.-à-d. le gyrus temporal supérieur, la partie postérieure du sillon temporal supérieur et la partie antérieure de l'insula) que sous-corticales (c.-à-d. l'hippocampe, le thalamus), seraient aussi associés aux comportements antisociaux (voir Figure 8). En effet, contrairement aux postulats indiquant une hypoactivation limbique chez les individus antisociaux

(Blair et al., 2014; Hyde et al., 2013; Viding, Fontaine, et al., 2012a), la majorité des résultats obtenus suggèrent des déficits au niveau cortical. Par exemple, dans l'article #2, l'hypoactivation de structures corticales (c.-à-d., insula, cortex cingulaire antérieur, cortex préfrontal dorsolatéral) et non subcorticales lors de tâches de détection de stimuli menaçants laisse croire que les individus antisociaux montreraient des déficits dans la perception plutôt que dans la réactivité physiologique. Il est donc possible que ces individus aient besoin de niveaux d'intensité plus élevés afin d'identifier correctement et répondre émotionnellement aux stimuli négatifs (Barbosa et al., 2016; Schönenberg et al., 2013; Sharp, van Goozen et Goodyer, 2006). Les recherches futures devraient étudier cette possibilité en utilisant la neuroimagerie.

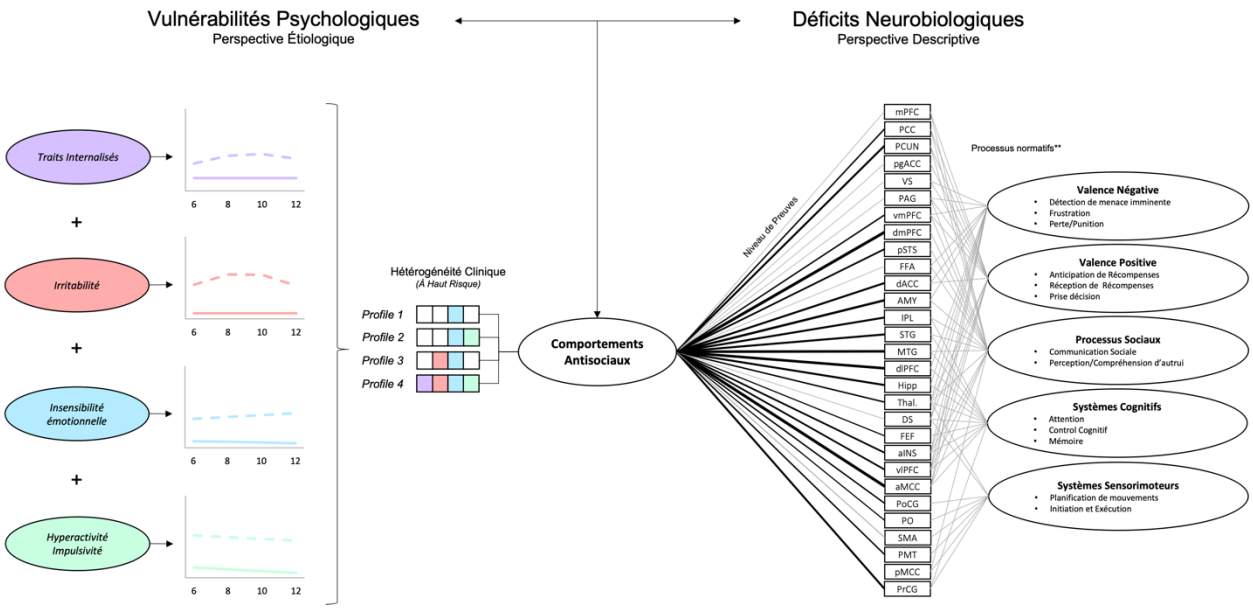

Figure 8. Synthèse des résultats obtenus dans la présente thèse

Cette figure représente les résultats obtenus sur les vulnérabilités psychologiques à travers le développement de l'enfant et les principaux déficits neurobiologiques caractérisant les individus ayant des comportements antisociaux. Le niveau de preuves concernant la structure cérébrale à travers les différentes études présentées est reflété par le caractère gras et l'épaisseur de l'association.

Il est aussi fort intéressant de constater un niveau de preuves élevé en ce qui a trait aux régions sous-jacentes au système sensorimoteur. En effet, il est important de souligner qu'on retrouver des déficits liés à ce réseau dans la totalité des résultats des articles présentés dans cette thèse. Bien que la littérature scientifique sur la délinquance fait souvent abstraction de ce système, celui-ci relève, selon le RDoC, de processus responsables du contrôle et de l'exécution des comportements moteurs. Au niveau comportemental, ce système peut être observé par des altérations motrices telles que des mouvements excessifs et de la difficulté à rester assis (ou « fidgeting »), symptômes fondamentaux du TDAH (Athanasiadou et al., 2020). Sur une base neurobiologique, les gyrus précentral et postcentral ainsi que l'aire motrice supplémentaire forment généralement le réseau somato-moteur (ou sensorimoteur), impliqué dans la planification et l'exécution des mouvements (Uddin et al., 2019). On peut ainsi présumer que les altérations dans l'activité et la connectivité de ces régions pourraient refléter des marqueurs neurobiologiques de l'impulsivité motrice et au manque de planification (par ex. symptômes d'hyperactivité/impulsivité) fréquemment observée chez les individus ayant des comportements antisociaux. En effet, les altérations des systèmes sensorimoteurs ne semblent pas être spécifique aux individus antisociaux (voir Article #3), mais augmenteraient le risque de comportements externalisés en général (c.-à-d., TC, TDAH et Trouble d'usage de substance) (voir Article #3 et Castellanos-Ryan et al., 2014). Par conséquent, il est d'une importance capitale de mieux comprendre le rôle que peuvent jouer les déficits du système sensorimoteur dans l'explication des comportements antisociaux.

Par ailleurs, on observe aussi un niveau faible de preuves quant à la présence de déficits relatifs aux systèmes à Valence positive. En effet, seulement les résultats des articles #5 et #6 semblent montrer l'importance du système à Valence positive. Comme mentionné dans l'introduction de cette présente thèse, certains sous-groupes pourraient présenter des différences neurobiologiques. Par exemple, dans l'article #6, on remarque que les lésions cérébrales au niveau du lobe frontal seraient significativement associées au réseau du traitement de la récompense et que celui-ci serait en lien avec les traits d'insensibilité émotionnelle et la malhonnêteté/tromperie. Aussi, les résultats de l'article #5 suggèrent que certaines régions cérébrales associées à la récompense (c.-à-d. cortex cingulaire périgénual) seraient

dysconnectées avec les régions du système sensorimoteur. Ces résultats pourraient en partie expliquer pourquoi les individus principalement caractérisés par l'insensibilité émotionnelle et l'hyperactivité/impulsivité (Article #1) seraient plus à risque de délinquance non-agressive, comparativement à l'agression. Par conséquent, on ne peut abandonner le rôle du système à Valence Positive dans notre compréhension de la délinquance. En sommes, les résultats obtenus dans les articles de cette thèse suggèrent que les comportements antisociaux pourraient être expliqués par des interactions entre les différents systèmes neuro-cognitifs au niveau clinique jusqu'au niveau de l'activité et de la connectivité cérébrales. Par exemple, dans l'article #5, nous avons observé que la sévérité des gestes antisociaux était caractérisée par des interactions spécifiques entre des régions cérébrales sous-jacentes aux systèmes sensorimoteurs (par ex. exécution de l'action), aux systèmes cognitifs (par ex. mémoire de travail et attention), aux systèmes à Valence négative (par ex. tristesse) et positive (par ex. récompense) et aux processus sociaux.

Limites de la thèse

Le but principal de cette thèse était d'identifier les systèmes neurocognitifs sous-jacents aux comportements antisociaux. Les résultats des 6 études présentées dans cette thèse nous dévoilent que les individus antisociaux seraient caractérisés par diverses trajectoires développementales axées sur la sévérité de traits internalisés, irritabilité, insensibilité émotionnelle et hyperactivité/impulsivité. Par ailleurs, ces individus présentent d'important déficits neurobiologiques associés à différents systèmes, notamment les systèmes à Valence négative, les systèmes cognitifs et les processus sociaux. Il est intéressant de constater le chevauchement entre les résultats de l'étude des facteurs psychologiques et ceux des études neurobiologiques. En effet, les irrégularités décelées à travers les systèmes à Valence négative (c.-à-d., anxiété, irritabilité), les processus sociaux (c.-à-d. insensibilité émotionnelle) et des systèmes cognitifs et sensorimoteurs (c.-à-d. hyperactivité/impulsivité et inattention) pourraient être à l'origine de l'hétérogénéité de trajectoires développementales à risque de comportements antisociaux. Ainsi, ces traits ou vulnérabilités définis comme facteurs de risque dynamiques

stables augmenteraient le risque de comportements antisociaux spécifiques tels que l'agression versus la délinquance non-agressive ou encore l'agression proactive versus réactive. Par exemple, tel qu'observé dans l'article #1 de cette thèse, les enfants suivants une trajectoire développementale défini par de hauts niveaux d'irritabilité et d'insensibilité émotionnelle seraient davantage à risque d'agression que de délinquance et à l'inverse, ceux suivant une trajectoire développementale définie par des hauts niveaux d'hyperactivité/impulsivité et d'insensibilité émotionnelle auraient plus tendance à la délinquance non-agressive. Or, les comportements antisociaux sont complexes et sont modulés par une variété de facteurs (c.-à-d., facteurs dynamiques stables, dynamiques aïgues, facteurs historiques et statiques, contextuels et les désinhibteurs). La Figure 9, inspirée par les travaux de Beech et Ward (2004) sur l'étiologie de la délinquance sexuelle, donne un portrait global de la complexité du phénomène étudié. Il importe donc de présenter les principales limites des études de cette thèse.

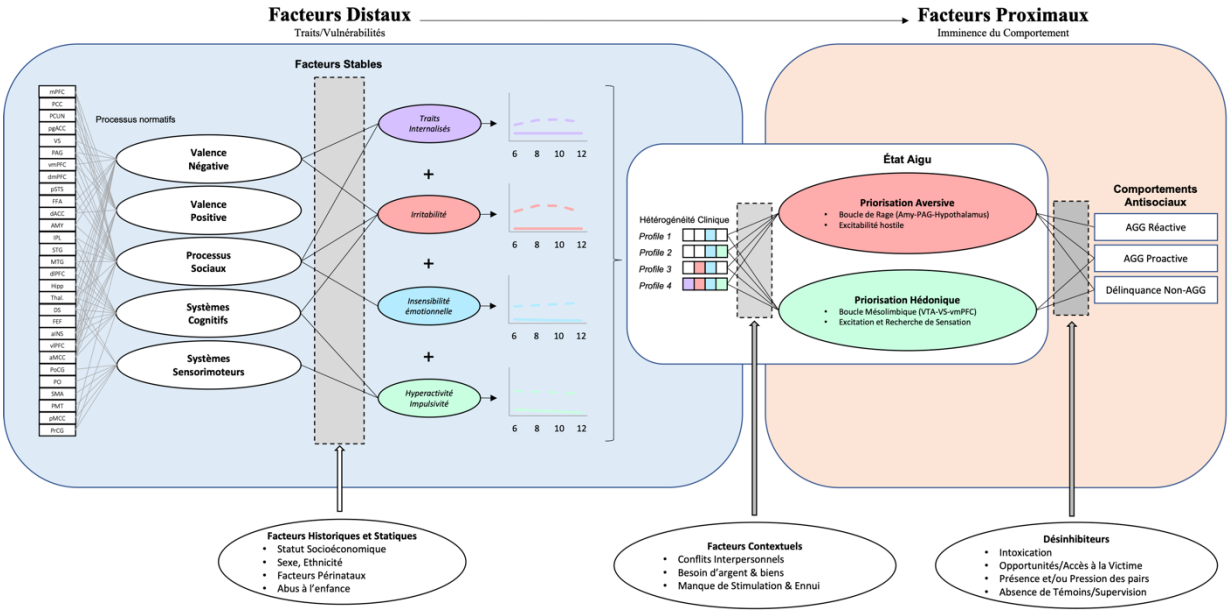

Figure 9. Représentation psychobiologique de la perpétration de comportements antisociaux

Cette figure représente la complexité des comportements antisociaux, allant de facteurs distaux (par ex. vulnérabilité psychologique), aux facteurs relatifs à l'imminence de l'agir délictuel.

Premièrement, les études présentées dans cette thèse ne tiennent pas compte des facteurs historiques et statiques tels que le sexe, l'ethnicité, le statut socioéconomique, l'abus et la victimisation durant l'enfance. Or, un bon nombre d'études indiquent que ces facteurs pourraient moduler le fonctionnement cérébral d'une personne, déterminer leur trajectoire développementale, et par conséquent, augmenter (ou réduire) le risque de comportements antisociaux. Par exemple, bien que les hommes et les femmes ne différeraient pas sur les critères de TPA (Chun et al., 2017) ni sur une variété de facteurs étiologiques (par ex. génétiques et environnementaux (Burt et al., 2019), on rapporte d'importantes différences de sexe nécessaire à notre compréhension du passage à l'acte délinquant. En effet, les garçons semblent montrer significativement plus d'agression directe (c.-à-d. agression physique incluant l'intimidation physique et l'utilisation d'armes) tandis que les filles seraient plus propices aux comportements d'agression indirecte (ou relationnelle) tels que la manipulation et l'intimidation verbale (Archer, 2004; Björkqvist, Lagerspetz, & Kaukiainen, 1992; Côté, 2007; Séguin & Tremblay, 2013). Ceci pourrait être expliqué par le fait que les garçons semblent une plus grande sévérité de traits d'insensibilité émotionnelle et d'impulsivité (Euler et al., 2017; Fontaine et al., 2010; Mitchell & Potenza, 2015) tandis que les adolescentes agressives montreraient plutôt des problèmes internalisés (Keiley, Lofthouse, Bates, Dodge, & Pettit, 2003; Lehto-Salo, Närhi, Ahonen, & Marttunen, 2009; Polier, Vloet, Herpertz-Dahlmann, Laurens, & Hodgins, 2012b). Ces résultats concorderaient avec les travaux épidémiologiques indiquant qu'on rapporte un ratio hommes:femmes de 3:1 et 1:3 en ce qui a trait, respectivement, au TPA et au trouble de la personnalité limite (Compton, Conway, Stinson, Colliver, & Grant, 2005). Par conséquent, on peut présupposer certaines différences de sexes dans les déficits de l'activité cérébrale associés aux comportements lors de tâches sous-jacentes aux systèmes à Valence négative (hyperréactivité émotionnelle chez les filles/femmes), aux systèmes cognitifs et des processus sociaux (hypoactivité chez les garçons/hommes) qui seraient à l'origine des différences dans la prévalence des comportements antisociaux. Il importe aussi de mentionner le rôle que peut jouer l'ethnicité, les facteurs socio-culturels et socio-économiques dans l'explication dans l'explication des résultats de la présente thèse. En effet, malgré sa taille modeste taille d'effet, le statut socio-économique est un facteur important dans l'explication des comportements antisociaux

(Letourneau et al., 2011; Piotwoska et al., 2015). Or, de récents résultats méta-analytiques indiquent que l'association entre le statut socio-économique et les comportements antisociaux seraient plus importante chez les jeunes en âge préscolaire (*r*=-.13) que chez les adolescents (*r*=-.066) (Piotwoska et al., 2015), indiquant l'impact que ce statut peut avoir sur l'apprentissage socio-affectif des enfants. Il est intéressant de constater que les résultats d'une étude portant sur 1,480 jumeaux suggèrent que le rôle des facteurs génétiques sous-jacents les comportements antisociaux seraient davantage important chez les individus provenant de milieux plus favorisés, tandis que l'influence de facteurs environnementaux partagés serait plus élevée chez ceux provenant de milieu moins favorisés (Tuvblad et al., 2005). En d'autres mots, l'émergence de comportements antisociaux pourrait provenir de différentes étiologies dépendamment du statut socio-économique. Dans la présente thèse, la majorité des échantillons proviennent de garçons et d'hommes caucasiens tandis que le statut socioéconomique est largement négligé. Il est donc primordial que les recherches futures tentent de mieux comprendre à quel degré les résultats en neuroimagerie portant chez les individus antisociaux sont modulés à travers différents groupes d'individus, basés sur le sexe, l'ethnicité, et le statut socioéconomique. D'autres facteurs environnementaux, tels que l'abus durant l'enfance (Braga et al., 2017), la victimisation des pairs (Reijntjes et al., 2010), mais aussi la fréquentation de pairs délinquants (Monahan et al., 2009; Fergusson et al., 2002, ne sont pas abordés dans la présente thèse. Malgré qu'ils représentent d'importants prédicteurs de délinquance, on peut présumer que ceux-ci pourraient, respectivement, altérés les systèmes à Valence négative (Hein & Monk, 2017) et positive (Smith, Rosenbaum, Botdorf, Steinberg, & Chein, 2018).

Deuxièmement, l'une des plus grandes limites de cette thèse (et de la neuroimagerie en général) est l'emphase mis sur des marqueurs neurobiologiques stables et distaux à l'agir délinquant. En effet, on tente de trouver des corrélats neurobiologiques aux individus antisociaux en utilisant diverse tâches. Or, bien que ces tâches aient été développées afin d'étudier des processus relativement stables à travers le temps, les réponses neurobiologiques ne peuvent qu'être le reflet de traits que les individus partagent à différent niveaux de sévérité. En d'autres mots, comment réagissent, de manière générale, ces individus lors de tâches d'empathie? Les résultats obtenus dans la présente thèse ne reflètent qu'une mineure partie de la complexité des

comportements antisociaux (facteurs de risques dynamiques stables). Qu'en est-il des facteurs de risques aigus, c'est-à-dire relatifs à l'imminence à l'agir délictuel? Tel que soulevé dans la partie précédente, il est nécessaire de mettre en place des tâches en neuroimagerie qui produisent un comportement similaire à l'agir délinquant (c.-à-d. de manière virtuel). En effet, mieux comprendre les réponses neurobiologiques *immédiates* lors d'agression et de délinquance non-agressive nous permettrait de cibler certains mécanismes afin de mieux les réguler. Par exemple, les études criminologiques ont permis d'identifier que les conflits interpersonnels, le besoin d'argent et de biens ainsi que le manque de stimulation et l'ennui seraient tous des facteurs contextuels importants qui motiveraient les individus à commettre des comportements délinquants (Farrington, 1993). D'après la littérature, l'imminence de l'agression réactive serait représentée par une priorisation du réseau sous-jacent à l'aversion et à l'excitabilité défensive (c.-à-d. l'amygdale, la substance grise périaqueducal et l'hypothalamus) (Panksepp, & Zellner, 2004) tandis que l'agression proactive et la délinquance non-agressive seraient plutôt représentées par une priorisation du réseau hédonique (c.-à-d. aire tegmentale ventrale, noyau accumbens et cortex préfrontal ventromédian) (Blair, 2022). Par exemple, les résultats d'une récente méta-analyse portant sur des études en neuroimagerie indiquent que le cortex préfrontal ventrolatéral, l'insula antérieure ainsi que l'aire motrice pré-supplémentaire seraient impliqués dans l'état de frustration suite à l'omission de récompense et aussi lors d'agression réactive (Dugré et Potvin, *Preprint*). Par ailleurs, une panoplie d'autres facteurs qualifiés comme « *désinhibiteurs* », notamment l'absence de témoins, la présence et/ou la pression des pairs, la présence d'opportunités ainsi que l'usage de substances seraient tous liés à l'imminence de comportements délinquants. Dans une perspective de prévention, il est sans équivoque que les recherches futures doivent mieux comprendre dans quelle mesure ces facteurs contextuels et désinhibiteurs peuvent moduler la réactivité émotionnelle, qu'elle soit aversive ou hédonique, et ainsi augmenter significativement l'imminence de l'agir délinquant.

Troisièmement, l'usage de substances est fréquemment rapporté chez les individus antisociaux. En effet, les jeunes ayant un TC commenceraient à consommer de l'alcool et du cannabis plus tôt (c.-à-d., vers 12 ans) que ceux issus de la population générale (approximativement16 ans) (Hopfer et al., 2013). Par ailleurs, les jeunes ayant un TC ainsi que les adultes ayant un TPA seraient

respectivement 5.9 (Nock et al., 2006b) et 7.2 (Lenzenweger, Lane, Loranger, & Kessler, 2007) fois plus à risque de recevoir un diagnostic de trouble d'usage de substance. En ce qui a trait aux déficits neurobiologiques associés aux comportements antisociaux, l'usage de substance pourrait avoir deux effets importants. D'une part, l'usage de substances répété pourrait avoir des effets délétères sur les vulnérabilités psychobiologiques pouvant ainsi influencer le risquede passage à l'acte. Par exemple, les résultats d'une récente méta-analyse indiquent que, chez les patients ayant une dépendance aux substances, le cortex préfrontal ventromédian serait hyperconnecté au striatum ventral, mais hypoconnecté à l'hippocampe et à l'amygdale (Dugré, Orban, & Potvin, 2022). En lien avec les comportements délinquants, ces dysconnectivités pourraient refléter la surévaluation des bénéfices sous-jacents la consommation ou la délinquance (par ex. vols, entrées par effraction) au détriment des risques. D'autre part, l'effet de substances peut exacerber l'impulsivité des individus au niveau aigu, tel que l'effet désinhibiteur de l'alcool sur la colère, l'irritabilité et les comportements agressifs (Chermack & Giancola, 1997) (Parrott & Zeichner, 2002; Pihl, Peterson, & Lau, 1993; Zeichner, Frey, & Parrott, 2003) qui pourrait être expliqué par des déficits au niveau de l'activité de l'insula et du cortex cingulaire antérieur (Bjork, 2021; Blair et al., 2021). Par conséquent, on peut émettre l'hypothèse que l'effet des substances pourrait impacter un nombre important de systèmes tels que les systèmes à Valence négative, à Valence positive et les systèmes cognitifs. Sur le plan psychologique, les recherches futures devraient tenir compte des trajectoires développementales sous-jacentes à la recherche de sensation forte dû à leur proximité avec les systèmes à Valence positive.

Dernièrement, certaines limites méthodologiques doivent être soulevées, notamment l'aspect corrélationnel des études en neuroimagerie mais aussi l'utilisation d'analyses méta-analytiques basées sur des coordonnées. En effet, malgré qu'on puisse détecter des différences dans l'activité cérébrale entre les sujets sains et les individus ayant des comportements antisociaux, il est impossible de savoir l'aspect causal de ces résultats. Par exemple, tel qu'observé dans l'article #6, les lésions à l'amygdale et au lobe frontal semblent êtredirectement associé à l'émergence de comportements antisociaux. Cependant, les individus antisociaux ne semblent pas rapporter de déficits de l'amygdale ni du cortex préfrontal ventromédian (résultats des articles #2 et #5). D'une part, on pourrait attribuer ces différences à l'importante hétérogénéité clinique chez cette

population. Par exemple, les individus ayant seulement des comportements délinquants non agressifs pourraient être plus enclins à démontrer des altérations du système de récompense (incluant le cortex préfrontal ventromédian), tandis que ceux ayant des comportements davantage agressifs (réactifs) seraient plutôt associés au dysfonctionnement cérébral sous-jacent à la détection de menace. D'autre part, ceci pourrait être aussi expliqué par le fait que les tâches utilisées ne reflètent pas réellement la réalité et l'imminence des comportements antisociaux. Autrement dit, les tâches utilisées à ce jour ne stimuleraient pas assez l'état d'excitabilité, qu'elle soit positive ou négative, afin d'apercevoir des différences significatives dans ces régions, entre les individus antisociaux et les sujets contrôles. Il demeure donc nécessaire de recourir aux nouvelles technologies, telles que la réalité virtuelle, afin d'augmenter la validité écologique des marqueurs neurobiologiques pour mieux étudier les comportements antisociaux (Lobbestael & Cima, 2021; Terbeck et al., 2022). Aussi, les méthodes méta-analytiques basées sur les coordonnées comportement plusieurs limites. En effet, bien que l'on tente de récréer des images similaires aux données d'origine à partir des coordonnées rapportées par les auteurs, les résultats de recherche indiquent une faible similarité (Coéfficient de Dice = .45) entre les résultats analysés à partir d'images réels et à partir de coordonnées (Salimi-Khorshidi et al., 2009). Dans leur étude, les auteurs ont utilisé seulement 15 études ce qui laisse croire qu'un plus grand nombre d'études pourrait augmenter la similarité entre les deux types de méta-analyse. Il aurait donc été préférable d'utiliser les données d'origine. Toutefois, il importe de mentionner que cette technique comporte aussi ses limites. Par exemple, les difficultés associées la disponibilité des données des groupes de recherche (par ex. refus de transmettre, données non-retrouvées) réduit significativement le nombre final d'études inclus dans la méta-analyse ce qui augmente nécessairement le risque de biais. Par ailleurs, différents choix méthodologiques ont été utilisés dépendamment de la question de recherche, c'est-à-dire le fait de prioriser l'étude de la taille d'effets des résultats ou la convergence spatiale. Tel que décrit dans l'article #1, la méthode SDM utilise la taille d'effets des coordonnées (Hedge's d ou g) ainsi qu'un noyau d'une largeur mi-hauteur de 20mm afin de créer une image similaire à l'originale, tandis que la méthode ALE repose sur la convergence spatiale, c'est-à-dire l'union des probabilités de noyaux ayant une largeur mi-hauteur qui dépendent de la taille de l'échantillon (majoritairement entre 8.5 mm et

10 mm). Les auteurs des méthodes méta-analytiques suggèrent un critère de $p<0.005$ avec un seuil de 10 voxels au niveau du regroupement pour la méthode SDM, ainsi qu'un critère de $p<0.001$ avec une correction de $p<0.05$ (Family-Wise Error) afin de balancer entre la sensibilité et la spécificité des résultats (Müller et al., 2018). Bien que les critères choisis pour la première méthode est une approximation de résultats corrigés, il est possible que le contrôle des faux positifs ait pu être trop conservateur ou trop libéral (Müller et al., 2018). Afin de réduire les biais associés au choix méta-analytique, les recherches futures devraient utiliser les deux méthodes afin d'évaluer le degré de convergence des résultats. Finalement, le nombre d'études inclus dans les méta-analyses des articles #2, #3 et #4 sont relativement petit. Par exemple, dans l'Article #3, on ne trouve que la nosologie psychiatrique et les tâches ne diffèrent que très peu entre les groupes de co-activations. En effet, tandis que les réseaux de co-activations ne sembleraient pas souffrir du manque de puissance statistique, les analyses subséquentes elles oui. En d'autres mots, la convergence spatiale des réseaux semble adéquate, mais les dysfonctions cérébrales dans ces réseaux pourraient varier à travers les différentes tâches et à travers les troubles psychiatriques. Il se pourrait que même si la tâche est cognitive (c.-à-d., N-Back, Stroop), les enfants ayant un trouble psychiatrique particulier (par ex. trouble anxieux), puissent être caractérisé par une activité aberrante de régions « émotionnelles » (par ex. amygdale). Il est donc nécessaire que les recherches futures tentent de mieux comprendre les interactions tâches*diagnostics afin de mieux comprendre les effets spécifiques et transdiagnostiques.

En somme, les comportements antisociaux sont complexes. Ceux-ci sont générés par de multiples mécanismes, et par le fait même, modulés par un nombre substantiel de facteurs biopsychosociaux. Par ailleurs, les individus commettant de la délinquance diffèrent largement sur une panoplie de caractéristiques. Les résultats obtenus dans cette thèse soutiennent néanmoins l'importance des traits d'insensibilité émotionnelle, mais aussi des traits d'hyperactivité/impulsivité, de l'irritabilité et des traits anxio-dépressifs, dans l'explication générale du passage à l'acte. Au niveau neurobiologique,les résultats présentés dans cette thèse indiquent un rôle crucial des systèmes à Valence négative, des processus sociaux et des systèmes cognitifs. Les altérations dans ces systèmes pourraient ainsi refléter le manque d'empathie, l'insensibilité à la peur ainsi que l'impulsivité qui caractérise fréquemment la population

antisociale. Bien que le travail présenté offre les bases comportementales et neurobiologiques communes dans cette population, un manque flagrant d'études portant sur la variabilité interindividuelle restreint notre compréhension du caractère idiosyncrasique de la délinquance. En effet, les résultats obtenus dans cette thèse ne permettent pas de mieux comprendre les corrélats neurobiologiques entre différents groupes d'individus à risque de comportements antisociaux, tel que rapporté dans l'article #1. Il va de soi que les recherches futures doivent centraliser les efforts afin de mieux comprendre les altérations communes et distinctes chez les sous-groupes d'individus à risque de délinquance de manière à déconstruire l'hétérogénéité clinique dans cette population. Or, l'identification des principaux domaines neurocognitifs sous-jacente à l'antisocialité nous éclaire cependant sur les possibles sources de variabilité inter-individuelle et ce, dans une perspective étiologique plutôt qu'athéorique et descriptive. Ainsi, bien que les méthodes méta-analytiques ne sont pas optimales afin d'étudier ces épineuses questions, les recherches futures devraient utiliser diverses techniques axées sur les données afin de mieux comprendre variabilité inter-individuelle des systèmes identifiés dans cette thèse.

Pertinence scientifique et perspectives de recherche

La présente thèse soulève l'importance de mieux déconstruire la complexité des processus neurobiologiques entourant les comportements antisociaux. En effet, les résultats des études présentées dans cette thèse indiquent, d'une part, que les traits d'insensibilité émotionnelle,l'irritabilité, les traits internalisés et les traits d'hyperactivité/impulsivité sont au cœur de l'hétérogénéité des individus ayant des comportements antisociaux. D'autre part, on suggère que les plus importantes altérations cérébrales lors de tâches en neuroimagerie proviennent de systèmes à Valence Négative, de systèmes cognitifs et des Processus Sociaux. On note aussi que les individus antisociaux seraient principalement caractérisés par des dysconnectivités entre des régions impliquées dans les systèmes à processus sociaux et aux systèmes attentionnels tandis que la sévérité des comportements antisociaux serait plutôt associéeaux dysconnectivités des systèmes à valence négative (saillance, cingulo-operculaire) systèmes attentionnels (VentAttn et DorsAttn) et du contrôle cognitif (FP), des systèmes à

processus sociaux (DMN) et du système somatomoteur. Finalement, la dernière étude de cette thèse portant sur les lésions cérébrales renforce l'idée selon laquelle le système à Valence négative, la reconnaissance émotionnelle faciale et le traitement de la récompense seraient associés, potentiellement de manièrecausale, à l'émergence de comportements antisociaux. Ces résultats ouvrent la porte à l'étude des variations interindividuelles en lien avec les comportements antisociaux et pourraient avoir d'importantes retombées dans le domaine scientifique, tel que sur la prédiction du risque ainsi que sur la médecine personnalisée.

Premièrement, les résultats obtenus dans les études présentées dans cette thèse indiquent que les individus antisociaux rapporteraient des déficits importants dans plusieurs domaines neurocognitifs. Or, comme observée dans le premier article, la population étudiée serait hautement hétérogène. Bien qu'on puisse observer des altérations comportementales et neurobiologiques communes à travers cette population, l'étude des différences neurobiologiques entre des sous- groupes demeure cruciale. Or, la majorité des études ayant cet objectif focalise souvent sur la présence ou non de traits d'insensibilité émotionnelle. Les résultats obtenus dans cette thèse suggèrent cependant que l'hétérogénéité sous-jacente à la population antisociale serait plus complexe. Par conséquent, les recherches futures pourraient donc tenter de mieux comprendre la variabilité interindividuelle sous-jacente à la population antisociale par l'entremise d'analyses axées sur les données (par ex., analyse de classes latentes) plutôt que sur une catégorie ou une dimension. D'une part, on pourrait tenter de regrouper les individus sur la base de vulnérabilités psychologiques (c.-à-d. incluant les traits d'insensibilité émotionnelle, l'irritabilité, les traits anxio-dépressifs et les symptômes de TDAH) afin de mieux comprendre les différences neurobiologiques entre certains sous-groupes. D'autre part, le regroupement d'individus sur une base neurobiologique (incluant les systèmes étudiés dans cette thèse) pourrait nous permettre d'identifier les différences comportementales entre des sous-groupes. Ces deux approches sont distinctes, mais complémentaires, du fait que la première approche est plutôt descriptive tandis que la deuxième serait plutôt étiologique en mettant l'emphase sur le fonctionnement cérébral « normal » qui augmenterait ou réduirait le risque de comportements antisociaux. Ainsi, on pourrait envisager l'utilisation de techniques statistiques avancées afin d'identifier des sous-groupes neurobiologiques et/ou des signatures

neurobiologiques sous-jacents aux comportements antisociaux. Récemment, des chercheurs ont démontré l'efficacité de la régression des moindres carrés partiels afin d'identifier des composantes latentes reliant une panoplie de variables cliniques aux patrons de connectivité cérébrale au repos (Kebets et al., 2019; Mihalik et al., 2022). Cette technique pourrait bel et bien nous permettre d'identifier des composantes associées à des vulnérabilités psychobiologiques qui augmenteraient le risque de comportements antisociaux. Bien que ces techniques soient de plus en plus utilisées, on doit d'abord se questionner sur l'homogénéité de nos construits et de nos échantillons, ainsi que sur le rôle que doit jouer la neuroimagerie dans notre compréhension de cette problématique.

Deuxièmement, les résultats de cette thèse peuvent stimuler la recherche sur la neuroprédiction du risque de comportements antisociaux, c'est-à-dire la capacité à pouvoir prédire l'émergence ou la récidive de comportements antisociaux. Par exemple, certains ont trouvé que l'hypoactivité du cortex cingulaire antérieure lors d'une tâche d'inhibition (système cognitif) était significativement associée à une future réarrestation (Aharoni et al., 2013). D'autres ont montré que le flux sanguin du lobe pariétal (systèmes cognitifs et processus sociaux) était associé à la récidive criminelle et offrirait un poids additionnel aux caractéristiques cliniques afin de prédire lerisque de récidive criminelle chez les patients en contexte médico-légal (augmentation l'aire sous la courbe ROC de .69 à .81) (Delfin et al., 2019). Outre le peu d'études et les échantillons limités,il est important de constater que les caractéristiques neurobiologiques n'expliqueraient qu'entre 8 % (Aharoni et al., 2013) et 12.5 % (Kiehl et al., 2018) de la variance de la récidive criminelle. Bien qu'elles puissent être associé à celle-ci, elles n'expliquent qu'une infime proportion de la problématique. Ceci pourrait principalement être dû au fait que la récidive criminelle est multifactorielle et serait davantage expliquée par des facteurs proximaux à l'agir délictuel. On pourrait émettre l'hypothèse que la réponse cérébrale aux systèmes à Valence négative serait davantage associée à la récidive violente tandis que la délinquance non-agressive serait plutôt liée à l'activité cérébrale des systèmes à Valence positive et/ou aux systèmes cognitifs. En effet, l'activité cérébrale lors de tâches à Valence négative pourrait en partie reflété le contexte dans lequel une potentielle récidive surgit. Depuis les dernières années, les méthodes d'apprentissage automatique ont suscité un engouement pour leur flexibilité et leur performance afin de prédire

un comportement. Des modèles d'apprentissage automatique pourraient donc être développés afin de mieux comprendre les patrons d'activité cérébral associés à la récidive. Cependant, la valeur ajoutée de la neuroimagerie demeure à prouver, considérant notamment les coûts importants associés à cette technique. De manière à augmenter l'efficacité de la prédiction du risque, j'encourage fortement les chercheurs à développer de nouvelles tâches en neuroimagerie afin de recréer une variété de situations « *écologiquement valide* » à la récidive (c.-à-d. conflits interpersonnels, besoins d'argent/de stimulations, etc).

Troisièmement, les résultats de cette thèse pourraient nous éclairer sur les pistes de traitements afin de réduire le risque de comportements antisociaux. Par exemple, les résultats de méta-analyses suggèrent une efficacité limitée des traitements psychologiques chez les jeunes ayant un TC (Bakker, Greven, Buitelaar, & Glennon, 2017; Hendriks, Bartels, Colins, & Finkenauer, 2018) et les adultes ayant un TPA (Gibbon, Khalifa, Cheung, Völlm, & McCarthy, 2020; H. A. Wilson, 2014). Aussi, ceux-ci ne seraient pas associés à une réduction du risque de récidive (Gabrielle Beaudry, Yu, Perry, & Fazel, 2021). Par ailleurs, on note que la prise de rispéridone (et les antipsychotiques en général) semble réduire la sévérité des comportements agressifs (Balia, Carucci, Coghill, & Zuddas, 2018; Pringsheim, Hirsch, Gardner, & Gorman, 2015b; van Schalkwyk, Beyer, Johnson, Deal, & Bloch, 2018) et les symptômes d'irritabilité (Breaux et al., 2022), tandis que la prise de psychostimulants semble avoir des effets particulièrement bénéfiques envers les problèmes de comportements chez les jeunes ayant un TDAH avec ou sans TC/TOP (Pringsheim, Hirsch, Gardner, & Gorman, 2015a). Cependant, chez les adultes ayant un TPA, l'efficacité du traitement pharmacologique demeure particulièrement limitée (Khalifa, Gibbon, Völlm, Cheung, & McCarthy, 2020). Tel que décrit dans cette thèse, les mécanismes neurobiologiques sous-jacents aux comportements antisociaux sont multiples etcomplexes. Par conséquent, regrouper les individus dans une seule catégorie (TC ou TPA) ainsi que le traitement universel (« One Size Fits All ») devient donc contre-productif dans une perspective de traitement. Dans le même ordre d'idées, chaque individu présente unfonctionnement plus ou moins normatif des systèmes neurocognitifs, augmentant ou réduisant le risque de comportements antisociaux. Par conséquent, l'identification des altérations de cessystèmes bonifierait notre compréhension du risque de passage à l'acte, mais aussi des cibles thérapeutiques. Par exemple, les individus

antisociaux semblent être insensibles à la punition, maisrépondre *normalement* au système à Valence positive. Le traitement psychologique basé sur le renforcement positif (plutôt que négatif) pourrait donc être à privilégier. Ceci concorde avec les résultats de travaux suggérant que le renforcement positif (par la mère) réduirait le risque de développer des traits d'insensibilité émotionnelle (Hyde et al., 2016) et augmenterait la réponse au traitement de jeunes ayant un TC et des traits d'insensibilité émotionnelle (Hawes et al., 2014).

Épilogue et Perspectives Cliniques

À la lecture de cette thèse, plusieurs questions restent sans réponse. Quelle est l'origine de la délinquance, serait-elle innée ou acquise? Comment crée-t-on un de la délinquance? Est-ce que, et dans quelle mesure, des déficits neurobiologiques pourraient altérer la Mens Rea[2] ? Pourrait-on déterminer la responsabilité criminelle d'une personne avec la neuroimagerie? Considérant l'optimisme derrière l'usage de la neuroimagerie en criminologie, cette dernière section sera dédiée au rôle que pourrait jouer (ou non) cette technique dans la pratique clinique de manière à évaluer ou prévenir le risque de comportements antisociaux.

Premièrement, Au Canada, la défense de non-responsabilité criminelle pour cause de troubles mentaux fait souvent l'objet de débats sociaux, à savoir si la Mens Rea d'un tel était, ou non, affectée au moment du délit. L'article 16 (paragraphe 1) du Code Criminel du Canada indique que « *La responsabilité criminelle d'une personne n'est pas engagée à l'égard d'un acte ou d'une omission de sa part survenu alors qu'elle était atteinte de troubles mentaux qui la rendaient incapable de juger de la nature et de la qualité de l'acte ou de l'omission, ou de savoir que l'acte ou l'omission était mauvais.* ». Bien que les résultats obtenus dans cette thèse défendent l'hypothèse selon laquelle les individus antisociaux seraient caractérisés par des altérations au niveau du fonctionnement cérébral, la neuroimagerie ne peut en aucun cas nous permettre de valider la présence ou non d'un « trouble mental » dans le cas d'individus antisociaux. Or, la

[2] La Mens Rea est un terme juridique employée afin de signifier l'intention coupable qui doit être démontré lors d'un procès afin de trouver (ou non) coupable l'individu lors d'une infraction criminelle

définition d'un trouble mental est davantage complexe qu'une simple déviation de la fonction mentale dite normale. En effet, si le trouble des conduites et le trouble de la personnalité antisociale sont des troubles mentaux au sens médico-légal, alors près de 50 % de la population carcérale et de la population juvénile en centre jeunesse pourraient se démettre de leur responsabilité criminelle. Plus important encore, la neuroimagerie n'est pas une machine à remonter dans le temps. Il m'apparaît évident qu'on ne peut revenir au moment de l'agir délictuel pour évaluer l'état mental de la personne présumée coupable. Seul le débat entre experts peut nous guider vers la version la plus « convaincante » sous-jacente à la chronologie des événements afin de déterminer l'état mental de l'accusé. Bien qu'on puisse en déterminer des vulnérabilités psychobiologiques, la responsabilité criminelle vogue dans le gris, demeurant floue et difficilement mesurable.

Deuxièmement, dans certains cas juridique la défense d'automatisme pourrait être soulevée. En effet, selon un jugement de la Cour Suprême du Canada (voir R.*c*.Stone, 1999, p.292-293) : « *le droit présume que les gens agissent volontairement. […] la défense doit établir les fondements de l'automatisme. Elle ne se sera acquittée de cette charge que si le juge du procès conclut qu'il existe une preuve qui permettrait à un jury ayant reçu des directives appropriées de conclure, selon la prépondérance des probabilités, que l'accusé a agi involontairement. Dans tous les cas, la défense devra présenter une allégation de caractère involontaire, confirmée par le témoignage d'un psychiatre.* ». Tel qu'observé dans l'article #6 de cette thèse, la présence de lésions cérébrales pourrait avoir des répercussions causales sur l'émergence de comportements antisociaux. Malgré leur rareté, certaines lésions cérébrales pourraient altérer le caractère volontaire de l'agir délictuel. Or, il est encore difficile de prouver le rôle causal d'une lésion cérébrale. Par exemple, un bon nombre d'études portant sur des sujets rapportant des lésions cérébrales aux mêmes régions identifiées (c.-à-d. le cortex préfrontal ventromédian et l'amygdale/cortex temporal) ne font aucune mention de comportements agressifs ni de délinquance non-agressive. Ainsi comment peut-on expliquer que des individus ayant des lésions similaires ne commettent pas de comportements antisociaux? Tandis que certains peuvent soulever la notion de réorganisation compensatoire du fonctionnement cérébrale, on peut aussi se demander si la présence de facteurs individuels avant la lésion pourrait expliquer ces

différences (Adolph et al., 2018). Dans toute sa complexité, le comportement antisocial serait observable et mesurable que lorsque les facteurs de risque historiques, individuels et contextuels sont présents. La proposition selon laquelle seule la lésion expliquerait l'émergence du geste délinquant est donc réductive. Par conséquent, il est fort probable que l'aspect *causal* du lien entre la lésion cérébrale et le crime soit médié par une panoplie de facteurs inter-individuels (c.-à-d. psychologiques et contextuels) qui, ne seraient pas suffisant afin d'établir une défense d'automatisme. Il est sans équivoque que davantage de recherches sont nécessaires afin de mieux comprendre les facteurs de risque d'individus ayant des lésions cérébrales.

Finalement, encore aujourd'hui, il est difficile de lier la neuroimagerie à la pratique clinique. Il va de soi que le manque flagrant de modèles théoriques, intégrant à la fois les notions criminologiques, psychologiques et neurobiologiques nuit excessivement à notre compréhension du phénomène étudié. Quel est l'objectif principal de l'utilisation de la neuroimagerie en criminologie? Dans quelle mesure pourrait-on utiliser la neuroimagerie comme stratégie de prévention primaire (c.-à-d. évaluer/intervenir avant l'émergence de comportements antisociaux), prévention secondaire (c.-à-d. identifier les individus à haut risque) et/ou prévention tertiaire (c.-à-d. gérer le risque de récidive ou réduire la sévérité de la pathologie)? Est-il réaliste d'utiliser la neuroimagerie dans le cas de la mise en place de stratégies de prévention primaires et secondaires, en sachant les coûts exorbitant liés à celle-ci? Malgré l'optimisme derrière cette technique, la neuroimagerie n'a pas encore démontré avec succès ses retombés cliniques. Par exemple, les corrélats neurobiologiques n'expliquent qu'une infime proportion de la variance associée aux comportements (Marek et al., 2022) et les effets bénéfiques associés à la stimulation transcrânienne sont limités et sont encore trop mal compris (Sergiou et al., 2020). L'évaluation clinique (au sens large) et la mise en place de stratégies de prévention individualisées demeurent encore aujourd'hui les des méthodes les plus efficaces afin de mieux comprendre et gérer le passage à l'acte délictuel. Tel qu'observé dans les articles de cette thèse, il m'apparait nécessaire que les stratégies de prévention primaires et secondaires devraient cibler principalement les traits d'insensibilité émotionnelle, l'hyperactivité/impulsivité et l'irritabilité afin de réduire l'émergence éventuelle de la délinquance. En effet, l'emphase mis sur des facteurs psychologiques relativement stable à travers le temps pourrait permettre de

réduire le risque que les individus commettent des gestes de délinquance. Par exemple, dans le cas de la prévention de problèmes d'usage de substance, les stratégies axées sur les traits de personnalité semblent réduire significativement le risque la quantité et la fréquence de consommation d'alcool et de drogues (Edalati, Conrod, 2018). Ainsi, prévenir très tôt durant l'enfance et l'adolescence l'exacerbation des psychopathologies pourraient avoir des bénéfices substantiels sur la réduction des comportements antisociaux. Contrairement à la prévention primaire et secondaire, la neuroimagerie pourrait nous être utile dans la mise en place de stratégies de prévention tertiaire. En effet, on sait que l'un des meilleurs prédicteurs de la récidive générale, violente et sexuelles est l'historique de comportements antisociaux (incluant les antécédents criminels) (Hanson et Morton-Bourgon, 2004, Bonta, Blais, Wilson, 2014); Katsiyannis et al., 2018; Cottle, Lee, Heilbrun, 2001). Au niveau clinique, il est difficile, voire impossible, de prendre l'historique de comportements ou l'âge du début de l'agir délinquant comme cible de traitement. Considérant que le début précoce et la persistance de comportements antisociaux sont fondamentaux à la définition du TC et du TPA (APA, 2013), il est donc à se questionner si la neuroimagerie pourrait nous éclairer sur des modalités de prévention tertiaire en ce qui a trait à ce type d'individus? Longuement définis comme étant « life-course persistent offenders » (Moffitt, 1993) ces individus pourraient-ils *souffrir* d'un trouble caractérisé par l'habitude de commettre des comportements antisociaux? Dans le même ordre d'idées, dans quelle mesure pourrait-on désapprendre un comportement antisocial? Serait-il possible que ces individus, souvent réticent au changement, puissent bénéficier des techniques de stimulation transcrânienne et aux tâches de contre-conditionnement. Il m'apparait évident que les recherches futures tenteront de répondre à ces questions.

En somme, l'étude des corrélats neurobiologiques sous-jacents aux comportements antisociaux est complexe. La définition même du comportement antisocial repose largement sur la dichotomie distinguant l'anormalité de la normalité qui contribue au manque de progression dans le domaine. Bien que le but de cette thèse fût de décortiquer les principaux systèmes associés aux comportements antisociaux, les recherches futures devront étudier le rôle de la variabilité interindividuelle de ces systèmes dans l'explication des comportements antisociaux. Dans toute sa complexité, le comportement antisocial pourrait être mieux défini comme étant :

« *une réponse comportementale brimant les droits d'autrui et/ou transgressant les normes sociales, déclenchée par une situation favorable à la manifestation de prédispositions psychobiologiques de l'individu. »* Un changement de paradigme est donc nécessaire, replaçant l'étiologie et l'hétérogénéité clinique au cœur du débat, au détriment de la description athéorique d'un diagnostic limitant.

Références bibliographiques

Achenbach, T. M., & Edelbrock, C. S. (1983). Manual for the child behavior checklist and revised child behavior profile.

Achenbach, T. M., & Rescorla, L. A. (2001). *Manual for the ASEBA school-age forms & profiles: child behavior checklist for ages 6-18, teacher's report form, youth self-report: an integrated system of multi-informant assessment*: University of Vermont, research center for children youth & families.

Acikalin, M. Y., Gorgolewski, K. J., & Poldrack, R. A. (2017). A Coordinate-Based Meta-Analysisof Overlaps in Regional Specialization and Functional Connectivity across Subjective Value and Default Mode Networks. *Front Neurosci, 11*, 1. doi:10.3389/fnins.2017.00001

Adler, H. M. (1917). A Psychiatric Contribution to the Study of Delinquency. *Journal of the American Institute of Criminal Law and Criminology, 8*(1), 45-68. doi:10.2307/1133711

Adolphs, R., Gläscher, J., & Tranel, D. (2018). Searching for the neural causes of criminal behavior. *Proc Natl Acad Sci U S A, 115*(3), 451-452. doi:10.1073/pnas.1720442115

Adolphs, R., Gosselin, F., Buchanan, T. W., Tranel, D., Schyns, P., & Damasio, A. R. (2005). A mechanism for impaired fear recognition after amygdala damage. *Nature, 433*(7021), 68- 72. doi:10.1038/nature03086

Adolphs, R., Tranel, D., Damasio, H., & Damasio, A. R. (1995). Fear and the human amygdala. *J Neurosci, 15*(9), 5879-5891. doi:10.1523/jneurosci.15-09-05879.1995

Adolphs, R., Tranel, D., Hamann, S., Young, A. W., Calder, A. J., Phelps, E. A., . . . Damasio, A.

R. (1999). Recognition of facial emotion in nine individuals with bilateral amygdala damage. *Neuropsychologia, 37*(10), 1111-1117. doi:10.1016/s0028-3932(99)00039-1

Afzali, M. H., Dagher, A., Edalati, H., Bourque, J., Spinney, S., Sharkey, R. J., & Conrod, P. (2020). Adolescent resting-state brain networks and unique variability of conduct problemswithin the

externalizing dimension. *Journal of personality disorders, 34*(5), 609-627.

Agustín-Pavón, C., Braesicke, K., Shiba, Y., Santangelo, A. M., Mikheenko, Y., Cockroft, G., . . . Roberts, A. C. (2012). Lesions of ventrolateral prefrontal or anterior orbitofrontal cortex in primates heighten negative emotion. *Biological psychiatry, 72*(4), 266-272.

Aharoni, E., Vincent, G. M., Harenski, C. L., Calhoun, V. D., Sinnott-Armstrong, W., Gazzaniga,

M. S., & Kiehl, K. A. (2013). Neuroprediction of future rearrest. *Proceedings of the National Academy of Sciences, 110*(15), 6223-6228. doi:10.1073/pnas.1219302110

Airdrie, Langley, Thapar, & van Goozen. (2018). Facial Emotion Recognition and Eye Gaze in Attention-Deficit/Hyperactivity Disorder With and Without Comorbid Conduct Disorder. *J Am Acad Child Adolesc Psychiatry, 57*(8), 561-570. doi:10.1016/j.jaac.2018.04.016

Airdrie, J. N., Langley, K., Thapar, A., & van Goozen, S. H. (2018). Facial emotion recognition and eye gaze in attention-deficit/hyperactivity disorder with and without comorbid conductdisorder. *Journal of the American Academy of Child & Adolescent Psychiatry, 57*(8), 561-570.

Albajes-Eizagirre, A., Solanes, A., & Radua, J. (2018). Meta-analysis of non-statistically significant unreported effects. *Statistical methods in medical research*, 0962280218811349.

Albajes-Eizagirre, A., Solanes, A., Vieta, E., & Radua, J. (2019). Voxel-based meta-analysis via permutation of subject images (PSI): Theory and implementation for SDM. *NeuroImage, 186*, 174-184.

Alegria, A. A., Radua, J., & Rubia, K. (2016). Meta-analysis of fMRI studies of disruptive behavior disorders. *American journal of psychiatry, 173*(11), 1119-1130.

Alexander, G. E., DeLong, M. R., & Strick, P. L. (1986). Parallel organization of functionally segregated circuits linking basal ganglia and cortex. *Annual review of neuroscience, 9*(1), 357-381.

Alexander, L. M., Escalera, J., Ai, L., Andreotti, C., Febre, K., Mangone, A., . . . Milham, M. P. (2017). An open resource for transdiagnostic research in pediatric mental health and learning disorders.

Sci Data, 4, 170181. doi:10.1038/sdata.2017.181

Allan, N. P., Capron, D. W., Lejuez, C. W., Reynolds, E. K., MacPherson, L., & Schmidt, N. B. (2014). Developmental trajectories of anxiety symptoms in early adolescence: the influenceof anxiety sensitivity. *J Abnorm Child Psychol, 42*(4), 589-600. doi:10.1007/s10802-013- 9806-0

Amft, M., Bzdok, D., Laird, A. R., Fox, P. T., Schilbach, L., & Eickhoff, S. B. (2015). Definition and characterization of an extended social-affective default network. *Brain Structure and Function, 220*(2), 1031-1049.

Anderson, S. W., Bechara, A., Damasio, H., Tranel, D., & Damasio, A. R. (1999). Impairment of social and moral behavior related to early damage in human prefrontal cortex. *Nat Neurosci,2*(11), 1032-1037. doi:10.1038/14833

Andreasen, N. C. (2007). DSM and the death of phenomenology in america: an example of unintended consequences. *Schizophr Bull, 33*(1), 108-112. doi:10.1093/schbul/sbl054

Ang, R. P., Huan, V. S., Li, X., & Chan, W. T. (2016). Factor Structure and Invariance of the Reactive and Proactive Aggression Questionnaire in a Large Sample of Young Adolescentsin Singapore. *Child Psychiatry Hum Dev, 47*(6), 883-889. doi:10.1007/s10578-015-0619- y

Angold, A., & Costello, E. J. (2006). Puberty and depression. *Child and Adolescent Psychiatric Clinics, 15*(4), 919-937.

Angold, A., Costello, E. J., & Erkanli, A. (1999). Comorbidity. *The Journal of Child Psychology and Psychiatry and Allied Disciplines, 40*(1), 57-87.

Angold, A., Costello, E. J., & Worthman, C. M. (1998). Puberty and depression: the roles of age, pubertal status and pubertal timing. *Psychological Medicine, 28*(1), 51-61.

Anticevic, A., Cole, M. W., Murray, J. D., Corlett, P. R., Wang, X.-J., & Krystal, J. H. (2012). Therole of default network deactivation in cognition and disease. *Trends in cognitive sciences,16*(12), 584-592.

Aoki, Y., Inokuchi, R., Nakao, T., & Yamasue, H. (2013). Neural bases of antisocial behavior: a voxel-based meta-analysis. *Social cognitive and affective neuroscience, 9*(8), 1223-1231.

APA. (1952). *Diagnostic and statistical manual of mental disorders* (1st Ed. ed.). Washington DC: American Psychiatric Association.

APA. (1968). *Diagnostic and statistical manual of mental disorders* (2nd Ed. ed.). Washington DC.: American Psychiatric Association.

APA. (1980). *Diagnostic and statistical manual of mental disorders* (3rd ed. ed.).APA. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed. ed.).

APA. (2013). *Diagnostic and statistical manual of mental disorders (5th ed.)*: Arlington, VA: Author.

Archer, J. (2004). Sex Differences in Aggression in Real-World Settings: A Meta-AnalyticReview. *Review of General Psychology, 8*(4), 291-322. doi:10.1037/1089-2680.8.4.291

Arioli, & Canessa. (2019). Neural processing of social interaction: Coordinate-based meta-analytic evidence from human neuroimaging studies. *Human brain mapping, 40*(13), 3712-3737.

Arioli, Cattaneo, Ricciardi, & Canessa. (2021). Overlapping and specific neural correlates for empathizing, affective mentalizing, and cognitive mentalizing: A coordinate-based meta- analytic study. *Hum Brain Mapp, 42*(14), 4777-4804. doi:10.1002/hbm.25570

Armstrong, Wells, Boisvert, Lewis, Cooke, Woeckener, & Kavish. (2019). Skin conductance, heart rate and aggressive behavior type. *Biol Psychol, 141*, 44-51.doi:10.1016/j.biopsycho.2018.12.012

Armstrong, T., & Olatunji, B. O. (2012). Eye tracking of attention in the affective disorders: A meta-analytic review and synthesis. *Clinical psychology review, 32*(8), 704-723.

Arnone, M., & Dantzer, R. (1980). Does frustration induce aggression in pigs? *Applied Animal Ethology*.

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2014). Inhibition and the right inferior frontal cortex: one decade on. *Trends in cognitive sciences, 18*(4), 177-185.

American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders (5th ed.)*:Arlington, VA: Author.

Athanasiadou, A., Buitelaar, J. K., Brovedani, P., Chorna, O., Fulceri, F., Guzzetta, A., & Scattoni, M. L. (2020). Early motor signs of attention-deficit hyperactivity disorder: a systematic review. *Eur Child Adolesc Psychiatry, 29*(7), 903-916. doi:10.1007/s00787-019-01298-5

Aupperle Robin, L., & Martin, P. P. (2010). Neural systems underlying approach and avoidance in anxiety disorders. *Dialogues in clinical neuroscience, 12*(4), 517.

Axelrud, L. K., Simioni, A. R., Pine, D. S., Winkler, A. M., Pan, P. M., Sato, J. R., . . . Salum, G.

A. (2021). Neuroimaging Association Scores: reliability and validity of aggregate measuresof brain structural features linked to mental disorders in youth. *Eur Child Adolesc Psychiatry, 30*(12), 1895-1906. doi:10.1007/s00787-020-01653-x

Azevedo, Pais-Ribeiro, Coelho, & Figueiredo-Braga. (2018). Validation of the Portuguese Version of Impulsive-Premeditated Aggression Scale in an Inmate Population. *Front Psychiatry, 9*,10. doi:10.3389/fpsyt.2018.00010

Azevedo, Vieira-Coelho, Castelo-Branco, Coelho, & Figueiredo-Braga. (2020). Impulsive and premeditated aggression in male offenders with antisocial personality disorder. *PloS one, 15*(3), e0229876. doi:10.1371/journal.pone.0229876

Azrin, N., Hutchinson, R. R., & Hake, D. (1966). EXTINCTION-INDUCED AGGRESSION. *Journal of the Experimental Analysis of behavior, 9*(3), 191-204.

Babinski, L. M., Hartsough, C. S., & Lambert, N. M. (1999). Childhood conduct problems, hyperactivity-impulsivity, and inattention as predictors of adult criminal activity. *J Child Psychol Psychiatry, 40*(3), 347-355.

Baker, C. L., Jara-Ettinger, J., Saxe, R., & Tenenbaum, J. B. (2017). Rational quantitativeattribution of beliefs, desires and percepts in human mentalizing. *Nature Human Behaviour, 1*(4), 0064. doi:10.1038/s41562-017-0064

Bakker, M. J., Greven, C. U., Buitelaar, J. K., & Glennon, J. C. (2017). Practitioner Review: Psychological treatments for children and adolescents with conduct disorder problems - a systematic review and meta-analysis. *J Child Psychol Psychiatry, 58*(1), 4-18. doi:10.1111/jcpp.12590

Balia, C., Carucci, S., Coghill, D., & Zuddas, A. (2018). The pharmacological treatment of aggression in children and adolescents with conduct disorder. Do callous-unemotional traitsmodulate the efficacy of medication? *Neurosci Biobehav Rev, 91*, 218-238. doi:10.1016/j.neubiorev.2017.01.024

Bandelow, B., & Wedekind, D. (2015). Possible role of a dysregulation of the endogenous opioid system in antisocial personality disorder. *Hum Psychopharmacol, 30*(6), 393-415. doi:10.1002/hup.2497

Bandura, A., Ross, D., & Ross, S. A. (1963). VICARIOUS REINFORCEMENT AND IMITATIVE LEARNING. *J Abnorm Psychol, 67*, 601-607. doi:10.1037/h0045550

Baranyi, G., Cassidy, M., Fazel, S., Priebe, S., & Mundt, A. P. (2018). Prevalence of Posttraumatic Stress Disorder in Prisoners. *Epidemiol Rev, 40*(1), 134-145. doi:10.1093/epirev/mxx015

Barbey, A. K., Koenigs, M., & Grafman, J. (2013). Dorsolateral prefrontal contributions to human working memory. *cortex, 49*(5), 1195-1205.

Barbosa, F., Almeida, P. R., Ferreira-Santos, F., & Marques-Teixeira, J. (2016). Using signal detection theory in the analysis of emotional sensitivity of male recidivist offenders. Criminal behaviour and mental health : CBMH, 26(1), 18–29. https://doi.org/10.1002/cbm.1950

Bard. (1928). A diencephalic mechanism for the expression of rage with special reference to the sympathetic nervous system. *American Journal of Physiology, 84*, 490-515.

Bard. (1934). On emotional expression after decortication with some remarks on certain theoreticalviews: Part II. *Psychological review, 41*(5), 424.

Barker, E. D., Tremblay, R. E., Nagin, D. S., Vitaro, F., & Lacourse, E. (2006). Development of male proactive and reactive physical aggression during adolescence. *J Child Psychol Psychiatry, 47*(8), 783-790. doi:10.1111/j.1469-7610.2005.01585.x

Barker, E. D., Vitaro, F., Lacourse, E., Fontaine, N. M., Carbonneau, R., & Tremblay, R. E. (2010). Testing the developmental distinctiveness of male proactive and reactive aggression with anested longitudinal experimental intervention. *Aggress Behav, 36*(2), 127-140. doi:10.1002/ab.20337

Barratt, E. S., & Felthous, A. R. (2003). Impulsive versus premeditated aggression: implications for mens rea decisions. *Behav Sci Law, 21*(5), 619-630. doi:10.1002/bsl.555

Bartels, M., Hudziak, J. J., van den Oord, E. J., van Beijsterveldt, C. E., Rietveld, M. J., & Boomsma, D. I. (2003). Co-occurrence of aggressive behavior and rule-breaking behaviorat age 12: multi-rater analyses. *Behav Genet, 33*(5), 607-621. doi:10.1023/a:1025787019702

Bartra, O., McGuire, J. T., & Kable, J. W. (2013). The valuation system: a coordinate-based meta-analysis of BOLD fMRI experiments examining neural correlates of subjective value. *Neuroimage, 76*, 412-427. doi:10.1016/j.neuroimage.2013.02.063

Baskin-Sommers, A., & Brazil, I. A. (2022). The importance of an exaggerated attention bottleneck for understanding psychopathy. *Trends Cogn Sci, 26*(4), 325-336. doi:10.1016/j.tics.2022.01.001

Bazett, H. C., & Penfield, W. G. (1922). A Study of the Sherrington Decerebrate Animal in the Chronic as well as the Acute Condition. *Brain: A Journal of Neurology, 45*, 185-265. doi:10.1093/brain/45.2.185

Beaudry, G., Yu, R., Långström, N., & Fazel, S. (2021). An Updated Systematic Review and Meta-regression Analysis: Mental Disorders Among Adolescents in Juvenile Detention and Correctional Facilities. *J Am Acad Child Adolesc Psychiatry, 60*(1), 46-60. doi:10.1016/j.jaac.2020.01.015

Beaudry, G., Yu, R., Perry, A. E., & Fazel, S. (2021). Effectiveness of psychological interventionsin prison to reduce recidivism: a systematic review and meta-analysis of randomised controlled trials. *The Lancet Psychiatry, 8*(9), 759-773. doi:https://doi.org/10.1016/S2215-0366(21)00170-X

Becht, A. I., Prinzie, P., Deković, M., van den Akker, A. L., & Shiner, R. L. (2016). Child personality facets and overreactive parenting as predictors of aggression and rule-breaking trajectories from childhood to adolescence. *Dev Psychopathol, 28*(2), 399-413. doi:10.1017/s0954579415000577

Bedaso, A., Ayalew, M., Mekonnen, N., & Duko, B. (2020). Global Estimates of the Prevalence of Depression among Prisoners: A Systematic Review and Meta-analysis. *Depress Res Treat, 2020*, 3695209. doi:10.1155/2020/3695209

Behar, L. B. (1977). The preschool behavior questionnaire. *Journal of abnormal child psychology, 5*(3), 265-275.

Behzadi, Y., Restom, K., Liau, J., & Liu, T. T. (2007). A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. *Neuroimage, 37*(1), 90-101. doi:10.1016/j.neuroimage.2007.04.042

Beissner, F., Meissner, K., Bär, K. J., & Napadow, V. (2013). The autonomic brain: an activation likelihood estimation meta-analysis for central processing of autonomic function. *J Neurosci, 33*(25), 10503-10511. doi:10.1523/jneurosci.1103-13.2013

Bellesi, G., Barker, E. D., Brown, L., & Valmaggia, L. (2019). Pediatric traumatic brain injury and antisocial behavior: are they linked? A systematic review. *Brain Inj, 33*(10), 1272-1292. doi:10.1080/02699052.2019.1641621

Berkowitz, L. (1989). Frustration-aggression hypothesis: examination and reformulation. *Psychological bulletin, 106*(1), 59.

Berlin, Rolls, & Iversen. (2005). Borderline personality disorder, impulsivity, and the orbitofrontal cortex. *American Journal of Psychiatry, 162*(12), 2360-2373.

Berlin, Rolls, & Kischka. (2004). Impulsivity, time perception, emotion and reinforcement sensitivity in patients with orbitofrontal cortex lesions. *Brain, 127*(5), 1108-1126.

Berrios, G. E. (1999). J.C. Prichard and the concept of "moral insanity". Classic text no.37. *Hist Psychiatry, 10*(37), 111-126. doi:10.1177/0957154x9901003706

Bertsch, K., Florange, J., & Herpertz, S. C. (2020). Understanding brain mechanisms of reactive aggression. *Current psychiatry reports, 22*(12), 1-16.

Bettencourt, B. A., Talley, A., Benjamin, A. J., & Valentine, J. (2006). Personality and aggressive behavior under provoking and neutral conditions: a meta-analytic review. *Psychol Bull, 132*(5), 751-777. doi:10.1037/0033-2909.132.5.751

Bevilacqua, Hale, Barker, & Viner. (2018). Conduct problems trajectories and psychosocial outcomes: a systematic review and meta-analysis. *Eur Child Adolesc Psychiatry, 27*(10), 1239-1260. doi:10.1007/s00787-017-1053-4

Bevilacqua, L., Hale, D., Barker, E. D., & Viner, R. (2018). Conduct problems trajectories and psychosocial outcomes: a systematic review and meta-analysis. *European Child & Adolescent Psychiatry, 27*(10), 1239-1260.

Bevilacqua, L., Hale, D., Barker, E. D., Viner, R. J. E. c., & psychiatry, a. (2018). Conduct problems trajectories and psychosocial outcomes: a systematic review and meta-analysis. *27*(10), 1239-1260.

Bezdjian, S., Baker, L. A., & Tuvblad, C. (2011). Genetic and environmental influences on impulsivity: a meta-analysis of twin, family and adoption studies. *Clin Psychol Rev, 31*(7),1209-1223. doi:10.1016/j.cpr.2011.07.005

Biderman, A. D., & Reiss, A. J. (1967). On Exploring the "Dark Figure" of Crime. *The ANNALS of the American Academy of Political and Social Science, 374*(1), 1-15. doi:10.1177/000271626737400102

Biggs, E. E., Timmers, I., Meulders, A., Vlaeyen, J. W. S., Goebel, R., & Kaas, A. L. (2020). Theneural correlates of pain-related fear: A meta-analysis comparing fear conditioning studiesusing painful and non-painful stimuli. *Neurosci Biobehav Rev, 119*, 52-65. doi:10.1016/j.neubiorev.2020.09.016

Billeci, L., Muratori, P., Calderoni, S., Chericoni, N., Levantini, V., Milone, A., . . . Dadds, M. (2019). Emotional processing deficits in Italian children with Disruptive Behavior Disorder: The role of callous unemotional traits. *Behav Res Ther, 113*, 32-38. doi:10.1016/j.brat.2018.12.011

Birbaumer, N., Veit, R., Lotze, M., Erb, M., Hermann, C., Grodd, W., & Flor, H. (2005). Deficientfear conditioning in psychopathy: a functional magnetic resonance imaging study. *Arch Gen Psychiatry, 62*(7), 799-805. doi:10.1001/archpsyc.62.7.799

Bird, Davies, Duarte, Shen, Loeber, & Canino. (2006). A study of disruptive behavior disorders in Puerto Rican youth: II. Baseline prevalence, comorbidity, and correlates in two sites. *J AmAcad Child Adolesc Psychiatry, 45*(9), 1042-1053.

Bird, H. R., Davies, M., Duarte, C. S., Shen, S., Loeber, R., & Canino, G. J. (2006). A study of disruptive behavior disorders in Puerto Rican youth: II. Baseline prevalence, comorbidity,and correlates in two sites. *Journal of the American Academy of Child & Adolescent Psychiatry, 45*(9), 1042-1053.

Biswal, B., Yetkin, F. Z., Haughton, V. M., & Hyde, J. S. (1995). Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magn Reson Med, 34*(4), 537- 541. doi:10.1002/mrm.1910340409

Bjork. (2021). The Neurocircuit Signature of Retaliation in Adolescents With Alcohol Problems. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 6*(5), 503-505. doi:https://doi.org/10.1016/j.bpsc.2021.02.007

Bjork, Chen, Smith, & Hommer. (2010). Incentive-elicited mesolimbic activation and externalizing symptomatology in adolescents. *Journal of Child Psychology and Psychiatry, 51*(7), 827- 837.

Bjork, & Pardini. (2015). Who are those "risk-taking adolescents"? Individual differences in developmental neuroimaging research. *Dev Cogn Neurosci, 11*, 56-64.

doi:10.1016/j.dcn.2014.07.008

Bjork, J. M., Chen, G., & Hommer, D. W. (2012). Psychopathic tendencies and mesolimbic recruitment by cues for instrumental and passively obtained rewards. *Biological psychology, 89*(2), 408-415.

Bjork, J. M., Chen, G., Smith, A. R., & Hommer, D. W. (2010). Incentive-elicited mesolimbic activation and externalizing symptomatology in adolescents. *Journal of Child Psychology and Psychiatry, 51*(7), 827-837.

Bjork, J. M., Smith, A. R., & Hommer, D. W. (2008). Striatal sensitivity to reward deliveries and omissions in substance dependent patients. *Neuroimage, 42*(4), 1609-1621.

Björkqvist, K., Lagerspetz, K. M., & Kaukiainen, A. (1992). Do girls manipulate and boys fight? Developmental trends in regard to direct and indirect aggression. *Aggressive behavior, 18*(2), 117-127. doi:10.1002/1098-2337(1992)18:2<117::AID-AB2480180205>3.0.CO;2-3

Black, D. W., Gunter, T., Loveless, P., Allen, J., & Sieleni, B. (2010). Antisocial personality disorder in incarcerated offenders: Psychiatric comorbidity and quality of life. *Ann Clin Psychiatry, 22*(2), 113-120.

Blackford, J. U., & Pine, D. S. (2012). Neural substrates of childhood anxiety disorders: a review of neuroimaging findings. *Child and Adolescent Psychiatric Clinics, 21*(3), 501-525.

Blair. (2016). The neurobiology of impulsive aggression. *Journal of child and adolescent psychopharmacology, 26*(1), 4-9.

Blair. (2018). Traits of empathy and anger: implications for psychopathy and other disorders associated with aggression. *Philos Trans R Soc Lond B Biol Sci, 373*(1744). doi:10.1098/rstb.2017.0155

Blair, Bajaj, Sherer, Bashford-Largo, Zhang, Aloi, . . . Blair. (2021). Alcohol Use Disorder and Cannabis Use Disorder Symptomatology in Adolescents and Aggression: Associations With Recruitment of Neural Regions Implicated in Retaliation. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 6*(5), 536-544.

Blair, Bashford-Largo, Zhang, Lukoff, Elowsky, Leibenluft, . . . Blair. (2020). Temporal Discounting Impulsivity and Its Association with Conduct Disorder and Irritability. *J Child Adolesc Psychopharmacol, 30*(9), 542-548. doi:10.1089/cap.2020.0001

Blair, Leibenluft, & Pine. (2014). Conduct disorder and callous–unemotional traits in youth. *New England Journal of Medicine, 371*(23), 2207-2216.

Blair, Mitchell, Leonard, Budhani, Peschardt, & Newman. (2004). Passive avoidance learning in individuals with psychopathy: modulation by reward but not by punishment. *Personality and Individual Differences, 37*(6), 1179-1192. doi:https://doi.org/10.1016/j.paid.2003.12.001

Blair, Veroude, & Buitelaar. (2018a). Neuro-cognitive system dysfunction and symptom sets: a review of fMRI studies in youth with conduct problems. *Neuroscience & Biobehavioral Reviews, 91*, 69-90.

Blair, Veroude, & Buitelaar. (2018b). Neuro-cognitive system dysfunction and symptom sets: A review of fMRI studies in youth with conduct problems. *Neurosci Biobehav Rev, 91*, 69- 90. doi:10.1016/j.neubiorev.2016.10.022

Blair, R., Veroude, K., & Buitelaar, J. (2018). Neuro-cognitive system dysfunction and symptom sets: a review of fMRI studies in youth with conduct problems. *Neuroscience & Biobehavioral Reviews, 91*, 69-90.

Blair, R. J. (2016). The neurobiology of impulsive aggression. *Journal of child and adolescent psychopharmacology, 26*(1), 4-9.

Blair, R. J. R. (2010). Neuroimaging of psychopathy and antisocial behavior: a targeted review. *Current psychiatry reports, 12*(1), 76-82.

Blair, R. J. R. (2013). Psychopathy: cognitive and neural dysfunction. *Dialogues in clinical neuroscience, 15*(2), 181.

Blair, R. J. R., Leibenluft, E., & Pine, D. S. (2014). Conduct disorder and callous–unemotional traits in youth. *New England Journal of Medicine, 371*(23), 2207-2216.

Blair, R. J. (2022). The motivation of aggression: A cognitive neuroscience approach and neurochemical speculations. Motivation Science, 8(2), 106–120. https://doi.org/10.1037/mot0000247.

Blais, J., Solodukhin, E., & Forth, A. E. (2014). A Meta-Analysis Exploring the Relationship Between Psychopathy and Instrumental Versus Reactive Violence. *Criminal Justice and Behavior, 41*(7), 797-821. doi:10.1177/0093854813519629

Blonigen, Carlson, Krueger, & Patrick. (2003). A twin study of self-reported psychopathic personality traits. *Personality and Individual Differences, 35*(1), 179-197. doi:10.1016/S0191-8869(02)00184-8

Blonigen, Hicks, Krueger, Patrick, & Iacono. (2005). Psychopathic personality traits: heritability and genetic overlap with internalizing and externalizing psychopathology. *Psychol Med, 35*(5), 637-648. doi:10.1017/s0033291704004180

Boccadoro, S., Wagels, L., Henn, A. T., Hüpen, P., Graben, L., Raine, A., & Neuner, I. (2021). Proactive vs. Reactive Aggression Within Two Modified Versions of the Taylor Aggression Paradigm. *Front Behav Neurosci, 15*, 749041. doi:10.3389/fnbeh.2021.749041

Boccia, M., Dacquino, C., Piccardi, L., Cordellieri, P., Guariglia, C., Ferlazzo, F., . . . Giannini, A. M. (2017). Neural foundation of human moral reasoning: an ALE meta-analysis about therole of personal perspective. *Brain Imaging Behav, 11*(1), 278-292. doi:10.1007/s11682- 016-9505-x

Boes, A. D. (2020). Lesion network mapping: where do we go from here? *Brain, 144*(1), e5-e5. doi:10.1093/brain/awaa350

Bolhuis, K., Lubke, G. H., van der Ende, J., Bartels, M., van Beijsterveldt, C. E. M., Lichtenstein,P., . . . Tiemeier, H. (2017). Disentangling Heterogeneity of Childhood Disruptive BehaviorProblems Into Dimensions and Subgroups. *J Am Acad Child Adolesc Psychiatry, 56*(8), 678-686. doi:10.1016/j.jaac.2017.05.019

Boll, S., & Gamer, M. (2016). Psychopathic traits affect the visual exploration of facial expressions. *Biol Psychol, 117*, 194-201. doi:10.1016/j.biopsycho.2016.03.010

Bongers, Koot, van der Ende, & Verhulst. (2004). Developmental trajectories of externalizing behaviors in childhood and adolescence. *Child Dev, 75*(5), 1523-1537. doi:10.1111/j.1467-8624.2004.00755.x

Bongers, I. L., Koot, H. M., Van der Ende, J., & Verhulst, F. C. (2003). The normative developmentof child and adolescent problem behavior. *Journal of abnormal psychology, 112*(2), 179.

Bonta, J., Blais, J., & Wilson, H. A. (2014). A theoretically informed meta-analysis of the risk for general and violent recidivism for mentally disordered offenders. Aggression and violent behavior, 19(3), 278-287.

Borich, M., Brodie, S., Gray, W., Ionta, S., & Boyd, L. (2015). Understanding the role of the primary somatosensory cortex: Opportunities for rehabilitation. *Neuropsychologia, 79*, 246-255.

Bours, C., Bakker-Huvenaars, M., Tramper, J., Bielczyk, N., Scheepers, F., Nijhof, K., . . . Glennon, J. (2018). Emotional face recognition in male adolescents with autism spectrum disorder or disruptive behavior disorder: an eye-tracking study. *European Child & Adolescent Psychiatry, 27*(9), 1143-1157.

Bouzat, P., & Pinatel, J. (1963). *Traité de droit pénal et de criminologie: Criminologie, par Jean Pinatel*: Dalloz.

Boxer, A. L., & Miller, B. L. (2005). Clinical features of frontotemporal dementia. *Alzheimer Dis Assoc Disord, 19 Suppl 1*, S3-6. doi:10.1097/01.wad.0000183086.99691.91

Boylan, K., Vaillancourt, T., Boyle, M., & Szatmari, P. (2007). Comorbidity of internalizing disorders in children with oppositional defiant disorder. *European Child & Adolescent Psychiatry, 16*(8), 484-494.

Braga, T., Gonçalves, L. C., Basto-Pereira, M., & Maia, Â. (2017). Unraveling the link between maltreatment and juvenile antisocial behavior: A meta-analysis of prospective longitudinal studies. Aggression and Violent Behavior, 33, 37–50. https://doi.org/10.1016/j.avb.2017.01.006.

Brazil, I. A., van Dongen, J. D. M., Maes, J. H. R., Mars, R. B., & Baskin-Sommers, A. R. (2018). Classification and treatment of antisocial individuals: From behavior to biocognition. *Neurosci Biobehav Rev, 91*, 259-277. doi:10.1016/j.neubiorev.2016.10.010

Breaux, R., Baweja, R., Eadeh, H. M., Shroff, D. M., Cash, A. R., Swanson, C. S., . . . Waxmonsky, J. G. (2022). Systematic Review and Meta-analysis: Pharmacological and Non- pharmacological Interventions for Persistent Non-episodic Irritability. *J Am Acad Child Adolesc Psychiatry*. doi:10.1016/j.jaac.2022.05.012

Brendgen, M., Vitaro, F., Boivin, M., Dionne, G., & Pérusse, D. (2006). Examining genetic and environmental effects on reactive versus proactive aggression. *Dev Psychol, 42*(6), 1299- 1312. doi:10.1037/0012-1649.42.6.1299

Bresin, K. (2019). Impulsivity and aggression: A meta-analysis using the UPPS model of impulsivity. *Aggression and Violent Behavior, 48*, 124-140. doi:https://doi.org/10.1016/j.avb.2019.08.003

Broeren, S., Muris, P., Diamantopoulou, S., & Baker, J. R. (2013). The course of childhood anxiety symptoms: developmental trajectories and child-related factors in normal children. *JAbnorm Child Psychol, 41*(1), 81-95. doi:10.1007/s10802-012-9669-9

Broidy, L. M., Nagin, D. S., Tremblay, R. E., Bates, J. E., Brame, B., Dodge, K. A., . . . Vitaro, F.(2003). Developmental trajectories of childhood disruptive behaviors and adolescent delinquency: a six-site, cross-national study. *Dev Psychol, 39*(2), 222-245. doi:10.1037//0012-1649.39.2.222

Brotman, M. A., Schmajuk, M., Rich, B. A., Dickstein, D. P., Guyer, A. E., Costello, E. J., . . . Leibenluft, E. (2006). Prevalence, clinical correlates, and longitudinal course of severe mood dysregulation in children. *Biol Psychiatry, 60*(9), 991-997. doi:10.1016/j.biopsych.2006.08.042

Brower, M. C., & Price, B. H. (2001). Neuropsychiatry of frontal lobe dysfunction in violent and criminal behaviour: a critical review. *J Neurol Neurosurg Psychiatry, 71*(6), 720-726. doi:10.1136/jnnp.71.6.720

Bruno, A., Celebre, L., Torre, G., Pandolfo, G., Mento, C., Cedro, C., . . . Muscatello, M. R. A. (2019). Focus on Disruptive Mood Dysregulation Disorder: A review of the literature. *Psychiatry Res, 279*, 323-330. doi:10.1016/j.psychres.2019.05.043

Brunoni, A. R. (2017). Beyond the DSM: trends in psychiatry diagnoses. *Archives of Clinical Psychiatry (São Paulo), 44*, 154-158.

Bucholz, K. K., Hesselbrock, V. M., Heath, A. C., Kramer, J. R., & Schuckit, M. A. (2000). A latent class analysis of antisocial personality disorder symptom data from a multi-centre family study of alcoholism. *Addiction, 95*(4), 553-567. doi:10.1046/j.1360- 0443.2000.9545537.x

Buchsbaum, B. R., Greer, S., Chang, W. L., & Berman, K. F. (2005). Meta-analysis of neuroimaging studies of the Wisconsin card-sorting task and component processes. *Hum Brain Mapp, 25*(1), 35-45. doi:10.1002/hbm.20128

Buckley, L., Kaye, S.-A., Stork, R. P., Heinze, J. E., & Eckner, J. T. (2017). Traumatic brain injuryand aggression: A systematic review and future directions using community samples. *Aggression and Violent Behavior, 37*, 26-34. doi:https://doi.org/10.1016/j.avb.2017.08.004

Buhle, J. T., Silvers, J. A., Wager, T. D., Lopez, R., Onyemekwu, C., Kober, H., . . . Ochsner, K. N. (2014). Cognitive reappraisal of emotion: a meta-analysis of human neuroimaging studies. *Cerebral Cortex, 24*(11), 2981-2990.

Burke, J. D., Loeber, R., & Lahey, B. B. (2007). Adolescent conduct disorder and interpersonal callousness as predictors of psychopathy in young adults. *Journal of Clinical Child and Adolescent*

Psychology, 36(3), 334-346.

Burns, G. L., Boe, B., Walsh, J. A., Sommers-Flanagan, R., & Teegarden, L. A. (2001). A confirmatory factor analysis on the DSM-IV ADHD and ODD symptoms: What is the best model for the organization of these symptoms? *Journal of abnormal child psychology, 29*(4), 339-349.

Burokas, A., Gutiérrez-Cuesta, J., Martín-García, E., & Maldonado, R. (2012). Operant model of frustrated expected reward in mice. *Addiction biology, 17*(4), 770-782.

Burt. (2009a). Are there meaningful etiological differences within antisocial behavior? Results of a meta-analysis. *Clinical psychology review, 29*(2), 163-178.

Burt. (2009b). Rethinking environmental contributions to child and adolescent psychopathology: a meta-analysis of shared environmental influences. *Psychol Bull, 135*(4), 608-637. doi:10.1037/a0015702

Burt. (2013). Do etiological influences on aggression overlap with those on rule breaking? A meta-analysis. *Psychol Med, 43*(9), 1801-1812. doi:10.1017/s0033291712001894

Burt, Donnellan, Iacono, & McGue. (2011). Age-of-onset or behavioral sub-types? A prospective comparison of two approaches to characterizing the heterogeneity within antisocial behavior. *Journal of abnormal child psychology, 39*(5), 633-644.

Burt, Slawinski, Carsten, Harden, Hyde, & Klump. (2019). How should we understand the absence of sex differences in the genetic and environmental origins of antisocial behavior? *PsycholMed, 49*(10), 1600-1607. doi:10.1017/s0033291719000771

Burt, S. (2013). Do etiological influences on aggression overlap with those on rule breaking? A meta-analysis. *Psychological medicine, 43*(9), 1801-1812.

Byrd, Loeber, & Pardini. (2014). Antisocial behavior, psychopathic features and abnormalities in reward and punishment processing in youth. *Clinical Child and Family Psychology Review,17*(2), 125-156.

Byrd, A. L., Hawes, S. W., Waller, R., Delgado, M. R., Sutherland, M. T., Dick, A. S., . . . Gonzalez, R. (2021). Neural response to monetary loss among youth with disruptive behavior disorders and callous-unemotional traits in the ABCD study. *Neuroimage Clin, 32*, 102810. doi:10.1016/j.nicl.2021.102810

Byrd, A. L., Loeber, R., & Pardini, D. A. (2014). Antisocial behavior, psychopathic features and abnormalities in reward and punishment processing in youth. *Clinical Child and Family Psychology Review, 17*(2), 125-156.

Bzdok, D., Schilbach, L., Vogeley, K., Schneider, K., Laird, A. R., Langner, R., & Eickhoff, S. B.(2012). Parsing the neural correlates of moral cognition: ALE meta-analysis on morality, theory of mind, and empathy. *Brain Structure and Function, 217*(4), 783-796.

Cai, W., Duberg, K., Padmanabhan, A., Rehert, R., Bradley, T., Carrion, V., & Menon, V. (2019). Hyperdirect insula-basal-ganglia pathway and adult-like maturity of global brain responsespredict inhibitory control in children. *Nat Commun, 10*(1), 4798. doi:10.1038/s41467-019-12756-8

Cai, W., Ryali, S., Chen, T., Li, C.-S. R., & Menon, V. (2014). Dissociable roles of right inferior frontal cortex and anterior insula in inhibitory control: evidence from intrinsic and task- related functional parcellation, connectivity, and response profile analyses across multiple datasets. *Journal of Neuroscience, 34*(44), 14652-14667.

Calder, A. J., Ewbank, M., & Passamonti, L. (2011). Personality influences the neural responses to viewing facial expressions of emotion. *Philos Trans R Soc Lond B Biol Sci, 366*(1571), 1684-1701. doi:10.1098/rstb.2010.0362

Canada, S. (2007). National Longitudinal Survey of Children and Youth - Cycle 2 Survey Instruments 1996-97 Book 2 - Education, 10-11 and 12-13 year-olds. Retrieved from https://www23.statcan.gc.ca/imdb/p3Instr.pl?Function=getInstrumentList&Item_Id=33636&UL=1V&

Cannon, W. B., & Britton, S. W. (1925). STUDIES ON THE CONDITIONS OF ACTIVITY IN ENDOCRINE GLANDS. *American Journal of Physiology-Legacy Content, 72*(2), 283- 294.

doi:10.1152/ajplegacy.1925.72.2.283

Cantor, J., Lafaille, S., Hannah, J., Kucyi, A., Soh, D., Girard, T., & Mikulis, D. (2016).Independent component analysis of resting-state functional magnetic resonance imaging inpedophiles. *The journal of sexual medicine, 13*(10), 1546-1554.

Cao, W., Li, C., Zhang, J., Dong, D., Sun, X., Yao, S., . . . Liu, J. (2019). Regional homogeneity abnormalities in early-onset and adolescent-onset conduct disorder in boys: a resting-statefMRI study. *Frontiers in Human Neuroscience, 13*, 26.

Caramaschi, D., de Boer, S. F., & Koolhaas, J. M. (2007). Differential role of the 5-HT1A receptorin aggressive and non-aggressive mice: an across-strain comparison. *Physiol Behav, 90*(4),590-601. doi:10.1016/j.physbeh.2006.11.010

Card, N. A., & Little, T. D. (2006). Proactive and reactive aggression in childhood and adolescence:A meta-analysis of differential relations with psychosocial adjustment. *International Journal of Behavioral Development, 30*(5), 466-480. doi:10.1177/0165025406071904

Cardinale, E. M., & Marsh, A. A. (2020). The Reliability and Validity of the Inventory of Callous Unemotional Traits: A Meta-Analytic Review. *Assessment*, *27*(1), 57–71. https://doi.org/10.1177/1073191117747392

Cardoos, S. L., Loya, F., & Hinshaw, S. P. (2013). Adolescent girls' ADHD symptoms and youngadult driving: the role of perceived deviant peer affiliation. *J Clin Child Adolesc Psychol, 42*(2), 232-242. doi:10.1080/15374416.2012.759117

Carré, J. M., Hyde, L. W., Neumann, C. S., Viding, E., & Hariri, A. R. (2013). The neural signaturesof distinct psychopathic traits. *Soc Neurosci, 8*(2), 122-135. doi:10.1080/17470919.2012.703623

Carvalho, L. d. F., Hauck, N., Pianowski, G., & Muner, L. C. (2019). Latent structure of antisocialand borderline personality disorders: a taxometric research. *Paidéia (Ribeirão Preto), 29*.

Caspers, S., Geyer, S., Schleicher, A., Mohlberg, H., Amunts, K., & Zilles, K. (2006). The human

inferior parietal cortex: cytoarchitectonic parcellation and interindividual variability. *Neuroimage, 33*(2), 430-448.

Castellanos-Ryan, N., Struve, M., Whelan, R., Banaschewski, T., Barker, G. J., Bokde, A. L., . . .Conrod, P. J. (2014). Neural and cognitive correlates of the common and specific varianceacross externalizing problems in young adolescence. *Am J Psychiatry, 171*(12), 1310-1319. doi:10.1176/appi.ajp.2014.13111499

Cecil, C. A., McCrory, E. J., Barker, E. D., Guiney, J., & Viding, E. (2018). Characterising youthwith callous–unemotional traits and concurrent anxiety: evidence for a high-risk clinical group. *European child & adolescent psychiatry, 27*(7), 885-898.

Celeux, G., & Soromenho, G. (1996). An entropy criterion for assessing the number of clusters in a mixture model. *Journal of classification, 13*(2), 195-212.

Centifanti, L. C., Fanti, K. A., Thomson, N. D., Demetriou, V., & Anastassiou-Hadjicharalambous, X. (2015). Types of Relational Aggression in Girls Are Differentiated by Callous- Unemotional Traits, Peers and Parental Overcontrol. *Behav Sci (Basel), 5*(4), 518-536. doi:10.3390/bs5040518

Cerdá, M., Sagdeo, A., Johnson, J., & Galea, S. (2010). Genetic and environmental influences on psychiatric comorbidity: a systematic review. *Journal of affective disorders, 126*(1-2), 14-38.

Chai, X. J., Castañón, A. N., Ongür, D., & Whitfield-Gabrieli, S. (2012). Anticorrelations in resting state networks without global signal regression. *Neuroimage, 59*(2), 1420-1428. doi:10.1016/j.neuroimage.2011.08.048

Chamberlain, S. R., Derbyshire, K. L., Leppink, E. W., & Grant, J. E. (2016). Neurocognitive deficits associated with antisocial personality disorder in non-treatment-seeking young adults. *Journal of the American Academy of Psychiatry and the Law Online, 44*(2), 218- 225.

Chapman, H., Gillespie, S. M., & Mitchell, I. J. (2018). Facial affect processing in incarcerated violent males: A systematic review. *Aggression and Violent Behavior, 38*, 123-138.

Chen, Yang, & Qian. (2013). Chinese Version of Impulsive/Premeditated Aggression Scale: Validation and its Psychometric Properties. *Journal of Aggression, Maltreatment & Trauma, 22*(2), 175-191. doi:10.1080/10926771.2013.741664

Chen, C., Zhou, J., Liu, C., Witt, K., Zhang, Y., Jing, B., . . . Li, L. (2015). Regional homogeneityof resting-state brain abnormalities in violent juvenile offenders: a biomarker of brain immaturity? *The Journal of neuropsychiatry and clinical neurosciences, 27*(1), 27-32.

Chermack, S. T., & Giancola, P. R. (1997). The relation between alcohol and aggression: An integrated biopsychosocial conceptualization. *Clinical psychology review, 17*(6), 621-649. doi:https://doi.org/10.1016/S0272-7358(97)00038-X

Chun, S., Harris, A., Carrion, M., Rojas, E., Stark, S., Lejuez, C., . . . Bornovalova, M. A. (2017).A psychometric investigation of gender differences and common processes across borderline and antisocial personality disorders. *J Abnorm Psychol, 126*(1), 76-88. doi:10.1037/abn0000220

Cieslik, E. C., Mueller, V. I., Eickhoff, C. R., Langner, R., & Eickhoff, S. B. (2015). Three key regions for supervisory attentional control: evidence from neuroimaging meta-analyses. *Neurosci Biobehav Rev, 48*, 22-34. doi:10.1016/j.neubiorev.2014.11.003

Cleckley, H. M. (1941). *The mask of sanity; an attempt to reinterpret the so-called psychopathic personality*: St. Louis : The C.V. Mosby Company, 1941.

Clithero, J. A., & Rangel, A. (2014). Informatic parcellation of the network involved in the computation of subjective value. *Soc Cogn Affect Neurosci, 9*(9), 1289-1302. doi:10.1093/scan/nst106

Cloninger, C. R. (1987). A systematic method for clinical description and classification of personality variants. A proposal. *Arch Gen Psychiatry, 44*(6), 573-588. doi:10.1001/archpsyc.1987.01800180093014

Clotfelter, E. D., O'Hare, E. P., McNitt, M. M., Carpenter, R. E., & Summers, C. H. (2007). Serotonin decreases aggression via 5-HT1A receptors in the fighting fish Betta splendens. *Pharmacol*

Biochem Behav, 87(2), 222-231. doi:10.1016/j.pbb.2007.04.018

Cohen, A. L., Soussand, L., Corrow, S. L., Martinaud, O., Barton, J. J. S., & Fox, M. D. (2019). Looking beyond the face area: lesion network mapping of prosopagnosia. *Brain, 142*(12), 3975-3990. doi:10.1093/brain/awz332

Cohen, P., Cohen, J., Aiken, L. S., & West, S. G. (1999). The problem of units and the circumstance for POMP. *Multivariate behavioral research, 34*(3), 315-346.

Cohn, Pape, Schmaal, van den Brink, van Wingen, Vermeiren, . . . Popma. (2015a). Differential relations between juvenile psychopathic traits and resting state network connectivity. *HumBrain Mapp, 36*(6), 2396-2405. doi:10.1002/hbm.22779

Cohn, Pape, Schmaal, van den Brink, van Wingen, Vermeiren, . . . Popma. (2015b). Differential relations between juvenile psychopathic traits and resting state network connectivity.*Human brain mapping, 36*(6), 2396-2405.

Cohn, Popma, van den Brink, Pape, L., Kindt, van Domburgh, . . . Veltman. (2013). Fear conditioning, persistence of disruptive behavior and psychopathic traits: an fMRI study. *Transl Psychiatry, 3*(10), e319. doi:10.1038/tp.2013.89

Cohn, Veltman, Pape, van Lith, Vermeiren, van den Brink, . . . Popma. (2015). Incentive processing in persistent disruptive behavior and psychopathic traits: A functional magnetic resonance imaging study in adolescents. *Biological psychiatry, 78*(9), 615-624.

Cole, D. M., Smith, S. M., & Beckmann, C. F. (2010). Advances and pitfalls in the analysis and interpretation of resting-state FMRI data. *Frontiers in systems neuroscience, 4*, 8.

Colins, Van Damme, Hendriks, & Georgiou. (2020). The DSM-5 with Limited Prosocial Emotions Specifier for Conduct Disorder: a Systematic Literature Review. *Journal of Psychopathology and Behavioral Assessment, 42*(2), 248-258. doi:10.1007/s10862-020- 09799-3

Colins, O. F. (2016). Assessing Reactive and Proactive Aggression in Detained Adolescents Outside

of a Research Context. *Child Psychiatry Hum Dev, 47*(1), 159-172. doi:10.1007/s10578-015-0553-z

Colins, O. F., Andershed, H., Salekin, R. T., & Fanti, K. A. (2018). Comparing DifferentApproaches for Subtyping Children with Conduct Problems: Callous-Unemotional Traits Only Versus the Multidimensional Psychopathy Construct. *J Psychopathol Behav Assess, 40*(1), 6-15. doi:10.1007/s10862-018-9653-y

Colins, O. F., & Vermeiren, R. R. (2013). The usefulness of DSM-IV and DSM-5 conduct disorder subtyping in detained adolescents. *J Nerv Ment Dis, 201*(9), 736-743. doi:10.1097/NMD.0b013e3182a20e94

Colman, I., Murray, J., Abbott, R. A., Maughan, B., Kuh, D., Croudace, T. J., & Jones, P. B. (2009). Outcomes of conduct problems in adolescence: 40 year follow-up of national cohort. *Bmj,338*, a2981.

Compton, W. M., Conway, K. P., Stinson, F. S., Colliver, J. D., & Grant, B. F. (2005). Prevalence, correlates, and comorbidity of DSM-IV antisocial personality syndromes and alcohol and specific drug use disorders in the United States: results from the national epidemiologic survey on alcohol and related conditions. *J Clin Psychiatry, 66*(6), 677-685. doi:10.4088/jcp.v66n0602

Consortium, C.-D. G. o. t. P. G. (2013). Identification of risk loci with shared effects on five major psychiatric disorders: a genome-wide analysis. *The lancet, 381*(9875), 1371-1379.

Corbetta, M., Patel, G., & Shulman, G. L. (2008). The reorienting system of the human brain: from environment to theory of mind. *Neuron, 58*(3), 306-324.

Cortese, S., Aoki, Y. Y., Itahashi, T., Castellanos, F. X., & Eickhoff, S. B. (2020). Systematic Review and Meta-analysis: Resting State Functional Magnetic Resonance Imaging Studiesof Attention-Deficit/Hyperactivity Disorder. *Journal of the American Academy of Child &Adolescent Psychiatry*.

Cortese, S., Kelly, C., Chabernaud, C., Proal, E., Di Martino, A., Milham, M. P., & Castellanos, F.X. (2012). Toward systems neuroscience of ADHD: a meta-analysis of 55 fMRI studies. *American*

Journal of Psychiatry, 169(10), 1038-1055.

Costello, E. J., Mustillo, S., Erkanli, A., Keeler, G., & Angold, A. (2003). Prevalence and development of psychiatric disorders in childhood and adolescence. *Archives of general psychiatry, 60*(8), 837-844.

Côté. (2007). Sex Differences in Physical and Indirect Aggression: A Developmental Perspective. *European Journal on Criminal Policy and Research, 13*(3), 183-200. doi:10.1007/s10610-007-9046-3

Côté, Vaillancourt, Barker, Nagin, & Tremblay. (2007). The joint development of physical and indirect aggression: Predictors of continuity and change during childhood. *DevPsychopathol, 19*(1), 37-55. doi:10.1017/s0954579407070034

Cote, S., Tremblay, R. E., Nagin, D. S., Zoccolillo, M., & Vitaro, F. (2002). Childhood behavioral profiles leading to adolescent conduct disorder: Risk trajectories for boys and girls. *Journalof the American Academy of Child & Adolescent Psychiatry, 41*(9), 1086-1094.

Côté, S. M., Orri, M., Brendgen, M., Vitaro, F., Boivin, M., Japel, C., . . . Falissard, B. (2017). Psychometric properties of the Mental Health and Social Inadaptation Assessment for Adolescents (MIA) in a population-based sample. *International journal of methods in psychiatric research, 26*(4), e1566.

Cottle, C. C., Lee, R. J., & Heilbrun, K. (2001). The prediction of criminal recidivism in juveniles: A meta-analysis. Criminal justice and behavior, 28(3), 367-394.

Craig, S. G., Goulter, N., & Moretti, M. M. (2021). A Systematic Review of Primary and Secondary Callous-Unemotional Traits and Psychopathy Variants in Youth. *Clin Child Fam Psychol Rev, 24*(1), 65-91. doi:10.1007/s10567-020-00329-x

Criaud, M., & Boulinguez, P. (2013). Have we been asking the right questions when assessing response inhibition in go/no-go tasks with fMRI? A meta-analysis and critical review. *Neurosci Biobehav Rev, 37*(1), 11-23. doi:10.1016/j.neubiorev.2012.11.003

Crick, N. R., & Dodge, K. A. (1996). Social information-processing mechanisms in reactive and proactive aggression. *Child Development, 67*(3), 993-1002.

Crocetti, E., Klimstra, T., Keijsers, L., Hale, W. W., 3rd, & Meeus, W. (2009). Anxiety trajectoriesand identity development in adolescence: a five-wave longitudinal study. *J Youth Adolesc,38*(6), 839-849. doi:10.1007/s10964-008-9302-y

Crowe, S. L., & Blair, R. J. R. (2008). The development of antisocial behavior: What can we learn from functional neuroimaging studies? *Development and psychopathology, 20*(4), 1145- 1159.

Cui, L., Colasante, T., Malti, T., Ribeaud, D., & Eisner, M. P. (2016). Dual Trajectories of Reactiveand Proactive Aggression from Mid-childhood to Early Adolescence: Relations to Sensation Seeking, Risk Taking, and Moral Reasoning. *J Abnorm Child Psychol, 44*(4), 663-675. doi:10.1007/s10802-015-0079-7

Cuthbert. (2015). Research Domain Criteria: toward future psychiatric nosologies. *Dialogues Clin Neurosci, 17*(1), 89-97. doi:10.31887/DCNS.2015.17.1/bcuthbert

Cuthbert, & Insel. (2013). Toward the future of psychiatric diagnosis: the seven pillars of RDoC. *BMC medicine, 11*(1), 126. doi:10.1186/1741-7015-11-126

da Cunha-Bang, S., & Knudsen, G. M. (2021). The Modulatory Role of Serotonin on Human Impulsive Aggression. *Biol Psychiatry, 90*(7), 447-457. doi:10.1016/j.biopsych.2021.05.016

Dadds, El Masry, Wimalaweera, & Guastella. (2008). Reduced eye gaze explains “fear blindness” in childhood psychopathic traits. *Journal of the American Academy of Child & Adolescent Psychiatry, 47*(4), 455-463.

Dadds, Jambrak, Pasalich, Hawes, & Brennan. (2011). Impaired attention to the eyes of attachment figures and the developmental origins of psychopathy. *J Child Psychol Psychiatry, 52*(3), 238-245. doi:10.1111/j.1469-7610.2010.02323.x

Damasio, H., Grabowski, T., Frank, R., Galaburda, A. M., & Damasio, A. R. (1994). The return of Phineas Gage: clues about the brain from the skull of a famous patient. *Science, 264*(5162),1102-1105. doi:10.1126/science.8178168

Damoiseaux, J. S., Rombouts, S. A. R. B., Barkhof, F., Scheltens, P., Stam, C. J., Smith, S. M., & Beckmann, C. F. (2006). Consistent resting-state networks across healthy subjects. *Proceedings of the National Academy of Sciences, 103*(37), 13848-13853. doi:10.1073/pnas.0601417103

Dantzer, R., Arnone, M., & Mormede, P. (1980). Effects of frustration on behaviour and plasma corticosteroid levels in pigs. *Physiology & Behavior, 24*(1), 1-4.

Darby, R. R., Horn, A., Cushman, F., & Fox, M. D. (2018). Lesion network localization of criminal behavior. *Proc Natl Acad Sci U S A, 115*(3), 601-606. doi:10.1073/pnas.1706587115

Darby, R. R., Joutsa, J., Burke, M. J., & Fox, M. D. (2018). Lesion network localization of freewill. *Proc Natl Acad Sci U S A, 115*(42), 10792-10797. doi:10.1073/pnas.1814117115

Darby, R. R., Joutsa, J., & Fox, M. D. (2019). Network localization of heterogeneous neuroimaging findings. *Brain, 142*(1), 70-79. doi:10.1093/brain/awy292

Darby, R. R., Laganiere, S., Pascual-Leone, A., Prasad, S., & Fox, M. D. (2017). Finding the imposter: brain connectivity of lesions causing delusional misidentifications. *Brain, 140*(2), 497-507. doi:10.1093/brain/aww288

Dargis, M., Wolf, R. C., & Koenigs, M. (2018). Psychopathic traits are associated with reduced fixations to the eye region of fearful faces. *J Abnorm Psychol, 127*(1), 43-50. doi:10.1037/abn0000322

Dawel, O'Kearney, McKone, & Palermo. (2012). Not just fear and sadness: meta-analytic evidence of pervasive emotion recognition deficits for facial and vocal expressions in psychopathy. *Neurosci Biobehav Rev, 36*(10), 2288-2304. doi:10.1016/j.neubiorev.2012.08.006

de Almeida, R. M., & Miczek, K. A. (2002). Aggression escalated by social instigation or by

discontinuation of reinforcement (“frustration”) in mice: inhibition by anpirtoline: a 5- HT1B receptor agonist. *Neuropsychopharmacology, 27*(2), 171-181.

de Boer, S. F., & Koolhaas, J. M. (2005). 5-HT1A and 5-HT1B receptor agonists and aggression:a pharmacological challenge of the serotonin deficiency hypothesis. *Eur J Pharmacol, 526*(1-3), 125-139. doi:10.1016/j.ejphar.2005.09.065

De Brito, Viding, Kumari, Blackwood, & Hodgins. (2013). Cool and hot executive function impairments in violent offenders with antisocial personality disorder with and without psychopathy. *PloS one, 8*(6), e65566. doi:10.1371/journal.pone.0065566

De Brito, S. A., Forth, A. E., Baskin-Sommers, A. R., Brazil, I. A., Kimonis, E. R., Pardini, D., . .

. Viding, E. (2021). Psychopathy. *Nature Reviews Disease Primers, 7*(1), 49. doi:10.1038/s41572-021-00282-1

De Luca, M., Beckmann, C. F., De Stefano, N., Matthews, P. M., & Smith, S. M. (2006). fMRI resting state networks define distinct modes of long-distance interactions in the human brain. *Neuroimage, 29*(4), 1359-1367. doi:10.1016/j.neuroimage.2005.08.035

Decety, J., Michalska, K. J., Akitsuki, Y., & Lahey, B. B. (2009). Atypical empathic responses in adolescents with aggressive conduct disorder: a functional MRI investigation. *Biological psychology, 80*(2), 203-211.

Decuyper, M., De Pauw, S., De Fruyt, F., De Bolle, M., & De Clercq, B. J. (2009). A meta-analysisof psychopathy-, antisocial PD- and FFM associations. *European Journal of Personality, 23*(7), 531-565. doi:10.1002/per.729

Del Casale, A., Kotzalidis, G. D., Rapinesi, C., Di Pietro, S., Alessi, M. C., Di Cesare, G., . . . Ferracuti, S. (2015). Functional Neuroimaging in Psychopathy. *Neuropsychobiology, 72*(2), 97-117. doi:10.1159/000441189

Delfin, C., Krona, H., Andiné, P., Ryding, E., Wallinius, M., & Hofvander, B. (2019). Prediction of

recidivism in a long-term follow-up of forensic psychiatric patients: Incremental effects of neuroimaging data. *PloS one, 14*(5), e0217127. doi:10.1371/journal.pone.0217127

Delvecchio, G., Fossati, P., Boyer, P., Brambilla, P., Falkai, P., Gruber, O., . . . McIntosh, A. M. (2012). Common and distinct neural correlates of emotional processing in bipolar disorderand major depressive disorder: a voxel-based meta-analysis of functional magnetic resonance imaging studies. *European Neuropsychopharmacology, 22*(2), 100-113.

Deming, P., & Koenigs, M. (2020). Functional neural correlates of psychopathy: a meta-analysis of MRI data. *Transl Psychiatry, 10*(1), 133. doi:10.1038/s41398-020-0816-8

Deming, P., Heilicher, M., & Koenigs, M. (2022). How reliable are amygdala findings in psychopathy? A systematic review of MRI studies. Neuroscience and biobehavioral reviews, 142, 104875. https://doi.org/10.1016/j.neubiorev.2022.104875

Derrfuss, J., Brass, M., Neumann, J., & von Cramon, D. Y. (2005). Involvement of the inferior frontal junction in cognitive control: meta-analyses of switching and Stroop studies. *Hum Brain Mapp, 25*(1), 22-34. doi:10.1002/hbm.20127

Déry, M., Bégin, V., Toupin, J., & Temcheff, C. (2019). Clinical Utility of the Limited Prosocial Emotions Specifier in the Childhood-Onset Subtype of Conduct Disorder. *Can J Psychiatry, 64*(12), 838-845. doi:10.1177/0706743719885469

DeSerisy, M., Ramphal, B., Pagliaccio, D., Raffanello, E., Tau, G., Marsh, R., . . . Margolis, A. E. (2021). Frontoparietal and default mode network connectivity varies with age and intelligence. *Developmental cognitive neuroscience, 48*, 100928.

Deyoung, C. G., & Gray, J. R. (2009). Personality neuroscience: Explaining individual differencesin affect, behaviour and cognition. In *The Cambridge handbook of personality psychology.*(pp. 323-346). New York, NY, US: Cambridge University Press.

Dickstein, S. G., Bannon, K., Xavier Castellanos, F., & Milham, M. P. (2006). The neural correlatesof attention deficit hyperactivity disorder: An ALE meta-analysis. *Journal of Child Psychology and*

Psychiatry, 47(10), 1051-1062.

Diekhof, E. K., Kaps, L., Falkai, P., & Gruber, O. (2012). The role of the human ventral striatum and the medial orbitofrontal cortex in the representation of reward magnitude - an activationlikelihood estimation meta-analysis of neuroimaging studies of passive reward expectancyand outcome processing. *Neuropsychologia, 50*(7), 1252-1266.

doi:10.1016/j.neuropsychologia.2012.02.007

Ding, R., Ren, J., Li, S., Zhu, X., Zhang, K., & Luo, W. (2020). Domain-general and domain-preferential neural correlates underlying empathy towards physical pain, emotional situation and emotional faces: An ALE meta-analysis. *Neuropsychologia, 137*, 107286. doi:10.1016/j.neuropsychologia.2019.107286

Docherty, M., Boxer, P., Huesmann, L. R., O'Brien, M., & Bushman, B. J. (2016). Exploring primary and secondary variants of psychopathy in adolescents in detention and in the community. *Journal of Clinical Child & Adolescent Psychology, 45*(5), 564-578.

Dodge, K. A., & Coie, J. D. (1987). Social-information-processing factors in reactive and proactive aggression in children's peer groups. *J Pers Soc Psychol, 53*(6), 1146-1158. doi:10.1037//0022-3514.53.6.1146

Dollard, Miller, Doob, Mowrer, & Sears. (1939b). *Frustration and aggression*. New Haven, CT, US: Yale University Press.

Dong, D., Wang, Y., Chang, X., Luo, C., & Yao, D. (2018). Dysfunction of large-scale brain networks in schizophrenia: a meta-analysis of resting-state functional connectivity. *Schizophrenia bulletin, 44*(1), 168-181.

Döpfner, M., Hautmann, C., Görtz-Dorten, A., Klasen, F., Ravens-Sieberer, U., & Group, B. S. (2015). Long-term course of ADHD symptoms from childhood to early adulthood in a community sample. *European child & adolescent psychiatry, 24*(6), 665-673.

Dotterer, H. L., Hyde, L. W., Shaw, D. S., Rodgers, E. L., Forbes, E. E., & Beltz, A. M. (2020). Connections that characterize callousness: Affective features of psychopathy are associatedwith personalized patterns of resting-state network connectivity. *NeuroImage: Clinical, 28*,102402.

Doucet, G. E., Janiri, D., Howard, R., O'Brien, M., Andrews-Hanna, J. R., & Frangou, S. (2020). Transdiagnostic and disease-specific abnormalities in the default-mode network hubs in psychiatric disorders: A meta-analysis of resting-state functional imaging studies. *Eur Psychiatry, 63*(1), e57. doi:10.1192/j.eurpsy.2020.57

Doucet, G. E., Janiri, D., Howard, R., O'Brien, M., Andrews-Hanna, J. R., & Frangou, S. (2020). Transdiagnostic and disease-specific abnormalities in the default-mode network hubs in psychiatric disorders: A meta-analysis of resting-state functional imaging studies. *European psychiatry, 63*(1).

Downar, J., Crawley, A. P., Mikulis, D. J., & Davis, K. D. (2000). A multimodal cortical networkfor the detection of changes in the sensory environment. *Nature neuroscience, 3*(3), 277- 283.

Dricu, M., & Frühholz, S. (2016). Perceiving emotional expressions in others: Activation likelihood estimation meta-analyses of explicit evaluation, passive perception and incidental perception of emotions. *Neurosci Biobehav Rev, 71*, 810-828. doi:10.1016/j.neubiorev.2016.10.020

Duchesne, S., Larose, S., Vitaro, F., & Tremblay, R. E. (2010). Trajectories of anxiety in a population sample of children: clarifying the role of children's behavioral characteristics and maternal parenting. *Dev Psychopathol, 22*(2), 361-373. doi:10.1017/s0954579410000118

Dugré, Dumais, Bitar, & Potvin. (2018). Loss anticipation and outcome during the Monetary Incentive Delay Task: a neuroimaging systematic review and meta-analysis. *PeerJ, 6*, e4749.

Dugré, Dumais, Dellazizzo, & Potvin. (2019). Developmental joint trajectories of anxiety-depressive trait and trait-aggression: implications for co-occurrence of internalizing and externalizing problems. *Psychological medicine*, 1-10.

Dugré, Giguére, Percie du Sert, Potvin, & Dumais. (2019). The Psychometric Properties of a Short

UPPS-P Impulsive Behavior Scale Among Psychiatric Patients Evaluated in an EmergencySetting. *Front Psychiatry, 10*, 139. doi:10.3389/fpsyt.2019.00139

Dugré, Orban, & Potvin. (Preprint). Disrupted functional connectivity of the brain reward system in substance use problems: a meta-analysis of functional neuroimaging studies. *medRxiv*.

Dugré, & Potvin. (2020). Developmental multi-trajectory of irritability, anxiety, and hyperactivity as psychological markers of heterogeneity in childhood aggression. *Psychological medicine*, 1-10.

Dugré, Potvin, Dellazizzo, & Dumais. (2021). Aggression and delinquent behavior in a large representative sample of high school students: Cannabis use and victimization as key discriminating factors. *Psychiatry Res, 296*, 113640. doi:10.1016/j.psychres.2020.113640

Dugré, J. R., Dumais, A., Bitar, N., & Potvin, S. (2018). Loss anticipation and outcome during the Monetary Incentive Delay Task: a neuroimaging systematic review and meta-analysis. *PeerJ, 6*, e4749.

Dugré, J. R., Dumais, A., Dellazizzo, L., & Potvin, S. (2019). Developmental joint trajectories of anxiety-depressive trait and trait-aggression: implications for co-occurrence of internalizing and externalizing problems. *Psychological Medicine*, 1-10.

Dugré, J. R., Eickhoff, S. B., & Potvin, S. (2022). Meta-analytical transdiagnostic neural correlatesin common pediatric psychiatric disorders. *Scientific reports, 12*(1), 4909. doi:10.1038/s41598-022-08909-3

Dugré, J. R., & Potvin, S. (2020). Multiple developmental pathways underlying conduct problems: A multitrajectory framework. *Development and psychopathology*, 1-10.

Dugré, J. R., & Potvin, S. (2021). Impaired attentional and socio-affective networks in subjects with antisocial behaviors: a meta-analysis of resting-state functional connectivity studies. *Psychol Med*, 1-11. doi:10.1017/s0033291721001525

Dugré, J. R., Potvin, S. (2021). Impaired attentional and socio-affective networks in subjects with

antisocial behaviors: A meta-analysis of resting-state functional connectivity studies. *Psychol Med.* 51(8), 1249-1259.

Dugré, J. R., Radua, J., Carignan-Allard, M., Dumais, A., Rubia, K., & Potvin, S. (2020). Neurofunctional abnormalities in antisocial spectrum: A meta-analysis of fMRI studies onFive distinct neurocognitive research domains. *Neuroscience & Biobehavioral Reviews*.

Dukart, J., Holiga, S., Rullmann, M., Lanzenberger, R., Hawkins, P. C. T., Mehta, M. A., . . . Eickhoff, S. B. (2021). JuSpace: A tool for spatial correlation analyses of magneticresonance imaging data with nuclear imaging derived neurotransmitter maps. *Human brainmapping, 42*(3), 555-566. doi:10.1002/hbm.25244

Duke, A. A., Bègue, L., Bell, R., & Eisenlohr-Moul, T. (2013). Revisiting the serotonin-aggression relation in humans: a meta-analysis. *Psychol Bull, 139*(5), 1148-1172.doi:10.1037/a0031544

Duncan, I., & Wood-Gush, D. (1971). Frustration and aggression in the domestic fowl. *Animal Behaviour, 19*(3), 500-504.

Durand, E., Chevignard, M., Ruet, A., Dereix, A., Jourdan, C., & Pradat-Diehl, P. (2017). Historyof traumatic brain injury in prison populations: A systematic review. *Ann Phys Rehabil Med, 60*(2), 95-101. doi:10.1016/j.rehab.2017.02.003

Easton, S., Brantingham, P., & Furness, H. (2014). *The cost of crime in Canada*: desLibris.

Edalati, H., & Conrod, P. J. (2019). A Review of Personality-Targeted Interventions for Prevention of Substance Misuse and Related Harm in Community Samples of Adolescents. *Frontiers in Psychiatry*, 9, 770. https://doi.org/10.3389/fpsyt.2018.00770

Edens, J. F., Marcus, D. K., Lilienfeld, S. O., & Poythress Jr, N. G. (2006). Psychopathic, not psychopath: taxometric evidence for the dimensional structure of psychopathy. *Journal of abnormal psychology, 115*(1), 131.

Egger, M., Smith, G. D., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a

simple, graphical test. *Bmj, 315*(7109), 629-634.

Eickhoff, S. B., Bzdok, D., Laird, A. R., Kurth, F., & Fox, P. T. (2012). Activation likelihood estimation meta-analysis revisited. *Neuroimage, 59*(3), 2349-2361.

Eickhoff, S. B., Laird, A. R., Fox, P. T., Bzdok, D., & Hensel, L. (2016). Functional segregation of the human dorsomedial prefrontal cortex. *Cerebral Cortex, 26*(1), 304-321.

Eickhoff, S. B., Laird, A. R., Grefkes, C., Wang, L. E., Zilles, K., & Fox, P. T. (2009). Coordinate-based activation likelihood estimation meta-analysis of neuroimaging data: A random- effects approach based on empirical estimates of spatial uncertainty. *Human brain mapping, 30*(9), 2907-2926.

Eickhoff, S. B., Nichols, T. E., Laird, A. R., Hoffstaedter, F., Amunts, K., Fox, P. T., . . . Eickhoff, C. R. (2016). Behavior, sensitivity, and power of activation likelihood estimation characterized by massive empirical simulation. *Neuroimage, 137*, 70-85.

Eickhoff, S. B., Stephan, K. E., Mohlberg, H., Grefkes, C., Fink, G. R., Amunts, K., & Zilles, K. (2005). A new SPM toolbox for combining probabilistic cytoarchitectonic maps andfunctional imaging data. *Neuroimage, 25*(4), 1325-1335.

Eickhoff, S. B., Thirion, B., Varoquaux, G., & Bzdok, D. (2015). Connectivity-based parcellation: Critique and implications. *Human brain mapping, 36*(12), 4771-4792.

Eimontaite, I., Schindler, I., De Marco, M., Duzzi, D., Venneri, A., & Goel, V. (2019). Left amygdala and putamen activation modulate emotion driven decisions in the iteratedPrisoner's Dilemma Game. *Frontiers in neuroscience, 13*, 741.

Eklund, A., Nichols, T. E., & Knutsson, H. (2016). Cluster failure: Why fMRI inferences for spatial extent have inflated false-positive rates. *Proceedings of the National Academy of Sciences, 113*(28), 7900-7905.

Elgar, F. J., McKinnon, B., Walsh, S. D., Freeman, J., P, D. D., de Matos, M. G., . . . Currie, C. (2015). Structural Determinants of Youth Bullying and Fighting in 79 Countries. *J AdolescHealth, 57*(6),

643-650. doi:10.1016/j.jadohealth.2015.08.007

Enzmann, D., Marshall, I. H., Killias, M., Junger-Tas, J., Steketee, M., & Gruszczynska, B. (2010).Self-reported youth delinquency in Europe and beyond: First results of the Second International Self-Report Delinquency Study in the context of police and victimization data.*European Journal of Criminology, 7*(2), 159-183. doi:10.1177/1477370809358018

Eres, R., Louis, W. R., & Molenberghs, P. (2018). Common and distinct neural networks involvedin fMRI studies investigating morality: an ALE meta-analysis. *Soc Neurosci, 13*(4), 384- 398. doi:10.1080/17470919.2017.1357657

Erskine, H. E., Norman, R. E., Ferrari, A. J., Chan, G. C., Copeland, W. E., Whiteford, H. A., & Scott, J. G. (2016). Long-term outcomes of attention-deficit/hyperactivity disorder and conduct disorder: a systematic review and meta-analysis. *Journal of the American Academy of Child & Adolescent Psychiatry, 55*(10), 841-850.

Essau, C. A., Sasagawa, S., & Frick, P. J. (2006). Callous-unemotional traits in a community sample of adolescents. *Assessment*, *13*(4), 454–469. https://doi.org/10.1177/1073191106287354

Etkin, A., Büchel, C., & Gross, J. J. (2015). The neural bases of emotion regulation. *Nature reviews neuroscience, 16*(11), 693.

Etkin, A., & Wager, T. D. (2007). Functional neuroimaging of anxiety: a meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. *American Journal of Psychiatry, 164*(10), 1476-1488.

Euler, F., Steinlin, C., & Stadler, C. (2017). Distinct profiles of reactive and proactive aggression in adolescents: associations with cognitive and affective empathy. *Child Adolesc Psychiatry Ment Health, 11*, 1. doi:10.1186/s13034-016-0141-4

Ewbank, M. P., Passamonti, L., Hagan, C. C., Goodyer, I. M., Calder, A. J., & Fairchild, G. (2018). Psychopathic traits influence amygdala–anterior cingulate cortex connectivity during facial emotion processing. *Social cognitive and affective neuroscience, 13*(5), 525-534.

Eysenck. (1997). Personality and the biosocial model of anti-social and criminal behaviour. In *Biosocial bases of violence.* (pp. 21-37). New York, NY, US: Plenum Press.

Eysenck, & Eysenck. (1970). CRIME AND PERSONALITY: AN EMPIRICAL STUDY OF THE THREE-FACTOR THEORY. *The British Journal of Criminology, 10*(3), 225-239. Retrieved from http://www.jstor.org/stable/23635921

Ezpeleta, L., Granero, R., de la Osa, N., Trepat, E., & Domènech, J. M. (2016). Trajectories of Oppositional Defiant Disorder Irritability Symptoms in Preschool Children. *J Abnorm Child Psychol, 44*(1), 115-128. doi:10.1007/s10802-015-9972-3

Fadok, J. P., Krabbe, S., Markovic, M., Courtin, J., Xu, C., Massi, L., . . . Lüthi, A. (2017). A competitive inhibitory circuit for selection of active and passive fear responses. *Nature, 542*(7639), 96-100. doi:10.1038/nature21047

Fairchild, Baker, & Eaton. (2018). Hypothalamic-Pituitary-Adrenal Axis Function in Children and Adults with Severe Antisocial Behavior and the Impact of Early Adversity. *Curr Psychiatry Rep, 20*(10), 84. doi:10.1007/s11920-018-0952-5

Fairchild, Hagan, Passamonti, Walsh, Goodyer, & Calder. (2014). Atypical neural responses during face processing in female adolescents with conduct disorder. *Journal of the American Academy of Child & Adolescent Psychiatry, 53*(6), 677-687. e675.

Fairchild, van Goozen, Calder, & Goodyer. (2013). Research review: evaluating and reformulating the developmental taxonomic theory of antisocial behaviour. *J Child Psychol Psychiatry, 54*(9), 924-940. doi:10.1111/jcpp.12102

Fairchild, G., Baker, E., & Eaton, S. (2018). Hypothalamic-pituitary-adrenal axis function in children and adults with severe antisocial behavior and the impact of early adversity. *Current psychiatry reports, 20*(10), 84.

Fairchild, G., Hawes, D. J., Frick, P. J., Copeland, W. E., Odgers, C. L., Franke, B., . . . De Brito, S. A. (2019). Conduct disorder. *Nat Rev Dis Primers, 5*(1), 43. doi:10.1038/s41572-019- 0095-y

Falkenbach, D., Poythress, N., & Creevy, C. (2008). The exploration of subclinical psychopathic subtypes and the relationship with types of aggression. *Personality and Individual Differences, 44*(4), 821-832.

Fallon, N., Roberts, C., & Stancak, A. (2020). Shared and distinct functional networks for empathy and pain processing: a systematic review and meta-analysis of fMRI studies. *Soc Cogn Affect Neurosci, 15*(7), 709-723. doi:10.1093/scan/nsaa090

Fan, Duncan, de Greck, & Northoff. (2011). Is there a core neural network in empathy? An fMRI based quantitative meta-analysis. *Neurosci Biobehav Rev, 35*(3), 903-911. doi:10.1016/j.neubiorev.2010.10.009

Fan, Y., Duncan, N. W., de Greck, M., & Northoff, G. (2011). Is there a core neural network in empathy? An fMRI based quantitative meta-analysis. *Neuroscience & Biobehavioral Reviews, 35*(3), 903-911.

Fanti, Demetriou, & Kimonis. (2013). Variants of callous-unemotional conduct problems in a community sample of adolescents. *Journal of youth and adolescence, 42*(7), 964-979.

Fanti, K. A. (2018). Understanding heterogeneity in conduct disorder: A review of psychophysiological studies. *Neuroscience & Biobehavioral Reviews, 91*, 4-20.

Fanti, K. A., Demetriou, C. A., & Kimonis, E. R. (2013). Variants of callous-unemotional conduct problems in a community sample of adolescents. *J Youth Adolesc, 42*(7), 964-979. doi:10.1007/s10964-013-9958-9

Fanti, K. A., Eisenbarth, H., Goble, P., Demetriou, C., Kyranides, M. N., Goodwin, D., . . . Cortese, S. (2019). Psychophysiological activity and reactivity in children and adolescents with conduct problems: A systematic review and meta-analysis. *Neurosci Biobehav Rev, 100*, 98-107. doi:10.1016/j.neubiorev.2019.02.016

Fanti, K. A., & Henrich, C. C. (2010). Trajectories of pure and co-occurring internalizing and externalizing problems from age 2 to age 12: findings from the National Institute of Child Health

and Human Development Study of Early Child Care. *Developmental psychology, 46*(5), 1159.

Faraone, S. V., Biederman, J., & Mick, E. (2006). The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. *Psychological Medicine,36*(2), 159-165.

Farrer, T. J., Frost, R. B., & Hedges, D. W. (2013). Prevalence of traumatic brain injury in juvenile offenders: a meta-analysis. *Child Neuropsychol, 19*(3), 225-234. doi:10.1080/09297049.2011.647901

Farrington, D. (1993). Motivations for conduct disorder and delinquency. Development and Psychopathology, 5(1-2), 225-241. doi:10.1017/S0954579400004363.

Fasano, A., Laganiere, S. E., Lam, S., & Fox, M. D. (2017). Lesions causing freezing of gait localize to a cerebellar functional network. *Ann Neurol, 81*(1), 129-141. doi:10.1002/ana.24845

Fazel, & Danesh. (2002). Serious mental disorder in 23000 prisoners: a systematic review of 62 surveys. *Lancet, 359*(9306), 545-550. doi:10.1016/s0140-6736(02)07740-1

Fazel, S., & Danesh, J. (2002). Serious mental disorder in 23 000 prisoners: a systematic review of 62 surveys. *The lancet, 359*(9306), 545-550.

Fazel, S., & Seewald, K. (2012). Severe mental illness in 33,588 prisoners worldwide: systematic review and meta-regression analysis. *Br J Psychiatry, 200*(5), 364-373. doi:10.1192/bjp.bp.111.096370

Fede, S., & Kiehl, K. (2020). Meta-analysis of the moral brain: patterns of neural engagement assessed using multilevel kernel density analysis. *Brain Imaging and behavior, 14*. doi:10.1007/s11682-019-00035-5

Feng, X., Shaw, D. S., & Silk, J. S. (2008). Developmental trajectories of anxiety symptoms among boys across early and middle childhood. *J Abnorm Psychol, 117*(1), 32-47. doi:10.1037/0021-843x.117.1.32

Ferguson, Lim, Cooke, Darby, Wu, Rost, . . . Fox. (2019). A human memory circuit derived from brain lesions causing amnesia. *Nat Commun, 10*(1), 3497. doi:10.1038/s41467-019-11353-z

Ferguson, C. J. (2010). Genetic contributions to antisocial personality and behavior: a meta-analytic review from an evolutionary perspective. *J Soc Psychol, 150*(2), 160-180. doi:10.1080/00224540903366503

Fergusson, D. M., Swain-Campbell, N. R., & Horwood, L. J. (2002). Deviant peer affiliations, crime and substance use: a fixed effects regression analysis. Journal of abnormal child psychology, 30(4), 419–430. https://doi.org/10.1023/a:1015774125952

Ficks, C. A., & Waldman, I. D. (2014). Candidate genes for aggression and antisocial behavior: a meta-analysis of association studies of the 5HTTLPR and MAOA-uVNTR. *Behav Genet, 44*(5), 427-444. doi:10.1007/s10519-014-9661-y

Finger, Marsh, Blair, Reid, Sims, Ng, . . . Blair. (2011). Disrupted reinforcement signaling in the orbitofrontal cortex and caudate in youths with conduct disorder or oppositional defiant disorder and a high level of psychopathic traits. *American Journal of Psychiatry, 168*(2), 152-162.

Finger, E. C., Marsh, A. A., Blair, K. S., Reid, M. E., Sims, C., Ng, P., . . . Blair, R. J. (2011). Disrupted reinforcement signaling in the orbitofrontal cortex and caudate in youths with conduct disorder or oppositional defiant disorder and a high level of psychopathic traits. *Am J Psychiatry, 168*(2), 152-162. doi:10.1176/appi.ajp.2010.10010129

Finger, E. C., Marsh, A. A., Mitchell, D. G., Reid, M. E., Sims, C., Budhani, S., . . . Leibenluft, E.(2008). Abnormal ventromedial prefrontal cortex function in children with psychopathic traits during reversal learning. *Archives of general psychiatry, 65*(5), 586-594.

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. (1995). The structured clinical interviewfor DSM-III-R personality disorders (SCID-II). Part I: Description. *Journal of personalitydisorders, 9*(2), 83-91.

Fischer, R., & Milfont, T. L. (2010). Standardization in psychological research. *International*

Journal of Psychological Research, 3(1), 88-96.

Fisher, P. M., & Hariri, A. R. (2013). Identifying serotonergic mechanisms underlying the corticolimbic response to threat in humans. *Philos Trans R Soc Lond B Biol Sci, 368*(1615), 20120192. doi:10.1098/rstb.2012.0192

Fite, P. J., Raine, A., Stouthamer-Loeber, M., Loeber, R., & Pardini, D. A. (2009). REACTIVE AND PROACTIVE AGGRESSION IN ADOLESCENT MALES: Examining Differential Outcomes 10 Years Later in Early Adulthood. *Crim Justice Behav, 37*(2), 141-157.doi:10.1177/0093854809353051

Fitzgerald, P. B., Laird, A. R., Maller, J., & Daskalakis, Z. J. (2008). A meta-analytic study of changes in brain activation in depression. *Human brain mapping, 29*(6), 683-695.

Flannery, J. S., Riedel, M. C., Bottenhorn, K. L., Poudel, R., Salo, T., Hill-Bowen, L. D., . . . Sutherland, M. T. (2020). Meta-analytic clustering dissociates brain activity and behavior profiles across reward processing paradigms. *Cognitive, Affective, & BehavioralNeuroscience, 20*(2), 215-235.

Fontaine, Hanscombe, Berg, McCrory, & Viding. (2018). Trajectories of Callous-Unemotional Traits in Childhood Predict Different Forms of Peer Victimization in Adolescence. *J Clin Child Adolesc Psychol, 47*(3), 458-466. doi:10.1080/15374416.2015.1105139

Fontaine, Lacourse, Vitaro, & Tremblay. (2014). Links between trajectories of self-reported violent and nonviolent offending and official offending during adolescence and adulthood. *Crim Behav Ment Health, 24*(4), 277-290. doi:10.1002/cbm.1935

Fontaine, McCrory, Boivin, Moffitt, & Viding. (2011). Predictors and outcomes of joint trajectories of callous–unemotional traits and conduct problems in childhood. *Journal of abnormal psychology, 120*(3), 730.

Fontaine, Rijsdijk, McCrory, & Viding. (2010). Etiology of different developmental trajectories of callous-unemotional traits. *J Am Acad Child Adolesc Psychiatry, 49*(7), 656-664. doi:10.1016/j.jaac.2010.03.014

Fontaine, N., Carbonneau, R., Barker, E. D., Vitaro, F., Hébert, M., Côté, S. M., . . . Tremblay, R.E. (2008). Girls' hyperactivity and physical aggression during childhood and adjustment problems in early adulthood: a 15-year longitudinal study. *Archives of general psychiatry,65*(3), 320-328.

Fontaine, N. M., McCrory, E. J., Boivin, M., Moffitt, T. E., & Viding, E. (2011). Predictors and outcomes of joint trajectories of callous–unemotional traits and conduct problems in childhood. *Journal of abnormal psychology, 120*(3), 730.

Fox. (2018). Mapping Symptoms to Brain Networks with the Human Connectome. *N Engl J Med, 379*(23), 2237-2245. doi:10.1056/NEJMra1706158

Fox, C., Snow, P. C., & Holland, K. (2014). The relationship between sensory processingdifficulties and behaviour in children aged 5–9 who are at risk of developing conduct disorder. *Emotional and behavioural difficulties, 19*(1), 71-88.

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., & Raichle, M. E. (2005).The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences, 102*(27), 9673-9678.

Frances, A. (2013). The past, present and future of psychiatric diagnosis. *World Psychiatry, 12*(2), 111-112. doi:10.1002/wps.20027

Frick, Lahey, Loeber, Stouthamer-Loeber, Green, Hart, & Christ. (1991). Oppositional defiant disorder and conduct disorder in boys: Patterns of behavioral covariation. *Journal of Clinical Child Psychology, 20*(2), 202-208. doi:10.1207/s15374424jccp2002_12

Frick, Lahey, Loeber, Tannenbaum, Van Horn, Christ, . . . Hanson. (1993). Oppositional defiant disorder and conduct disorder: A meta-analytic review of factor analyses and cross-validation in a clinic sample. *Clinical psychology review, 13*(4), 319-340. doi:https://doi.org/10.1016/0272-7358(93)90016-F

Frick, Ray, Thornton, & Kahn. (2014a). Annual research review: A developmental psychopathology approach to understanding callous-unemotional traits in children and

adolescents with serious conduct problems. *Journal of Child Psychology and Psychiatry, 55*(6), 532-548.

Frick, Ray, Thornton, & Kahn. (2014b). Can callous-unemotional traits enhance the understanding, diagnosis, and treatment of serious conduct problems in children and adolescents? A comprehensive review. *Psychol Bull, 140*(1), 1-57. doi:10.1037/a0033076

Frick, & White. (2008). Research review: The importance of callous-unemotional traits for developmental models of aggressive and antisocial behavior. *Journal of Child Psychologyand Psychiatry, 49*(4), 359-375.

Frick, P. J., Ray, J. V., Thornton, L. C., & Kahn, R. E. (2014). Annual research review: A developmental psychopathology approach to understanding callous-unemotional traits in children and adolescents with serious conduct problems. *Journal of Child Psychology and Psychiatry, 55*(6), 532-548.

Frick, P. J., & White, S. F. (2008). Research review: The importance of callous-unemotional traits for developmental models of aggressive and antisocial behavior. *Journal of Child Psychology and Psychiatry, 49*(4), 359-375.

Friston, K. J. (2011). Functional and effective connectivity: a review. *Brain Connect, 1*(1), 13-36. doi:10.1089/brain.2011.0008

Frith, C., & Frith, U. (2005). Theory of mind. *Curr Biol, 15*(17), R644-646. doi:10.1016/j.cub.2005.08.041

Fullana, M. A., Albajes-Eizagirre, A., Soriano-Mas, C., Vervliet, B., Cardoner, N., Benet, O., . . . Harrison, B. J. (2018). Fear extinction in the human brain: A meta-analysis of fMRI studiesin healthy participants. *Neurosci Biobehav Rev, 88*, 16-25. doi:10.1016/j.neubiorev.2018.03.002

Fullana, M. A., Albajes-Eizagirre, A., Soriano-Mas, C., Vervliet, B., Cardoner, N., Benet, O., . . .Harrison, B. J. (2019). Amygdala where art thou? *Neurosci Biobehav Rev, 102*, 430-431. doi:10.1016/j.neubiorev.2018.06.003

Fullana, M. A., Harrison, B. J., Soriano-Mas, C., Vervliet, B., Cardoner, N., Àvila-Parcet, A., & Radua, J. (2016). Neural signatures of human fear conditioning: an updated and extended meta-analysis of fMRI studies. *Mol Psychiatry, 21*(4), 500-508. doi:10.1038/mp.2015.88

Fusar-Poli, P., Placentino, A., Carletti, F., Landi, P., Allen, P., Surguladze, S., Barale, F. (2009). Functional atlas of emotional faces processing: a voxel-based meta-analysis of 105 functional magnetic resonance imaging studies. *Journal of psychiatry & neuroscience*.

Galéra, C., Côté, S. M., Bouvard, M. P., Pingault, J. B., Melchior, M., Michel, G., Tremblay, R. E. (2011). Early risk factors for hyperactivity-impulsivity and inattention trajectories from age 17 months to 8 years. *Arch Gen Psychiatry, 68*(12), 1267-1275. doi:10.1001/archgenpsychiatry.2011.138

Galera, C., Orri, M., Vergunst, F., Melchior, M., Van der Waerden, J., Bouvard, M. P., Côté, S. M. (2020). Developmental profiles of childhood attention-deficit/hyperactivity disorder and irritability: association with adolescent mental health, functional impairment, and suicidal outcomes. *Journal of Child Psychology and Psychiatry*.

Gallup, G. G. (1965). Aggression in rats as a function of frustrative nonreward in a straight alley. *Psychonomic Science, 3*(1), 99-100.

Gao, Y., Rogers, J. C., Pauli, R., Clanton, R., Baker, R., Birch, P., . . . De Brito, S. A. (2019). Neural correlates of theory of mind in typically-developing youth: Influence of sex, age and callous-unemotional traits. *Scientific reports, 9*(1), 16216. doi:10.1038/s41598-019-52261-y

Gard, A. M., Dotterer, H. L., & Hyde, L. W. (2019). Genetic influences on antisocial behavior: recent advances and future directions. *Curr Opin Psychol, 27*, 46-55. doi:10.1016/j.copsyc.2018.07.013

Garofalo, C., & Velotti, P. (2017). Negative emotionality and aggression in violent offenders: The moderating role of emotion dysregulation. *Journal of Criminal Justice, 51*, 9-16. doi:https://doi.org/10.1016/j.jcrimjus.2017.05.015

Geerlings, Y., Asscher, J. J., Stams, G.-J. J. M., & Assink, M. (2020). The association between psychopathy and delinquency in juveniles: A three-level meta-analysis. *Aggression and Violent Behavior, 50*, 101342. doi:https://doi.org/10.1016/j.avb.2019.101342

Geurts, D. E., von Borries, K., Volman, I., Bulten, B. H., Cools, R., & Verkes, R. J. (2016). Neural connectivity during reward expectation dissociates psychopathic criminals from non-criminal individuals with high impulsive/antisocial psychopathic traits. *Soc Cogn Affect Neurosci, 11*(8), 1326-1334. doi:10.1093/scan/nsw040

Ghanizadeh, A. (2011). Sensory processing problems in children with ADHD, a systematic review. *Psychiatry Investigation, 8*(2), 89.

Ghanizadeh, A. (2012). Psychometric analysis of the new ADHD DSM-V derived symptoms. *BMC psychiatry, 12*(1), 1-6.

Giannotta, & Rydell. (2016a). The Prospective Links Between Hyperactive/Impulsive, Inattentive, and Oppositional-Defiant Behaviors in Childhood and Antisocial Behavior in Adolescence: The Moderating Influence of Gender and the Parent-Child Relationship Quality. *Child Psychiatry Hum Dev, 47*(6), 857-870. doi:10.1007/s10578-015-0617-0

Giannotta, & Rydell. (2016b). The Prospective Links Between Hyperactive/Impulsive, Inattentive, and Oppositional-Defiant Behaviors in Childhood and Antisocial Behavior in Adolescence: The Moderating Influence of Gender and the Parent–Child Relationship Quality. *Child Psychiatry & Human Development, 47*(6), 857-870. doi:10.1007/s10578-015-0617-0

Gibbon, S., Khalifa, N. R., Cheung, N. H., Völlm, B. A., & McCarthy, L. (2020). Psychological interventions for antisocial personality disorder. *Cochrane Database Syst Rev, 9*(9), Cd007668. doi:10.1002/14651858.CD007668.pub3

Gillespie, S. M., Kongerslev, M. T., Sharp, C., Bo, S., & Abu-Akel, A. M. (2018). Does Affective Theory of Mind Contribute to Proactive Aggression in Boys with Conduct Problems and Psychopathic Tendencies? *Child Psychiatry Hum Dev, 49*(6), 906-916. doi:10.1007/s10578-018-0806-8

Gillespie, S. M., Rotshtein, P., Wells, L. J., Beech, A. R., & Mitchell, I. J. (2015). Psychopathic traits are associated with reduced attention to the eyes of emotional faces among adult male non-offenders. *Front Hum Neurosci, 9*, 552. doi:10.3389/fnhum.2015.00552

Givens, E. M., & Reid, J. A. (2019). Developmental Trajectories of Physical Aggression and Nonaggressive Rule-Breaking During Late Childhood and Early Adolescence. *Criminal Justice and Behavior, 46*(3), 395-414. doi:10.1177/0093854818803652

Glenn, A. L., & Raine, A. (2008). The neurobiology of psychopathy. *Psychiatric Clinics of North America, 31*(3), 463-475.

Goldstein, R. B., Chou, S. P., Saha, T. D., Smith, S. M., Jung, J., Zhang, H., . . . Grant, B. F. (2017).The Epidemiology of Antisocial Behavioral Syndromes in Adulthood: Results From the National Epidemiologic Survey on Alcohol and Related Conditions-III. *J Clin Psychiatry, 78*(1), 90-98. doi:10.4088/JCP.15m10358

Gong, Fan, Liu, Yang, Zhang, & Zhou. (2017). Revisiting the impact of OXTR rs53576 on empathy: A population-based study and a meta-analysis. *Psychoneuroendocrinology, 80*, 131-136. doi:10.1016/j.psyneuen.2017.03.005

Gong, Q., Scarpazza, C., Dai, J., He, M., Xu, X., Shi, Y., . . . Ai, Y. (2019). A transdiagnostic neuroanatomical signature of psychiatric illness. *Neuropsychopharmacology, 44*(5), 869- 875.

Goodkind, M., Eickhoff, S. B., Oathes, D. J., Jiang, Y., Chang, A., Jones-Hagata, L. B., . . . Korgaonkar, M. S. (2015). Identification of a common neurobiological substrate for mental illness. *JAMA psychiatry, 72*(4), 305-315.

Goodman, R. (2001). Psychometric properties of the strengths and difficulties questionnaire. *J Am Acad Child Adolesc Psychiatry, 40*(11), 1337-1345. doi:10.1097/00004583-200111000- 00015

Gordon, Spielman, Hahn-Ketter, & Sy. (2017). The Relationship Between Traumatic Brain Injury and Criminality in Juvenile Offenders. *J Head Trauma Rehabil, 32*(6), 393-403. doi:10.1097/htr.0000000000000274

Gordon, E. M., Laumann, T. O., Adeyemo, B., Huckins, J. F., Kelley, W. M., & Petersen, S. E. (2016). Generation and evaluation of a cortical area parcellation from resting-state correlations. *Cerebral Cortex, 26*(1), 288-303.

Gorin, H. M., Kosson, D. S., Miller, S. A., Fontaine, N. M., Vitaro, F., Séguin, J. R., . . . Tremblay, R. E. (2019). Psychopathic Traits in Middle Childhood: Evidence of a Hierarchical Three- Factor Structure. *Journal of Psychopathology and Behavioral Assessment, 41*(3), 341-352.

Gottfredson, M. R., & Hirschi, T. (1990). *A general theory of crime*: Stanford University Press.

Goulter, N., Kimonis, E. R., Hawes, S. W., Stepp, S., & Hipwell, A. E. (2017). Identifying stable variants of callous-unemotional traits: A longitudinal study of at-risk girls. *Dev Psychol, 53*(12), 2364-2376. doi:10.1037/dev0000394

Gourley, L., Wind, C., Henninger, E. M., & Chinitz, S. (2013). Sensory processing difficulties, behavioral problems, and parental stress in a clinical population of young children. *Journalof child and family studies, 22*(7), 912-921.

Grace, S. A., Rossell, S. L., Heinrichs, M., Kordsachia, C., & Labuschagne, I. (2018). Oxytocin and brain activity in humans: A systematic review and coordinate-based meta-analysis of functional MRI studies. *Psychoneuroendocrinology, 96*, 6-24. doi:10.1016/j.psyneuen.2018.05.031

Grafman, J., Schwab, K., Warden, D., Pridgen, A., Brown, H. R., & Salazar, A. M. (1996). Frontallobe injuries, violence, and aggression: a report of the Vietnam Head Injury Study.*Neurology, 46*(5), 1231-1238. doi:10.1212/wnl.46.5.1231

Graham, Devinsky, & Labar. (2007). Quantifying deficits in the perception of fear and anger in morphed facial expressions after bilateral amygdala damage. *Neuropsychologia, 45*(1), 42-54. doi:10.1016/j.neuropsychologia.2006.04.021

Graham, J., Salimi-Khorshidi, G., Hagan, C., Walsh, N., Goodyer, I., Lennox, B., & Suckling, J. (2013). Meta-analytic evidence for neuroimaging models of depression: state or trait? *Journal of affective disorders, 151*(2), 423-431.

Gray, J. A. (1970). The psychophysiological basis of introversion-extraversion. *Behav Res Ther, 8*(3), 249-266. doi:10.1016/0005-7967(70)90069-0

Grayson, D. S., & Fair, D. A. (2017). Development of large-scale functional networks from birth to adulthood: A guide to the neuroimaging literature. NeuroImage, 160, 15–31.

Greenwald, R. M., Gwin, J. T., Chu, J. J., & Crisco, J. J. (2008). Head impact severity measures for evaluating mild traumatic brain injury risk exposure. *Neurosurgery, 62*(4), 789-798; discussion 798. doi:10.1227/01.neu.0000318162.67472.ad

Gregory, S., Blair, R. J., Simmons, A., Kumari, V., Hodgins, S., & Blackwood, N. (2015). Punishment and psychopathy: A case-control functional MRI investigation of reinforcement learning in violent antisocial personality disordered men. *The Lancet Psychiatry, 2*(2), 153-160.

Greicius, M. D., Krasnow, B., Reiss, A. L., & Menon, V. (2003). Functional connectivity in the resting brain: A network analysis of the default mode hypothesis. *Proceedings of the National Academy of Sciences, 100*(1), 253-258. doi:10.1073/pnas.0135058100

Gross, C. T., & Canteras, N. S. (2012). The many paths to fear. *Nat Rev Neurosci, 13*(9), 651-658. doi:10.1038/nrn3301

Grupe, D. W., Wielgosz, J., Davidson, R. J., & Nitschke, J. B. (2016). Neurobiological correlates of distinct PTSD symptom profiles during threat anticipation in combat veterans. *Psychological medicine, 46*(9), 1885.

Gu, X., Hof, P. R., Friston, K. J., & Fan, J. (2013). Anterior insular cortex and emotional awareness. *Journal of Comparative Neurology, 521*(15), 3371-3388.

Guay, J. P., Ruscio, J., Knight, R. A., & Hare, R. D. (2007). A taxometric analysis of the latent structure of psychopathy: evidence for dimensionality. *J Abnorm Psychol, 116*(4), 701-716. doi:10.1037/0021-843x.116.4.701

Guillory, S. A., & Bujarski, K. A. (2014). Exploring emotions using invasive methods: review of 60

years of human intracranial electrophysiology. *Soc Cogn Affect Neurosci, 9*(12), 1880- 1889. doi:10.1093/scan/nsu002

Gunn, J. (1998). Psychopathy: An elusive concept with moral overtones. In *Psychopathy: Antisocial, criminal, and violent behavior.* (pp. 32-39). New York, NY, US: The Guilford Press.

Guo, Y., Schmitz, T. W., Mur, M., Ferreira, C. S., & Anderson, M. C. (2018). A supramodal role of the basal ganglia in memory and motor inhibition: Meta-analytic evidence.*Neuropsychologia, 108*, 117-134.

Gürsel, D. A., Avram, M., Sorg, C., Brandl, F., & Koch, K. (2018). Frontoparietal areas link impairments of large-scale intrinsic brain networks with aberrant fronto-striatal interactionsin OCD: a meta-analysis of resting-state functional connectivity. *Neuroscience & Biobehavioral Reviews, 87*, 151-160.

Haber, S. N., & Knutson, B. (2010). The reward circuit: linking primate anatomy and human imaging. *Neuropsychopharmacology, 35*(1), 4-26.

Hagberg, A., Swart, P., & S Chult, D. (2008). *Exploring network structure, dynamics, and function using NetworkX*. Retrieved from

Hamilton, J. P., Etkin, A., Furman, D. J., Lemus, M. G., Johnson, R. F., & Gotlib, I. H. (2012). Functional neuroimaging of major depressive disorder: a meta-analysis and new integrationof baseline activation and neural response data. *American Journal of Psychiatry, 169*(7), 693-703.

Hamilton, R. K., Hiatt Racer, K., & Newman, J. P. (2015). Impaired integration in psychopathy: A unified theory of psychopathic dysfunction. *Psychological review, 122*(4), 770.

Hammerton, G., Heron, J., Mahedy, L., Maughan, B., Hickman, M., & Murray, J. (2018). Low resting heart rate, sensation seeking and the course of antisocial behaviour across adolescence and young adulthood. *Psychol Med, 48*(13), 2194-2201.doi:10.1017/s0033291717003683

Hampson, M., Olson, I. R., Leung, H. C., Skudlarski, P., & Gore, J. C. (2004). Changes in functional

connectivity of human MT/V5 with visual motion input. *Neuroreport, 15*(8), 1315-1319. doi:10.1097/01.wnr.0000129997.95055.15

Han, H. (2017). Neural correlates of moral sensitivity and moral judgment associated with brain circuitries of selfhood: A meta-analysis. *Journal of Moral Education, 46*(2), 97-113. doi:10.1080/03057240.2016.1262834

Hanley, J. A., & McNeil, B. J. (1982). The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology, 143*(1), 29-36. doi:10.1148/radiology.143.1.7063747

Hanson, R. K., & Morton-Bourgon, K. (2004). Predictors of sexual recidivism: An updated meta-analysis 2004-02. Public Safety and Emergency Preparedness Canada.

Hare, R. D. (1980). A research scale for the assessment of psychopathy in criminal populations. *Personality and Individual Differences, 1*(2), 111-119. doi:10.1016/0191-8869(80)90028-8

Hare, R. D. (2003a). The psychopathy checklist–Revised. *Toronto, ON, 2003*.Hare, R. D. (2003b). The psychopathy checklist–Revised. *Toronto, ON, 412*.

Hare, R. D. (2021). The PCL-R assessment of psychopathy. In *The Wiley international handbookon psychopathic disorders and the law: Diagnosis and treatment, Vol. 1, 2nd ed.* (pp. 63- 106). Hoboken, NJ, US: Wiley Blackwell.

Harenski, C. L., Thornton, D. M., Harenski, K. A., Decety, J., & Kiehl, K. A. (2012). Increased frontotemporal activation during pain observation in sexual sadism: preliminary findings. *Arch Gen Psychiatry, 69*(3), 283-292. doi:10.1001/archgenpsychiatry.2011.1566

Hariri, A. R., Mattay, V. S., Tessitore, A., Kolachana, B., Fera, F., Goldman, D., Weinberger,D. R. (2002). Serotonin transporter genetic variation and the response of the human amygdala. *Science, 297*(5580), 400-403. doi:10.1126/science.1071829

Harlow. (1869). *Recovery from the passage of an iron bar through the head*. Boston: Clapp.

Harrendorf, S., & Heiskanen, M. (2010). International statistics on crime and justice. S. Malby

(Ed.). Helsinki: European Institute for Crime Prevention and Control, affiliated with the United Nations (HEUNI).

Hart, H., Radua, J., Mataix-Cols, D., & Rubia, K. (2012). Meta-analysis of fMRI studies of timingin attention-deficit hyperactivity disorder (ADHD). *Neuroscience & Biobehavioral Reviews, 36*(10), 2248-2256.

Hart, H., Radua, J., Nakao, T., Mataix-Cols, D., & Rubia, K. (2013). Meta-analysis of functional magnetic resonance imaging studies of inhibition and attention in attention- deficit/hyperactivity disorder: exploring task-specific, stimulant medication, and age effects. *JAMA psychiatry, 70*(2), 185-198.

Hartley, C. A., & Phelps, E. A. (2010). Changing fear: the neurocircuitry of emotion regulation. *Neuropsychopharmacology, 35*(1), 136.

Hasratian, A. M., Meuret, A. E., Chmielewski, M., & Ritz, T. (2022). An Examination of the RDoC Negative Valence Systems Domain Constructs and the Self-Reports Unit of Analysis. *Behavior Therapy*. doi:https://doi.org/10.1016/j.beth.2022.04.009

Hawes, D. J. (2014). Disruptive behaviour disorders and DSM-5. *Asian journal of psychiatry, 11*, 102-105.

Hawes, D. J., Price, M. J., & Dadds, M. R. (2014). Callous-unemotional traits and the treatment of conduct problems in childhood and adolescence: a comprehensive review. *Clin Child FamPsychol Rev, 17*(3), 248-267. doi:10.1007/s10567-014-0167-1

Hay, Castle, & Davies. (2000). Toddlers' use of force against familiar peers: a precursor of serious aggression? *Child Dev, 71*(2), 457-467. doi:10.1111/1467-8624.00157

Hay, D., Tremblay, R., Hartup, W., & Archer, J. (2005). Developmental origins of aggression. He, J. L., Wodka, E., Tommerdahl, M., Edden, R. A., Mikkelsen, M., Mostofsky, S. H., & Puts, N.A. (2021). Disorder-specific alterations of tactile sensitivity in neurodevelopmental disorders. *Communications biology, 4*(1), 1-15.

Hein, T. C., & Monk, C. S. (2017). Research Review: Neural response to threat in children, adolescents, and adults after child maltreatment - a quantitative meta-analysis. *J Child Psychol Psychiatry, 58*(3), 222-230. doi:10.1111/jcpp.12651

Hendriks, A. M., Bartels, M., Colins, O. F., & Finkenauer, C. (2018). Childhood aggression: A synthesis of reviews and meta-analyses to reveal patterns and opportunities for preventionand intervention strategies. *Neurosci Biobehav Rev, 91*, 278-291. doi:10.1016/j.neubiorev.2018.03.021

Henry, J., Pingault, J. B., Boivin, M., Rijsdijk, F., & Viding, E. (2016). Genetic and environmental aetiology of the dimensions of Callous-Unemotional traits. *Psychol Med, 46*(2), 405-414. doi:10.1017/s0033291715001919

Herpers, P. C., Scheepers, F. E., Bons, D. M., Buitelaar, J. K., & Rommelse, N. N. (2014). The cognitive and neural correlates of psychopathy and especially callous–unemotional traits in youths: A systematic review of the evidence. *Development and psychopathology, 26*(1), 245-273.

Hester, R., Fassbender, C., & Garavan, H. (2004). Individual differences in error processing: a review and reanalysis of three event-related fMRI studies using the GO/NOGO task. *Cerebral Cortex, 14*(9), 986-994.

Hewitt, L. E., & Jenkins, R. L. (1946). *Fundamental patterns of maladjustment; the dynamics of their origin; a statistical analysis based upon five hundred case records of children examined at the Michigan Child Guidance Institute*. Oxford, England: State of Illinois.

Hiser, J., & Koenigs, M. (2018). The multifaceted role of the ventromedial prefrontal cortex in emotion, decision making, social cognition, and psychopathology. *Biological psychiatry, 83*(8), 638-647.

Hobson, C. W., Scott, S., & Rubia, K. (2011). Investigation of cool and hot executive function in ODD/CD independently of ADHD. *Journal of Child Psychology and Psychiatry, 52*(10), 1035-1043.

Hodgdon, E. A., Yu, Q., Kryza-Lacombe, M., Liuzzi, M. T., Aspe, G. I., Menacho, V. C., . . . Wiggins,

J. L. (2021). Irritability-related neural responses to frustrative nonreward in adolescents with trauma histories: A preliminary investigation. *Dev Psychobiol, 63*(6), e22167. doi:10.1002/dev.22167

Hodgins, De Brito, Chhabra, & Côté. (2010). Anxiety disorders among offenders with antisocial personality disorders: a distinct subtype? *Can J Psychiatry, 55*(12), 784-791. doi:10.1177/070674371005501206

Hodgins, S., & Guberman, G. I. (2022). Disentangling antecedents from consequences of traumatic brain injury: The need for prospective longitudinal studies. *Cellular, Molecular, Physiological, and Behavioral Aspects of Traumatic Brain Injury*, 553-561.

Hodsoll, S., Lavie, N., & Viding, E. (2014). Emotional attentional capture in children with conduct problems: the role of callous-unemotional traits. *Front Hum Neurosci, 8*, 570. doi:10.3389/fnhum.2014.00570

Homberg, J. R., & Lesch, K. P. (2011). Looking on the bright side of serotonin transporter gene variation. *Biol Psychiatry, 69*(6), 513-519. doi:10.1016/j.biopsych.2010.09.024

Hopfer, C., Salomonsen-Sautel, S., Mikulich-Gilbertson, S., Min, S. J., McQueen, M., Crowley, T., . . . Hewitt, J. (2013). Conduct disorder and initiation of substance use: a prospective longitudinal study. *J Am Acad Child Adolesc Psychiatry, 52*(5), 511-518.e514. doi:10.1016/j.jaac.2013.02.014

Horley, K., Williams, L. M., Gonsalvez, C., & Gordon, E. (2003). Social phobics do not see eye to eye:: A visual scanpath study of emotional expression processing. *Journal of anxiety disorders, 17*(1), 33-44.

Horley, K., Williams, L. M., Gonsalvez, C., & Gordon, E. (2004). Face to face: visual scanpath evidence for abnormal processing of facial expressions in social phobia. *Psychiatry Research, 127*(1-2), 43-53.

Hosking, J. G., Kastman, E. K., Dorfman, H. M., Samanez-Larkin, G. R., Baskin-Sommers, A., Kiehl, K. A., . . . Buckholtz, J. W. (2017). Disrupted prefrontal regulation of striatal subjective value

signals in psychopathy. *Neuron, 95*(1), 221-231. e224.

Hoza, B., Mrug, S., Gerdes, A. C., Hinshaw, S. P., Bukowski, W. M., Gold, J. A., . . . Arnold, L.E. (2005). What aspects of peer relationships are impaired in children with attention-deficit/hyperactivity disorder? *J Consult Clin Psychol, 73*(3), 411-423. doi:10.1037/0022-006x.73.3.411

Huang, J., Fan, L., Lin, K., & Wang, Y. (2020). Variants of children with psychopathic tendenciesin a community sample. *Child Psychiatry and Human Development, 51*(4), 563-571. doi:10.1007/s10578-019-00939-9

Hubbard, J. A., McAuliffe, M. D., Morrow, M. T., & Romano, L. J. (2010). Reactive and proactive aggression in childhood and adolescence: precursors, outcomes, processes, experiences, and measurement. *J Pers, 78*(1), 95-118. doi:10.1111/j.1467-6494.2009.00610.x

Hulvershorn, L. A., Cullen, K., & Anand, A. (2011). Toward dysfunctional connectivity: a reviewof neuroimaging findings in pediatric major depressive disorder. *Brain Imaging andbehavior, 5*(4), 307-328.

Hung, Gaillard, Yarmak, & Arsalidou. (2018). Dissociations of cognitive inhibition, response inhibition, and emotional interference: Voxelwise ALE meta-analyses of fMRI studies. *Hum Brain Mapp, 39*(10), 4065-4082. doi:10.1002/hbm.24232

Hung, Y., Gaillard, S. L., Yarmak, P., & Arsalidou, M. (2018). Dissociations of cognitiveinhibition, response inhibition, and emotional interference: Voxelwise ALE meta-analysesof fMRI studies. *Human brain mapping, 39*(10), 4065-4082.

Hwang, S., Nolan, Z. T., White, S. F., Williams, W. C., Sinclair, S., & Blair, R. (2016). Dual neurocircuitry dysfunctions in disruptive behavior disorders: emotional responding and response inhibition. *Psychological medicine, 46*(7), 1485-1496.

Hyde, Shaw, & Hariri. (2013). Understanding youth antisocial behavior using neuroscience through a developmental psychopathology lens: Review, integration, and directions for research.

Developmental Review, 33(3), 168-223.

Hyde, Waller, Trentacosta, Shaw, Neiderhiser, Ganiban, . . . Leve. (2016). Heritable and Nonheritable Pathways to Early Callous-Unemotional Behaviors. *Am J Psychiatry, 173*(9),903-910. doi:10.1176/appi.ajp.2016.15111381

Hyde, L. W., Byrd, A. L., Votruba-Drzal, E., Hariri, A. R., & Manuck, S. B. (2014). Amygdala reactivity and negative emotionality: Divergent correlates of antisocial personality and psychopathy traits in a community sample. *Journal of abnormal psychology, 123*(1), 214.

Hyde, L. W., Shaw, D. S., & Hariri, A. R. (2013). Understanding youth antisocial behavior using neuroscience through a developmental psychopathology lens: Review, integration, and directions for research. *Developmental Review, 33*(3), 168-223.

Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D. S., Quinn, K., . . . Wang, P. (2010). Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. *Am J Psychiatry, 167*(7), 748-751. doi:10.1176/appi.ajp.2010.09091379

Isen, J., Tuvblad, C., Younan, D., Ericson, M., Raine, A., & Baker, L. A. (2022). Developmental Trajectories of Delinquent and Aggressive Behavior: Evidence for Differential Heritability. *Child Psychiatry Hum Dev, 53*(2), 199-211. doi:10.1007/s10578-020-01119-w

Izquierdo, A., Suda, R. K., & Murray, E. A. (2005). Comparison of the effects of bilateral orbital prefrontal cortex lesions and amygdala lesions on emotional responses in rhesus monkeys. *Journal of Neuroscience, 25*(37), 8534-8542.

Janiri, D., Moser, D. A., Doucet, G. E., Luber, M. J., Rasgon, A., Lee, W. H., . . . Frangou, S. (2020). Shared neural phenotypes for mood and anxiety disorders: a meta-analysis of 226 task-related functional imaging studies. *JAMA psychiatry, 77*(2), 172-179.

Janson, H., & Kjelsberg, E. (2006). Factor structure and individual patterns of DSM-IV conduct disorder criteria in adolescent psychiatric inpatients. *Nordic journal of psychiatry, 60*(2), 168-175.

Jauniaux, Khatibi, Rainville, & Jackson. (2019). A meta-analysis of neuroimaging studies on pain empathy: investigating the role of visual information and observers' perspective. *Soc CognAffect Neurosci, 14*(8), 789-813. doi:10.1093/scan/nsz055

Jauniaux, J., Khatibi, A., Rainville, P., & Jackson, P. L. (2019). A meta-analysis of neuroimaging studies on pain empathy: investigating the role of emotional information and observer's perspective.

Jetté, M., & Des Groseilliers, L. (2000). Longitudinal study of child development in Québec (ELDEQ 1998-2000). Survey Description and Methodology, 1. In.

Johanson, M., Vaurio, O., Tiihonen, J., & Lähteenvuo, M. (2019). A Systematic Literature Reviewof Neuroimaging of Psychopathic Traits. *Front Psychiatry, 10*, 1027. doi:10.3389/fpsyt.2019.01027

Jones. (2012). A critique of the DSM-5 field trials. *J Nerv Ment Dis, 200*(6), 517-519. doi:10.1097/NMD.0b013e318257c699

Jones, Barrera, Brothers, Ring, & Wahlestedt. (2017). Oxytocin and social functioning. *Dialogues Clin Neurosci, 19*(2), 193-201. doi:10.31887/DCNS.2017.19.2/cjones

Jones, Laurens, Herba, Barker, & Viding. (2009). Amygdala hypoactivity to fearful faces in boys with conduct problems and callous-unemotional traits. *American Journal of Psychiatry, 166*(1), 95-102.

Jones, S. E., Miller, J. D., & Lynam, D. R. (2011). Personality, antisocial behavior, and aggression:A meta-analytic review. *Journal of Criminal Justice, 39*(4), 329-337. doi:10.1016/j.jcrimjus.2011.03.004

Joutsa, J., Corp, D. T., & Fox, M. D. (2022). Lesion network mapping for symptom localization: recent developments and future directions. *Curr Opin Neurol, 35*(4), 453-459. doi:10.1097/wco.0000000000001085

Joutsa, J., Horn, A., Hsu, J., & Fox, M. D. (2018). Localizing parkinsonism based on focal brain

lesions. *Brain, 141*(8), 2445-2456. doi:10.1093/brain/awy161

Joutsa, J., Moussawi, K., Siddiqi, S. H., Abdolahi, A., Drew, W., Cohen, A. L., . . . Fox, M. D. (2022). Brain lesions disrupting addiction map to a common human brain circuit. *Nat Med,28*(6), 1249-1255. doi:10.1038/s41591-022-01834-y

Joutsa, J., Shih, L. C., Horn, A., Reich, M. M., Wu, O., Rost, N. S., & Fox, M. D. (2018). Identifying therapeutic targets from spontaneous beneficial brain lesions. *Ann Neurol, 84*(1), 153-157. doi:10.1002/ana.25285

Jung, T., & Wickrama, K. A. (2008). An introduction to latent class growth analysis and growth mixture modeling. *Social and personality psychology compass, 2*(1), 302-317.

Kaczkurkin, A. N., Moore, T. M., Calkins, M. E., Ciric, R., Detre, J. A., Elliott, M. A., . . . Rosen, A. (2018). Common and dissociable regional cerebral blood flow differences associate with dimensions of psychopathology across categorical diagnoses. *Molecular psychiatry, 23*(10), 1981-1989.

Kahn, R. E., Frick, P. J., Youngstrom, E. A., Kogos Youngstrom, J., Feeny, N. C., & Findling, R. L. (2013). Distinguishing primary and secondary variants of callous-unemotional traits among adolescents in a clinic-referred sample. *Psychol Assess, 25*(3), 966-978.doi:10.1037/a0032880

Kaiser, R. H., Andrews-Hanna, J. R., Wager, T. D., & Pizzagalli, D. A. (2015). Large-scale network dysfunction in major depressive disorder: a meta-analysis of resting-state functional connectivity. *JAMA psychiatry, 72*(6), 603-611.

Kaller, S., Rullmann, M., Patt, M., Becker, G. A., Luthardt, J., Girbardt, J., . . . Sabri, O. (2017). Test-retest measurements of dopamine D(1)-type receptors using simultaneous PET/MRI imaging. *Eur J Nucl Med Mol Imaging, 44*(6), 1025-1032. doi:10.1007/s00259-017-3645-0

Kärgel, C., Massau, C., Weiß, S., Walter, M., Kruger, T. H., & Schiffer, B. (2015). Diminished functional connectivity on the road to child sexual abuse in pedophilia. *The journal of sexual medicine, 12*(3), 783-795.

Karpman, B. (1941). On the need of separating psychopathy into two distinct clinical types: the symptomatic and the idiopathic. *Journal of Criminal Psychopathology, 3*, 112-137.

Karpman, B. (1948). Conscience in the psychopath; another version. *Am J Orthopsychiatry, 18*(3), 455-491. doi:10.1111/j.1939-0025.1948.tb05109.x

Katsiyannis, A., Whitford, D. K., Zhang, D., & Gage, N. A. (2018). Adult recidivism in United States: A meta-analysis 1994–2015. Journal of Child and Family Studies, 27(3), 686-696.

Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., . . . Ryan, N. (1997). Schedulefor Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. *J Am Acad Child Adolesc Psychiatry, 36*(7), 980-988. doi:10.1097/00004583-199707000-00021

Kavish, N., Vaughn, M. G., Cho, E., Barth, A., Boutwell, B., Vaughn, S., . . . Martinez, L. (2017). Physiological Arousal and Juvenile Psychopathy: Is Low Resting Heart Rate Associated with Affective Dimensions? *Psychiatr Q, 88*(1), 103-114. doi:10.1007/s11126-016-9437-z

Kebets, V., Holmes, A. J., Orban, C., Tang, S., Li, J., Sun, N., Kong, R., Poldrack, R. A., & Yeo, B. T. T. (2019). Somatosensory-Motor Dysconnectivity Spans Multiple Transdiagnostic Dimensions of Psychopathology. Biological psychiatry, 86(10), 779–791. https://doi.org/10.1016/j.biopsych.2019.06.013

Keiley, M. K., Lofthouse, N., Bates, J. E., Dodge, K. A., & Pettit, G. S. (2003). Differential risks of covarying and pure components in mother and teacher reports of externalizing and internalizing behavior across ages 5 to 14. *J Abnorm Child Psychol, 31*(3), 267-283. doi:10.1023/a:1023277413027

Keltikangas-Järvinen, L., Puttonen, S., Kivimäki, M., Elovainio, M., Pulkki-Råback, L., Koivu, M., . . . Lehtimäki, T. (2008). Serotonin receptor genes 5HT1A and 5HT2A modify the relation between childhood temperament and adulthood hostility. *Genes Brain Behav, 7*(1), 46-52. doi:10.1111/j.1601-183X.2007.00324.x

Kennis, M., Rademaker, A. R., & Geuze, E. (2013). Neural correlates of personality: an integrative review. *Neuroscience & Biobehavioral Reviews, 37*(1), 73-95.

Kennis, M., Rademaker, A. R., & Geuze, E. (2013). Neural correlates of personality: an integrative review. *Neurosci Biobehav Rev, 37*(1), 73-95. doi:10.1016/j.neubiorev.2012.10.012

Kerr, Z. Y., Evenson, K. R., Rosamond, W. D., Mihalik, J. P., Guskiewicz, K. M., & Marshall, S.W. (2014). Association between concussion and mental health in former collegiate athletes. *Injury epidemiology, 1*(1), 28-28. doi:10.1186/s40621-014-0028-x

Keyes, K. M., Eaton, N. R., Krueger, R. F., McLaughlin, K. A., Wall, M. M., Grant, B. F., & Hasin, D. S. (2012). Childhood maltreatment and the structure of common psychiatric disorders. *The British Journal of Psychiatry, 200*(2), 107-115.

Khalifa, N. R., Gibbon, S., Völlm, B. A., Cheung, N. H., & McCarthy, L. (2020). Pharmacological interventions for antisocial personality disorder. *Cochrane Database Syst Rev, 9*(9), Cd007667. doi:10.1002/14651858.CD007667.pub3

Kiehl, K. A., Anderson, N. E., Aharoni, E., Maurer, J. M., Harenski, K. A., Rao, V., . . . Steele, V. R. (2018). Age of gray matters: Neuroprediction of recidivism. *NeuroImage: Clinical, 19*,813-823. doi:https://doi.org/10.1016/j.nicl.2018.05.036

Kim, Cilles, Johnson, & Gold. (2012). Domain general and domain preferential brain regions associated with different types of task switching: a meta-analysis. *Hum Brain Mapp, 33*(1),130-142. doi:10.1002/hbm.21199

Kim, Hsu, Talmasov, Joutsa, Soussand, Wu, . . . Fox. (2021). Lesions causing hallucinations localize to one common brain network. *Mol Psychiatry, 26*(4), 1299-1309. doi:10.1038/s41380-019-0565-3

Kim, H. (2014). Involvement of the dorsal and ventral attention networks in oddball stimulus processing: A meta-analysis. *Human brain mapping, 35*(5), 2265-2284.

Kim, H., Daselaar, S. M., & Cabeza, R. (2010). Overlapping brain activity between episodic memory encoding and retrieval: roles of the task-positive and task-negative networks. *Neuroimage, 49*(1), 1045-1054.

Kim, J. I., Kang, Y.-H., Lee, J.-M., Cha, J., Park, Y.-H., Kweon, K.-J., & Kim, B.-N. (2018). Resting-state functional magnetic resonance imaging investigation of the neural correlatesof cognitive-behavioral therapy for externalizing behavior problems in adolescent bullies. *Progress in neuro-psychopharmacology and biological psychiatry, 86*, 193-202.

Kim, J. S. (2016). Post-stroke Mood and Emotional Disturbances: Pharmacological Therapy Based on Mechanisms. *J Stroke, 18*(3), 244-255. doi:10.5853/jos.2016.01144

Kimonis, E. R., Frick, P. J., Munoz, L. C., & Aucoin, K. J. (2008). Callous-unemotional traits andthe emotional processing of distress cues in detained boys: testing the moderating role of aggression, exposure to community violence, and histories of abuse. *Dev Psychopathol, 20*(2), 569-589. doi:10.1017/s095457940800028x

Kimonis, E. R., Graham, N., & Cauffman, E. (2018). Aggressive Male Juvenile Offenders with Callous-Unemotional Traits Show Aberrant Attentional Orienting to Distress Cues. *J Abnorm Child Psychol, 46*(3), 519-527. doi:10.1007/s10802-017-0295-4

Kimonis, E. R., Skeem, J. L., Cauffman, E., & Dmitrieva, J. (2011). Are secondary variants of juvenile psychopathy more reactively violent and less psychosocially mature than primaryvariants? *Law Hum Behav, 35*(5), 381-391. doi:10.1007/s10979-010-9243-3

Klapwijk, E. T., Aghajani, M., Colins, O. F., Marijnissen, G. M., Popma, A., van Lang, N. D., . . . Vermeiren, R. R. (2016). Different brain responses during empathy in autism spectrum disorders versus conduct disorder and callous-unemotional traits. *Journal of Child Psychology and Psychiatry, 57*(6), 737-747.

Knutson, & Greer. (2008). Anticipatory affect: neural correlates and consequences for choice. *Philosophical Transactions of the Royal Society B: Biological Sciences, 363*(1511), 3771-3786.

Knutson, Westdorp, Kaiser, & Hommer. (2000). FMRI visualization of brain activity during a monetary incentive delay task. *Neuroimage, 12*(1), 20-27. doi:10.1006/nimg.2000.0593

Knutson, B., & Greer, S. M. (2008). Anticipatory affect: neural correlates and consequences for choice. *Philosophical Transactions of the Royal Society B: Biological Sciences, 363*(1511),3771-3786.

Koenigs, M., Kruepke, M., & Newman, J. P. (2010). Economic decision-making in psychopathy: a comparison with ventromedial prefrontal lesion patients. *Neuropsychologia, 48*(7), 2198-2204.

Kogler, Müller, Werminghausen, Eickhoff, & Derntl. (2020). Do I feel or do I know? Neuroimaging meta-analyses on the multiple facets of empathy. *cortex, 129*, 341-355. doi:10.1016/j.cortex.2020.04.031

Kogler, L., Müller, V. I., Chang, A., Eickhoff, S. B., Fox, P. T., Gur, R. C., & Derntl, B. (2015). Psychosocial versus physiological stress—Meta-analyses on deactivations and activationsof the neural correlates of stress reactions. *NeuroImage, 119*, 235-251.

Kohls, Fairchild, Bernhard, Martinelli, Smaragdi, Gonzalez-Madruga, . . . Konrad. (2020). Neuropsychological Subgroups of Emotion Processing in Youths With Conduct Disorder.*Front Psychiatry, 11*, 585052. doi:10.3389/fpsyt.2020.585052

Kohls, G., Baumann, S., Gundlach, M., Scharke, W., Bernhard, A., Martinelli, A., . . . Oldenhof, H. (2020). Investigating sex differences in emotion recognition, learning, and regulation among youths with conduct disorder. *Journal of the American Academy of Child &Adolescent Psychiatry, 59*(2), 263-273.

Kokkinos, C. M., Kirpitsi, E., Voulgaridou, I., & Markos, A. (2022). Reactive and proactive aggression subgroups in early adolescents and the interplay among callous-unemotional traits, moral disengagement, empathy and functions of aggression. *Current Psychology: AJournal for Diverse Perspectives on Diverse Psychological Issues, 41*(6), 3551-3564. doi:10.1007/s12144-020-00858-2

Kolesar, T. A., Bilevicius, E., Wilson, A. D., & Kornelsen, J. (2019). Systematic review and meta-analyses of neural structural and functional differences in generalized anxiety disorder and healthy controls using magnetic resonance imaging. *NeuroImage: Clinical, 24*, 102016.

Konstenius, M., Larsson, H., Lundholm, L., Philips, B., van de Glind, G., Jayaram-Lindström, N.,& Franck, J. (2015). An epidemiological study of ADHD, substance use, and comorbid problems in incarcerated women in Sweden. *J Atten Disord, 19*(1), 44-52. doi:10.1177/1087054712451126

Korponay, C., Pujara, M., Deming, P., Philippi, C., Decety, J., Kosson, D. S., . . . Koenigs, M. (2017). Impulsive-antisocial psychopathic traits linked to increased volume and functionalconnectivity within prefrontal cortex. *Social cognitive and affective neuroscience, 12*(7), 1169-1178.

Koster, R., Guitart-Masip, M., Dolan, R. J., & Düzel, E. (2015). Basal ganglia activity mirrors a benefit of action and reward on long-lasting event memory. *Cerebral Cortex, 25*(12), 4908-4917.

Kozak, M. J., & Cuthbert, B. N. (2016). The NIMH Research Domain Criteria Initiative: Background, Issues, and Pragmatics. *Psychophysiology, 53*(3), 286-297. doi:10.1111/psyp.12518

Kraepelin, E. (1909). *Psychiatrie : ein Lehrbuch fu□□r studierende und A□□rzte*. Leipzig: J.A. Barth.

Krall, S. C., Rottschy, C., Oberwelland, E., Bzdok, D., Fox, P. T., Eickhoff, S. B., . . . Konrad, K.(2015). The role of the right temporoparietal junction in attention and social interaction asrevealed by ALE meta-analysis. *Brain Struct Funct, 220*(2), 587-604. doi:10.1007/s00429-014-0803-z

Krueger, R. F., Markon, K. E., Patrick, C. J., & Iacono, W. G. (2005). Externalizing psychopathology in adulthood: a dimensional-spectrum conceptualization and its implications for DSM-V. *J Abnorm Psychol, 114*(4), 537-550. doi:10.1037/0021- 843x.114.4.537

Kühn, S., & Gallinat, J. (2012). The neural correlates of subjective pleasantness. *Neuroimage, 61*(1), 289-294. doi:10.1016/j.neuroimage.2012.02.065

Kujawa, A., Klein, D. N., Pegg, S., & Weinberg, A. (2020). Developmental trajectories to reduced activation of positive valence systems: A review of biological and environmental contributions.

Dev Cogn Neurosci, 43, 100791. doi:10.1016/j.dcn.2020.100791

Kuniishi, H., Ichisaka, S., Matsuda, S., Futora, E., Harada, R., & Hata, Y. (2017). Chronic inactivation of the orbitofrontal cortex increases anxiety-like behavior and impulsive aggression, but decreases depression-like behavior in rats. *Frontiers in Behavioral Neuroscience, 10*, 250.

Kurth, F., Zilles, K., Fox, P. T., Laird, A. R., & Eickhoff, S. B. (2010). A link between the systems: functional differentiation and integration within the human insula revealed by meta-analysis. *Brain Structure and Function, 214*(5-6), 519-534.

Lai, C.-H. (2014). Patterns of cortico-limbic activations during visual processing of sad faces in depression patients: a coordinate-based meta-analysis. *The Journal of neuropsychiatry andclinical neurosciences, 26*(1), 34-43.

Laird, McMillan, Lancaster, Kochunov, Turkeltaub, Pardo, & Fox. (2005). A comparison of label-based review and ALE meta-analysis in the Stroop task. *Hum Brain Mapp, 25*(1), 6-21. doi:10.1002/hbm.20129

Laird, A. R., Eickhoff, S. B., Rottschy, C., Bzdok, D., Ray, K. L., & Fox, P. T. (2013). Networks of task co-activations. *Neuroimage, 80*, 505-514. doi:10.1016/j.neuroimage.2013.04.073

Laird, A. R., Riedel, M. C., Sutherland, M. T., Eickhoff, S. B., Ray, K. L., Uecker, A. M., . . . Fox, P. T. (2015). Neural architecture underlying classification of face perception paradigms. *Neuroimage, 119*, 70-80.

Lamm, Decety, & Singer. (2011). Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. *Neuroimage, 54*(3), 2492-2502. doi:10.1016/j.neuroimage.2010.10.014

Lamm, C., Decety, J., & Singer, T. (2011). Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. *NeuroImage, 54*(3), 2492-2502.

Lancaster, J. L., Laird, A. R., Eickhoff, S. B., Martinez, M. J., Fox, P. M., & Fox, P. T. (2012). Automated regional behavioral analysis for human brain images. *Frontiers in neuroinformatics, 6*, 23.

Langner, & Eickhoff. (2013). Sustaining attention to simple tasks: a meta-analytic review of the neural mechanisms of vigilant attention. *Psychol Bull, 139*(4), 870-900. doi:10.1037/a0030694

Langner, R., & Camilleri, J. A. (2021). Meta-Analytic Connectivity Modelling (MACM): A Toolfor Assessing Region-Specific Functional Connectivity Patterns in Task-Constrained States. In *Brain Network Dysfunction in Neuropsychiatric Illness* (pp. 93-104): Springer.

Langner, R., & Eickhoff, S. B. (2013). Sustaining attention to simple tasks: a meta-analytic review of the neural mechanisms of vigilant attention. *Psychological bulletin, 139*(4), 870.

Langner, R., Rottschy, C., Laird, A. R., Fox, P. T., & Eickhoff, S. B. (2014). Meta-analytic connectivity modeling revisited: controlling for activation base rates. *Neuroimage, 99*, 559- 570. doi:10.1016/j.neuroimage.2014.06.007

Larson, C. L., Baskin-Sommers, A. R., Stout, D. M., Balderston, N. L., Curtin, J. J., Schultz, D. H., . . . Newman, J. P. (2013). The interplay of attention and emotion: top-down attention modulates amygdala activation in psychopathy. *Cognitive, Affective, & Behavioral Neuroscience, 13*(4), 757-770.

Larsson, Dilshad, Lichtenstein, & Barker. (2011). Developmental trajectories of DSM-IV symptoms of attention-deficit/hyperactivity disorder: genetic effects, family risk and associated psychopathology. *J Child Psychol Psychiatry, 52*(9), 954-963. doi:10.1111/j.1469-7610.2011.02379.x

Larsson, H., Andershed, H., & Lichtenstein, P. (2006). A genetic factor explains most of the variation in the psychopathic personality. *Journal of abnormal psychology, 115*(2), 221- 230. doi:10.1037/0021-843X.115.2.221

Larsson, H., Dilshad, R., Lichtenstein, P., & Barker, E. D. (2011). Developmental trajectories of

DSM-IV symptoms of attention-deficit/hyperactivity disorder: Genetic effects, family risk and associated psychopathology. *Journal of Child Psychology and Psychiatry, 52*(9), 954-963.

Latzman, R. D., Patrick, C. J., & Lilienfeld, S. O. (2019). Heterogeneity matters: implications for Poeppl et al.'s (2019) meta-analysis and future neuroimaging research on psychopathy. *Molecular psychiatry*, 1-2.

Leaberry, K. D., Walerius, D. M., Rosen, P. J., & Fogleman, N. D. (2020). Emotional Lability. In

V. Zeigler-Hill & T. K. Shackelford (Eds.), *Encyclopedia of Personality and Individual Differences* (pp. 1319-1329). Cham: Springer International Publishing.

LeDoux. (2015). Anxious. Retrieved from http://public.ebookcentral.proquest.com/choice/publicfullrecord.aspx?p=2126068

LeDoux, & Pine. (2016). Using Neuroscience to Help Understand Fear and Anxiety: A Two- System Framework. *Am J Psychiatry, 173*(11), 1083-1093. doi:10.1176/appi.ajp.2016.16030353 LeDoux, J. (2015). *Anxious*: Oneworld Publications.

Lee, S. J., Park, S. H., Jeong, A., Chae, H., & Oh, K. (2017). Temperamental predictors of developmental trajectories of inattention and hyperactivity-impulsivity problems in schoolchildren. *Integr Med Res, 6*(1), 33-40. doi:10.1016/j.imr.2016.11.002

Lees, B., Squeglia, L. M., McTeague, L. M., Forbes, M. K., Krueger, R. F., Sunderland, M., . . .Mewton, L. (2021). Altered Neurocognitive Functional Connectivity and Activation Patterns Underlie Psychopathology in Preadolescence. *Biol Psychiatry Cogn Neurosci Neuroimaging, 6*(4), 387-398. doi:10.1016/j.bpsc.2020.09.007

Lehto-Salo, P., Närhi, V., Ahonen, T., & Marttunen, M. (2009). Psychiatric comorbidity more common among adolescent females with CD/ODD than among males. *Nordic journal of psychiatry, 63*(4), 308-315.

Lei, D., Du, M., Wu, M., Chen, T., Huang, X., Du, X., Gong, Q. (2015). Functional MRI reveals

different response inhibition between adults and children with ADHD. *Neuropsychology, 29*(6), 874.

Leibenluft, E. (2017). Pediatric Irritability: A Systems Neuroscience Approach. *Trends Cogn Sci, 21*(4), 277-289. doi:10.1016/j.tics.2017.02.002

Lenzenweger, M. F., Lane, M. C., Loranger, A. W., & Kessler, R. C. (2007). DSM-IV personality disorders in the National Comorbidity Survey Replication. *Biological psychiatry, 62*(6), 553-564.

Leppanen, J., Ng, K. W., Tchanturia, K., & Treasure, J. (2017). Meta-analysis of the effects of intranasal oxytocin on interpretation and expression of emotions. *Neurosci Biobehav Rev, 78*, 125-144. doi:10.1016/j.neubiorev.2017.04.010

Letourneau, N. L., Duffett-Leger, L., Levac, L., Watson, B., & Young-Morris, C. (2013). Socioeconomic status and child development: A meta-analysis. Journal of Emotional and Behavioral Disorders, 21(3), 211-224.

Lev, A., Braw, Y., Elbaum, T., Wagner, M., & Rassovsky, Y. (2020). Eye Tracking During a Continuous Performance Test: Utility for Assessing ADHD Patients. *Journal of Attention Disorders*, 1087054720972786.

Li, C.-S. R., Yan, P., Sinha, R., & Lee, T.-W. (2008). Subcortical processes of motor response inhibition during a stop signal task. *NeuroImage, 41*(4), 1352-1363.

Li, S., Hu, N., Zhang, W., Tao, B., Dai, J., Gong, Y., . . . Lui, S. (2019). Dysconnectivity of multiplebrain networks in schizophrenia: a meta-analysis of resting-state functional connectivity. *Frontiers in psychiatry, 10*, 482.

Li, Y., Aggen, S., Shi, S., Gao, J., Tao, M., Zhang, K., . . . Liu, Y. (2014). The structure of the symptoms of major depression: exploratory and confirmatory factor analysis in depressed Han Chinese women. *Psychological medicine, 44*(7), 1391-1401.

Liang, K.-Y., & Zeger, S. L. (1986). Longitudinal data analysis using generalized linear models.

Biometrika, 73(1), 13-22.

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P., . . . Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Journal of clinical epidemiology, 62*(10), e1-e34.

Lieberman, & Cunningham. (2009). Type I and Type II error concerns in fMRI research: re-balancing the scale. *Soc Cogn Affect Neurosci, 4*(4), 423-428. doi:10.1093/scan/nsp052

Lieberman, M. D., & Cunningham, W. A. (2009). Type I and Type II error concerns in fMRI research: re-balancing the scale. *Social cognitive and affective neuroscience, 4*(4), 423-428.

Liew, S. L., Lo, B. P., Donnelly, M. R., Zavaliangos-Petropulu, A., Jeong, J. N., Barisano, G., . . .Yu, C. (2022). A large, curated, open-source stroke neuroimaging dataset to improve lesion segmentation algorithms. *Sci Data, 9*(1), 320. doi:10.1038/s41597-022-01401-7

Liew, S. L., Zavaliangos-Petropulu, A., Jahanshad, N., Lang, C. E., Hayward, K. S., Lohse, K. R., . . . Thompson, P. M. (2022). The ENIGMA Stroke Recovery Working Group: Big data neuroimaging to study brain-behavior relationships after stroke. *Hum Brain Mapp, 43*(1), 129-148. doi:10.1002/hbm.25015

Lilienfeld, Sauvigné, Reber, Watts, Hamann, Smith, . . . Tranel. (2018). Potential effects of severe bilateral amygdala damage on psychopathic personality features: A case report. *Personality disorders, 9*(2), 112-121. doi:10.1037/per0000230

Lilienfeld, S. O., & Waldman, I. D. (1990). The relation between childhood attention-deficit hyperactivity disorder and adult antisocial behavior reexamined: The problem of heterogeneity. *Clinical psychology review, 10*(6), 699-725. doi:https://doi.org/10.1016/0272-7358(90)90076-M

Lischinsky, J. E., & Lin, D. (2020). Neural mechanisms of aggression across species. *Nature neuroscience, 23*(11), 1317-1328. doi:10.1038/s41593-020-00715-2

Liu, Hairston, Schrier, & Fan. (2011). Common and distinct networks underlying reward valence and processing stages: a meta-analysis of functional neuroimaging studies. *Neuroscience & Biobehavioral Reviews, 35*(5), 1219-1236.

Liu, Liu, Zheng, Zhao, & Fu. (2021). Reexamining the neural network involved in perception of facial expression: A meta-analysis. *Neurosci Biobehav Rev, 131*, 179-191. doi:10.1016/j.neubiorev.2021.09.024

Liu, X., Hairston, J., Schrier, M., & Fan, J. (2011). Common and distinct networks underlying reward valence and processing stages: a meta-analysis of functional neuroimaging studies. *Neuroscience & Biobehavioral Reviews, 35*(5), 1219-1236.

Livanou, M., Furtado, V., Winsper, C., Silvester, A., & Singh, S. P. (2019). Prevalence of Mental Disorders and Symptoms Among Incarcerated Youth: A Meta-Analysis of 30 Studies. *International Journal of Forensic Mental Health, 18*(4), 400-414. doi:10.1080/14999013.2019.1619636

Lo, Y., Mendell, N. R., & Rubin, D. B. (2001). Testing the number of components in a normal mixture. *Biometrika, 88*(3), 767-778.

Lobbestael, J., & Cima, M. J. (2021). Virtual Reality for Aggression Assessment: The Development and Preliminary Results of Two Virtual Reality Tasks to Assess Reactive andProactive Aggression in Males. *Brain Sci, 11*(12). doi:10.3390/brainsci11121653

Lobo, R. P., Bottenhorn, K. L., Riedel, M. C., Toma, A. I., Hare, M. M., Smith, D. D., . . . Laird, A. R. (2022). Neural systems underlying RDoC social constructs: An activation likelihood estimation meta-analysis. *bioRxiv*, 2022.2004.2004.487016. doi:10.1101/2022.04.04.487016

Lockwood, P. L., Sebastian, C. L., McCrory, E. J., Hyde, Z. H., Gu, X., De Brito, S. A., & Viding, E. (2013). Association of callous traits with reduced neural response to others' pain inchildren with conduct problems. *Current Biology, 23*(10), 901-905.

Loeber, R. (1990). Development and risk factors of juvenile antisocial behavior and delinquency. *Clinical psychology review, 10*(1), 1-41. doi:https://doi.org/10.1016/0272-7358(90)90105-J

Loeber, R., & Stouthamer-Loeber, M. (1998). Development of juvenile aggression and violence: Some common misconceptions and controversies. *American Psychologist, 53*(2), 242-259. doi:10.1037/0003-066X.53.2.242

Loney, B. R., Frick, P. J., Clements, C. B., Ellis, M. L., & Kerlin, K. (2003). Callous-unemotionaltraits, impulsivity, and emotional processing in adolescents with antisocial behavior problems. *J Clin Child Adolesc Psychol, 32*(1), 66-80. doi:10.1207/s15374424jccp3201_07

Longman, T., Hawes, D. J., & Kohlhoff, J. (2016). Callous-Unemotional Traits as Markers for Conduct Problem Severity in Early Childhood: A Meta-analysis. *Child Psychiatry Hum Dev, 47*(2), 326-334. doi:10.1007/s10578-015-0564-9

Lorber, M. F. (2004). Psychophysiology of aggression, psychopathy, and conduct problems: a meta-analysis. *Psychological bulletin, 130*(4), 531.

Lozier, L. M., Cardinale, E. M., VanMeter, J. W., & Marsh, A. A. (2014). Mediation of the relationship between callous-unemotional traits and proactive aggression by amygdala response to fear among children with conduct problems. *JAMA psychiatry, 71*(6), 627-636.

Luijten, M., Schellekens, A. F., Kühn, S., Machielse, M. W., & Sescousse, G. (2017). Disruptionof reward processing in addiction: an image-based meta-analysis of functional magnetic resonance imaging studies. *JAMA psychiatry, 74*(4), 387-398.

Lundervold, A. J., Bøe, T., & Lundervold, A. (2017). Inattention in primary school is not good for your future school achievement-A pattern classification study. *PloS one, 12*(11), e0188310. doi:10.1371/journal.pone.0188310

Lynam, D. R. (1996). Early identification of chronic offenders: who is the fledgling psychopath? *Psychol Bull, 120*(2), 209-234. doi:10.1037/0033-2909.120.2.209

Lynam, D. R. (1998). Early identification of the fledgling psychopath: locating the psychopathic child in the current nomenclature. *J Abnorm Psychol, 107*(4), 566-575. doi:10.1037//0021-843x.107.4.566

Lynam, D. R., Charnigo, R., Moffitt, T. E., Raine, A., Loeber, R., & Stouthamer-Loeber, M. (2009). The stability of psychopathy across adolescence. *Development and psychopathology, 21*(4), 1133-1153.

Madonna, D., Delvecchio, G., Soares, J. C., & Brambilla, P. (2019). Structural and functional neuroimaging studies in generalized anxiety disorder: a systematic review. *BrazilianJournal of Psychiatry, 41*(4), 336-362.

Mann, Engelhardt, Briley, Grotzinger, Patterson, Tackett, . . . Harden. (2017). Sensation seeking and impulsive traits as personality endophenotypes for antisocial behavior: Evidence fromtwo independent samples. *Pers Individ Dif, 105*, 30-39. doi:10.1016/j.paid.2016.09.018

Mann, Paul, Tackett, Tucker-Drob, & Harden. (2018). Personality risk for antisocial behavior: Testing the intersections between callous-unemotional traits, sensation seeking, and impulse control in adolescence. *Dev Psychopathol, 30*(1), 267-282. doi:10.1017/s095457941700061x

Mann, Tackett, Tucker-Drob, & Harden. (2018). Callous-Unemotional Traits Moderate Genetic and Environmental Influences on Rule-Breaking and Aggression: Evidence for Gene × Trait Interaction. *Clin Psychol Sci, 6*(1), 123-133. doi:10.1177/2167702617730889

Mar, R. A. (2011). The neural bases of social cognition and story comprehension. *Annual review of psychology, 62*(1), 103-134.

Marcus, D. K., John, S. L., & Edens, J. F. (2004). A taxometric analysis of psychopathicpersonality. *J Abnorm Psychol, 113*(4), 626-635. doi:10.1037/0021-843x.113.4.626

Marcus, D. K., Lilienfeld, S. O., Edens, J. F., & Poythress, N. G. (2006). Is antisocial personality disorder continuous or categorical? A taxometric analysis. *Psychol Med, 36*(11), 1571- 1581. doi:10.1017/s0033291706008245

Marcus, D. K., Ruscio, J., Lilienfeld, S. O., & Hughes, K. T. (2008). Converging Evidence for the Latent Structure of Antisocial Personality Disorder:Consistency of Taxometric and LatentClass Analyses. *Criminal Justice and Behavior, 35*(3), 284-293.doi:10.1177/0093854807311679

Marek, S., Hwang, K., Foran, W., Hallquist, M. N., & Luna, B. 2015. The Contribution of Network Organization and Integration to the Development of Cognitive Control. PLoS biology, 13(12)

Marek, S., Tervo-Clemmens, B., Nielsen, A. N., Wheelock, M. D., Miller, R. L., Laumann, T. O., Earl, E., Foran, W. W., Cordova, M., Doyle, O., Perrone, A., Miranda-Dominguez, O., Feczko, E., Sturgeon, D., Graham, A., Hermosillo, R., Snider, K., Galassi, A., Nagel, B. J., Ewing, S. W. F., … Dosenbach, N. U. F. (2019). Identifying reproducible individual differences in childhood functional brain networks: An ABCD study. *Developmental cognitive neuroscience*, *40*, 100706. https://doi.org/10.1016/j.dcn.2019.100706

Marek, S., Tervo-Clemmens, B., Calabro, F. J., Montez, D. F., Kay, B. P., Hatoum, A. S., . . . Dosenbach, N. U. F. (2022). Reproducible brain-wide association studies require thousands of individuals. *Nature, 603*(7902), 654-660. doi:10.1038/s41586-022-04492-9

Marsee, M. A., Frick, P. J., Barry, C. T., Kimonis, E. R., Muñoz Centifanti, L. C., & Aucoin, K. J.(2014). Profiles of the forms and functions of self-reported aggression in three adolescent samples. *Dev Psychopathol, 26*(3), 705-720. doi:10.1017/s0954579414000339

Marsh. (2022). Comment: Getting Our Affect Together: Shared Representations as the Core of Empathy. *Emotion Review, 14*(3), 184-187. doi:10.1177/17540739221107029

Marsh, & Blair. (2008). Deficits in facial affect recognition among antisocial populations: a meta-analysis. *Neurosci Biobehav Rev, 32*(3), 454-465. doi:10.1016/j.neubiorev.2007.08.003

Marsh, Finger, Fowler, Adalio, Jurkowitz, Schechter, . . . Blair. (2013). Empathic responsiveness in amygdala and anterior cingulate cortex in youths with psychopathic traits. *J Child Psychol Psychiatry, 54*(8), 900-910. doi:10.1111/jcpp.12063

Marsh, A. A., & Blair, R. J. R. (2008). Deficits in facial affect recognition among antisocial populations: a meta-analysis. *Neuroscience & Biobehavioral Reviews, 32*(3), 454-465.

Marsh, A. A., Finger, E. C., Fowler, K. A., Jurkowitz, I. T., Schechter, J. C., Henry, H. Y., . . . Blair, R. (2011). Reduced amygdala–orbitofrontal connectivity during moral judgments in youths with

disruptive behavior disorders and psychopathic traits. *Psychiatry Research: Neuroimaging, 194*(3), 279-286.

Marsh, A. A., Finger, E. C., Mitchell, D. G., Reid, M. E., Sims, C., Kosson, D. S., . . . Blair, R. (2008). Reduced amygdala response to fearful expressions in children and adolescents with callous-unemotional traits and disruptive behavior disorders. *American Journal of Psychiatry, 165*(6), 712-720.

Marshal, M. P., & Molina, B. S. (2006). Antisocial behaviors moderate the deviant peer pathway to substance use in children with ADHD. *J Clin Child Adolesc Psychol, 35*(2), 216-226. doi:10.1207/s15374424jccp3502_5

Martin-Key, N., Brown, T., & Fairchild, G. (2017). Empathic accuracy in male adolescents with conduct disorder and higher versus lower levels of callous-unemotional traits. *Journal of abnormal child psychology, 45*(7), 1385-1397.

Martin-Key, N. A., Graf, E., Adams, W., & Fairchild, G. (2018). Facial emotion recognition and eye movement behaviour in conduct disorder. *Journal of Child Psychology and Psychiatry,59*(3), 247-257.

Martino, S. C., Ellickson, P. L., Klein, D. J., McCaffrey, D., & Edelen, M. O. (2008). Multiple trajectories of physical aggression among adolescent boys and girls. *Aggress Behav, 34*(1),61-75. doi:10.1002/ab.20215

Matthys, Vanderschuren, & Schutter. (2013a). The neurobiology of oppositional defiant disorder and conduct disorder: altered functioning in three mental domains. *Dev Psychopathol, 25*(1), 193-207. doi:10.1017/s0954579412000272

Matthys, Vanderschuren, & Schutter. (2013b). The neurobiology of oppositional defiant disorder and conduct disorder: altered functioning in three mental domains. *Development and psychopathology, 25*(1), 193-207.

Matthys, W., van Goozen, S. H., de Vries, H., Cohen-Kettenis, P. T., & van Engeland, H. (1998).The

dominance of behavioural activation over behavioural inhibition in conduct disorderedboys with or without attention deficit hyperactivity disorder. *J Child Psychol Psychiatry, 39*(5), 643-651.

Matthys, W., Vanderschuren, L. J., & Schutter, D. J. (2013). The neurobiology of oppositional defiant disorder and conduct disorder: altered functioning in three mental domains. *Development and psychopathology, 25*(1), 193-207.

Maughan, B., Rowe, R., Messer, J., Goodman, R., & Meltzer, H. (2004). Conduct disorder and oppositional defiant disorder in a national sample: developmental epidemiology. *J Child Psychol Psychiatry, 45*(3), 609-621. doi:10.1111/j.1469-7610.2004.00250.x

Mayes, S. D., Waxmonsky, J. D., Calhoun, S. L., & Bixler, E. O. (2016). Disruptive Mood Dysregulation Disorder Symptoms and Association with Oppositional Defiant and Other Disorders in a General Population Child Sample. *J Child Adolesc Psychopharmacol, 26*(2),101-106. doi:10.1089/cap.2015.0074

McKee, A. C., Stern, R. A., Nowinski, C. J., Stein, T. D., Alvarez, V. E., Daneshvar, D. H., . . . Cantu, R. C. (2013). The spectrum of disease in chronic traumatic encephalopathy. *Brain, 136*(Pt 1), 43-64. doi:10.1093/brain/aws307

McTeague, L. M., Huemer, J., Carreon, D. M., Jiang, Y., Eickhoff, S. B., & Etkin, A. (2017). Identification of common neural circuit disruptions in cognitive control across psychiatric disorders. *American Journal of Psychiatry, 174*(7), 676-685.

McTeague, L. M., Rosenberg, B. M., Lopez, J. W., Carreon, D. M., Huemer, J., Jiang, Y., . . . Etkin, A. (2020). Identification of common neural circuit disruptions in emotional processing across psychiatric disorders. *American Journal of Psychiatry, 177*(5), 411-421.

Mechias, Etkin, & Kalisch. (2010). A meta-analysis of instructed fear studies: implications for conscious appraisal of threat. *Neuroimage, 49*(2), 1760-1768. doi:10.1016/j.neuroimage.2009.09.040

Mechias, M.-L., Etkin, A., & Kalisch, R. (2010). A meta-analysis of instructed fear studies:

implications for conscious appraisal of threat. *NeuroImage, 49*(2), 1760-1768.

Meehan, A. J., Maughan, B., Cecil, C. A., & Barker, E. D. (2017). Interpersonal callousness and co-occurring anxiety: Developmental validity of an adolescent taxonomy. *Journal of abnormal psychology, 126*(2), 225.

Meffert, H., Gazzola, V., Den Boer, J. A., Bartels, A. A., & Keysers, C. (2013). Reduced spontaneous but relatively normal deliberate vicarious representations in psychopathy. *Brain, 136*(8), 2550-2562.

Mellentin, A. I., Dervisevic, A., Stenager, E., Pilegaard, M., & Kirk, U. (2015). Seeing enemies? A systematic review of anger bias in the perception of facial expressions among anger- prone and aggressive populations. *Aggression and Violent Behavior, 25*, 373-383.

Meloy, J. R. (2006). Empirical basis and forensic application of affective and predatory violence. *Aust N Z J Psychiatry, 40*(6-7), 539-547. doi:10.1080/j.1440-1614.2006.01837.x

Mende-Siedlecki, P., Said, C. P., & Todorov, A. (2013). The social evaluation of faces: a meta-analysis of functional neuroimaging studies. *Soc Cogn Affect Neurosci, 8*(3), 285-299. doi:10.1093/scan/nsr090

Mendez, M. F. (2022). Behavioral Variant Frontotemporal Dementia and Social and Criminal Transgressions. *J Neuropsychiatry Clin Neurosci*, appineuropsych21080224. doi:10.1176/appi.neuropsych.21080224

Menks, Fehlbaum, Borbás, Sterzer, Stadler, & Raschle. (2021). Eye gaze patterns and functional brain responses during emotional face processing in adolescents with conduct disorder. *Neuroimage Clin, 29*, 102519. doi:10.1016/j.nicl.2020.102519

Menks, W. M., Fehlbaum, L. V., Borbás, R., Sterzer, P., Stadler, C., & Raschle, N. M. (2020). Eyegaze patterns and functional brain responses during emotional face processing in adolescents with conduct disorder. *NeuroImage: Clinical, 29*, 102519.

Metcalf, S., Dickerson, K. L., Milojevich, H. M., & Quas, J. A. (2021). Primary and Secondary Variants of Psychopathic Traits in at-Risk Youth: Links with Maltreatment, Aggression, and Empathy. *Child Psychiatry Hum Dev, 52*(6), 1060-1070. doi:10.1007/s10578-020- 01083-5

Michalska, K. J., Machlin, L., Moroney, E., Lowet, D. S., Hettema, J. M., Roberson-Nay, R., . . . Leibenluft, E. (2017). Anxiety symptoms and children's eye gaze during fear learning. *Journal of Child Psychology and Psychiatry, 58*(11), 1276-1286.

Mihalik, A., Chapman, J., Adams, R. A., Winter, N. R., Ferreira, F. S., Shawe-Taylor, J., Mourão-Miranda, J., & Alzheimer's Disease Neuroimaging Initiative (2022). Canonical Correlation Analysis and Partial Least Squares for Identifying Brain-Behavior Associations: A Tutorial and a Comparative Study. Biological psychiatry. Cognitive neuroscience and neuroimaging, 7(11), 1055–1067. https://doi.org/10.1016/j.bpsc.2022.07.012

Mikton, C. R., Butchart, A., Dahlberg, L. L., & Krug, E. G. (2016). Global Status Report on Violence Prevention 2014. *Am J Prev Med, 50*(5), 652-659. doi:10.1016/j.amepre.2015.10.007

Milad, M. R., Pitman, R. K., Ellis, C. B., Gold, A. L., Shin, L. M., Lasko, N. B., Rauch, S. L. (2009). Neurobiological basis of failure to recall extinction memory in posttraumatic stress disorder. *Biological psychiatry, 66*(12), 1075-1082.

Milani, A. C. C., Hoffmann, E. V., Fossaluza, V., Jackowski, A. P., & Mello, M. F. (2017). Does pediatric post-traumatic stress disorder alter the brain? Systematic review and meta-analysis of structural and functional magnetic resonance imaging studies. *Psychiatry and Clinical Neurosciences, 71*(3), 154-169.

Miller, C. H., Hamilton, J. P., Sacchet, M. D., & Gotlib, I. H. (2015). Meta-analysis of functional neuroimaging of major depressive disorder in youth. *JAMA psychiatry, 72*(10), 1045-1053.

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual review of neuroscience, 24*(1), 167-202.

Miller, M. W., Wolf, E. J., Kilpatrick, D., Resnick, H., Marx, B. P., Holowka, D. W., . . . Friedman, M. J. (2013). The prevalence and latent structure of proposed DSM-5 posttraumatic stress disorder symptoms in US national and veteran samples. *Psychological trauma: theory, research, practice, and policy, 5*(6), 501.

Miller-Johnson, S., Coie, J. D., Maumary-Gremaud, A., & Bierman, K. (2002). Peer rejection and aggression and early starter models of conduct disorder. *J Abnorm Child Psychol, 30*(3), 217-230. doi:10.1023/a:1015198612049

Mitchell, & Potenza. (2015). Importance of sex differences in impulse control and addictions. *Front Psychiatry, 6*, 24. doi:10.3389/fpsyt.2015.00024

Mitchell, Smid, Troelstra, Wever, Ziegler, & Beech. (2013). Psychopathic characteristics are related to high basal urinary oxytocin levels in male forensic patients. *The Journal of Forensic Psychiatry & Psychology, 24*(3), 309-318. doi:10.1080/14789949.2013.773455

Mitchell, D. G., Colledge, E., Leonard, A., & Blair, R. J. (2002). Risky decisions and response reversal: is there evidence of orbitofrontal cortex dysfunction in psychopathic individuals? *Neuropsychologia, 40*(12), 2013-2022. doi:10.1016/s0028-3932(02)00056-8

Moffitt. (2003). Life-course-persistent and adolescence-limited antisocial behavior: A 10-year research review and a research agenda. In *Causes of conduct disorder and juveniledelinquency.* (pp. 49-75). New York, NY, US: The Guilford Press.

Moffitt, T. E. (1993). A developmental taxonomy. *Psychological review, 100*(4), 674-701.

Moffitt, T. E. (2006). Life-course-persistent versus adolescence-limited antisocial behavior. In D. Cicchetti & D. J. Cohen (Eds.), Developmental psychopathology: Risk, disorder, and adaptation (pp. 570–598). John Wiley & Sons, Inc.

Moffitt, T. E. (2018). Male antisocial behaviour in adolescence and beyond. *Nature Human Behaviour, 2*(3), 177.

Mohammadi, M. R., Salmanian, M., & Keshavarzi, Z. (2021). The Global Prevalence of Conduct Disorder: A Systematic Review and Meta-Analysis. *Iran J Psychiatry, 16*(2), 205-225. doi:10.18502/ijps.v16i2.5822

Mohan-Gibbons, H., Weiss, E., & Slater, M. (2012). Preliminary Investigation of Food Guarding Behavior in Shelter Dogs in the United States. *Animals (Basel), 2*(3), 331-346. doi:10.3390/ani2030331

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of internal medicine, 151*(4), 264-269.

Mok, J. N. Y., Green, L., Myerson, J., Kwan, D., Kurczek, J., Ciaramelli, E., . . . Rosenbaum, S.R. (2021). Does Ventromedial Prefrontal Cortex Damage Really Increase Impulsiveness? Delay and Probability Discounting in Patients with Focal Lesions. *J Cogn Neurosci, 33*(9), 1-19. doi:10.1162/jocn_a_01721

Molenberghs, P., Johnson, H., Henry, J. D., & Mattingley, J. B. (2016). Understanding the minds of others: A neuroimaging meta-analysis. *Neuroscience & Biobehavioral Reviews, 65*, 276-291.

Monahan, K. C., Steinberg, L., & Cauffman, E. (2009). Affiliation with antisocial peers, susceptibility to peer influence, and antisocial behavior during the transition to adulthood. Developmental psychology, 45(6), 1520–1530. https://doi.org/10.1037/a0017417

Moore, Sunjic, Kaye, Archer, & Indig. (2016). Adult ADHD Among NSW Prisoners: Prevalence and Psychiatric Comorbidity. *J Atten Disord, 20*(11), 958-967. doi:10.1177/1087054713506263

Moore, C. C., Hubbard, J., Morrow, M. T., Barhight, L. R., Lines, M. M., Sallee, M., & Hyde, C.T. (2018). The simultaneous assessment of and relations between children's sympathetic and parasympathetic psychophysiology and their reactive and proactive aggression. *Aggress Behav, 44*(6), 614-623. doi:10.1002/ab.21786

Morandini, H. A. E., Silk, T. J., Griffiths, K., Rao, P., Hood, S. D., & Zepf, F. D. (2020). Meta- analysis

of the neural correlates of vigilant attention in children and adolescents. *cortex, 132*, 374-385. doi:https://doi.org/10.1016/j.cortex.2020.08.008

Morawetz, C., Bode, S., Derntl, B., & Heekeren, H. R. (2017). The effect of strategies, goals and stimulus material on the neural mechanisms of emotion regulation: a meta-analysis of fMRI studies. *Neuroscience & Biobehavioral Reviews, 72*, 111-128.

Moreau, G. (2020). Statistiques sur les crimes déclarés par la police au Canada. *Juristat, 85*(2), 3-70. Retrieved from https://www150.statcan.gc.ca/n1/pub/85-002-x/2021001/article/00013-fra.htm

Morgan, A. B., & Lilienfeld, S. O. (2000). A meta-analytic review of the relation between antisocial behavior and neuropsychological measures of executive function. *Clinical psychology review, 20*(1), 113-136.

Morin, A. J. S., Maïano, C., Nagengast, B., Marsh, H. W., Morizot, J., & Janosz, M. (2011). General Growth Mixture Analysis of Adolescents' Developmental Trajectories of Anxiety:The Impact of Untested Invariance Assumptions on Substantive Interpretations. *StructuralEquation Modeling: A Multidisciplinary Journal, 18*(4), 613-648. doi:10.1080/10705511.2011.607714

Morris, S. E., & Cuthbert, B. N. (2012). Research Domain Criteria: cognitive systems, neural circuits, and dimensions of behavior. *Dialogues Clin Neurosci, 14*(1), 29-37. doi:10.31887/DCNS.2012.14.1/smorris

Morriss, J., Hoare, S., & van Reekum, C. M. (2018). It's time: A commentary on fear extinction in the human brain using fMRI. *Neurosci Biobehav Rev, 94*, 321-322. doi:10.1016/j.neubiorev.2018.06.025

Motzkin, J. C., Newman, J. P., Kiehl, K. A., & Koenigs, M. (2011). Reduced prefrontal connectivity in psychopathy. *Journal of Neuroscience, 31*(48), 17348-17357.

Motzkin, J. C., Philippi, C. L., Wolf, R. C., Baskaya, M. K., & Koenigs, M. (2015). Ventromedial prefrontal cortex is critical for the regulation of amygdala activity in humans. *Biological*

psychiatry, 77(3), 276-284.

Müller, Höhner, & Eickhoff. (2018). Influence of task instructions and stimuli on the neural network of face processing: An ALE meta-analysis. *cortex, 103*, 240-255. doi:10.1016/j.cortex.2018.03.011

Müller, N. G., Machado, L., & Knight, R. T. (2002). Contributions of subregions of the prefrontal cortex to working memory: evidence from brain lesions in humans. *J Cogn Neurosci, 14*(5),673-686. doi:10.1162/08989290260138582

Müller, V. I., Cieslik, E. C., Laird, A. R., Fox, P. T., Radua, J., Mataix-Cols, D., . . . Turkeltaub, P. E. (2018). Ten simple rules for neuroimaging meta-analysis. *Neuroscience & Biobehavioral Reviews, 84*, 151-161.

Müller, V. I., Cieslik, E. C., Serbanescu, I., Laird, A. R., Fox, P. T., & Eickhoff, S. B. (2017). Altered brain activity in unipolar depression revisited: meta-analyses of neuroimaging studies. *JAMA psychiatry, 74*(1), 47-55.

Muñoz, L. C., Frick, P. J., Kimonis, E. R., & Aucoin, K. J. (2008). Types of aggression,responsiveness to provocation, and callous-unemotional traits in detained adolescents. *J Abnorm Child Psychol, 36*(1), 15-28. doi:10.1007/s10802-007-9137-0

Murray, Lopez-Duran, Mitchell, Monk, & Hyde. (2022). Antisocial behavior is associated with reduced frontoparietal activity to loss in a population-based sample of adolescents. *PsycholMed*, 1-9. doi:10.1017/s0033291722000307

Murray, Shaw, Forbes, & Hyde. (2017a). Reward-Related Neural Correlates of Antisocial Behavior and Callous-Unemotional Traits in Young Men. *Biol Psychiatry Cogn Neurosci Neuroimaging, 2*(4), 346-354. doi:10.1016/j.bpsc.2017.01.009

Murray, Shaw, Forbes, & Hyde. (2017b). Reward-related neural correlates of antisocial behavior and callous–unemotional traits in young men. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 2*(4), 346-354.

Murray, Waller, & Hyde. (2018). A systematic review examining the link between psychopathic personality traits, antisocial behavior, and neural reactivity during reward and loss processing. *Personality Disorders: Theory, Research, and Treatment, 9*(6), 497.

Murray, L., Shaw, D. S., Forbes, E. E., & Hyde, L. W. (2017). Reward-related neural correlates of antisocial behavior and callous–unemotional traits in young men. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 2*(4), 346-354.

Murray-Close, D., Holterman, L. A., Breslend, N. L., & Sullivan, A. (2017). Psychophysiology of proactive and reactive relational aggression. *Biological psychology, 130*, 77-85. doi:https://doi.org/10.1016/j.biopsycho.2017.10.005

Murrie, D. C., Marcus, D. K., Douglas, K. S., Lee, Z., Salekin, R. T., & Vincent, G. (2007). Youthwith psychopathy features are not a discrete class: a taxometric analysis. *J Child Psychol Psychiatry, 48*(7), 714-723. doi:10.1111/j.1469-7610.2007.01734.x

Musser, Karalunas, Dieckmann, Peris, & Nigg. (2016). Attention-deficit/hyperactivity disorder developmental trajectories related to parental expressed emotion. *Journal of abnormal psychology, 125*(2), 182.

Musser, E. D., Karalunas, S. L., Dieckmann, N., Peris, T. S., & Nigg, J. T. (2016). Attention-deficit/hyperactivity disorder developmental trajectories related to parental expressed emotion. *J Abnorm Psychol, 125*(2), 182-195. doi:10.1037/abn0000097

Muthén, B., & Muthén, B. O. (2009). *Statistical analysis with latent variables*: Wiley New York.
Muthén, B., & Muthén, L. K. (2000). Integrating person-centered and variable-centered analyses:

Growth mixture modeling with latent trajectory classes. *Alcoholism: Clinical and experimental research, 24*(6), 882-891.

Nagin, & Tremblay. (1999). Trajectories of boys' physical aggression, opposition, and hyperactivity on the path to physically violent and nonviolent juvenile delinquency. *Child Dev, 70*(5), 1181-1196. doi:10.1111/1467-8624.00086

Nagin, D., & Tremblay, R. E. (1999). Trajectories of boys' physical aggression, opposition, and hyperactivity on the path to physically violent and nonviolent juvenile delinquency. *Child Development, 70*(5), 1181-1196.

Nagin, D. S., Jones, B. L., Passos, V. L., & Tremblay, R. E. (2018). Group-based multi-trajectory modeling. *Statistical methods in medical research, 27*(7), 2015-2023.

Nagin, D. S., & NAGIN, D. (2005). *Group-based modeling of development*: Harvard University Press.

Nakaji, P., Meltzer, H. S., Singel, S. A., & Alksne, J. F. (2003). Improvement of aggressive and antisocial behavior after resection of temporal lobe tumors. *Pediatrics, 112*(5), e430. doi:10.1542/peds.112.5.e430

Nee, D. E., Wager, T. D., & Jonides, J. (2007). Interference resolution: insights from a meta-analysis of neuroimaging tasks. *Cognitive, Affective, & Behavioral Neuroscience, 7*(1), 1- 17.

Nelson, R. J., & Trainor, B. C. (2007). Neural mechanisms of aggression. *Nature reviews neuroscience, 8*(7), 536-546. doi:10.1038/nrn2174

Network, T., O'Dushlaine, C., Rossin, L., Lee, P. H., Duncan, L., Parikshak, N. N., . . . Purcell, S. M. (2015). Psychiatric genome-wide association study analyses implicate neuronal, immune and histone pathways. *Nature neuroscience, 18*(2), 199.

Neumann, J., Lohmann, G., Derrfuss, J., & von Cramon, D. Y. (2005). Meta-analysis of functional imaging data using replicator dynamics. *Hum Brain Mapp, 25*(1), 165-173. doi:10.1002/hbm.20133

Newman, J. P., & Kosson, D. S. (1986). Passive avoidance learning in psychopathic and nonpsychopathic offenders. *J Abnorm Psychol, 95*(3), 252-256.

Newman, J. P., Widom, C. S., & Nathan, S. (1985). Passive avoidance in syndromes of disinhibition: psychopathy and extraversion. *J Pers Soc Psychol, 48*(5), 1316-1327.

doi:10.1037//0022-3514.48.5.1316

NICHD. (2004). Trajectories of physical aggression from toddlerhood to middle childhood: predictors, correlates, and outcomes. *Monogr Soc Res Child Dev, 69*(4), vii, 1-129. doi:10.1111/j.0037-976x.2004.00312.x

Nikolas, M. A., & Burt, S. A. (2010). Genetic and environmental influences on ADHD symptom dimensions of inattention and hyperactivity: a meta-analysis. *J Abnorm Psychol, 119*(1), 1-17. doi:10.1037/a0018010

Nock, M. K., Kazdin, A. E., Hiripi, E., & Kessler, R. C. (2006a). Prevalence, subtypes, and correlates of DSM-IV conduct disorder in the National Comorbidity Survey Replication. *Psychological medicine, 36*(5), 699.

Noiret, N., Carvalho, N., Laurent, É., Vulliez, L., Bennabi, D., Chopard, G., . . . Vandel, P. (2015). Visual scanning behavior during processing of emotional faces in older adults with major depression. *Aging & Mental Health, 19*(3), 264-273.

Noordermeer, Luman, & Oosterlaan. (2016). A Systematic Review and Meta-analysis of Neuroimaging in Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD) TakingAttention-Deficit Hyperactivity Disorder (ADHD) Into Account. *Neuropsychol Rev, 26*(1), 44-72. doi:10.1007/s11065-015-9315-8

Noordermeer, S. D., Luman, M., & Oosterlaan, J. (2016). A systematic review and meta-analysis of neuroimaging in oppositional defiant disorder (ODD) and conduct disorder (CD) taking attention-deficit hyperactivity disorder (ADHD) into account. *Neuropsychology review, 26*(1), 44-72.

Northam, J. C., & Dadds, M. R. (2020). Is Callous Always Cold? A Critical Review of the Literature on Emotion and the Development of Callous–Unemotional Traits in Children. *Clinical Child and Family Psychology Review*, 1-19.

Nylund, K. L., Asparouhov, T., & Muthén, B. O. (2007). Deciding on the number of classes in latent

class analysis and growth mixture modeling: A Monte Carlo simulation study. *Structural Equation Modeling: A Multidisciplinary Journal, 14*(4), 535-569.

O'Nions, E., Sebastian, C. L., McCrory, E., Chantiluke, K., Happe, F., & Viding, E. (2014). Neuralbases of Theory of Mind in children with autism spectrum disorders and children with conduct problems and callous-unemotional traits. *Developmental science, 17*(5), 786-796.

Odgers, C. L., Moretti, M. M., Burnette, M. L., Chauhan, P., Waite, D., & Reppucci, N. D. (2007).A latent variable modeling approach to identifying subtypes of serious and violent female juvenile offenders. *Aggress Behav, 33*(4), 339-352. doi:10.1002/ab.20190

Ogilvie, J. M., Stewart, A. L., Chan, R. C., & Shum, D. H. (2011). Neuropsychological measures of executive function and antisocial behavior: A meta-analysis. *Criminology, 49*(4), 1063-1107.

Olbert, C. M., Gala, G. J., & Tupler, L. A. (2014). Quantifying heterogeneity attributable to polythetic diagnostic criteria: theoretical framework and empirical application. *Journal of abnormal psychology, 123*(2), 452.

Oldham, S., Murawski, C., Fornito, A., Youssef, G., Yücel, M., & Lorenzetti, V. (2018). The anticipation and outcome phases of reward and loss processing: A neuroimaging meta- analysis of the monetary incentive delay task. *Human brain mapping, 39*(8), 3398-3418.

Olino, T. M. (2016). Future Research Directions in the Positive Valence Systems: Measurement, Development, and Implications for Youth Unipolar Depression. *J Clin Child Adolesc Psychol, 45*(5), 681-705. doi:10.1080/15374416.2015.1118694

Oliver, B. R., Barker, E. D., Mandy, W. P., Skuse, D. H., & Maughan, B. (2011). Social cognitionand conduct problems: a developmental approach. *Journal of the American Academy of Child & Adolescent Psychiatry, 50*(4), 385-394.

Omalu, B. I., Hamilton, R. L., Kamboh, M. I., DeKosky, S. T., & Bailes, J. (2010). Chronic traumatic encephalopathy (CTE) in a National Football League Player: Case report and emerging medicolegal practice questions. *J Forensic Nurs, 6*(1), 40-46. doi:10.1111/j.1939-

3938.2009.01064.x

Orri, Galera, Turecki, Boivin, Tremblay, Geoffroy, & Côté. (2019). Pathways of Association Between Childhood Irritability and Adolescent Suicidality. *J Am Acad Child Adolesc Psychiatry, 58*(1), 99-107.e103. doi:10.1016/j.jaac.2018.06.034

Orri, M., Galera, C., Turecki, G., Forte, A., Renaud, J., Boivin, M., . . . Geoffroy, M.-C. (2018). Association of childhood irritability and depressive/anxious mood profiles with adolescentsuicidal ideation and attempts. *JAMA psychiatry, 75*(5), 465-473.

Padmala, S., & Pessoa, L. (2010). Interactions between cognition and motivation during response inhibition. *Neuropsychologia, 48*(2), 558-565.

Pagani, L. S., Fitzpatrick, C., Barnett, T. A., & Dubow, E. (2010). Prospective associations between early childhood television exposure and academic, psychosocial, and physical well-being by middle childhood. *Archives of pediatrics & adolescent medicine, 164*(5), 425-431.

Palmer, S. M., Crewther, S. G., & Carey, L. M. (2015). A meta-analysis of changes in brain activityin clinical depression. *Frontiers in Human Neuroscience, 8*, 1045.

Palomero-Gallagher, N., Vogt, B. A., Schleicher, A., Mayberg, H. S., & Zilles, K. (2009). Receptor architecture of human cingulate cortex: evaluation of the four-region neurobiological model. *Human brain mapping, 30*(8), 2336-2355.

Panksepp. (1998). *Affective neuroscience: The foundations of human and animal emotions*. New York, NY, US: Oxford University Press.

Panksepp. (2010). Affective neuroscience of the emotional BrainMind: evolutionary perspectives and implications for understanding depression. *Dialogues Clin Neurosci, 12*(4), 533-545. doi:10.31887/DCNS.2010.12.4/jpanksepp

Panksepp, & Zellner. (2004). Towards a neurobiologically based unified theory of aggression. *REVUE INTERNATIONALE DE PSYCHOLOGIE SOCIALE., 17*, 37-62.

Paquin, S., Lacourse, E., Brendgen, M., Vitaro, F., Dionne, G., Tremblay, R. E., & Boivin, M. (2014). The Genetic-environmental Architecture of Proactive and Reactive Aggression Throughout Childhood. *97*(5-6), 398-420. doi:doi:10.1515/mks-2014-975-609

Pardini, Obradović, & Loeber. (2006). Interpersonal callousness, hyperactivity/impulsivity, inattention, and conduct problems as precursors to delinquency persistence in boys: a comparison of three grade-based cohorts. *J Clin Child Adolesc Psychol, 35*(1), 46-59. doi:10.1207/s15374424jccp3501_5

Pardini, D., & Frick, P. J. (2013). Multiple developmental pathways to conduct disorder: Current conceptualizations and clinical implications. *Journal of the Canadian Academy of Child and Adolescent Psychiatry, 22*(1), 20.

Park, K. J., Lee, J. S., & Kim, H.-W. (2017). Medical and psychiatric comorbidities in korean children and adolescents with attention-deficit/hyperactivity disorder. *Psychiatry Investigation, 14*(6), 817.

Parrott, D. J., & Zeichner, A. (2002). Effects of alcohol and trait anger on physical aggression in men. *J Stud Alcohol, 63*(2), 196-204. doi:10.15288/jsa.2002.63.196

Passamonti, L., Fairchild, G., Goodyer, I. M., Hurford, G., Hagan, C. C., Rowe, J. B., & Calder, J. (2010). Neural abnormalities in early-onset and adolescence-onset conduct disorder. *Archives of general psychiatry, 67*(7), 729-738.

Passingham, D., & Sakai, K. (2004). The prefrontal cortex and working memory: physiology and brain imaging. *Curr Opin Neurobiol, 14*(2), 163-168. doi:10.1016/j.conb.2004.03.003

Patton, J. H., Stanford, M. S., & Barratt, E. S. (1995). Factor structure of the Barratt impulsiveness scale. *J Clin Psychol, 51*(6), 768-774. doi:10.1002/1097-4679(199511)51:6<768::aid-jclp2270510607>3.0.co;2-1

Pechorro, P., DeLisi, M., Andrade, J., Gonçalves, R. A., & Quintas, J. (2021). Primary and secondary variants of psychopathy in incarcerated youth: An investigation with a focus onsocial anxiety.

Deviant Behavior, 1-13.

Pechorro, P., Maroco, J., Ray, J. V., & Gonçalves, R. A. (2015). Psychometric properties of the Barratt Impulsiveness Scale version 11 among a Portuguese sample of incarcerated juvenile offenders. *Psychology, Crime & Law, 21*(9), 854-870. doi:10.1080/1068316X.2015.1054386

Pedregosa, F., Varoquaux, G., Gramfort, A., Michel, V., Thirion, B., Grisel, O., Dubourg, V. (2011). Scikit-learn: Machine learning in Python. *the Journal of machine Learningresearch, 12*, 2825-2830.

Philippi, C. L., Bruss, J., Boes, A. D., Albazron, F. M., Deifelt Streese, C., Ciaramelli, E., . . . Tranel, D. (2021). Lesion network mapping demonstrates that mind-wandering isassociated with the defaultmode network. *J Neurosci Res, 99*(1), 361-373. doi:10.1002/jnr.24648.

Pihl, R. O., Peterson, J. B., & Lau, M. A. (1993). A biosocial model of the alcohol-aggression relationship. *J Stud Alcohol Suppl, 11*, 128-139. doi:10.15288/jsas 1993.s11.128

Pillow, D. R., Pelham, W. E., Jr., Hoza, B., Molina, B. S., & Stultz, C. H. (1998). Confirmatory factor analyses examining attention deficit hyperactivity disorder symptoms and other childhood disruptive behaviors. *J Abnorm Child Psychol, 26*(4), 293-309. doi:10.1023/a:1022658618368

Pine, D. S., Guyer, A. E., & Leibenluft, E. (2008). Functional magnetic resonance imaging and pediatric anxiety. *Journal of the American Academy of Child and Adolescent Psychiatry, 47*(11), 1217.

Pingault, Côté, Vitaro, Falissard, Genolini, & Tremblay. (2014). The developmental course of childhood inattention symptoms uniquely predicts educational attainment: a 16-year longitudinal study. *Psychiatry Res, 219*(3), 707-709. doi:10.1016/j.psychres.2014.06.022

Pingault, J.-B., Côté, S. M., Lacourse, E., Galéra, C., Vitaro, F., & Tremblay, R. E. (2013). Childhood hyperactivity, physical aggression and criminality: a 19-year prospective population-based study.

PloS one, 8(5).

Piotrowska, P. J., Stride, C. B., Croft, S. E., & Rowe, R. (2015). Socioeconomic status and antisocial behaviour among children and adolescents: a systematic review and meta-analysis. Clinical psychology review, 35, 47–55. https://doi.org/10.1016/j.cpr.2014.11.003.

Poeppl, T. B., Donges, M. R., Mokros, A., Rupprecht, R., Fox, P. T., Laird, A. R., . . . Eickhoff, S. (2019). A view behind the mask of sanity: meta-analysis of aberrant brain activity in psychopaths. *Molecular psychiatry, 24*(3), 463.

Polanczyk, G. V., Salum, G. A., Sugaya, L. S., Caye, A., & Rohde, L. A. (2015). Annual research review: A meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. *Journal of Child Psychology and Psychiatry, 56*(3), 345-365.

Poldrack, R. A. (2007). Region of interest analysis for fMRI. *Social cognitive and affective neuroscience, 2*(1), 67-70.

Polier, Vloet, Herpertz-Dahlmann, Laurens, & Hodgins. (2012a). Comorbidity of conduct disorder symptoms and internalising problems in children: investigating a community and a clinicalsample. *Eur Child Adolesc Psychiatry, 21*(1), 31-38. doi:10.1007/s00787-011-0229-6

Polier, Vloet, Herpertz-Dahlmann, Laurens, & Hodgins. (2012b). Comorbidity of conduct disorder symptoms and internalising problems in children: investigating a community and a clinicalsample. *European Child & Adolescent Psychiatry, 21*(1), 31-38.

Polman, H., Orobio de Castro, B., Koops, W., van Boxtel, H. W., & Merk, W. W. (2007). A meta-analysis of the distinction between reactive and proactive aggression in children and adolescents. *J Abnorm Child Psychol, 35*(4), 522-535. doi:10.1007/s10802-007-9109-4

Pondé, M. P., Freire, A. C., & Mendonça, M. S. (2011). The prevalence of mental disorders in prisoners in the city of Salvador, Bahia, Brazil. *Journal of forensic sciences, 56*(3), 679- 682.

Popova, N. K., & Naumenko, V. S. (2013). 5-HT1A receptor as a key player in the brain 5-HT

system. *Rev Neurosci, 24*(2), 191-204. doi:10.1515/revneuro-2012-0082

Portnoy, J., & Farrington, D. P. (2015). Resting heart rate and antisocial behavior: An updated systematic review and meta-analysis. *Aggression and Violent Behavior, 22*, 33-45. doi:https://doi.org/10.1016/j.avb.2015.02.004

Portnoy, J., Raine, A., Chen, F. R., Pardini, D., Loeber, R., & Jennings, J. R. (2014). Heart rate and antisocial behavior: The mediating role of impulsive sensation seeking. *Criminology: An Interdisciplinary Journal, 52*(2), 292-311. doi:10.1111/1745-9125.12038

Potegal, M., & Davidson, R. J. (2003). Temper tantrums in young children: 1. Behavioral composition. *J Dev Behav Pediatr, 24*(3), 140-147. doi:10.1097/00004703-200306000- 00002

Power, J. D., Mitra, A., Laumann, T. O., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. J. N. (2014). Methods to detect, characterize, and remove motion artifact in resting state fMRI. *84*, 320-341.

Pozzi, E., Vijayakumar, N., Rakesh, D., & Whittle, S. (2021). Neural Correlates of Emotion Regulation in Adolescents and Emerging Adults: A Meta-analytic Study. *Biol Psychiatry, 89*(2), 194-204. doi:10.1016/j.biopsych.2020.08.006

Prehn, K., Schlagenhauf, F., Schulze, L., Berger, C., Vohs, K., Fleischer, M., . . . Herpertz, S. C. (2013). Neural correlates of risk taking in violent criminal offenders characterized by emotional hypo-and hyper-reactivity. *Social neuroscience, 8*(2), 136-147.

Pringsheim, T., Hirsch, L., Gardner, D., & Gorman, D. A. (2015a). The pharmacological management of oppositional behaviour, conduct problems, and aggression in children and adolescents with attention-deficit hyperactivity disorder, oppositional defiant disorder, and conduct disorder: a systematic review and meta-analysis. Part 1: psychostimulants, alpha-2 agonists, and atomoxetine. *Can J Psychiatry, 60*(2), 42-51. doi:10.1177/070674371506000202

Pringsheim, T., Hirsch, L., Gardner, D., & Gorman, D. A. (2015b). The pharmacological management of oppositional behaviour, conduct problems, and aggression in children and adolescents with attention-deficit hyperactivity disorder, oppositional defiant disorder, and

conduct disorder: a systematic review and meta-analysis. Part 2: antipsychotics and traditional mood stabilizers. *Can J Psychiatry, 60*(2), 52-61. doi:10.1177/070674371506000203

Pu, W., Luo, Q., Jiang, Y., Gao, Y., Ming, Q., & Yao, S. (2017). Alterations of brain functional architecture associated with psychopathic traits in male adolescents with conduct disorder. *Scientific reports, 7*(1), 1-11.

Puiu, A. A., Wudarczyk, O., Kohls, G., Bzdok, D., Herpertz-Dahlmann, B., & Konrad, K. (2020).Meta-analytic evidence for a joint neural mechanism underlying response inhibition and state anger. *Hum Brain Mapp, 41*(11), 3147-3160. doi:10.1002/hbm.25004

Pujara, M., Motzkin, J. C., Newman, J. P., Kiehl, K. A., & Koenigs, M. (2014). Neural correlates of reward and loss sensitivity in psychopathy. *Soc Cogn Affect Neurosci, 9*(6), 794-801. doi:10.1093/scan/nst054

Pujol, Batalla, Contreras-Rodríguez, Harrison, Pera, Hernández-Ribas, . . . Cardoner. (2012). Breakdown in the brain network subserving moral judgment in criminal psychopathy. *SocCogn Affect Neurosci, 7*(8), 917-923. doi:10.1093/scan/nsr075

Pujol, J., Batalla, I., Contreras-Rodríguez, O., Harrison, B. J., Pera, V., Hernández-Ribas, R., . . . Deus, J. (2012). Breakdown in the brain network subserving moral judgment in criminal psychopathy. *Social cognitive and affective neuroscience, 7*(8), 917-923.

Puts, N. A., Harris, A. D., Mikkelsen, M., Tommerdahl, M., Edden, R. A., & Mostofsky, S. H. (2017). Altered tactile sensitivity in children with attention-deficit hyperactivity disorder. *Journal of neurophysiology, 118*(5), 2568-2578.

Quay, H. C. (1964). Dimensions of personality in delinquent boys as inferred from the factor analysis of case history data. *Child Development, 35*(2), 479-484.

Quay, H. C. (1988). The behavioral reward and inhibition system in childhood behavior disorder. In *Attention deficit disorder, Vol. 3: New research in attention, treatment, and psychopharmacology.* (pp. 176-186). Elmsford, NY, US: Pergamon Press.

Quay, H. C. (1993). The psychobiology of undersocialized aggressive conduct disorder: A theoretical perspective. *Development and psychopathology, 5*(1-2), 165-180. doi:10.1017/S0954579400004326

Radua, J., Borgwardt, S., Crescini, A., Mataix-Cols, D., Meyer-Lindenberg, A., McGuire, P., & Fusar-Poli, P. (2012). Multimodal meta-analysis of structural and functional brain changes in first episode psychosis and the effects of antipsychotic medication. *Neuroscience & Biobehavioral Reviews, 36*(10), 2325-2333.

Radua, J., Mataix-Cols, D., Phillips, M. L., El-Hage, W., Kronhaus, D., Cardoner, N., & Surguladze, S. (2012). A new meta-analytic method for neuroimaging studies that combines reported peak coordinates and statistical parametric maps. *European psychiatry,27*(8), 605-611.

Rae, Hughes, Weaver, Anderson, & Rowe. (2014). Selection and stopping in voluntary action: a meta-analysis and combined fMRI study. *Neuroimage, 86*, 381-391. doi:10.1016/j.neuroimage.2013.10.012

Rae, C. L., Hughes, L. E., Weaver, C., Anderson, M. C., & Rowe, J. B. (2014). Selection and stopping in voluntary action: a meta-analysis and combined fMRI study. *NeuroImage, 86*,381-391.

Rafiei, D., & Kolla, N. J. (2021). DAT1 polymorphism associated with poor decision-making in males with antisocial personality disorder and high psychopathic traits. *Behav Sci Law, 39*(5), 583-596. doi:10.1002/bsl.2537

Raine. (2019). The neuromoral theory of antisocial, violent, and psychopathic behavior. *Psychiatry Res, 277*, 64-69. doi:10.1016/j.psychres.2018.11.025

Raine, & Yang. (2006). Neural foundations to moral reasoning and antisocial behavior. *Soc Cogn Affect Neurosci, 1*(3), 203-213. doi:10.1093/scan/nsl033

Raine, A., Dodge, K., Loeber, R., Gatzke-Kopp, L., Lynam, D., Reynolds, C., . . . Liu, J. (2006). The reactive–proactive aggression questionnaire: Differential correlates of reactive and proactive aggression in adolescent boys. *Aggressive Behavior: Official Journal of the International Society*

for Research on Aggression, 32(2), 159-171.

Raine, A., & Yang, Y. (2006). Neural foundations to moral reasoning and antisocial behavior.*Social cognitive and affective neuroscience, 1*(3), 203-213.

Ramautar, J. R., Slagter, H. A., Kok, A., & Ridderinkhof, K. R. (2006). Probability effects in the stop-signal paradigm: the insula and the significance of failed inhibition. *Brain research, 1105*(1), 143-154.

Ran, G., Cao, X., & Chen, X. (2018). Emotional prediction: An ALE meta-analysis and MACM analysis. *Conscious Cogn, 58*, 158-169. doi:10.1016/j.concog.2017.10.019

Raschle, N. M., Menks, W. M., Fehlbaum, L. V., Tshomba, E., & Stadler, C. (2015). Structural and Functional Alterations in Right Dorsomedial Prefrontal and Left Insular Cortex Co- Localize in Adolescents with Aggressive Behaviour: An ALE Meta-Analysis. *PloS one, 10*(9), e0136553. doi:10.1371/journal.pone.0136553

Ratiu, P., Talos, I. F., Haker, S., Lieberman, D., & Everett, P. (2004). The tale of Phineas Gage, digitally remastered. *J Neurotrauma, 21*(5), 637-643. doi:10.1089/089771504774129964

Regier, D. A., Narrow, W. E., Clarke, D. E., Kraemer, H. C., Kuramoto, S. J., Kuhl, E. A., & Kupfer, D. J. (2013). DSM-5 field trials in the United States and Canada, Part II: test-retest reliability of selected categorical diagnoses. *Am J Psychiatry, 170*(1), 59-70. doi:10.1176/appi.ajp.2012.12070999

Reijntjes, A., Kamphuis, J. H., Prinzie, P., Boelen, P. A., van der Schoot, M., & Telch, M. J. (2011). Prospective linkages between peer victimization and externalizing problems in children: a meta-analysis. Aggressive behavior, 37(3), 215–222. https://doi.org/10.1002/ab.20374.

Ren, F., Li, X., Chen, G., Wang, M. C., & Xia, F. (2020). A taxometric analysis of psychopathy ina Chinese prison sample. *Psych J, 9*(6), 924-933. doi:10.1002/pchj.396

Rey, J. M., Sawyer, M. G., & Prior, M. R. (2005). Similarities and differences between aggressive

and delinquent children and adolescents in a national sample. *Aust N Z J Psychiatry, 39*(5),366-372. doi:10.1080/j.1440-1614.2005.01583.x

Rhee, S. H., Lahey, B. B., & Waldman, I. D. (2015). Comorbidity among dimensions of childhood psychopathology: Converging evidence from behavior genetics. *Child development perspectives, 9*(1), 26-31.

Riedel, M. C., Yanes, J. A., Ray, K. L., Eickhoff, S. B., Fox, P. T., Sutherland, M. T., & Laird, A.R. (2018). Dissociable meta-analytic brain networks contribute to coordinated emotional processing. *Human brain mapping, 39*(6), 2514-2531.

Robinson, J. L., Laird, A. R., Glahn, D. C., Lovallo, W. R., & Fox, P. T. (2010). Metaanalytic connectivity modeling: delineating the functional connectivity of the human amygdala. *Human brain mapping, 31*(2), 173-184.

Roelofs, K., & Dayan, P. (2022). Freezing revisited: coordinated autonomic and central optimization of threat coping. *Nature reviews neuroscience*. doi:10.1038/s41583-022-00608-2

Rogers, Duncan, Lynett, & Sewell. (1994). Prototypical analysis of antisocial personality disorder.*Law and human behavior, 18*(4), 471-484. doi:10.1007/BF01499051

Rogers, J. C., & De Brito, S. A. (2016). Cortical and subcortical gray matter volume in youths with conduct problems: a meta-analysis. *JAMA psychiatry, 73*(1), 64-72.

Romer, A. L., Elliott, M. L., Knodt, A. R., Sison, M. L., Ireland, D., Houts, R., . . . Melzer, T. R. (2020). Pervasively thinner neocortex as a transdiagnostic feature of general psychopathology. *American Journal of Psychiatry*, appi. ajp. 2020.19090934.

Romer, A. L., Knodt, A. R., Houts, R., Brigidi, B. D., Moffitt, T. E., Caspi, A., & Hariri, A. R. (2018). Structural alterations within cerebellar circuitry are associated with general liabilityfor common mental disorders. *Molecular psychiatry, 23*(4), 1084-1090.

Romer, A. L., Knodt, A. R., Sison, M. L., Ireland, D., Houts, R., Ramrakha, S., . . . Moffitt, T. E. (2019).

Replicability of structural brain alterations associated with general psychopathology: evidence from a population-representative birth cohort. *Molecular psychiatry*, 1-8.

Roos, L. E., Fisher, P. A., Shaw, D. S., Kim, H. K., Neiderhiser, J. M., Reiss, D., . . . Leve, L. D. (2016). Inherited and environmental influences on a childhood co-occurring symptom phenotype: Evidence from an adoption study. *Dev Psychopathol, 28*(1), 111-125. doi:10.1017/s0954579415000322

Rosell, D. R., & Siever, L. J. (2015). The neurobiology of aggression and violence. *CNS Spectr, 20*(3), 254-279. doi:10.1017/s109285291500019x

Rösler, M., Retz, W., Yaqoobi, K., Burg, E., & Retz-Junginger, P. (2009). Attention deficit/hyperactivity disorder in female offenders: prevalence, psychiatric comorbidity and psychosocial implications. *Eur Arch Psychiatry Clin Neurosci, 259*(2), 98-105. doi:10.1007/s00406-008-0841-8

Ross, & Margolis. (2018). Research Domain Criteria: Cutting Edge Neuroscience or Galen's Humors Revisited? *Mol Neuropsychiatry, 4*(3), 158-163. doi:10.1159/000493685

Ross, Roule, Deveney, Towbin, Brotman, Leibenluft, & Tseng. (2020). A preliminary study on functional activation and connectivity during frustration in youths with bipolar disorder. *Bipolar Disorders*.

Rottschy, C., Eickhoff, S. B., Schleicher, A., Mohlberg, H., Kujovic, M., Zilles, K., & Amunts, K.(2007). Ventral visual cortex in humans: cytoarchitectonic mapping of two extrastriate areas. *Human brain mapping, 28*(10), 1045-1059.

Rottschy, C., Langner, R., Dogan, I., Reetz, K., Laird, A. R., Schulz, J. B., . . . Eickhoff, S. B. (2012). Modelling neural correlates of working memory: a coordinate-based meta-analysis.*Neuroimage, 60*(1), 830-846.

Rowe, R., Maughan, B., Pickles, A., Costello, E. J., & Angold, A. (2002). The relationship between DSM-IV oppositional defiant disorder and conduct disorder: findings from the Great Smoky

Mountains Study. *J Child Psychol Psychiatry, 43*(3), 365-373. doi:10.1111/1469- 7610.00027

Rubia, K. (2018). Cognitive neuroscience of attention deficit hyperactivity disorder (ADHD) and its clinical translation. *Frontiers in Human Neuroscience, 12*, 100.

Sadeh, T., Shohamy, D., Levy, D. R., Reggev, N., & Maril, A. (2011). Cooperation between the hippocampus and the striatum during episodic encoding. *Journal of Cognitive Neuroscience, 23*(7), 1597-1608.

Sakai, J. T., Dalwani, M. S., Mikulich-Gilbertson, S. K., Raymond, K., McWilliams, S., Tanabe, J., . . . Crowley, T. J. (2017). Imaging decision about whether to benefit self by harming others: Adolescents with conduct and substance problems, with or without callous- unemotionality, or developing typically. *Psychiatry Research: Neuroimaging, 263*, 103- 112.

Salekin, R. T., Rosenbaum, J., & Lee, Z. (2008). Child and adolescent psychopathy: Stability and change. *Psychiatry, Psychology and Law, 15*(2), 224-236.

Salimi-Khorshidi, G., Smith, S. M., Keltner, J. R., Wager, T. D., & Nichols, T. E. (2009). Meta-analysis of neuroimaging data: a comparison of image-based and coordinate-based poolingof studies. *Neuroimage, 45*(3), 810-823.

Salla, J., Michel, G., Pingault, J. B., Lacourse, E., Paquin, S., Galéra, C., . . . Côté, S. M. (2016). Childhood trajectories of inattention-hyperactivity and academic achievement at 12 years.*Eur Child Adolesc Psychiatry, 25*(11), 1195-1206. doi:10.1007/s00787-016-0843-4

Sallet, J., Mars, R. B., Noonan, M. P., Neubert, F.-X., Jbabdi, S., O'Reilly, J. X., . . . Rushworth, M. F. (2013). The organization of dorsal frontal cortex in humans and macaques. *Journal of Neuroscience, 33*(30), 12255-12274.

Salo, T., Bottenhorn, K. L., Nichols, T. E., Riedel, M. C., Sutherland, M. T., Yarkoni, T., & Laird, A.R. (2018). NiMARE: a neuroimaging meta-analysis research environment. *F1000Research, 7*.

Samea, F., Soluki, S., Nejati, V., Zarei, M., Cortese, S., Eickhoff, S. B., . . . Eickhoff, C. R. (2019).Brain

alterations in children/adolescents with ADHD revisited: A neuroimaging meta- analysis of 96 structural and functional studies. *Neuroscience & Biobehavioral Reviews, 100*, 1-8.

Sasser, T. R., Beekman, C. R., & Bierman, K. L. (2015). Preschool executive functions, single- parent status, and school quality predict diverging trajectories of classroom inattention in elementary school. *Dev Psychopathol, 27*(3), 681-693. doi:10.1017/s0954579414000947

Scerbo, A., Raine, A., O'Brien, M., Chan, C. J., Rhee, C., & Smiley, N. (1990). Reward dominanceand passive avoidance learning in adolescent psychopaths. *J Abnorm Child Psychol, 18*(4),451-463. doi:10.1007/bf00917646

Schaefer, A., Kong, R., Gordon, E. M., Laumann, T. O., Zuo, X.-N., Holmes, A. J., . . . Yeo, B. T.(2018). Local-global parcellation of the human cerebral cortex from intrinsic functional connectivity MRI. *Cerebral Cortex, 28*(9), 3095-3114.

Schiffer, B., Pawliczek, C., Müller, B. W., Wiltfang, J., Brüne, M., Forsting, M., . . . Hodgins, S. (2017). Neural mechanisms underlying affective theory of mind in violent antisocial personality disorder and/or schizophrenia. *Schizophrenia bulletin, 43*(6), 1229-1239.

Schmaal, L., van Harmelen, A.-L., Chatzi, V., Lippard, E. T., Toenders, Y. J., Averill, L. A., . . . Blumberg, H. P. (2020). Imaging suicidal thoughts and behaviors: a comprehensive reviewof 2 decades of neuroimaging studies. *Molecular psychiatry, 25*(2), 408-427.

Schönenberg, M., Louis, K., Mayer, S., & Jusyte, A. (2013). Impaired identification of threat-related social information in male delinquents with antisocial personality disorder. Journal of personality disorders, 27(4), 496–505.

Schreuders, E., Klapwijk, E. T., Will, G.-J., & Güroğlu, B. (2018). Friend versus foe: Neural correlates of prosocial decisions for liked and disliked peers. *Cognitive, Affective, & Behavioral Neuroscience, 18*(1), 127-142.

Schüller, C. B., Kuhn, J., Jessen, F., & Hu, X. (2019). Neuronal correlates of delay discounting in healthy subjects and its implication for addiction: an ALE meta-analysis study. *Am J DrugAlcohol*

Abuse, 45(1), 51-66. doi:10.1080/00952990.2018.1557675

Schultz, W. (2016). Dopamine reward prediction error coding. *Dialogues Clin Neurosci, 18*(1), 23-32. doi:10.31887/DCNS.2016.18.1/wschultz

Schurz, Aichhorn, Martin, & Perner. (2013). Common brain areas engaged in false belief reasoning and visual perspective taking: a meta-analysis of functional brain imaging studies. *Frontiers in Human Neuroscience, 7*, 712.

Schurz, Radua, Tholen, Maliske, Margulies, Mars, . . . Kanske. (2021). Toward a hierarchical model of social cognition: A neuroimaging meta-analysis and integrative review of empathy and theory of mind. *Psychol Bull, 147*(3), 293-327. doi:10.1037/bul0000303

Schurz, M., Radua, J., Aichhorn, M., Richlan, F., & Perner, J. (2014). Fractionating theory of mind:a meta-analysis of functional brain imaging studies. *Neuroscience & Biobehavioral Reviews, 42*, 9-34.

Schwarzlose, R. F., Tillman, R., Hoyniak, C. P., Luby, J. L., & Barch, D. M. (2023). Sensory Over-responsivity: A Feature of Childhood Psychiatric Illness Associated With Altered Functional Connectivity of Sensory Networks. Biological psychiatry, 93, 92–101.

Seara-Cardoso, A., & Viding, E. (2015). Functional Neuroscience of Psychopathic Personality in Adults. *J Pers, 83*(6), 723-737. doi:10.1111/jopy.12113

Sebastian, McCrory, Cecil, Lockwood, De Brito, Fontaine, & Viding. (2012). Neural responses to affective and cognitive theory of mind in children with conduct problems and varying levelsof callous-unemotional traits. *Archives of general psychiatry, 69*(8), 814-822.

Sebastian, McCrory, Dadds, Cecil, Lockwood, Hyde, . . . Viding. (2014). Neural responses to fearful eyes in children with conduct problems and varying levels of callous–unemotional traits. *Psychological medicine, 44*(1), 99-109.

Sebastian, C., McCrory, E., Dadds, M., Cecil, C., Lockwood, P., Hyde, Z., . . . Viding, E. (2014). Neural

responses to fearful eyes in children with conduct problems and varying levels of callous–unemotional traits. *Psychological medicine, 44*(1), 99-109.

Séguin. (2004). Neurocognitive elements of antisocial behavior: Relevance of an orbitofrontal cortex account. *Brain Cogn, 55*(1), 185-197. doi:10.1016/s0278-2626(03)00273-2

Séguin. (2009). The frontal lobe and aggression. *Eur J Dev Psychol, 6*(1), 100-119. doi:10.1080/17405620701669871

Séguin, & Tremblay. (2013). 507Aggression and Antisocial Behavior: A Developmental Perspective. In *The Oxford Handbook of Developmental Psychology, Vol. 2: Self and Other*(pp. 0). doi:10.1093/oxfordhb/9780199958474.013.0020

Séguin, J. R., Sylvers, P., & Lilienfeld, S. O. (2007). The neuropsychology of violence. *The Cambridge handbook of violent behavior and aggression*, 187-214.

Seo, D., Patrick, C. J., & Kennealy, P. J. (2008). Role of Serotonin and Dopamine System Interactions in the Neurobiology of Impulsive Aggression and its Comorbidity with other Clinical Disorders. *Aggress Violent Behav, 13*(5), 383-395. doi:10.1016/j.avb.2008.06.003

Servaas, M. N., van der Velde, J., Costafreda, S. G., Horton, P., Ormel, J., Riese, H., & Aleman, A. (2013). Neuroticism and the brain: a quantitative meta-analysis of neuroimaging studies investigating emotion processing. *Neurosci Biobehav Rev, 37*(8), 1518-1529. doi:10.1016/j.neubiorev.2013.05.005

Sescousse, G., Caldú, X., Segura, B., & Dreher, J. C. (2013). Processing of primary and secondary rewards: a quantitative meta-analysis and review of human functional neuroimaging studies. *Neurosci Biobehav Rev, 37*(4), 681-696. doi:10.1016/j.neubiorev.2013.02.002

Sethi, A., O'Nions, E., McCrory, E., Bird, G., & Viding, E. (2018). An fMRI investigation of empathic processing in boys with conduct problems and varying levels of callous- unemotional traits. *NeuroImage: Clinical, 18*, 298-304.

Shackman, A. J., Salomons, T. V., Slagter, H. A., Fox, A. S., Winter, J. J., & Davidson, R. J. (2011). The integration of negative affect, pain and cognitive control in the cingulate cortex. *Nat Rev Neurosci, 12*(3), 154-167. doi:10.1038/nrn2994

Shader, M. (2001). Risk factors for delinquency: An overview: US Department of Justice. Office of Justice Programs, Office of Juvenile Justice and Delinquency Prevention.

Shahrestani, S., Kemp, A. H., & Guastella, A. J. (2013). The impact of a single administration of intranasal oxytocin on the recognition of basic emotions in humans: a meta-analysis. *Neuropsychopharmacology, 38*(10), 1929-1936. doi:10.1038/npp.2013.86

Shanmugan, S., Wolf, D. H., Calkins, M. E., Moore, T. M., Ruparel, K., Hopson, R. D., . . . Jackson, C. (2016). Common and dissociable mechanisms of executive system dysfunction across psychiatric disorders in youth. *American Journal of Psychiatry, 173*(5), 517-526.

Shannon, Raichle, Snyder, Fair, Mills, Zhang, . . . Kiehl. (2011). Premotor functional connectivity predicts impulsivity in juvenile offenders. *Proc Natl Acad Sci U S A, 108*(27), 11241- 11245. doi:10.1073/pnas.1108241108

Shannon, B. J., Raichle, M. E., Snyder, A. Z., Fair, D. A., Mills, K. L., Zhang, D., . . . Nagel, B. J.(2011). Premotor functional connectivity predicts impulsivity in juvenile offenders. *Proceedings of the National Academy of Sciences, 108*(27), 11241-11245.

Sharp, C., van Goozen, S., & Goodyer, I. (2006). Children's subjective emotional reactivity to affective pictures: Gender differences and their antisocial correlates in an unselected sample of 7-11-year-olds. Journal of Child Psychology and Psychiatry, 47(2), 143–150. https://doi.org/10.1111/j.1469-7610.2005.01464.x

Shiba, Y., Kim, C., Santangelo, A. M., & Roberts, A. C. (2015). Lesions of either anterior orbitofrontal cortex or ventrolateral prefrontal cortex in marmoset monkeys heighten innatefear and attenuate active coping behaviors to predator threat. *Frontiers in systems neuroscience, 8*, 250.

Shiroma, E. J., Ferguson, P. L., & Pickelsimer, E. E. (2012). Prevalence of traumatic brain injury in an offender population: a meta-analysis. *J Head Trauma Rehabil, 27*(3), E1-10. doi:10.1097/HTR.0b013e3182571c14

Shulman, G. L., Corbetta, M., Buckner, R. L., Fiez, J. A., Miezin, F. M., Raichle, M. E., & Petersen,

S. E. (1997). Common blood flow changes across visual tasks: I. Increases in subcortical structures and cerebellum but not in nonvisual cortex. *Journal of Cognitive Neuroscience,9*(5), 624-647.

Siddiqi, S. H., Kording, K. P., Parvizi, J., & Fox, M. D. (2022). Causal mapping of human brain function. *Nat Rev Neurosci, 23*(6), 361-375. doi:10.1038/s41583-022-00583-8

Siegel, A., & Victoroff, J. (2009). Understanding human aggression: New insights from neuroscience. *Int J Law Psychiatry, 32*(4), 209-215. doi:10.1016/j.ijlp.2009.06.001

Siep, N., Tonnaer, F., van de Ven, V., Arntz, A., Raine, A., & Cima, M. (2019). Anger provocation increases limbic and decreases medial prefrontal cortex connectivity with the left amygdalain reactive aggressive violent offenders. *Brain Imaging and behavior, 13*(5), 1311-1323.

Sigvardsson, S., Bohman, M., & Cloninger, C. R. (1987). Structure and stability of childhood personality: prediction of later social adjustment. *Journal of Child Psychology and Psychiatry, 28*(6), 929-946.

Sijtsema, J. J., Veenstra, R., Lindenberg, S., van Roon, A. M., Verhulst, F. C., Ormel, J., & Riese, H. (2010). Mediation of sensation seeking and behavioral inhibition on the relationship between heart rate and antisocial behavior: the TRAILS study. *J Am Acad Child Adolesc Psychiatry, 49*(5), 493-502. doi:10.1097/00004583-201005000-00010

Silverman, M. H., Jedd, K., & Luciana, M. (2015). Neural networks involved in adolescent reward processing: An activation likelihood estimation meta-analysis of functional neuroimaging studies. *Neuroimage, 122*, 427-439. doi:10.1016/j.neuroimage.2015.07.083

Simard, V., Nielsen, T. A., Tremblay, R. E., Boivin, M., & Montplaisir, J. Y. (2008). Longitudinalstudy

of preschool sleep disturbance: the predictive role of maladaptive parental behaviors, early sleep problems, and child/mother psychological factors. *Archives of pediatrics & adolescent medicine, 162*(4), 360-367.

Simmonds, D. J., Pekar, J. J., & Mostofsky, S. H. (2008). Meta-analysis of Go/No-go tasks demonstrating that fMRI activation associated with response inhibition is task-dependent. *Neuropsychologia, 46*(1), 224-232. doi:10.1016/j.neuropsychologia.2007.07.015

Simonoff, E., Pickles, A., Meyer, J. M., Silberg, J. L., Maes, H. H., Loeber, R., . . . Eaves, L. J. (1997). The Virginia Twin Study of Adolescent Behavioral Development. Influences of age, sex, and impairment on rates of disorder. *Arch Gen Psychiatry, 54*(9), 801-808. doi:10.1001/archpsyc.1997.01830210039004

Skeem, J. L., Poythress, N., Edens, J. F., Lilienfeld, S. O., & Cale, E. M. (2003). Psychopathic personality or personalities? Exploring potential variants of psychopathy and their implications for risk assessment. *Aggression and Violent Behavior, 8*(5), 513-546. doi:https://doi.org/10.1016/S1359-1789(02)00098-8

Smeets, K. C., Oostermeijer, S., Lappenschaar, M., Cohn, M., van der Meer, J. M., Popma, A.,. Buitelaar, J. K. (2017). Are Proactive and Reactive Aggression Meaningful Distinctions in Adolescents? A Variable- and Person-Based Approach. *J Abnorm Child Psychol, 45*(1), 1-14. doi:10.1007/s10802-016-0149-5

Smith, Rosenbaum, Botdorf, Steinberg, & Chein. (2018). Peers influence adolescent reward processing, but not response inhibition. *Cognitive, Affective, & Behavioral Neuroscience, 18*(2), 284-295. doi:10.3758/s13415-018-0569-5

Smith, S. M., & Nichols, T. E. (2009). Threshold-free cluster enhancement: addressing problems of smoothing, threshold dependence and localisation in cluster inference. *NeuroImage, 44*(1), 83-98.

Sobanski, E., Banaschewski, T., Asherson, P., Buitelaar, J., Chen, W., Franke, B., . . . Sonuga- Barke, E. (2010). Emotional lability in children and adolescents with attention deficit/hyperactivity

disorder (ADHD): clinical correlates and familial prevalence. *Journal of Child Psychology and Psychiatry, 51*(8), 915-923.

Solmi, M., Radua, J., Olivola, M., Croce, E., Soardo, L., de Pablo, G. S., . . . Kim, J. H. (2021). Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies. *Molecular psychiatry*, 1-15.

Song, S., Zilverstand, A., Song, H., d'Oleire Uquillas, F., Wang, Y., Xie, C., . . . Zou, Z. (2017). The influence of emotional interference on cognitive control: A meta-analysis of neuroimaging studies using the emotional Stroop task. *Sci Rep, 7*(1), 2088. doi:10.1038/s41598-017-02266-2

Sonuga-Barke, E. J., Cortese, S., Fairchild, G., & Stringaris, A. (2016). Annual Research Review: Transdiagnostic neuroscience of child and adolescent mental disorders–differentiating decision making in attention-deficit/hyperactivity disorder, conduct disorder, depression, and anxiety. *Journal of Child Psychology and Psychiatry, 57*(3), 321-349.

Sorella, S., Grecucci, A., Piretti, L., & Job, R. (2021). Do anger perception and the experience of anger share common neural mechanisms? Coordinate-based meta-analytic evidence of similar and different mechanisms from functional neuroimaging studies. *Neuroimage*, 117777.

Sosa, R., Mata-Luévanos, J., & Buenrostro-Jáuregui, M. (2021). The Role of the Lateral Habenula in Inhibitory Learning from Reward Omission. *ENeuro, 8*(3). doi:10.1523/eneuro.0016- 21.2021

Sperber, C., & Dadashi, A. (2020). The influence of sample size and arbitrary statistical thresholds in lesion-network mapping. *Brain, 143*(5), e40-e40. doi:10.1093/brain/awaa094

Spreng, R. N., & Mar, R. A. (2012). I remember you: a role for memory in social cognition and the functional neuroanatomy of their interaction. *Brain research, 1428*, 43-50.

Spreng, R. N., Mar, R. A., & Kim, A. S. (2009). The common neural basis of autobiographical memory, prospection, navigation, theory of mind, and the default mode: a quantitative meta-analysis. *Journal of Cognitive Neuroscience, 21*(3), 489-510.

Sprooten, E., Rasgon, A., Goodman, M., Carlin, A., Leibu, E., Lee, W. H., & Frangou, S. (2017). Addressing reverse inference in psychiatric neuroimaging: Meta-analyses of task-related brain activation in common mental disorders. *Human brain mapping, 38*(4), 1846-1864.

Stahl, S. M. (2014). Deconstructing violence as a medical syndrome: mapping psychotic, impulsive, and predatory subtypes to malfunctioning brain circuits. *CNS Spectr, 19*(5), 357-365. doi:10.1017/s1092852914000522

Stanger, C., Achenbach, T. M., & Verhulst, F. C. (1997). Accelerated longitudinal comparisons of aggressive versus delinquent syndromes. *Development and psychopathology, 9*(1), 43-58.

Sterne, J. A., Sutton, A. J., Ioannidis, J. P., Terrin, N., Jones, D. R., Lau, J., . . . Schmid, C. H. (2011). Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *Bmj, 343*, d4002.

Stringaris, A. (2011). Irritability in children and adolescents: a challenge for DSM-5. *Eur Child Adolesc Psychiatry, 20*(2), 61-66. doi:10.1007/s00787-010-0150-4

Stringaris, A., Goodman, R., Ferdinando, S., Razdan, V., Muhrer, E., Leibenluft, E., & Brotman, M. A. (2012). The Affective Reactivity Index: a concise irritability scale for clinical and research settings. *Journal of child psychology and psychiatry, and allied disciplines*, *53*(11), 1109–1117. https://doi.org/10.1111/j.1469-7610.2012.02561.x

Stringaris, A., Vidal-Ribas, P., Brotman, M. A., & Leibenluft, E. (2018). Practitioner Review: Definition, recognition, and treatment challenges of irritability in young people. *Journal ofChild Psychology and Psychiatry, 59*(7), 721-739.

Sukhodolsky, D. G., Ibrahim, K., Kalvin, C. B., Jordan, R. P., Eilbott, J., & Hampson, M. (2022). Increased amygdala and decreased frontolimbic r esting- s tate functional connectivity in children with aggressive behavior. *Soc Cogn Affect Neurosci, 17*(7), 634-644. doi:10.1093/scan/nsab128

Sullivan, P. F., Daly, M. J., & O'donovan, M. (2012). Genetic architectures of psychiatric disorders: the emerging picture and its implications. *Nature Reviews Genetics, 13*(8), 537-551.

Sutcubasi, B., Metin, B., Kurban, M. K., Metin, Z. E., Beser, B., & Sonuga-Barke, E. (2020). Resting-state network dysconnectivity in ADHD: A system-neuroscience-based meta-analysis. *The World Journal of Biological Psychiatry*, 1-74.

Swann, A. C., Lijffijt, M., Lane, S. D., Steinberg, J. L., & Moeller, F. G. (2009). Trait impulsivity and response inhibition in antisocial personality disorder. *J Psychiatr Res, 43*(12), 1057- 1063. doi:10.1016/j.jpsychires.2009.03.003

Swanson, J. M., Schuck, S., Porter, M. M., Carlson, C., Hartman, C. A., Sergeant, J. A., Clevenger, W., Wasdell, M., McCleary, R., Lakes, K., & Wigal, T. (2012). Categorical and Dimensional Definitions and Evaluations of Symptoms of ADHD: History of the SNAP and the SWAN Rating Scales. *The International journal of educational and psychological assessment*, *10*(1), 51–70.

Swick, D., Ashley, V., & Turken, U. (2011). Are the neural correlates of stopping and not going identical? Quantitative meta-analysis of two response inhibition tasks. *Neuroimage, 56*(3),1655-1665. doi:10.1016/j.neuroimage.2011.02.070

Sylvester, C. M., Yu, Q., Srivastava, A. B., Marek, S., Zheng, A., Alexopoulos, D., . . . Dierker, D.L. (2020). Individual-specific functional connectivity of the amygdala: A substrate forprecision psychiatry. *Proceedings of the National Academy of Sciences, 117*(7), 3808-3818. Tackett, Krueger, Iacono, & McGue. (2005). Symptom-based subfactors of DSM-defined conductdisorder: evidence for etiologic distinctions. *Journal of abnormal psychology, 114*(3), 483. Tackett, Krueger, Sawyer, & Graetz. (2003). Subfactors of DSM-IV conduct disorder: Evidenceand connections with syndromes from the Child Behavior Checklist. *Journal of abnormal child psychology, 31*(6), 647-654. doi:10.1023/A:1026214324287

Tackett, J. L., Lahey, B. B., Van Hulle, C., Waldman, I., Krueger, R. F., & Rathouz, P. J. (2013). Common genetic influences on negative emotionality and a general psychopathology factorin childhood and adolescence. *Journal of abnormal psychology, 122*(4), 1142.

Tao, Wang, Zhu, & Cai. (2021). Bilingualism and domain-general cognitive functions from a neural perspective: A systematic review. *Neurosci Biobehav Rev, 125*, 264-295.

doi:10.1016/j.neubiorev.2021.02.029

Tao, D., He, Z., Lin, Y., Liu, C., & Tao, Q. (2021). Where does fear originate in the brain? A coordinate-based meta-analysis of explicit and implicit fear processing. *Neuroimage, 227*, 117686. doi:10.1016/j.neuroimage.2020.117686

Taschereau-Dumouchel, V., Kawato, M., & Lau, H. (2020). Multivoxel pattern analysis reveals dissociations between subjective fear and its physiological correlates. *Mol Psychiatry, 25*(10), 2342-2354. doi:10.1038/s41380-019-0520-3

Taschereau-Dumouchel, V., Michel, M., Lau, H., Hofmann, S. G., & LeDoux, J. E. (2022). Puttingthe "mental" back in "mental disorders": a perspective from research on fear and anxiety. *Mol Psychiatry, 27*(3), 1322-1330. doi:10.1038/s41380-021-01395-5

Taubert, J., Flessert, M., Wardle, S. G., Basile, B. M., Murphy, A. P., Murray, E. A., & Ungerleider,

L. G. (2018). Amygdala lesions eliminate viewing preferences for faces in rhesus monkeys. *Proc Natl Acad Sci U S A, 115*(31), 8043-8048. doi:10.1073/pnas.1807245115

Terbeck, S., Case, C., Turner, J., Spencer, V., Bacon, A., Howard, C., & Howard, I. S. (2022). Assessing reactive violence using immersive virtual reality. *PloS one, 17*(5), e0268191.

Thomson, & Centifanti. (2018). Proactive and Reactive Aggression Subgroups in Typically Developing Children: The Role of Executive Functioning, Psychophysiology, and Psychopathy. *Child Psychiatry Hum Dev, 49*(2), 197-208. doi:10.1007/s10578-017-0741- 0

Thomson, N. D., & Centifanti, L. C. M. (2018). Proactive and Reactive Aggression Subgroups in Typically Developing Children: The Role of Executive Functioning, Psychophysiology, and Psychopathy. *Child Psychiatry & Human Development, 49*(2), 197-208. doi:10.1007/s10578-017-0741-0

Tian, J., & Uchida, N. (2015). Habenula Lesions Reveal that Multiple Mechanisms Underlie Dopamine Prediction Errors. *Neuron, 87*(6), 1304-1316. doi:10.1016/j.neuron.2015.08.028

Tiihonen, J., Koskuvi, M., Lähteenvuo, M., Virtanen, P. L. J., Ojansuu, I., Vaurio, O., . . . Lehtonen,Š. (2020). Neurobiological roots of psychopathy. *Mol Psychiatry, 25*(12), 3432-3441.

doi:10.1038/s41380-019-0488-z

Timmers, I., Park, A. L., Fischer, M. D., Kronman, C. A., Heathcote, L. C., Hernandez, J. M., & Simons, L. E. (2018). Is Empathy for Pain Unique in Its Neural Correlates? A Meta- Analysis of Neuroimaging Studies of Empathy. *Front Behav Neurosci, 12*, 289. doi:10.3389/fnbeh.2018.00289

Tippett, D. C., Godin, B. R., Oishi, K., Oishi, K., Davis, C., Gomez, Y., . . . Hillis, A. E. (2018). Impaired Recognition of Emotional Faces after Stroke Involving Right Amygdala or Insula.*Semin Speech Lang, 39*(1), 87-100. doi:10.1055/s-0037-1608859

Tonkonogy, J. M. (1991). Violence and temporal lobe lesion: head CT and MRI data. *J Neuropsychiatry Clin Neurosci, 3*(2), 189-196. doi:10.1176/jnp.3.2.189

Topping, R. (1941). Case studies of aggressive delinquents. *American Journal of Orthopsychiatry, 11*(3), 485-492. doi:10.1111/j.1939-0025.1941.tb05831.x

Tremblay, Japel, Pérusse, McDuff, Boivin, Zoccolillo, & Montplaisir. (1999). The search for the age of 'onset' of physical aggression: Rousseau and Bandura revisited. *Criminal Behaviourand Mental Health, 9*(1), 8-23. doi:10.1002/cbm.288

Tremblay, Nagin, Séguin, Zoccolillo, Zelazo, Boivin, . . . Japel. (2004). Physical aggression during early childhood: Trajectories and predictors. *Pediatrics, 114*(1), e43-e50.

Tremblay, Pihl, Vitaro, & Dobkin. (1994). Predicting early onset of male antisocial behavior from preschool behavior. *Arch Gen Psychiatry, 51*(9), 732-739. doi:10.1001/archpsyc.1994.03950090064009

Tremblay, R. E. (2010). Developmental origins of disruptive behaviour problems: the 'original sin'hypothesis, epigenetics and their consequences for prevention. *Journal of Child Psychology*

and Psychiatry, 51(4), 341-367.

Tremblay, R. E., Pihl, R. O., Vitaro, F., & Dobkin, P. L. (1994). Predicting early onset of male antisocial behavior from preschool behavior. *Archives of general psychiatry, 51*(9), 732- 739.

Tseng, W. L., Deveney, C. M., Stoddard, J., Kircanski, K., Frackman, A. E., Yi, J. Y., . . .Leibenluft, E. (2019). Brain Mechanisms of Attention Orienting Following Frustration: Associations With Irritability and Age in Youths. *Am J Psychiatry, 176*(1), 67-76. doi:10.1176/appi.ajp.2018.18040491

Tseng, W. L., Kawabata, Y., Gau, S. S., Banny, A. M., Lingras, K. A., & Crick, N. R. (2012). Relations of inattention and hyperactivity/impulsivity to preadolescent peer functioning: the mediating roles of aggressive and prosocial behaviors. *J Clin Child Adolesc Psychol, 41*(3), 275-287. doi:10.1080/15374416.2012.656556

Ttofi, M. M., Farrington, D. P., & Lösel, F. (2012). School bullying as a predictor of violence laterin life: A systematic review and meta-analysis of prospective longitudinal studies. *Aggression and Violent Behavior, 17*(5), 405-418.

Tully, Gabay, Brown, Murphy, & Blackwood. (2018). The effect of intranasal oxytocin on neural response to facial emotions in healthy adults as measured by functional MRI: A systematicreview. *Psychiatry Res Neuroimaging, 272*, 17-29. doi:10.1016/j.pscychresns.2017.11.017

Tully, Sethi, Griem, Paloyelis, Craig, Williams, Blackwood. (2022). *Oxytocin normalises theimplicit processing of fearful faces in psychopathy: a randomised crossover study using fMRI*.

Tulving, E., & Markowitsch, H. J. (1998). Episodic and declarative memory: role of the hippocampus. *Hippocampus, 8*(3), 198-204.

Turtonen, O., Saarinen, A., Nummenmaa, L., Tuominen, L., Tikka, M., Armio, R. L.,Hietala,J. (2021). Adult Attachment System Links With Brain Mu Opioid Receptor AvailabilityIn Vivo. *Biol Psychiatry Cogn Neurosci Neuroimaging, 6*(3), 360-369. doi:10.1016/j.bpsc.2020.10.013.

Tuvblad, C., Raine, A., Zheng, M., & Baker, L. A. (2009). Genetic and environmental stability differs in reactive and proactive aggression. *Aggress Behav, 35*(6), 437-452. doi:10.1002/ab.20319

Tuvblad, C., Grann, M., & Lichtenstein, P. (2006). Heritability for adolescent antisocial behavior differs with socioeconomic status: gene-environment interaction. Journal of child psychology and psychiatry, and allied disciplines, 47(7), 734–743. https://doi.org/10.1111/j.1469-7610.2005.01552.x

Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., . . .Joliot, M. (2002). Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *NeuroImage, 15*(1), 273-289.

Uddin, Yeo, & Spreng. (2019). Towards a universal taxonomy of macro-scale functional human brain networks. *Brain topography, 32*(6), 926-942.

Uddin, L. Q. (2015). Salience processing and insular cortical function and dysfunction. *Nat Rev Neurosci, 16*(1), 55-61. doi:10.1038/nrn3857

Umbach, R. H., & Tottenham, N. (2020). Callous-unemotional traits and reduced default mode network connectivity within a community sample of children. *Development and psychopathology*, 1-14.

Underwood, M. K., Beron, K. J., & Rosen, L. H. (2011). Joint trajectories for social and physical aggression as predictors of adolescent maladjustment: internalizing symptoms, rule- breaking behaviors, and borderline and narcissistic personality features. *Dev Psychopathol,23*(2), 659-678. doi:10.1017/s095457941100023x

Vachon, D. D., Lynam, D. R., & Johnson, J. A. (2014). The (non)relation between empathy and aggression: surprising results from a meta-analysis. *Psychol Bull, 140*(3), 751-773. doi:10.1037/a0035236

Van Dam, N. T., O'Connor, D., Marcelle, E. T., Ho, E. J., Craddock, R. C., Tobe, R. H., . . . Leventhal, B. L. (2017). Data-driven phenotypic categorization for neurobiological analyses: beyond DSM-5 labels. *Biological psychiatry, 81*(6), 484-494.

van Dijk, J. J. M. (2010). Revisiting the 'dark number of crime. In *Revisiting the 'dark number of crime'. In M. Herzog-Evans (Ed.), Transnational Criminology Manual.* : Wolf Legal Publishers (WLP).

Van IJzendoorn, & Bakermans-Kranenburg. (2012). A sniff of trust: meta-analysis of the effects of intranasal oxytocin administration on face recognition, trust to in-group, and trust to out-group. *Psychoneuroendocrinology, 37*(3), 438-443. doi:10.1016/j.psyneuen.2011.07.008

van Lier, P. A., Vitaro, F., Barker, E. D., Koot, H. M., & Tremblay, R. E. (2009). Developmental links between trajectories of physical violence, vandalism, theft, and alcohol-drug use fromchildhood to adolescence. *J Abnorm Child Psychol, 37*(4), 481-492. doi:10.1007/s10802- 008-9289-6

van Lith, K., Veltman, D. J., Cohn, M. D., Pape, L. E., van den Akker-Nijdam, M. E., van Loon, A. W. G., . . . Doreleijers, T. (2018). Effects of Methylphenidate During Fear Learning in Antisocial Adolescents: A Randomized Controlled fMRI Trial. *Journal of the American Academy of Child & Adolescent Psychiatry, 57*(12), 934-943.

van Schalkwyk, G. I., Beyer, C., Johnson, J., Deal, M., & Bloch, M. H. (2018). Antipsychotics for aggression in adults: A meta-analysis. *Prog Neuropsychopharmacol Biol Psychiatry, 81*, 452-458.

doi:10.1016/j.pnpbp.2017.07.019

VanElzakker, M. B., Staples-Bradley, L. K., & Shin, L. M. (2018). The neurocircuitry of fear and PTSD. In *Sleep and Combat-Related Post Traumatic Stress Disorder* (pp. 111-125):Springer.

Vargha-Khadem, F., Gadian, D. G., Watkins, K. E., Connelly, A., Van Paesschen, W., & Mishkin, M. (1997). Differential effects of early hippocampal pathology on episodic and semantic memory. *Science, 277*(5324), 376-380.

Vassos, E., Collier, D. A., & Fazel, S. (2014). Systematic meta-analyses and field synopsis of genetic association studies of violence and aggression. *Mol Psychiatry, 19*(4), 471-477. doi:10.1038/mp.2013.31

Vaughn, M. G., Edens, J. F., Howard, M. O., & Smith, S. T. (2009). An Investigation of Primary and Secondary Psychopathy in a Statewide Sample of Incarcerated Youth. *Youth Violenceand Juvenile Justice, 7*(3), 172-188. doi:10.1177/1541204009333792

Verbruggen, F., & Logan, G. D. (2008). Response inhibition in the stop-signal paradigm. *Trends Cogn Sci, 12*(11), 418-424. doi:10.1016/j.tics.2008.07.005

Vergunst, F., Tremblay, R. E., Galera, C., Nagin, D., Vitaro, F., Boivin, M., & Côté, S. M. (2019).Multi-rater developmental trajectories of hyperactivity-impulsivity and inattention symptoms from 1.5 to 17 years: a population-based birth cohort study. *Eur Child Adolesc Psychiatry, 28*(7), 973-983. doi:10.1007/s00787-018-1258-1

Veroude, K., Zhang-James, Y., Fernàndez-Castillo, N., Bakker, M. J., Cormand, B., & Faraone, S.V. (2016). Genetics of aggressive behavior: An overview. *Am J Med Genet B Neuropsychiatr Genet, 171b*(1), 3-43. doi:10.1002/ajmg.b.32364

Vidal-Ribas, P., Brotman, M. A., Valdivieso, I., Leibenluft, E., & Stringaris, A. (2016). The Statusof Irritability in Psychiatry: A Conceptual and Quantitative Review. *J Am Acad Child Adolesc Psychiatry, 55*(7), 556-570. doi:10.1016/j.jaac.2016.04.014

Viding, Fontaine, & McCrory. (2012a). Antisocial behaviour in children with and without callous-unemotional traits. *Journal of the Royal Society of Medicine, 105*(5), 195-200.

Viding, Fontaine, & McCrory. (2012b). Antisocial behaviour in children with and without callous-unemotional traits. *J R Soc Med, 105*(5), 195-200. doi:10.1258/jrsm.2011.110223

Viding, Sebastian, Dadds, Lockwood, Cecil, De Brito, & McCrory. (2012). Amygdala response to preattentive masked fear in children with conduct problems: the role of callous-unemotionaltraits. *American Journal of Psychiatry, 169*(10), 1109-1116.

Viding, E., Blair, R. J., Moffitt, T. E., & Plomin, R. (2005). Evidence for substantial genetic risk for psychopathy in 7-year-olds. *J Child Psychol Psychiatry, 46*(6), 592-597. doi:10.1111/j.1469-7610.2004.00393.x

Viding, E., Fontaine, N. M., & McCrory, E. J. (2012). Antisocial behaviour in children with and without callous-unemotional traits. *Journal of the Royal Society of Medicine, 105*(5), 195-200.

Viding, E., Jones, A. P., Frick, P. J., Moffitt, T. E., & Plomin, R. (2008). Heritability of antisocial behaviour at 9: do callous-unemotional traits matter? *Dev Sci, 11*(1), 17-22. doi:10.1111/j.1467-7687.2007.00648.x

Viding, E., Sebastian, C. L., Dadds, M. R., Lockwood, P. L., Cecil, C. A., De Brito, S. A., & McCrory, E. J. (2012). Amygdala response to preattentive masked fear in children with conduct problems: the role of callous-unemotional traits. *American Journal of Psychiatry,169*(10), 1109-1116.

Vindas, M. A., Folkedal, O., Kristiansen, T. S., Stien, L. H., Braastad, B. O., Mayer, I., & Øverli, Ø. (2012). Omission of expected reward agitates Atlantic salmon (Salmo salar). *Animal Cognition, 15*(5), 903-911.

Vindas, M. A., Johansen, I. B., Vela-Avitua, S., Nørstrud, K. S., Aalgaard, M., Braastad, B. O., ... Øverli, Ø. (2014). Frustrative reward omission increases aggressive behaviour of inferiorfighters. *Proceedings of the Royal Society B: Biological Sciences, 281*(1784), 20140300.

Vize, C. E., Collison, K. L., Miller, J. D., & Lynam, D. R. (2019). Using Bayesian methods to update and expand the meta-analytic evidence of the five-factor model's relation to antisocial behavior. *Clin Psychol Rev, 67*, 61-77. doi:10.1016/j.cpr.2018.09.001

VOGT, B. A., VOGT, L. J., & HOF, P. R. (2004). Cingulate gyrus. In *The human nervous system.* (pp. 915-949): Elsevier.

Völlm, B., Richardson, P., McKie, S., Elliott, R., Dolan, M., & Deakin, B. (2007). Neuronal correlates of reward and loss in Cluster B personality disorders: a functional magnetic resonance imaging study. *Psychiatry Res, 156*(2), 151-167. doi:10.1016/j.pscychresns.2007.04.008

von Polier, G. G., Greimel, E., Konrad, K., Großheinrich, N., Kohls, G., Vloet, T. D., Schulte Rüther, M. (2020). Neural correlates of empathy in boys with early onset conduct disorder. *Frontiers in psychiatry, 11*, 178.

Vossel, S., Geng, J. J., & Fink, G. R. (2014). Dorsal and ventral attention systems: distinct neural circuits but collaborative roles. *The Neuroscientist, 20*(2), 150-159.

Vuong, Q. H. (1989). Likelihood ratio tests for model selection and non-nested hypotheses. *Econometrica: Journal of the Econometric Society*, 307-333.

Vytal, K., & Hamann, S. (2010). Neuroimaging support for discrete neural correlates of basic emotions: a voxel-based meta-analysis. *J Cogn Neurosci, 22*(12), 2864-2885. doi:10.1162/jocn.2009.21366

Wager, T. D., Jonides, J., & Reading, S. (2004). Neuroimaging studies of shifting attention: a meta-analysis. *Neuroimage, 22*(4), 1679-1693.

Wahlund, K., & Kristiansson, M. (2009). Aggression, psychopathy and brain imaging—review and future recommendations. *International Journal of law and Psychiatry, 32*(4), 266-271.

Waller, R., & Hicks, B. M. (2019). Trajectories of alcohol and marijuana use among primary versus secondary psychopathy variants within an adjudicated adolescent male sample. *Personality*

disorders, 10(1), 87-96. doi:10.1037/per0000303

Waller, R., Wagner, N. J., Barstead, M. G., Subar, A., Petersen, J. L., Hyde, J. S., & Hyde, L. W. (2020). A meta-analysis of the associations between callous-unemotional traits and empathy, prosociality, and guilt. *Clin Psychol Rev, 75*, 101809. doi:10.1016/j.cpr.2019.101809

Wallis, G., Stokes, M., Cousijn, H., Woolrich, M., & Nobre, A. C. (2015). Frontoparietal and Cingulo-opercular Networks Play Dissociable Roles in Control of Working Memory. *J Cogn Neurosci, 27*(10), 2019-2034. doi:10.1162/jocn_a_00838

Walters, Diamond, Magaletta, Geyer, & Duncan. (2007). Taxometric analysis of the antisocial features scale of the personality assessment inventory in federal prison inmates. *Assessment, 14*(4), 351-360. doi:10.1177/1073191107304353

Walters, Duncan, & Mitchell-Perez. (2007). The latent structure of psychopathy: a taxometric investigation of the Psychopathy Checklist Revised in a heterogeneous sample of male prison inmates. *Assessment, 14*(3), 270-278. doi:10.1177/1073191107299594

Walters, Ermer, Knight, & Kiehl. (2015). Paralimbic biomarkers in taxometric analyses of psychopathy: does changing the indicators change the conclusion? *Personality disorders, 6*(1), 41-52. doi:10.1037/per0000097

Walters, Gray, Jackson, Sewell, Rogers, Taylor, & Snowden. (2007). A taxometric analysis of the Psychopathy Checklist: Screening Version (PCL:SV): further evidence of dimensionality.*Psychol Assess, 19*(3), 330-339. doi:10.1037/1040-3590.19.3.330

Walters, R. K., Polimanti, R., Johnson, E. C., McClintick, J. N., Adams, M. J., Adkins, A. E., . . . Bertelsen, S. (2018). Transancestral GWAS of alcohol dependence reveals common genetic underpinnings with psychiatric disorders. *Nature neuroscience, 21*(12), 1656-1669.

Wang, H., He, W., Wu, J., Zhang, J., Jin, Z., & Li, L. (2019). A coordinate-based meta-analysis ofthe n-back working memory paradigm using activation likelihood estimation. *Brain Cogn,132*, 1-12. doi:10.1016/j.bandc.2019.01.002

Waschbusch, D. A. (2002). A meta-analytic examination of comorbid hyperactive-impulsive-attention problems and conduct problems. *Psychol Bull, 128*(1), 118-150. doi:10.1037/0033-2909.128.1.118

Watson, D., Stanton, K., & Clark, L. A. (2017). Self-report indicators of negative valenceconstructs within the research domain criteria (RDoC): A critical review. *J Affect Disord, 216*, 58-69. doi:10.1016/j.jad.2016.09.065

Weathersby, F. L., King, J. B., Fox, J. C., Loret, A., & Anderson, J. S. (2019). Functional connectivity of emotional well-being: Overconnectivity between default and attentional networks is associated with attitudes of anger and aggression. *Psychiatry Research:Neuroimaging, 291*, 52-62.

Weder, N. D., Aziz, R., Wilkins, K., & Tampi, R. R. (2007). Frontotemporal dementias: a review. *Ann Gen Psychiatry, 6*, 15. doi:10.1186/1744-859x-6-15

Weeks, J. W., Howell, A. N., & Goldin, P. R. (2013). Gaze avoidance in social anxiety disorder. *Depression and anxiety, 30*(8), 749-756.

Weller, Blanford, & Butler. (2018). Estimated Prevalence of Psychiatric Comorbidities in U.S. Adolescents With Depression by Race/Ethnicity, 2011-2012. *J Adolesc Health, 62*(6), 716-721. doi:10.1016/j.jadohealth.2017.12.020

Weller, B. E., Blanford, K. L., & Butler, A. M. (2018). Estimated Prevalence of Psychiatric Comorbidities in US Adolescents With Depression by Race/Ethnicity, 2011–2012. *Journal of Adolescent Health, 62*(6), 716-721.

Wesley, M. J., & Bickel, W. K. (2014). Remember the future II: meta-analyses and functional overlap of working memory and delay discounting. *Biol Psychiatry, 75*(6), 435-448. doi:10.1016/j.biopsych.2013.08.008

Westmoreland, P., Gunter, T., Loveless, P., Allen, J., Sieleni, B., & Black, D. W. (2010). Attention deficit hyperactivity disorder in men and women newly committed to prison: clinical

characteristics, psychiatric comorbidity, and quality of life. *Int J Offender Ther Comp Criminol, 54*(3), 361-377. doi:10.1177/0306624x09332313

Wetzell, R. (2010). Criminology in Weimar and Nazi Germany. 401-423. doi:10.1017/CBO9781139052405.019

White, Clanton, Brislin, Meffert, Hwang, Sinclair, & Blair. (2014). Reward: empirical contribution. Temporal discounting and conduct disorder in adolescents. *J Pers Disord, 28*(1), 5-18. doi:10.1521/pedi.2014.28.1.5

White, Marsh, Fowler, Schechter, Adalio, Pope, . . . Blair. (2012). Reduced amygdala response in youths with disruptive behavior disorders and psychopathic traits: decreased emotional response versus increased top-down attention to nonemotional features. *American Journalof Psychiatry, 169*(7), 750-758.

White, Pope, Sinclair, Fowler, Brislin, Williams, . . . Blair. (2013a). Disrupted expected value and prediction error signaling in youths with disruptive behavior disorders during a passive avoidance task. *Am J Psychiatry, 170*(3), 315-323. doi:10.1176/appi.ajp.2012.12060840

White, Pope, Sinclair, Fowler, Brislin, Williams, . . . Blair. (2013b). Disrupted expected value and prediction error signaling in youths with disruptive behavior disorders during a passive avoidance task. *American Journal of Psychiatry, 170*(3), 315-323.

White, Williams, Brislin, Sinclair, Blair, Fowler, . . . Blair. (2012). Reduced activity within the dorsal endogenous orienting of attention network to fearful expressions in youth with disruptive behavior disorders and psychopathic traits. *Development and psychopathology, 24*(3), 1105-1116.

White, S. F., VanTieghem, M., Brislin, S. J., Sypher, I., Sinclair, S., Pine, D. S., ... & Blair, R. J.R. (2015). Neural correlates of the propensity for retaliatory behavior in youths with disruptive behavior disorders. *American Journal of Psychiatry, 173*(3), 282-290.

Whiteside, S. P., & Lynam, D. R. (2001). The Five Factor Model and impulsivity: using a structural

model of personality to understand impulsivity. *Personality and Individual Differences, 30*(4), 669-689. doi:https://doi.org/10.1016/S0191-8869(00)00064-7

Whitfield-Gabrieli, S., & Nieto-Castanon, A. (2012). Conn: a functional connectivity toolbox for correlated and anticorrelated brain networks. *Brain Connect, 2*(3), 125-141. doi:10.1089/brain.2012.0073

Wichstrøm, Berg-Nielsen, Angold, Egger, Solheim, & Sveen. (2012). Prevalence of psychiatric disorders in preschoolers. *J Child Psychol Psychiatry, 53*(6), 695-705. doi:10.1111/j.1469-7610.2011.02514.x

Wiggins, J. L., Mitchell, C., Stringaris, A., & Leibenluft, E. (2014). Developmental trajectories of irritability and bidirectional associations with maternal depression. *J Am Acad Child Adolesc Psychiatry, 53*(11), 1191-1205, 1205.e1191-1194. doi:10.1016/j.jaac.2014.08.005

Williams, W. H., Cordan, G., Mewse, A. J., Tonks, J., & Burgess, C. N. (2010). Self-reported traumatic brain injury in male young offenders: a risk factor for re-offending, poor mental health and violence? *Neuropsychol Rehabil, 20*(6), 801-812. doi:10.1080/09602011.2010.519613

Wilson, Colizzi, Bossong, Allen, Kempton, & Bhattacharyya. (2018). The Neural Substrate of Reward Anticipation in Health: A Meta-Analysis of fMRI Findings in the Monetary Incentive Delay Task. *Neuropsychol Rev, 28*(4), 496-506. doi:10.1007/s11065-018-9385-5 Wilson, Juodis, & Porter. (2011). Fear and loathing in psychopaths: A meta-analytic investigationof the facial affect recognition deficit. *Criminal Justice and Behavior, 38*(7), 659-668. doi:10.1177/0093854811404120

Wilson, H. A. (2014). Can antisocial personality disorder be treated? A meta-analysis examining the effectiveness of treatment in reducing recidivism for individuals diagnosed with ASPD.*The International Journal of Forensic Mental Health, 13*(1), 36-46. doi:10.1080/14999013.2014.890682

Wong, T. Y., Sid, A., Wensing, T., Eickhoff, S. B., Habel, U., Gur, R. C., & Nickl-Jockschat, T. (2019).

Neural networks of aggression: ALE meta-analyses on trait and elicited aggression.*Brain Structure and Function, 224*(1), 133-148.

Woodworth, R. S., & Sherrington, C. S. (1904). A pseudaffective reflex and its spinal path. *J Physiol, 31*(3-4), 234-243. doi:10.1113/jphysiol 1904.sp001034

Worringer, B., Langner, R., Koch, I., Eickhoff, S. B., Eickhoff, C. R., & Binkofski, F. C. (2019). Common and distinct neural correlates of dual-tasking and task-switching: a meta-analyticreview and a neuro-cognitive processing model of human multitasking. *Brain Struct Funct,224*(5), 1845-1869. doi:10.1007/s00429-019-01870-4

Wrangham, R. W. (2018). Two types of aggression in human evolution. *Proc Natl Acad Sci U S A, 115*(2), 245-253. doi:10.1073/pnas.1713611115

Xie, H., Drabick, D. A., & Chen, D. (2011). Developmental trajectories of aggression from late childhood through adolescence: similarities and differences across gender. *Aggress Behav,37*(5), 387-404. doi:10.1002/ab.20404

Xu, Raine, Yu, & Krieg. (2014). Resting Heart Rate, Vagal Tone, and Reactive and Proactive Aggression in Chinese Children. *Journal of abnormal child psychology, 42*(3), 501-514. doi:10.1007/s10802-013-9792-2

Xu, J., Van Dam, N. T., Feng, C., Luo, Y., Ai, H., Gu, R., & Xu, P. (2019). Anxious brain networks:A coordinate-based activation likelihood estimation meta-analysis of resting-state functional connectivity studies in anxiety. *Neuroscience & Biobehavioral Reviews, 96*, 21-30.

Xu, Y., Farver, J. A. M., & Zhang, Z. (2009). Temperament, harsh and indulgent parenting, and Chinese children's proactive and reactive aggression. *Child Development, 80*(1), 244-258.

Yang, J. (2015). The influence of motor expertise on the brain activity of motor task performance: A meta-analysis of functional magnetic resonance imaging studies. *Cogn Affect Behav Neurosci, 15*(2), 381-394. doi:10.3758/s13415-014-0329-0

Yang, M., Tsai, S. J., & Li, C. R. (2020). Concurrent amygdalar and ventromedial prefrontal cortical responses during emotion processing: a meta-analysis of the effects of valence of emotion and passive exposure versus active regulation. *Brain Struct Funct, 225*(1), 345- 363. doi:10.1007/s00429-019-02007-3

Yang, Y., & Raine, A. (2009). Prefrontal structural and functional brain imaging findings in antisocial, violent, and psychopathic individuals: a meta-analysis. *Psychiatry Research: Neuroimaging, 174*(2), 81-88.

Yarkoni, T., Poldrack, R. A., Nichols, T. E., Van Essen, D. C., & Wager, T. D. (2011). Large-scale automated synthesis of human functional neuroimaging data. *Nature methods, 8*(8), 665- 670.

Yeo, B. T., Krienen, F. M., Sepulcre, J., Sabuncu, M. R., Lashkari, D., Hollinshead, M., . . . Polimeni, J. R. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of neurophysiology*.

Yoder, K., Harenski, C., Kiehl, K., & Decety, J. (2015). Neural networks underlying implicit and explicit moral evaluations in psychopathy. *Translational psychiatry, 5*(8), e625-e625.

Young, S., Moss, D., Sedgwick, O., Fridman, M., & Hodgkins, P. (2015). A meta-analysis of the prevalence of attention deficit hyperactivity disorder in incarcerated populations. *Psychol Med, 45*(2), 247-258. doi:10.1017/s0033291714000762

Yu, L. Q., Kan, I. P., & Kable, J. W. (2020). Beyond a rod through the skull: A systematic reviewof lesion studies of the human ventromedial frontal lobe. *Cogn Neuropsychol, 37*(1-2), 97-141. doi:10.1080/02643294.2019.1690981

Yu-Feng, Z., Yong, H., Chao-Zhe, Z., Qing-Jiu, C., Man-Qiu, S., Meng, L., . . . Yu-Feng, W. (2007). Altered baseline brain activity in children with ADHD revealed by resting-state functional MRI. *Brain and Development, 29*(2), 83-91.

Yule, A. M., DiSalvo, M., Wilens, T. E., Wozniak, J., Faraone, S. V., Lyons, R. M., Woodworth, K. Y., & Biederman, J. (2020). High Correspondence Between Child Behavior Checklist Rule Breaking

Behavior Scale with Conduct Disorder in Males and Females. *Child psychiatry and human development*, *51*(6), 978–985. https://doi.org/10.1007/s10578-020-00978-7

Zang, Y., Jiang, T., Lu, Y., He, Y., & Tian, L. (2004). Regional homogeneity approach to fMRI data analysis. *Neuroimage, 22*(1), 394-400.

Zeichner, A., Frey, F. C., & Parrott, D. J. (2003). Correlates of delayed physical aggression in response to provocation. *Revue Internationale de Psychologie Sociale, 16*(3), 81-100.

Zeier, J. D., Baskin-Sommers, A. R., Hiatt Racer, K. D., & Newman, J. P. (2012). Cognitive control deficits associated with antisocial personality disorder and psychopathy. *Personality Disorders: Theory, Research, and Treatment, 3*(3), 283.

Zhang, Z., Peng, P., Eickhoff, S. B., Lin, X., Zhang, D., & Wang, Y. (2021). Neural substrates of the executive function construct, age-related changes, and task materials in adolescents andadults: ALE meta-analyses of 408 fMRI studies. *Dev Sci, 24*(6), e13111. doi:10.1111/desc.13111

Zhu, W., Zhou, X., & Xia, L.-X. (2019). Brain structures and functional connectivity associated with individual differences in trait proactive aggression. *Scientific reports, 9*(1), 1-12.

Zilverstand, A., Parvaz, M. A., & Goldstein, R. Z. (2017). Neuroimaging cognitive reappraisal in clinical populations to define neural targets for enhancing emotion regulation. A systematic review. *Neuroimage, 151*, 105-116.

Zinchenko, O., Yaple, Z. A., & Arsalidou, M. (2018). Brain Responses to Dynamic Facial Expressions: A Normative Meta-Analysis. *Front Hum Neurosci, 12*, 227. doi:10.3389/fnhum.2018.00227.

Annexes

Suite au comité d'examen

Bonjour,

Votre projet intitulé « Hétérogénéité clinique des jeunes à risque de comportements antisociaux : analyses multi-trajectoires du développement de traits de personnalité» a été accepté par les des membres du comité d'examen. Voici toutefois certains commentaires et avertissements des membres du comité d'examen.

- Les membres du comité d'examen recommandent un échéancier de 1 ½ an (novembre 2020) d'accès pour commencer dans le cas de correction ou d'analyses supplémentaires.
- La méthodologiste a remarqué que vous utiliseriez les questionnaires enseignants. Elle voulait vous aviser qu'il y a beaucoup de valeurs manquantes dans ceux-ci.
- L'ELDEQ étant une enquête longitudinale, il faudra disposer d'une stratégie pour tenir compte du plan de sondage complexe dans l'ELDEQ, surtout comme l'utilisation de plusieurs cycles et variables fera diminuer le nombre de répondants. Voir à ce sujet : http://www.jesuisjeserai.stat.gouv.qc.ca/pdf/doc_tech/Document_de_reference_ponderations.pdf. De plus, je pourrais aussi vous mettre en contact avec la méthodologiste pour qu'elle puisse vous aviser de la meilleure pondération à utiliser pour vos analyses.

Voilà l'essentiel des commentaires et avertissements. Finalement, je prépare l'entente qui sera ensuite révisée par les services juridiques de l'Institut avant de vous l'envoyer pour approbation. Pour toutes questions, vous pouvez me rejoindre par courriel ou téléphone.

Sincèrement,

Institut de la statistique Québec

Marc-Antoine Côté-Marcil
Analyste-conseil

Centre d'accès aux données de recherche de l'Institut de la statistique du Québec (CADRISQ)
Direction de la diffusion et des communications (DDC)

Institut de la statistique du Québec

Centre intégré
universitaire de santé
et de services sociaux
de l'Est-de-
l'Île-de-Montréal
Québec

Le 11 mars 2020

Monsieur Stéphane Potvin
CIUSSS de l'Est-de-l'Île-de-Montréal
Installation Intitut universitaire en santé mentale de Montréal

Objet : Approbation conditionnelle du Comité d'évaluation scientifique

Projet nº 2020-2067

Titre : *La spécificité des marqueurs neurobiologiques dans la classification des sous-types du trouble des conduites.*

Monsieur Potvin,

Le Comité d'évaluation scientifique en santé en santé mentale et populationnelle du CIUSSS de l'Est-de-l'Île-de-Montréal, a passé en revue, à sa réunion du 10 mars 2020, votre protocole de recherche pour le projet mentionné en rubrique.

Les membres du CÉS, après avoir examiné le protocole de recherche et échangé, demandent de faire les modifications ou ajouts suivants et de répondre à certaines interrogations :

Problématique

On mentionne que bien qu'il y ait eu des avancées considérables sur le thème de la violence chez les jeunes, un nombre limité d'études a été publié sur la compréhension du lien entre les trajectoires développementales des traits/tempéraments et le risque de violence chez les adolescents. L'objectif général de la présente recherche est d'étudier les marqueurs neurobiologiques (imagerie cérébrale) associés à l'hétérogénéité de tempéraments/traits de personnalité sous-jacents au risque de comportements antisociaux de l'enfance à l'adolescence. Le tout sera tiré d'une base de données anonymisée de plus de 2000 personnes intitulées Child Mind Institute. | Quelques points sont à peaufiner. Il faudrait préciser la définition de certains construits. Par exemple, pour ce qui est de la violence, un des problèmes, dans la recension des écrits portant sur la jeunesse, est le manque de consensus sur les définitions et il est donc difficile de tirer des conclusions et de comparer les résultats d'études. Ici, on semble interchanger les termes violence et comportements antisociaux, mais ils ne le sont pas (c.-à-d. pas tous les comportements violents sont antisociaux, tel que l'automutilation). Cela est particulièrement sensible comme définition dans le domaine de l'enfance, notamment parce qu'il est question d'intention ou non. Dans le domaine de la santé mentale (p.ex.: déficience intellectuelle, schizophrénie), il est important de mettre en contexte. Un autre point est qu'il faudrait préciser certains passages. Par exemple on mentionne que "Ceci serait principalement expliqué par la présence d'une importante hétérogénéité entre les adolescents à risque de passage à l'acte criminel". Ici, il faut préciser ce que vous voulez apporter en lien avec les objectifs. Par ailleurs, il est parfois difficile de percevoir le fil conducteur vers la pertinence du projet et des objectifs sous un principe d'entonnoir. Par exemple, on apporte de façon subite les divergences entre les actes violents présentés chez les adolescents anxieux vs psychopathes. Ceci arrive de façon inattendue et il faudrait peut-être justifier cet exemple, si cela est important. Enfin, plusieurs sections contiennent des références, mais on soulève plusieurs concepts dans la section problématique qui ne sont pas référencés.

Hypothèses

Il est proposé que les systèmes dysfonctionnels prédominants seront le système du mode par défaut, du traitement des émotions, du contrôle cognitif, ainsi que les systèmes associés au traitement de la récompense et de la punition. Ces derniers seront significativement associés à leur phénotype(s) respectif(s). Plus de précisions sur les liens spécifiques auraient facilité la compréhension et les idées. Aussi, de nouveaux concepts non discutés préalablement ont été introduits dans les objectifs/hypothèses (système de mode par défaut/système lié à la récompense).

Analyses

Pour ce qui est des analyses, il manque certains détails qui pourraient permettre d'utiliser cette base de données de façon optimum et des questions subsistent. Par exemple, de quelle façon sont sélectionnées les composantes liées aux domaines neurocognitifs d'intérêt? Concernant les associations entre ces composantes et les mesures phénotypiques, de quelle façon sera implémentée la correction pour comparaisons multiples? Sur le plan de la régression logistique, pourquoi ne pas l'appliquer dans une perspective d'apprentissage automatique, avec validation croisée? La taille de l'échantillon permettrait aisément cette démarche statistique.

Décision

Il s'agit d'un projet tout à fait pertinent qui puise dans une base de données importante. Par contre, le texte nécessitera d'être révisé sur le plan de la rédaction de l'introduction. Ainsi, la problématique devrait être clairement soutenue par la recension et ici, il faudra ajouter des citations. Similairement, il faudrait décrire tous les concepts liés aux hypothèses (p.ex., système du mode par défaut et le système lié à la récompense dans l'introduction ou la problématique). De plus, développer des objectifs et des hypothèses plus spécifiques faciliterait l'évaluation. Les variables et les analyses demeurent vagues et nombreuses, ce qui risque de produire beaucoup de faux positifs. Une alternative pourrait être de diminuer le nombre d'analyses ou de variables ou d'appliquer une correction pour que les résultats demeurent valides.

Pour l'ensemble des raisons soulevées, le comité est d'avis que le présent projet pourrait être accepté conditionnellement aux corrections demandées.

Si vous êtes en désaccord avec les conditions du CÉS, nous vous remercions de justifier votre position en répondant dans la rubrique appropriée de Nagano. Veuillez noter que l'intégration des suggestions du CÉS est laissée à la discrétion des auteurs.

Après réception du protocole dûment revu et corrigé ainsi que des réponses soumises dans Nagano, en fonction des remarques indiquées plus haut, votre recherche pourra faire l'objet d'une approbation finale par le président du CÉS, lequel est autorisé par le CÉS à approuver définitivement ce projet de recherche en accéléré.

Si vous désirez déposer votre projet pour la réunion du CÉR du CIUSSS de l'Est-de-l'Île-de-Montréal du 1er avril 2020, vous devez répondre à toutes les conditions du CÉS et soumettre votre nouvelle version du protocole dans Nagano, d'ici le 24 mars 2020.

En terminant, nous vous remercions d'apporter les modifications demandées au protocole et de le joindre, en mode revision, dans une des conditions qui vous ont été soumises par le président du CÉS dans Nagano.

La procédure à suivre dans Nagano :

1. Cliquer sur l'onglet "Message"
2. Choisir une discussion (n'importe laquelle)
3. Inscrire votre réponse dans l'encadré "Message" - Obligatoire
4. Cliquer sur "ajouter une révision de fichier", le cas échéant
5. Fichier : choisir le fichier à remplacer qui est déjà dans Nagano
6. Révision : joindre vos fichiers amendés
7. **IMPORTANT** cliquer sur le bouton "Répondre" après avoir répondu à chacun des messages.

N.B. Vous devez répondre à chacune des questions. Par contre, il n'est pas nécessaire de joindre votre protocole amendé à chacune des réponses, une seule fois est suffisante.

Avec l'expression de nos sentiments les meilleurs.

Monsieur Marc Lavoie, Ph. D
Président
Comité d'évaluation scientifique en santé mentale et populationnelle
CIUSSS de l'Est-de-l'Île-de-Montréal