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Intégration sensorielle chez les individus ayant un trouble du spectre de l'autisme

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Résumé

La capacité du cerveau humain à intégrer les informations issues d'une ou de plusieurs modalités sensorielles est essentielle pour percevoir le monde de manière unifiée et cohérente. Il a été suggéré que le trouble du spectre de l'autisme (TSA) puisse être associé à une dysfonction de la capacité à intégrer les informations provenant de différentes modalités sensorielles. Toutefois, les données empiriques à cet effet demeurent complexes et équivoques. Dans ce contexte, le présent projet de thèse a pour but de permettre une meilleure compréhension du lien qui existe entre le TSA et les performances d'intégration sensorielle. Les résultats obtenus suggèrent que le TSA est associé à une diminution de la capacité à intégrer des informations provenant de différentes modalités sensorielles (IMS). Contrairement à ce qui était suggéré dans la littérature, cette atteinte serait présente indépendamment du type de stimuli traités, mais semble un peu plus manifeste pour les informations de nature sociale. Celle-ci semble également spécifique au traitement multisensoriel, dans le contexte où aucun déficit n'a été objectivé lors de l'intégration de stimuli de même modalité chez les individus ayant un TSA. Par ailleurs, ce déficit d'IMS n'est pas sous-tendu par une atteinte des processus attentionnels nécessaires pour la transition d'une modalité à l'autre lors du traitement multisensoriel. De façon générale, ces résultats ont permis d'approfondir les connaissances en lien avec l'intégration sensorielle chez les individus ayant un TSA. Ceux-ci témoignent de la présence d'atypies au niveau des processus d'IMS qui devront être approfondies davantage, et ouvrent la voie à des études futures qui tenteront de préciser l'étiologie, les corrélats neuronaux et, de façon primordiale, l'impact clinique associés à ces difficultés d'IMS.

Mots-clés : Intégration sensorielle; Trouble du spectre de l'autisme; Vision; Audition; Tact.

Abstract

The ability to integrate information from one or more sensory modalities is essential to perceive the world as unified and coherent. It has been suggested that autism spectrum disorder (ASD) may be associated with difficulties to integrate sensory information from different modalities. However, the empirical evidences remain complex and equivocal. In this context, the purpose of this thesis is to provide a better understanding of the relationship between ASD and sensory integration. The results suggest that ASD is associated with a decrease in the ability to integrate information from different sensory modalities (MSI). Contrary to what was suggested in the literature, this difficulty generalizes to social and non-social stimuli. It also seems specific to MSI, since no deficit was observed for the integration of stimuli coming from the same modality. Moreover, the reduced MSI observed in ASD is not related to atypical attentional shift between modalities, which is similar in both groups. Overall, these results improve knowledge related to sensory integration in individuals with ASD. These demonstrate atypical MSI processes in ASD, and pave the way for future studies that will attempt to clarify the etiology, the neural correlates and, more importantly, the clinical impact associated with these MSI difficulties.

Keywords: Sensory integration; Autism spectrum disorder; Vision; Audition; Somatosensory.

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Liste des sigles et abréviations

ADI-R	*Autism Diagnostic Interview - Revised*
ADOS-G	*Autistic Diagnostic Observation Schedule - Generic*
AES	*Anterior ectosylvian sulcus*
ANOVA	*Analysis of variance*
ASD	*Autism spectrum disorder*s
AUT	*Autism*
ASP	*Asperger's syndrome*
Cm	*Centimeter*
CS	Colliculus supérieur
CDF	*Cumulative distribution function*
Db	*Decibel*
DT	Développement typique
DSM-5	*Diagnostic and Statistical Manual of Mental Disorders, Fifth edition*
ERP	*Event related potential*
FFA	*Fusiform face area*
GR	Gain de redondance
HIT	*Percentage of correct responses*
Hz	*Hertz*
IMS	Intégration multisensorielle
IE	*Inverse efficiency*
IQ	*Intellectual quotient*
LED	*Light-emitting diode*
M	*Meter*
MSI	*Multisensory integration*
Ms	*Millisecond*
pSTS	*posterior superior temporal sulcus*
SACS	*Speed-accuracy composite score*
S	*Second*
RG	*Redundancy gain*

rLS	*Lateral suprasylavian sulcus*
RSE	*Redundant signal effect*
TD	*Typically developing*
TR	Temps de réaction
TSA	Trouble du spectre de l'autisme
WCC	*Weak central coherence*

« Une question qui me rend parfois perplexe :
Est-ce moi ou les autres qui sont fous? »
- *Albert Einstein*

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Chapitre 1 : Introduction Générale

L’intégration sensorielle permet d’accéder à une perception unifiée de l’environnement en combinant les différentes informations obtenues via un et/ou plusieurs des organes sensoriels propres à l’humain (Stein et Meredith, 1993). Il a été suggéré que le trouble du spectre de l’autisme (TSA), une condition neurodéveloppementale caractérisée par des atypies au niveau de la communication et des interactions sociales, de même que par la présence de comportements et d’intérêts restreints et répétitifs (American Psychiatric Association, 2013), puisse être associé à une dysfonction de l’intégration multisensorielle (IMS), c’est-à-dire de la capacité à intégrer des informations provenant de différentes modalités sensorielles (Wallace et Stevenson, 2014; Bahrick et Todd, 2011; Iarocci et McDonald, 2006; Marco et al., 2011). Cette hypothèse est appuyée par la présence de particularités sensorielles supra-modales (ou non spécifiques à une seule modalité) chez les individus ayant un TSA (Marco, Hinkley, Hill et Nagarajan, 2011; Baranek, David, Poe, Stone et Watson, 2006), de même que par les principaux modèles théoriques qui suggèrent un avantage pour le traitement perceptif local comparativement à celui nécessitant une approche globale ou intégrative (Frith et Happe, 1994; Brock, Brown, Boucher et Rippon, 2002; Mottron, Dawson, Soulieres, Hubert et Burack, 2006). De ce fait, une atteinte des processus d’IMS pourrait avoir un effet en cascade sur les étapes subséquentes de la hiérarchie de traitement de l’information, et ultimement affecter les habiletés cognitives plus complexes, telles que la communication et les interactions sociales qui sont particulièrement touchées dans le TSA (Stevenson et al., 2014a; Bahrick et Lickliter, 2000; 2002; Bahrick, 2010; Bahrick et Todd, 2011).

Plusieurs études se sont intéressées à la question de l’IMS chez les individus ayant un TSA au cours des dernières années, mais jusqu’à présent le portrait demeure complexe et équivoque (Wallace et Stevenson, 2014). Dans ce contexte, le présent projet de thèse a pour but de permettre une meilleure compréhension du lien qui existe entre le TSA et les performances d’intégration sensorielle. Le premier objectif sera de déterminer si la capacité d’intégrer des informations provenant de différentes modalités sensorielles diffère entre les individus ayant un TSA et ceux avec développement typique (DT), puis de préciser si celle-ci est tributaire de la nature des stimuli traités, une hypothèse actuellement proposée dans la littérature (Bebko, Weiss, Demark et Gomez, 2006; Magnée et al., 2008; Mongillo et al., 2008). Le second objectif sera de comparer les performances d’IMS à celles retrouvées lors de l’intégration de stimuli d’une même modalité sensorielle chez les personnes ayant un TSA. De façon complémentaire, nous évaluerons également si le changement d’allocation des ressources attentionnelles entre les modalités est susceptible d’expliquer la présence de différences au niveau de l’IMS entre les groupes, puis proposerons un paradigme pouvant éventuellement être utilisé chez les individus ayant un TSA pour préciser l’impact de la saillance des stimuli sur l’IMS.

En guise d’introduction aux articles qui composent ce projet de thèse, nous présenterons d’abord une revue des concepts de base en lien avec l’IMS, soit les fondements neuronaux, les enjeux développementaux et les implications comportementales. Le concept d’IMS ou inter-modale sera ensuite comparé à celui d’intégration unisensorielle ou intra-modale, qui réfère à l’intégration d’informations provenant d’une même modalité sensorielle. Finalement, l’hypothèse d’une dysfonction des processus d’intégration sensorielle associée au TSA sera discutée, puis suivie d’une revue de la littérature témoignant de l’état actuel des connaissances à ce sujet.

Chapitre 2 : Intégration sensorielle

L’humain possède différents organes sensoriels, à travers lesquels il perçoit son environnement (Stein et Meredith, 1993). Chacun d’entre eux permet d’accéder à une représentation distincte de l’environnement, pour laquelle il n’y a parfois aucun équivalent dans une autre modalité, et encode les influx sensoriels dans un cadre de référence qui lui est spécifique (Harris, Blakemore et Donaghy, 1980; Morrell, 1972; Russell, 1992; Spence et Driver, 2004). Dans ce contexte, une question cruciale ayant suscité l’intérêt dans le milieu philosophique et scientifique depuis plusieurs décennies (Spence, Pavani, Maravita et Holmes, 2004) est : comment arrive-t-on à une représentation cohérente du monde qui nous entoure? L’intégration sensorielle des informations obtenues via un et/ou différents systèmes sensoriels serait ce qui permet d’accéder à cette perception unifiée de l’environnement (Stein et Stanford, 2008).

2.1 Intégration multisensorielle ou inter-modale

2.1.1 Fondements neuronaux de l’intégration multisensorielle

Il importe de d’abord comprendre les principes neurophysiologiques qui sous-tendent l’IMS, car la façon de conceptualiser l’intégration sensorielle au niveau comportemental est principalement fondée sur ceux-ci. La majorité de ces principes sont tirés d’une série d’études produites par Stein et collaborateurs vers la fin des années 1970, portant sur les neurones du colliculus supérieur (CS) chez le chat.

Chez le mammifère, le CS présente une organisation laminaire. Les couches superficielles (I-III) sont unisensorielles et les neurones qui s’y trouvent ne répondent qu’à des stimulations visuelles. Les couches profondes (IV-VII) contiennent différents types de neurones unisensoriels (visuels, auditifs et tactiles), de même que des neurones multisensoriels, c’est-à-dire qui répondent à une combinaison d’informations visuelle, auditive et/ou tactile (Knudsen, 1982; Meredith et Stein, 1983; King et Palmer, 1985; Stein, Stanford et Rowland, 2009). Cette structure a pour fonction de permettre l’orientation rapide vers une stimulation extérieure, en contrôlant les mouvements oculaires et de la tête, via des projections au niveau des aires motrices du tronc cérébral et de la moelle épinière (Stein, Jiang, Wallace et Stanford, 2001; Sparks et Mays, 1990; Stein et Meredith, 1991; Wurtz et Munoz, 1995). Les neurones multisensoriels retrouvés dans le CS ont des champs récepteurs spécifiques pour chacune des modalités sensorielles auxquelles ils répondent (Stein et Stanford, 2008). La transposition dans un cadre de référence oculocentrique commun permet aux signaux sensoriels issus d'un même événement d'activer les mêmes neurones du CS, permettant ainsi leur combinaison (Stein, 1998).

Il a été démontré, au moyen d'enregistrements unicellulaires, que le neurone multisensoriel ne fait pas que combiner ces influx sensoriels, mais qu'il peut les intégrer. En effet, lorsque deux stimuli de modalités différentes sont présentés simultanément et à proximité l'un de l'autre, la réponse du neurone multisensoriel est supérieure à celle observée pour la plus efficace des deux composantes individuelles (Meredith et Stein, 1983; 1986; 1996; Wallace, Meredith et Stein, 1993; 1998; Wallace, Wilkinson et Stein, 1996; Kadunce, Vaughan, Wallace et Stein, 2001). Cet effet synergique, associé à l'excitation répétée d'un même neurone, est plus marqué pour les stimuli de faible intensité (Meredith et Stein, 1986; Stein et Meredith, 1993; Stein et al., 2009). Au contraire, une diminution de la réponse neuronale est notée lorsque les stimuli sont présentés de façon spatialement discordante (Meredith et Stein, 1986; 1996; Kadunce, Vaughan, Wallace, Benedek et Stein, 1997; Kadunce et al., 2001; Wallace et al., 1998), ce qui s'explique possiblement par le fait qu'une région inhibitrice borde les champs récepteurs excitateurs (Kadunce et al., 1997). Il a été montré qu'il existe une fenêtre temporelle à travers laquelle l'intégration est possible, celle-ci variant généralement entre 100 à 500 ms (Meredith, Nemitz et Stein, 1987; Wallace et Stein, 1994), puisque le temps nécessaire au traitement des signaux varie d'une modalité à l'autre.

De ces études sont nés trois principes de base sous-tendant l'IMS (Stein et Meredith, 1993), c'est-à-dire que celle-ci est inversement proportionnelle au niveau d'intensité des stimuli (loi de l'efficacité inversée), et qu'elle est possible lorsque les stimuli sont présentés à proximité dans l'espace (loi spatiale) et de façon rapprochée dans le temps (loi temporelle). D'un point de vue intuitif, ces principes sont logiques en ce sens que la congruence spatiale et temporelle est généralement un indicateur de l'appartenance à un même évènement, et que les signaux les moins saillants sont ceux qui bénéficient le plus d'être amplifiés (Wallace et Stevenson, 2014).

À noter que l'IMS au niveau du CS est dépendante des projections provenant de certaines aires corticales associatives, soit le sulcus ectosylvien antérieur (AES) et le sulcus suprasylvien latéral (rLS) (Wallace et Stein, 1994; 1997). Des neurones multisensoriels ont également été identifiés à d'autres niveaux dans le système nerveux central, notamment au niveau cortical (Stein et Meredith, 1993; Stein et Stanford, 2008). Les propriétés et patrons de réponse y sont toutefois peu documentés, et seraient possiblement moins systématisés qu'au niveau des CS (Wallace, Meredith et Stein, 1992; Calvert et Thesen, 2004). En plus des trois principes décrits précédemment, il semble que la congruence sémantique entre les stimuli présentés serait particulièrement importante pour l'IMS au niveau cortical (Stein et Stanford, 2008; Laurienti et al., 2003).

2.1.2 Développement de l'IMS

Il est important de savoir que les propriétés nécessaires à l'IMS des neurones du CS et du cortex ne sont pas innées, mais qu'elles s'acquièrent progressivement en lien avec l'expérience sensorielle (Wallace et Stein, 1997; 2001; 2007; Stein et Rowland, 2011; Carriere et al., 2007; Wallace et al., 1993; Wallace, Carriere, Perrault, Vaughan et Stein, 2006). L'objectif n'étant pas d'effectuer une revue de littérature extensive à ce sujet, il paraît toutefois pertinent de décrire quelques éléments clés associés au développement de l'IMS, qui permettront de mieux saisir les résultats obtenus chez les individus ayant un TSA.

Les études chez le primate non humain et le chat suggèrent que l'apparition des neurones multisensoriels suit celle des neurones unisensoriels au niveau des CS, et survient une à deux semaines après la naissance (Stein et Rowland, 2011; Stein, Labos et Kruger, 1973; Wallace et Stein, 1997). Par contre, cela prendrait plusieurs semaines supplémentaires avant que ces neurones n'acquièrent leurs propriétés adultes, notamment la capacité d'intégrer les informations multisensorielles (Wallace et Stein, 1997; Wallace et Stein, 2001; Wallace et al., 1996). Celle-ci se développerait de façon parallèle à la maturation des projections provenant des aires corticales associatives AES et rLS (Wallace et Stein, 1997; 2000; Stein, Wallace, Stanford et Jiang, 2002). Chez l'humain, la capacité de combiner de façon synergique l'information multisensorielle semble également s'acquérir progressivement en lien avec l'expérience postnatale (Gori, Del, Sandini et Burr, 2008; Putzar, Goerendt, Lange, Rosler et Roder, 2007;

Nardini, Bales et Mareschal, 2015; Brandwein et al., 2011; Gori, Sandini et Burr, 2012). L’exposition au monde extérieur, où l’individu est confronté à de multiples informations sensorielles, lui permettrait d’apprendre que certaines propriétés des stimuli tendent à co-varier ensemble, et contribuerait au développement de sa capacité à déterminer s’ils appartiennent ou non au même événement (Stein et Rowland, 2011). L’étude d’individus atteints de cataractes congénitales ayant été opérées en jeune âge a démontré que la privation sensorielle durant les deux premières années de vie affecte l’IMS une fois le sens de la vue retrouvé (Putzar et al., 2007). Les propriétés des neurones multisensoriels s’adapteraient également en fonction de la configuration des stimuli présents dans l’environnement durant les premiers mois de vie (Wallace et Stein, 2007). Des résultats similaires ont été obtenus chez l’animal (Wallace, Perrault, Hairston et Stein, 2004; Carriere et al., 2007; Stein et Rowland, 2011).

2.1.3 Modèles anatomofonctionnels de l’IMS

Tel qu’exposé précédemment, les principes de base qui sous-tendent l’IMS proviennent principalement d’enregistrements unicellulaires au niveau des neurones multisensoriels du CS, qui sont impliqués dans la détection et l’orientation par rapport aux évènements extérieurs. Après avoir transigé par ce relais, les informations sensorielles sont traditionnellement acheminées vers leurs aires corticales primaires respectives. D’un point de vue plus macroscopique, la compréhension anatomofonctionnelle de l’organisation des réseaux corticaux impliqués dans l’IMS a beaucoup évolué au cours des dernières années et sera décrite brièvement.

Initialement, on croyait que l’IMS était sous-tendue par un phénomène de convergence hiérarchique et unidirectionnel, c’est-à-dire que les informations sensorielles étaient d’abord traitées séparément dans les aires corticales sensorielles primaires, puis qu’elles convergeaient vers une région hétéromodale où elles étaient combinées entre elles (Stein et Meredith, 1993; Meredith, 2002). Plusieurs zones de convergence potentielles ont été identifiées, dont le sulcus temporal supérieur (STS) (Baylis, Rolls et Leonard, 1987; Benevento, Fallon, Davis et Rezak, 1977; Bruce, Desimone et Gross, 1981; Neal, Pearson et Powell, 1990; Watanabe et Iwai, 1991; Desimone et Ungerleider, 1986), le sulcus intrapariétal, le cortex pariétal (Bremmer et al., 2001; Lewis et Van Essen, 2000; Linden, Grunewald et Anderson, 1999), ainsi que les régions frontales incluant les aires prémotrices et préfrontales (Graziano, Reiss et Gross, 1999; Watanabe, 1992; Romanski, 2007). Celles-ci sont caractérisées par le fait qu'elles reçoivent des afférences provenant de différentes aires cérébrales sensorielles primaires, et qu'elles semblent contenir des neurones multisensoriels.

Par contre, cette vision très hiérarchique du traitement multisensoriel a été récemment remplacée par une compréhension plus complexe et nuancée (Kayser et Logothetis, 2007; Ghazanfar et Schroeder, 2006; Driver et Spence, 2000; Foxe et Schroeder, 2005; Mesulam, 1998), selon laquelle il n'y a pas que les zones hétéro-modales qui sont impliquées dans l'IMS, mais également les aires sensorielles primaires que l'on croyait auparavant purement unimodales. Des projections descendantes provenant des zones de convergence hétéro-modales et influençant de façon rétroactive des aires sensorielles primaires ont été identifiées, en plus des projections ascendantes déjà connues (Calvert et Thesen, 2004). Des connexions directes entre les aires sensorielles ont également été observées (Driver et Spence, 2000; Falchier, Clavagnier, Barone et Kennedy, 2002; Rockland et Ojima, 2003). Bien qu'hypothétique, il est suggéré que ces connexions directes sont associées à un traitement multisensoriel rapide, mais peu spécifique. Elles pourraient s'activer en présence d'une co-stimulation, sans qu'il n'y ait de relation particulière entre les stimuli de différentes modalités, permettant ainsi de générer un état d'alerte ou une réponse rapide (Driver et Noesselt, 2008; Murray et al., 2005). Au contraire, les projections descendantes provenant des zones hétéro-modales pourraient être impliquées lors de tâches multisensorielles plus complexes, impliquant par exemple l'attention (Macaluso, 2006). En effet, il n'est pas exclu que des mécanismes différents puissent être impliqués selon le niveau de complexité des stimuli traités, de même que la tâche effectuée (Wallace et Stevenson, 2014).

2.1.4 Implications comportementales de l'IMS

Sur le plan de l'activation neuronale, il a donc été démontré que la présentation d'un stimulus bimodal est avantageuse par rapport à chacune de ses composantes unimodales. La question suivante est de déterminer ce qu'il en est des corrélats au niveau comportemental.

Les premières études chez le chat montrent que les données comportementales sont similaires à celles retrouvées au niveau de la réponse neuronale. En effet, les configurations de stimuli augmentant et/ou réduisant la réponse physiologique des neurones des CS ont, respectivement, le même impact sur les comportements d'orientation et les performances de localisation (Stein, Huneycut et Meredith, 1988; Stein, Meredith, Huneycutt et McDade, 1989; Wilkinson, Meredith et Stein, 1996; Jiang, Jiang et Stein, 2002; Burnett, Stein, Chaponis et Wallace, 2004; Burnett, Stein, Perrault et Wallace, 2007). Ces résultats suggèrent que ces comportements sont, du moins en partie, sous-tendus par l'activité neuronale au niveau des CS.

Chez l'humain, il a aussi été démontré que la précision et les temps de réaction (TRs) sont significativement améliorés par la présentation simultanée d'un stimulus d'une autre modalité lors de tâches de détection simples (Stein et al., 1989; Frassinetti, Bolognini et Làdavas, 2002; Hughes, Reuter-Lorenz, Nozawa et Fendrich, 1994; Frens, Van Opstal et Van der Willigen, 1995; Goldring, Dorris, Corneil, Ballantyne et Munoz, 1996; Nozawa, Reuter-Lorenz et Hugues, 1994; Colonius et Arndt, 2001; Diederich et Colonius, 2004; Forster, Cavina-Pratesi, Aglioti et Berlucchi, 2002; Làdavas, 2008; Rowland, Quessy, Stanford et Stein, 2007). Des résultats similaires ont été obtenus pour des tâches plus complexes, par exemple de localisation (Bolognini, Leo, Passamonti, Stein et Làdavas, 2007) ou de discrimination d'objets (Giard et Peronnet, 1999; Molholm, Ritter, Javitt et Foxe, 2004).

Dans ce contexte, la façon d'opérationnaliser l'IMS au niveau neurophysiologique a été transposée aux données comportementales. Elle se définit par la présence d'une différence statistiquement significative entre la réponse comportementale à un stimulus multisensoriel et la réponse à la plus efficace de ses deux composantes unisensorielles (Meredith et Stein, 1983; Stein, Stanford, Ramachandran, Perrault et Rowland, 2009). Le terme gain de redondance (GR) est utilisé pour quantifier cette différence. Toutefois, cette définition ne permet pas d'éliminer la possibilité que les deux stimuli aient été traités de façon indépendante, sans qu'il n'y ait eu d'intégration entre les signaux sensoriels. En effet, le principe de facilitation statistique prédit que, même lorsque les stimuli sont traités de façon indépendante, les TRs sont plus rapides pour la condition multisensorielle. On réfère à ce principe sous le terme de « modèle de course » (Miller, 1982; Raab, 1962). Celui-ci peut être représenté en imaginant deux courbes de distribution normales indépendantes, l'une représentant la distribution des TRs pour une composante auditive unique et l'autre représentant la distribution des TRs pour une composante visuelle unique. Si l'on établit une courbe de distribution prédite pour un stimulus audio-visuel à partir des TRs aux composantes auditive et visuelle uniques, en présumant qu'elles sont traitées de façon indépendante, le TR le plus rapide sera enregistré comme étant la réponse prédite à la présentation du stimulus audio-visuel pour chacun des essais. Cette distribution prédite pour un stimulus audio-visuel deviendra alors le point de référence pour déterminer s'il y a réellement présence d'un phénomène d'IMS. Si les résultats obtenus pour une condition multisensorielle surpassent les prédictions basées sur cette distribution audio-visuelle prédite, cela implique que le modèle de course ne peut expliquer à lui seul le phénomène de facilitation observé dans la condition multisensorielle, et donc qu'il y a présence d'IMS. Le GR et l'analyse des données basée sur le modèle de course seront donc les analyses statistiques principales utilisées pour les études incluses dans ce projet de thèse.

Concernant l'application au comportement des trois principes de base qui sous-tendent l'IMS au niveau de la réponse neuronale (Stein et Meredith, 1993), celle-ci est plus nuancée. Rappelons que ces principes stipulent que la réponse neuronale est maximisée par la présentation de stimuli qui sont spatialement (loi spatiale) et temporellement (loi temporelle) congruents, de même que de faible intensité (loi de la faible efficacité inversée).

De façon générale, au niveau comportemental, le GR serait maximal lorsque les stimuli sont présentés de façon simultanée (Frassinetti et al., 2002; Shore, Barnes et Spence, 2006; Diederich et Colonius, 2004; Làdavas, 2008; Frassinetti, Bolognini, Bonora et Làdavas, 2005). Comme pour l'animal, il existe chez l'humain une fenêtre d'IMS, c'est-à-dire un intervalle de temps durant lequel deux stimuli présentés sont perçus comme étant simultanés et peuvent être intégrés (Diederich et Colonius, 2009; Hairston, Laurienti, Mischra, Burdette et Wallace, 2003; Stevenson et Wallace, 2013; Stevenson, Wallace et Altieri, 2014), celle-ci variant d'un individu à l'autre (Vatakis et Spence, 2006; Stevenson et Wallace, 2013; Boer-Schellekens, Eussen et Vroomen, 2013) et selon le type d'information traitée (Stevenson, Zemtsov et Wallace, 2012). Concernant l'impact de la congruence spatiale sur l'IMS, son application serait possiblement tâche-dépendante, celle-ci étant marquée principalement pour les tâches de nature spatiale (Girard, Collignon et Lepore, 2011; Cappe, Thelen, Romei, Thut et Murray, 2012; Sperdin, Cappe et Murray, 2010; Spence, McDonald et Driver, 2004; Fiebelkorn, Foxe, Butler et Molholm, 2011; Vroomen et Keetels, 2006). Finalement, la généralisation du principe d'efficacité inversée au comportement demeure très controversée, certaines études étant en faveur de cette hypothèse (Diederich et Colonius, 2004; Corneil, Van Wanrooij, Munoz et Van Opstal, 2002) et d'autres l'infirmant (Holmes, 2007; 2009; Ross, Saint-Amour, Leavitt, Javitt et Foxe, 2007; Stein, Stanford, Ramachandran, Perrault et Rowland, 2009). Récemment, il a été suggéré qu'il y aurait une certaine flexibilité dans l'application de ces principes en lien avec les besoins de la tâche (Wallace et Stevenson, 2014; Doehrmann et Naumer, 2008; van Atteveldt, Murray, Thut et Schroeder, 2014; Ursino, Cuppini et Magosso, 2014).

Toutefois, il importe de spécifier qu'il s'agit de principes de base, tenant peu compte des processus cognitifs de plus hauts niveaux qui demeurent moins bien compris à l'heure actuelle (Stein et Rowland, 2011). À cet effet, il a, par exemple, été démontré que la congruence sémantique, qui réfère à l'identité et/ou au sens (Chen et Spence, 2010; 2011; Doehrmann et Naumer, 2008; Grassi et Casco, 2010; Laurienti, Kraft, Maldjian, Burdette et Wallace, 2004; Ursino et al., 2014) contribuerait grandement à l'IMS.

2.1.5 Informations incongruentes et IMS

D'un point de vue adaptatif, il est avantageux de combiner ensemble les stimuli sensoriels appartenant à un même événement. Cela explique le fait que la présentation d'informations bimodales congruentes est associée à un GR, tel que discuté dans la précédente section. Par contre, dans le quotidien, il arrive fréquemment d'être confronté simultanément à des informations contradictoires. Par exemple, si un automobiliste entend le bruit d'une sirène alors qu'il conduit sur la route et qu'il voit simultanément une voiture de police devant lui, il est possible qu'il ait l'impression que le son provient de la voiture, alors qu'en réalité, il est produit par une ambulance se trouvant derrière. Dans ce cas, les informations auditives et visuelles ont été combinées, et le percept biaisé en faveur de la modalité visuelle. Une autre possibilité peut être que le chauffeur perçoive le bruit de la sirène comme étant plus proche qu'il ne l'est en réalité. Il est suggéré que l'humain arrive à adapter de façon optimale la stratégie avec laquelle il combine ces informations incongruentes, en fonction de la fiabilité de chaque type d'indice, afin d'arriver au percept représentant le mieux la réalité extérieure (Ernst et Bank, 2002; Alais et Burr, 2004; Helbig et Ernst, 2007). Les phénomènes d'illusions multisensorielles représentent une façon intéressante d'observer les conséquences de la perturbation des relations typiques entre les indices sensoriels (Stein, 1998). Les illusions les plus communément utilisées, notamment dans l'étude de l'IMS chez les individus ayant un trouble du spectre de l'autisme, seront donc décrites brièvement ci-dessous.

Un phénomène illusoire bien connu est l'*effet ventriloque* (Howard et Templeton, 1966). En présence d'informations audio-visuelles spatialement incongruentes, la localisation du stimulus auditif se trouve biaisée dans la direction d'un stimulus visuel présenté simultanément (Radeau et Bertelson, 1987; Bertelson et Radeau, 1981; Slutsky et Recanzone, 2001; Radeau, 1994; Radeau et Bertelson, 1977; 1978; Vroomen et de Gelder, 2004; Spence et Driver, 2000; Pavani, Spence et Driver, 2000). De façon concrète, ce phénomène se produit lors de la projection d'un film au cinéma, et explique pourquoi la voix des acteurs semble provenir de leur bouche, alors que celle-ci est projetée via des haut-parleurs situés de chaque côté de l'écran. Sur le plan langagier, l'*effet McGurk* (McGurk et MacDonald, 1976) a aussi été grandement étudié. Celui-ci a permis de démontrer que lorsque le mouvement des lèvres perçu indique une syllabe différente de celle entendue de façon simultanée, il y a intégration en un seul percept qui combine ces deux syllabes. Par exemple, si un individu entend le mot « paire » et voit les lèvres prononcer le mot « frère », la perception sera une synthèse de ces deux mots, par exemple « faire » ou « traire ». Dans l'*illusion visuelle par le son* (en anglais « sound-induced flash illusion »), il a été démontré qu'un stimulus visuel unique peut être perçu comme étant double s'il est présenté simultanément à une paire de stimuli auditifs (effet de scission) et qu'une paire de stimuli visuels peut être perçue comme un seul stimulus si elle est présentée au même moment qu'un stimulus auditif unique (effet de fusion) (Shams, Kamitani et Shimojo, 2000; Shams, Kamitani, Thompson et shimojo, 2001; Watkins, Shams, Tanaka, Haynes et Rees, 2006; Shams, Kamitani et Shimojo, 2002; Shams et Kim, 2010). Finalement, une illusion développée plus récemment, l'*effet Pip et Pop*, a montré que la présentation simultanée d'un stimulus individuel sans lien sémantique avec la tâche permet d'augmenter la saillance de la cible lors d'une tâche de recherche visuelle (Van der Burg, Olivers, Bronkhorst et Theeuwes, 2008; Van der Burg, Talsma, Olivers, Hickey et Theeuwes, 2011; Vroomen et de Gelder, 2000).

2.1.6 Perception des émotions et IMS

La capacité de reconnaître les émotions exprimées par autrui est une habileté fondamentale pour la régulation des interactions interpersonnelles (Izard et al., 2001). Un aspect crucial de celle-ci est qu'elle implique généralement l'activation simultanée de différents canaux sensoriels (Campanella et Belin, 2007; Klasen, Chen et Mathiak, 2012). L'intégration de ces informations, qui sont le plus souvent congruentes sur le plan sémantique, permet d'arriver à un estimé plus juste de la réalité et ainsi d'optimiser la communication (Ernst et Bülthoff, 2004; de Gelder et Vroomen, 2000; de Gelder, Morris et Dolan, 2005). Les études portant sur l'IMS des émotions sont le plus souvent basées sur la combinaison d'informations sensorielles provenant de l'expression faciale et de la voix (Schirmer et Adolphs, 2017). En effet, les expressions faciales sont généralement apparentes et facilement accessibles dans la vie de tous les jours et leur utilisation peut être aisément adaptée en contexte expérimental (Schirmer et Adolphs, 2017). La voix a l'avantage de transmettre des signaux émotionnels pouvant être dissociés du contenu verbal, notamment via la prosodie (Schirmer et Adolphs, 2017; Banse et Scherer, 1996). Le décodage émotionnel basé sur le langage corporel (ex. posture) serait moins utilisé chez l'humain (Enea et Iancu, 2016).

Afin d'étudier la capacité des individus à intégrer les informations auditive et visuelle de nature émotionnelle, Collignon et collaborateurs (2008; 2010) ont développé un paradigme rigoureux basé sur l'utilisation de stimuli émotionnels écologiques non-verbaux et dynamiques (Belin, Fillion-Bilodeau et Gosselin, 2008; Simon, Craig, Gosselin, Belin et Rainville, 2008). Ce protocole consiste en une tâche de discrimination des émotions présentées sous forme auditive, visuelle et audio-visuelle. Les résultats ont montré une accélération significative des TRs pour la condition multisensorielle comparativement aux conditions unisensorielles, surpassant les prédictions basées sur le modèle de course. Cela suggère que la perception des émotions est une situation multisensorielle robuste qui respecte les principes généraux retrouvés au niveau cellulaire (Collignon et al., 2008; 2010). Les conclusions de cette étude concordent avec d'autres travaux qui ont démontré que l'IMS de la prosodie et de l'expression faciale permet une reconnaissance plus rapide et précise des expressions émotionnelles (Paulmann et Pell, 2011; Kreifelts, Ethofer, Grodd, Erb et Wildgruber, 2007; Föcker, Gondan et Röder, 2011; Chen, Han, Pan, Luo et Wang, 2016; Chen et al., 2016).

Comme les expressions émotionnelles provenant du visage et de la voix ne sont pas toujours sémantiquement congruentes, notamment dans le contexte d'interactions sociales plus complexes, certaines études ont tenté de préciser comment le cerveau combine ce type d'information lorsqu'elles sont conflictuelles. Lorsque libres de baser leur jugement sur l'une ou l'autre des modalités présentées, la majorité des individus tendent à catégoriser l'émotion par rapport à l'expression faciale (Takagi, Hiramatsu, Tabei et Tanaka, 2015; Massaro et Egan, 1996; Collignon et al., 2008; Jacob, Kreifelts, Brück, Erb, Hösl et Wildgruber, 2012; Watson et al., 2013; 2014). Cet avantage en faveur de la modalité visuelle est compatible avec le fait que celle-ci est considérée comme étant la plus représentative du véritable contenu émotionnel (Jacob et al., 2012). Par contre, la tendance opposée, soit un avantage en faveur de la modalité auditive, est observée lorsque l'on réduit la saillance du stimulus visuel, ce qui suggère que les règles demeurent flexibles (Collignon et al., 2008). Lorsque l'on demande aux individus de baser leur jugement spécifiquement sur l'une des modalités, la présentation d'une information sensorielle contradictoire affecte la discrimination émotionnelle, et ce même si les participants ont pour consigne d'ignorer cette information (de Gelder et Vroomen, 2000; Ethofer et al., 2006; Collignon et al., 2008). Cela suggère qu'il s'agit d'un processus automatique, se produisant, du moins partiellement, à un niveau pré-attentionnel (Vroomen, Driver et de Gelder, 2001).

Les études en neuroimagerie qui se sont intéressées à l'intégration audio-visuelle des émotions ont permis de mettre en lumière un réseau de régions cérébrales pouvant être impliquées dans ce processus. Le contraste entre des stimuli émotionnels audio-visuels et leurs composantes unisensorielles respectives serait principalement associé à une augmentation de l'activation au niveau du gyrus temporal moyen, du gyrus temporal supérieur et du sulcus temporal supérieur postérieur (STSp; Pourtois, de Gelder, Bol et Crommelinck, 2005; Ethofer, Pourtois et Wildgruber, 2006; Kreifelts et al., 2007; Kreifelts, Ethofer, Huberle, Grodd et Wildgruber, 2010; Robins, Hunyadi et Schultz, 2009). En tentant d'éviter certaines limites propres aux protocoles d'imagerie conventionnels, un phénomène d'adaptation multisensorielle a été observé au niveau du STSp droit, suggérant également l'implication de cette région dans l'intégration audio-visuelle des émotions (Watson et al., 2014). Cette notion est supportée par les études neuroanatomiques décrites précédemment qui démontrent que le STS représente une zone de convergence pour les projections issues des cortex auditif et visuel (Jones et Powell, 1970; Seltzer et Pandya, 1978).

2.2 Intégration unisensorielle ou intra-modale

Il est surprenant de noter qu'il demeure assez récent que l'un des aspects les plus fondamentaux de l'intégration multisensorielle a été exploré, à savoir si les mécanismes qui sous-tendent l'intégration des stimuli provenant de différentes modalités sensorielles (intégration multisensorielle ou inter-modale) sont les mêmes que ceux impliqués lors de la combinaison de stimuli provenant d'une même modalité sensorielle (intégration unisensorielle ou intra-modale) (Stein et Stanford, 2008; Alvarado, Vaughan, Stanford et Stein, 2007a).

Certaines études comportementales ont observé un GR lors de tâches de détection et de localisation impliquant des paires de stimuli de la même modalité sensorielle (Schröter, Ulrich et Miller, 2007; Savazzi et Marzi, 2002; 2008; Cavina-Pratesi, Bricolo, Prior et Marzi, 2001; Laurienti, Burdette, Maldjian et Wallace, 2006). Par contre, lorsque l'on compare directement le GR entre les paires de stimuli unimodales et bimodales, celui-ci est beaucoup plus marqué pour les stimuli multisensoriels tant chez l'animal (Gingras, Rowland et Stein, 2009) que chez l'humain (Girard, Pelland, Lepore et Collignon, 2013; Forster et al., 2002; Laurienti et al., 2006; Miniussi, Girelli et Marzi, 1998). De plus, la majorité de ces études ont démontré que l'amélioration de la performance ne surpasse pas les prédictions du modèle de course pour les paires de stimuli unisensoriels visuels (Girard et al., 2013; Murray, Foxe, Higgins, Javitt et Schroeder, 2001; Corballis, 1998; Reuter Lorenz, Nozawa, Gazzaniga et Hughes, 1995; Badzakova-Traikov, Hamm et Waldie, 2005) et tactiles (Girard et al., 2013; Forster et al., 2002), ce qui suggère que celle-ci peut s'expliquer par un effet de facilitation statistique plutôt que par un phénomène d'intégration neuronale. Quelques rares études ont tout de même montré un certain degré de violation du modèle de course, mais moindre que pour les stimuli multisensoriels (Forster et al., 2002; Cavina-Pratesi et al., 2001; Miniussi et al., 1998).

Sur le plan neurophysiologique, il a été montré que l'IMS engendre un produit plus important que l'intégration unisensorielle. En effet, Alvarado et ses collaborateurs (2007a; 2007b) se sont intéressés à la réponse des neurones unisensoriels visuels et multisensoriels du

CS à des paires de stimuli visuo-visuels et audio-visuels, l'objectif étant de comparer les propriétés de réponse en conditions uni- et multi-modales. Contrairement aux stimuli multisensoriels, les paires unimodales n'engendraient que très rarement une amélioration de la réponse neuronale, celle-ci étant généralement égale ou inférieure à la réponse neuronale pour la plus efficace de ses deux composantes visuelles, et ce tant pour les neurones unisensoriels que multisensoriels. Ces résultats suggèrent que les processus impliqués dans l'intégration de stimuli d'une même modalité diffèrent de ceux qui sous-tendent l'IMS. La modulation du traitement sensoriel par les projections des aires corticales associatives AES et rLS au niveau des neurones des CS serait également spécifique à l'IMS (Alvarado et al., 2007b). En effet, il a été démontré que la désactivation de ces régions altère l'IMS, mais n'a pas d'impact sur l'intégration d'informations de même modalité (Alvarado et al., 2007b). Cela témoigne encore une fois de différences fondamentales dans les circuits qui sous-tendent ces deux fonctions.

À la lumière des résultats expérimentaux et des théories plus récentes sur l'intégration sensorielle, notamment des modèles bayésiens, l'un des éléments qui paraît central pour expliquer cette différence réside dans le fait que les informations qui proviennent de différents organes sensitifs procurent des estimés indépendants par rapport à un même événement, qui ne sont pas contaminés par les mêmes sources de bruit interne, alors que les informations issues d'une même modalité sensorielle sont moins indépendantes l'une de l'autre et présentent généralement une certaine covariance (Ernst et Banks, 2002; Alvarado, Rowland, Stanford et Stein, 2008). En effet, les indices multisensoriels tendent à procurer des estimés complémentaires du même événement, alors que ce n'est pas autant le cas pour les indices provenant d'une même modalité sensorielle (Van Atteveldt et al., 2014). La combinaison de plusieurs mesures indépendantes est ce qui permet de réduire l'incertitude d'un estimé sensoriel (Ernst et Banks, 2002; Knill et Pouget, 2004; Fetsch, DeAngelis et Angelaki, 2013). Dans ce contexte, les combinaisons qui ne permettent pas d'augmenter la précision des informations transmises au système nerveux central ont moins de chances d'améliorer le comportement. Par exemple, deux stimuli sensoriels identiques, issus de la même modalité sensorielle, qui sont présentés simultanément et approximativement au même endroit dans l'espace ne seront pas associés à un GR équivalent à celui obtenu pour une paire de stimuli audio-visuels, car ils covarient au point où le bénéfice d'être intégrés devient minimal (Girard et al., 2013).

Chapitre 3 : Trouble du spectre de l'autisme et intégration sensorielle

3.1 Trouble du spectre de l'autisme

Le TSA est une condition neurodéveloppementale caractérisée par des atypies au niveau de la communication et des interactions sociales, de même que par la présence de comportements et d'intérêts restreints et répétitifs (American Psychiatric Association, 2013). À ce jour, il n'existe pas de marqueur biologique permettant de diagnostiquer le TSA, celui-ci étant plutôt effectué sur la base d'une anamnèse clinique et de l'observation des comportements (Sadock, Sadock & Ruiz, 2015). Selon les critères diagnostiques établis par le DSM-5, les atteintes socio-communicatives retrouvées dans le TSA peuvent toucher la réciprocité sociale et émotionnelle (ex. difficulté à entretenir une conversation partagée), l'utilisation et la compréhension des comportements non verbaux (ex. diminution du contact visuel, expression faciale inappropriée au contexte), de même que le développement et le maintien de relations interpersonnelles (ex. faible niveau d'empathie, difficulté à développer des amitiés). Au niveau des comportements et des intérêts répétitifs, on peut retrouver la présence de mouvements stéréotypés, l'adhésion à des routines et rituels fixes associée à une difficulté à tolérer le changement, des intérêts circonscrits et atypiques dans leur contenu ou leur intensité, de même que des atypies au niveau du traitement sensoriel (ex. intérêt spécifique envers certains attributs sensoriels, tendance à éviter les environnements surstimulants). Bien que cela ne figure pas parmi les critères diagnostiques, le TSA peut être accompagné, dans certains cas souvent plus sévères, d'un trouble du langage et/ou d'une déficience intellectuelle (American Psychiatric Association, 2013).

Au Canda, la prévalence du TSA est actuellement estimée à 1 enfant sur 66 (Agence de la santé publique du Canada, 2018). Cette condition est retrouvée 4 fois plus fréquemment chez les garçons que chez les filles, la prévalence étant de 1 garçon sur 42 et de 1 fille sur 165 (Agence de la santé publique du Canada, 2018). L'étiologie demeure imprécise à ce jour, bien qu'il soit clair qu'une composante génétique est impliquée (Sadock et al., 2015). L'hétérogénéité dans l'expression des symptômes suggère qu'il y a possiblement différents patrons de transmission génétique, impliquant chacun l'interaction entre plusieurs gènes, pour lesquels la pénétrance serait incomplète (Mottron et Caron, 2016). La présence de certains facteurs prénataux (ex. saignement gestationnel, diabète gestationnel, âge avancé des parents) et périnataux (ex. petit poids de naissance, détresse fœtale, trauma, incompatibilité du groupe sanguin ABO ou du facteur Rh, hyperbilirubinémie) pourrait possiblement augmenter le risque de TSA, bien qu'aucun d'entre eux ne puisse à lui seul expliquer le diagnostic (Sadock et al., 2015). À noter qu'il existe une comorbidité fréquente avec certains syndromes génétiques, notamment le syndrome du X fragile et la sclérose tubéreuse, ainsi qu'avec l'épilepsie. Le TSA associé à des affections neurologiques ou génétiques identifiées, dits TSA étiologique, est fréquemment exclu des études cliniques, en ce sens qu'il représente possiblement une entité différente du TSA idiopathique (primaire ou sans cause apparente) (Mottron et Caron, 2016).

Des changements significatifs ont été apportés dans les critères de l'autisme entre la 4^{e} version révisée et la 5^{e} version du DSM, ceux-ci ayant, entre autres, comme objectif que davantage d'importance soit accordée à la présence de symptômes de nature sensorielle (American Psychiatric Association, 2013). En effet, depuis les premières descriptions effectuées par Kanner au milieu des années quarante (Kanner, 1943), plusieurs études ont démontré des atypies dans le traitement sensoriel chez les individus ayant un TSA, et ce pour chacune des modalités sensorielles (Marco et al., 2011). Ces informations ont d'abord majoritairement été obtenues au moyen de questionnaires et d'entrevues auprès de proches d'enfants ayant un TSA (Baranek et al., 2006; O'Neill et Jones, 1997; Kasari et Sigman, 1997; Kern et al., 2007; Rogers, Hepburn et Wehner, 2003). Bien qu'hétérogènes, les symptômes sensoriels ont classiquement été divisés en trois catégories principales, soit une hypersensibilité sensorielle (réaction négative à des stimuli de l'environnement qui sont généralement considérés comme étant plutôt neutres), une hyposensibilité sensorielle (diminution ou absence de réponse à certains stimuli) et une recherche de stimulation (attrait pour certains types d'expériences sensorielles) (Baranek et al., 2006). Plus récemment, des études ont empiriquement confirmé la présence d'altération dans le traitement sensoriel chez les individus ayant un TSA (par exemple, O'Connor, 2012; Simmons et al., 2009; Baum, Stevenson et Wallace, 2015; Baranek, Little, Parham, Ausderau & Sabatos-Devito, 2014). Par contre, plusieurs d'entre elles ont aussi montré que dans certains domaines, notamment pour les tâches nécessitant un traitement sensoriel local ou de bas niveau (comparativement à un traitement global ou holistique), les fonctions sensorielles sont intactes et même augmentées en lien avec le TSA (Bertone, Mottron, Jelenic et Faubert, 2005; Almeida, Dickinson, Maybery, Badcock et Badcock, 2013; Bonnel et al., 2003; 2010; Mottron, Peretz et Ménard, 2000; Samson, Mottron, Soulières et Zeffiro, 2012).

Plusieurs théories ont été développées pour tenter d'expliquer de façon unifiée les particularités sensorielles associées au TSA (Baum et al., 2015). Un survol des principaux modèles est exposé dans le paragraphe suivant. Bien qu'il n'y ait pas de consensus, certains éléments sont similaires pour plusieurs d'entre eux, notamment la présence d'un avantage chez les individus ayant un TSA lors de tâches impliquant un traitement local ou de bas niveau comparativement à celles nécessitant une approche plus globale ou intégrative.

La *théorie de la faible cohérence centrale* (Frith et Happe, 1994; Happe, 1999; Happe et Frith, 2006; Burnette et al., 2005) suggère que le TSA est caractérisé par une altération au niveau de la communication ou de la connectivité entre les différents réseaux cérébraux. Sur le plan comportemental, cela se manifeste par la présence de difficultés dans le traitement global ou holistique, alors que le traitement d'éléments locaux demeure intact. Selon la *théorie du déficit d'intégration temporelle* (en anglais « temporal binding deficit »; Brock et al., 2002), le TSA serait associé à une atteinte des processus permettant la synchronisation de l'activité entre les réseaux neuronaux, principalement en ce qui a trait aux oscillations gamma de haute fréquence. On suggère que cela pourrait avoir un impact négatif sur les capacités d'intégration multisensorielle. De façon similaire, le *modèle du fonctionnement perceptuel augmenté* (Mottron et al., 2006) décrit chez les individus ayant un TSA la présence d'un mode perceptuel davantage orienté vers les éléments locaux associé à sur-fonctionnement perceptuel de bas niveau, avec une diminution relative de la performance pour les tâches perceptuelles complexes ou nécessitant un traitement plus global. Selon ce modèle, les individus ayant un TSA présentent également une plus grande indépendance de la perception par rapport aux processus rétroactifs de haut niveau (en anglais « top-down »). Cela pourrait expliquer la présence d'un biais favorable pour le traitement local versus global. Cet élément est également retrouvé dans une théorie perceptuelle de l'autisme développée plus récemment, basée sur les modèles bayésiens, soit l'*hypothèse de l'a priori diminué* (en anglais « hypo-priors » ; Pellicano et Burr, 2012). L'une des prémisses de ce modèle est que le processus de prise de décision par rapport à un influx sensoriel est basé sur deux éléments, soit la fiabilité de l'information sensorielle traitée et l'expérience antérieure (l'a priori). Chez les individus ayant un TSA, la prise de décision serait davantage influencée par l'influx sensoriel, et moins par l'expérience antérieure. Ce mode de fonctionnement serait associé à une perception plus littérale de l'environnement.

3.2 Trouble du spectre de l'autisme et Intégration multisensorielle

La présence d'atypies sensorielles non spécifiques à une seule modalité, de même que les modèles suggérant un avantage pour le traitement perceptif local et une diminution de la connectivité entre les différents réseaux cérébraux ont contribué au développement de l'hypothèse d'une dysfonction de l'IMS dans le TSA (Wallace et Stevenson, 2014). Il a été suggéré qu'une difficulté à intégrer les informations provenant de différentes modalités sensorielles puisse en partie expliquer certains symptômes propres à cette condition (Bahrick et Todd, 2011; Magnée, de Gelder, van Engeland et Kemner, 2007; 2008; Russo et al., 2010; Russo, Mottron, Burack et Jemel, 2012; Iarocci et McDonald, 2006; Marco et al., 2011), incluant les particularités sensorielles (ex. tendance à éviter les environnements surstimulants, intérêt spécifique envers certains attributs sensoriels), mais également les atteintes au niveau des habiletés sociales et de la communication (Monk et al., 2010; Bachevalier et Loveland, 2006; Sigman, Dijamco, Gratier et Rozga, 2004). Le percept représentant l'élément de base sur lequel se construisent les représentations perceptuelles et cognitives, il fait sens qu'un changement au niveau des processus d'IMS puisse avoir un effet en cascade sur les étapes subséquentes de traitement de l'information, et que cela affecte ultimement les sphères cognitives plus complexes, telles que la communication et les interactions sociales (Stevenson et al., 2014a; Bahrick et Lickliter, 2000; 2002; Bahrick, 2010; Bahrick et Todd, 2011).

Plusieurs études se sont intéressées à la question de l'IMS chez les individus ayant un TSA au cours des dernières années, mais jusqu'à présent le portrait demeure complexe et confus (Wallace et Stevenson, 2014). Une hypothèse est que la capacité des individus ayant un TSA à intégrer des informations provenant de différentes modalités sensorielles pourrait varier selon le type d'informations qui sont intégrées (Bebko et al., 2006; Magnée et al., 2008; Mongillo et al., 2008). Les informations de nature sociale (ex. émotions, langage) étant généralement plus complexes et variables que les stimuli non sociaux (Adolphs, 2001; Dawson et al., 2004), il a été suggéré qu'elles pourraient être associées à des difficultés d'IMS beaucoup plus marquées chez les individus ayant un TSA.

3.2.1 Trouble du spectre de l'autisme et IMS d'informations sociales

Les études portant sur l'IMS d'informations sociales chez les personnes ayant un TSA sont principalement basées sur deux grands domaines, soit l'intégration audio-visuelle des émotions et du langage verbal. Quelques rares travaux se sont également intéressés à l'impact de l'interaction entre les informations visuelles et tactiles de nature sociale sur la proprioception et la représentation corporelle.

Concernant l'IMS des émotions, la majorité des études effectuées chez les individus ayant un TSA portent sur la capacité à reconnaître la congruence émotionnelle entre des paires de visage et de voix exprimant une émotion. Ces études suggèrent une diminution de la capacité à faire correspondre l'expression faciale et la prosodie qui sont associées à la même émotion (Hobson, 1986; Hobson, Ouston et Lee, 1988; Loveland et al., 1995; O'Connor, 2007; but see Prior, Dahlstrom et Squires, 1990). Il semble également que les individus ayant un TSA bénéficient moins de l'ajout d'une composante auditive lors d'une tâche de discrimination émotionnelle à partir d'expressions faciales (Xavier et al., 2015). La réponse électrophysiologique à des paires visage-voix a été comparée entre les individus ayant un TSA et ceux ayant un DT. Pour le groupe avec DT, l'amplitude de la composante N2 au niveau occipito-temporal était augmentée par l'ajout d'une voix exprimant la peur à la présentation d'un visage exprimant cette même émotion. Au contraire, les adultes ayant un TSA présentaient une diminution de la composante N2 dans cette condition multisensorielle, suggérant une différence chez cette population dans la façon d'intégrer les informations audio-visuelles de nature émotionnelle (Magnée et al., 2008). Il a toutefois été suggéré par la suite que celle-ci puisse être attribuée à une différence au niveau des mécanismes attentionnels (Magnée, de Gelder, van Engeland et Kemner, 2011). Dans le même sens, une étude en tomographie par émission de positron a montré une diminution de l'activation au niveau du gyrus fusiforme droit et du cortex frontal inférieur en lien avec la présentation simultanée d'une voix et d'une expression faciale exprimant la même émotion chez les individus ayant un TSA (Hall, Szechtman et Nahmias, 2003). Deux études en IRMf, dont l'une sur un très petit échantillon de participants (Loveland, Steinberg, Pearson, Mansour et Reddoch, 2008), ont également démontré certaines atypies dans les réseaux cérébraux recrutés par les adolescents ayant un TSA lors de tâches multisensorielles émotionnelles, notamment une diminution de l'activation des régions frontale médiale et orbitofrontale lors d'une tâche de congruence émotionnelle (Loveland et al., 2008) et une hypoactivation des aires associatives frontales et temporales lorsqu'on leur demandait d'identifier l'émotion associée à des paires audio-visuelles (Boer-Schellekens et al., 2013).

Par contre, il est important de noter que les études empiriques portant sur l'intégration des émotions chez les individus ayant un TSA présentent certaines limites importantes. En effet, la grande majorité d'entre elles ont employé des stimuli visuels statiques, notamment des photos de visages exprimant une émotion, et très peu ont utilisé des vidéos représentant des expressions faciales dynamiques (Golan, Baron-Cohen et Golan, 2008; Loveland et al., 1997; Loveland et al., 2008). Il est démontré que les stimuli statiques ont une faible validité écologique, alors que le mouvement facial contribue à l'identification des émotions et joue un rôle important dans la perception de leur intensité (Ambadar, Schooler et Cohn, 2005; Biele et Grabowska, 2006). Les régions cérébrales impliquées dans le traitement des expressions faciales, telles que le STSp, l'amygdale et l'insula, s'activent également différemment en réponse à des expressions émotionnelles dynamiques versus statiques (Haxby, Hoffman et Gobbini, 2000; 2002; LaBar, Crupain, Voyvodic et McCarthy, 2003; Miki, Takeshima, Watanabe, Honda et Kakigi, 2011). De plus, seulement quelques études portant sur l'IMS des émotions chez les individus ayant un TSA ont utilisé des vocalisations affectives comme stimulus auditif, la majorité d'entre elles ayant employé des mots ou des phrases susceptibles d'induire un biais sémantique ou lexical, augmentant ainsi le risque que les différences obtenues soient liées à des variations dans le niveau de compréhension du langage (Haviland, Walker-Andrews, Huffman, Toci et Alton, 1996; Paul, Augustyn, Klin et Volkmar, 2005; Lindner et Rosen, 2006). Finalement, aucune de ces études n'a utilisé un paradigme et des analyses statistiques permettant de calculer le GR multisensoriel et de le comparer à un modèle prédictif. Tel que décrit précédemment, d'un point de vue neurophysiologique, l'IMS implique que l'interaction entre deux influx sensoriels produit un signal qui diffère de la réponse neuronale à la meilleure de ses composantes individuelles (Stein et Meredith, 1993). Ces études, à partir desquelles des inférences par rapport à l'IMS chez les individus ayant un TSA ont été tirées, sont donc basées sur des protocoles qui ne tiennent pas compte de cette définition (Stein et al., 2010).

La compréhension du langage est une autre habileté du registre social nécessitant l'intégration d'informations audio-visuelles, soit le mouvement des lèvres et le son de la voix. Plusieurs études basées sur l'*effet McGurk* décrit précédemment (McGurk et MacDonald, 1976), ont montré que les enfants et les adolescents ayant un TSA démontrent une diminution de l'influence de la vision sur l'audition lors de ce type de paradigme (de Gelder, Vroomen et Van der Heide, 1991; Mongillo et al., 2008; Irwin, Tornatore, Brancazio et Whalen, 2011; Bebko, Schroeder et Weiss, 2014; Stevenson et al., 2014a; mais voir Stevenson et al., 2017; Stevenson et al., 2014c; Williams, Massaro, Peel, Bosseler et Suddendorf, 2004; Iarocci, Rombough, Yager, Weeks et Chua, 2010). Certaines études ont observé que ces différences dans l'IMS d'informations de nature linguistique semblaient se résorber chez l'adulte, possiblement en lien avec le développement (Taylor, Isaac et Milne, 2010; Foxe et al., 2015; Keane, Rosenthal, Chun et Shams, 2010; Saalasti et al., 2012).

Une difficulté supplémentaire associée au fait de percevoir les expressions émotionnelles et le langage en contexte naturaliste est le fait que la saillance de ces informations est souvent diminuée par le bruit environnant. Par exemple, la voix d'un individu peut être masquée par le son des objets à proximité ou par la voix d'autres personnes. De la même façon, l'expression faciale d'un individu peut être partiellement cachée par une partie de son corps ou en lien avec l'angle dans lequel il est positionné par rapport à l'observateur. Dans ces contextes, il devient nécessaire de pouvoir extraire de façon efficace les informations émotionnelles ou langagières du bruit environnant, afin d'en saisir le contenu et de pouvoir interagir de façon appropriée avec l'autre (Pelli et Farell, 1999). Comparativement aux individus ayant un DT, il a été démontré que, dans un environnement bruyant, les enfants ayant un TSA bénéficient moins de voir le mouvement des lèvres lors d'une tâche de discrimination langagière auditive (Smith et Benetto, 2008). Les difficultés d'IMS en contexte linguistique retrouvées dans le TSA seraient inversement corrélées au ratio signal/bruit lors de la présentation des stimuli (Foxe et al., 2015; Stevenson et al., 2017). À notre connaissance, à ce jour, aucune étude n'a évalué la capacité des individus ayant un TSA à percevoir et intégrer les émotions dans le bruit.

À noter que la quasi-totalité des études portant sur l'intégration d'information de nature sociale chez les individus ayant un TSA sont basées sur l'utilisation de stimuli auditifs et visuels, possiblement en lien avec leur rôle apparent dans la communication et les relations interpersonnelles (Cascio, Lorenzi et Baranek, 2016). Toutefois, le toucher est également reconnu comme étant impliqué dans le développement social (Myers, 1984; Hertenstein, 2002; Hertenstein, Keltner, App, Bulleit et Jaskolla, 2006; Thye, Bednarz, Herringshaw, Sartin et Kana, 2018; Dunbar, 2010; Cascio et al., 2016; Field, 2001), en plus de contribuer au processus d'acquisition d'un sens du soi (Schütz-Bosbach, Musil et Haggard, 2009) qui sous-tend certaines fonctions sociales, telles que la capacité d'imitation et l'empathie (Schütz-Bosbach, Mancini, Aglioti et Haggard, 2006). La majorité des études qui se sont intéressées à l'intégration d'informations visuo-tactiles de nature sociale en autisme ont utilisé un effet d'illusion que l'on appelle l'impression de la main de caoutchouc (en anglais « rubber hand illusion »; Botvinick, 2004), dans lequel la fusion d'informations visuelles et tactiles permet d'influencer la représentation corporelle et la proprioception. Il a été démontré que la susceptibilité à cette illusion est réduite (Paton, Hohwy et Enticott, 2012) et retardée (Cascio, Foss-Feig, Burnette, Heacock et Cosby, 2012) chez les individus ayant un TSA. Un paradigme similaire a été adapté en réalité virtuelle. Deux images de la main du participant étaient produites, l'une positionnée au même endroit que la vraie main et l'autre à côté, et des stimulations visuo-tactiles étaient transmises, de façon synchrone ou asynchrone, sur l'une de ces images virtuelles et sur la vraie main du participant. Cela a permis de démontrer que les participants ayant un TSA, comme les enfants plus jeunes, ne s'approprient pas l'image de la main dont la position est discordante par rapport à la leur, mais qui est stimulée de façon synchrone, comme c'est le cas pour les enfants avec un DT du même âge chronologique, ce qui suggère la possibilité d'un retard dans le développement de l'intégration visuo-tactile d'informations sociales chez cette population (Ropar, Greenfield, Smith, Carey et Newport, 2018; Greenfield, Ropar, Smith, Carey et Newport, 2015).

3.2.2 Trouble du spectre de l'autisme et IMS d'informations non sociales

Afin de préciser la capacité d'individus ayant un TSA à intégrer des informations non-sociales, plusieurs études ont utilisé l'*illusion visuelle par le son* (en anglais « sound-induced flash illusion »; Shams et al., 2000), dans laquelle un stimulus visuel unique peut être perçu comme étant double s'il est présenté simultanément à une paire de stimuli auditifs et qu'une paire de stimuli visuels peut être perçue comme un seul stimulus si elle est présentée simultanément à un stimulus auditif unique. De façon générale, ces études suggèrent que la sensibilité à cette illusion multisensorielle est indépendante du diagnostic de TSA (Van der Smagt, Van Engeland et Kemner, 2007; Keane et al., 2010; Foss-Feig et al., 2010; Stevenson et al., 2017; mais voir Stevenson et al., 2014b; Bao, Doobay, Mottron, Collignon et Bertone, 2017). De plus, aucune différence n'a été observée entre les enfants et adolescents ayant un TSA et ceux avec un DT lors de tâches de discrimination spatiale de stimuli audio-visuels et visuo-vestibulaires (Stewart et al., 2016; Zaidel, Goin-Kochel et Angelaki, 2015). Par contre, les deux études ayant employé un paradigme de détection simple suggèrent au contraire la présence d'un déficit dans la capacité des enfants ayant un TSA à intégrer des informations multisensorielles de nature non-sociale (Brandwein et al., 2013; Brandwein et al., 2015). En effet, elles ont démontré que les performances dans la condition multimodale excédaient celles prédites par le modèle de course chez les enfants ayant un DT, mais pas chez ceux avec un diagnostic de TSA (Brandwein et al., 2013; 2015).

De la même façon que pour les informations de nature sociale, la majorité des études comportementales portant sur l'intégration de stimuli non sociaux en autisme sont basées sur les modalités auditives et visuelles. À notre connaissance, Poole et ses collaborateurs (2015; 2018) sont les seuls à avoir utilisé le tact en tant que modalité principale. Ils ont démontré que lorsqu'on leur demande de déterminer s'ils perçoivent une seule ou deux vibrations tactiles, pendant qu'un nombre congruent ou incongruent de stimuli visuels sont présentés, les individus ayant un TSA témoignent d'une plus grande difficulté à supprimer le traitement des distracteurs plus distants et controlatéraux, suggérant une altération dans la modulation spatiale des interactions visuo-tactiles (Poole et al., 2015; 2018).

Au moyen d'enregistrements électrophysiologiques durant la présentation passive de stimuli de bas niveau auditifs, tactiles et audio-tactiles, un phénomène d'IMS a été observé chez les participants ayant un DT entre 100 et 200 ms, mais pas chez les enfants ayant un TSA, suggérant une diminution de l'intégration automatique des informations sensorielles chez les enfants ayant un TSA comparativement à ceux ayant un DT (Russo et al., 2010). Des résultats similaires ont été obtenus lors d'une tâche de détection simple basée sur des stimuli audio-visuels. Les enfants ayant un TSA ont démontré une diminution de l'intégration au niveau neuronal, entre 100 et 150 ms post-stimulation, qui semblait associée à l'utilisation d'un réseau cortical différent de celui retrouvé chez les enfants avec DT (Brandwein et al., 2013). Ces corrélats neuronaux de l'IMS (mesurés entre 100 et 130 ms) corréleraient avec le niveau de sévérité du TSA (Brandwein et al., 2015).

En somme, bien que plusieurs études aient démontré une difficulté à intégrer les stimuli de nature sociale chez les individus ayant un TSA, les résultats demeurent plus équivoques en ce qui concerne l'intégration d'information exempte de contenu social.

3.3 Trouble du spectre de l'autisme et intégration unisensorielle ou intra-modale

Plusieurs des principaux modèles perceptifs du TSA proposent donc un avantage en faveur d'un traitement local et de bas niveau, avec une difficulté relative pour les tâches nécessitant une approche plus globale ou intégrative (Dakin et Frith, 2005). Tel que mentionné précédemment, il est également suggéré que le TSA est associé à une diminution de la connectivité globale, mais à une augmentation de la connectivité à l'intérieur des réseaux cérébraux locaux (Brock et al., 2002). Ces hypothèses suscitent une question importante, à savoir si les altérations observées au niveau de l'intégration sensorielle sont spécifiques aux conditions multisensorielles, qui impliquent de combiner des signaux provenant de régions cérébrales différentes et souvent plus distantes, ou si elles touchent également l'intégration unisensorielle ou intra-modale. Les capacités d'intégration inter-modale et intra-modale n'ont jamais été directement comparées chez les individus ayant un TSA.

Chapitre 4 : Objectifs et hypothèses de recherche

Comme en témoignent les chapitres précédents, le portrait actuel concernant l'intégration sensorielle chez les personnes ayant un TSA demeure complexe et équivoque. Les conclusions varient grandement d'une étude à l'autre, passant d'une atteinte importante de l'intégration sensorielle à une absence complète de différence entre les groupes. L'hypothèse d'un déficit qui serait spécifique aux informations de nature sociale est proposée, mais demeure à confirmer. La variabilité dans les paradigmes et les analyses utilisées, de même que dans les caractéristiques des participants inclus dans les échantillons est significative et complexifie la comparaison des résultats entre les études. De plus, plusieurs d'entre elles infèrent des conclusions concernant l'intégration sensorielle chez les individus ayant un TSA, alors qu'il n'est pas clair qu'il s'agit réellement de ce processus qui est mesuré, par exemple lors de tâches d'appariement multisensoriel. Il est également surprenant de constater que l'on n'a pas évalué si les résultats obtenus sont spécifiques l'IMS ou s'ils se généralisent à l'intégration d'informations de même modalité.

Dans ce contexte, l'objectif général de ce projet de thèse est d'arriver à une meilleure compréhension du lien qui existe entre le TSA et les performances d'intégration sensorielle. À cette fin, la première question est de déterminer si la capacité d'intégrer des informations provenant de différentes modalités sensorielles diffère entre les individus ayant un TSA et ceux avec DT, puis de préciser si celle-ci dépend du type de stimulus, c'est-à-dire de sa nature sociale versus non sociale. Le second objectif est d'évaluer comment les performances d'IMS se comparent à celles retrouvées lors de l'intégration de stimuli de même modalité sensorielle chez les personnes ayant un TSA. Par ailleurs, nous évaluerons également si le changement d'allocation des ressources attentionnelles entre les modalités est susceptible d'expliquer les différences d'IMS entre les groupes, et proposerons un paradigme pouvant éventuellement être utilisé chez les individus ayant un TSA pour évaluer l'impact de la saillance des stimuli sur l'IMS.

Pour ce faire, les études 1, 2 et 3 compareront les performances comportementales d'un groupe d'adultes ayant un TSA à celles d'individus ayant un DT, appariés selon l'âge, le genre et le quotient intellectuel (QI). Afin de faciliter la comparaison des résultats entre les études, les participants inclus dans chacune d'entre elles présenteront des profils similaires en ce qui a trait à l'âge, au QI et aux modalités diagnostiques du TSA. Le type de paradigme utilisé permettra de calculer le GR et de comparer les résultats obtenus à ceux prédits par le modèle de course pour l'ensemble des conditions à l'étude (intégration inter- versus intra-modale, stimuli de nature sociale versus non sociale). Finalement, l'étude 4, dont l'objectif est d'élaborer et de tester un protocole visant à déterminer l'impact du niveau de saillance des stimuli sur le traitement multisensoriel, sera effectuée auprès d'un échantillon d'adultes ayant un DT.

Article 1 : Intégration multisensorielle d'expressions émotionnelles chez les individus ayant un TSA.

L'objectif principal de cette étude est d'explorer la capacité des individus ayant un TSA à intégrer des informations de nature sociale de différentes modalités sensorielles. Dans ce cadre, la performance d'un groupe d'adultes ayant un diagnostic de TSA est comparée à celle d'un groupe contrôle avec DT lors d'une tâche de discrimination émotionnelle d'informations auditives (prosodie), visuelles (expressions faciales) et audio-visuelles. Afin de compenser pour les limites majeures des études précédentes, des stimuli visuels dynamiques, écologiques et empiriquement validés sont utilisés (Belin et al., 2008; Simon et al., 2008). Les stimuli auditifs sont exempts de contenu verbal, dans l'optique d'éliminer la présence d'un biais sémantique ou lexical. Le paradigme utilisé permet de mesurer le GR associé au traitement multisensoriel et de le comparer entre les groupes, puis de déterminer si le gain multisensoriel surpasse les prédictions du modèle de course.

Plusieurs études ont observé un déficit d'IMS pour les stimuli complexes de nature sociale (ex. émotions, langage) chez les individus ayant un TSA (Bebko et al., 2006; Magnée et al., 2008; Mongillo et al., 2008). Dans ce sens, nous émettons l'hypothèse que les participants ayant un TSA bénéficieront moins de l'exposition à l'information bimodale de nature émotionnelle que les individus ayant un DT. Cela se traduira par la présence d'un GR diminué chez les adultes ayant un TSA par rapport aux participants ayant un DT, de même que par une absence de violation du modèle de course, suggérant ainsi une atteinte des processus d'IMS en contexte social.

Article 2 : Intégration multisensorielle d'informations non sociales chez les individus ayant un TSA.

Cette étude a pour objectif de déterminer si les difficultés suggérées au niveau de l'IMS d'informations de nature sociale chez les individus ayant un TSA peuvent être généralisées à l'intégration de stimuli exempts de contenu social. Pour ce faire, les performances à une tâche de recherche visuelle complexe durant laquelle un indice sonore peut être présenté simultanément au changement de couleur de la cible ont été comparées entre les individus ayant un TSA et les participants contrôles. Ce paradigme a été validé antérieurement chez les personnes ayant un DT (Van der Burg et al., 2008), et démontre de façon générale une augmentation de l'efficacité à identifier la cible visuelle en présence de l'indice sonore, suggérant un effet bénéfique associé à la combinaison de ces informations multisensorielles.

Tel que mentionné, plusieurs études ont suggéré que les déficits d'IMS retrouvés chez les personnes avec un TSA sont limités aux stimuli de nature sociale (Bebko et al., 2006; Magnée et al., 2008; Mongillo et al., 2008). Par contre, des travaux récents ont montré que ce déficit d'intégration est aussi observé lors du traitement d'informations non-sociales de bas niveau (Brandwein et al., 2013; 2015). Puisque le phénotype inhérent au TSA inclut des atypies qui affectent à la fois le fonctionnement social (ex. difficultés de communication) et non-social (ex. évitement des environnements surstimulants, attirance envers certains attributs sensoriels spécifiques), nous croyons que l'intégration d'informations non-sociales de bas niveau sera également touchée. Donc, nous prédisons que l'avantage associé à l'ajout d'un indice sonore sur la précision et la vitesse de réponse lors de la tâche de recherche visuelle sera moindre chez les individus ayant un TSA que chez ceux avec un DT.

Article 3 : Intégration intra-modale et inter-modale chez les adultes ayant un TSA.

La troisième étude incluse dans ce projet de thèse a trois objectifs principaux. Premièrement, celle-ci vise à confirmer les résultats obtenus lors de la deuxième étude à savoir si les difficultés d'IMS observées pour les informations de nature sociale sont généralisables à des stimuli de nature non sociale. Cette fois, cela sera évalué au moyen d'une tâche de détection simple, récemment validée par notre équipe auprès d'adultes ayant un DT. Ce paradigme a l'avantage de limiter l'influence potentielle de processus de plus haut niveau sur l'IMS. Le second objectif est de comparer les performances d'intégration inter-modale (multisensorielle) et intra-modale (unisensorielle) chez les participants ayant un TSA, puis de mettre celle-ci en perspective avec les données obtenues chez les personnes ayant un DT. Finalement, nous évaluerons l'impact du changement d'allocation des ressources attentionnelles entre les modalités sensorielles sur la performance de détection, et le cas échéant, la possibilité que cela explique les différences entre les groupes au niveau de l'IMS. À noter que pour cette étude, il a été décidé d'utiliser des stimuli de modalité visuelle et tactile. Ce choix est basé principalement sur le fait que la modalité tactile n'a été que très peu étudiée en lien avec l'IMS chez les individus ayant un TSA, bien que son rôle dans le développement social soit clairement démontré (Cascio et al., 2016; Field, 2001; Myers, 1984) et que les atypies somatosensorielles figurent parmi les symptômes sensitifs les plus fréquemment retrouvés dans cette population (Rogers et al., 2003).

De la même façon que pour l'étude précédente, nous émettons l'hypothèse que le GR visuo-tactile sera diminué chez les individus ayant un TSA comparativement aux participants avec un DT, et que les TRs pour la condition multisensorielle ne surpasseront pas les prédictions du modèle de course, témoignant d'une atteinte des processus d'IMS pour les stimuli non sociaux chez cette population. Concernant la comparaison entre les capacités d'intégration inter-modale et intra-modale, il a été montré que celles-ci diffèrent chez les personnes ayant un DT en raison d'une plus grande indépendance entre les informations provenant de plusieurs modalités (Girard et al., 2013; Forster et al., 2002). Nous émettons l'hypothèse que le déficit d'intégration chez les individus ayant un TSA sera limité aux informations multisensorielles, et que ces capacités seront préservées lors de l'intégration de signaux unisensoriels. Précisément, nous prédisons que le groupe d'individus ayant un TSA aura un GR inférieur à celui du groupe contrôle pour l'intégration inter-modale, mais pas pour l'intégration intra-modale.

Article 4 : Impact du niveau de saillance basé sur l'excentricité lors d'une tâche d'intégration multisensorielle.

Tel que mentionné, l'un des principes de base de l'IMS au niveau neurobiologique est que l'amélioration de la réponse neuronale associée à la présentation d'une paire de stimuli bimodale congruente est généralement inversement proportionnelle au niveau de saillance des stimuli qui composent cette paire. Cela fait référence à la loi de l'efficacité inversée (Stein et

Meredith, 1993). Par contre, la possibilité de généraliser cette observation neurophysiologique au comportement demeure controversée (Holmes, 2007; 2009; Ross et al., 2007; Stein et al., 2009). Lors de la présentation de paires bimodales incongruentes, il est plutôt suggéré que le percept puisse être biaisé en faveur de la plus saillante des deux composantes, augmentant ainsi la probabilité d'obtenir une perception juste de la réalité (Ernst et Bank, 2002; Alais et Burr, 2004; Helbig et Ernst, 2007). Afin de préciser ces hypothèses, l'objectif de cette étude est de développer un protocole permettant d'évaluer l'impact du niveau de saillance des stimuli sur le traitement multisensoriel. Le paradigme développé permet de localiser la position de cibles auditives, visuelles et audio-visuelles à travers l'espace frontal (180 degrés), et d'ainsi évaluer l'effet de la diminution de saillance associée à l'excentricité sur le GR pour les stimuli audio-visuels spatialement congruents et sur l'effet de capture multisensorielle (ou effet ventriloque) pour les paires audio-visuelles spatialement incongruentes.

Basé sur le principe d'efficacité inversée, notre hypothèse est que le GR augmentera progressivement en lien avec le niveau d'excentricité, c'est-à-dire à mesure que la saillance des informations auditives et visuelles diminue. Comme il est suggéré que la perception multimodale est basée sur une pondération des différents influx sensoriels en fonction de leur niveau de fiabilité (Alais et Burr, 2004; Ernst et Bülthoff, 2004), et que la saillance des informations visuelles est susceptible d'être davantage affectée par la périphérie, nous prévoyons une diminution de l'effet de capture visuelle (ou effet ventriloque) en en lien avec l'augmentation du degré d'excentricité auquel les stimuli seront présentés.

Une fois le protocole développé et testé auprès d'une population ayant un DT, celui-ci pourra éventuellement être utilisé chez les individus ayant un TSA, afin de préciser comment varie l'impact du niveau de saillance sur le traitement multisensoriel chez cette population. Il n'y a pas d'élément qui suggère que l'impact de la saillance sur le gain de redondance en présence de stimuli spatialement congruents puisse différer entre ces groupes. Par contre, en ce qui concerne le traitement de stimuli spatialement incongruents, une hypothèse est que le moindre poids accordé aux aprioris dans la prise de décision en contexte sensoriel (Pellicano et Burr, 2012) engendre une réponse différente chez les personnes ayant un TSA.

Chapitre 5

Article 1: Multilevel alterations in the processing of audio-visual emotion expressions in autism spectrum disorders.

Multilevel alterations in the processing of audio-visual emotion expressions in autism spectrum disorders.

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5.1 Abstract

The abilities to recognize and integrate emotions from another person's facial and vocal expressions are fundamental cognitive skills involved in the effective regulation of social interactions. Deficits in such abilities have been suggested as a possible source for certain atypical social behaviors manifested by persons with autism spectrum disorders (ASD). In the present study, we assessed the recognition and integration of emotional expressions in ASD using a validated set of ecological stimuli comprised of dynamic visual and auditory (non-verbal) vocal clips. Autistic participants and typically developing controls (TD) were asked to discriminate between clips depicting expressions of disgust and fear presented either visually, auditorily or audio-visually. The group of autistic participants was less efficient to discriminate emotional expressions across all conditions (unimodal and bimodal). Moreover, they necessitated a higher signal-to-noise ratio for the discrimination of visual or auditory presentations of disgust versus fear expressions. These results suggest an altered sensitivity to emotion expressions in this population that is not modality-specific. In addition, the group of autistic participants benefited from exposure to bimodal information to a lesser extent than did the TD group, indicative of a decreased multisensory gain in this population. These results are the first to compellingly demonstrate joint alterations for both the perception and the integration of multisensory emotion expressions in ASD.

Keywords : Autism spectrum disorder; multisensory; emotion expressions; audition; vision.

5.2 Introduction

The ability to recognize emotional expressions is a fundamental cognitive ability for the regulation of interpersonal interactions (Adolph, 2002; Custrini & Feldman, 1989; Izard et al., 2001). The tone of the voice and the facial expression are two crucial cues that we constantly use to predict others' actions and to react appropriately in a social situation. An important aspect of affect perception in everyday life is that it usually involves, like speech, the activation of several sensory channels simultaneously. Therefore, the combination of information from facial expression (visual signal) and prosody (auditory signal) usually results in a unified and more optimal representation of the expressed emotion (de Gelder, Bocker, Tuomainen, Hensen, & Vroomen, 1999; de Gelder & Vroomen, 2000; de Gelder et al., 2005). For example, it has been shown that the multisensory integration (MSI) of these two types of information typically allows for faster and more accurate recognition of emotion expressions in human observers (Collignon et al., 2008, 2010; de Gelder & Vroomen, 2000; Dolan, Morris, & de Gelder, 2001; Kreifelts, Ethofer, Grodd, Erb, & Wildgruber, 2007; Massaro & Egan, 1996) and in human- machine interfaces (Busso et al., 2004).

Deficits in the perception of emotion expressions have been suggested as possible causes of atypical social and communicative interactions that are a striking part of the behavioral phenotype of autistic spectrum disorders (ASD) (Bachevalier & Loveland, 2006; Monk et al., 2010; Sigman, Dijamco, Gratier, & Rozga, 2004). However, a majority of the empirical investigations in the field have focused on the facial expression of emotions using static stimuli such as photographs (Bal et al., 2010), with only a few studies using video representing dynamic facial movements (Golan, Baron-Cohen, & Golan, 2008; Loveland, Steinberg, Pearson, Mansour, & Reddoch, 2008; Loveland et al., 1997). The former static stimuli have limited ecological validity and neglect the intrinsic dynamic nature of facial expressions. Indeed, facial movements have been shown to enrich emotional expression, contributing to its identification and playing an important role in the perception of its intensity (Ambadar, Schooler, & Cohn, 2005; Biele & Grabowska, 2006). Also, neuroimaging studies have shown that the brain regions involved in the processing of facial affect, such as the posterior superior temporal sulcus (pSTS), the amygdala and the insula, respond differently to dynamic than to static emotional expressions (Haxby, Hoffman, & Gobbini, 2000, 2002; LaBar, Crupain, Voyvodic, &

McCarthy, 2003; Miki, Takeshima, Watanabe, Honda, & Kakigi, 2011). Moreover, only a few studies explored the processing of affective vocalizations in ASD (Baker, Montgomery, & Abramson, 2010; Hall, Szechtman, & Nahmias, 2003; Loveland et al., 2008; Wang, Lee, Sigman, & Dapretto, 2007). In most cases, these studies included semantic or lexical confounds in the tasks (Lindner & Rosen, 2006) raising the possibility that the results were influenced by differences in language comprehension (Haviland, Walker-Andrews, Huffman, Toci, & Alton, 1996; Paul, Augustyn, Klin, & Volkmar, 2005). Finally, most studies investigating the recognition of emotions in autistic individuals explored a single sensory modality at a time, whereas in natural settings, emotions are expressed both facially and vocally, allowing the combination of these sources of information by human observers for optimal recognition (Collignon et al., 2008; de Gelder et al., 1999; de Gelder & Vroomen, 2000; de Gelder et al., 2005). The use of multisensory conditions to explore the recognition of emotional expressions in ASD is of particular interest since differences in multisensory processing between ASD and typically developing controls (TD) has recently been demonstrated (Collignon et al., 2012; Magnee, de Gelder, van Engeland, & Kemner, 2007; 2008; Russo et al., 2010; Russo, Mottron, Burack, & Jemel, 2012).

An additional challenge associated with the processing of emotional expressions in natural settings is related to the fact that the saliency of emotional information in faces and voices is often reduced by environmental noise. In signal processing, noise can be considered unwanted data that is not being used to transmit a signal, but is simply a by-product of other activities. For example, the voice of an individual can be masked by noise from other human voices or from objects surrounding him. Similarly, a person's facial expression can be partially hidden by an object or because of the angle in which the observer is positioned. Therefore, the ability of the observer to extract efficiently emotional information from noise appears crucial for effective social interactions and therefore it is relevant to evaluate the perception of emotional expressions in noisy situations (Pelli & Farell, 1999). Some studies have suggested that ASD have a specific difficulty in perceiving speech when presented in a noisy background compared to TD (Alcantara, Weisblatt, Moore, & Bolton, 2004; Smith & Bennetto, 2007). To our knowledge, no study has investigated the perception of visual or auditory emotional expressions in noise in ASD.

The goal of the present study was therefore to explore the perception and the integration of emotion expressions in ASD by using ecological and validated sets of dynamic visual and non-verbal vocal clips of emotional expressions (Belin, Fillion- Bilodeau, & Gosselin, 2008; Simon, Craig, Gosselin, Belin, & Rainville, 2008). Participants were asked to categorize expressions of fear or disgust as quickly and accurately as possible when presented with auditory, visual and audio–visual stimuli. This task allowed us to compare recognition and MSI performance of emotional expressions between ASD and TD. We also compared unisensory performance of ASD and TD participants by measuring their ability to discriminate emotional expressions when presented auditorily and visually in individually adapted levels of noise. Similar paradigms have been previously successfully used to demonstrate that the perception of emotional expressions is a robust multisensory situation which follows rules that have been observed in other perceptual domains (Collignon et al., 2008) and to illustrate gender differences in the processing of emotion expressions (Collignon et al., 2010).

5.3 Material and Methods

5.3.1 Subjects

Thirty-two autistic participants (30 males; mean age 21 years; range 14–32 years) and 18 TD controls (18 males; mean age 21 years; range 15–27 years) participated in this study. Participants were recruited from the database of the Rivière-des-Prairies Hospital's autism clinic (Montreal, Canada). ASD participants were defined using DSM-IV-TR diagnostic criteria, as operationalized by the Autism Diagnostic Interview – Revised (ADI-R) (Lord, Rutter, & Le Couteur, 1994) and the Autistic Diagnostic Observation Schedule-Generic (ADOS-G) (Lord et al., 2000) algorithms. Control participants and their first-degree relatives were screened with a questionnaire for any history of neurological or psychiatric disorders. The groups were closely matched in terms of laterality and Weschler IQ ([Full-scale = ASD: 105 ± 15; TD 111 ± 9]; [Performance = ASD: 102 ± 13; TD 108 ± 10]; [Verbal = ASD: 106 ± 16; TD 112 ± 11]). All participants had a global Wechsler score of 80 or more. They all had normal or corrected to normal far and near vision assessed before testing using near and far Snellen acuity charts. The ethics board of both the Rivière-des-Prairies Hospital and University of Montreal approved the study.

Autism lies on a spectrum and comprises two major subgroups: individuals with classic autism and those with Asperger's syndrome. These groups share the combination of social-communication difficulties, repetitive behaviors and restricted interests. In classic autism, language development in children is also delayed and their intelligence level range from intellectual disability to superior intelligence, while criteria for Asperger excludes cognitive impairment. Following the DSM-5 decision to adopt a dimensional view of heterogeneity in autism spectrum, we subsequently merged the subgroups in a common sample of ASD. However, since previous experiments suggested that classic autism and Asperger's syndrome might differ in terms of perceptual abilities (Brochu-Barbeau, Soulie`res, Dawson, Zeffiro, & Mottron, 2013; Bonnel et al., 2010; Jones et al., 2009), we also analyzed the data by separating the two subgroups and no significant difference was observed between them (see supplemental analyses; SFigs. 2–5).

5.3.2 Stimuli

As in our previous experiments, fear and disgust expressions were used because, from an evolutionary perspective, these emotions may be more important for survival than other basic emotions. Indeed, in the multisensory domain, Dolan et al. (2001) suggested that the rapid integration across modalities is not as automatic for happy expressions as it is for fear signals. More specifically, the goal of fear would be to augment sensory vigilance (Davis & Whalen, 2001) whereas disgust is associated with sensory rejection (Rozin & Fallon, 1987). Consistent with this idea, it has been demonstrated that fear enhances sensory acquisition and perception, whereas disgust dampens it (Susskind et al., 2008), therefore giving empirical support to the Darwinian hypothesis that some basic emotion expressions may have originated in altering the sensory interface with the physical world (Darwin, 1972/1998). Furthermore, disgust and fear expressions convey highly discriminable signals (Belin et al., 2008; Ekman & Friesen, 1976; Simon et al., 2008; Susskind et al., 2008) and serve as a model to study the existence of separate neural substrates underlying the processing of individual emotion expressions (Calder, Lawrence, & Young, 2001).

The visual stimuli used in this study were selected from a standardized set of dynamic color stimuli of actors and actresses displaying prototypical facial expressions (Simon et al., 2008). One actor and one actress who best depicts facial expressions of fear and disgust based on a previous control study (Collignon et al., 2008) were selected. The facial expressions were “prototypical” and “natural” insofar as they possessed the key features (identified using the Facial Action Coding System: FACS) identified by Ekman and Friesen (1976) as being representative of everyday facial expressions (Simon et al., 2008). The same actor and actress portrayed the two emotions. The selected clips were edited in short segments of 500 ms with a size of 350 x 430 pixels using Adobe Premiere and Adobe Aftereffect (Adobe Systems Inc., San Jose, US). The clips always started with a neutral face, which then continuously evolves into full expression (Fig. 1).

The auditory stimuli used were selected from the “Montreal affective voices”, a standardized set of emotional vocal expressions designed for research on auditory affective processing with the avoidance of potential confound from linguistic content (Belin et al., 2008). Among this set, we selected fear and disgust vocalizations portrayed by one actor and one actress producing the stimuli with the highest level of distinctiveness. Again, each actor portrayed both emotions. The selected affective interjections were then edited in short meaningful segments of 500 ms (10 ms sinusoidal rise/fall ramp time) and normalized peak values (90%) using Adobe Audition 2.0 (Adobe Systems Inc., San Jose, US) (see the Supplementary material section for further details about the selection of the stimuli).

5.3.3 Procedure

Participants sat in a silent and darkened room with their head supported by a chinrest in front of a computer screen at a viewing distance of 57 cm. Visual stimuli (width = 10° and height = 12.5° of visual angle) were presented in the center of the screen over a constant gray background. Auditory stimuli were presented binaurally through headphones (Philips HJ030) at a self-adjusted comfort level.

5.3.3.1 Task 1: Discrimination of emotional expressions and multisensory integration.

Participants were asked to discriminate fear and disgust stimuli presented auditorily, visually, or audio-visually. The bimodal (audio–visual) stimuli consisted in the synchronous presentation of visual and auditory clips depicting the same emotion (e.g. fearful face/fearful voice). Each actor or actress in the visual clips has been associated with a specific voice, and these pairs remained the same for all experimental conditions. Participants were asked to respond as quickly and as accurately as possible in a forced two-choice discrimination paradigm, by pressing the appropriate keyboard keys with the index (left key) and the middle finger (right key) of their right hand. The response keys were counterbalanced across subjects so that for half of the participants the left key corresponded to fear and the right key to disgust and for the other half the opposite was true. The participants were presented a total of 120 stimuli randomly interleaved (2 [emotions: fear, disgust] x 2 [actors: 1 actor, 1 actress] x 3 [modalities: visual, auditory, audio- visual] x 10 repetitions). These stimuli were displayed in 4 separate blocks of 30 stimuli lasting approximately 10 min. Each stimulus presentation was followed by a 2000 ms gray background (the response period), and then a central cross appeared for 500–1500 ms (uniformly distributed random duration) prior to the next stimulus (Mean ISI 3000 ms; range 2500–3500 ms, uniformly distributed).

5.3.3.2 Task 2: Signal/Noise ratio for auditory and visual emotional expressions recognition.

The participants had to discriminate between fear and disgust stimuli presented visually or auditorily. They were asked to respond as accurately as possible, without time constraint, by pressing the appropriate keyboard keys with the index (left key) and the middle finger (right key) of their right hand. The response keys were counterbalanced across subjects, so that for half of the participants the left key corresponded to fear and the right key to disgust and for the other half the left key corresponded to disgust and the right key to fear. Each stimulus presentation lasted until the participant pressed one of the response keys. The next stimulus appeared immediately after the participant's response. After each correct response, white Gaussian noise was randomly added to the presented audio (sequence of normally distributed random numbers at a sample rate of 44.1 kHz) or video (Gaussian noise in each of the three color channels) clips. Similarly, noise was removed from the following stimulus each time the participant made a wrong choice. This individual adjustment was carried out using the QUEST adaptive staircase (Watson & Pelli, 1983) implemented in the Psychtoolbox (Brainard, 1997; Pelli, 1997) for Matlab (The MathWorks, Inc.). The signal-to-noise ratio of the video and audio clips was adjusted in order to target a 80% accuracy rate in each participant. The participants viewed a total of 320 stimuli (2 [emotions: fear, disgust] x 2 [actors: 1 actor, 1 actress] x 2 [modalities: visual, auditory] x 40 repetitions). These stimuli were separated in 4 “visual blocks” each including 40 video clips and 4 “auditory blocks” each comprising 40 audio clips. The blocks were counterbalanced between modalities.

5.3.4 Data Analysis

5.3.4.1 Task 1.

Task accuracy was estimated by the calculation of the d' sensitivity index computed following Snodgrass and Corwin (1988). Only latencies of correct responses were considered in the analysis of reaction times (RTs). In experiments equally emphasizing accuracy and processing speed, it is, in principle, possible that each subject (group) may adopt different response strategies, by varying RT inversely with accuracy (and thus show speed-accuracy trade-off). Therefore, overall performance (and variance) may best be reflected by a single variable that simultaneously takes into account speed and accuracy. We recently introduced the “speed-accuracy composite score (SACS)”, which is an extension of the widely used “inverse efficiency scores” (Townsend & Ashby, 1983), and demonstrated its utility in investigating between-groups differences in performance (Collignon et al., 2010). With SACS, in order to attribute the same weight to accuracy and RTs performances across the participants, we normalized the d’ and the RT scores obtained across all conditions and we subtracted the normalized RTs from the normalized d’ [Z(d’) - Z(RTs)]. Differences in performance were then analyzed by submitting the d’, RTs and SACS to a repeated measures ANOVA. Based on significant F-values, Bonferroni post-hoc analyses were performed when appropriate. Percentage of correct responses (HIT) and of false alarms (and related statistics) are illustrated separately in a supporting figure (Fig. S1).

5.3.4.2 Multisensory Integration.

We first calculated separately in each participant the redundancy gain (RG) as defined by the decrease (in percent) of the mean RT obtained in the multisensory condition when compared with the mean RT obtained in the best unisensory condition (Girard, Collignon, & Lepore, 2011). The RG was then submitted to an independent samples t-test to test for a statistical difference between ASD and TD. Different explanations have been put forward to account for the observation of the RG. The most commons are the race and the coactivation models. The race model proposes that each individual stimulus elicits an independent detection process. For a given trial, the fastest stimulus determines the observable RT. On average, the time to detect the fastest of several redundant signals is faster than the detection time for a single signal. Therefore, the speeding up of reaction time is attributable to statistical facilitation (Raab, 1962). When the race model's prediction is violated, the speedup of RTs cannot be attributed to a statistical effect alone but some kind of coactivation must have occurred. To account for violations of the race model's prediction, the coactivation model (Miller, 1982) proposes that the neural activations of both stimuli combine to induce faster responses. Testing the race model inequality is widely used as an indirect behavioral measure of neurophysiological integrative processes underlying RT facilitation (see for example Girard, Pelland, Lepore, and Collignon (2013); but see Otto and Mamassian (2012)). To further investigate multisensory integration differences between ASD and TD, the race model inequality was evaluated (Miller, 1982) using the RMITest software, which implements the algorithm described at length in Ulrich, Miller, and Schröter (2007). This procedure involves several steps. First, cumulative distribution functions (CDFs) of the RT distributions were estimated for every participant and for each condition (visual, auditory and audio–visual conditions). Second, the bounding sum of the two CDFs obtained from the two unimodal conditions (visual and auditory) were computed for each participant. This measure provided an estimate of the boundary at which the race model is violated, given by Boole's inequality. Third, percentile points were determined for every distribution of RT, including the estimated bound for each participant. In the present study, the race model inequality was evaluated at the 5th, 15th, 25th ... 95th percentile points of the RT distributions. Fourth, for each percentile, mean RTs from redundant conditions were subtracted from the mean RTs from the bound. If these scores were above 0, it exceeded the race model prediction and therefore supported the existence of an integrative process (Miller, 1982; but see Otto and Mamassian (2012)).

5.3.4.3 Task 2.

The signal-to-noise ratios, corresponding to the detection thresholds, were analyzed using a repeated measures ANOVA (2 [groups: ASD, TD; between subjects factor] x 2 [modalities:

auditory, visual; within subject factor]). Based on significant F-values, Bonferroni post-hoc analyses were performed when appropriate.

5.4 Results

In all the analyses presented in the main manuscript, data obtained for fear and disgust stimuli are collapsed. Results (and related statistics) obtained for each emotion separately are presented in the supplementary material (Sfig. 6, Sfig. 7, Sfig. 8).

5.4.1 Task 1.

For the SACS (Fig. 2A), we observed a main effect of the factor "group" (F(1,48) = 5.27, $p \leq .05$, $\eta^2_{partial}=.10$), revealing superior general performance in the TD group compared to the ASD group. The analysis also yielded a main effect of the factor "modality" (F(2,96) = 31.82, $p \leq .0005$, $\eta^2_{partial}=.61$). Post-hoc comparisons demonstrated superior performance with bimodal stimuli compared to visual ($p \leq .0005$) and auditory ($p \leq .0005$) stimuli alone, and superior performance with visual stimuli compared to auditory stimuli ($p \leq .05$). A "modality" by "group" interaction was not evidenced (F(2,96) = .082, p=.92, $\eta^2_{partial}=.002$), suggesting that lower performance in the ASD group was generalized across stimulus presentation conditions. For d' scores (Fig. 2B), we did not observe any significant difference in performance between TD and ASD (F(1,48) = .21, p=.65, $\eta^2_{partial}=.004$). However, we observed a main effect of the factor "modality" (F(1,48) = 12.18, $p \leq .005$, $\eta^2_{partial}=.20$) with superior performance for bimodal stimuli compared to auditory ($p \leq .005$) but not visual (p=.56) stimuli and no difference between visual and auditory (p=.1) stimuli. There was no interaction between "group" and "modality" factors (F(2,96) = .97, p=.38, $\eta^2_{partial}= .02$). For RTs (Fig. 2C), we observed a main effect of the factor "group" (F(1,48) = 6.12, $p \leq .05$, $\eta^2_{partial}=.11$), revealing superior general performance (faster RTs) in TD compared to ASD. It also yielded a main effect of the factor "modality" (F(1,48) = 70.66, $p \leq .005$, $\eta^2_{partial}=.60$), with superior performance for bimodal stimuli compared to visual ($p \leq .0005$) and auditory ($p \leq .0005$) stimuli alone and no difference between visual and auditory (p=.32) stimuli. There was no interaction between "group" and "modality" factors (F(2,96) = 1.54, p=.22, $\eta^2_{partial}= .03$).

5.4.2 Multisensory Integration.

Although ASD ($t(31) = 4.73$, $p \leq .001$, $\eta^2 = .42$) and TD ($t(17) = 9.43$, $p \leq .001$, $\eta^2 = .84$) showed a reliable RG, there was a superior multisensory gain in the TD group compared to the ASD group ($t(48) = -3.21$, $p \leq .005$, $\eta^2 = .18$) (Fig. 3). To further test for differences in multisensory integration abilities in ASD and TD, we used a one-sampled t-test against '0' in order to investigate whether the positive difference between the redundant condition and the probabilistic bound was significant (meaning a violation of the race model prediction) in TD and ASD. For TD, the difference was significant for the fastest 5th percentiles of the RTs distribution ($t(17) = 2.1$, $p \leq .05$, $\eta^2 = .21$) whereas for ASD, no violation of the race model inequality was found ($t(31) = .44$, $p = .66$, $\eta^2 = .01$) (Fig. 4).

5.4.3 Task 2.

We observed a main effect of the factor "group" ($F(1,48) = 3.93$, $p \leq .05$, $\eta^2_{\text{partial}} = .08$), with lower detection thresholds for the TD group. There was also a main effect for the factor "modality" ($F(1,48) = 159.58$, $p \leq .0005$, $\eta^2_{\text{partial}} = .77$), with lower detection thresholds for visual than for auditory stimuli (Fig. 5). A "modality" by "group" interaction was not found ($F(1,48) = 1.54$, $p = .22$, $\eta^2_{\text{partial}} = .003$), suggesting lower detection thresholds in the TD group for both visual and auditory modalities.

5.5 Discussion

Alterations in the ability to recognize emotional expressions in ASD is often suggested as a possible source for certain atypical social and communicative behaviors that characterize this population. The first aim of this study was to empirically test this hypothesis by exploring the perception of emotion in autistic individuals using ecological and validated sets of dynamic visual and non-verbal vocal clips of emotional expressions. We found a decreased performance in ASD compared to TD for the recognition of emotion expressions in every condition of stimulus presentation (auditory, visual, bimodal; see Fig. 2). These results suggest the existence of a generalized alteration in the perception of emotion expressions in ASD that is apparent in different sensory channels. Group differences are mainly (but not only) noticeable in their response speed (Fig. 2C). Perceptual decisions involve the accumulation of sensory evidence over time, a process that is corrupted by noise (Gold & Shadlen, 2007). The basic principle is that noisy evidence for a sensory signal is accumulated over time until a criterion is reached and a decision is made (Bogacz, Wagenmakers, Forstmann, & Nieuwenhuis, 2010). It is possible that auditory and visual estimates of emotional expressions are noisier in ASD leading to the necessity to accumulate more evidence before taking a perceptual decision on the emotional expression displayed. This is partly supported by the observation that ASD also necessitate a higher signal-to-noise ratio than TD for the recognition of unimodal auditory and visual emotion expressions in noise. Pellicano and Burr (2012) recently relied on a Bayesian framework to suggest that altered autistic perception might result from attenuated priors resulting in fewer internal constraints on perception (hypo-priors). The authors suggested that hypo-priors in ASD should impede/improve performance in situations where priors help/bias perceptual decisions, respectively. It might therefore be hypothesized that in the context of the discrimination of emotion expressions, individuals with ASD might lack priors that typically improve the efficiency of perceptual computations by reducing overall noise or error (e.g. this mouth's shape means this expression). Overall, this impairment in the extraction of meaningful emotional information might be related to the prominent atypical behavior of ASD in social contexts, by preventing them from engaging in "expected" behaviors, such as quickly and efficiently adjusting to a particular theme in a conversation conveyed by the facial or vocal emotional information originating from the expression of the interlocutor, particularly in situation when the environment is noisy. Our experiment however focused on a subset of emotional expressions, which do not preclude the possibility that the results might be different with other emotional expressions (e.g. happiness, anger). Also, because the present study does not indicate what specific features of the facial and vocal expressions are processed abnormally in ASD during the perception of emotion expression (i.e. changes in the shapes of the eyes for facial expressions or changes in the pitch of the voice for vocal expressions), further research is needed to investigate in more details which are the specific underlying mechanisms of this impairment (Neumann, Spezio, Piven, & Adolphs, 2006; Spezio, Adolphs, Hurley, & Piven, 2007; Song, Kawabe, Hakoda, & Du, 2012).

Our results agree with previous studies pointing toward inferior performance by ASD for the recognition of emotional expressions. Deficits in the recognition of visual emotional expressions were previously found in ASD (Celani, Battacchi, & Arcidiacono, 1999; Kuusikko et al., 2009; Pelphrey et al., 2002; Teunisse & de Gelder, 2001). It was also demonstrated that ASD were markedly impaired in selecting the appropriated facial expression of emotions associated with a vocalization (Hobson, 1986a, 1986b). In addition, ASD were found to have lower performance than TD when asked to match faces on the basis of emotional expressions (Hobson, Ouston, & Lee, 1988), and were shown to be much better for matching corresponding objects than facial expressions (Braverman, Fein, Lucci, & Waterhouse, 1989). These results are also consistent with a recent study by Hubert, Wicker, Monfardini, and Deruelle (2009) measuring electro-dermal response during perception of emotional expressions in ASD. The authors found that autistic persons, unlike TD, do not present any variation of the skin conductance response when presented with facial emotional expressions. Because of the important role of the amygdala in the modulation of autonomic response (Bagshaw & Benzies, 1968; Lang, Tuovinen, & Valleala, 1964; Mangina & Beuzeron-Mangina, 1996) and in the processing of emotions expressions (Adolph, 2002; Critchley et al., 2000; LeDoux, 2000), Hubert et al. (2009) attributed their results to a putative dysfunction of this brain region in ASD. This hypothesis is coherent with several studies that have reported structural, functional and connectivity alterations of the amygdala in ASD (Baron-Cohen et al., 1999; Corbett et al., 2009; Critchley et al., 2000; Kleinhans et al., 2008; Monk et al., 2010; Munson et al., 2006; Murphy et al., 2012; Nacewicz et al., 2006; Pelphrey, Morris, McCarthy, & Labar, 2007; Schumann, Barnes, Lord, & Courchesne, 2009; Schumann et al., 2004; Shalom, 2009; Stanfield et al., 2008; Weng et al., 2011). Such alteration in the function of the amygdala may also, at least in part, explain the generalized (amodal) deficit observed in ASD in the current study, since this core brain structure in affective processing receives input from all sensory modalities (LeDoux, 2007; Macdonald, 1998) and has been demonstrated to be involved in the processing of both visual (Costafreda, Brammer, David, & Fu, 2008) and auditory (Fecteau, Belin, Joanette, & Armony, 2007) emotional expressions. This hypothesis of a general alteration in the processing of emotional expressions may also relate to the observation that individuals with ASD show reduced processing of affective meaning of actions (Grezes, Wicker, Berthoz, & de Gelder, 2009) and body postures (Hadjikhani et al., 2009).

Aside from atypicalities in emotional brain centers, some neuroimaging studies in ASD also showed alterations in sensory-specific brain regions dedicated to the processing of facial or vocal information. For example, a reduction of activity of the fusiform face area (FFA) has been found in ASD during the discrimination of different faces (Critchley et al., 2000; Hubl et al., 2003; Pierce, Muller, Ambrose, Allen, & Courchesne, 2001; Schultz, 2005). However, a recent meta-analysis (Samson, Mottron, Soulieres, & Zeffiro, 2012) suggested that these results depend on particular task characteristics and are not explained by a generalized disruption of the mechanisms of the fusiform gyrus or by a reduced face expertise (Hadjikhani et al., 2004; Hadjikhani, Joseph, Snyder, & Tager-Flusberg, 2007; Pierce, Haist, Sedaghat, & Courchesne, 2004). It has also been hypothesized that this hypoactivation of FFA results from diminished gaze fixation during face processing in autism (Dalton et al., 2005) or from a slight displacement of the face activation region (Scherf, Luna, Minshew, & Behrmann, 2010). A study involving only five ASD individuals has also suggested that ASD failed to activate superior temporal sulcus (STS), a voice-selective region, in response to vocal sounds, whereas a normal pattern of brain activation is present in response to non-vocal sounds (Gervais et al., 2004). Altogether, these results suggest atypical cortical processing of socially relevant visual and auditory information in ASD and again may be related to our observation of a generalized alteration in the processing of emotional expression irrespective of the sensory modality conveying such information.

One might wonder if the alteration observed here for the discrimination of emotional expressions reflects a general deficit in the processing of any sensory/perceptual information in ASD. Previous results from our team and from several other groups strongly argue against such interpretation. Brochu-Barbeau et al. (2013) recently suggested that when ASD are matched with control participants on the basis of Weschler scores (like here), this might result in the ASD being superior in various perceptual domains. Actually, several participants from the present study were enrolled in a recent experiment demonstrating faster visual-search abilities in ASD, despite reduced multisensory integration (Collignon et al., 2012). Therefore, such dissociation between the presence (in comparison with a Wechsler matched control group) of diminished processing of social information and preserved or even enhanced processing of non-social stimuli (Bertone, Mottron, Jelenic, & Faubert, 2005; Caron, Mottron, Berthiaume, & Dawson, 2006), which is especially evident for visuo-spatial processing (Collignon et al., 2012; Jolliffe & Baron-Cohen, 1997; Joseph, Keehn, Connolly, Wolfe, & Horowitz, 2009; O'Riordan, Plaisted, Driver, & Baron-Cohen, 2001; Pellicano, Gibson, Maybery, Durkin, & Badcock, 2005;

Shah & Frith, 1983) and for pitch perception (Bonnel et al., 2010; Jones et al., 2009), may represent a behavioral marker for ASD and may explain the classical observation of an avoidance of socially complex environment concomitant with an enhanced investment in restricted domain of expertise in ASD.

It is worth noting here that all the participants of the current study were late adolescents and young adults, between 15 and 27 years. Many studies suggested an improvement in emotional recognition during the course of development in TD and ASD children (Lindner & Rosen, 2006; Wright et al., 2008). Moreover, Smith, Montagne, Perrett, Gill and Gallagher (2010) reported a significant relationship between age and accuracy at identifying the emotional expression of disgust in ASD. A meta-analysis by Stanfield et al. (2008) also demonstrated that as age increased the volume difference of the amygdala between ASD and TD decreased. Therefore, it would be interesting to carry out further research to investigate whether differences in the perception of multisensory emotion expressions between ASD and TD are amplified during childhood and reduced in older adults.

The second main objective of the present experiment was to investigate the ability to integrate audio-visual emotional expressions in ASD. The results obtained in the present study support our previous findings (Collignon et al., 2008, 2010) by showing that the information from the visual and auditory sensory modalities interact to produce a redundancy gain, which is expressed by a significant reduction in RTs in the bimodal condition when compared to the best modality. However, even if a RG was found in both groups, it was reduced in the ASD compared to TD group. Consistently with previous studies (Collignon et al., 2008, 2010), we found that in TD, for the fastest latencies (percentiles) of the RT distributions, the RT probability in the bimodal condition exceeded the probabilistic sum of the RT observed in the auditory or visual unisensory conditions, suggesting that signal integration occurred (Fig. 4; Miller, 1982; but see Otto and Mamassian (2012)). This was however not observed in ASD. These results therefore indicate that in addition to a general alteration in the recognition of emotions, individuals with ASD also present altered ability to integrate separate sensory representations of the emotional expressions. It is important here to understand that this result is not a direct outcome of the unimodal inferiority in ASD. In contrast, according to the "inverse effectiveness” principle, a basic concept in multisensory integration stating that the multisensory gain is inversely proportional to the saliency of unisensory signals (Stein & Meredith, 1993), one may have predicted greater integration in ASD on the basis of their inferior performance in unisensory conditions. We therefore postulate that ASD might present a specific alteration in the integration of socially-contingent information coming from separate auditory and visual modalities.

Because the combination of multiple sensory inputs into a single percept requires the integration of different sensory areas of the brain, the reduced MSI in ASD is coherent with models suggesting reduced communication between functionally specialized brain regions (Belmonte et al., 2004; Brock, Brown, Boucher, & Rippon, 2002; Liu, Cherkassky, Minshew, & Just, 2011; Rippon, Brock, Brown, & Boucher, 2007; Schipul, Keller, & Just, 2011), as exemplified by altered anatomical and functional inter-regional connectivity (Cherkassky, Kana, Keller, & Just, 2006; Thomas, Humphreys, Jung, Minshew, & Behrmann, 2011; Weinstein et al., 2011). Supporting this hypothesis, Hall et al. (2003) found a decrease in the activity of the right fusiform region and a reduced frontal activation in ASD when congruent prosodic content was added to emotional facial stimuli. Also, an electroencephalographic study, measuring event related potentials (ERPs) in response to cross-modal presentation of emotional expressions in ASD, suggested impaired functional connectivity between the fusiform gyrus and STS, which is involved in MSI (Magnée, de Gelder, van Engeland, & Kemner, 2008). Finally, several evoked potential studies have demonstrated that ASD present delayed latencies of the N170 face-sensitive component to faces compared to TD (McPartland, Dawson, Webb, Panagiotides, & Carver, 2004; O’Connor, Hamm, & Kirk, 2005). This delay in processing facial information during social interactions could lead to an inaccurate association between facial expressions and the auditory information coming from a person’s voice (O’Connor, 2007).

Interestingly, MSI deficit in ASD does not appear to be selective to complex social stimuli. In a recent study, we showed that ASD do not benefit from the presence of a typically advantageous temporally relevant tone during a complex visual search task (Collignon et al., 2012). Along the same lines, a recent electroencephalographic study demonstrated that ASD children do not automatically combine sensory inputs early in the processing hierarchy as efficiently as TD individuals (Russo et al., 2010; but see Russo et al. (2012)). Also, Brandwein et al. (2012) recorded high-density electrophysiology during a simple audio-visual task and showed reduced behavioral facilitation and altered early neurophysiological processing of multisensory stimuli in children with ASD when compared to TD. Reduced MSI abilities might therefore be grounded on impairments in neural communication across distant brain systems that generalize across cognitive domains (i.e. social versus non-social).

Previous studies reported that persons with classic autism (AUT) and Asperger's syndrome (ASP), two sub-populations in the broad ASD, might differ in terms of perceptual skills (Bonnel et al., 2010; Mazefsky & Oswald, 2007; Rinehart, Bradshaw, Moss, Brereton, & Tonge, 2000; Sahyoun, Soulieres, Belliveau, Mottron, & Mody, 2009). As individuals with AUT have developmental communication/language impairments whereas persons with ASP do not exhibit language delay or disruption during development (see Section 2.1), one might have expected that AUT might be associated with more detrimental effects when perceiving emotions (Mazefsky & Oswald, 2007). Interestingly, we did not find any significant differences between the AUT and ASP sub-groups for the perception and MSI of emotion expressions (see SFigs. 2–5). In contrast, our results suggest that the history of language development in the ASD population has no significant impact on the atypical perception of emotional expressions observed in this population.

In conclusion, the data presented here provides strong evidence that alterations in the processing of emotion expressions is a prominent perceptual feature of ASD and that such disruption is not associated to a specific sensory modality. This difficulty is manifested during the perception of visual and auditory emotional expressions and suggests noisier amodal perceptual estimates of emotional expressions in ASD. Finally, these results compellingly demonstrate joint alteration in the perception and the integration of multisensory emotion expression in ASD.

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Emotion recognition in faces and the use of visual context in young people with high-functioning autism spectrum disorders. *Autism*, 12(6), 607-626.

5.8 Figures

Fig. 1. Schematic representation of the stimuli

Participants were required to discriminate between affective expressions of fear and disgust displayed either by an actress or an actor. Stimuli consisted in video and non-linguistic vocal clips and were either displayed alone or together (bimodal condition).

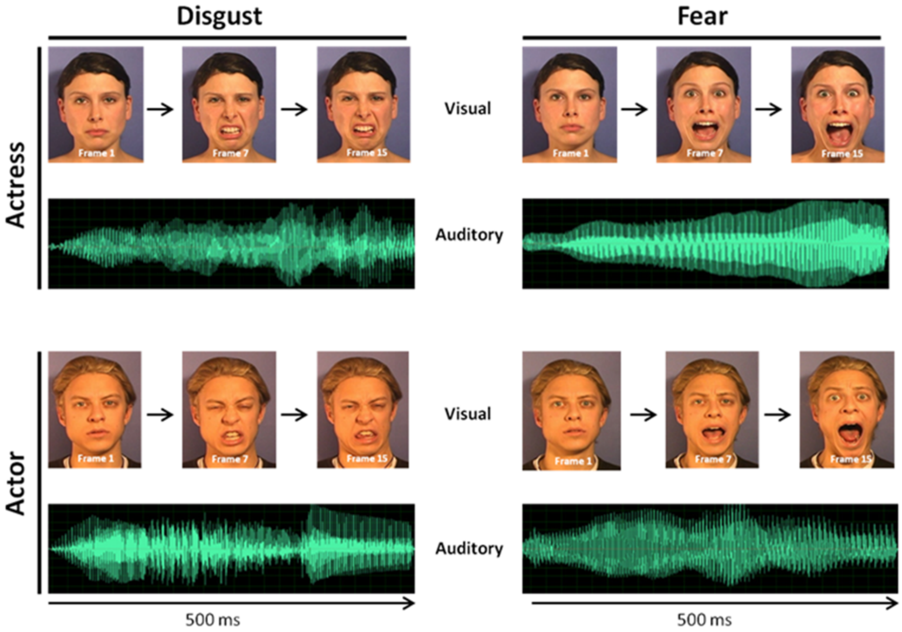


Fig. 2. Discrimination performance

Speed-accuracy composite scores (A; see material and methods), d' scores (B) and mean reaction times (C) for the discrimination of emotional expressions presented auditorily, visually and audio-visually in ASD and TD. In all the figures, error bars denote the standard error of the group.

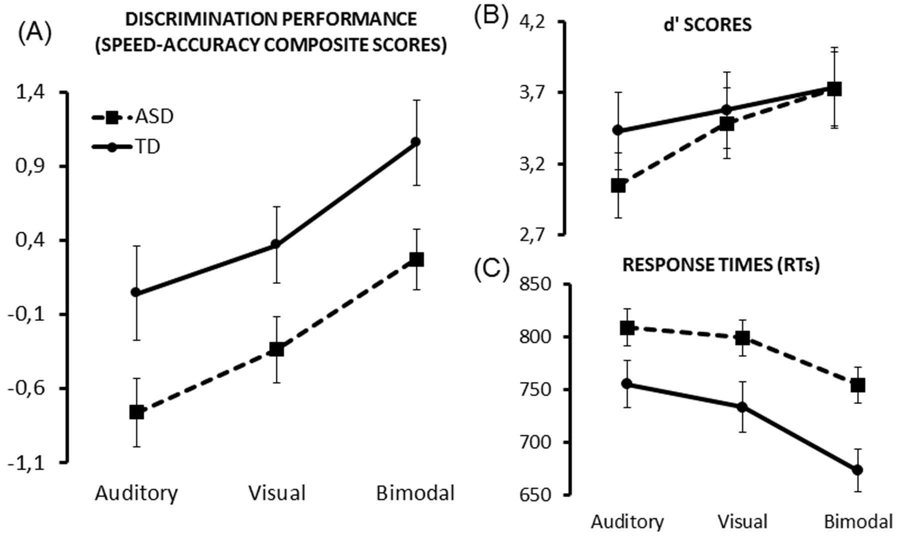


Fig. 3. Redundancy gain

Redundancy gain (in percent; see material and methods) for ASD and TD. Error bars denote the standard error of the group. The figure illustrates a superior redundancy gain in TD than in ASD (**: p≤.005).

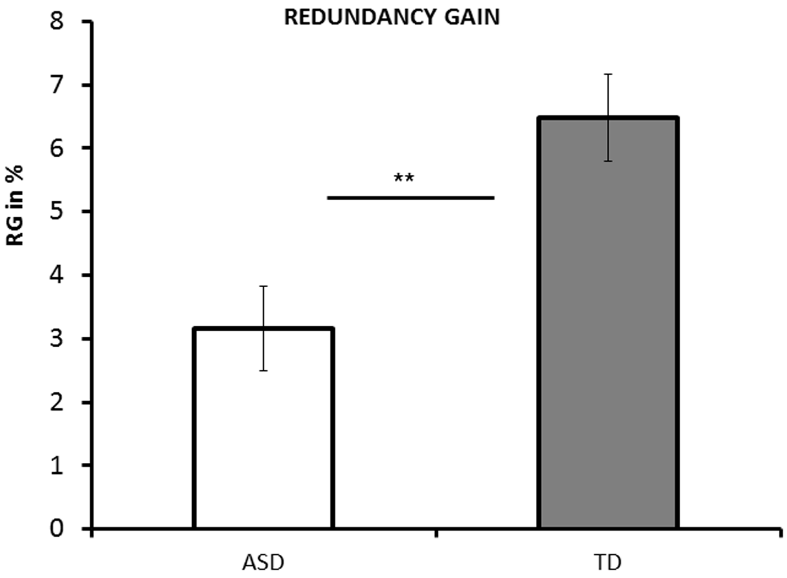


Fig. 4. Race model inequality

Test for violation of the race model inequality (Miller, 1982; Ulrich, Miller & Schröter, 1982). The graph represents the difference in milliseconds (on the Y axis) between the model prediction computed from the RTs of each unisensory counterpart (the model bound) and the RTs obtained in the redundant conditions. Positive values on the graph refer to RTs that were faster than the race model prediction. Negative values on the graph refer to RTs that were slower than the race model prediction. The difference between the bound and the RTs of the redundant condition are computed for each percentile of the RT distribution (on the X axis). For TD, the difference significantly exceeded the race model inequality for the 5th percentiles of the RTs distribution. For ASD, no violation of the race model inequality was found (*: p≤.05).

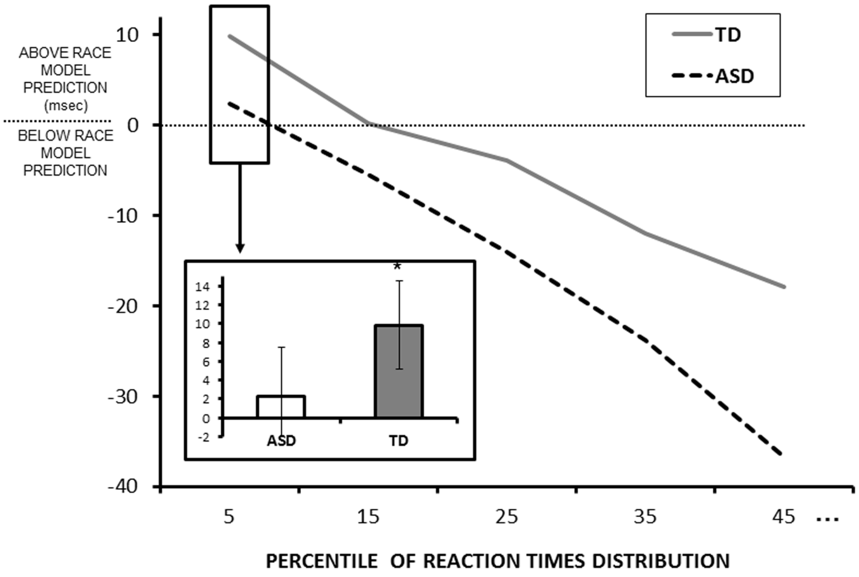
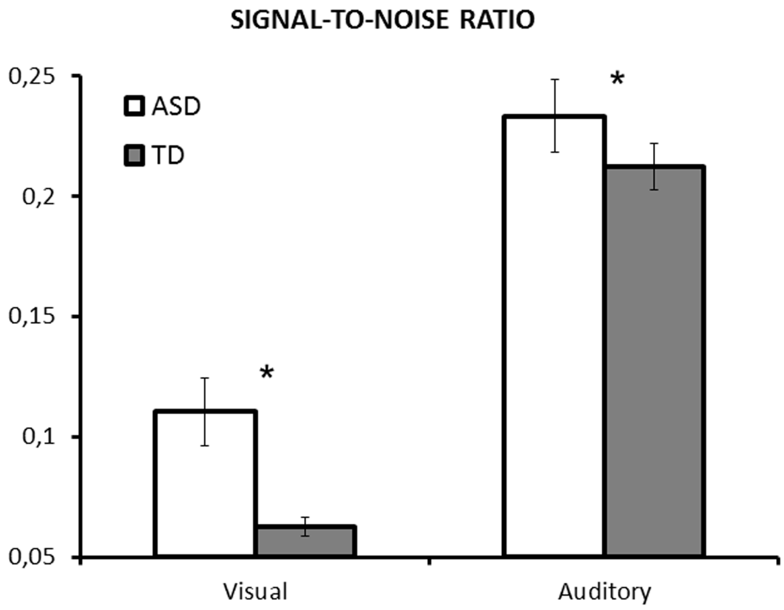


Fig. 5. Signal-to-noise ratio

Signal-to-noise ratio for an 80% accuracy rate in the discrimination of emotional expressions presented auditorily and visually in ASD and TD. This graphic illustrates the main effect of the factor “group”, suggesting inferior detection thresholds in TD than ASD for both modalities (*: p≤.05).



Chapitre 6

Article 2: Reduced multisensory facilitation in persons with autism.

Reduced multisensory facilitation in persons with autism.

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6.1 Abstract

Although the literature concerning auditory and visual perceptual capabilities in the autism spectrum is growing, our understanding of multisensory integration (MSI) is rather limited. In the present study, we assessed MSI in autism by measuring whether participants benefited from an auditory cue presented in synchrony with the color change of a target during a complex visual search task. The synchronous auditory pip typically increases search efficacy (pip and pop effect), indicative of the beneficial use of sensory input from both modalities. We found that for conditions without auditory information, autistic participants were better at visual search compared to neurotypical participants. Importantly, search efficiency was increased by the presence of auditory pip for neurotypical participants only. The simultaneous occurrence of superior unimodal performance with altered audio-visual integration in autism suggests autonomous sensory processing in this population.

Keywords: Autism; multisensory integration; visual search; vision; audition.

6.2 Introduction

Our perceptual world is made up of events that usually stimulate more than one sense at a given time. The brain must therefore integrate sources of information originating from multiple sensory modalities in order to create a unified and coherent internal representation of our external environment (Stein and Meredith, 1993). This process, referred to as multisensory integration (MSI), ultimately allows us to interact with our surroundings and others in an adaptive manner. It has been previously suggested that atypical MSI may plausibly be the origin for certain characteristic behaviors in autism (Iarocci and McDonald, 2006; Marco et al., 2011), including the avoidance of overstimulating environments and the focus on repetitive sensory attributes (Lovaas et al., 1979). Major cognitive theories in autism such as the Weak Central Coherence (WCC) theory (Frith and Happe, 1994), the temporal binding deficit hypothesis (Brock et al., 2002) and the Enhanced Perceptual Functioning theory (Mottron et al., 2006) have evolved from the tenet that autistic (AUT) perception is best defined as being locally-oriented, often resulting in superior performance when a local or detailed processing strategy is advantageous, and a concurrent, inferior performance on tasks necessitating a global or integrative approach (Behrmann et al., 2006; Dakin and Frith, 2005). Such a perceptual approach is consistent with the premise of impaired MSI in autism (Iarocci and McDonald, 2006).

Despite the fact that sensory integration therapies are routinely proposed in rehabilitation (Dawson and Watling, 2000), experimental studies directly investigating MSI abilities in autism are relatively sparse and have yielded equivocal results (Foxe and Molholm, 2009). Most multisensory processing paradigms resulting in MSI deficits in autism have used socially-contingent type stimuli, such as human speech or faces (Magnée et al., 2007, 2008; Silverman et al., 2010; Smith and Bennetto, 2007); but see (Magnée et al., 2009). Importantly, some studies suggested that MSI deficits in autism might actually be limited for more complex “social” stimuli (e.g., speech), with intact integration of simple (non- linguistic, non-social) information (Bebko et al., 2006; Magnee et al., 2008; Mongillo et al., 2008). Therefore, the available literature suggests that MSI impairment in autism may be contingent on the type of information - social or non-social - being integrated across modalities.

In order to investigate if MSI deficit could be observed in autism using non-social stimuli, we assessed MSI within the context of the challenging pip and pop visual search paradigm (Van der Burg et al., 2008). In this task, the presence of an auditory cue (auditory tone or pip) presented in synchrony with the color change of a target during a complex visual search task typically results in more efficient search performance. The synchronous pip makes the target pop-out from its complex visual environment, suggesting the beneficial and spontaneous use of multiple sources of sensory information when available. This task is particularly relevant for investigating MSI in autism since this effect has proven to be purely multisensory (the visual cue alone cannot trigger the effect), is largely automatic (the effect is stimulus-driven and mainly independent of higher-level goals or expectations), and is believed to isolate integration occurring at lower-levels (non-social) within the sensory processing hierarchy (Van der Burg et al., 2008, 2011).

6.3 Methods

6.3.1 Subjects

Nineteen participants (16 M) diagnosed with AUT disorder (AUT - referred to as autism throughout) and 20 typically developing (TD) participants (19 M) were recruited from the database of the Rivière-des-Prairies Hospital (Montréal, Canada). The data of three participants with AUT disorder and one TD participant were not included in the analysis due to the impossibility of the subject to do the task adequately (less than 65% of correct responses when all the conditions were mixed). The resulting groups were closely matched in terms of gender (AUT: 15 M/1 F; TD: 19 M/0 F), age (AUT: mean age 24.5 years ± 5; range 14-31 years; TD: mean age 21 years ± 4; range 14-27 years), and Wechsler IQ [(full-scale = AUT: 102 ± 15; TD: 110 ± 9); (Performance = AUT: 101 ± 13; TD: 108 ± 10); (Verbal = AUT: 102 ± 17; TD: 111 ± 12)]. AUT Disorder was defined using stringent Diagnostic and Statistical Manual of Mental Disorders, 4th edition text revision diagnostic criteria, as operationalized by the combination of Autism Diagnostic Interview - Revised (ADI-R) (Lord et al., 1994) and the Autism Diagnostic Observation Schedule - Generic (ADOS-G) (Lord et al., 2000) algorithms. All AUT participants experienced language delay (acquisition of the first words or sentences ≤36 months) or atypical language during development (echolalia, stereotypic sentences, pronoun inversion, etc.), therefore representing a clinically homogenous group representative of prototypical autism. Control participants and their first-degree relatives were screened with a questionnaire for any history of neurological or psychiatric disorders. All participants had normal or corrected-to-normal vision as evaluated by a Snellen chart prior the beginning of the experiment. The ethics boards of both the Rivière-des-Prairies Hospital and the University of Montreal (where testing took place) approved the study. Written informed consent was obtained for all of the participants, who received financial compensation for their participation in the study.

6.3.2 Apparatus, stimuli and procedure

Stimulus presentation and data collection were controlled by an Hewlett–Packard DC5800 computer equipped with a built in ATI Radeon 3100 graphic card and a C-Media PCI CMI8738 sound card. Visual stimuli were presented on a 17-inch color CRT monitor refreshed at rate of 75 cycles/sec (Hz) with a screen resolution of 1024 x 768 pixels. Stimuli generation and animation were controlled with Matlab R2009b (Mathworks Inc., Sherborn, MA, USA). Participants sat in a silent and dimly lit room with their head positioned on a chinrest 59 cm away from the monitor. They were instructed to search for a horizontal or vertical line segment (target) among displays of 24, 36 or 48 oblique line segments (length .57° visual angle) of various orientations (distracters) (see Fig. 1A). The orientation of each distracter deviated randomly by either plus or minus 22.5° from horizontal or vertical; the target was always either horizontally- or vertically-oriented. At random intervals (on average once every 100 ms), a random number of items changed color between red and green with the constraint that the color of the target always changed alone, never coinciding with the color change of any distracter. The target and distracter line segments were presented on a black background. On average, target color changes occurred once every nine items color changes (on average once every 900 ms). Therefore, the more frequent distracter color changes around the target resulted in a complex and difficult visual search. A more extended description of the stimuli and procedure can be found in the methods of the Experiment 1 of the original paper of Van der Burg et al. (2008). A demonstration can be found on http://www.psy.vu.nl/pippop

Two task conditions were presented: (1) a tone-present condition, in which the visual target change of color was accompanied by a short sound or pip, and (2) a tone-absent condition, in which no sound was presented during the task. For both task conditions, participants were instructed to search for the target and to respond as quickly and accurately as possible by pressing one of two keys with the index and major fingers of their right hand when the target orientation was horizontal or vertical, respectively. The auditory stimulus consisted of a 500 Hz tone (90% normalized peak value, plateau time 50 ms, rise/fall time 5 ms) presented for 60 ms at 70 db-SPL via stereo speakers (Gigaworks T20, Creative Technology Ltd., USA) placed at the left and right side of the CRT screen used to display the visual stimuli. It is important to note that the tone did not provide information regarding the location, color, or orientation of the visual target; it was simply synchronized to the target color change. Participants completed two tone-absent blocks and two tone-present blocks presented in counterbalanced orders. Each block consisted of 24 trials comprising eight trials for each set size (24, 36 or 48), with half of the trials containing a vertical target, and the other half a horizontal target. For all conditions, the color of the target could not change during the first 500 ms of each trial. The order of the trials was counterbalanced within each block. Each trial was displayed until participants responded, with a maximal duration of 18 sec. Participants were asked to keep fixation on a dot presented at the center of the screen. Breaks were encouraged between blocks to maintain a high concentration level and prevent fatigue. The participants' gaze was monitored throughout the experiment via a camera to ensure that they maintained central fixation. Participants practiced one block of six trials before the start of the experiment.

6.3.3 Statistical analysis

Task accuracy (HITs) was estimated by calculating the proportion of correct responses. The reaction times (RTs) reflected the time between search display onset and response to the target color change. Only latencies for correct responses were considered in the analysis. These two measures were submitted to a repeated measure analysis of variance (ANOVA) with set size (24, 36 & 48) and tone-presence (present vs absent) as within-subject variables, and experimental group (AUT and TD) as the between-subject variable. The reported values for p are those after a Greenhouse-Geisser correction for sphericity violations, with alpha set at .05. Based on significant F-values, Bonferroni post-hoc analyses were performed when appropriate. Proportions of correct responses, errors and omissions as well as RTs data are reported as supporting information.

6.4 Results

Fig. 1B illustrates the accuracy scores (proportion of correct responses) and mean RTs obtained in the “tone absent” and “tone present” conditions for TD and AUT participants.

6.4.1 HITs

No main effect of group was observed [F(1,33) = .17, p = .9]. As expected, a highly significant main effect of the set size was found [F(2,66) = 35, $p \leq$ 10E-3], revealing that the increase of the number of distracters in the visual search display (24, 36 & 48) dramatically impaired the performance across groups. We also observed a significant main effect of tone-presence [F(1,33) = 4.5, p = .04] revealing higher accuracy in the tone present condition. Importantly, the ANOVA also revealed a significant group x tone-presence interaction [F(1,33) = 5.8, p = .021] which indicated that performance was significantly higher in the tone-present condition in the TD group (p = .002), whereas tone-presence did not affect performance (i.e., no bimodal enhancement) for the AUT group (p = .847).

6.4.2 RTs

No main effect of group was observed [F(1,33) = .66, p = .42]. As was found with the HIT performance, a highly significant main effect of the set size was found [F(2,66) = 112, $p \leq$ 10E-3], revealing that the increase of the number of distracters in the visual search display (24, 36 & 48) dramatically slowed down response speed across groups (all $p \leq$ 10E-3 for the post-hoc comparisons) for both tone-present/absent conditions. We also observed a significant group x tone-presence interaction [F(1,33) = 8.8, p = .006] which indicated that RTs were significantly faster in the tone-present condition in the TD group (p = .003), whereas tone-presence did not affect RTs (i.e., no bimodal improvement) for the AUT group (p = .269). Finally, we also observed that the RTs of the AUT group were significantly faster compared to that of the TD group (p = .036) for the tone-absent condition only.

6.5 Discussion

The present study demonstrates that AUT individuals do not benefit from the presence of a typically facilitatory, temporally relevant tone during a demanding visual search task. The absence of this pip and pop effect in the autism group is suggestive of atypical integration of low-level, non-social perceptual cues originating from different sensory modalities. In contrast to what was previously suggested (Mongillo et al., 2008; van der Smagt et al., 2007), our research compellingly demonstrates that reduced MSI in autism is not selective to complex social stimuli, but can also be observed with low- level sensory information.

The demonstration of altered MSI in autism, defined in the present study by a lack of bimodal facilitation during visual search task, may be related to the reduced efficacy for integrating local information into complex perceptual information in autism, whether assessed within (intra-modal) or between sensory modalities (intermodal), as defined by the Bertone et al's (2003, 2005) complexity-specific hypothesis. Such a tendency for detail- or feature-based perception (also referred to as "local processing bias") instead of more holistic stimulus processing is also congruent with the WCC model (Frith, 1989), which in the present study, would represents a reduction in integrative processing between modalities, rather that within a single modality. This alteration of integration mechanisms has recently been established in the form of local neural alterations involved in intra-modal information processing (Bertone et al., 2010; Casanova, 2007; Keita et al., 2010) and reduced functional connectivity between specialized brain regions, as exemplified by altered anatomical and functional inter-regional connectivity (Anderson et al., 2011; Barttfeld et al., 2011; Belmonte et al., 2004; Brock et al., 2002; Horwitz et al., 1988; Just et al., 2007, 2004; Liu et al., 2011; Schipul et al., 2011; Thomas et al., 2011; Weinstein et al., 2011); but see (Leveille et al., 2010). Moreover, it has been recently suggested that some of the genes implicated in autism might play a role in the development of such atypical pattern of neural connectivity (Scott-Van Zeeland et al., 2010). Long-distance underconnectivity in autism implies that any facet of psychological function that is dependent on the coordination or integration of brain regions is susceptible to disruption (Brock et al., 2002; Just et al., 2004). Such atypical brain connectivity might therefore impair MSI processes since merging separate sensory inputs into a common percept necessarily requires inter-regional collaboration between separate sensory brain areas (Driver and Noesselt, 2008; Ghazanfar and Schroeder, 2006).

Consistent with this interpretation, Van der Burg et al. (2011) recently used electroencephalographic recordings to demonstrate that the multisensory facilitative effect observed with a task similar as the one used in the present study relies on early MSI (50-60 ms post-stimulus onset). Such early MSI processes putatively rely on long-range connections implicating primary sensory cortical areas (Falchier et al., 2002). It is therefore possible that it is the development of such connections that is particularly affected in autism (Courchesne et al., 2007). Supporting this hypothesis, a recent electroencephalographic study demonstrated that children with autism do not automatically combine sensory inputs early in the processing hierarchy to the same degree as TD individuals (Russo et al., 2010).

Aside from the underconnectivity hypothesis, the present results may be related to recent studies that have demonstrated that AUT children have a prolonged temporal window within which they integrate multisensory stimuli (Foss-Feig et al., 2010; Kwakye et al., 2011). A specific deficit in temporal processing of multisensory information will plausibly result in atypical MSI abilities, which intrinsically rely on the ability to temporally synchronize information originating across sensory systems (Stein and Meredith, 1993). A protracted temporal binding window in the autism group may therefore have impeded the time-locked association between the tone and the target's color change, ultimately resulting in the absence of the MS facilitation in the autism group.

Our results also demonstrated that atypical MSI in the AUT group is concomitant to more efficient unimodal visual search performance (e.g., shorter RTs in the AUT than in the TD group in the tone-absent condition). This result is consistent with previous demonstrations of superior visual search in autism (Joseph et al., 2009; O'Riordan et al., 2001), and an increased ability to detect visual targets embedded among distracters (Jolliffe and Baron-Cohen, 1997; Pellicano et al., 2005; Shah and Frith, 1983). This well replicated ability has been demonstrated to have a perceptual rather than attentional origin (Joseph et al., 2009), and has been associated with multiple other lower, and mid-level perceptual superiorities (Caron et al., 2006). Similar perceptual superiorities in autism have been also recently demonstrated in the auditory modality (Bonnel et al., 2010; Jones et al., 2009). The existence of multiple lower- (discrimination), mid- (visual search) and higher- (pattern manipulation) level perceptual superiorities in autism might therefore be an important determinant of cognition and behavior in this population (Mottron et al., 2006; Bertone et al., 2010).

The presence of such efficient, unisensory-based performance in the autism group is exemplary of autonomous sensory processing, where maximal performance on a visual task is not contingent on using multiple available sources of sensory information. Such autonomous processing has been postulated to be the collateral consequence of impaired large-scale, integrative connectivity (Belmonte et al., 2004) or be rooted in the altered development of local neural networks operating within each sensory modality (Bertone et al., 2010; Mottron et al., 2006). Accordingly, the concomitance of enhanced unimodal visuo-spatial performance and the lack of MSI facilitation in the autism group may be related, to some extent, to the "inverse effectiveness" principle, which states that the result of MSI is inversely proportional to the effectiveness of the relevant stimuli (Stein and Meredith, 1993). This principle highlights the fact that MSI is usually more efficient when the reliability of one of the sensory channels is reduced (Ernst and Bülthoff, 2004). Enhanced visuo-spatial processing in autism may therefore reduce the tendency to take into account auditory information in order to resolve a visual search task. In a similar vein, a recent study using the rubber hand illusion demonstrated a reduction in sensitivity to visuotactile-proprioceptive discrepancy (reflecting atypical MSI) but more accurate proprioception in autism Spectrum disorders (Paton et al., in press). In order to explore if the reduced MSI observed in our autism group was directly related to their enhanced unimodal performance, we carried out additional analysis on a sub-sample of TD participants who had visual search performance comparable to that of the autism group in the tone-absent condition (see Supplementary Fig. 1). Results demonstrated that a facilitatory effect was still manifested for the tone-present condition in this TD sub-group, arguing against the idea that the reduced MSI observed in the autism group was solely due to difference of performance in the unimodal condition (e.g., enhanced visual search skills).

In the original study demonstrating the "pip and pop effect", Van der Burg et al. (2008) carried out control experiments, notably varying the probability of synchrony between target change and the auditory cue. They found that search benefited when the target color change was accompanied by a tone, even though this co-occurrence was relatively rare (occurring on only 20% of the trials; on 80% of the trials the tone accompanied a distractor event instead). The auditory event was therefore rather uninformative with regards to when to expect the target color change, and did not affect the overall pattern of results. Van der Burg et al. (2008) suggested that the integration of the synchronous auditory and visual signals is mostly automatic (because it still occurs when the pip is synchronized with distractors on the majority of trials). However, our observation of a strong effect of task difficulty (set size) on RTs in the "pip" (MSI) condition in TD does not support the presence of a real pop-out effect, which typifies automatic, bottom-up type processing. Therefore, it may be argued that, at least in part, the beneficial effect of sound synchrony is gated by a strategic, top-down control, and that it is such a process which may have been altered in the autism group. In fact, Van der Burg and colleagues already suggested that the effect diminishes if observers adopt a small, focused window of attention, suggesting that at least some distributed attention is necessary for observers to notice, and take advantage of the synchronized event (Van der Burg et al., 2008). This would be consistent with other evidence suggesting that attention plays a crucial role in audio-visual integration at multiple stages of information processing (Alsius et al., 2005; Talsma et al., 2007, 2010). This interaction between MSI and attention is of particular importance here, given that a recent electrophysiological study exploring face-voice interaction, demonstrated that MSI might be particularly impaired in autism under situations requiring high-level of attentional resources (e.g., divided attention) but not in situation where the attentional charge is lower (e.g., selective attention) (Magnée et al., 2011). Further works should therefore explore how the interplay between attention and MSI might explain the atypical MSI abilities observed in autism.

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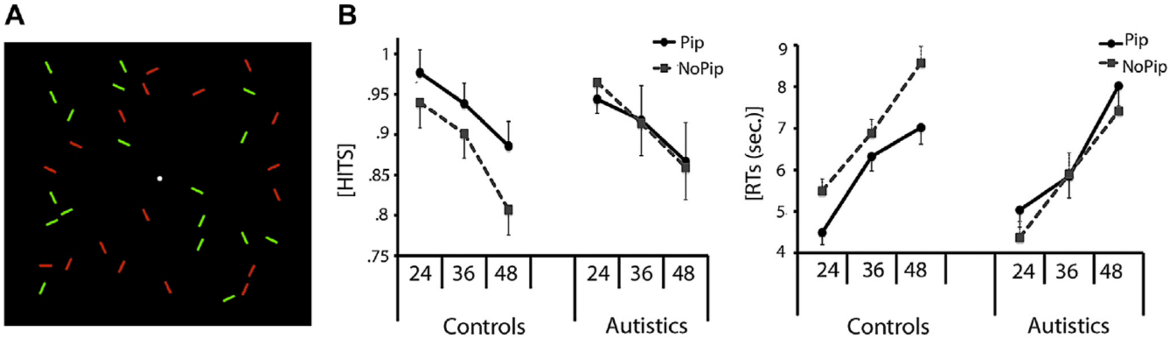
6.8 Figures

Fig. 1. Visual search performance

Panel A: example of the visual search displays used in the present study. Set size varied among 24, 36 & 48 items. Participants were instructed to respond as soon as they found a vertical or horizontal line segment. During the search, the distracters as well as the target continuously changed color between red and green. Panel B: the figure displays accuracy scores (HITs: proportion of correct responses) and mean RTs obtained in the “tone absent” (square-dashed line) and “tone present” (circle-straight line) conditions of stimulation in TD and AUT participants. Error bars denote standard error. A synchronous, non-spatial auditory event increased the number of hits and decreased search times for a visual target in the TD group, but not in the AUT group.



Chapitre 7

Article 3: Within- and Cross-modal integration in the Autism Spectrum.

Within- and Cross-modal integration in the Autism Spectrum.

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7.1 Abstract

Although specific impairment in the integration of sensory information has been suggested in autism spectrum (AS), empirical evidences remain equivocal. Importantly, the differing behavioral outcome of combining unisensory versus multisensory inputs has never been directly investigated in AS. In the current study, we assessed the integration of low-level visual and tactile information both within and across modalities in AS and typically developing (TD) individuals. TD individuals demonstrated increased redundancy gain for cross-modal conditions relative to both within-modal conditions (visual and tactile). In contrast, the AS group showed enhanced facilitation for the cross-modal compared to the within-visual conditions only; no difference in redundancy gain was observed between the cross-modal and the within-tactile conditions. We observed that the reaction time distributions of redundant cross-modal targets, but not those of within-modal targets, exceeded the reaction time distribution predicted by Miller's race model in both groups, but less in the AS than in the TD. Importantly, the reduced bimodal integration observed in AS was not related to atypical attentional shift between modalities, which was similar in both groups. In conclusion, AS displays a selective alteration of multisensory integration of low-level non-social information.

Keywords: Autism Spectrum; Sensory integration; Visual; Tactile.

7.2 Introduction

The autism spectrum (AS) is a complex neurodevelopmental condition that is defined by socio-communicative difficulties and the presence of restricted interests and repetitive behaviours. Although atypical sensory abilities have always been associated with AS's behavioural and cognitive profiles, they are now considered as one of AS's core clinical features, defined by the hyper- or hypo-reactivity to different sensory inputs or unusual interests in sensory aspects of the environment (DSM-5-American Psychiatric Association, 2013). Although most research regarding sensory abilities in AS has focused on unimodal visual or auditory processes, understanding the different aspects of cross-modal (or multisensory) sensory integration and how they relate to characteristic behaviors in AS (Baum, Stevenson & Wallace, 2015; Stevenson et al., 2016; Wallace & Stevenson, 2014; Iarocci & McDonald, 2006; Marco, Hinkley, Hill & Nagarajan, 2011) is arguably more representative of subjective reports of "sensory overload" in this population (O'Neill & Jones, 1997; Bonneh et al., 2008). Specifically, there is growing evidence that multisensory integration is associated with higher-level socio-communicative functioning, repetitive behavior and restricted interests in AS (Baum et al., 2015; Cascio, Woynaroski, Baranek & Wallace, 2016; Stevenson et al., 2017).

The benefit of multisensory integration is often investigated using the Redundant Signal Effect (RSE; Hershenson, 1962; Raab, 1962), a popular experimental procedure that typically shows significant decrease in reaction times when detecting two or more stimuli if presented simultaneously rather than individually (Todd, 1912). In particular, testing for the Miller's race model inequality has been widely used as an indirect behavioral measure of non-probabilistic integrative processes underlying reaction time (RT) facilitation (so-called violations of Miller's bound). This model predicts that RT to a cross-modal stimulus will be based on the RT for the fastest of its unisensory components. If RTs to detect multisensory stimuli are significantly faster than what is predicted based on unisensory performance, the race model prediction is violated, meaning that the RSE (faster RTs in redundant conditions) reflects a true non-probabilistic multisensory integrative process. Used sparingly to assess multimodal integration in AS individuals, studies using this paradigm and analyses have demonstrated an atypically diminished integration of low-level non-social multisensory inputs in children (Brandwein et al., 2013; 2015), and of emotional face-voice stimuli in AS adults (Charbonneau et al., 2013).

These aforementioned RSE studies that concluded reduced multisensory integration in AS individuals assumed contextual invariance in reaction times to the stimuli sequence. In other words, they did not consider that sensory information is not processed independently, as the perception of a stimulus is largely influenced by previously presented sensory inputs (Miller, 1982; Otto & Mamassian, 2012; Gondan, Lange, Rösler & Röder, 2004). In TD individuals, RTs to a sensory input are faster when preceded by a stimulus from the same modality. In contrast, when the stimuli in successive trials come from different modalities, attention need to shift from one modality to another resulting in longer RTs. The cognitive effort associated to the change in attention between modalities on consecutive trials is referred as the modality shift cost. This may explain why, at a perceptual level, participants respond faster to simultaneously presented bimodal signals compared to unimodal signals (Gondan, Lange, Rösler & Röder, 2004; Spence, Nicholls & Driver, 2001; Harrar et al., 2014). In order to specifically assess multisensory integration abilities in AS individuals, it is critical to evaluate whether the atypical multisensory integration documented in AS individuals originate from difference in the way they engage and disengage their attention to separate sensory inputs (Harrar et al., 2014; de Heering et al., 2016). This is particularly crucial since studies have shown that the ability to shift or disengage attention is often impaired in AS individuals (for example, Courchesne et al., 1994; Landry & Bryson, 2004; Renner, Klinger & Klinger, 2006; Wainwright-Sharp & Bryson, 1993). It is therefore necessary to investigate the allocation of attentional resources during cross-modal processing when assessing multisensory integration abilities in AS individuals.

Major cognitive theories in autism research, including the Weak Central Coherence theory (Frith & Happe, 1994), the Enhanced Perceptual Functioning theory (Mottron, Dawson, Soulières, Hubert & Burack, 2006), and the temporal binding deficit hypothesis (Brock, Brown, Boucher & Rippon, 2002), emphasize that locally-oriented sensory processing in AS individuals is associated with superior performance on tasks where local analysis is advantageous with concurrent inferior performance on tasks requiring a global or integrative approach (Dakin & Frith, 2005; Behrmann, Thomas & Humphreys, 2006). It was suggested that AS was associated with reductions in global connectivity, with typical or even increased connectivity within local networks (Brock et al., 2002). This leads to the important question of whether the putative sensory integration atypicalities observed in AS are specific to multisensory conditions that involve combining signals coming from multiple and more distant cortical areas (i.e, by synchronization of high-frequency gamma oscillations), or if they also apply to within-modal interactions that are mediated by the same cortical areas (see Simon & Wallace, 2016 for review). Although reasearch in TD individuals suggest that within- and cross-modal integration differ by the amount of facilitation that they produce at the behavioral (Girard, Pelland, Lepore & Collignon, 2013; Forster, Cavina-Pratesi, Aglioti & Berlucchi, 2002; Laurienti, Burdette, Maldjian & Wallace, 2006; Miniussi, Girelli & Marzi, 1998; Murray, Foxe, Higgins, Javitt & Schroeder, 2001; Corballis, 1998; Reuter Lorenz, Nozawa, Gazzaniga & Hughes, 1995; Badzakova-Traikov, Hamm & Waldie, 2005) and neurophysiological level (Alvarado, Vaughan, Stanford & Stein, 2007a; Alvarado, Stanford, Vaughan & Stein, 2007b), differences regarding within-modal and cross-modal integration have yet to be directly compared in AS individuals .

Somatosensory processing is known to play a crucial role in the social development of TD individuals (Maitre et al., 2017; Myers, 1984; Hertenstein, 2002; Hertenstein, Keltner, App, Bulleit & Jaskolla, 2006; Thye, Bednarz, Herringshaw, Sartin & Kana, 2018; Dunbar, 2010), notably for the pre-verbal socio-communicative development (Cascio et al., 2016; Field, 2001), and may contribute to the acquisition of a sense of self (Schütz-Bosbach, Musil & Haggard, 2009) which underlies some social skills, including imitation and empathizing (Schütz-Bosbach, Mancini, Aglioti & Haggard, 2006). Despite the importance of somatosensory perception on such higher-level abilities, the literature on multisensory processing in AS has mainly been confined to the auditory and visual modalities, possibly because of their obvious role in verbal and nonverbal communication that is frequently found to be atypical in AS (Baum, Stevenson & Wallace, 2015; Cascio, Lorenzi & Baranek, 2016). However, somatosensory atypicalities are among the most frequently reported sensory complaints in AS (Rogers, Hepburn & Wehner, 2003; Tomchek & Dunn, 2007) and mechanisms mediating low-level somatosensory perception in AS individuals have been found to be atypical (i.e., Kahn et al., 2015; Puts et al., 2017) and related to AS symptomatology (Tavassoli et al., 2016). It is therefore highly relevant to include the tactile modality when investigating cross-modal integration in AS individuals.

In the present study, we used a visuo-tactile RSE paradigm to simultaneously assess and compare the ability of AS and TD individuals to detect and integrate simple visual and tactile stimuli both within and across modalities, and to shift attention from one modality to another during multisensory processing. We used easily detectable, suprathreshold stimuli to measure performance in both groups that was subjected to three different types of analyses: (i) reaction times and redundancy gains, (ii) Miller's race model analyses, and (iii) modality switch cost analyses (see the Experimental Procedures for details). Crucially, the redundancy gain associated with visuo-tactile integration in AS individuals was compared to that associated to the integration of redudant visual and tactile stimuli, allowing us to directly compare within- and cross-modal integration performances in the AS.

7.3 Material and Methods

7.3.1 Participants

Fourteen AS individuals and 14 typically developing (TD) controls participated in this study. Participants were recruited from the database of the Rivière-des-Prairies Hospital's autism clinic (Montréal, Canada). Thirteen participants from the AS group were diagnosed with the Autism Diagnostic Interview (ADI-R ; Lord, Rutter & Le Couteur, 1994) and/or the Autistic Diagnostic Observation Schedule (ADOS-G ; Lord et al., 2000) (ADI only : two ; ADI and ADOS : eleven). One participant from the AS group was diagnosed based on DSM-IV-TR criterias (American Psychiatric Association, 2000) and expert clinical judgment. Trained clinical professionals working at the specialized clinic at the Rivière-des-Prairies Hospital conducted both diagnostic tests. TD participants and their first-degree relatives were screened with a questionnaire for any history of neurological or psychiatric disorder. All participants in both groups were males and had normal or corrected to normal near and far vision assessed before testing using near and far Snellen acuity charts. The groups were closely matched in terms of age ($t(26) = .35, p = .73$; AS : mean age 25 years $\pm$ 5 ; range 18-35 years ; TD : mean age 24 years $\pm$ 4 ; range 16-30), laterality and global Wechsler intellectual quotient [(Full-scale IQ : $t(25) = -1.955, p = .06$; AS : mean 100 $\pm$ 13, range 84-126 ; TD : mean 111 $\pm$

13, range 87-130); (Performance IQ : AS : mean 104 ± 13, range 77-123 ; TD : mean 109 ± 12, range 82-131); (Verbal IQ : AS : mean 99 ± 16, range 72-128 ; TD : 112 ± 10, range 94-125)]. All participants had a full-scale Wechsler score of 80 or more. Each participant gave informed consent to participate in the study and received monetary compensation for this. The ethics board of the Rivière-des-Prairies Hospital approved the study.

7.3.2 Stimuli

Tactile stimuli were delivered using a pneumatic stimulator that was located outside the testing room in order to reduce any distraction produced by the system. Rigid plastic tubes connected the stimulator to four plastic membranes (one centimeter of diameter) positioned on the ventral surface of the particpnats' distal third of their index and the middle fingers. Tactile stimulation consisted of the inflation of the plastic membrane by a pulse of air pressure sent through the plastic tube from the pneumatic stimulator. Each tactile stimulation lasted for 100 ms. Given the significant interindividual variability in the sensitivity to tactile stimulation, the intensity at which it was delivered was calibrated individually to obtain reliable stimulations (see Girard et al., 2013). Participants' hands were positioned at a distance of 57 cm from their head. The tips of their index fingers were placed at 3° of eccentricity below a central fixation cross, and at 2.5° to the left (index of the left hand) or the the right (index of the right hand) of it. The tips of their middle fingers were placed at 3° of eccentricity above the central fixation cross, and at 2.5° to the left (middle finger of the left hand) or to the right (middle finger of the right hand) (see SFig. 1). Participants' fingers were positioned in a fixed apparatus (150 x 120 x 75 mm). The index finger and the middle finger of the left hand were inserted in separe holes (25 mm of diameter and 35 mm of depth) located on the left side of the box, with a distance of 60 mm between the tips of both fingers. The same configuration was used on the right side of the box for the index and the middle finger of the right hand.

Visual stimuli were presented on a plastic board (120 x 150 mm) located on the top of the apparatus via a projector suspended on the ceiling of the testing room, approximately 50 mm above the fingertips of the participants. Each visual stimulation consisted in white circle subtending 1° of visual angle presented on a black background, and lasted for 100 ms. As for tactile stimulations, visual stimuli were delivered at 3° degrees of eccentricity below or above the central fixation cross, and at 2.5° to its left or to its right (SFig. 1). For the misaligned double visual and visuo-tactile conditions (see procedure below for a description of the experimental conditions), visual stimuli were presented at 1.5° of eccentricity below or above the central fixation cross, and at 2.5° to its left or to its right, in order to maintain a similar interstimuli distance for the aligned and the misaligned conditions.

7.3.3 Procedure

The paradigm was adapted from Girard and colleagues (2013). Participants sat in a silent and darkened room with their head positioned on a chinrest. They were instructed to press on a response button with their left or their right thumb as fast as possible each time a stimulation was presented. The hand used to respond alternated between each block, and the order was counterbalanced across participants. Participants' gaze was monitored throughout the experiment via a camera to ensure that participants maintained central fixation. Stimuli were displayed, and RTs were recorded using Presentation software (Neurobehavioral Systems, Inc., Albany, USA).

Participants were presented with eight different conditions : (1) simple tactile stimulus (T1, T2, T3, T4); (2) aligned double tactile stimuli (T1/T2, T3/T4); (3) misaligned double tactile stimuli (T1/T4, T2/T3); (4) simple visual stimulus (V1, V2, V3, V4); (5) aligned double visual stimuli (V1/V2, V3/V4); (6) misaligned double visual stimuli ($V1_{prime}/V4_{prime}$, $V2_{prime}/V3_{prime}$); (7) aligned visuo-tactile stimuli (V1/T2, V2/T1, V3/T4, V4/T3) and (8) misaligned visuo-tactile stimuli ($V1_{prime}$/T4, $V4_{prime}$/T1, $V2_{prime}$/T3, $V3_{prime}$/T2). Aligned conditions consisted of two stimuli presented in the same hemispace (left or right), while misaligned conditions were made up of two stimuli from opposite hemispace. For the aligned conditions, one of the stimuli was presented on (tactile) or above (visual) the index finger of one hand, and the other was presented on (tactile) or above (visual) the middle finger of the same hand. For the misaligned conditions, one of the stimuli was presented on (tactile) or above (visual) the index finger of one hand, and the other was presented on (tactile) or above (visual) the middle finger of the opposite hand. Participants completed six blocks of 260 experimental trials. Each block contained 10 repetitions of the 24 stimuli configurations, and 20 catch trials (8%) to restrict the tendency of participants to produce anticipatory responses. A total of 60 trials per condition were therefore recorded. Inter-trial interval randomly varied between 1500 and 3500 ms (mean 2500 ms). The central fixation cross was displayed throughout the experiment. Each block lasted approximately 11 minutes. Breaks were encouraged between the blocks to keep an optimal level of attention.

7.3.4 Data Analysis

Since the effect of alignment was the same for both groups of participants, the scores for aligned and misaligned conditions were combined for all analysis (see Supplementary Material for the detailed statistical analysis and separate graphical representation of aligned and misaligned conditions).

7.3.4.1 Reaction Times and Accuracy

Both accuracy and response speed were examined in order to investigate the general ability to detect sensory inputs. Task accuracy was estimated by the proportion of detected stimuli (in percent). RTs ranging from 100 to 1000 ms were analyzed. In experiments that place equal emphasis on accuracy and processing speed, it is possible that participants adopt different response strategies by varying RTs inversely with accuracy (and thus resulting in a speed/accuracy trade-off). We therefore calculated the Inverse Efficiency (IE) scores which constitute a standard approach to combine mean RTs and accuracy measures of performance (Townsend & Ashby, 1978), and considered as “corrected RTs” that discount possible criterion shifts or speed/ accuracy trade-offs. The IE scores were obtained by dividing RTs by the proportion of detected stimuli separately for each condition, with higher IE scores indicated worse performance. IE scores were submitted to repeated measures ANOVAs 2 (Group: AS, TD ; between-subjects factor) x 5 (Condition : simple tactile, double tactile, simple visual, double visual, visuo-tactile). Based on significant F-values, Bonferonni post-hoc analysis were performed when appropriate. For the sake of completeness, a similar ANOVA was also carried out for accuracy and RTs and are presented as supplemental materials.

7.3.4.2 Within-modal and Cross-modal Integration

Sensory integration was first investigated by calculating the redundancy gain (RG), which corresponded to the decrease (in percent) in the mean IE scores obtained in the redundant conditions as compared to the mean IE scores obtained for the best single condition (Stein & Meredith, 1993; Girard, Collignon & Lepore, 2011; Charbonneau, Véronneau, Boudrias-Fournier, Lepore & Collignon, 2013). For each condition and each participant separately, the mean IE score for the redundant condition was subtracted from the mean IE score for the fastest stimulus of the pair, and then divided by the latter, which yielded to the percentage of decrease in IE score between the redundant condition and its best constituent [RG = (IE score best single condition – IE score redundant condition) / IE score best single condition]. The RGs were then submitted to a 2 (Group: AS, TD; between-subjects factor) x 3 (Modality: double tactile, double visual, visuo-tactile) repeated measures ANOVA.

Miller (1982) provided a method to test whether or not the redundant target effect (faster RTs in redundant conditions) reflects a true sensory integrative process. For a given trial, the fastest stimulus determines the observable RT. On average, the time to detect the fastest of several pairs of redundant signals is faster than the detection time for a single signal. The speeding up of reaction time can therefore be attributable to statistical facilitation (Raab, 1962). However, if the race model's prediction is violated, the speedup of RTs cannot be attributed to a statistical effect alone, and some kind of integrative processes is assumed (Miller, 1982). More recent and parsimonious interpretations of violations of the race model do not assume that the signals interact at a neuronal level (Otto & Mamassian, 2012; Otto, Dassy & Mamassian, 2013). Like others (Harrar et al., 2014; De heering et al., 2016), we assume here that integration is anything that cannot be explained only by probabilistic unisensory processing alone (Stein et al. 2010). Analyses of violation of the race model inequality were carried out using the RMITest software which implements the algorithm described in Ulrich, Miller and Schroter (2007). The algorithm estimates the cumulative probability distributions of RTs in the two unimodal simple conditions and the redundant condition, and tests whether redundant-targets RTs are significantly faster than would be predicted by a race model (with t-tests). We then calculated the proportion of percentiles showing faster RTs than the prediction of the race model, and compared it using a 2 (Group: AS, TD; between-subjects factor) x 3 (Modality: double tactile, double visual, visuo-tactile) repeated measures ANOVA.

7.3.4.3 Modality Switch Cost

Since one of the effects potentially driving violation of the race model is the cost of switching attention between modalities (Otto & Mamassian, 2012; Gondan et al., 2004), we compared the modality switch cost in AS and TD. To determine whether the RTs to a stimulus were influenced by the modality of the stimulus presented in the previous trial, the RTs obtained in the single and within-modal conditions were classified in function of their previous trial (previous trial of the same modality and previous trial of a different modality). The modality switch cost was then calculated by subtracting the mean RTs for conditions in which the stimuli were preceded by a stimulus of the same modality to the mean RTs for conditions in which the stimuli were preceded by a stimulus of a different modality (Harrar et al., 2014; Otto & Mamassian, 2012). These scores were submitted to a 2 (Group: AS, TD; between-subject factor) x 2 (Modality: tactile, visual) repeated measures ANOVA, in order to test whether it differed according to the group or the modality of the stimulation.

7.4 Results

7.4.1 Reaction Times and Accuracy

Overall, both groups performed the detection task accurately. TD participants detected 97.5% of all tactile stimuli (range from 91 to 100%), 98% of visual stimuli (range from 92 to 100%) and 98% of cross-modal pairs (range from 92 to 100%). AS participants detected 96% of tactile stimuli (range from 87 to 100%), 97% of visual stimuli (range from 87 to 100%) and 98% of visuo-tactile stimuli (range from 91 to 100%). TD participants responded to 4% of the catch trials throughout the experiment, whereas AS participants responded to 2% of the trials ($t(26) = -1.419, p = .17$) (see Supplementary Material for detailed analysis on accuracy and RTs separately).

When comparing IE scores across groups and conditions (Fig. 1A), we found main effects for both the "group" ($F(1,26) = 4.90, p \leq .05$, $n2_{\text{partial}} = .16$) and "condition" factors ($F(4,104) = 39.03, p \leq .001$, $n2_{\text{partial}} = .60$). There was an interaction between those two factors ($F(4,104) = 3.31, p \leq .05$, $n2_{\text{partial}} = .11$), as differences in performance between the conditions of presentation changed according to the group. For the TD group, we found lower IE scores for visuo-tactile conditions than for simple tactile ($p \leq .001$) and simple visual ($p \leq .001$) conditions whereas in AS group, there was no significant difference in performance between cross-modal, within-modal and simple auditory and tactile conditions.

7.4.2 Within-modal and Cross-modal Integration

RGs were significantly different from 0 for the three redundant conditions in both TD (double tactile : $t(13) = 7.26, p \leq .001$; double visual : $t(13) = 13.16, p \leq .001$; visuo-tactile : $t(13) = 13.40, p \leq .001$) and AS groups (double tactile : $t(13) = 7.83, p \leq .001$; double visual : $t(13) = 5.42, p \leq .001$; visuo-tactile : $t(13) = 7.36, p \leq .001$). When comparing RGs between groups and modalities (Fig. 1B), we found no main effect for the "group" factor ($F(1,26) = .03, p = .88$), but there was a main effect for the factor "modality" ($F(2,52) = 30.08, p \leq .05$, $n^2_{\text{partial}} = .54$), and a significant interaction between those two variables ($F(2,52) = 3.11, p \leq .05$, $n^2_{\text{partial}} = .11$). Cross-modal visuo-tactile stimuli produced greater RG compared to both double tactile and double visual conditions in TD, while RGs for the visuo-tactile and the double tactile conditions were both superior to RG for the double visual conditions in AS.

To further test for group differences in the within- and cross-modal integration conditions, we examined whether the RTs obtained in the redundant conditions exceeded the statistical facilitation predicted by Miller's race model inequality (Miller, 1982). For the cross-modal visuo-tactile conditions, the race model inequality was significantly violated up to the 50th percentiles of the RTs distribution in TD (Fig. 1C), while it was only significantly violated for the 10th to the 30th percentiles of the RTs distribution in AS (Fig. 1C). Consistent with previous results (Girard et al., 2013), no significant violation of the race model inequality was demonstrated for the double visual and the double tactile conditions, suggesting that the faster RTs in these conditions could be explained by simple probability summation for both AS and TD participants.

When assessing whether the proportion of percentiles where RTs were faster than predicted by the race model (Fig. 1D), we observed a group by modality interaction ($F(2,52) = 8.01, p \leq .001$, $n^2_{\text{partial}} = .24$), suggesting that the proportion of percentiles for which the race model was violated was significantly higher in TD individuals compared to AS individuals for cross-modal visuo-tactile condition. There were no group-difference for the double tactile and double visual conditions.

7.4.3 Modality Switch Cost

The modality switch cost was significantly different from 0 for the two modalities in both AS (tactile : $t(13) = 2.44, p \leq .05$; visual : $t(13) = 8.81, p \leq .001$) and TD groups (tactile : $t(13) = 2.32, p \leq .05$; visual : $t(13) = 5.77, p \leq .001$). This confirmed that the RTs are faster when stimuli are preceded by a stimulation of the same, rather than different modality (Fig. 1E-F). We found no main effect for the "group" factor ($F(1{,}26) = .03, p = .86$). We observed a main effect of the "modality" factor ($F(1{,}26) = 4.64, p \leq .05$, $n^2_{\text{partial}} = .15$), as participants in both groups were faster to switch from visual to tactile stimuli. There was no interaction between these two factors ($F(1{,}26) = .50, p = .49$).

7.5 Discussion

We investigated the ability of AS individuals to integrate cross-modal and within-modal low-level information, and to shift attention from one modality to another during multisensory processing. Our results demonstrate that AS individuals can integrate cross-modal visuo-tactile information, although this integrative process is decreased compared to TD. When comparing within-modal and cross-modal integration performances across groups, we found that cross-modal visuo-tactile stimuli (or conditions) produced greater RTs facilitation compared to both double tactile and visual conditions in TD, while redundancy gains for visuo-tactile and double tactile were both superior to those in the double visual condition in AS individuals. Importantly, the attentional processes needed to shift from one modality to another were found to be similar in TD and AS, suggesting that the alteration in multisensory integration observed in AS individuals is not due to an impaired capacity to switch attention across the senses, but rather, has a perceptual origin.

Cross-modal integration in AS

In AS individuals, the RTs for the cross-modal conditions exceeded to a lesser extent the probabilistic sum of the RTs predicted from the visual and tactile conditions relative to TD participants, suggesting that AS individuals are able to integrate low-level visuo-tactile information, albeit in a relatively altered manner.

Interestingly, we also found that overall, AS participants responded more slowly than controls to any sensory stimuli (see SFig. 2). Application of the race model is thus advantageous to factor out this unisensory delay since integration is calculated on probability summation of individual unisensory reaction times distributions (see Harrar et al. (2014) for similar discussion in dyslexic individuals). Moreover, according to the inverse effectiveness principle (Stein & Meredith, 1993), a basic concept in sensory integration stating that the multisensory gain is inversely proportional to the saliency of unisensory signals, one may have predicted greater cross-modal integration in AS based on their slower RTs for single visual and tactile conditions, which reinforce our results of a specific alteration of the multisensory integration process in AS (Brandwein et al., 2013; 2015; Charbonneau et al., 2013).

Until now, multisensory integration of visuo-tactile information in AS has mainly been investigated based on visuo-tactile illusions, like the rubber hand illusion (Botvinick, 2004), in which information from vision and touch are merged to influence proprioception and body representation. The experience of this illusion has been shown to be reduced in AS individuals (Paton, Hohwy & Enticott, 2012) and delayed (Cascio, Foss-Feig, Burnette, Heacock & Cosby, 2012). To our knowledge, only the studies of Poole and collaborators (2015; 2018) have used an approach void of socially salient stimuli to investigate visuo-tactile processing in AS individuals. In these studies, participants were asked to judge whether a tactile stimulation was a single or two separate (double) vibrations while presented with a congruent or incongruent number of distracting light flashes, a paradigm somewhat analogous to the sound-induced flash illusion (Shams, Kamitani & Shimojo, 2000). Their results demonstrated that AS individuals showed a difficulty for suppressing the processing of distant contralateral distractors, and suggested reduced spatial modulation of visuo-tactile interactions (Poole et al., 2015; 2018). Therefore, results from the current study confirm and extend previous research showing an alteration of visuo-tactile integration in AS (Paton et al., 2012; Cascio et al., 2012; Poole et al., 2015; 2018).

The current study is the first to rely on a simple reaction time paradigm in AS adults that allow to measure responses for both unisensory and multisensory conditions to simple low-level visuo-tactile stimuli, and to directly compare the benefits of multisensory information to a predicted model (i.e. the race model; Miller, 1982; 1986) based on responses to the unisensory conditions (see Brandwein et al. (2013; 2015) for similar paradigm with audio-visual stimuli in children and adolescents). Some studies based on audio-visual interactions suggested an improvement in the ability to integrate cross-modal sensory information with development in AS (Foxe et al., 2015; Taylor, Isaac & Milne, 2010). It is interesting to note that we found reduced violation of the race model inequality for the fastest latencies of the RTs distribution in AS adults, while a complete absence of violation of the race model inequality was found when performing a similar task in AS children and adolescents aged between 7 and 16 years old (Brandwein et al., 2013; 2015). Although speculative, these results may suggest that developmental changes due to neurobiological or experiential factors (or both), progressively regularize multisensory integration abilities in AS (Poole et al., 2015). Studies examining developmental trajectories of multisensory processing for linguistic information in AS individuals have observed an improvement in the ability to integrate audio-visual syllables with age (Foxe et al., 2015; Taylor et al., 2010; although see Stevenson et al., 2014c). Cross-modal integration abilities are far from mature at birth, but rather develop over a protracted period of time and strongly depend on sensory experiences (see Stein, Stanford & Rowland, 2014 for a review). For example, experiments in animals suggested that multisensory plasticity persisted into adulthood (Stein et al., 2014). Therefore, relevant cross-modal experiences or training could compensate, at least to some extent, for an absence of typical development early in life (Stein et al., 2014). It therefore seems promising to develop longitudinal protocols intended to measure cross-modal integration abilities across the life-span in AS individuals, and eventually use those data to adapt the sensory therapies that are currently proposed in rehabilitation (Powers, Hillock-Dunn & Wallace, 2016; Powers, Hevey & Wallace, 2012).

Multisensory atypicalities in AS individuals could, at least partly, be underpinned by alterations in temporal aspects of sensory processing. This is supported by findings demonstrating an extended temporal binding window for low-level non social (Kwakye, Foss-Feig, Cascio, Stone & Wallace, 2011; Foss-Feig et al., 2010; Greenfield et al., 2015; Noel, Lytle, Cascio & Wallace, 2018; although see: Poole et al., 2018; Noel, De Niear, Stevenson, Alais & Wallace, 2017; Stevenson et al., 2017) and linguistic information (Woynaroski et al., 2013; Stevenson et al., 2014a; Noel, Stevenson & Wallace, 2018) in AS. Temporal binding windows were found to correlate with performance on the McGurk effect (Stevenson et al., 2017; Stevenson et al., 2014a), which subsequently impacted speech perception (Stevenson et al., 2017). Given that that our paradigm has proved efficient to investigate within-modal and cross-modal integration in AS individuals, an interesting avenue would be to manipulate the time interval between unisensory and multisensory pairs of stimuli and to evaluate how our results extended to different degrees of temporal synchrony between the stimuli.

Within-modal integration in AS

Gains observed for cross-modal visuo-tactile stimuli was stronger compared to double visual and double tactile conditions in TD individuals, and no significant violation of the race model inequality was found for any redundant visual or tactile condition. These results reproduce and extend previous observations of reduced redundancy gain for unisensory compared to multisensory information in both human (Girard et al., 2013; Forster et al., 2002; Laurienti et al., 2006; Miniussi et al., 1998) and animal (Gingras et al., 2009), as well as an absence of violation of Miller's race model inequality for pairs of visual (Girard et al., 2013; Murray et al., 2001; Corballis, 1998; Reuter Lorenz et al., 1995; Badzakova-Traikov et al., 2005) and tactile stimuli (Girard, Pelland et al., 2013; Forster et al., 2002). RG from intra-modal interactions therefore seems to be explained by simple probalistic facilitation while multisensory integration violates such pure statistical facilitation. It is worth nothing that these results are somewhat consistent with those of studies showing that unimodal pairs were generally associated with subadditive reponses, while cross-modal pairs generated additive or superadditive neural signals, at least when recorded in the superior colliculus in non-humans (Alvarado et al., 2007a;b). Moreover, the deactivation of the anterior ectosylvian sulcus (AES) and the rostral aspect of the lateral suprasylvian sulcus (rLS), which are mandatory for multisensory integration, had no impact on the integration of within-modal pairs, suggesting fundamental differences in the circuits underlying within- and cross-modal integration (Alvarado et al., 2007b). The most likely explanation seems to be that cross-modal integration combines sensory inputs from more independent sources, therefore allowing to reduce the uncertainty of the sensory estimates, while within-modal integration rather reflects the covariance between similar information (Ernst & Banks, 2002; Alvarado et al., 2008; Girard et al., 2013; Van Atteveldt et al., 2014).

AS individuals also exhibited a RG for the within-modal conditions, which was expressed by a significant reduction in RTs in the double tactile and the double visual conditions compared to the simple tactile and visual conditions. Similar to the TD group, the RTs in the within-modal conditions did not exceed the probabilistic sum of the RTs observed in the visual or tactile conditions. However, we found an interesting difference when comparing the performance of the two groups, as cross-modal visuo-tactile stimuli produced greater RT facilitation compared to both double tactile and visual conditions in TD, while RGs for visuo-tactile and double tactile RGs were both superior to RG for the double visual condition in AS. It might be hypothesized that tactile inputs were processed more independently from one another in AS, which may have led to higher RGs associated with integration of tactile stimuli in this population.

Modality switch cost in AS

Sequential stimuli presented during a simple detection task are not processed independently as RT to a sensory input is faster when preceded by a stimulus from the same modality (Harrar et al., 2014; Otto & Mamassian, 2012 ; Gondan et al., 2004). In contrast, when the stimuli in successive trials originate from different modalities, attention needed to shift from one modality to another leads to longer RTs (modality shift cost). Since several studies have shown impairments in the disengagement of attention in autistic population (Courchesne et al., 1994 ; Landry & Bryson, 2004 ; Renner et al., 2006 ; Wainwright-Sharp & Bryson, 1993 ; but see Boer-Schellekens et al., 2013 ; Iarocci & Burack, 2004 ; Senju et al., 2004 ; Leekam et al., 2000), we investigated whether alteration in sensory integration may relate to atypical modality switch cost in AS individuals. We observed a classic modality switch cost for both visual and tactile modalities, as RTs were faster when consecutive stimuli were coming from the same modality. Importantly, this effect was similar between the two groups. This result therefore minimizes the possibility that the atypical cross-modal integration observed in AS could be explained by an alteration of switching attention from one stimulus to another.

Conclusion

In conclusion, the present study demonstrates specific alteration in the integration of low-level, visuo-tactile stimuli in AS adults. When comparing within- and cross-modal integration, we found that cross-modal stimuli produced greater RT facilitation compared to within-modal conditions, except for the double tactile pairs in AS, leading to the hypothesis that neural representations for visual and tactile stimuli could be associated with different level of independency in AS individuals. Finally, using our novel approach, we ruled out the possibility that the atypical multisensory integration in the AS is explained by an altered ability to switch attention from one stimulus to another, by finding identical modality switch cost effect in AS and TD between the visual and tactile modalities.

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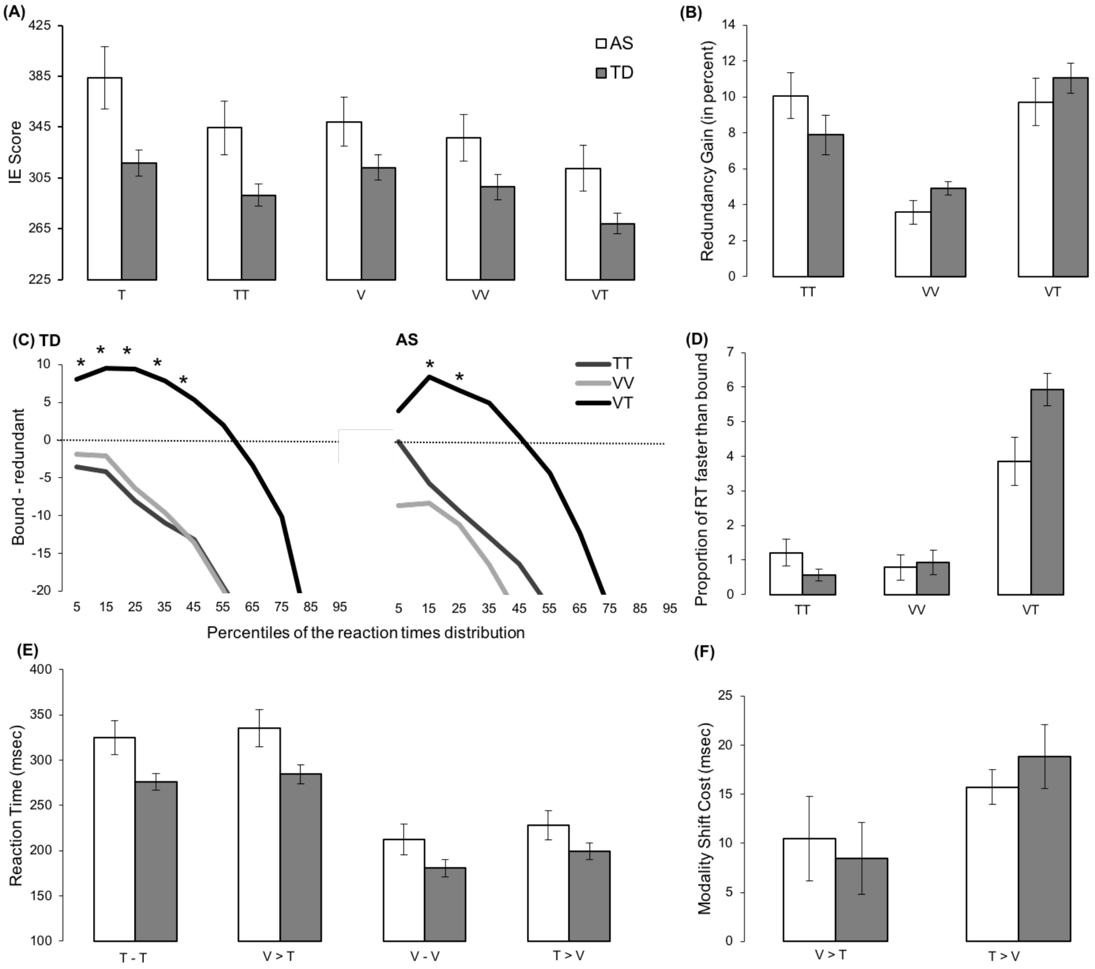
7.8 Figures

Fig. 1. Detection performance et integration

(A) Mean IE scores (in ms) for single, within-modal and cross-modal conditions in TD and in AS. Error bars represented standard error of the mean. Capital letters referred to the modality (T tactile, TT double tactile, V visual, VV double visual, VT visuo-tactile). (B) Mean redundancy gains (RGs) for double within- and cross-modal conditions in TD and in AS. (C) Test for violation of the race model inequality (Miller, 1982) in TD (left panel) and in AS (right panel). Y axis represented the difference in ms between the race model prediction computed from the RT of each single sensory component and the RT obtained in the redundant conditions for within- and cross-modal pairs. This value was computed for each percentile of the RT distribution represented on the X axis. Positive values on the Y axis of the graph referred to RTs that were faster than the race model prediction. When this difference was statistically significant, RTs were marked with an asterisk, which indicated a violation of the race model inequality. (D) Mean proportion of percentiles (out of ten) for which RTs were faster than predicted by the race model for double within- and cross-modal conditions in TD and in AS. (E) Modality Shift Cost effects for single and within-modal conditions were calculated according to whether the previous stimulus was from the same or from a different modality. (F) Modality Shift Cost indexes (in ms) calculated by subtracting the mean RTs for conditions in which the stimuli were preceded by a stimulus of the same modality to the mean RTs for conditions in which the stimuli were preceded by a stimulus of a different modality, as a function of the modality in both groups.

Fig. 1



(A)
425
385
345
305
265
225
IE Score
AS
TD
T
TT
V
VV
VT
(B)
14
12
10
8
6
4
2
0
Redundancy Gain (in percent)
TT
VV
VT
(C) TD
AS
*
10
5
0
-5
-10
-15
-20
Bound - redundant
5
15
25
35
45
55
65
75
85
95
TT
VV
VT
Percentiles of the reaction times distribution
(D)
7
6
5
4
3
2
1
0
Proportion of RT faster than bound
TT
VV
VT
(E)
400
350
300
250
200
150
100
Reaction Time (msec)
T - T
V > T
V - V
T > V
(F)
25
20
15
10
5
0
Modality Shift Cost (msec)
V > T
T > V

Chapitre 8

Article 4: The ventriloquist in periphery: Impact of eccentricity-related reliability on audio-visual localization.

The ventriloquist in periphery: Impact of eccentricity-related reliability on audio-visual localization.

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8.1 Abstract

The relative reliability of separate sensory estimates influences the way they are merged into a unified percept. We investigated how eccentricity-related changes in reliability of auditory and visual stimuli influence their integration across the entire frontal space. First, we surprisingly found that despite a strong decrease in auditory and visual unisensory localization abilities in periphery, the redundancy gain resulting from the congruent presentation of audio-visual targets was not affected by stimuli eccentricity. This result therefore contrasts with the common prediction that a reduction in sensory reliability necessarily induces an enhanced integrative gain. Second, we demonstrate that the visual capture of sounds observed with spatially incongruent audio-visual targets (ventriloquist effect) steadily decreases with eccentricity, paralleling a lowering of the relative reliability of unimodal visual over unimodal auditory stimuli in periphery. Moreover, at all eccentricities, the ventriloquist effect positively correlated with a weighted combination of the spatial resolution obtained in unisensory conditions. These findings support and extend the view that the localization of audio-visual stimuli relies on an optimal combination of auditory and visual information according to their respective spatial reliability. All together, these results evidence that the external spatial coordinates of multisensory events relative to an observer's body (e.g., eyes' or head's position) influence how this information is merged, and therefore determine the perceptual outcome.

Keywords: Multisensory integration; ventriloquist effect; spatial localization; reliability; eccentricity.

8.2 Introduction

Through the integration of information acquired by the different senses, our brain is able to construct a unified and more robust representation of our environment. The respective reliability of distinct sensory inputs strongly influences how they are merged in a single coherent percept (Sumby & Pollack, 1954). Probably one of the best examples of how the perceptual system deals with intersensory reliability is the ventriloquist effect (Howard & Templeton, 1966), in which the localization of auditory information is biased in the direction of a synchronously presented, but spatially misaligned, visual stimulus. In this perceptual situation, because the visual system typically provides the more accurate and reliable spatial information, the brain attributes more weight to vision in localizing the audio-visual event, thus inducing a visual capture of acoustic space (Pick, Warren, & Hay, 1969). This effect explains why although a movie actor's voice comes from loud-speakers far away from the screen, our brain recalibrates this discrepancy to give us the false impression that sound is actually coming from his mouth. Such visual capture does not occur in a rigid, hardwired manner, but follows flexible situation-dependent rules that allow information to be combined with maximal efficacy. Some experiments demonstrated that when the reliability of visual input is reduced, for example when visual information is blurred (Alais & Burr, 2004), presented at a low perceptual threshold (Bolognini, Leo, Passamonti, Stein, & Làdavas, 2007), near the onset of a visual saccade (Binda, Bruno, Burr, & Morrone, 2007) or degraded with myopia-inducing lenses (Hairston, Laurienti, Mishra, Burdette, & Wallace, 2003), the relative reliability of the auditory spatial cues increases and more weight is attributed to sounds in the localization of bimodal stimuli. Therefore, the ventriloquist effect may be considered as a specific example of near-optimal statistical (Bayesian) combination of visual and auditory spatial cues, where each cue is weighted in proportion of its relative reliability, rather than one modality capturing the other (Alais & Burr, 2004; Battaglia, Jacobs, & Aslin, 2003; Ernst & Bülthoff, 2004).

In daily life, a frequent situation inducing a decrease in visual and auditory reliability is when the same event appears in periphery rather than in the central spatial field relative to our sensory receptors. Auditory information is less reliably localized when it is presented in the periphery versus in front of the head (Barfield, Cohen, & Rosenberg, 1997; Makous & Middlebrooks, 1990; Nguyen, Suied, Viaud-Delmon, & Warusfel, 2009; Thurlow & Runge,

1967) due to change in interaural cues (Middlebrooks, 1991). Similarly, it is more difficult for a human observer to localize visual inputs when presented in the periphery compared to the center of the visual field because the central (foveal) part of retina contains a greater density of cone photoreceptors compared to the retinal periphery, leading to a more fine-grained representation of the information being processed (Baizer, Ungerleider, & Desimone, 1991; Dacey & Petersen, 1992; Stephen et al., 2002).

Such systematic reduction in the ability of the human observer to locate peripheral auditory and visual targets therefore affords a unique ecological opportunity to investigate how the reliability of sensory stimulations impact audio-visual integration across space (Collignon, 2007). Surprisingly, if the impact of the reliability on audio-visual integration has been massively investigated in the central visual field, only a few studies explored this phenomenon throughout the frontal space. Hairston and collaborators (2003b) studied how the absolute location in space modifies the ability of an irrelevant visual signal to influence the localization of an auditory target. They showed that auditory localization is more affected by the simultaneous presentation of a visual input coming from the center rather than from the periphery of the visual field. However, because these authors did not explore the far periphery (+30°), and because their paradigm was not designed to jointly investigate the redundancy gain (presentation of spatially aligned multisensory sources) and sensory capture (presentation of spatially misaligned multisensory sources), the impact of eccentricity-related reliability on audio-visual spatial integration remains elusive.

The goal of the present study was therefore to investigate further how spatial signals acquired by different sensory systems are integrated in the context of their position relative to the observer. To do so, we used a design allowing us to probe how the position of audio-visual targets in the entire frontal space (180°) affect the cross-modal capture and the multisensory integration (MSI) resulting from the presentation of spatially incongruent and congruent audio-visual events, respectively.

8.3 Methods

8.3.1 Subjects

Thirty-two right-handed participants (16 males; mean age of 24 years ± 3; range 20-30 years) were recruited and participated in this experiment. None of the subjects reported a history of neurological or psychiatric disorders. They all had normal hearing and normal or corrected-to-normal vision. The study was approved by the Comité d'Éthique de la Recherche de la Faculté des Arts et des Sciences (CERFAS) of the University of Montreal. All participants provided written informed consent and received financial compensation for their participation in the study.

8.3.2 Apparatus and stimuli

The entire experiment took place in a darkened, double-walled audiometric room (3.49 m x 1.94 m x 1.89 m), which was insulated by 7.5 cm width wedges on five sides (the floor was made of carpeting). Stimuli were presented on a semi-circular perimeter of 180° with a diameter of 150 cm. A height-adjustable chair and a keypad with two response buttons were installed at the center of the semicircle. The distance between the participant's head and the perimeter was 75 cm. Thirteen white light-emitting diodes (LEDs) and 13 small loudspeakers (Beyer Dynamics, DT-48) were positioned on this unit. A LED was placed directly above each speaker at eye level of the participant. Each pair, composed of a LED and a speaker, was separated by 15° of visual angle. These pairs were located at 0°, ±15°, ±30°, ±45°, ±60°, ±75°, and ±90° relative to the central fixation point, with positive values representing areas to the right and negative values representing areas to the left of the fixation point (Figure 1A). An additional red LED was used as a fixation spot placed at 0°, just above the central target white LED. The whole perimeter was covered with a semi-transparent black fabric so that the participants could not see the speakers and the LEDs when they were turned off.

Visual stimuli consisted in a 15 ms illumination of a white LED (48 cd/m^2). Auditory stimuli were 15 ms bursts of white noise (5 ms rise/fall time, 5 ms plateau). The level of intensity was adjusted to 65 dB SPL at the position of the participants' head. Bimodal (audio-visual) stimuli consisted in the simultaneous occurrence of a visual and an auditory stimulus. Stimuli delivery was controlled with Presentation software (Neurobe- havioral Systems, Inc., Albany, CA).

8.3.3 Procedure

A pair of two stimulations (always consisting of a probe and of a target stimulus) was presented on each trial (see Figure 1B for an example). The first stimulation (probe) was composed of an audio-visual pair, in which the auditory and visual stimuli were always delivered simultaneously at the same location. The probe could originate from seven different locations: 0°, ±15°, ±45°, or ±75° of eccentricity from midline. The second stimulation (target) could be (a) a visual stimulus alone, (b) an auditory stimulus alone, or (c) both visual and auditory stimuli presented simultaneously in a congruent or incongruent fashion. For the congruent matching, the visual and auditory stimuli were presented at the same location. In contrast, for the incongruent matching, the visual and auditory stimuli came from separate eccentricities. The target stimulus was presented between 100 and 150 ms after the probe either to its right (+15°) or to its left (-15°). For the incongruent conditions, one component of the target stimulus (e.g., visual stimulus) was presented to the right (+15°) of the probe while the other (e.g., auditory stimulus) appeared to its left (-15°). Each pair of stimuli was followed by a 1000 ms interval for response production. The central red LED was lit for 500 ms preceding the occurrence of a stimulus to ensure central fixation.

Participants were instructed to judge as accurately and as fast as possible whether the target stimulus, which could be an auditory, a visual, or an audio-visual stimulation, was located to the left or to the right of the probe by pressing the appropriate buttons of the keypad with the index (leftward response) or the middle fingers (rightward response) of their right hand. They were asked to localize the target stimulus based on their initial reaction to the stimulation even if they perceived a conflict between the senses. A total of 1,680 randomly interleaved stimuli [7 (position of the probe: 0°, ±15°, ±45°, ±75°) x 2 (target's location: right, left) x 4 (modality: visual, auditory, bimodal congruent, bimodal incongruent) x 30 repetitions] were presented to each subject. These stimuli were displayed in 15 blocks of 112 stimuli lasting approximately 4 minutes each. Breaks were encouraged between blocks to maintain a high concentration level and prevent mental fatigue.

8.3.4 Data analysis

In order to investigate the participants' ability to localize auditory, visual, and congruent audio-visual stimuli across the external frontal space, we computed the sensitivity index (d') to obtain a measure of the discriminability between leftward versus rightward targets relative to the probe and the position bias (β). The d' were calculated as $[(z_{\text{proportion correct}} - z_{\text{proportion incorrect}})/\sqrt{2}]$ and the β as $[-(z_{\text{proportion correct}} + z_{\text{proportion incorrect}})/2]$ (Macmillan & Creelman, 1991). Correct mean reaction times (RTs; ranging from 150 ms to 1000 ms) were also analyzed. In experiments that place equal emphasis on accuracy and processing speed, it is possible that subjects adopt different response strategies by varying RT inversely with accuracy (and thus show speed/accuracy trade-off). Therefore, overall performance may be best reflected by a single variable that simultaneously takes into account speed and accuracy. We have therefore also calculated the Inverse Efficiency (IE) scores which constitute a standard approach to combine mean RTs and accuracy measures of performance (Townsend & Ashby, 1978) and can be considered as "corrected reaction times" that discount possible criterion shifts or speed/accuracy trade-offs (Collignon et al., 2008; Röder, Kusmierek, Spence, & Schicke, 2007; Spence, Shore, Gazzaniga, Soto-Faraco, & Kingstone, 2001). The IE scores were obtained by dividing response times by the rate of correct responses separately for each condition (thus, a higher value indicates worse performance).

MSI was investigated by calculating the redundancy gain (RG) based on d', RTs and IE scores. RG was defined as the difference (in percent) between the mean d', mean RTs, or IE scores obtained in the multisensory condition and the mean d', RTs, or IE scores obtained in the best unisensory condition. RG was measured separately for each participant and level of eccentricity. Different explanations have been put forward to account for the observation of the RG. The most commons are the race and the coactivation models. The race model proposes that each individual stimulus elicits an independent detection process. For a given trial, the fastest stimulus determines the observable RT. On average, the time to detect the fastest of several redundant signals is faster than the detection time for a single signal. Therefore, the speeding up of reaction time is attributable to statistical facilitation (Raab, 1962). When the race model's prediction is violated, the speedup of RTs cannot be attributed to a statistical effect alone but some kind of coactivation must have occurred. To account for violations of the race model's prediction, the coactivation model (Miller, 1982) proposes that the neural activations of both stimuli combine to induce faster responses. Testing the race model inequality is widely used as an indirect behavioral measure of neurophysiological integrative processes underlying RT facilitation (see for example Girard, Pelland, Lepore, & Collignon, 2013; but also see Otto & Mamassian, 2012). To further investigate MSI, the race model inequality was evaluated (Miller, 1982) using the RMITest software, which implements the algorithm described at length in Ulrich, Miller & Schröter (2007). This procedure involves several steps. First, cumulative distribution functions (CDFs) of the RT distributions were estimated for every participant, eccentricity, and condition (visual, auditory, and audio-visual conditions). Second, the bounding sum of the two CDFs obtained from the two unimodal conditions (visual and auditory) were computed for each participant. This measure provided an estimate of the boundary at which the race model is violated, given by Boole's inequality. Third, percentile points were determined for every distribution of RT, including the estimated bound for each participant. In the present study, the race model inequality was evaluated at the 2.5, 7.5, 12.5, . . . 97.5 percentile points of the RT distributions. Fourth, for each percentile, mean RTs from redundant conditions were subtracted to the mean RTs from the bound. If those scores were above 0, the results exceeded the race model prediction and therefore supported the existence of a facilitation process (Miller, 1982; but see also Otto & Mamassian, 2012).

In order to quantify sensory dominance (the "ventriloquist effect") in incongruent conditions, the percentage of responses toward the sound (i.e., when a sound is coming from the right side and a flash is coming from the left side of the probe, and the participant reports the stimulus as coming from the right side) was subtracted from the percentage of responses toward the flash (i.e., when a sound is coming from the right side and a flash is coming from the left side of the probe, and the participant reports the stimulus as coming from the left side) for each eccentricity separately. A positive score would therefore indicate a visual capture over audition, while a negative score would suggest the reverse.

The relative performances obtained in visual and auditory unisensory conditions were directly compared by subtracting visual from auditory d', RTs, and IE scores and respectively dividing the score obtained by the auditory d', RTs, and IE scores, (d', RTs, or IE auditory – d', RTs, or IE visual)/d', RTs, or IE auditory. Positive scores therefore attest higher unisensory spatial performance in vision expressed in percent of the unisensory auditory results. These scores could then be correlated with the visual capture observed in the bimodal incongruent condition in order to investigate whether the relative superiority of vision over audition in unisensory conditions relates to the ventriloquist effect.

Since there was no difference in performances for the eccentricities to the left (-15°, -45°, -75°) and to the right (+15°, +45°, +75°) of the central fixation point, these scores were combined (see Supplementary Material for the details of the statistical analyses), at the exception of the β analysis which differ depending on which side the stimuli were presented. Statistical analyses were therefore conducted on four levels of eccentricity, which enhance statistical power by reducing the number of multiple comparisons: |0°| (central); |15°| (mean: -15°, +15°), |45°| (mean: -45°, +45°), |75°| (mean: -75°, +75°). Each result's figure (Figure 2 through Figure 6) represents the performance obtained in the full frontal space as well as the figures for the combined eccentricities.

8.4 Results

8.4.1 Localization of auditory, visual and audio-visual congruent stimuli: General Performance

Differences in general performance were analyzed by submitting d', β, RTs, and IE scores to repeated-measures ANOVAs (4 [eccentricities: |0°|, |15°|, |45°|, |75°|] x 3 [modalities: auditory, visual, bimodal congruent]). Based on significant F values, Bonferroni post-hoc analyses were performed when appropriate.

d' (Figure 2A): We observed a main effect for the "modality" factor, $F(2, 248) = 153.75$, $p \leq 0.0001$, $\eta^2 = 0.55$, reflecting inferior performance for auditory stimuli compared to both visual and bimodal stimuli and inferior performance for visual than for bimodal stimuli. We also obtained a main effect for the "eccentricity" factor, $F(3, 124) = 38.69$, $p \leq 0.0001$, $\eta^2 = 0.48$. Overall, this effect revealed that performance steadily decreased with eccentricity, with superior performance when comparing eccentricities |0°| and |45°|, |15°| and |45°| or |45°| and |75°|. Finally, an "eccentricity" by "modality" interaction was also found, $F(6, 248) = 3.02$, $p \leq 0.05$, $\eta^2 = 0.07$, driven by the fact that auditory performance only (not visual or bimodal) decreased between eccentricities |0°| and |15°|.

β (Figure 3): We found a main effect for the "eccentricity" factor, $F(6, 217) = 7.18$, $p \leq 0.001$, $\eta^2 = 0.17$, with a leftward bias for stimuli presented at the eccentricities -75°, -45°, -15°, 0°, and 15° compared to 75° and for the stimuli presented at the eccentricity -75° compared to 45°. There was no main effect for the "modality" factor, $F(2, 434) = 0.99$, $p = 0.37$, $\eta^2 = 0.005$, and no interaction was identified between the factors "modality" and "eccentricity", $F(12, 434) = 1.71$, $p = 0.06$, $\eta^2 = 0.05$.

RTs (Figure 2B): First, a main effect was found for the "modality" factor, $F(2, 248) = 114.94$, $p \leq 0.0001$, $\eta^2 = 0.48$, with higher RTs for auditory stimuli compared to both visual and bimodal stimuli and higher RTs for visual than bimodal stimuli. We also observed a main effect for the "eccentricity" factor, $F(3, 124) = 2.76$, $p \leq 0.05$, $\eta^2 = 0.06$, revealing a general slowdown of RTs with eccentricity. Finally, an "eccentricity" by "modality" interaction was found, $F(6, 248) = 10.11$, $p \leq 0.0001$, $\eta^2 = 0.20$, revealing that only RTs to auditory targets were not influenced by the eccentricity of the stimuli (p = 1.0 for all comparisons).

IE scores (Figure 2C): We observed a main effect of the factor "modality", $F(2, 248) = 204.58$, $p \leq 0.0001$, $\eta^2 = 0.62$, with worst performance for auditory stimuli compared to both visual and bimodal stimuli and a worst performance for visual than bimodal stimuli. We also found a main effect for the "eccentricity" factor, $F(3, 124) = 20.52$, $p \leq 0.0001$, $\eta^2 = 0.33$, again showing a decrease of performance with eccentricity. No interaction was identified between the factors "modality" and "eccentricity", $F(6, 248) = 2.65$, $p = 0.13$, $\eta^2 = 0.04$.

The relative unimodal performance of vision over audition (see data analysis section for details) was compared across the eccentricities using one-way ANOVAs. When based on d' scores, the relative unimodal performance of vision over audition changed across the eccentricities, $F(3, 127) = 6.01$, $p \leq 0.005$, $\eta^2 = 0.13$, with lower visual dominance for eccentricity |0°| than |45°| (Figure 2D). If measured using the RTs, the relative performance of vision over audition significantly decreased in periphery, $F(3, 127) = 14.59$, $p \leq 0.001$, $\eta^2 = 0.26$), with higher visual dominance when comparing eccentricities |0°| than |45°|, |15°| than |45°| and |45°| than |75°| (Figure 2E). No significant effect of eccentricity, $F(3, 127) = 2.12$, $p = 0.10$, $\eta^2 = 0.05$) was found when the relative performance of vision over audition was calculated based on IE scores, even if the scores tended to be lower at the largest eccentricity (|75°|; Figure 2F).

8.4.2 Localization of spatially congruent audio-visual stimuli: Redundancy Gain

There was no significant difference in RG throughout the different eccentricities when derived from the d', $F(3, 124) = 2.32$, $p = 0.08$, $\eta^2 = 0.05$ (Figure 4A), or the IE scores, $F(3, 124) = 0.23$, $p = 0.88$, $\eta^2 = 0.006$ (Figure 4C). If measured using the RTs, RG showed fluctuations according to the degree of eccentricity, $F(3, 124) = 4.55$, $p \leq 0.005$, $\eta^2 = 0.10$, with higher RG for eccentricity |0°| and |15°| compared to |75°| (Figure 4B). A positive difference (meaning a violation of the race model prediction) was observed between the redundant condition and the probabilistic bound for the first three percentiles of the RT distribution at eccentricity |0°| and for the first percentile at eccentricity |15°|. No violation of the race model estimation was found for the eccentricities |45°| and |75°| (Figure 5, see Supplementary Material for the figure representing the results obtained in the full frontal space).

In order to further investigate the association between the RG and the localization performance for unisensory information, we correlated (using Pearson product-moment correlation coefficient) the RG with the mean d', RTs, and IE scores for the best unisensory modality across eccentricities (Gingras, Rowland, & Stein, 2009). According to the principle of inverse effectiveness (IE), stating that the multisensory gain produced by the integration of separate sensory estimates is enhanced when the reliability of these stimuli is low (Stein & Meredith, 1993), these variables are generally inversely correlated; that is, lower accuracy in localizing single stimuli is associated with maximal RG when adding another stimulus (Stanford, Quessy, & Stein, 2005; Stein & Meredith, 1993). We obtained no significant correlation between the RG and the best unisensory d' ($r = -0.33$, $p = 0.47$), RTs ($r = -0.72$, $p = 0.07$), or IE scores ($r= -0.27$, $p = 0.55$) (Figure 4D), meaning that RG was relatively constant regardless of the reliability of the best unisensory component. The marginal tendency observed with RTs was in opposite direction of the predictions made from the IE principle: Shorter RTs in the best modality (at more central location) were associated with a higher RG.

8.4.3 Localization of spatially incongruent audio-visual stimuli: The Ventriloquist Effect

We observed a main effect of the factor "eccentricity", $F(3, 124) = 17.67, p \leq 0.0001, \eta^2 = 0.30$, revealing a decrease in the ventriloquist effect with eccentricity. Post-hoc comparisons demonstrated a higher visual capture for eccentricity |0°| compared to |45°| and |75°|, for eccentricity |15°| compared to |45°| and |75°|, and for eccentricity |45°| compared to |75°| (Figure 6A).

In order to investigate the association between the ventriloquist effect and the relative reliability of unisensory visual over auditory stimuli, we correlated the relative reliability of visual over auditory unimodal information in d' scores, RTs, and IE scores (reflecting both the discriminability and processing speed of the stimuli) with the visual capture effect separately for each eccentricity. For all eccentricities, we obtained a positive correlation between the ventriloquist effect and the scores of visual reliability based on IE scores [|0°| (r = 0.63, $p \leq 0.001$), |15°| (r = 0.70, $p \leq 0.001$), |45°| (r = 0.69, $p \leq 0.001$), and |75°| (r = 0.77, $p \leq 0.001$); Figure 6B], d' [|0°| (r = 0.42, $p \leq 0.05$), |15°| (r = 0.21, $p = 0.24$), |45°| (r = 0.32, p = 0.07), and |75°| (r = 0.18, p = 0.33); Supplementary Figure S2A] and RTs [|0°| (r = 0.55, $p \leq 0.001$), |15°| (r = 0.72, $p \leq 0.0001$), |45°| (r = 0.62, $p \leq 0.0001$) and |75°| (r = 0.56, $p \leq 0.001$); Supplementary Figure S2B], meaning that individuals having higher visual localization abilities relative to auditory ones also show an enhanced visual capture at every level of eccentricity.

8.4.4 Control experiment

In the main experiment, the probe always consisted in an audio-visual pair of stimuli while the target could either be a unimodal (auditory or visual) or a bimodal (audio-visual) stimulation. Therefore, the unisensory trials were not purely unimodal as they contained a bimodal probe, and the amount of noise associated with the two types of multisensory pairs was not equal to that associated with the unisensory auditory and visual pairs. In order to test if the differences we observed between unisensory and multisensory stimulations was associated to the difference in the level of noise between those conditions, we conducted a control experiment in which the first stimulation of each pair was always presented in the same modality as the second stimulus of the pair (either auditory, visual, or audio-visual), instead of always being an audio-visual stimulation (Supplementary Figure S3A and S3B).

Results (and related statistics) are presented in the Supplementary Material (Supplementary Figure S4 through S8) and are consistent with what was found in the main experiment. Therefore, using a constant level of noise for each pair of stimulation, we observed that despite a strong decrease in auditory and visual unisensory localization abilities in periphery (see Supplementary Figure S4A through S4C), the RG resulting from the congruent presentation of audio-visual targets was not affected by stimuli eccentricity (see Supplementary Figure S6). We also confirmed that the ventriloquist effect steadily decreased with eccentricity (see Supplementary Figure S8A), paralleling a lowering of the relative reliability of unimodal visual over unimodal auditory stimuli in periphery (see Supplementary Figure S4D through S4F), and that it positively correlated with a weighted combination of the spatial resolution obtained in unisensory conditions (see Supplementary Figure S8B).

8.5 Discussion

By exploring how the spatial location of auditory and visual targets affects both the multisensory gain and the ventriloquist effect, the current study shed new lights on how the natural eccentricity-related changes in reliability of audio-visual stimuli impact their integration across the entire external frontal space.

We first examined how the position of auditory-alone and visual-alone stimuli influences our spatial discrimination abilities. Regarding the localization of the visual stimuli, we observed higher discriminability (Figure 2A) and faster RTs (Figure 2B) when the information was presented in the center of the frontal field rather than in the periphery. This reduction in the reliability of visual information with eccentricity is consistent with the fact that, through its physiological properties (higher density of cones than rods in the fovea and the reverse in the periphery of the retina), the visual system has a better spatial resolution for central vision (Baizer et al., 1991; Dacey & Petersen, 1992; Stephen et al., 2002). When looking at the ability to localize the auditory stimuli, we also observed a severe reduction in the discriminability of information presented in the periphery (Figure 2A). This finding is in accordance with studies showing that higher auditory spatial resolution is achieved for information presented directly in front of the head, due to the spatial dependence of the interaural difference cues (Blauert, 1997;

Middlebrooks, 1991). Interestingly, the RTs for the auditory targets remained similar across all the frontal space (Figure 2B), which therefore contrasts with the results obtained in vision where eccentricity similarly affected both the discriminability and the RTs of the stimuli. These results suggest that, at least in terms of RTs, the detrimental effect of peripheral stimuli appearance is lower in audition than in vision (see also Figure 2E–F). This outcome might be related to studies reporting that saccadic reaction time toward auditory (but not visual) stimuli accelerated as a function of target eccentricity, whereas accuracy decreased (as for visual targets) with increasing eccentricity (Gabriel, Munoz, & Boehnke, 2010; Yao & Peck, 1997), suggesting that there is a speed-accuracy trade-off in the localization of peripheral auditory targets. The mechanisms underlying this effect still remain elusive, but have been suggested to be related to spatial receptive field attributes of neurons in the superior colliculus (Zambarbieri, 2002; Zambarbieri, Beltrami, & Versino, 1995; Zambarbieri, Schmid, Magenes, & Prablanc, 1982), as it changes with eye position or when the fixation point disappear before the onset of the target.

The first main objective of the current study was to explore the impact of the eccentricity-related reliability of auditory and visual information on the RG. Based on the inverse efficiency (IE) principle in MSI stating that the multisensory gain produced by the integration of separate sensory estimates coming from the same event is enhanced when the reliability of these stimuli is low (Stein & Meredith, 1993), one may have expected a positive relation between the RG and the eccentricities of the targets since the reliability of visual and auditory information dramatically decrease when presented in periphery (Figure 2C). Moreover, the observation of direct projections between caudal region of the auditory cortex and visual areas representing peripheral visual space in monkeys (Falchier, Clavagnier, Barone, & Kennedy, 2002; Rockland & Ojima, 2003) and humans (Beer, Plank, & Greenlee, 2011) provided a neurophysiological support to hypothesize enhanced audio-visual integration in periphery. Surprisingly, we did not observe a significant influence of the eccentricity of our targets on the RG derived from d’ or IE scores (Figure 4A and Figure 4C). Rather, we even observed a stronger RG for central locations with RT measurements (Figure 4B and Supplementary Figure S4B). In support of these results, we observed that for the fastest latencies (percentiles) of the RT distributions, the RT probability in the bimodal condition exceeded the probabilistic sum of the RT observed in the auditory or visual unisensory conditions (Figure 5 and Supplementary Figure S7; Miller, 1982; but see also Otto & Mamassian, 2012). This violation of the race model prediction was however not observed for more peripheral locations (|45°| and |75°|), which indicates a reduced ability to integrate separate sensory information when presented in the periphery of the frontal space.

Gingras and collaborators (2009) examined the performance of cats in localizing auditory, visual, and spatio-temporally congruent audio-visual stimuli at different eccentricities of the frontal space (±45°). They found that the enhanced performance obtained with audio-visual stimuli was inversely proportional to the best single stimulus accuracy at each location, a result which is consistent with the IE principle. In contrast with these results and reinforcing the hypothesis that the IE principle is not observed in our experiment, we found no correlation between the performance for the best unisensory modality and the RG (Figure 4D).

As such, we show that IE does not strictly apply to the multisensory enhancements seen during audio-visual localization in humans. These results therefore contradict simple models predicting that the rules of IE governing MSI derived from unicellular studies in the brainstem (see for example Rowland, Stanford, & Stein, 2007; Stein, Stanford, Ramachandran, Perrault, & Rowland, 2009) directly relates to multisensory phenomena at the level of perception and behavior (Holmes & Spence, 2005). Actually, even at a neurophysiological level, it was already suggested that setting stimulus intensity such that both significant facilitation and suppression relative to the unisensory response could reasonably arise, and measuring absolute changes of multisensory gain as a function of unisensory responsiveness, are parameters that have been shown to reduce the likelihood that the rule of IE will be followed (Holmes, 2009).

Although IE has been shown in numerous behavioral studies (Bolognini, Frassinetti, Serino, & Làdavas, 2005; Gondan, Niederhaus, Rösler, & Röder, 2005; Stein, Huneycutt, & Meredith, 1988), several reports also failed to show support for this principle (Diederich & Colonius, 2008; Kim & James, 2010; Ross et al., 2007; Ross, Saint-Amour, Leavitt, Javitt, & Foxe, 2007; Stevenson, Krueger Fister, Barnette, Nidiffer, & Wallace, 2012). For example, Ross and colleagues (2007) investigated whether seeing a speaker's articulatory movements would influence a listener's ability to recognize spoken words under noisy environmental conditions, and found that the redundancy RG is higher at intermediate auditory signal-to-noise ratios (and not at lowest signal-to-noise ratios as predicted by the IE principle). The authors interpreted their results by suggesting that there is a maximal integration window at intermediate signal-to-noise ratios, where the perceptual system can build on either the visual or the auditory modality. These findings appear to be consistent with those from our experiment, as RG tended to be greatest at intermediate eccentricities (|15°|, |45°|; see Figure 4C). A reason why these results were not observed from previous studies investigating audio-visual perception across the frontal space (Bolognini et al., 2005) could be that none of them presented the information in the far periphery (>55°). Therefore, these studies cut off approximately at the same eccentricity at which we observed a maximal gain.

Another related question is whether the same mechanisms are implicated when comparing multisensory enhancement in the same brain receptive field (RF) or across different RFs. The vast majority of experiments explored the multisensory enhancement at a unique position in space while changing the level of stimulus intensity, therefore activating a unique RF with different level of intensity. However, in the current study, we varied the strength of the sensory signal by presenting it through different RFs having different spatial resolution. It might therefore be interesting to investigate if different level of stimulus intensity (i.e., high and low intensity) at each of the eccentricities may induce performances compatible with the principle of IE.

The second main interest of the current study was to explore the impact of eccentricity-related reliability of auditory and visual information on the ventriloquist effect. The ventriloquist effect is a perceptual condition wherein a visual stimulus biases (captures) the localization of a spatially incongruent sound. It was first thought to reflect a winner-take-all advantage that favors visual over non-visual spatial information because vision typically provides the most reliable information for space perception (Welch & Warren, 1980). However, more recent studies demonstrated that information from independent sensory channels is integrated with a near-optimal or Bayesian strategy, such that the perceived location of the sound rather depends on the weighted sum of the sensory cues based on their respective reliability (Alais & Burr, 2004; Ernst & Bülthoff, 2004). In the spatial domain, Hairston et al. (2003b) examined the ability of a visual signal to influence the localization of an auditory target according to their eccentricity (±40° in fontal space). They found that the visual bias was strongly dependent on the location of the visual stimulus, with greatest bias in the center of visual space where the reliability of the visual targets is the greatest. Moreover, Teramoto and collaborators (2012) showed that the perceived direction of visual motion could be modulated by the presence of a moving sound and that the more the visual stimuli originated from the periphery, the stronger the effect. The current study supports and extends these results by demonstrating that the ventriloquist effect steadily decreases with eccentricity over the whole frontal space (Figure 6A). Moreover, we show that this reduction of visual capture is associated with more similar unimodal localization performance between vision and audition in periphery (Figure 2D-F; Supplementary Figure S4D through S4F). It is however important to note here that regarding the relation between the relative unisensory performances for visual over auditory targets, we observed a speed/accuracy tradeoff effect, as the performance based on d' increased with eccentricity and the opposite effect was found for RTs (Figure 2D through E). The combination of both scores in the IE scores still indicated a reduction in visual dominance as a function of the eccentricity (Figure 2F).

We also demonstrate for the first time that the ventriloquist effect strongly correlates with the relative unisensory reliability between visual over auditory information for each eccentricity across the frontal space (Figure 6B): The better the unisensory localization abilities in vision compared to audition, the stronger the ventriloquist effect. These results further bolster the idea that, based on the relative spatial reliability of auditory and visual unisensory information, the ventriloquist effect results from a weighted combination of the information gathered from the two modalities (Alais & Burr, 2004). Audio-visual integration in space is therefore not an absolute process but relative to the location of the multisensory event from the observer's body position, which location differently impact on the reliability of the unisensory components.

It is hypothesized that the topography of the auditory space is constantly calibrated by retino-visuomotor feedback in order to maintain stable spatial alignment with the visual space (Lewald, 2013; 2002a, b). This was notably evidenced by studies demonstrating that following an exposure period to spatially disparate audio-visual stimuli, the perceived location of a sound is being translocated in the direction of the visual stimuli to which observers had previously been exposed, known as the ventriloquist after-effect (Can- on, 1970; Frissen, Vroomen, de Gelder, & Bertelson, 2003; Lewald, 2002a, b; Radeau & Bertelson, 1974; Recanzone, 1998). Based on the results of the current study, we hypothesize that the magnitude of this after-effect may vary according to the eccentricity where the audio-visual stimuli are presented during the exposure period, with stronger ventriloquist after-effect in the central visual field where the reliability of the visual target is the highest.

8.6 Conclusion

The current study provides new insights into how the eccentricity of separate sensory estimates influences the merging of these inputs into a unified percept. First, we found that the multisensory gain was not affected by stimuli reliability, contrasting with the prediction made from the principle of IE. This finding suggests that multisensory principles derived from unicellular experiment carried out in the superior colliculus (Stein and Meredith, 1993) are not straightforward in their explanation of multisensory phenomena at the level of perception and behavior (Spence, 2013). Second, we demonstrated that the visual capture of sounds observed with spatially incongruent audio-visual targets steadily decreased with eccentricity. Finally, we showed that at every level of eccentricity, the ventriloquist effect directly relates to a weighted combination of the spatial resolution obtained in unisensory conditions. These results evidence that the external spatial coordinates of multisensory events relative to an observer's body (e.g., eyes' or head's position) influence how this information is merged, and therefore determine the perceptual outcome. These results might have implications for the design of optimal ergonomic environment where the attention of an observer has to be captured by auditory, visual or audio-visual cues delivered at various spatial locations.

8.7 Acknowledgments

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8.9 Figures

Fig.1. Schematic representation of the apparatus and experimental trial

(A) Schematic representation of the apparatus. Thirteen LEDs and 13 small loudspeakers were positioned on a 180° semi- circular perimeter. (B) Schematic example of an experimental trial. Pairs consisting of a LED placed above a speaker were located at 0°, ±15°, ±30°, ±45°, ±60°, ±75°, and ±90° relative to the fixation point of the subject. The probe could originate from seven different locations, either 0°, ±15°, ±45°, or ±75° from midline, while the comparison stimulus was presented either to the right (+15°) or/and to the left (-15°) of this reference.

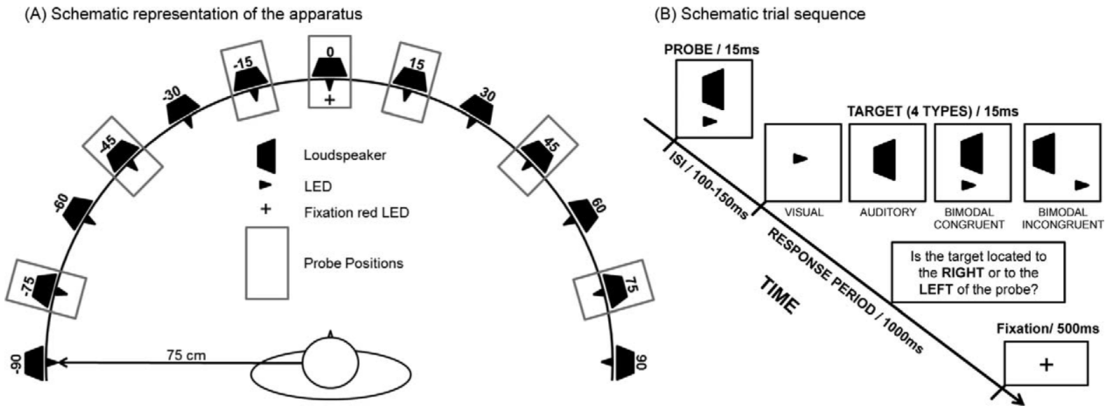


Fig. 2. Localization performance

Left panel: d’ scores (A), RTs (B), and IE scores (see Methods) (C) for the discrimination of auditory, visual, and audio-visual stimuli as a function of the eccentricity. Right panel: relative performance for visual over auditory targets as a function of the eccentricity based on d’ scores (D), RTs (E), and IE scores (F). Error bars denote standard errors of the mean corrected for between-subjects variability (Cousineau, 2005).

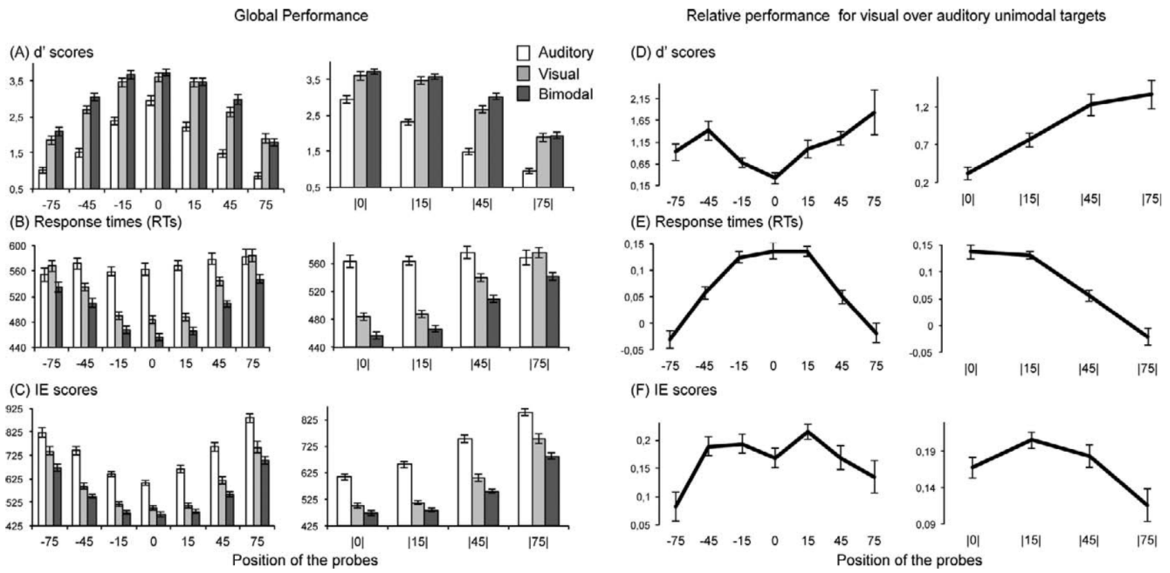


Fig 3. Bias

β scores for the discrimination of auditory, visual, and audio-visual stimuli as a function of the eccentricity. Positive values reflected a leftward response bias, while negative values represented a rightward response bias. Error bars denote standard errors of the mean corrected for between-subjects variability (Cousineau, 2005).

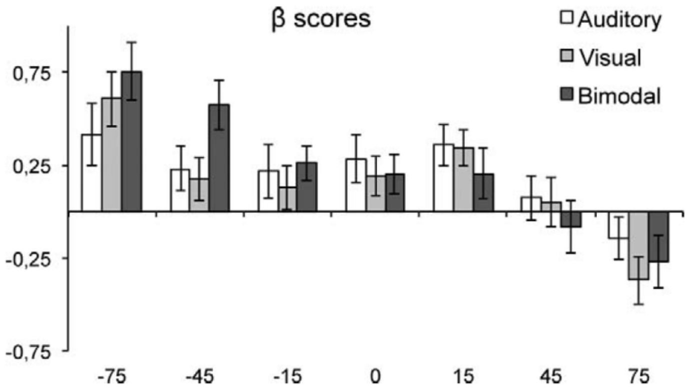


Fig. 4. Redundancy gain

RG (in percent) based on d’ scores (A), RTs (B), and IE scores (C) as a function of the eccentricity. (D) RG in function of the performance for the best unisensory component based on d’, RTs, and IE scores. Error bars denote standard errors of the mean corrected for between-subjects variability (Cousineau, 2005).

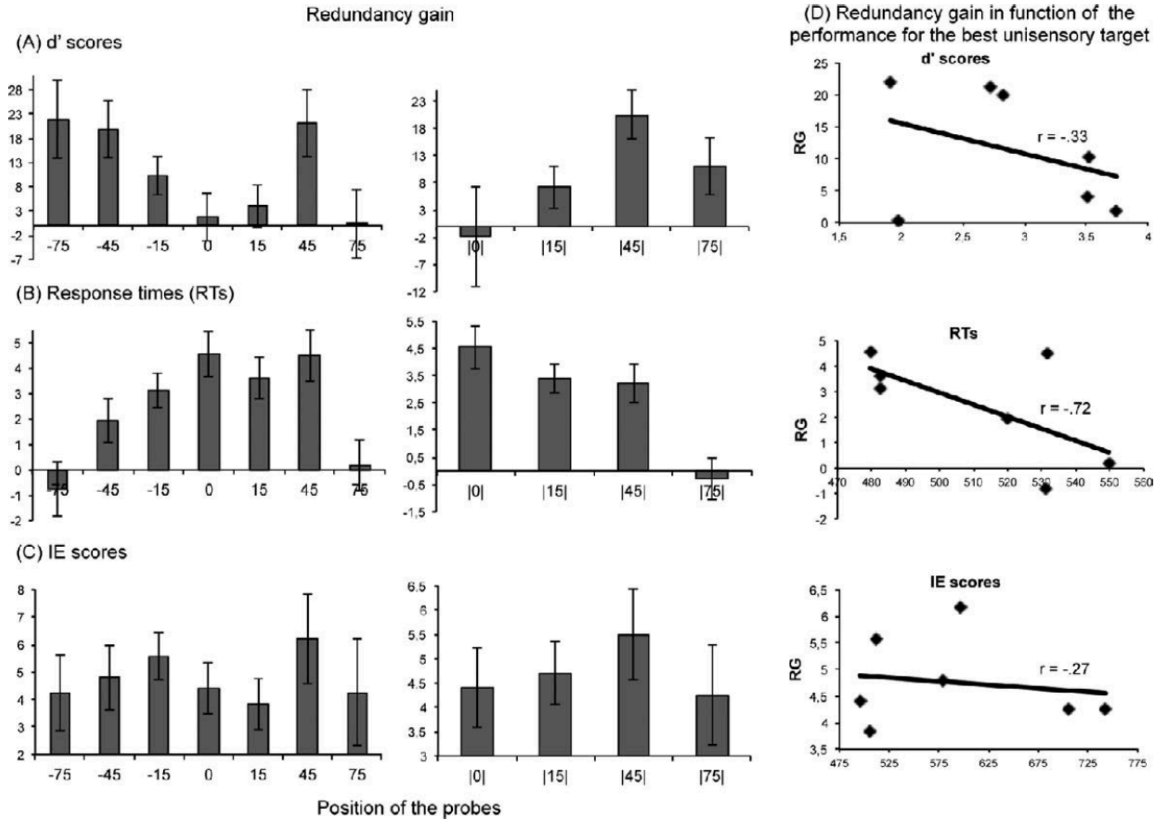


Fig. 5. Race model inequality

Test for violation of the race model inequality (Miller, 1982; Ulrich, Miller, & Schröter, 2007). The graph represents the difference in milliseconds (on the y-axis) between the model prediction computed from the RTs of each unisensory counterpart (the model bound) and the RTs obtained in the redundant conditions. Positive values on the graph refer to RTs that were faster than the race model prediction. Negative values on the graph refer to RTs that were slower than the race model prediction. The difference between the bound and the RTs of the redundant condition are computed for each percentile of the RT distribution (on the x-axis).

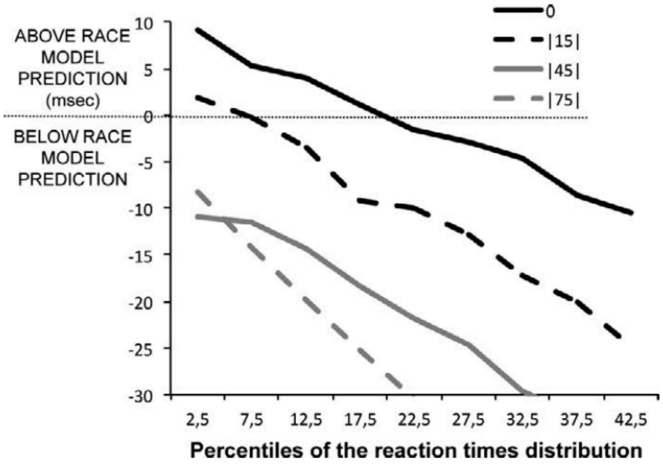
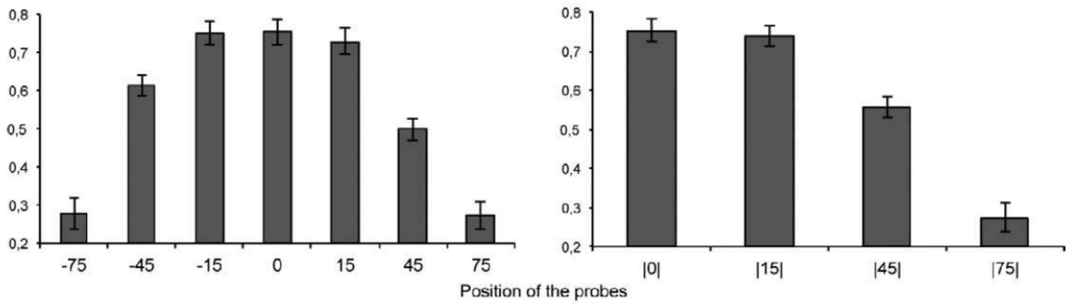


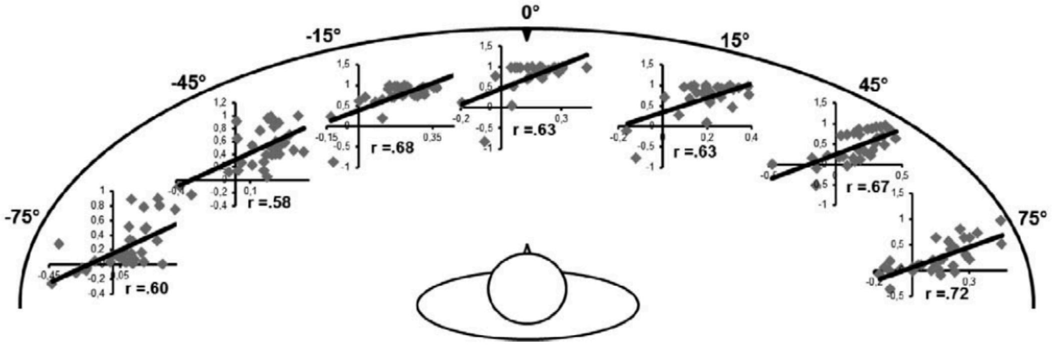
Fig. 6. Ventriloquist effect

(A) Ventriloquist effect as a function of the eccentricity. This score is obtained by subtracting the percentage of responses guided by hearing to the percentage of responses guided by vision for each eccentricity. Error bars denote standard errors of the mean corrected for between-subjects variability (Cousineau, 2005). (B) Ventriloquist effect as a function of the relative reliability between visual and auditory targets. This figure shows a significant positive correlation between the ventriloquist effect and the visual reliability scores for each eccentricity.

(A) Ventriloquist effect



(B) Ventriloquist in function of the relative performance of visual over auditory unimodal targets based on IE scores



8.10 Supplementary Material

Main Experiment: Effect of the position in relation to the central fixation point

Statistical analysis were made to compare performances for the eccentricities to the left (-15°, -45°, -75°) and to the right (+15°, +45°, +75°) of the central fixation point. An absence of difference between scores for right and left eccentricities would allow us to combine these scores and therefore to conduct statistical analyses on four levels of eccentricity, which enhance statistical power by reducing the number of multiple comparisons: |0°| (central); |15°| (mean: -15°, +15°), |45°| (mean: -45°, 45°), |75°| (mean: -75°, +75°).

Localization of auditory, visual and audio-visual congruent stimuli: General Performance

The effect of the position of the stimulus (left versus right) in relation to the central fixation point on the general performance was measured by submitting d', β, RTs and IE scores to repeated measures ANOVAs (2 [hemispaces: left, right] x 3 [eccentricities: |15°|, |45°|, |75°|] x 3 [modalities: auditory, visual, bimodal congruent]).

d': No main effect was observed for the "hemispace" factor ($F(1,62) = .30$, $p=.59$, $\eta^2 =.005$), revealing that there was no difference in performance when stimuli were presented to the right compared to the left of the central fixation point. We did not found any interaction between the "hemispace" and the "modality" factors ($F(2,124) = .69$, $p=.50$, $\eta^2 =.01$) or between the "hemispace" and the "eccentricity" factors ($F(2,124) = .22$, $p=.81$, $\eta^2 =.003$).

β: We found a main effect for the "hemispace" factor ($F(1,62) = 8.86$, $p \leq .05$, $\eta^2 =.13$), with a stronger leftward bias for stimuli presented to the left compared to the right of the central fixation. There was an interaction between the factors "hemispace" and "modality" ($F(2,124) = 61.0$, $p \leq .05$, $\eta^2 =.17$), as well as between the factors "hemispace" and "eccentricity" ($F(2,124) = 61.0$, $p \leq .0001$, $\eta^2 =.38$), suggesting that the effect of the hemispace on the performances changed according to the modality of the stimuli and the eccentricity where they originated. Therefore,

RTs: No main effect was observed for the factor "hemispace" ($F(1,62) = .12$, $p=.73$, $\eta^2 =.001$), showing similar performance when stimuli were presented to the right compared to the left of the central fixation point. We did not found any interaction between the "hemispace" and the "modality" factors ($F(2,124) = .39$, $p=.68$, $\eta^2 =.006$) or between the "hemispace" and the "eccentricity" factors ($F(2,124) = 1.85$, $p=.16$, $\eta^2 =.03$).

IE scores: No main effect was found for the “hemispace” factor (*F*(1,62) = .31, *p*=.58, η^2=.005), revealing that there was no difference in performance when stimuli were presented to the right compared to the left of the central fixation point. We did not identified any interaction between the “hemispace” and the “modality” factors (*F*(2,124) = .52, *p*=.60, η^2 =.008) or between the “hemispace” and the “eccentricity” factors (*F*(2,124) = 1.37, *p*=.26, η^2=.02).

The effect of the position of the stimulus (left versus right) in relation to the central fixation point on the relative unimodal performance of vision over audition was compared across the eccentricities using repeated measures ANOVAs (2 [hemispaces: left, right] x 3 [eccentricities: |15°|, |45°|, |75°|]). When based on d’ scores, there was no main effect of the “hemispace” factor on the relative unimodal performance of vision over audition (*F*(1,62) = 1.5, *p*=.23, η^2=.02) or interaction between the “hemispace” and “eccentricity” factors (*F*(2,124) = 1.68, *p*=.19, η^2=.03). If measured using the RTs, we did not observed any main effect of the “hemispace” factor on the relative unimodal performance of vision over audition (*F*(1,62) = .05, *p*=.82, η^2=.001) or interaction between the “hemispace” and “eccentricity” factors (*F*(2,124) = .29, *p*=.75, η^2=.005). No significant effect of the “hemispace” factor (*F*(1,62) = .28, *p*=.60, η^2 =.004) or interaction between the “hemispace” and “eccentricity” factors (*F*(2,124) = 1.23, *p*=.30, η^2=.02) was found when the relative performance of vision over audition was calculated based on IE scores.

Localization of spatially congruent audio-visual stimuli: Redundancy gain

The effect of the position of the stimulus (left versus right) in relation to the central fixation point on the RG was compared across the eccentricities using repeated measures ANOVAs (2 [hemispaces: left, right] x 3 [eccentricities: |15°|, |45°|, |75°|]). When based on d’ scores, there was no main effect of the “hemispace” factor on the RG (*F*(1,62) = 1.64, *p*=.20, η^2=.03) or interaction between the “hemispace” and “eccentricity” factors (*F*(2,124) = 1.37, *p*=.26, η^2 =.02). If measured using the RTs, we did not observed any main effect of the “hemispace” factor on the RG (*F*(1,62) = 1.0, *p*=.32, η^2 =.01) or interaction between the “hemispace” and “eccentricity” factors (*F*(2,124) = .60, *p*=.55, η^2=.01). No significant effect of the “hemispace” factor (*F*(1,62) = .007, *p*=.93, η^2=.0) or interaction between the “hemispace” and “eccentricity” factors (*F*(2,124) = .52, *p*=.60, η^2 =.008) was found when the RG was calculated based on IE scores.

Localization of spatially incongruent audio-visual stimuli: the Ventriloquist Effect

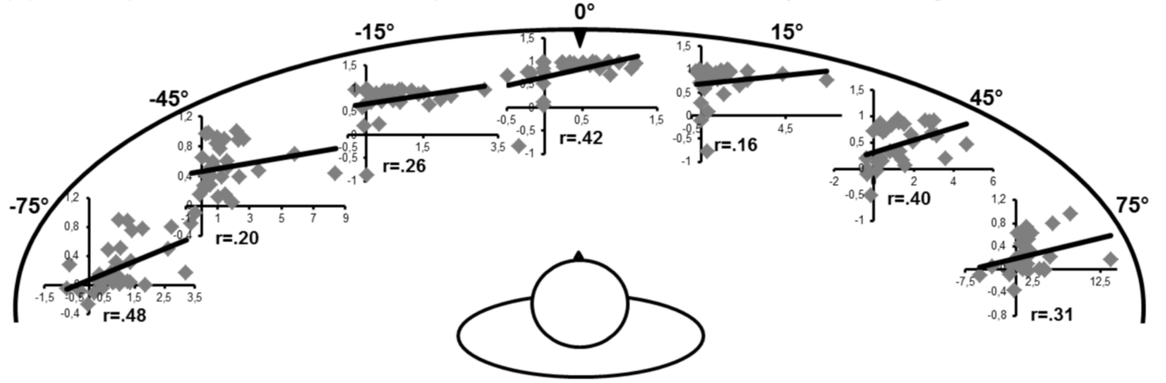
The effect of the position of the stimulus (left versus right) in relation to the central fixation point on the ventriloquist effect was compared across the eccentricities using repeated measures ANOVAs (2 [hemispaces: left, right] x 3 [eccentricities: |15˚|, |45˚|, |75˚|]). There was no main effect of the "hemispace" factor on the ventriloquist effect (*F*(1,62) = .16, *p*=.69, η^2 =.003) or interaction between the "hemispace" and "eccentricity" factors (*F*(2,124) = .48, *p*=.62, η^2 =.008).

<u>Main experiment: Ventriloquist in function of the relative performance of visual over auditory unimodal targets</u>

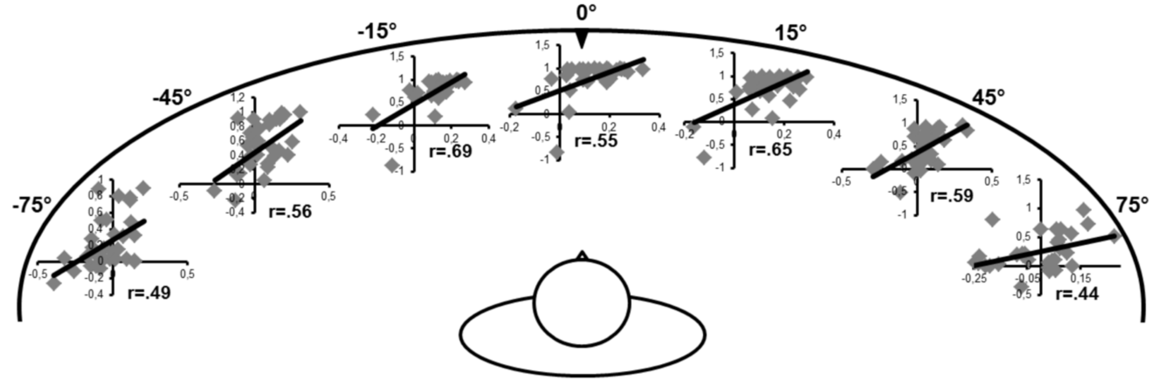
Sfig. 1. Ventriloquist effect as a function of the relative reliability between visual and auditory targets based on **(A)** d'scores and **(B)** RTs.

Sfig. 1

(A) Ventriloquist in function of the relative performance of visual over auditory unimodal targets based on d' scores



(B) Ventriloquist in function of the relative performance of visual over auditory unimodal targets based on RTs



Control Experiment

Methods

Subjects

Twelve right-handed participants (6 males; mean age of 25 years ± 3; range 21–30 years) were recruited and participated in this experiment. None of the subjects reported a history of neurological or psychiatric disorders. They all had normal hearing and normal or corrected-to-normal vision. The study was approved by the « Comité d'Éthique de la Recherche de la Faculté des Arts et des Sciences » (CÉRFAS) of the University of Montreal. All participants provided written informed consent for their participation in the study.

Procedure

The apparatus and the stimuli were the same as in the main experiment (Sfig. 2A). However, the first stimulation (probe) of each pair was always presented in the same modality (either auditory, visual or audio-visual) as the second stimulus (target) of the pair, instead of always being an audio-visual stimulation (Sfig. 2B). Therefore, each pair of stimulations (always consisting of a probe and of a target stimulus) could comprise (1) two visual stimuli, (2) two auditory stimuli or (3) two audio-visual stimuli. For the audio-visual pairs, the target could be presented in a congruent or incongruent fashion. For the congruent matching, the visual and auditory stimuli were presented at the same location. In contrast, for the incongruent matching, the visual and auditory stimuli came from separate eccentricities. The probe could originate from 7 different locations: 0, ±15, ±45 or ±75 degrees of eccentricity from midline. The target stimulus was presented between 100 and 150msec after the probe either to its right (+15°) or to its left (-15°). For the incongruent conditions, one component of the target stimulus (e.g. visual stimulus) was presented to the right (+15°) of the probe while the other (e.g. auditory stimulus) appeared to its left (-15°). Each pair of stimuli was followed by a 1000msec interval for response production. The central red LED was lit for 500msec preceding the occurrence of a stimulus to ensure central fixation.

Participants were instructed to judge as accurately and as fast as possible whether the target stimulus, which could be an auditory, a visual or an audio-visual stimulation, was located to the left or to the right of the probe by pressing the appropriate buttons of the keypad with the index (leftward response) or the middle fingers (rightward response) of their right hand. They were asked to localize the target stimulus based on their initial reaction to the stimulation even if they perceived a conflict between the senses.

A total of 1680 randomly interleaved stimuli (7 [position of the probe: 0°, ±15°, ±45°, ±75°] x 2 [target's location: right, left] x 4 [modality: visual, auditory, bimodal congruent, bimodal incongruent] x 30 repetitions) were presented to each subject. These stimuli were displayed in 15 blocks of 112 stimuli lasting approximately 4 minutes each. Breaks were encouraged between blocks to maintain a high concentration level and prevent mental fatigue.

Results

Localization of auditory, visual and audio-visual congruent stimuli: General Performance

Differences in general performance were analyzed by submitting d', β, RTs and IE scores to repeated measures ANOVAs (4 [eccentricities: |0˚|, |15˚|, |45˚|, |75˚|] x 3 [modalities: auditory, visual, bimodal congruent]). Based on significant F-values, Bonferroni post-hoc analyses were performed when appropriate.

d' (Sfig. 3A): We observed a main effect for the "modality" factor ($F(2,88) = 21.07$, $p \leq .0001$, $\eta^2 = .32$), reflecting inferior performance for auditory stimuli compared to both visual and bimodal stimuli and inferior performance for visual than bimodal stimuli. We also obtained a main effect for the "eccentricity" factor ($F(3,44) = 42.41$, $p \leq .0001$, $\eta^2 = .74$). Overall, this effect revealed that performance steadily decreased with eccentricity, with superior performance when comparing eccentricities |0°| and |45°|, |15°| and |45°| or |45°| and |75°|. No interaction was found between the "eccentricity" and the "modality" factors ($F(6,88) = .48$, $p = .82$, $\eta^2 = .03$).

β (Sfig. 4): As mentioned, β analysis differed for the eccentricities to the left and to the right of the central fixation and therefore were not combined. We found a main effect for the "eccentricity" factor ($F(6,77) = 3.83$, $p \leq .05$, $\eta^2 = .23$), with a leftward bias for stimuli presented at the eccentricities -75 compared to 45 and 75. There was also a small effect for the "modality" factor ($F(2,154) = 3.41$, $p \leq .05$, $\eta^2 = .04$), with a larger leftward bias for auditory than for bimodal stimuli. Finally, an interaction was identified between the factors "modality" and "eccentricity" ($F(12,154) = 2.55$, $p \leq .05$, $\eta^2 = .17$), revealing that only bias to visual targets was influenced by the eccentricity of the stimuli, and that the stronger leftward bias found for auditory compared to bimodal stimuli was significant only for eccentricity 75.

RTs (Sfig. 3B): First, a main effect was found for the "modality" factor ($F(2,88) = 46.99$, $p \leq .0001$, $\eta^2 = .52$), with higher RTs for auditory and visual stimuli compared to bimodal stimuli. We also observed a main effect for the "eccentricity" factor ($F(3,44) = 5.99$, $p \leq .05$, $\eta^2 = .29$), revealing a general slow down of RTs with eccentricity. Finally, an "eccentricity" by "modality" interaction was found ($F(6,88) = 5.60$, $p \leq .0001$, $\eta^2 = .28$), which was driven by the fact that only RTs to auditory targets were not influenced by the eccentricity of the stimuli ($p = .26$).

IE scores (Sfig. 3C): We observed a main effect of the factor "modality" ($F(2,88) = 35.15$, $p \leq .0001$, $\eta^2 = .44$), with worst performance for auditory and visual stimuli compared to bimodal stimuli. We also found a main effect for the "eccentricity" factor ($F(3,44) = 15.51$, $p \leq .0001$, $\eta^2 = .51$) again showing a decrease of performance with eccentricity. Finally, an interaction was identified between the factors "modality" and "eccentricity" ($F(6,88) = 3.72$, $p \leq .05$, $\eta^2 = .20$), as the superior performance for bimodal stimuli was observed only for the more peripheral eccentricity.

The relative unimodal performance of vision over audition (see data analysis section for details) was compared across the eccentricities using one-way ANOVAs. No significant effect of eccentricity ($F(3,47) = 1.08$, $p = .37$, $\eta^2 = .07$) was found when the relative performance of vision over audition was calculated based on d' scores (Sfig. 3D). When based on RTs, the relative unimodal performance of vision over audition changed across the eccentricities ($F(3,47) = 7.87$, $p \leq .0001$, $\eta^2 = .35$), with higher visual dominance for eccentricity |0°| and |15°| than |75°| (Sfig. 3E). If measured using the IE scores, the relative performance of vision over audition also significantly decreased in periphery ($F(3,47) = 3.84$, $p \leq .05$, $\eta^2 = .21$), with higher visual dominance when comparing eccentricities |45°| than |75°| (Sfig. 3F).

Localization of spatially congruent audio-visual stimuli: Redundancy gain

There was no significant difference in RG throughout the different eccentricities when derived from the d' ($F(3,47) = .81$, $p = .50$, $\eta^2 = .05$) (Sfig. 5A), the RTs ($F(3,47) = 2.60$, $p = .15$, $\eta^2 = .15$) (Sfig. 5B) or the IE scores ($F(3,47) = 2.18$, $p = .10$, $\eta^2 = .13$) (Sfig. 5C). A positive difference (meaning a violation of the race model prediction) was found between the redundant condition and the probabilistic bound at eccentricity |0°| for the fastest 7.5, 12.5 and 22.5 percentiles of the RTs distribution. This difference was not found for the eccentricities |15°|,

|45°| and |75°|, which suggest a higher RG for central (|0°|) compared to peripheral (|15°|, |45°| and |75°|) eccentricities (Sfig. 6).

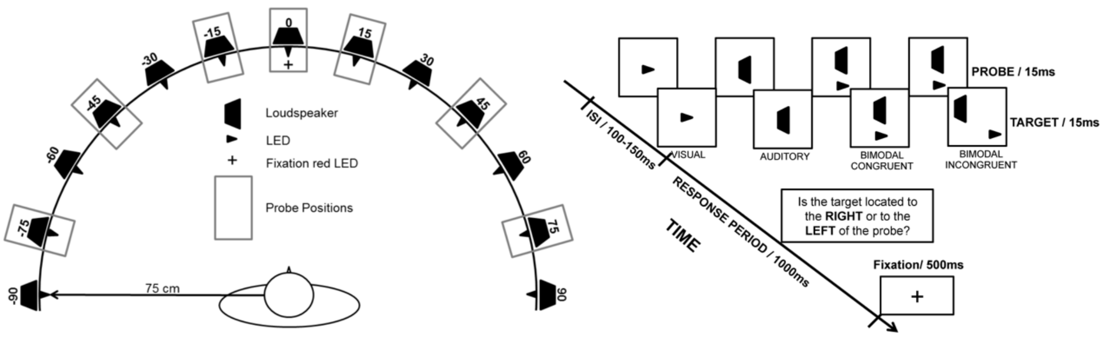
Localization of spatially incongruent audio-visual stimuli: the Ventriloquist Effect

We observed a main effect of the factor "eccentricity" ($F(3,47) = 10.35$, $p \leq .0001$, $\eta^2 = .41$), revealing a decrease in the ventriloquist effect with eccentricity. Post-hoc comparisons demonstrated an higher visual capture for eccentricity |0˚|, |15˚| and |45˚| compared to |75˚| (Sfig. 7A).

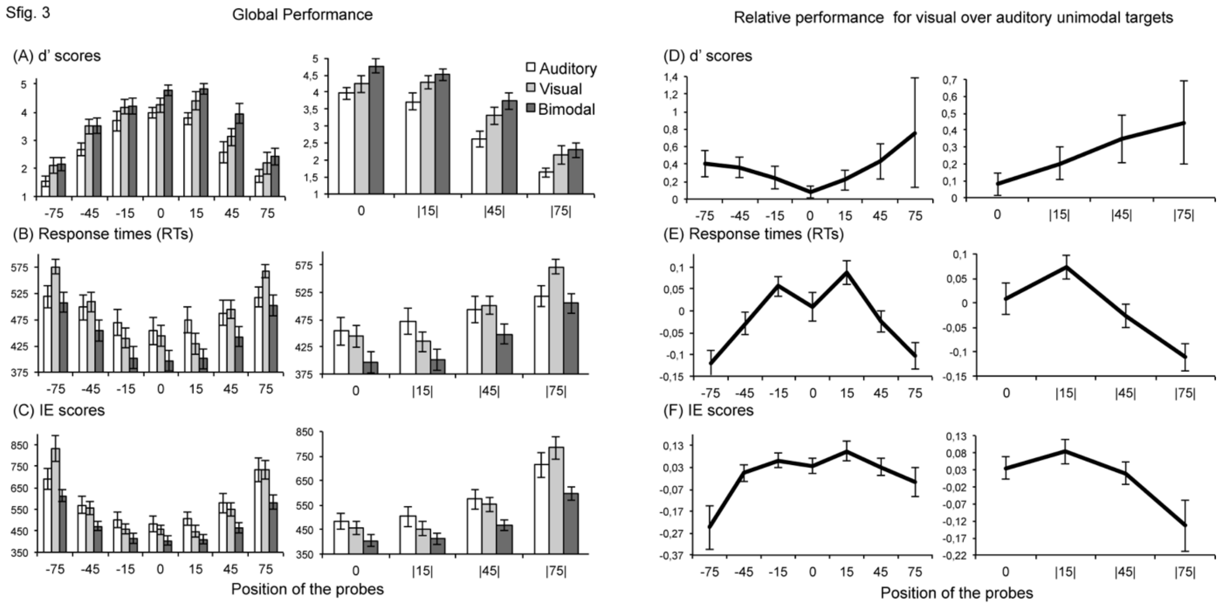
In order to investigate the association between the ventriloquist effect and the relative reliability of unisensory visual over auditory stimuli, we correlated the relative reliability of visual over auditory unimodal information in IE scores (reflecting both the discriminability and processing speed of the stimuli) with the visual capture effect separately for each eccentricity. We obtained a positive correlation between the ventriloquist effect and the scores of visual reliability based on IE scores for all eccentricities (|0˚| ($r = .47$, p=.12), |15˚| ($r = .57$, p≤.05), |45˚| ($r = .31$, p=.33) and |75˚| ($r = .77$, p≤.01); Sfig.7B), meaning that individuals having higher visual localization abilities relative to auditory ones, also show an enhanced visual capture at every level of eccentricity.

Sfig. 2. (A) Schematic representation of the apparatus. Thirteen LEDs and 13 small loudspeakers were positioned on a 180° semi-circular perimeter. **(B)** Schematic example of an experimental trial. Pairs consisting of a LED placed above a speaker were located at 0°, ±15°, ±30°, ±45°, ±60°, ±75° and ±90° relative to the fixation point of the subject. The probe could originate from 7 different locations, either 0°, ±15°, ±45° or ±75° from midline, while the comparison stimulus was presented either to the right (+15°) or/and to the left (-15°) of this reference.

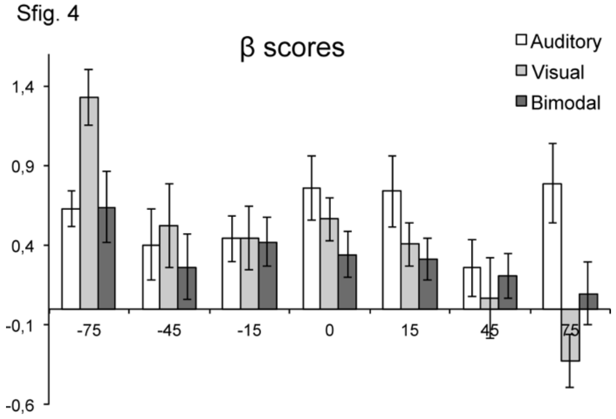
Sfig. 2



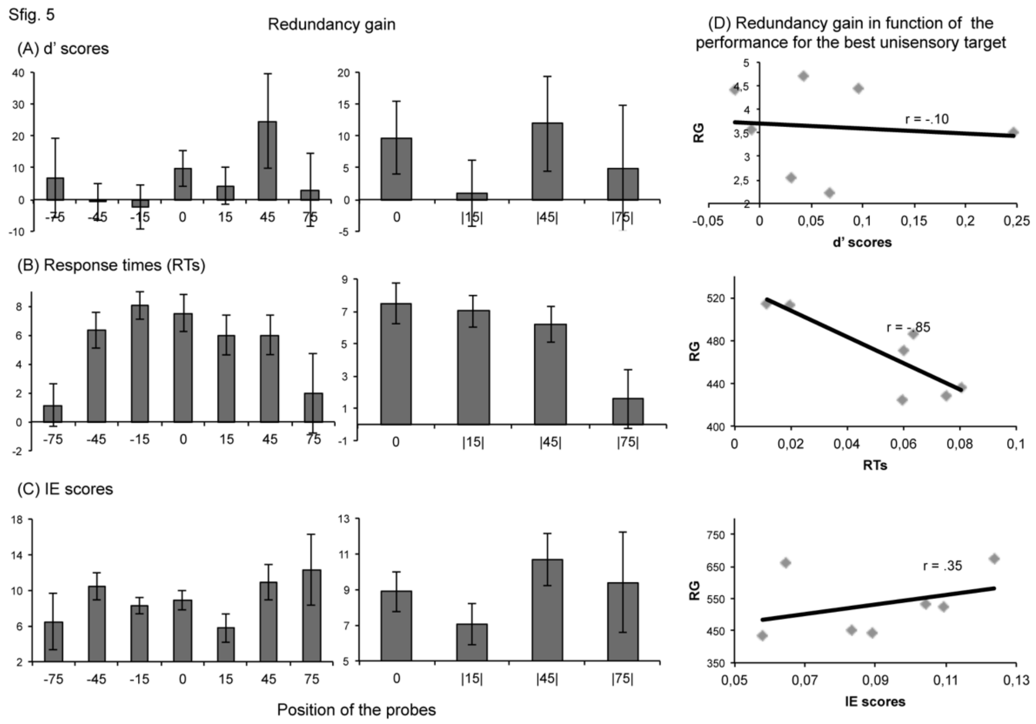
Sfig. 3. Left panel: d' scores **(A)**, RTs **(B)** and IE scores (see methods) **(C)** for the discrimination of auditory, visual and audio-visual stimuli as a function of the eccentricity. Right panel: relative performance for visual over auditory targets as a function of the eccentricity based on d' scores **(D)**, RTs **(E)** and IE scores **(F)**. Error bars denote standard errors of the mean corrected for between-subjects variability (Cousineau, 2005).



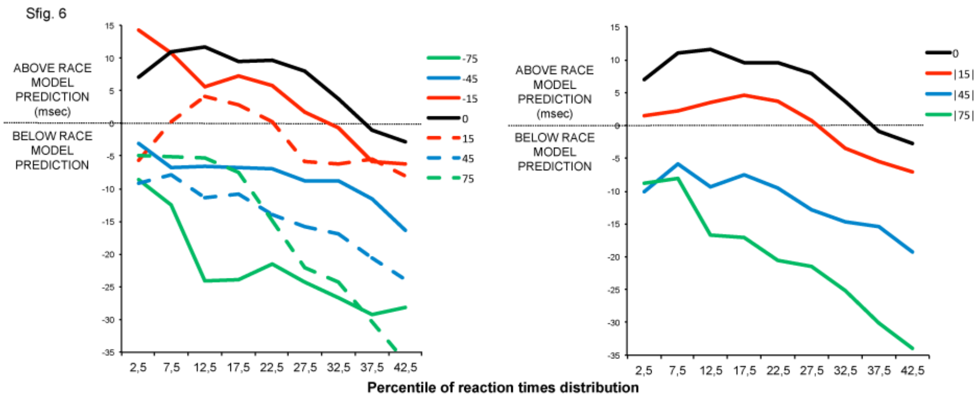
Sfig. 4. β scores for the discrimination of auditory, visual and audio-visual stimuli as a function of the eccentricity. Error bars denote standard errors of the mean corrected for between-subjects variability (Cousineau, 2005).



Sfig. 5. RG (in percent) based on d' scores **(A)**, RTs **(B)** and IE scores **(C)** as a function of the eccentricity. Error bars denote standard errors of the mean corrected for between-subjects variability (Cousineau, 2005).



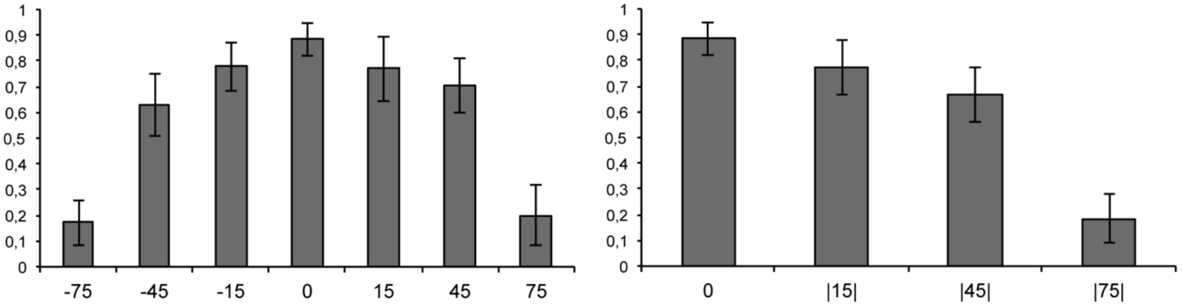
Sfig. 6. Test for violation of the race model inequality. The graph represents the difference in milliseconds (on the Y axis) between the model prediction computed from the RTs of each unisensory counterpart (the model bound) and the RTs obtained in the redundant conditions. Positive values on the graph refer to RTs that were faster than the race model prediction. Negative values on the graph refer to RTs that were slower than the race model prediction. The difference between the bound and the RTs of the redundant condition are computed for each percentile of the RT distribution (on the X axis).



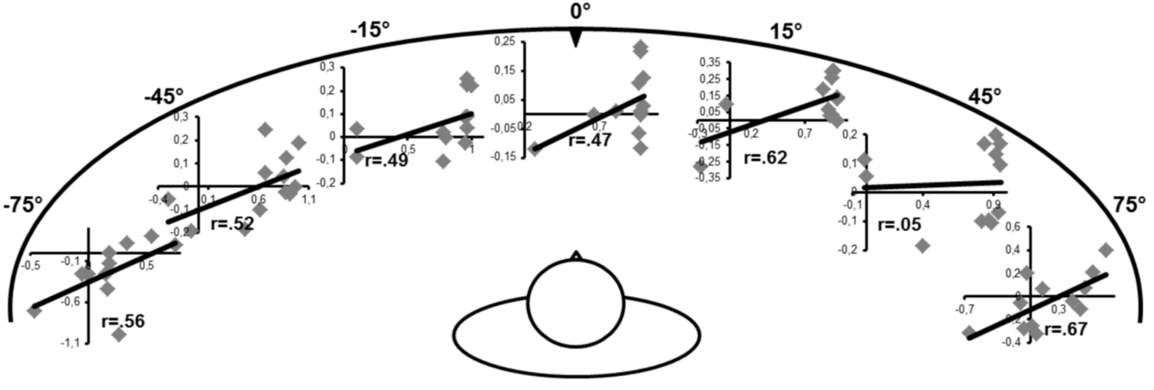
Sfig. 7. (A) Ventriloquist effect as a function of the eccentricity. This score is obtained by subtracting the percentage of responses guided by hearing to the percentage of responses guided by vision for each eccentricity. Error bars denote standard errors of the mean corrected for between-subjects variability (Cousineau, 2005). **(B)** Ventriloquist effect as a function of the relative reliability between visual and auditory targets. This figure shows a significant positive correlation between the ventriloquist effect and the visual reliability scores for each eccentricity.

Sfig. 7

(A) Ventriloquist effect



(B) Ventriloquist in function of the relative performance of visual over auditory unimodal targets based on IE scores



Chapitre 9 : Discussion Générale

L’objectif général de ce projet de thèse était donc de permettre une meilleure compréhension du lien qui existe entre le TSA et les performances d’intégration sensorielle. Pour ce faire, nous souhaitions d’abord confirmer que la capacité d’intégrer des informations provenant de différentes modalités sensorielles diffère entre les individus ayant un TSA et ceux avec DT, puis déterminer si celle-ci dépend du type de stimuli traité, soit de nature sociale versus non sociale. De plus, il nous semblait crucial d’évaluer si la capacité d’intégrer des informations multisensorielles se distingue de celle impliquée lors de l’intégration de stimuli d’une même modalité sensorielle (intégration intra-modale), ce qui n’avait jamais été directement évalué chez les individus ayant un TSA. Finalement, nous nous sommes intéressés à savoir si le changement d’allocation des ressources attentionnelles entre les modalités est susceptible d’expliquer les différences d’IMS entre les groupes, puis avons développé un paradigme permettant de mieux comprendre l’impact de la saillance des stimuli sur l’IMS qui pourra éventuellement être utilisé chez les individus ayant un TSA.

9.1 Objectif 1 : Intégration multisensorielle chez les individus ayant un TSA

9.1.1 Intégration multisensorielle d’informations sociales et TSA

La capacité des individus ayant un TSA à intégrer des informations de nature sociale a été explorée au moyen d’une tâche de discrimination émotionnelle. Celle-ci consistait à identifier l’émotion représentée au niveau de l’expression faciale (visuel), de la prosodie (auditif) ou de la combinaison de ces deux sources d’information (audio-visuel). Nous avons démontré que la combinaison des informations auditive et visuelle était associée à une amélioration des temps de réponse par rapport à la meilleure des composantes unimodales chez les individus ayant un TSA, suggérant un avantage associé au traitement d’informations multisensorielles chez cette population. Ce gain de redondance était toutefois moins important que celui observé pour le groupe contrôle avec DT. La comparaison des performances en condition bimodale aux prédictions du modèle de course a démontré une absence de différence significative chez les personnes ayant un TSA, alors que les temps de réponse surpassaient les prédictions du modèle de course chez les participants avec DT.

De façon générale, ces résultats suggèrent donc que les individus ayant un TSA bénéficient, comme ceux ayant un DT, de la combinaison d'informations multisensorielles congruentes de nature sociale, mais que leur capacité à les intégrer est diminuée.

9.1.2 Intégration multisensorielle d'informations non sociales et TSA

L'IMS d'informations de nature non sociale a été investiguée au moyen de deux tâches différentes. D'abord, nous avons comparé la performance entre les groupes à une tâche de recherche visuelle complexe durant laquelle un indice sonore était parfois présenté de façon simultanée au changement de couleur de la cible visuelle, l'objectif étant d'évaluer si les individus ayant un TSA étaient en mesure de bénéficier de la combinaison de ces deux sources d'informations multisensorielles. Les résultats ont montré que l'ajout de l'indice sonore n'affectait pas la précision, ni les temps de réponse pour identifier la cible chez les individus ayant un TSA, alors qu'un avantage clair associé à la combinaison audio-visuelle était retrouvé chez le groupe contrôle avec DT. De façon intéressante, en l'absence de l'indice sonore, les individus ayant un TSA étaient plus rapides que ceux avec DT pour identifier la cible.

Ces résultats témoignent de la présence d'atypies au niveau de l'IMS de stimuli non sociaux chez les personnes ayant un TSA, et suggèrent que la diminution de la capacité à intégrer des informations provenant de différentes modalités sensorielles n'est pas spécifique aux stimuli de nature sociale.

Une limite peut toutefois être soulevée en lien avec cette tâche. En effet, il est possible que l'amélioration de la performance de recherche visuelle en présence de l'indice sonore s'explique, du moins en partie, par un processus de contrôle rétroactif (en anglais « top-down »), et que ce soit plutôt ce processus qui soit utilisé de façon moins spontanée chez les individus ayant un TSA. Cette hypothèse serait compatible avec les résultats obtenus par Boer-Schellekens et collaborateurs (Boer-Schellekens, Keetels, Eussen et Vroomen, 2013). En effet, ces derniers ont répliqué la tâche de recherche visuelle incluse dans le présent projet de thèse, à l'exception près que les participants étaient explicitement avisés avant de débuter la tâche que certains essais seraient accompagnés d'un indice sonore synchronisé avec le changement de couleur de la cible visant à les aider à résoudre la tâche. Les participants étaient également autorisés à utiliser la stratégie de recherche visuelle souhaitée, alors que dans la présente étude, l'instruction était de maintenir le regard sur le point de fixation central. Les résultats de cette étude n'ont montré aucune différence entre les participants ayant un TSA et ceux avec DT. Pour les deux groupes, la performance était diminuée en lien avec l'augmentation du nombre de distracteurs visuels, et optimisée par l'ajout d'un indice sonore présenté de façon synchronisée au changement de couleur de la cible. Dans ce cadre, il est possible que le fait d'avoir explicité le rôle de l'indice sonore sur la tâche ait incité les participants à utiliser une stratégie de traitement rétroactive, ce qui semble avoir fait disparaître les différences de performance entre les groupes. Il est donc possible que les adultes ayant un TSA puissent bénéficier de la présentation synchrone d'un son durant une tâche de recherche visuelle, mais que cet avantage soit moins automatique, comme il disparaît lorsque sa fonction n'est pas décrite de façon explicite.

Cette hypothèse concorde avec le fait que l'utilisation de processus cognitifs descendants, c'est-à-dire qui appliquent des connaissances générales pour influencer la perception, serait automatique ou obligatoire chez les individus ayant un DT, mais pas chez les personnes ayant un TSA (Mottron et al., 2006). En effet, chez ces derniers, l'utilisation de processus de traitement descendants ou rétroactifs serait plus malléable et pourrait dépendre, par exemple, du profil spécifique de la tâche ou des consignes données. Cela expliquerait, entre autres, le fait que les individus ayant un TSA sont généralement moins trompés par les illusions sensorielles que ceux avec DT (Mottron et al., 2006).

Entre autres dans le contexte de la limite précédemment soulevée, il semblait pertinent de réévaluer la capacité des individus ayant un TSA à intégrer des informations de nature non sociale. Au moyen d'une étude subséquente, l'IMS d'informations non sociales de bas niveau a été comparée entre les participants ayant un TSA et ceux avec DT lors d'une tâche de détection visuo-tactile extrêmement simple, limitant l'influence de processus de plus haut niveau. Comme pour les informations de nature sociale, les résultats ont montré un gain de redondance chez les individus ayant un TSA, c'est-à-dire une diminution des temps de réponse en condition visuo-tactile comparativement à la plus efficace de ses deux composantes individuelles. Pour les deux groupes, la distribution des temps de réponse en condition bimodale surpassait les prédictions basées sur le modèle de course, bien que dans une proportion moindre chez les individus ayant un TSA. Précisément, les résultats surpassaient les prédictions du modèle de course pour les 50 premiers percentiles de la distribution des temps de réponse chez les individus ayant un DT et entre les 10^{e} et 30^{e} percentiles de la distribution des temps de réponse pour le groupe de participants ayant un TSA.

Ces résultats suggèrent que les individus ayant un TSA peuvent intégrer les informations non sociales de bas niveau, mais possiblement de façon moins efficace ou atypique par rapport aux personnes avec DT.

9.1.3 Impact de la nature du stimulus sur l'intégration multisensorielle chez les individus ayant un TSA

Dans l'ensemble, les résultats obtenus suggèrent donc que le TSA est associé à une diminution de la capacité à intégrer des informations provenant de différentes modalités sensorielles. Cette atteinte est présente indépendamment du type de stimuli traités, mais semble un peu plus manifeste pour les informations de nature sociale. En effet, bien que les différences entre les tâches ne permettent pas une comparaison directe des résultats, nous notons une absence complète de violation du modèle de course pour les paires bimodales de nature sociale, alors que les résultats surpassent les prédictions du modèle de course, mais dans une proportion moindre que chez les contrôles avec DT, pour les paires bimodales non sociales. De façon importante, nous observons une diminution de l'IMS chez les individus ayant un TSA comparativement à ceux avec DT, et non pas d'une absence complète d'intégration ni une détérioration de la performance en contexte multisensoriel. En effet, excepté pour la tâche de recherche visuelle (mais voir Boer-Schellekens et al., 2013), les participants ayant un TSA ont bénéficié de la présentation d'informations bimodales, bien que le gain de redondance fût moindre que celui retrouvé chez les individus ayant un DT.

Tel que mentionné précédemment, plusieurs études ont observé un déficit d'IMS pour les stimuli de nature sociale chez les individus ayant un TSA, alors que les résultats sont plus mitigés pour ce qui est des informations de nature non sociale (Bebko et al., 2006; Magnée et al., 2008; Mongillo et al., 2008). La démonstration que l'atteinte des processus d'IMS n'est pas spécifique au traitement d'information de nature sociale est importante. En effet, en raison des difficultés socio-communicationnelles inhérentes au diagnostic de TSA, il n'est pas exclu que l'utilisation de stimuli impliquant le langage ou les émotions empêche d'isoler l'effet propre de l'IMS, ce qui complexifie les conclusions pouvant être tirées sur la base de ces études (Bao et al., 2017). De plus, les stimuli langagiers et émotionnels sont généralement beaucoup plus riches et complexes que ceux utilisés pour évaluer l'IMS de stimuli non sociaux, ce qui peut être problématique, puisqu'il a été suggéré que les individus ayant TSA présentent des difficultés perceptuelles qui sont sélectives au traitement d'information plus complexe et globale (Minshew, Sweeney et Luna, 2002). Les résultats du présent projet de thèse suggèrent plutôt une atteinte générale des processus d'IMS chez les individus ayant un TSA, qui persiste au-delà du type d'information traitée.

De façon intéressante, dans certains contextes particuliers, cette diminution de la capacité à intégrer les informations provenant de différentes modalités sensorielles pourrait avantager les individus ayant un TSA, en ce sens qu'elle faciliterait la ségrégation de différentes sources d'informations contradictoires (Stevenson et al., 2014b). Par exemple, en présence d'informations incongruentes, les individus ayant un TSA auraient la capacité de traiter indépendamment l'un des stimuli en limitant l'influence de l'autre, ce qui est presqu'impossible à faire pour les personnes ayant un DT (Stevenson et al., 2014b).

9.1.4 Intégration multisensorielle chez les individus ayant un TSA

L'un des facteurs qui contribue fort probablement à l'hétérogénéité des résultats dans la littérature portant sur l'IMS chez les individus ayant un TSA est la variabilité importante au niveau des tâches et des techniques d'analyse qui sont employées (Laurienti et al., 2006). Le principal paradigme utilisé dans les études comprises dans ce projet de thèse, soit l'effet de redondance du signal (en anglais « Redundancy Signal Effect »; Hershenson, 1962; Raab, 1962), est très fréquemment utilisé dans les études auprès d'individus ayant un DT. De la même façon, la comparaison des résultats obtenus en contexte multisensoriel avec les prédictions du modèle de course (Miller, 1982) est largement employée comme mesure comportementale indirecte des processus d'intégration qui sous-tendent la facilitation des temps de réponse. Cependant, chez les individus ayant un TSA, ce type de paradigme et d'analyse n'ont été que très peu appliqués. À notre connaissance, seulement deux études l'ont fait. Celles-ci ont été effectuées auprès d'une population d'enfants, et ont démontré un déficit d'IMS pour les stimuli non-sociaux de bas niveau chez les participants ayant un TSA. Précisément, la distribution des temps de réponse pour la condition bimodale surpassait les prédictions du modèle de course chez les enfants avec DT, mais pas chez ceux ayant un TSA (Brandwein et al., 2013; 2015), ce qui concorde avec les résultats obtenus dans le présent projet de thèse. L'utilisation de ce type de paradigme et d'analyse a l'avantage significatif de contrôler pour les différences au niveau des performances unisensorielles (Harrar et al., 2014). De plus, il est important de considérer que plusieurs études à partir desquelles des conclusions par rapport à l'IMS chez les individus ayant un TSA ont été émises (entre autres les tâches d'appariement multisensoriel, certaines études basées sur des phénomènes d'illusions ou d'autres comparant la performance en condition multisensorielle à une seule condition unisensorielle) ne tiennent pas compte du fait que, par définition, l'évaluation du gain multisensoriel nécessite qu'une condition bimodale soit être comparée à la plus rapide de ses composantes unimodales (Stein et al., 2010).

La présence d'une atteinte des processus d'IMS, généralisée pour les différents types de stimuli, peut être interprété à la lumière des modèles perceptifs décrits précédemment, soit la *théorie de la faible cohérence centrale* (Frith et Happe, 1994; Happe, 1999; Happe et Frith, 2006; Burnette et al., 2005), le *modèle du fonctionnement perceptuel augmenté* (Mottron et al., 2006) et la théorie du *déficit d'intégration temporelle* (en anglais « temporal binding deficit »; Brock et al., 2002), selon lesquels les individus ayant un TSA présenteraient un mode perceptuel davantage orienté vers les éléments locaux, avec une atteinte de la performance pour les tâches nécessitant un traitement plus global ou intégratif. En effet, les difficultés d'IMS peuvent se traduire par une diminution de la capacité à intégrer les informations locales pour former une représentation perceptuelle multisensorielle plus complexe. De plus, les résultats obtenus lors de la tâche de recherche visuelle concordent avec l'hypothèse selon laquelle les individus ayant un TSA présenteraient une plus grande indépendance de la perception par rapport aux processus rétroactifs de haut niveau, émise dans le *modèle du fonctionnement perceptuel augmenté* (Mottron et al., 2006) et les théories bayésiennes (Pellicano et Burr, 2012). En effet, lorsqu'aucune explication n'est spécifiquement fournie par rapport à l'utilité de l'indice sonore lors de la tâche de recherche visuelle, les participants ayant un TSA tendent à utiliser un mode de traitement perceptuel basé sur les influx sensoriels visuels et ne bénéficient pas de l'ajout de cette composante. Par contre, lorsqu'il est spécifiquement explicité que le stimulus auditif peut être utilisé pour faciliter l'identification de la cible, les participants ayant un TSA utilisent également cette stratégie, et leur performance est similaire à celle observée chez les individus avec DT (Boer-Schellekens et al., 2013), suggérant que l'utilisation de stratégies de plus haut niveau est moins automatique chez les individus ayant un TSA.

Plusieurs études suggèrent que le TSA puisse être associé à une diminution de l'intégrité des connexions neuronales à longue portée, ayant pour conséquence une atteinte de l'intégration et de la synchronisation entre les régions cérébrales plus distantes (Foxe et al., 2015; Baum et al., 2015; Schipul, Keller et Just, 2011; Belmonte et al., 2004; Geschwind et Levitt, 2007; Minshew et Williams, 2007). Divers réseaux corticaux ont démontré un patron de connectivité fonctionnelle anormal chez les individus ayant un TSA lors de tâches cognitives, notamment lors de paradigmes évaluant le langage, l'attention, la mémoire, la perception des émotions et la théorie de l'esprit (Rudie et al., 2012; Kleinhans et al., 2008; Abrams et al., 2013; Just, Cherkassky, Keller et Minshew, 2004; Just, Cherkassky, Keller, Kana et Minshew, 2007; Kana, Keller, Cherkassky, Minshew et Just, 2009; Kana, Keller, Minshew et Just, 2007; Solomon et al., 2009), de même que lors de l'évaluation de l'activité cérébrale au repos (Anderson et al., 2011; Muller et al., 2011; Cherkassky, Kana, Keller et Just, 2006; Assaf et al., 2010; Weng et al., 2010). Sur le plan structurel, des études par imagerie en tenseur de diffusion ont démontré la présence de différences au niveau de l'intégrité des faisceaux de matière blanche chez les personnes ayant un TSA, suggestifs d'une hypo-connectivité neuronale (Shukla, Keehn et Muller, 2011; Weinstein et al., 2011; Thomas, Humphreys, Jung, Minshew et Behrmann, 2011; Lee et al., 2007; Langen et al., 2012; Chang et al., 2014), principalement au niveau frontal et temporal, incluant la région du STSp (Lee et al., 2007; Barnea-Goraly et al., 2004; Keller, Kana et Just, 2007; Ke et al., 2009). Ces conclusions demeurent toutefois controversées, et doivent être interprétées avec précaution (Visser, Cohen et Geurts, 2012; Vasa, Mostofsky et Ewen, 2016). En effet, plusieurs études n'ont pas observé de réduction de la connectivité chez les individus ayant un TSA ou ont plutôt démontré un patron mixte avec une augmentation de la connectivité entre certaines régions et une diminution pour d'autres (par exemple, Leveillé et al., 2010; Brieber et al., 2010; Lee et al., 2009; Monk et al., 2009). Certaines variables confondantes sont également susceptibles d'avoir eu un impact sur les résultats obtenus (Vasa et al., 2016), notamment des différences entre les groupes au niveau des mouvements de la tête lors des études en imagerie cérébrale (Power, Barnes, Snyder, Schlaggar et Peterson, 2012; Van Dijk, Sabuncu et Buckner, 2012; Koldewyn et al., 2014).

L'étiologie à l'origine de l'atteinte de la capacité à intégrer des informations provenant de différentes modalités sensorielles chez les individus ayant un TSA demeure inconnue à ce jour. L'IMS est un processus cérébral complexe, qui implique que de l'information traitée dans des régions cérébrales différentes soit transmise à travers des distances corticales prolongées, possiblement entre autres via des connexions monosynaptiques à longue distance (Falchier et al., 2010 ; Foxe et Schroeder, 2005 ; Keniston, Henderson et Meredith, 2010). En ce sens, il est possible que ce processus soit facilement vulnérable aux insultes neurologiques (Beker, Foxe et Molholm, 2018). Cela pourrait expliquer que des déficits d'IMS soient retrouvés dans plusieurs conditions neurodéveloppementales et neuropsychiatriques, telles que la dyslexie (Francisco, Jesse, Groen et McQueen, 2017 ; Hahn, Foxe et Molholm, 2014) et la schizophrénie (Ross et al., 2007). Certaines hypothèses ont également été émises sur le plan génétique. Il a été suggéré que le gène CNTNAP2, possiblement associé au TSA (Alarcon et al., 2008; Arking et al., 2008), puisse être impliqué dans le patron atypique de connectivité neuronale observé chez cette population dans certaines études (Scott-Van Zeeland et al., 2010). En ce sens, chez les adultes ayant un DT, il a été démontré qu'un polymorphisme au niveau du gène CNTNAP2 est associé à une diminution de l'anisotrophie fractionnelle pour plusieurs faisceaux de matière blanche, de même qu'à une diminution de la performance d'intégration audio-visuelle de stimuli langagiers (Ross et al., 2017). Par contre, une étude récente, qui a été effectuée sur un échantillon de taille significative regroupant plusieurs banques de données, suggère que plutôt que la distribution des variantes génétiques observées chez les patients ayant un diagnostic de TSA serait similaire à celle retrouvée dans la population générale, donc que l'implication de ce gène dans la condition neurodéveloppementale n'est pas si claire (Toma et al., 2018). Des changements comportementaux au niveau des performances d'IMS chez la souris ont aussi été observés suite à des modifications génétiques en lien avec un transporteur de la sérotonine, qui serait possiblement impliqué dans le TSA (Siemann et al., 2017). D'un point de vue développemental, sur la base d'un modèle cognitif théorique visant à identifier les mécanismes correspondant le mieux aux données observées chez les individus ayant un TSA, il a été suggéré que la diminution de l'exposition aux expériences multisensorielles en jeune âge puisse affecter la maturation des connexions entre les aires unisensorielles et les régions cérébrales de convergence hétéromodales, et ainsi expliquer les différences observées au niveau des performances d'IMS (Cuppini et al., 2017).

En somme, il semble clair que davantage d'études devront être effectuées au cours des prochaines années afin de préciser ce qui est à l'origine et sous-tend les déficits d'IMS retrouvés au niveau comportemental chez les individus ayant un TSA.

9.2 Objectif 2 : Intégration unisensorielle ou intra-modale chez les individus ayant un TSA

Dans le cadre du présent projet, les performances d'intégration inter-modale et intra-modale ont été comparées entre elles au moyen d'une tâche de détection visuo-tactile. Chez les personnes ayant un DT, il a été démontré que le gain de redondance pour les paires de stimuli visuelles ou tactiles était inférieur à celui observé en condition visuo-tactile. De plus, les résultats obtenus pour les conditions intra-modales ne surpassaient pas les prédictions basées sur le modèle de course, suggérant que l'accélération des temps de réponse dans les conditions unisensorielles peut s'expliquer par un simple effet de facilitation statistique. De la même façon, chez les participants ayant un TSA, l'amélioration des temps de réponse en condition intra-modale ne surpassait pas les prédictions du modèle de course. Toutefois, une différence intéressante a été notée en comparant les résultats entre les groupes. Alors que les paires visuo-tactiles étaient associées à un gain de redondance supérieur aux paires visuelles et tactiles pour le groupe de participants ayant un DT, on a noté que le gain de redondance pour les paires visuo-tactiles et tactiles était équivalent et supérieur à celui obtenu pour les paires visuelles chez les individus ayant un TSA.

Les résultats obtenus auprès du groupe d'individus ayant un DT concordent avec les études antérieures ayant montré un gain de redondance inférieur en condition intra-modale versus inter-modale chez l'humain (Girard et al., 2013; Forster et al., 2002; Laurienti et al., 2006; Miniussi et al., 1998) et l'animal (Gingras et al., 2009), de même qu'une absence de violation du modèle de course pour les paires visuelles (Girard et al., 2013; Murray et al., 2001; Corballis, 1998; Reuter Lorenz et al., 1995; Badzakova-Traikov et al., 2005) et tactiles (Girard et al., 2013; Forster et al., 2002). Cela est aussi compatible avec les données neurophysiologiques qui suggèrent que l'intégration intra- et inter-modale sont sous-tendues par des mécanismes différents. En effet, il a été démontré que la réponse des neurones unisensoriels et multisensoriels du CS diffère significativement lors de la présentation de paires de stimuli intra-modales versus inter-modales. De plus, la désactivation des aires associatives AES et rLS n'a aucun impact sur l'intégration intra-modale, alors que ces régions corticales sont essentielles au processus d'IMS (Alvarado et al., 2007a; b).

La principale hypothèse ayant été émise pour expliquer cette différence est que l'intégration inter-modale permet la combinaison de stimuli sensoriels provenant de sources indépendantes, qui ne sont pas contaminées par le même bruit interne, alors que l'intégration intra-modale reflète davantage la co-variation entre un même type d'information (Ernst et Banks, 2002; Alvarado et al., 2008; Girard et al., 2013; Van Atteveldt et al., 2014). Basé sur les modèles bayésiens, la combinaison de plusieurs stimuli indépendants provenant d'un même événement extérieur permet de réduire davantage l'incertitude associée à l'estimé sensoriel (Ernst et Banks, 2002; Knill et Pouget, 2004; Fetsch et al., 2013).

Basé sur cette hypothèse provenant des études chez les individus ayant un DT, nous pouvons suggérer que les stimuli tactiles sont traités de façon plus indépendante chez les personnes ayant un TSA, ce qui expliquerait que le gain de redondance observé pour les paires tactiles soit équivalent à celui retrouvé pour les conditions inter-modales. En ce sens, une étude récente de Poole et collaborateurs (2018) a comparé la performance d'un groupe individus ayant un TSA à celle de participants contrôles avec un DT lors d'une tâche de discrimination de stimuli visuels et tactiles présentés simultanément à des distracteurs visuels. Ils ont démontré qu'il n'y avait pas d'avantage à ce que les distracteurs soient présentés dans une modalité différente de la cible chez les participants ayant un TSA, c'est-à-dire qu'il n'y avait aucune différence de performance pour les combinaisons cible-distracteurs intra-modales versus inter-modales. Au contraire, la suppression des distracteurs était plus efficace lorsque ceux-ci étaient présentés dans une modalité différente de la cible chez les individus ayant un DT. En lien avec nos résultats, cela suggère la possibilité d'atypies au niveau du traitement d'informations intra-modales chez les individus ayant un TSA, possiblement en lien avec un traitement plus distinct ou indépendant des stimuli unisensoriels.

9.3 Effet de changement de modalité et intégration multisensorielle chez les individus ayant un TSA

Il est connu que l'information sensorielle n'est pas traitée de façon indépendante et que par exemple, lors d'une tâche de détection, la perception d'un stimulus est influencée par ceux qui ont été présentés précédemment (Harrar et al., 2014; Otto et Mamassian, 2012; Gondan, Lange, Rösler et Röder, 2004). Chez les individus ayant un DT, il a été démontré que la réponse à un stimulus sensoriel est plus rapide lorsque celui-ci est précédé d'un influx de même modalité. Au contraire, lorsque deux stimuli présentés de façon successive sont de différentes modalités sensorielles, l'attention doit transférer d'une modalité à l'autre, ce qui engendre une augmentation des temps de réponse. Le coût ou la demande cognitive associé à la transition entre les modalités d'un essai à l'autre est appelé l'effet de changement de modalité (en anglais « modality shift effect »; Harrar et al., 2014). Ce phénomène est susceptible de contribuer au fait que la vitesse de réponse est plus rapide pour les stimuli multisensoriels par rapport aux stimuli unisensoriels simples lors d'une tâche d'IMS (Gondan et al., 2004; Harrar et al., 2014). Pour cette raison, il est primordial de s'assurer que le déficit d'IMS précédemment observé chez les individus ayant un TSA comparativement à ceux avec DT n'est pas expliqué par une différence dans la capacité d'engager et de désengager l'attention par rapport aux différents stimuli sensoriels. Cela est d'autant plus important que plusieurs études ont démontré une difficulté au niveau du désengagement des fonctions attentionnelles chez les individus ayant un TSA (par exemple, Courchesne et al., 1994; Landry et Bryson, 2004; Renner, Klinger et Klinger, 2006; Wainwright-Sharp et Bryson, 1993), bien que cette hypothèse demeure controversée (Boer-Schellekens et al., 2013; Iarocci et Burack, 2004; Leekam, Lopez et Moore, 2000).

Dans ce contexte, l'impact du changement de modalité entre les essais sur les temps de réponse a été mesuré et comparé entre les groupes lors de la tâche de détection de stimuli visuels, tactiles et visuo-tactiles simples. Précisément, nous souhaitions préciser si les différences entre les groupes au niveau de l'IMS pouvaient s'expliquer par la présence d'atypies au niveau de l’effet de changement de modalité chez les participants ayant un TSA. Cette hypothèse a toutefois été infirmée par les résultats obtenus. En effet, nous avons observé un effet de changement de modalité classique pour les modalités visuelles et tactiles chez les individus ayant un TSA, c’est-à-dire des temps de réponse plus rapides pour les essais qui étaient précédés de la présentation d’un stimulus de même modalité. La magnitude de cet effet était similaire pour les deux groupes. Sur la base de ces résultats, il semble peu probable que la diminution de l’IMS observée chez les individus ayant un TSA puisse être expliquée par une atteinte des processus attentionnels nécessaires pour la transition d’une modalité à l’autre lors du traitement multisensoriel.

Ces résultats s’accordent avec ceux obtenus dans le cadre de la tâche de recherche visuelle incluse dans le présent projet. En effet, advenant une difficulté au niveau des processus de désengagement attentionnels, nous nous serions attendus à ce que la vitesse de traitement soit plus lente et qu’elle soit plus affectée par l’augmentation du nombre de distracteurs chez les individus ayant un TSA comparativement aux personnes ayant un DT (Boer-Schellekens et al., 2013). Toutefois, nous avons plutôt obtenu le résultat inverse, soit une plus grande rapidité pour identifier la cible lors de la recherche visuelle pour le groupe d’adultes ayant un TSA, et un impact similaire de la proportion de distracteurs sur la performance entre les groupes. Boer-Schellekens et collaborateurs (2013), qui ont répliqué cette étude, ont également observé une performance légèrement supérieure chez les individus ayant un TSA lors de la tâche de recherche visuelle en l’absence de son, ainsi qu’un effet similaire du nombre de distracteurs sur la performance pour les deux groupes, suggérant une absence de difficulté à désengager, rediriger et engager les processus attentionnels lors de cette tâche perceptuelle (Boer-Schellekens et al., 2013).

9.4 Impact du niveau de saillance sur l’intégration multisensorielle

L’un des objectifs du présent projet était de développer un protocole de recherche permettant d’évaluer l’effet du niveau de saillance des stimuli sur le traitement multisensoriel. À cette fin, nous avons créé un protocole basé sur la localisation de cibles auditives, visuelles et audio-visuelles à travers l’espace frontal (180 degrés), permettant ainsi d’évaluer l’effet de la diminution de saillance associée à l’excentricité sur le gain de redondance pour les paires de stimuli audio-visuels spatialement congruents, ainsi que sur l'effet de capture multisensorielle (ou effet ventriloque) pour les paires de stimuli audio-visuels spatialement incongruents. Ce paradigme a été testé auprès d'une population d'adultes ayant un DT.

En premier lieu, l'impact du degré de saillance associé à l'excentricité sur l'intégration d'informations audio-visuelles congruentes a été évalué. Basé sur le principe de l'efficacité inversée, selon lequel la magnitude de la réponse neuronale à un stimulus bimodal est inversement proportionnelle au niveau d'intensité ou de saillance de ses composantes (Stein et Meredith, 1993), nous avions émis l'hypothèse que le gain de redondance augmenterait avec le niveau d'excentricité. En d'autres termes, nous nous attendions à ce que le gain de redondance soit plus important pour les stimuli présentés en périphérie plutôt qu'en position centrale, car le niveau de saillance des informations auditives et visuelles diminue en périphérie. De façon surprenante, ce n'est pas ce qui a été observé. Le gain de redondance était même supérieur en position centrale. À l'appui de ce résultat, les performances en condition bimodale surpassaient les prédictions du modèle de course pour les conditions de présentation plus centrales, mais pas en périphérie. Ces résultats suggèrent que le principe d'efficacité inversé ne semble pas s'appliquer automatiquement au gain de redondance observé lors d'une tâche de localisation audio-visuelle, et remet en question le fait que ce principe, développé sur la base d'études neurophysiologiques par enregistrement unicellulaire, puisse être directement transposé au comportement.

Bien que le principe d'efficacité inversée ait été objectivé dans différentes études comportementales (Bolognini, Frassinetti, Serino et Làdavas, 2005; Gondan, Niederhaus, Rösler et Röder, 2005; Stein et al., 1988), plusieurs travaux n'ont pas réussi à mettre en évidence l'application de cette règle au niveau du comportement (Diederich et Colonius, 2008; Kim et James, 2010; Ross et al., 2007; Stevenson et al., 2012). Par exemple, une étude dont l'objectif était d'évaluer l'IMS de stimuli langagiers dans un environnement bruyant, a observé que le gain de redondance était maximal pour un ratio signal/bruit intermédiaire, et non pour le plus faible ratio signal/bruit tel que prédit par le principe d'efficacité inversée (Ross et al., 2007). Basé sur ces résultats, il a été suggéré qu'il existe un niveau de saillance minimal jusqu'auquel le principe d'IE peut s'appliquer, celui-ci devant être suffisamment important pour que le système sensoriel puisse s'appuyer sur les informations perçues. Cela pourrait expliquer le fait que le GR semble chuter au degré d'excentricité maximal ([75°]) dans la présente étude.

Le second objectif de cette étude était d'explorer l'impact du niveau de saillance basé sur l'excentricité sur l'effet ventriloque pouvant être observé en présence d'informations spatialement incongruentes. Cette étude a démontré que l'effet ventriloque, soit le fait que la perception d'une paire audio-visuelle dont les composantes ne sont pas positionnées au même endroit est biaisée en faveur du stimulus visuel, s'atténue en fonction de l'augmentation du niveau d'excentricité. Cet effet de capture visuel dépend donc du niveau de saillance de l'information visuelle par rapport à l'information auditive, en ce sens que plus la performance visuelle excède la performance auditive, plus fort est l'effet ventriloque. Ces résultats supportent l'hypothèse qu'en présence d'informations multisensorielles incongruentes, notre système perceptuel combine celles-ci de façon flexible en les pondérant selon leur niveau fiabilité relative, afin d'arriver à la représentation la plus juste possible de l'environnement extérieur (Alais et Burr, 2004).

Une prochaine étape serait d'investiguer comment les résultats à cette tâche se comparent entre les individus ayant un TSA et ceux avec DT. Il n'y a pas d'élément qui suggère que l'impact de la saillance sur le gain de redondance en présence de stimuli spatialement congruents puissent différer entre ces groupes. Par contre, en ce qui concerne le traitement de stimuli spatialement incongruents, une hypothèse est que la capacité à traiter les informations de façon plus indépendante (Stevenson et al., 2014b), de même que la diminution de l'influence de l'expérience antérieure sur le processus de prise de décision par rapport à un influx sensoriel (Pellicano et Burr, 2012) soient susceptibles d'engendrer une réponse différente chez les personnes ayant un TSA.

9.5 Intégration sensorielle et perception de la temporalité chez les individus ayant un TSA

Lorsque deux stimuli sont objectivement présentés au même moment, la probabilité que ceux-ci soient perçus par un observateur comme étant simultanés est très grande. Il est toutefois documenté que malgré un intervalle inter-stimuli allant jusqu'à quelques centaines de millisecondes, tout dépendant du type de stimulus, ceux-ci seront aussi perçus comme étant simultanés pour une certaine proportion des essais. La fenêtre d'IMS fait référence à cet intervalle de temps durant lequel les stimuli présentés ont une forte probabilité d'être combinés ou intégrés, car ils sont perçus comme étant simultanés et donc possiblement comme provenant d'un même événement (Wallace et Stevenson, 2014; Colonius et Diederich, 2004; Hairston, Burdette, Flowers, Wood et Wallace, 2005). L'existence d'une fenêtre temporelle durant laquelle les stimuli peuvent être intégrés est avantageuse d'un point de vue adaptatif, car il existe des différences considérables dans le temps nécessaire à la propagation des influx sensoriels selon la modalité (van eijk, Kohlrausch, Juola et Van de Par, 2008).

Il importe de discuter du fait que de plus en plus d'études suggèrent que les difficultés d'IMS chez les individus ayant un TSA puissent être en lien avec des atypies au niveau de la perception temporelle en contexte multisensoriel. Au niveau du traitement d'informations de nature sociale, il a été observé que les individus ayant un TSA présentent une fenêtre temporelle d'intégration prolongée par rapport aux individus ayant un DT (Noel, Lytle, Cascio et Wallace, 2018; Noel, Stevenson et Wallace, 2018; Woynaroski et al., 2013, mais voir : Grossman, Schneps et Tager-Flusberg, 2009; Irwin et al., 2011), la durée de celle-ci étant négativement corrélée avec l'IMS (Stevenson et al., 2018). Cette fenêtre d'intégration ressemblerait davantage à celle retrouvée chez les jeunes enfants, ces derniers présentant une fenêtre d'intégration plus large et symétrique que les adultes (Lewkowicz, 1996; 2000; Lewkowicz et Ghazanfar, 2009; Lewkowicz et Lickliter, 2013). Comparativement aux personnes avec DT, les individus ayant un TSA présenteraient également un plus faible degré de sensibilité lorsqu'il s'agit de discriminer l'ordre de présentation de paires de syllabes auditives et visuelles (Boer-Schellekens et al., 2013; Stevenson et al., 2014a), et passeraient moins de temps à fixer les paires de stimuli langagiers temporellement congruents qu'incongruents lors d'une tâche de regard préférentiel (Bebko et al., 2006; Grossman, Steinhart, Mitchell et McIlvane, 2015).

Des résultats similaires, mais plus mitigés sont obtenus en lien avec le traitement temporel d'informations non sociales de bas niveau. Quelques études ont observé une fenêtre d'IMS plus étendue pour les stimuli simples audio-visuels (Kwakye, Foss-Feig, Cascio, Stone et Wallace, 2011; Noel et al., 2018) et visuo-tactiles chez les individus ayant un TSA (Noel et al., 2018; Greenfield et al., 2015), de même qu'une diminution de la performance par rapport aux contrôles ayant un DT lorsqu'il s'agit de déterminer l'ordre de présentation de paires de stimuli audio-visuels (Boer-Schellekens et al., 2013). Par contre, d'autres n'ont observé aucune différence entre les individus ayant un TSA et ceux avec DT lors de tâches de discrimination de la synchronie pour des paires de stimuli multisensoriels (Stevenson et al., 2014a; Turi, Karaminis, Pellicano et Burr, 2016; Noel, De Niear, Stevenson, Alais et Wallace, 2017; Keane et al., 2010).

À noter qu'il n'y a pas de consensus à savoir si ces atypies dans le traitement temporel seraient spécifiques aux conditions multisensorielles (Falter, Elliott et Bailey, 2012; Stevenson et al., 2014a) ou plutôt généralisables à l'ensemble du traitement perceptuel et donc également présentes en contexte unisensoriel (Boer-Schellekens et al., 2013; Kwakye et al., 2011).

Bien que les conclusions demeurent mitigées pour l'instant, il semble clair qu'un déficit au niveau de la perception de la temporalité chez les individus ayant un TSA, notamment une augmentation de la fenêtre temporelle d'intégration sensorielle, serait susceptible d'altérer la capacité à intégrer des informations sensorielles. Lorsque la perception des relations temporelles entre les stimuli est moins précise, il y a perte d'un indice permettant de déterminer quelles informations doivent être intégrées ensemble. Il y a alors plus de risque d'intégrer des stimuli qui n'appartiennent pas au même évènement, et de créer un percept pouvant être ambigu (Wallace et Stevenson, 2014). La durée de la fenêtre d'intégration a un effet direct sur l'intégration sensorielle, en ce sens qu'elle détermine en partie quels stimuli seront combinés et lesquels ne le seront pas (Zhou et al., 2018). Chez les individus ayant un DT, il a été démontré que la durée de la fenêtre d'intégration sensorielle était corrélée négativement au degré d'intégration mesuré lors de l'illusion McGurk (Stevenson et al., 2014a; Stevenson et al., 2012).

9.6 Impact du développement sur l'intégration sensorielle chez les individus ayant un TSA

Certaines études suggèrent que les difficultés à intégrer des informations provenant de différentes modalités sensorielles chez les individus ayant un TSA s'atténueraient avec le développement. Par exemple, une amélioration de la performance d'IMS en fonction de l'âge a été observée lors de tâches multisensorielles impliquant des stimuli linguistiques audio-visuels (Foxe et al., 2015; Taylor et al., 2010; mais voir Stevenson et al., 2014c). Par contre, il est important de noter que ces résultats proviennent d'études transversales, et donc que les résultats sont susceptibles d'être influencés par des variables confondantes autres que l'âge des participants. De plus, celles-ci ne permettent pas d'évaluer si, pour un même enfant, les performances d'IMS ont progressé avec le développement.

Dans le cadre du présent projet, une atteinte de l'IMS a été observée chez les adultes ayant un TSA lors d'une tâche de détection de stimuli non sociaux de bas niveau, la distribution des temps de réponse surpassant les prédictions du modèle de course dans une moindre proportion que pour le groupe de participants ayant un DT. Sur la base d'une tâche et d'analyses similaires, une absence complète de violation du modèle de course a été observée chez les enfants et adolescents ayant un TSA, dont l'âge variait entre 7 et 16 ans (Brandwein et al., 2013; 2015). Bien que cela demeure spéculatif, ces résultats pourraient supporter l'hypothèse selon laquelle il existerait un délai dans la maturation des processus d'IMS chez les individus ayant un TSA, pouvant être partiellement compensé une fois à l'âge adulte.

Tel que discuté précédemment, la capacité d'intégrer les informations provenant de différentes modalités sensorielles n'est pas mature au moment de la naissance, et se développe plutôt sur une période de temps prolongée, en lien avec l'expérience sensorielle (Stein, Stanford & Rowland, 2014 pour une revue de la littérature sur le sujet). De ce fait, il est possible que l'exposition à des expériences multisensorielles ou l'entraînement à ce type d'habileté puisse permettre de compenser, du moins jusqu'à un certain point, pour une atteinte précoce au niveau de cette fonction (Stein et al., 2014).

9.7 Implications cliniques

9.7.1 Relation entre l'intégration sensorielle et le phénotype du TSA

L'une des questions qui demeure centrale est comment les difficultés observées au niveau de l'IMS peuvent-elles expliquer les particularités propres au phénotype du TSA. Un modèle explicatif est que les processus sensoriels, incluant l'IMS, représentent les unités de base à partir desquelles sont construites des représentations perceptuelles et cognitives plus complexes qui influenceront les habiletés cognitives de haut niveau (Wallace et Stevenson, 2014). L'IMS peut donc être conceptualisée comme étant l'un des blocs de construction qui permettra d'ériger des structures plus complexes, telles que les fonctions cognitives de haut niveau. Selon ce modèle, une atteinte des processus sensoriels ou multisensoriels primaires aura un effet en cascade sur la hiérarchie des processus de traitement de l'information, et par conséquent perturbera les fonctions cognitives complexes de plus haut niveau, telles que l'attention, le langage, la communication ou les interactions sociales (Bahrick et Todd, 2011; Bahrick, 2010).

Bien que cette hypothèse soit intéressante d'un point de vue théorique, il est important que sa validité soit testée empiriquement, notamment en étudiant les relations qui existent entre la performance aux tâches d'IMS et les fonctions cognitives de plus haut niveau qui sont fréquemment atypiques chez les individus ayant un TSA, telles que les habiletés interpersonnelles ou de communication (Wallace et Stevenson, 2014; Stevenson et al., 2014a). Par exemple, Stevenson et collaborateurs (2017) ont récemment démontré que l'IMS d'information linguistique corrélait positivement avec la capacité de percevoir le langage dans le bruit chez les individus ayant un TSA. Idéalement, ce type d'étude impliquerait le suivi longitudinal d'enfants ayant un TSA, afin d'évaluer si la présence d'atteintes au niveau de l'intégration sensorielle permet de prédire la survenue de difficultés cognitives et socio-communicationnelles chez un même individu (Cascio, Woynaroski, Baranek et Wallace, 2016).

9.7.2 Réadaptation multisensorielle et plasticité cérébrale

L'hypothèse d'une amélioration des capacités d'IMS avec le développement chez les individus ayant un TSA suggère que certaines stratégies pourraient être mises en place pour favoriser l'acquisition de cette habileté. Cette idée est renforcée par le fait que des études chez l'animal et l'humain suggèrent que l'IMS est un processus associé à une plasticité cérébrale importante, dont le développement est tributaire de l'expérience post-natale. Dans ce cadre, il est possible que l'entraînement à des tâches d'apprentissage perceptuelles multisensorielles en jeune âge puisse être utilisé afin d'améliorer les performances d'IMS (Beker et al., 2018).

Chez les adultes ayant un DT, il a été démontré que ce type d'entraînement permet d'améliorer la performance de discrimination de la synchronie temporelle de stimuli multisensoriels, c'est-à-dire de réduire la durée de la fenêtre d'intégration sensorielle (Powers, Hillock et Wallace, 2009; Powers, Hevey et Wallace, 2012), qui est corrélée à l'IMS (Stevenson et al., 2014a). Cette amélioration de la performance comportementale est aussi associée à des modifications au niveau des réseaux cérébraux centrés sur le STSp (Powers et al., 2012), suggérant une augmentation de l'efficacité du traitement et de la connectivité entre le STSp et un réseau de régions incluant les cortex auditifs et visuels. L'efficacité de ce type d'entraînement multisensoriel a aussi été démontré pour d'autres populations cliniques, notamment les enfants atteints de dyslexie (Kujala et al., 2001).

Sur le plan clinique, différents types de thérapie d'intégration sensorielle ont été développés. On note toutefois une grande variabilité dans les méthodes utilisées, et un manque de support empirique par rapport aux interventions qui sont proposées (Case-Smith, Weaver et Fristad, 2015). La thérapie d'intégration sensorielle basée sur les principes développés par Ayres (1972) est celle qui a obtenu le plus de support empirique. Celle-ci est basée sur l'utilisation d'activités proposées par un thérapeutes en fonction des besoins de l'enfant, qui visent à développer les fonctions sensorielles et motrices (ex. le fait de ramper dans un tunnel permet de travailler à la fois la modalité tactile et le mouvement du corps dans l'espace). Des essais cliniques randomisés ont démontré des impacts positifs de cette thérapie sur différents comportements adaptatifs, tels que l'autonomie et les interactions sociales (Schaaf et al., 2014; Pfeiffer, Koenig, Kinnealey, Sheppard et Henderson, 2011; Case-Smith et al., 2015). On note toutefois qu'il existe des divergences profondes par rapport à la terminologie utilisée pour décrire l'IMS entre les cliniciens et les scientifiques. Par exemple, en ergothérapie, on réfère généralement à l'intégration sensorielle comme la capacité d'organiser les différentes informations sensorielles dans le but de faire une tâche. Un objectif en lien avec l'IMS pourrait donc être d'améliorer le niveau d'indépendance lors de l'habillage, qui implique les praxies, de même qu'un traitement visuel et tactile de l'information. Ce type d'approche davantage écologique, n'est généralement pas fondée sur une définition de l'IMS basée sur la neurophysiologie, et le lien avec les performances comportementales à des tâches neurophysiologiques ou leurs corrélats neuronaux demeure imprécis (Cascio et al., 2016).

Davantage d'études nous paraissent donc nécessaires pour supporter empiriquement les thérapies actuellement proposées en cliniques. Celles-ci devraient préconiser une approche interdisciplinaire (Cascio et al., 2016), en incluant des mesures à la fois cliniques et neuroscientifiques (comportementales, neuropsychologiques et neurophysiologiques), de même que tenter de préciser si les impacts observés sur des habiletés de plus haut niveau semblent médiés par les effets de la thérapie sur les fonctions sensorielles plus primaires (Cascio et al., 2016).

9.8 Limites et perspectives futures

L'une des limites de cette étude est que ce ne sont pas les mêmes participants qui ont effectués chacune des tâches. Afin de comparer les résultats entre les études, notamment les performances d'intégration pour les stimuli de nature sociale versus non sociale, il aurait été intéressant que chaque participant complète l'ensemble des tâches proposées. Il aurait ensuite été possible de vérifier si les individus présentant un déficit d'IMS plus marqué pour les expressions émotionnelles le sont également pour le traitement de stimuli simples de bas niveau, renforçant ainsi les conclusions obtenues.

De plus, il aurait pu être pertinent d'inclure une tâche supplémentaire visant à comparer les performances d'IMS pour des stimuli non sociaux présentant un niveau de complexité équivalent à celui de stimuli émotionnels ou langagiers, par exemple des objets de la vie courante. En effet, tel que mentionné précédemment, les expressions émotionnelles se distinguent par leur caractère social, mais également par leur niveau de détail et de complexité important. De ce fait, les stimuli utilisés pour les deux tâches de détection incluses dans ce projet de thèse différaient non seulement sur la base de leur nature sociale versus non sociale, mais également par rapport à leur niveau de complexité. À noter que cela ne remet pas en question les conclusions obtenues, car une atteinte de l'IMS a été observée à la fois pour les stimuli plus complexes de nature sociale et les stimuli non sociaux de bas niveau. Par contre, cela aurait pu être problématique si des déficits n'avaient été obtenus que pour les stimuli émotionnels.

Dans le cadre de l’étude portant sur la détection de stimuli de bas niveau, il a été décidé d’utiliser des stimuli tactiles et visuels, plutôt qu’auditifs et visuels comme c’était le cas pour la tâche de discrimination émotionnelle. Ce choix a été basé sur le fait que les atypies somatosensorielles font partie des symptômes sensoriels les plus fréquemment rapportés par les individus ayant un TSA (Rogers et al., 2003), qu’il est reconnu que le tact joue un rôle important dans le développement social (Myers, 1984; Hertenstein, 2002; Hertenstein et al., 2006; Thye et al., 2018; Dunbar, 2010), et que cette modalité a été très peu étudiée en contexte multisensoriel chez les individus ayant un TSA. Il parait donc justifié et d’un grand intérêt d’avoir inclus la modalité tactile dans cette tâche. Par contre, dans l’optique de comparer les résultats entre les études, il aurait aussi pu être intéressant d’utiliser des stimuli audio-visuels de bas niveau, afin que les modalités sur lesquelles sont basées les deux tâches soient les mêmes.

Outre les éléments précédemment décrits, plusieurs avenues nous semblent cruciales à explorer en lien avec l’intégration sensorielle chez les individus ayant un TSA. D’abord, d’autres études comportementales devront être développées, afin de confirmer les résultats obtenus en ce qui a trait à la comparaison des processus d’intégration intra- et inter-modale. En effet, il s’agit de la première fois que ces processus sont directement comparés chez les personnes ayant un TSA. La possibilité d’un traitement plus indépendant des informations unisensorielles a été soulevée, sur la base de l’interprétation bayésienne des résultats obtenus auprès de populations ayant un DT, mais davantage de support empirique sera nécessaire pour confirmer cette hypothèse. À cette fin, un protocole similaire à celui utilisé dans le présent projet pourrait être répliqué en utilisant des stimuli de types et de modalités différentes, dans l’optique de déterminer si des résultats similaires sont reproduits et d’ainsi renforcer les conclusions proposées.

Ensuite, l’une des hypothèses ayant été émise récemment est que les difficultés d’IMS observées chez les individus ayant un TSA seraient sous-tendues, du moins en partie, par une atteinte au niveau de la perception des indices de temporalité associés au traitement sensoriel. Celle-ci est supportée par certaines études ayant démontré une fenêtre d’IMS prolongée dans cette population (Woynaroski et al., 2013; Stevenson et al., 2014a; Noel et al., 2018; Kwakye et al., 2011; Foss-Feig et al., 2010; Greenfield et al., 2015; mais voir: Poole et al., 2018; Noel et al., 2017; Stevenson et al., 2017). Dans ce contexte, une avenue intéressante serait de répliquer les tâches incluses dans ce projet de thèse en manipulant l'intervalle de temps inter-stimuli entre les paires multisensorielles et unisensorielles, afin d'évaluer l'impact de cette modification de la synchronie entre les stimuli sur l'intégration inter- et intra-modale. De plus, comme nous avons démontré que le déficit d'intégration chez les individus ayant un TSA est spécifique aux conditions inter-modales, il serait pertinent que des protocoles soient développés, afin de comparer directement les performances de discrimination temporelle en contexte unisensoriel et multisensoriel.

D'un point de vue théorique, il semble plausible que certaines atypies propres au phénotype du TSA soient expliquées par un déficit d'IMS. Par contre, très peu d'études ont validé cette hypothèse empiriquement. Dans ce cadre, il importe de préciser les relations qui existent entre la performance aux tâches d'IMS et les fonctions cognitives de plus haut niveau qui sont fréquemment atypiques chez les individus ayant un TSA, telles que les habiletés interpersonnelles ou de communication (Wallace et Stevenson, 2014; Stevenson et al., 2014a). Si possible, ce type d'étude impliquerait le suivi longitudinal d'enfants ayant un TSA, afin d'évaluer si la présence d'atteintes au niveau de l'intégration sensorielle permet de prédire la survenue de difficultés cognitives et socio-communicationnelles chez un même individu (Cascio et al., 2016). Des données génétiques et d'imagerie cérébrale structurale et fonctionnelle pourraient du même coup être recueillies, dans le but de préciser l'étiologie sous-jacente à ces difficultés d'IMS. Un effort particulier devrait être fait pour préciser le lien qui existe entre les performances comportementales, les données en imagerie structurale et fonctionnelle, de même que les génotypes et phénotypes des individus ayant un TSA (Baum et al., 2015).

La mise en place d'un protocole de recherche longitudinal permettrait également de mesurer l'évolution des capacités d'intégration sensorielle en fonction de l'âge, et d'ainsi confirmer ou infirmer l'hypothèse d'une amélioration spontanée de la capacité à intégrer les informations provenant de différentes modalités sensorielles avec l'expérience chez les personnes ayant un TSA. Advenant le fait que les difficultés d'IMS présentes en jeune âge puissent être, du moins partiellement, spontanément compensées en lien avec l'expérience, il en découlerait un impact clinique important, en ce sens que cela augmenterait l'espoir que des thérapies sensorielles puissent être utilisées à des fins de réadaptation (Powers, Hillock-Dunn et Wallace, 2016; Powers et al., 2012). Le cas échéant, davantage d'études seront nécessaires pour supporter empiriquement les thérapies actuellement proposées en cliniques. Tel que mentionné, celles-ci devront préconiser une approche interdisciplinaire (Cascio et al., 2016), en incluant des mesures à la fois cliniques et neuroscientifiques afin d'intégrer davantage ces deux façons très différentes de conceptualiser l'IMS.

9.9 Conclusion générale

Le présent projet de thèse avait pour objectif de permettre une meilleure compréhension du lien qui existe entre le TSA et les performances d'intégration sensorielle. Les résultats obtenus suggèrent que le TSA est associé à une diminution de la capacité à intégrer des informations provenant de différentes modalités sensorielles. Contrairement à ce qui était suggéré dans la littérature, cette atteinte serait présente indépendamment du type de stimuli traités, mais semble un peu plus manifeste pour les informations de nature sociale. Celle-ci semble également spécifique au traitement multisensoriel, dans le contexte où aucun déficit n'a été objectivé lors de l'intégration de stimuli de même modalité chez les individus ayant un TSA. Par ailleurs, la démonstration d'un effet de changement de modalité similaire chez les individus ayant un TSA et ceux avec DT, suggère que ce déficit d'IMS n'est pas sous-tendu par une atteinte des processus attentionnels nécessaires pour la transition d'une modalité à l'autre lors du traitement multisensoriel.

De façon générale, ces résultats ont permis de préciser le tableau actuel en lien avec l'intégration sensorielle et le TSA. Il semble clair que des atypies sont présentes à ce niveau chez les individus ayant un TSA, et méritent d'être approfondies davantage. À cette fin, beaucoup de travail demeure toutefois à entreprendre. Un protocole visant à évaluer l'effet du niveau de saillance des stimuli sur le traitement multisensoriel a été validé dans le cadre de ce projet, et pourra être appliqué auprès de populations d'individus ayant un TSA. Les études futures devront également adresser le développement longitudinal des processus d'IMS, l'impact de la perception temporelle sur le traitement sensoriel, de même que le lien entre les performances d'IMS, les corrélats neuronaux structurels et fonctionnels, la génétique et le phénotype des individus ayant un TSA.

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Curriculum Vitae abrégé (Formation et articles publiés)

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Résidence en Psychiatrie, Université de Montréal	2015 à ce jour
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Publications scientifiques

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