Université de Montréal

Exploration de la reconnaissance des émotions en schizophrénie comorbide

par Karine Paquin

Département de Psychologie, Faculté des Arts et des Sciences

Thèse présentée à la Faculté des Études supérieures en vue de l'obtention du grade de Philosophiæ Doctor (Ph.D.) en Psychologie Recherche et Intervention, option psychologie clinique

Novembre 2017

Résumé

La schizophrénie est un trouble mental complexe qui possède plusieurs étiologies possibles, enracinées à la fois dans la biologie et l'environnement. Ce trouble se manifeste par divers symptômes négatifs et positifs ainsi que de nombreux déficits neurocognitifs et sociocognitifs. Pour compliquer les choses, ce trouble est fortement comorbide avec plusieurs autres, dont l'un des plus répandus est le trouble d'abus de substances. La plupart des recherches se sont concentrées soit sur la neurobiologie de cette maladie, soit sur l'identification de structures cérébrales déficientes et la dérégulation de plusieurs systèmes neurotransmetteurs, ou encore sur la neurocognition en essayant de déceler les déficits dans des domaines tels que l'attention, l'apprentissage et la mémoire, via l'usage de technologies modernes telles que l'imagerie cérébrale fonctionnelle. Cependant, des études plus récentes ont démontré que ce qui caractérise le plus la schizophrénie serait plutôt lié au fonctionnement social. De plus, on peut prédire plus facilement le fonctionnement social lorsque l'on examine les domaines sociocognitifs plutôt que les domaines neurocognitifs. Plus précisément, il a été démontré que la capacité à reconnaître les émotions pouvait avoir une très forte association avec le fonctionnement social et les conséquences du trouble. Cependant, en ce qui concerne la reconnaissance des émotions, aucun consensus n'émerge de la littérature scientifique. Certains affirment que les déficits sociocognitifs sont globaux tandis que d'autres suggèrent qu'ils sont spécifiques à une ou certaines émotions. Pourtant, d'autres ont postulé que les résultats hétérogènes dans la reconnaissance des émotions pourraient être dus non pas aux décifits eux-mêmes, mais plutôt aux méthodes utilisées pour mesurer la reconnaissance des émotions. Il est également important de noter que la plupart des études ont porté uniquement sur les personnes atteintes de schizophrénie seule lorsque les statistiques montrent qu'environ 50% de ces personnes souffrent également d'un

trouble d'abus de substances. Par conséquent, essayer de déterminer les déficits sociocognitifs dans la schizophrénie seule pourrait ne pas permettre de généraliser les résultats.

Notre objectif premier était d'évaluer la reconnaissance des émotions à la fois globale et spécifique, dans la schizophrénie seule et dans la schizophrénie comorbide avec l'abus de substances, en utilisant des avatars virtuels comme outil de mesure (considéré plus naturel) et en examinant l'impact sur le fonctionnement social. Nos résultats pour l'ensemble de l'échantillon composé de personnes atteintes de schizophrénie seule et de schizophrénie et d'abus de substances ont montré une bonne reconnaissance générale des émotions, la tristesse étant la plus facile à identifier et la peur étant la plus difficile. Il y avait aussi des patrons d'interprétation erronés où la peur tendait à être confondue avec la surprise alors que la colère était confondue avec la neutralité. Il y avait une corrélation positive entre l'identification de la tristesse et la fréquence des interactions positives avec la famille et une corrélation négative entre les erreurs d'identification dans la neutralité et la fréquence de l'interaction positive avec la famille. Il est important de noter que les personnes présentant des comorbidités étaient plus à même de reconnaître les émotions négatives comme la colère et la peur, les amenant à interagir davantage avec les autres. Compte tenu de ces résultats paradoxaux, nous avons voulu dans notre deuxième article, mieux comprendre l'impact du trouble d'abus de substances - plus spécifiquement pour la consommation de cannabis qui a été la plus étudiée - sur la schizophrénie afin de donner un sens aux profils sociocognitifs que nous avons trouvé, avec comme objectif principal de trouver des moyens appropriés pour remédier aux déficits. Nous avons exploré différents modèles explicatifs tels que l'hypothèse neuroprotectrice, l'hypothèse de vulnérabilité inférieure et enfin l'hypothèse sociale qui est la plus prometteuse. Enfin, nous avons examiné la littérature pour voir ce qui a été fait le plus souvent en matière de remédiation cognitive en sociocognition. Nous pouvons

conclure qu'il serait préférable de créer un programme de remédiation hybride qui inclurait à la fois l'apprentissage via la pratique - en créant un programme d'entrainement à la reconnaissance des émotions adapté aux déficits individuels avec des avatars virtuels - et l'apprentissage stratégique par la thérapie de groupe pour intégrer les compétences sociales une fois la rééducation de la reconnaissance des émotions acquise.

En conclusion, alors que notre échantillon était petit, sans pouvoir prédictif ou de comparaison avec un groupe témoin, nos résultats soulignent toutefois l'importance de la remédiation ciblée et l'impact de l'abus de substances comorbides sur les profils sociocognitifs en schizophrénie. Nous suggérons que la schizophrénie est plutôt un «trouble social» qu'un trouble «du cerveau» ou «de la pensée». Nous explorons les diverses étiologies sociales telles que les expériences traumatiques de l'enfance, la déviance de la communication parentale et le concept 'd'émotion exprimée' tout en suggérant que la stigmatisation, l'isolement social et les mauvaises interactions sociales pourraient être à l'origine des nombreux dysfonctionnements. Par conséquent, nous suggérons que l'accent de la recherche future soit mis sur les comorbidités en schizophrénie, sur la cognition sociale et sur les impacts sur le fonctionnement social.

Mots clefs: schizophrénie, abus de substances, comorbidité, reconnaissance des émotions, fonctionnement social, avatars virtuels

Abstract

Schizophrenia is a complex mental disorder that has multiple possible aetiologies that are rooted in both biology and environment. It is manifested through various negative and positive symptoms as well as many neurocognitive and sociocognitive deficits. To complicate matters, this disorder is highly comorbid with several others, with one of the most prevalent one being substance use disorder. Most research in the past has focused on either the neurobiology of this illness, identifying deficient brain structures and dysregulation in several neurotransmitter systems or on neurocognition trying to decipher the deficits in domains like attention, learning and memory through the use of modern technology such as functioning imaging. However, more recent studies have shown that what could very well be the hallmark of schizophrenia, is rather more linked to social functioning. Furthermore, social functioning can be more readily predicted when we examine sociocognitive domains rather than neurocognitive ones. More specifically, it has been shown that emotion recognition ability could have a very strong association with social functioning and outcomes. However, where emotion recognition is concerned, there is no clear consensus in the literature. Some argue the deficits are global while others suggest that it is emotion specific. Yet others have posited that perhaps, the heterogeneous findings in emotion recognition could be due not to the deficits themselves to rather to the methods used to measure emotion recognition. Also of importance, is the fact that most studies will solely focus on individuals that have schizophrenia alone when statistics show that around 50% of these individuals also suffer from substance use disorder. Therefore, trying to ascertain sociocognitive deficits in schizophrenia alone might not be optimal to generalize the findings.

As such, it was our first objective to assess emotion recognition both global and specific, in schizophrenia alone and in comorbid schizophrenia and substance use disorder, using virtual

avatars as a more naturalistic measurement tool and also examining the impact of social functioning. Our results for the whole sample comprised of individuals with schizophrenia alone and schizophrenia and substance use disorder, showed good overall emotion recognition with sadness being the easiest to identify and fear the hardest. There were also specific misinterpretation patterns where fear tended to be misidentified as surprise while anger was perceived as neutrality. There was a positive correlation between identification sadness and frequency of positive interaction with family and a negative one between identification errors in neutrality and frequency of positive interaction with family. Importantly, individual with comorbid presentations were better at recognizing negative emotions like anger and fear leading to more interactions with others. Given those paradoxical results, we wanted in our second article, to better understand the impact of substance use disorder – more specifically for cannabis use which has been studied the most – on schizophrenia in order to make sense of the sociocognitive profiles we found, with the main objective of finding appropriate ways to remediate the deficits. We explored various explanatory models such as the neuroprotective hypothesis, the lower vulnerability hypothesis and finally the social hypothesis which is the one that holds the most promise. Finally, we examined the literature to see what was done the most often with regard to cognitive remediation in sociocognition. We can conclude that it would be preferable to create a hybrid remediation program that would include both practice learning – by creating a training program for emotion recognition tailor-fitted to individual deficits with virtual avatars – and strategy learning through group therapy to integrate social skills following retraining of emotion recognition.

To conclude, while our sample was small and did not allow us any predictive power or comparison with a control group, our results highlight the importance of targeted remediation and

the impact of comorbid substance use disorder on sociocognitive profiles. We suggest that schizophrenia is rather a "social disorder" than it is a "brain" or "thought disorder". We explore the various social aetiologies such as traumatic childhood experiences, communication deviance and expressed emotion for the disorder while proposing that stigmatisation, social isolation and overall poor social interactions could be at the source of the many dysfunctions found in the disorder. Therefore, we suggest that the focus of future research should be on both comorbidities in schizophrenia, social cognition and social functioning outcomes.

Key words: schizophrenia, substance use disorder, comorbidity, emotion recognition, social functioning, virtual avatars

Table of content

List of tables

Table 4. Studies that include both explicit and implicit methodologies

List of figures/images

Chapter 2 – Article #1

Chapter 3 – Book chapter (Article #2)

List of abbreviations

Δ^9-THC – delta-9-tetrahydrocannabinol

APT - Attention Process Training

BPRS-E - Brief Psychiatric Rating Scale-Extended

CHUM - Centre Hospitalier de l'Université de Montréal

CRT - Cognitive Remediation Therapy

DSM-IV - Diagnostic and Statistical Manual of Mental Disorders, 4th edition

ER - Emotion Recognition

FESFS - First Episode Social Functioning Scale

fMRI - Functional Magnetic Resonance Imaging

F-SCIT - Family-Social Cognition and Interaction Training

IUSMM - Institut Universitaire en Santé Mental de Montréal

MATRICS - Measurement And Treatment Research to Improve Cognition in Schizophrenia

NEAR - Neuropsychological Educational Approach to Remediation

PST - Problem Solving Training

REC - Cognition-Emotional Rehabilitation

SCET - Social Cognition Enhancement Training

SCID - Structured Clinical Interview for DSM-IV

SCIT - Social Cognition and Interaction Training

SPSS - Statistical Package for the Social Sciences

SRT - Standard Rehabilitation Training

SST - Social Skills Training

SUD - Substance Use Disorder

SZ+Can - Schizophrenia patients smoking cannabis

SZ - Schizophrenia patients not smoking cannabis

TAD - Targeted Auditory Discriminatino

TAR - Training of Affect Recognition

TAU - Treatment As Usual

TOM - Theory of Mind

VOC - Vocational Program

VR - Virtual Reality

WT - Work Therapy

Remerciements

À l'aube de l'achèvement de mon parcours doctoral qui aura duré 7 ans, j'ai peine à trouver les mots pour décrire comment je me sens. Mon cheminement fut certes fort différent de ce à quoi je m'attendais, comme c'est surement le cas pour plusieurs. Reste que ma première année doctorale fut remplie de défis, mais aussi de difficiles embuches qui ont fait en sorte que j'ai remis l'idée d'un doctorat en psychologie en question. C'est grâce à certaines personnes que je citerai plus bas, que j'ai pris la décision de poursuivre mes études malgré ceux qui voulaient me mettre des bâtons dans les roues. Je retire une grande fierté d'avoir su persévérer et de pouvoir aujourd'hui encourager d'autres étudiants à faire de même, malgré les difficultés rencontrées.

À Tania, merci de m'avoir supporté dès le premier jour et de m'avoir offert des opportunités en or au niveau de la recherche pour m'aider dans ma carrière. Je te remercie d'avoir cru en moi et de m'avoir encouragé à ne pas lâcher! Mais par-dessus tout, je te remercie d'avoir pris une chance en me "protégeant" et en prenant mon bord durant ma première année d'étude, et ce, sans vraiment me connaître. Je suis consciente que c'était un risque, ne sachant pas encore de quoi j'étais capable ou ce que j'allais accomplir ou pas. Je n'oublierai pas de ci tôt ce geste, qui t'a couté en plus, et qui m'a permis de poursuivre mes études. Je te suis éternellement reconnaissante et je crois que, même si je veux rendre honneur à ton dévouement et ton implication, ces quelques lignes de remerciements de thèse ne sauraient résumer cette reconnaissance.

À Stéphane, tu es un codirecteur hors pair! Le superviseur sérieux qui offre des directives claires et qui pose les bonnes questions au bon moment et à d'autres instants, le 'papa réconfortant' dont on a tant besoin durant ce cheminement, même si on n'ose pas toujours se l'avouer. Tu as toujours su bien doser entre les deux et je te remercie d'avoir été là pour moi du début à la fin.

À Sophie, je peux difficilement exprimer l'impact que tu as eu sur mon parcours. Sans toi,

et la confiance en moi et mes capacités cliniques qui semblait tout simplement inébranlable, je n'aurais sans doute pas été jusqu'au bout. Je ne suis pas la seule que tu aies 'sauvée', sache qu'une grosse partie du crédit te revient. Ne change surtout pas, nous avons vraiment besoin de gens comme toi pour nous aider à passer au travers cette étape pas toujours évidente!

À Kevin, tu m'as non seulement épaulé durant tout ce processus, mais tu es devenu un de mes amis les plus chers. Merci de m'avoir permis de m'appuyer sur toi quand j'en avais besoin, merci d'avoir enduré mes crises de stress et d'avoir continué à me faire rire même quand j'avais juste envie de pleurer. Ton amitié me tient à coeur par-dessus tout.

To Rick, my stats guru and my old teacher whom I shall never forget. You are still to this day, the only one that seems to understand anything I say when it is stats related! Thanks for your patience and your guidance throughout the years.

To my friend Leigh, thanks for your input, editing and support on my thesis and for pretty much everything else too. You have such a prodound sense of empathy that it makes every interaction with you a delight. Thanks for being who you are.

À Nathalie Langelier et toutes les infirmières du 404 à Louis H, un gros merci pour votre dévotion envers mon projet et l'attention que vous avez portée aux petits détails. C'est grâce à vous que mon recrutement à l'unité fut grandement amélioré.

Aussi, je voudrais prendre le temps de remercier tous les participants qui ont voulu m'aider dans mon projet de thèse en participant à cette étude.

Finalement, merci à mon merveilleux mari. J’aurais sans doute besoin de plusieurs pages pour décrire l’amour et la force que tu me donnes au quotidien. Le fait que tu crois en moi de façon aussi inébranlable ne peut que me donner la force de poursuivre. Merci d’avoir su endurer mes hauts et mes bas au travers les années. Merci d’avoir fait autant de sacrifice pour soutenir mon rêve et d’avoir parfois dû mettre les tiens de côté. Mais merci par-dessus tout pour ta

patience au quotidien et pour m'avoir donné une famille dont je suis si fière. Je t'aime et t'aimerai toujours.

À mon fils Lucas, lumière de ma vie, merci mon grand garçon de m'avoir permis de reprendre confiance en moi grâce à ton amour inconditionnel et ta joie de vivre.

À François

"It is the greatest gift we have: to bear their pain without breaking.
And it comes from the most human part of us: hope."

Introduction to the problem

Schizophrenia is a serious mental disorder that has many negative effects on the lives of individuals who are suffering from it. It is multifaceted, its causes being rooted in both biology and environmental conditions. It presents with a myriad of symptoms and deficits that are sometimes misunderstood. The stigma surrounding this disorder is as great as the accompanying severe social functioning difficulties. Individuals are often described as standing out because of behavioral quirks and social oddness, like having trouble starting a conversation, revealing too much about themselves to strangers, not understanding jokes or social rules, or even talking to themselves. The general public often has limited knowledge of these symptoms, which can lead to feelings of discomfort and fear when confronting these individuals. As with any type of disorder, being socially isolated will often worsen the condition. It is currently believed that the only hope these individuals have of a normal life is to take medication. However, studies in the past few decades have demonstrated that there are many targets – most of them social in nature – other than physically obvious symptoms to treat, and multiple interventions have proven useful in helping people in their recovery. These interventions may bring about more sustainable benefits than what medication alone is able to do and could even be implemented as prevention tools. Nevertheless, research in schizophrenia tends to be very focused, aiming to identify 'markers' or the hallmarks of the disorder, excluding from studies individuals with more complex clinical presentation. Yet, it is well known that schizophrenia is not a lone disorder and that it most often is accompanied by comorbid disorders such as social anxiety, depression, or substance abuse disorder, further worsening the prognosis and impeding the person's recovery. It is important to identify the impact such comorbidities can have on the person with schizophrenia's functioning. A more comprehensive approach to understanding and treating individuals with schizophrenia and comorbid presentation could improve the personal and social recovery of those concerned.

Literature review

Schizophrenia: definitions and causes

The term "schizophrenia" was coined back in 1908 by Bleuler who described the disorder as a splitting of the psychic functions, where there was a dissociation between thought processes, emotions, and behaviors, all of which lead to manifestations like hallucinations, delusions, and social withdrawal (Kyziridis, 2005). Although our understanding of this disorder has grown over the years, these symptoms and their social impact are still the target of both research projects and treatments. Schizophrenia is however a very heterogeneous disorder, with individuals presenting severe psychotic symptoms (hallucinations and delusions), but others presenting more cognitive deficits and negative symptoms (e.g. lack of motivation, poor emotional expression). The advent of the DSM-5 has brought the concern back to the forefront of discussions, highlighting limitations that result from trying to put individuals, who could be presenting with a wide range of severity and type of symptoms, in the same box. Furthermore, it is important to understand that, unfortunately, some individuals will receive a misdiagnosis of a psychotic disorder because of the presence of psychotic symptoms, although their symptoms do not alter their functioning or cause any kind of distress. On the one hand, it is not rare to hear members of the general population declare that they have heard voices in the past – van Os (2003) have documented that between 9 and 25 % of the general population experience psychotic symptoms, whereas only 1 to 2% will need psychiatric treatment. Studies support the notion of a continuum in the experience of psychotic symptoms, with only a select few experiencing severe distress and dysfunction. Auditory hallucinations, for example, can be heard by some individuals, sometimes daily, without the associated distress we would expect them to experience. In fact, these individuals differ from others because they report their voices as being positive and supportive experiences in their lives while those who suffer from auditory hallucinations in the context of schizophrenia,

will report that the voices they hear are often negative and threatening, causing significant negative impact on their daily functioning (Honig et al., 1998), high levels of distress (Birchwood & Chadwick, 1997), depression (Birchwood et al., 2004), and increasing the risks of suicide (Kjelby et al., 2015).

Schizophrenia and pharmaceutical treatments

Schizophrenia is a complex mental disorder affecting thinking, judgement, and reality assessment. It consists of positive symptoms, and, for some, negative and cognitive symptoms. Positive symptoms, such as visual or auditory hallucinations and delusions are the first criteria (mandatory to receive a diagnosis) of the disorder. There are also more discrete demonstrations – the negative symptoms – such as flat affect, social withdrawal, and the various cognitive symptoms or deficits, both neuro- and sociocognitive (APA, 2000). Although positive symptoms, such as strong and negative-content auditory hallucinations or obsessive persecutory delusions, can make daily living difficult, it is the negative and cognitive symptoms that have the strongest and most lasting impact on functioning. For years, the main objective of pharmaceutical treatment was to reduce positive symptoms resulting in antipsychotic medication that not only did not improve negative symptoms or cognitive deficits but that often made them worse. Furthermore, the side-effects of most antipsychotics are severe, in terms of their impact on the person's physical health (e.g. obesity, Parkinson's disease, sexual disorders) (Lacro, Dunn, Dolder, Leckband, & Jeste, 2002; Rummel-Kluge et al., 2010). As such, it is not surprising that adherence rates to medication are poor in schizophrenia, and medication cessation is the leading cause of psychotic relapses. All of the aforementioned reasons (more negative symptoms, more cognitive deficits, severe side-effects) as well as suboptimal efficacy of antipsychotic medication (close to 60% true benefit, with close to 30% of individuals suffering from treatment-resistant

schizophrenia, (Lally & MacCabe, 2015)), explain the poor adherence in schizophrenia. Treatments are needed that do not only focus on positive symptoms but that aim at improving other aspects of schizophrenia, such as cognitive deficits that are intimately linked with social functioning. In fact, our understanding of schizophrenia is more multi-factorial today, thanks to more complete and nuanced models to explain the causes of the disorder and its clinical presentation, thus allowing the development of useful treatment targets. However, the social impact of having cognitive deficits and its repercussion on the aetiology, course and remission from the disorder remains absent from most explanatory models.

The diathesis stress model and the various aetiologies

Schizophrenia has been understood as the interaction of genetic or biological predispositions and environmental stressors for some time now (Zubin & Spring, 1977). According to this model, individuals have various biological, genetic or neurological vulnerabilities that can lead to psychotic symptoms when stressors, such as trauma, substance abuse, or constant daily stressors (bullying, racism) are present. It also hints at the fact that certain individuals would be more sensitive than others to such stressors, also known as 'heightened reactivity to stressors' (Walker & Diforio, 1997). Not only does this heightened fragility to stress have an impact of the neurobiology of the individuals by having adverse effects on the dopamine system and cortisol release (dysregulation of the HPA axis) in childhood, but those dysfunctions remain in adulthood as well, potentially contributing to the development of severe mental disorders such as schizophrenia. Furthermore those neurobiological abnormalities, could lead to neurocognitive and sociocognitive degeneration and ultimately, impairments (Read, Perry, Moskowitz, & Connolly, 2001). This segment on the link between trauma and neuronal development is known as the Traumagenic Neurodevelopmental model and has been cited as a

satisfactory explanation of the vulnerability part of the diathesis stress model. Of great importance, is that studies have shown that the aforementioned abnormalities are reversible through psychotherapy and cognitive retraining (Brenner, 2000; Fuchs, 2004).

Trauma in childhood. Child abuse, including physical and sexual abuse as well as neglect, has been shown to play a causal role in the manifestation of various psychiatric complications, some which can lead to the onset of adult disorders such as depression, anxiety and substance abuse. Having been a victim of such abuse is also linked with the severity of the presenting problem in severe mental disorders like schizophrenia. For instance, it has been associated with earlier admission in hospital which is associated with earlier onset of the disorder, longer and more frequent hospitalizations, increase risk of self-arm and suicidality, presenting with more severe symptomatology as well as showing greater levels of social isolation (see Read, Van Os, Morrison, & Ross, 2005, for review), the latter being known to be one of the factors that has the most devastating impact on schizophrenia (as shown by various animal models such as Jiang, Rompala, Zhang, Cowell, & Nakazawa, 2013; Malone, Kearn, Chongue, Mackie, & Taylor, 2008).

Communication deviance and expressed emotion. On the one hand, communication deviance is defined as 'the degree to which a relative's communication lacks clarity and causes disruptions in the focus of the attention' during social interactions (Singer & Wynne, 1965). It manifests through the use of odd terms and unsound reasoning and it has been noted in both patients with schizophrenia and their parents. This ineffective style of communication has been suggested as leading to confusion, distress and dysfunctional communication (Wynne, Singer, & Toohey, 1976) which inadvertently, creates a stressful environment. Moreover, constant exposure

to this type of communication dysfunction could lead to deficits in attention (a neurocognitive domain) and difficulties in processing psychosocial information (a sociocognitive domain).

On the other hand, expressed emotion is described as 'critical, hostile or emotionally overinvolved attitudes' by the relatives of individuals suffering from severe mental disorders (Kavanagh, 1992). It is also associated with poorer course of illness as well as poorer outcome in severe mental disorders like schizophrenia (Kymalainen, Weisman, Rosales, & Armesto, 2006). Communication deviance is potentially an underlying factor that could affect emotion expression as studies have shown positive correlations between the two constructs (Kymalainen et al., 2006; Miklowitz et al., 1986). More concretely, family members that are high in both communication deviance and expressed emotions, will tend to address siblings using comments that are critical and intrusive, and express them in distorted and over-involved manners, causing the equivalent of a traumatic emotional experience for the person interacting with them. Family interactions being everyone's primary source of social interactions, it is easy to imagine the severe impact such hostile communication style could have on the social functioning for these individuals. Moreover, there is consensus in the literature that exposure to psychosocial stress can exacerbate symptoms when the disorder is already present, and that it could even trigger relapses after remission (Walker & Diforio, 1997).

The stress-vulnerability model was modified in 1982 by Liberman (Liberman, 1982) to include the concept of protective factors, whereby someone with strong family and social support, good social skills, a good self-esteem, good stress-management strategies and a large and efficacious inventory of coping strategies when symptoms arise, and who responds well and is adherent to his medication, is much less likely to experience a symptomatic relapse when faced

with stressors. These protective factors are all modifiable elements that can be learned, developed and worked on. As such, social skills, and the resulting social functioning, are important targets of treatment, acting as protective factors against the inevitable stressors that are encountered. Studies in the past decade on social skills have revealed how intrinsically related they are to cognitive deficits. Nevertheless, these deficits both neuro and sociocognitive in nature, have yet to be integrated in this model, though more and more studies have highlighted their link with functional outcome and its impact of recovery from the disorder.

Schizophrenia and cognitive deficits

Individuals suffering from schizophrenia have been shown to have important neurocognitive deficits, ranging from difficulties in concentration to poor attention, memory and executive functioning (Zubin & Spring, 1977). Socio-cognitive deficits have also been documented, namely difficulties in interpersonal relations due to misunderstanding of facial cues, emotional content, others' intentions, or even one's own emotions (Walker & Diforio, 1997). Around 80% of individuals suffering from schizophrenia will have some neuro- or socio-cognitive deficits over the course of the disorder and sometimes prior to its onset (Liberman, 1982). Although both neurocognition and sociocognition predict the functioning of individuals with schizophrenia, the latter has recently accumulated evidence as being a stronger predictor (Meesters et al., 2010; Nuechterlein et al., 2008; Raffard, Gely-Nargeot, Capdevielle, Bayard, & Boulenger, 2009), or at least an important mediator (Lecardeur et al., 2009; Lysaker et al., 2005; Wolwer & Frommann, 2011) of social functioning and quality of life in schizophrenia. As such, treatments focusing on sociocognitive deficits might have greater impacts on functioning, above and beyond the treatment of negative or positive symptoms, as well as improving upon neurocognitive deficits (Green, 1996, Lesh et al., 2011).

Schizophrenia and neurocognitive deficits

Cognitive dysfunctions are considered to be a core feature of schizophrenia, being strongly correlated with poor functional outcome (Goldberg, David, & Gold, 2011) as well as being a better predictors of general outcome and rehabilitation than the presence or absence of psychotic symptoms (Brune, Abdel-Hamid, Lehmakamper, & Sonntag, 2007; Roncone et al., 2004). It has been reported that around 70% of individuals suffering from schizophrenia have neurocognitive deficits (Addington, Saeedi, & Addington, 2006). Importantly, some even suggest that the deficits could be present even before the clinical onset of the disorder, making it an interesting target for prevention (Bourque et al., 2012). There are six major domains of neurocognitive symptoms, namely speed of processing, attention/vigilance, working memory, verbal learning, reasoning, and problem solving (Penk et al., 2000). Each of these have been linked with specific functional outcomes. For instance, data gathered from functional imaging studies have demonstrated that schizophrenia is characterized by impaired fronto-parietal, fronto-striatal, fronto-limbic, and frontal-temporal networks, with most of these impairments linked with deficits in working memory, executive functions, and episodic memory (Palmer, Heaton, Kuck, & Braff, 1997). Despite the obvious importance and contribution of neurocognitive deficits on the course of the disorder, over the last decade, many researchers have put forward the idea that deficits in social cognition specifically, rather than solely in neurocognition, might explain a large portion of the poor social functioning found in individuals with schizophrenia (M. Kurtz, 2005).

Schizophrenia and socio-cognitive deficits

Social cognition is defined as all the processes used to collect, interpret, and process social information in order to properly interact on an interpersonal level (MATRICS; Nuechterlein et al., 2008). It can typically be divided into five different domains, namely Theory

of Mind (recognizing mental states in others), social knowledge (knowing and being able to apply social rules given certain social situations), attribution style (blaming oneself or giving others negative intentions), emotion regulation (how one copes with strong emotions), and last but not least, emotion recognition (one's ability to recognize facial emotions) (Minzenberg, Laird, Thelen, Carter, & Glahn, 2009). Over the past decades, researchers have suggested that social cognition deficits could explain many, if not most, of the social dysfunctions and poor social functioning found in schizophrenia (Keefe et al., 2011; M. M. Kurtz, Seltzer, Shagan, Thime, & Wexler, 2007; Revheim et al., 2006). Importantly, while Theory of Mind has been a popular research topic in the last few years, it has been suggested that one of the most useful social cognitive skills in social situations is one's ability to recognize others' facial emotions (i.e.: emotion recognition (M. F. Green, 1996; Lesh, Niendam, Minzenberg, & Carter, 2011)). Indeed, when attempting social interactions, assessing the other person's reaction to us is something that can be accomplished by examining facial features even before actively engaging in conversation, making emotion recognition the primary source of evaluation of potential success or failure of the upcoming interaction.

Emotion Recognition in schizophrenia

Emotion recognition might be central to social functioning in schizophrenia because it has been associated with difficulties in interpersonal interactions and fulfilment of social roles (Pinkham et al., 2014). Numerous studies have shown that people diagnosed with schizophrenia often have a deficit in recognizing facial expressions in others. This deficit in emotion recognition includes both difficulties in identifying the proper emotion as well as discriminating between different emotions (Couture, Penn, & Roberts, 2006; Pinkham et al., 2014). It has been posited that, according to the universality hypothesis, there are six basic emotions that are

recognizable across cultures (see review by Couture et al., 2006), namely joy, surprise, sadness, disgust, fear, and anger. Because discrimination between emotions has been shown to be an issue with this population, recent research has included neutrality as the seventh 'emotion' of interest. A closer look at emotion recognition studies reveals that little information exists regarding the specificity of the emotions involved in the deficits (Corrigan & Penn, 2001, p. 3). While some will argue that emotion recognition deficits are general (i.e.: attributions; Mancuso, Horan, Kern, & Green, 2011) and not emotion specific, the literature brings about more questions than answers given the lack of consensus across studies. For instance, some results show that the deficit is worse in the case of deciphering negative emotions (P. Ekman, Sorenson, & Friesen, 1969; though this is an ongoing debate amonsgt researchers and academics). Others state that their results demonstrate that more ambiguous and subtle emotions (such a neutrality) are harder to detect by individuals with schizophrenia (Addington et al., 2006). Conversely, others have reported that emotion recognition deficits in schizophrenia are only found with positive emotions (Silver, Bilker, & Goodman, 2009). To shed some light on the intricacies of these deficits, some studies have investigated the underlying mechanisms related to emotion recognition. For instance, results from a study on individuals with schizophrenia and their unaffected biological siblings shows that on facial emotion recognitions task, even though siblings performed better than their affected family member, they still performed significantly worse than the control group (Amminger et al., 2012; Bediou et al., 2007; Comparelli, Corigliano, De Carolis, Mancinelli, Trovini, Ottavi, & Girardi, 2013; van't Wout et al., 2007). This is reported as potential evidence that emotion recognition deficits could be a heritable endophenotype in schizophrenia. Impairments in executive functions, memory, and attention have been investigated as potential culprits for difficulties in emotion recognition (Edwards, Jackson, & Pattison, 2002; Mandal, Pandey, & Prasad, 1998; Morrison, Bellack, & Mueser, 1988; Penn, Combs, & Mohamed, 2001)

and many studies have also tried to improve upon those neurocognitive functions in schizophrenia (Tsoi et al., 2008). However, none of these neurocognitive deficits has been linked to emotion recognition (Combs et al., 2007; Freeman et al., 2005; Garety & Freeman, 1999). A study by Mueser and colleagues (Tsoi et al., 2008) reports that, compared to controls, individuals with chronic schizophrenia had poorer performances on emotion recognition tasks and that those performances were linked to poor social competence such as the inability to maintain a conversation for 3 to 5 minutes. Similarly, difficulty in recognizing facial expressions predicts struggles in forming interpersonal relationships (Erol, Mete, Sonmez, & Unal, 2010) and is associated with lower global functioning and worse adaptive behaviours such as social skills. Therefore, some have suggested that emotion recognition in schizophrenia is not necessarily associated with a specific social skill but that it is rather an important predictor of overall social functioning (Nuechterlein et al., 2008), further highlighting the importance of establishing clear emotion recognition patterns for this population.

Schizophrenia, social skills, and social functioning

It is well recognized that individuals suffering from schizophrenia have poor interpersonal functioning and limited social skills and that those deficits are not only relatively stable over time but they are believed to be more pronounced in schizophrenia than in any other psychiatric disorder (see Paquin, Wilson, Cellard, Lecomte, & Potvin, 2014, for review). To reiterate, those limitations have severe negative consequences on the outcome of the disorder as well as on the quality of life of individuals suffering from schizophrenia. Even in the time of Bleuler, one's capacity to have a job or to take care of themselves outside the hospital setting was considered a good criterion to evaluate the severity of the disorder and the ability to recover from its devastating effects. It is therefore crucial to properly evaluate the social cognitive deficits that

could impact social outcomes, but also to be thorough in measuring the said outcomes.

Social functioning includes a variety of areas like one's capacity to engage in positive and meaningful relationships (i.e., friends and family), being able to care for oneself by cooking, cleaning, and maintaining proper hygiene without forgetting the very important areas of school and work (Mancuso et al., 2011). Over the years, several measurement tools have been used, few of which have included multiple aspects of social life such as work or school, although they are of key importance in the lives and the recovery of individuals suffering from schizophrenia (Poole, Tobias, & Vinogradov, 2000). Given that the disorder usually declares itself around the ages of 16 to 30 (Khoury, Lecomte, Comtois, & Nicole, 2013; Mueser & Bellack, 1998), it is not surprising that it can affects individuals' capacities to develop social networks, work and study skills, making assessment of deficits linked to precise social outcomes even more critical. Importantly, what is usually assessed in the context of social functioning is one's daily life behaviors (for e.g.: is the person working, taking care of his belongings, maintaining proper hygiene). However, these measures do not take into account the individuals' perception of his abilities, which could have significant impact of their capacities to use the skills they might have (Lecomte, Corbière, & Briand, 2008; Lin, Wood, & Yung, 2013). Of even greater importance is the crucial point that having comorbid mental health presentations always makes for a more complex picture. This is not different in schizophrenia; having a comorbid disorder can significantly impact social functioning.

Furthermore, schizophrenia is one of the most highly stigmatized mental disorder. Individuals suffering from schizophrenia are feared and misunderstood which often leads them to having very limited amounts of positive social interactions, if any at all besides perhaps with

family members admitting they have proper family support systems. This in turn leads to severe social isolation that could have a significant impact on the course of the disorder and on the recovery potential. However, deciphering when and where social difficulties interact with the presentation or course of the disorder is no easy matter. It could be argued that being socially isolated leads to difficulties in social interactions and therefore cause individuals to loose their ability to properly recognize facial expressions due to the lack of social interactions. Conversely, it could be that deficits in emotion recognition leads to constant social mistakes due to inappropriate evaluations of the reactions and emotions of others, causing a sense of failure, validating a sense of inadequacy already felt from the stigmas and resulting in individuals shying away from social interactions altogether. This is yet another reason why evaluation of sociocognition in schizophrenia and dual diagnosis schizophrenia is of paramount importance.

Schizophrenia and comorbid substance use

As mentioned previously, individuals with schizophrenia often present with comorbid manifestations. Among the most prevalent disorders, substance use disorder is found in around 50% of individuals diagnosed with schizophrenia (Lecomte et al., 2014; Regier et al., 1990). This statistic should not be taken lightly as having this comorbid presentation increases the risks of psychiatric relapses, hospitalizations (Drake et al, 1989), and rates of homelessness and unemployment (Drake et al., 1989, Soyka et al., 1993) as well as severely worsening social adjustment (Salyers et al., 2001). All these factors have important economic and societal repercussions. On their own, substance use disorders are associated with severe negative consequences such as psychotic relapses (Saha, Chant, Welham, & McGrath, 2005), poor adherence to medication, suicide, depression, issues with housing as well as finding and maintaining a job, and several legal and health problems (Lecomte et al., 2014). Among the most

commonly used drugs in comorbid schizophrenia are cannabis, stimulants, alcohol and nicotine (Winklbaur, Ebner, Sachs, Thau, & Fischer, 2006). Individuals with schizophrenia smoke cannabis 3 to 6 times more than the general population. Cannabis smoking has been associated with earlier age of onset of the disorder and a 2 to 3 fold increase in psychotic symptoms and schizophrenia-spectrum diagnoses (Beck, Emery and Greenburg in Wells et al., 1995). Research has also demonstrated that cannabis smoking in non-psychotic individuals has severe negative impact on the neurocognitive domains of working memory, executive functions, attention, and episodic memory (Agosti, Nunes, & Levin, 2002). Chronic cannabis smoking in normal individuals will produce neuro-functional alterations mirroring the neurophysiologic dysfunctions seen in schizophrenia (Bourque et al., 2013), causing researchers to hypothesize that the negative impact of cannabis smoking in schizophrenia could be tenfold. Nevertheless, it is not yet clear what effects substance use disorders have on the socio-cognitive deficits of individuals with comorbid schizophrenia or even if specific socio-cognitive profiles are more likely to be present in those with comorbid substance use disorder and psychotic disorders. A pilot functional imaging study comparing emotion recognition in healthy controls versus individuals with either schizophrenia alone or schizophrenia and comorbid substance use disorder showed that while positive emotion recall in schizophrenia was poorer than in controls, there were no significant differences between controls and those with schizophrenia and comorbid substance abuse (Potvin, Mancini-Marlë, Fahim, Mensour, & Stip, 2007). Those seemingly contradicting results have been labelled the “paradox of the dually diagnosed” (Moore et al., 2007; Myles, Newall, Nielssen, & Large, 2012) where individuals with comorbid substance use disorder are judged to be both behaviourally more disorganized while simultaneously being more socially competent, at least in some aspects. Moreover, conflicting results have been documented in the literature with some finding that having substance use disorder and schizophrenia leads to exacerbation of

cognitive deficits (Crean, Crane, & Mason, 2011) and others, reporting on the contrary that, substance use disorder is associated with having better cognitive performances (Bossong, Jansma, Bhattacharyya, & Ramsey, 2014), and yet others reporting that cognition remains intact whether there is substance use or not (Salyers & Mueser, 2001). A recent review of the literature as well as a meta-analysis from our group (Lev-Ran, Harrison, Ron, Barnes, & Joyce, 2012; Mata et al., 2008) report better cognitive performance when individuals are young and when they only use cannabis.

The research conducted to assess cognitive deficits in comorbid schizophrenia with other types of drugs is scarce. Most of the studies have used samples of individuals who have used cocaine and methamphetamines (both considered stimulants) but rarely has the effect of the specific drugs been looked at individually, meaning that most individuals in these studies present with polydrug use. Nevertheless, results in terms of neurocognition seem to indicate faster speed of processing, better attention, and psychomotor speed but worst performances on verbal learning and memory and spatial working memory (Coulston, Perdices, & Tennant, 2007; DeRosse, Kaplan, Burdick, Lencz, & Malhotra, 2010). To summarize, it is not yet clear whether having comorbid substance abuse disorder has a negative, a positive, or no effect at all on cognition. Furthermore, there is also the various aetiologies to consider and how they could impact the different presentations in comorbid schizophrenia and substance abuse disorder. One thing is however certain; studies looking into the type, the frequency, and the quantity of the drugs used in link with specific cognitive deficits are warranted. Most reviews and meta-analyses looking into comorbid schizophrenia have focused on neurocognition, with the exception of (Bahorik, Newhill, & Eack, 2013; Ringen et al., 2010) who examined emotional memory which could be argued to be a domain of sociocognition. Therefore, it becomes vital to define and understand

social cognitive processes in comorbid schizophrenia and substance use disorders.

Emotion recognition in substance use disorder

Studies on substance use disorder have documented potential emotion recognition deficits in these individuals. Firstly, and as we noted before, there are many drugs of choice available. While some studies investigate individual drug use such as cannabis or cocaine, others include participants with polydrug use, making the distinction in the patterns of recognition more difficult to identify and generalize. Secondly, some studies include participants that were abstinent for several months at the time the study was conducted, whereas others included active drug users, which could potentially influence the outcome. For instance, in the case of currently abstinent cannabis dependent individuals, emotion recognition deficits have been found for recognizing negative emotions, when compared to controls (Potvin, Joyal, Pelletier, & Stip, 2008). Similarly, but in the case of active polydrug use, (see both Donohue & Doody, 2012 for reviews; Potvin et al., 2008) deficits in negative emotion recognition were reported. Some even report specific deficits for fear recognition for regular cocaine users Mancini-Marlë et al. (2006), compared to occasional users and controls and for current methamphetamine abusers (Bayrakçi et al., 2015). All of these aforementioned studies investigated emotion recognition for substance abuse only. They give us ground to believe that, given the emotion recognition deficits reported in schizophrenia, the presence of comorbid substance abuse disorder could have an impact, on the social functioning of individuals with such comorbid presentations. No studies to date have explored the impact of socio-cognition on social functioning in samples of individuals with both schizophrenia and substance use disorders. It remains to be shown if there is a specific substance of use that could have a larger effect on emotion recognition, and subsequently on functioning, than others, in this population.

Assessment tools in emotion recognition

It has been argued in the past that discrepancies in emotion recognition results in schizophrenia could be due to the variety of evaluation tools (Couture et al., 2006)**,** with at times questionable sensitivity and validity. For starters, most of the studies interested in emotion recognition have used static measures of assessment. The most commonly used measure is Ekman's pictures that are presented in black and white and only include Caucasian individuals Fernàndez-Serrano, Lozano, Pérez-Garcia, and Verdejo-Garcia (2010). With the advent of virtual reality, the use of dynamic virtual avatars in various types of studies has gained interest. Virtual avatars have the advantage of being presented in color, of being animated with the degree of emotionality depicted by the characters being adjustable in intensity, of having the possibility to present the character depicting the emotion facing forward, facing at a 45 degree angle or shown in profile, and they include a variety of races (i.e., Asian, Hispanic, Black, etc.) making them a more realistic and a naturalistic assessment tool. Furthermore, recent studies have supported the ecological validity of their use in research, when compared to natural facial expressions (Kemmis, Hall, Kingston, & Morgan, 2007b) and Ekman's pictures (Kim, Kwon, & Chang, 2011). In our study, we further added the facial expression of neutrality to the regular six emotions used in the literature (sadness, anger, disgust, fear, joy, surprise). The reasoning stems from a concern of having a measuring tool that would be more realistic in nature. On a regular day we spend most of our time exhibiting a neutral facial expression, therefore understanding the identification patterns – recognizing neutrality for what it is truly, or conversely, recognizing it as either a positive or a negative emotion instead – could give us insight into the emotion recognition difficulties of individuals dual diagnosis schizophrenia. Once proper profiles of emotion recognition are established for this population, this aspect of social cognition could

become the target of both prevention intervention and concrete treatment of the deficits in the hopes of seeing positive impact on social functioning and therefore, on recovery.

Remediation of social cognition

Although more and more research efforts are put toward identifying the various deficits in emotion recognition and their impact in social functioning, many questions remain unanswered, especially regarding comorbid disorders. Many efforts in the last few years have been put forward to remedy the many deficits found in schizophrenia, with the field of social cognition gaining increasing interest. However, the various modalities of remediation of said deficits makes it difficult to decipher what is the most appropriate way to retrain the dysfunctions in order to gain benefits that could prevent the schizophrenia and help in the recovery from the disorder.

In schizophrenia. Research on social cognition is an emerging field that is so far showing great potential for rehabilitation of individuals suffering from schizophrenia (P Ekman & Friesen, 1976). It is considered by many researchers as holding a strong relationship with positive functional outcomes (Dyck, Winbeck, Leiberg, Chen, & Mathiak, 2010) and it has become an interesting target of remediation. Cognitive remediation in schizophrenia is defined as "a behavioral training based intervention that aims to improve cognitive processes (attention, memory, executive function, social cognition or metacognition) with the goal of durability and generalization" (Cognitive Remediation Experts Workshop in Florence, Italy, April 2010). Though many positive outcomes have been noted from the use of cognitive remediation in schizophrenia, on both cognition itself and of rehabilitation in many reviews and meta-analysis, the methodology used in those trainings has been called into question. There are generally two categories of training found in the cognitive training literature: (1) practice learning, in which

there is no explicit component to the learning process, it is solely based on repetition and the increasing difficulty of the task being presented thus generating implicit learning via trial and error, and, (2) strategy learning, where the main goal of the training is to teach an explicit and determined strategy to learn a specific skill (Cigna, Guay, & Renaud, 2015; Joyal, Jacob, Cigna, Guay, & Renaud, 2014). The methods or technologies used for either type of training are quite varied, including computed-assisted programs, community-based skills learning, group or individual therapy, pen-and-paper procedures, or combinations of some of these. More often than not, research on cognitive remediation of sociocognitive impairments have used explicit methodologies in their training with limited impact on improvement (Stopa & Clark, 1993). Also, most of the studies in the literature will tend to focus on sociocognition at large, neglecting to identify specific deficits and target those. This is especially true for emotion recognition; since there is still no consensus on which specific emotion this population has trouble identifying, most trainings cast a wider net and retrain emotion recognition as a whole, with some of them including most if not all domains of sociocognition in the remediation (Wykes, Huddy, Cellard, McGurk, & Czobor, 2011), making for less efficient trainings for one, but also creating difficulties in identifies the key ingredients that make for a successful training.

Given the variety of available training models, the often general and non-specific deficit treatments in addition to the various outcomes depending on the model chosen, it appears that more studies are warranted before recommending a specific treatment model for emotion recognition deficits in comorbid schizophrenia and substance use disorder.

Objectives

Although the initial goal of this doctoral project was to develop a novel remediation procedure, the investigations and literature reviews conducted as a first step changed the focus to increase our understanding of the targeted phenomena, i.e. social cognition in comorbid schizophrenia and substance use disorder. We first set out to examine emotion recognition patterns of individuals suffering from schizophrenia and schizophrenia and substance use disorder. It was not our original idea to compare groups but, rather, to explore a more naturalistic sample of individuals with schizophrenia given the fact that 50% of them suffer from comorbid substance use (Penn, Mueser, Doonan, & Nishith, 1995; Pinkham & D.L., 2006) and that they are generally excluded for studies when it is the case. Secondly, we explored in more details the various impacts of substance use disorder on schizophrenia by regrouping all findings on neurocognition, social functioning and social cognition in a book chapter (Horan, Kern, Green, & Penn, 2008). While it is generally expected that having comorbid substance use disorder would exacerbate the difficulties individuals with schizophrenia live with daily, highlighting the intriguing paradox found in neurocognitive studies of this population was paramount to set the groundwork for our preliminary study, that also showed the same counter-intuitive results. Lastly, before diving into cognitive remediation techniques to potentially improve emotion recognition, if any deficits were found in our sample, we examined the literature to see what types of remediation trainings appeared to be the most commonly used to improve cognition in schizophrenia. We therefore conducted a review of 99 articles that employed various methodologies to improve both neurocognition and social cognition (see Paquin et al., 2014, for review) to draw tentative conclusions and make suggestions for future research.

Chapter 2

Emotion recognition pattern in comorbid schizophrenia using virtual avatars: an exploratory study

Karine Paquin, Tania Lecomte & Stéphane Potvin

Article re-submitted in *The Journal of Dual Diagnosis* after reviews

Paquin, K., Lecomte, T., Renaud, P. & Potvin, S. (Re-*submitted*, February 2018). Emotion recognition in comorbid schizophrenia using virtual avatars: an exploratory study. *The Journal of Dual Diagnosis.*

Abstract

Exploration of emotion recognition (ER) and its impact on social functioning in schizophrenia has brought about some contradicting results with some finding deficits in recognition of negative emotions and others of positive or neutral ones. However, few are the studies that use dynamic ER measures or that study more naturalistic samples that include participants with comorbid presentations like substance use disorder. Objectives: to examine general and specific emotion recognition patterns using virtual avatars and its potential impact on social functioning while exploring the impact of substance use disorder of the results. Methods: 29 participants suffering from schizophrenia were selected, including the ones having comorbid substance use disorder. Dynamic virtual avatars were used to measure ER, and social functioning was measured with the First Episode Social Functioning Scale. Results: global ER was similar to normative data with sadness being the easiest to identify and fear the hardest. Fear tended to be misidentified as surprise while anger was wrongly perceived as neutrality. There was a positive correlation between identification of sadness and frequency of positive interaction with family as well as between better recognition of joy and improved perception of one's ability to work. Individuals with comorbid presentations were better at recognizing negative emotions (anger and fear) and lastly, those with comorbid cannabis use perceived having better capacities to interact with others and engage in social activities. Conclusions: results in ER for comorbid presentations appear counter-intuitive but are common in recent literature, with some potential explanations such as the social hypothesis attempting to explain them but remaining unsatisfactory. Difficulty recognizing fear is in line with normative studies reporting this emotion as the hardest to identify and the same can be said about the fear-surprise confusion. On the other hand, the anger-neutrality confusion is novel. Though preliminary and conducted on a small sample, our data

suggest more research is needed to properly identify the impact of substance use in schizophrenia on both ER and social functioning.

Keywords: emotion recognition, schizophrenia, comorbidity, substance use disorder, social functioning, dynamic avatars, virtual avatars

1. Introduction

Social cognition deficits in schizophrenia are recognized as severely impeding the quality of life of individuals and as being a direct predictor of social functioning (Brune et al., 2007; Roncone et al., 2004), and yet, there is still a lot of debate regarding which specific social deficits are central to social functioning. Social cognition is defined as all the processes used to collect, interpret, and process social information, as well as interact with others based on these interpretations (Corrigan & Penn, 2001; M.F. Green et al., 2008). It typically includes five domains, namely Theory of Mind (recognizing mental states of others), social knowledge (knowing and being able to apply social rules given certain social situations), attribution style (blaming oneself or giving others negative intentions), emotion regulation (how one copes with strong emotions), and last but not least, emotion recognition (one's ability to recognize facial emotions) (Minzenberg et al., 2009). Over the past decades, researchers have suggested that social cognition deficits could explain many, if not most, of the social dysfunctions and poor social functioning found in schizophrenia (Keefe et al., 2011; M. M. Kurtz et al., 2007; Revheim et al., 2006). Emotion recognition is undoubtedly the process that has been studied the most. It is now recognized that many individuals with schizophrenia have deficits in both identifying and discriminating facial expressions (Couture et al., 2006; Pinkham et al., 2014). Furthermore,

emotion recognition might be central to social functioning in schizophrenia because it has been associated with difficulties in interpersonal interactions and fulfilment of social roles (Pinkham et al., 2014). Nevertheless, the intricacies of where the deficits in emotion recognition lies and it impacts social functioning – which seems to be a crucial component in the aetiology, evolution of and remission from schizophrenia – remains elusive.

A closer look at emotion recognition studies reveals that little information exists regarding the specificity of the emotions involved in the deficits (Addington et al., 2006). While some will argue that the deficits in emotion recognition are global (Silver et al., 2009), others argue it is specific. Indeed, some find deficits in recognizing negative emotions (Amminger et al., 2012; Bediou et al., 2007; Comparelli, Corigliano, De Carolis, Mancinelli, Trovini, Ottavi, Dehning, et al., 2013; van't Wout et al., 2007), others find deficits in recognizing positive emotions (Tsoi et al., 2008) and yet others, identify the deficit as being more related to neutral expressions (Kohler et al., 2003). It has been argued that these discrepancies in results are due to testing modalities. While several studies used Ekman's facial expressions (P Ekman & Friesen, 1976; P Ekman, Friesen, & Hager, 2002) to measure emotion recognition, in the last few years, the emergence of virtual reality gave way to novel, more flexible ways to assess emotion recognition. Ekman's pictures are static in nature, are presented in black and white and only include Caucasian individuals. Virtual avatars, on the other hand, are dynamic (with the degree of emotional expression that can be adjusted), presented in color and include a variety of races (i.e. Asian, Hispanic, Black, etc.). Studies have already demonstrated the ecological validity of using virtual avatars in research, by comparing them to natural facial expressions (Dyck et al., 2010), and by comparing them to Ekman's facial expression (Cigna et al., 2015; Weyers, Mühlberger, Hefele, & Pauli, 2006).

Of importance is the fact that deficits in emotion recognition have also been found in substance use disorders (Bayrakçi et al., 2015; Fernandez-Serrano, Moreno-Lopez, Perez-Garcia, & Verdejo-Garcia, 2012; Henry, Mazur, & Rendell, 2009; Kemmis, Hall, Kingston, & Morgan, 2007a; Kim et al., 2011). Given the fact that close to 50% of individuals with schizophrenia have a lifetime substance use disorder (see Blanchard, Brown, Horan, & Sherwood, 2000 for review), it is highly surprising that no studies have investigated the potential impact of having this comorbid presentation on emotion recognition, making the samples less naturalistic and the results less generalizable (Humphreys, 2017; Stroup & Geddes, 2008). Interestingly, from knowing the deleterious impact of cannabis smoking of the cognitive capacities of normative groups (Crean et al., 2011), we would expect that having this comorbid presentation would exacerbate the cognitive deficits. However, it appears that cognition remains intact, and in some cases actually improves, for individuals that have this presentation. While perhaps counter-intuitive, these results have been replicated in close to 20 studies to date (see Paquin, Lecomte, & Potvin, 2017, for review), further highlighting the need to assess this population on social cognition measures.

The main objective of this study was to examine general and specific emotion recognition using virtual avatars. Secondly, we hoped to explore and establish a link between emotion recognition and social functioning. Lastly, we set to explore the impact of comorbid substance use disorder on the data.

2. Methods

2.1 Participants

A total of 29 out-patients from the Psychosis program of the *Institut Universitaire en Santé Mentale de Montréal* (IUSMM), a large psychiatric institution in Montreal, and the Jeunes Adultes Psychotiques clinic from the *Centre Hospitalier de l'Université de Montréal* (CHUM), accepted to participate in our study (see Table 1 for sociodemographic information). Inclusion criteria were: 1) having a diagnosis of schizophrenia according to DSM-IV, 2) having the capacity to consent to participation in this study, and 3) being between the age of 18 and 35 years old (as this study was part of a larger one, focused on first psychotic episodes). Exclusion criteria included: 1) not being fluent in English or French, 2) having an organic brain disorder or IQ below 70 (from chart review), and 3) having a non-corrected visual impairment. Noteworthy, patients with comorbid substance use disorders (DMS-IV diagnoses of either cannabis or stimulant abuse in our case) were not excluded. The eligible participants were informed about the study procedure and duration and gave their written consent. This study was approved by the University of Montreal's ethics board as well as by the IUSMM and the CHUM ethics board.

2.2 Study procedures and clinical evaluation

This current cross-sectional study took place within a larger study on comorbid substance use disorder in early psychosis. In order to assess inclusion and exclusion criteria, participants were administered the psychotic disorders and substance use disorders modules of the computerized version of the *Structured Clinical Interview for DSM-IV diagnosis for Axis I* (SCID-I, First, Spitzer, Gibbon, & Williams, 2002). Sociodemographic information was obtained with the *PSR Toolkit* (Arns, 1998). The SCID-I semi-structured interviews were administered by Ph.D. students in our laboratory that were trained to gold standard. Social functioning was measured with *First Episode Social Functioning Scale* (FESFS, Lecomte et al., 2014) which

includes the following domains: "intimacy", "social activities", "friends", "family", "living skills", "interacting with people", "school" and "work".

Using a PowerPoint presentation that lasted 30 minutes on a standard laptop pc, dynamic avatars were presented to assess emotion recognition (Cigna et al., 2015). Overall, 10 avatars in each category of universally recognized emotions (sadness, anger, disgust, joy, fear, surprise) and neutral expression (12 avatars) were presented for 2.5 seconds, with a delay of 10 seconds between each avatar (for a total of 72 avatars; see Image 1 for sample of avatar), during which participant gave their response by picking the appropriate emotion displayed by the avatars from the list of 7 emotions. An auditory signal at 7 seconds (following offset) gave the cue to participants that the next avatar was about to appear on the screen. The animation started with a neutral facial expression and over the course of 2.5 seconds, morphed into the appropriate facial expression. Intensity of emotional expression varied from 60% to 100% and avatars were presented only facing forward. Avatars were comprised of both male and female subjects that were either Caucasian, Hispanic or Black (12 Latinos women, 36 Caucasians (23 males, 13 females), 24 Blacks (12 males, 12 females) all selected randomly). Participants were instructed to look at each avatar on the computer and then indicate in their booklet the emotion the avatar was depicting by choosing between 7 previously described emotions. No feedback was given to let the participants know if they answered properly or not. The avatars were presented without interruption. We computed mean scores for each individual emotion as well as for positive (joy, surprise) and negative (sadness, fear, disgust, anger) emotions for our analyses. These avatars were tested for construct validity against Ekman's static pictures, measuring recognition, facial muscle activation and gaze time in the eye region. It was found that there was no difference in

any of these measures, confirming validity for their use for measuring emotion recognition (Joyal et al., 2014).

3. Statistical analyses

Analyses were conducted using SPSS version 24. We conducted ANOVAs for emotion recognition and diagnoses, using contrast orthogonal vectors for post hoc analyses to verify the impact of the type of substance use on the results. The group comparisons were as follows: schizophrenia alone, schizophrenia and cannabis abuse or schizophrenia and stimulant abuse. Specifically, we ran ANOVAs for global ER, for negative emotions (including sadness, fear, anger and disgust), for positive emotions (including joy and surprise) and for neutrality separately. When we needed to further explore the 7 emotions to decipher where the difference was, we used the Bonferonni correction for multiple comparisons. We further examined the descriptive data for emotion recognition in order to see if there was a pattern in misattributing certain emotions. Pearson correlations were used to analyze the relationship between social functioning and emotion recognition and, when significant, we conducted a linear regression to analyze the link between specific emotion recognition and social functioning domains. We used $p < .05$ for significance, including data with $p=.06$ only as showing potential trends and tentative interpretations.

4. Results

4.1 Emotion recognition

Overall emotion recognition showed an average of 70.4% of correct answers (29.6% of errors) for the whole sample with no significant between group differences. When we examined

the success scores for specific emotions, sadness got the highest recognition scores (82.1%) while fear got the worst results (42.6%) (see Table 2).

We then explored the attribution errors for specific emotions in our entire sample. Therefore, when an emotion was misinterpreted, we examined if there were any tendencies in the answers. Fear was misinterpreted as surprise 29.3% of the time, while anger was misinterpreted as neutrality 18.3% of the time. There was no specific pattern of responses for other emotions (with percentages all under 7%).

4.2 Associations with social functioning

Our second hypothesis posited a correlation between emotion recognition and social functioning. We therefore examined if recognition of certain categories of emotions (moreover, if recognizing of individual emotions) was linked with social functioning. There were no significant results when comparing overall scores of emotion recognition and overall scores of social functioning. There was a positive correlation (see Table 3) between sadness recognition and one's frequency of positive interaction with family (r=0.41, p=0.03), explaining 17% of the variance ($F_{(1,28)}$=5.44, p=.03). Moreover, – and despite the fact that only a very small portion of our sample reported working (N=10) – the data also showed a positive correlation between the recognition average for positive emotions and one's perceived abilities to work (r=0.64, p=.05). Specifically, average scores on emotion recognition for joy, predicted one's perceived abilities to work, explaining 43.8% of the variance ($F_{(1,9)}$=6.23, p=.04).

4.3 Associations with substance use disorders

Lastly, we explored the impact of substance use on the data. When comparing participants with schizophrenia alone and those with schizophrenia and comorbid substance use disorder in general (stimulant+cannabis abuse), we found that individuals with both schizophrenia and substance use disorder were better at recognizing negative emotions ($F_{(1,27)}$=7.32, p=.01, η^2=.21, see Table 4) particularly anger ($F_{(1,27)}$=5,54, p=.03, η^2=.17, see Table 4) and fear ($F_{(1,27)}$=8.94, p=.01, η^2=.25, see Table 4). As posthoc analyses, we examined if the type of substance of use – either cannabis or stimulant – could have an effect on the valence of emotion recognition. When comparing schizophrenia alone (N=13) with schizophrenia comorbid with specific types of substance (cannabis: N=10, stimulants: N=6), we found a significant difference in negative emotion recognition ($t_{(26)}$=-2.74, p=.02, see Table 5) with individuals with stimulant use disorder being better at recognizing negative emotions, specifically anger ($t_{(26)}$=-2.31, p=.03, see Table 5) and fear ($t_{(26)}$=-3.56, p=.001, see Table 5). We further found a significant difference in negative emotion recognition when comparing schizophrenia alone to schizophrenia with cannabis use disorder ($t_{(26)}$=-2.17, p=.05, see Table 6), with a trend for better fear recognition ($t_{(26)}$=-1.92, p=.06, see Table 6), in those with cannabis use disorder compared to participants with schizophrenia alone.

Upon further exploration of social functioning and the impact of substance use disorder, we found that in the case of the frequency of use of abilities to 'interact with others', there was a significant between group difference when comparing individuals with schizophrenia alone and those with schizophrenia and substance use ($F_{(2,28)}$=3.89, p=.03). More specifically, individuals with the comorbid presentation of cannabis use, tended to use their abilities more frequently than those with schizophrenia alone ($t_{(26)}$=2.74, p=.01, see Table 7). Running the same comparison, we

found similar results for the frequency of use of the abilities for 'social activities' with a trend toward a between group difference ($F_{(2,28)}$=3.15, p=.06, see Table 7), where individuals with schizophrenia and cannabis use disorder used their abilities more frequently than those with schizophrenia alone ($t_{(26)}$=2.48, p=.02, see Table 7). There was no group difference between those that have schizophrenia alone and schizophrenia with stimulant use disorder or when comparing individuals with comorbid cannabis use with those that had comorbid stimulant use.

5. Discussion

Our intentions were to firstly examine emotion recognition in individuals with schizophrenia using dynamic avatars, and try to identify emotion specific deficits, if any. We secondly intended to establish a link between emotion recognition and social functioning and lastly, we wished to explore if substance use disorder would have an impact on those results.

Interestingly, our data showed that individuals suffering from schizophrenia had overall emotion recognition scores that were similar to normal controls found in the literature using dynamic emotion recognition tools. Indeed, Cigna et al. (2015) – who conducted their preliminary validation studies for the use of the same dynamic avatars we used in our protocol – reports overall emotion recognition scores of 78% in their first study and 78.6% in their second study, with a normative sample of university students. Those results are surprising and cannot be explained by methodology. Tentatively, we suggest that these results could be due to the paradoxical explanation of conversation of cognitive functions in substance use disorders (Tiffany, Friedman, Greenfield, Hasin, & Jackson, 2011), since we did not exclude the participants that had this comorbidity. Close to 20 studies have reported that individuals suffering from both schizophrenia and substance use disorder maintain or even improve upon their

cognitive functions, specifically their neurocognitive abilities (see Paquin et al., 2017, for review). However, more studies are required to ascertain if this paradox is consistent for sociocognitive functions.

Where specific emotion recognition was concerned, we found that sadness was easily recognized and fear poorly recognized across all participants with schizophrenia. In comparison, Cigna et al. (2015) also reported fear as being the emotion that was the hardest to identify in university students (study 1: 39.9%, study 2: 49.6%). Contrastingly, it was surprise (study 1: 88.4%, study 2: 77.1%) and joy (study 1: 87.1%, study 2: 76.7%), rather than sadness, that were the easiest to identify in Cigna et al. (2015). Of note, Weyers et al. (2006) using a similar, though smaller sample of university students, also reported that joy was well identified (91%). It is unclear why this group would have more ease to recognize sadness but it could be suggested that stigmatisation surrounding this disorder could lead these individuals to become more alert to sign of sadness from others during their social interactions, therefore improving their emotion recognition of that specific emotion.

Regarding misinterpretation patterns, our data showed that fear was mistaken for surprise while anger was mistaken for neutrality in schizophrenia. The fear-surprise confusion is consistent with results seen in normative samples (Cigna et al., 2015; study 1: 49.6%, study 2: 33%). As for the anger-neutrality confusion, this result supports other studies suggesting that neutrality is difficult for many individuals with schizophrenia to recognize (Kohler et al. (2003), likely due to inadequate use of facial cues linked to the eyes and mostly using the mouth or other less useful facial information (Clark, Gosselin, & Goghari, 2013; Gosselin & Schyns, 2001).

Though the data did not allow us to examine any predictive link between emotion recognition and social functioning, correlations for specific emotions and specific social functioning subscales were revealing. The most relevant ones being the positive correlation between sadness recognition and frequency of positive interaction with family and recognition of joy and one's perceived ability to work. Given the confusion between anger and neutrality and the fact that fear is the emotion that seems to be the hardest to recognize, it appears that recognition and potentially interpretation of negative emotions is impaired, which could have negative repercussion on social functioning. Conversely, a better recognition of another negative emotion – sadness – leading to more positive interactions with family members, could be explained by a more supportive family environment that would foster more empathy in individuals. It is likely that those who live with family members interact more frequently and are therefore more exposed to various emotions, enabling them to be better at emotion recognition, compared to those who live alone for instance. We were however not able to verify this hypothesis.

Our data showed that individuals with a comorbid presentation were better at recognizing negative emotions like fear and anger and that their capacity to interact with others was essentially preserved. Similar findings have been emerging recently in the literature regarding fewer cognitive impairments in those with schizophrenia and substance disorders, compared to schizophrenia alone (see Paquin, Lecomte, & Potvin, 2016). Indeed, we found better emotion recognition for both cannabis and stimulant users with schizophrenia in our sample as well as more self-reported interactions with others and social activities. To our knowledge, this is the first study that suggests that emotion recognition would be relatively preserved in dual diagnosis schizophrenia. Functional imaging studies (Mancini-Marlë et al., 2006; Potvin et al., 2007) have also reported that individuals with schizophrenia and cannabis use have stronger emotional

reactions to negative emotional stimuli (than those with schizophrenia alone), as well as increased frontal activations, which could explain the better recognition of negative emotions. Given that a lifestyle of addiction requires certain social skills (socialize with drug users and dealers, to handle money and make transactions), a good recognition of negative emotions is an asset for substance users. This is know as 'the social hypothesis' (Mueser et al., 2000). However, this hypothesis remains unsatisfactory since it would imply that the differences are not related to the pharmacological effects of the drugs but rather to premorbid differences in social skills. This also leads to the conclusion that improvements in cognition in substance use would vary depending on the availability of the drug of choice, which is not the case (Paquin et al., 2017). However, one needs to remain cautious when interpreting these data; we are unaware of any substance having been shown to improve emotion recognition abilities in individuals having no psychiatric disorder. Quite to the contrary, most studies show that normative samples under the influence of cannabis, report marked deficits in neurocognition that often remain over time, even when drug use ceases (Crean et al., 2011). Therefore, more studies are required to determine if different substances (i.e. cannabis, alcohol or stimulants) have different impacts on social cognition as well as neurocognition in schizophrenia.

There are obvious limitations to our study. Our small sample size did not allow us to run robust statistical analysis to examine between group differences for substance use disorders. Furthermore, our data remain descriptive as we did not have a control group of normal individuals. Although our avatars have ecological and construct validity, future studies could look at various lengths of exposition and different degrees of intensity given that brief exposures or more subtle emotions could be more challenging and better discriminate between individuals (P Ekman, 2004). Moreover, it is paramount that sociocognitive evaluations of individuals with

comorbid substance disorder presentation be assessed in order to ascertain if a specific psycho-active substance brings about a different impact on social cognition and even more so, on social functioning.

References

Achim, A. M., Ouellet, R., Lavoie, M.-A., Vallières, C., Jackson, P. L., & Roy, M.-A. (2013). Impact of social anxiety on social cognition and functioning in patients with recent-onset schizophrenia spectrum disorders. *Schizophrenia Research, 145*(1–3), 75-81. doi:https://doi.org/10.1016/j.schres.2013.01.012

Addington, J., Saeedi, H., & Addington, D. (2006). Facial affect recognition: a mediator between cognitive and social functioning in psychosis? *Schizophrenia Research, 85*, 142-150.

Amminger, G. P., Schafer, M. R., Papageorgiou, K., Klier, C. M., Schlogelhofer, M., Mossaheb, N., . . . McGorry, P. D. (2012). Emotion recognition in individuals at clinical high-risk for schizophrenia. *Schizophrenia Bulletin, 38*(5), 1030-1039.

Arns, P. (1998). Canadian Version of the PSR Toolkit: Ontario Federation Community Mental Health and Addiction Programs.

Bayrakçi, A., Sert, E., Zorly, N., Erol, A., Sariçiçek, A., & Mete, L. (2015). Facial emotion recognition deficits in abstinent cannabis dependent patients. *Comprehensive Psychiatry, 58*, 160-164.

Bediou, B., Asri, F., Brunelin, J., Krolak-Salmon, P., D'Amato, T., Saoud, M., & Tazi, I. (2007). Emotion recognition and genetic vulnerability to schizophrenia. *British Journal of Psychiatry, 191*, 126-130.

Blanchard, J. J., Brown, S. A., Horan, W. P., & Sherwood, A. R. (2000). Substance use disorders in schizophrenia: Review, integration, and a proposed model. *Clinical Psychology Review, 20*(2), 207-234.

Bourke, C., Douglas, K., & Porter, R. (2010). Processing of facial emotion expression in major depression: a review. *Australian & New Zealand Journal of Psychiatry, 44*(8), 681-696.

Brekke, J. S., Kay, D. D., Kee, K. S., & Green, M. F. (2005). Biosocial pathways to functional outcome in schizophrenia. *Schizophrenia Research, 80*, 213-225.

Brune, M., Abdel-Hamid, M., Lehmakamper, C., & Sonntag, C. (2007). Mental state attribution, neurocognitive functioning, and psychopathology: What predicts poor social competence in schizophrenia best? *Schizophrenia Research, 92*(1-3), 151-159.

Cigna, M.-H., Guay, J.-P., & Renaud, P. (2015). La reconnaissance émotionnelle faciale: validation préliminaire de stimuli virtuels dynamiques et comparaison avec les Pictures of Facial Affect (POFA). *Criminologie, 48*(2), 237-263.

Clark, C., Gosselin, F., & Goghari, V. M. (2013). Aberrant patterns of visual facial information usage in schizophrenia. *Journal of Abnormal Psychology, 122*, 513-519.

Comparelli, A., Corigliano, V., De Carolis, A., Mancinelli, I., Trovini, G., Ottavi, G., . . . Girardi, P. (2013). Emotion recognition impairment is present early and is stable throughout the course of schizophrenia. *Schizophrenia Research, 143*(1), 65-69.

Corrigan, P. W., & Penn, D. L. (2001). Introduction: Framing models of social cognition and schizophrenia. In P. W. Corrigan & D. L. Penn (Eds.), *Social cognition and schizophrenia* (pp. 3-37). Washington, D.C.: American Psychological Association.

Dyck, M., Winbeck, M., Leiberg, S., Chen, Y., & Mathiak, K. (2010). Virtual faces as a tool to study emotion recognition deficits in schizophrenia. *Psychiatry Research, 179*(3), 247-252.

Edwards, J., Jackson, H. J., & Pattison, P. E. (2002). Emotion recognition via facial expression and affective prosody in schizophrenia: A methodological review. *Clinical Psychology Review, 22*(6), 789-832.

Ekman, P. (2004). Micro Expression Training Tool (METT) Online.

Ekman, P., & Friesen, W. V. (1976). *Pictures of facial affect*: Consulting Psychologists Press.

Ekman, P., Friesen, W. V., & Hager, J. C. (2002). *Facial Action Coding System: The Manual*: Consulting Psychologists Press.

Fernandez-Serrano, M. J., Moreno-Lopez, L., Perez-Garcia, M., & Verdejo-Garcia, A. (2012). Inteligencia emocional en individuos dependientes de cocaina. *Trastornos Adictivos, 14*(1), 27-33.

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (2002). *Structured Clinical Interview for DSM-IV-TR Axis I Disorders - Patient edition. (SCID-I/P)*. New York.

Gosselin, F., & Schyns, P. (2001). Bubbles: a technique to reveal the use of information in recognition tasks. *Vision Research, 41*(17), 2261-2271.

Green, M. F., Penn, D. L., Bentall, R., Carpenter, W. T., Gaebel, W., Gur, R. C., . . . Heinssen, R. (2008). Social cognition in schizophrenia: an NIMH workshop on definitions, assessment, and research opportunities. *Schizophrenia Bulletin, 34*(6), 1211-1220.

Henry, J. D., Mazur, M., & Rendell, P. G. (2009). Social-cognitive difficulties in former users of methamphetamine. *British Journal of Clinical Psychology, 48*, 323-327.

Herberner, E. S., Harrow, M., & Sands, J. (2000). The influence of depression on the course, functioning and treatment of patients with schizophrenia. *Psychiatric Annals, 30*(10), 653-658.

Hooker, C., & Park, S. (2002). Emotion processing and its relationship to social functioning in schizophrenia patients. *Psychiatry Research, 112*, 41-50.

Humphreys, K. (2017). A review of the impact of exclusion criteria on the generalizability of schizophrenia treatment reserach. *Clinical Schizophrenia & Related Psychoses, 11*(1), 49-57.

Joyal, C. C., Jacob, L., Cigna, M.-H., Guay, J.-P., & Renaud, P. (2014). Virtual faces expressing emotions: An initial concomitant and construct validity study. *Frontiers in Human Neuroscience, 8*. doi: 10.3389/fnhum.2014.00787

Kemmis, L., Hall, J. K., Kingston, R., & Morgan, M. J. (2007). Impaired fear recognition in regular recreational cocaine users. *Psychopharmacology, 194*, 151-159.

Kim, Y. T., Kwon, D. H., & Chang, Y. (2011). Impairments of facial emotion recognition and theory of mind in methamphetamine abusers. *Psychiatry Research, 186*, 80-84.

Kohler, C. G., Turner, T. H., Bilker, W. B., Brensinger, C. M., Siegel, S. J., Kanes, S. J., . . . Gur, R. C. (2003). Facial emotion recognition in schizophrenia: Intensity effects and error pattern. *American Journal of Psychiatry, 160*(10), 1768-1774.

Lecomte, T., Corbière, M., Ehmann, T., Addington, J., Abdel-Baki, A., & Macewan, B. (2014). Development and preliminary validation of the First Episode Social Functioning Scale for early psychosis. *Psychiatric Research, 216*(3), 412-417. doi:10.1016/j.psychres.2014.01.044

Mancini-Marlë, A., Potvin, S., Fahim, C., Mensour, B., Beauregard, M., Roy, J. Y., & Stip, E. (2006). Neural correlates of the affect regulation model in schizophrenia patients with a substance use history: A functional magnetic resonance imagine study. *Journal of Clinical Psychiatry, 67*(3), 342-350.

Mandal, M. K., Pandey, R., & Prasad, A. B. (1998). Facial expressions of emotions and schizophrenia: A review. *Schizophrenia Bulletin, 24*(3), 399-412.

Paquin, K., Lecomte, T., & Potvin, S. (2016). *Cannabis smoking in adult schizophrenia: A cognitive and functional magnetic resonance imaging perspective*. London, United Kingdom: Academic Press.

Pinkham, A. E., Penn, D. L., Green, M. F., Buck, B., Healey, K. M., & Harvey, P. D. (2014). The social cognition psychometric evaluation study: results of the expert survey and RAND panel. *Schizophrenia Bulletin, 40*(4), 813-823.

Potvin, S., Mancini-Marlë, A., Fahim, C., Mensour, B., & Stip, E. (2007). A functional magnetic resonance imaging study of social emotion in schizophrenia patients with and without comorbid substance use disorder. *Social Neuroscience, 2*(2), 1-11.

Roncone, R., Mazza, M., Frangou, I., De Risio, A., Ussorio, D., Tozzini, C., & Casacchia, M. (2004). Rehabilitation of theory of mind deficit in schizophrenia: a pilot study of metacognitive strategies in group treatment. *Neuropsychological rehabilitation, 14*(4), 421-435.

Silver, H., Bilker, W. B., & Goodman, C. (2009). Impaired recognition of happy, sad and neutral expressions in schizophrenia is emotion, but no valence, specific and context dependent. *Psychiatry Research, 169*(2), 101-106.

Stroup, T. S., & Geddes, J. R. (2008). Randomized controlled trials for schizophrenia: Study designs targeted to distinct goals. *Schizophrenia Bulletin, 34*(2), 266-274.

Tiffany, S. T., Friedman, L., Greenfield, S. F., Hasin, D. S., & Jackson, R. (2011). Beyond drug use: A systematic consideration of other outcomes in evaluations of treatments for substance use disorders. *Addiction, 107*, 709-718.

Tsoi, D. T., Lee, K. H., Khokhar, W. A., Mir, N. U., Swalli, J. S., Gee, K. A., . . . Woodruff, P. W. R. (2008). Is facial emotion recognition impairment in schizophrenia identical for different emotions? A signal detection analysis. *Schizophrenia Research, 99*(1-3), 263-269.

van't Wout, M., Aleman, A., Kessels, R. P., Cahn, W., de Haan, E. H., & Kahn, R. S. (2007). Exploring the nature of facial affect processing deficits in schizophrenia. *Psychiatry Research, 150*(3), 227-235.

Ventura, J., Green, M. F., Shaner, A., & Liberman, R. P. (1993). Training and quality assurance with the Brief Psychiatric Rating Scale. *International Journal of Methods in Psychiatric Research, 3*, 221-244.

Weyers, P., Mühlberger, A., Hefele, C., & Pauli, P. (2006). Electromyographic responses to static and dynamic avatar emotional facial expressions. *Psychophysiology, 43*(5), 450-453.

Image 1

Avatar of Caucasian male displaying neutral facial expression.

Table 1

Sociodemographic information on participants

Gender	Male	Female		
	23	6		
Marital status	Single	Other		
	25	4		
Level of education	Partial highschool	Completed highschool	Partial college	Completed college
	15	8	3	3
Residential status	Independent	Lives with family	Supervised housing	Other
	12	4	5	8
Age average	25.3			

N=29.

Table 2

Success rates for emotion recognition of specific emotions in percentages

Emotion	Success (%)	*SEM*
Anger	69.0	4.2
Fear	42.6	3.8
Sadness	82.1	4.5
Disgust	73.0	5.1
Joy	80.5	3.9
Surprise	69.3	5.2
Neutral	79.0	3.2

SEM=Standard Error of the Mean

Table 3

Correlations between emotion recognition and social functioning domains

Mesures		1	2	3	4
1. Sadness	Pearson *r*				
	N				
2. Positive	Pearson *r*	.78**			
	N	29			
3. Frequency of positive interactions with family	Pearson *r*	.41*	.22		
	N	29	29		
4. Perceived capacities for work	Pearson *r*	.56	.64*	.26	
	N	10	10	10	

* $p < .05$, ** $p < .01$

Table 4

Comparison between schizophrenia alone and schizophrenia comorbid with substance abuse on emotion recognition

Emotion	SZ		SZ+Subs	
	M	*SD*	*M*	*SD*
Negative	0.58	0.23	0.78	0.08
Anger	0.58	0.24	0.78	0.20
Fear	0.32	0.18	0.52	0.18

SZ: Schizophrenia alone, N=13; SZ+Subs: Schizophrenia+cannabis and stimulant abuse, N=16.

Table 5

Comparison between schizophrenia alone and schizophrenia comorbid with stimulant abuse on emotion recognition

Emotion	SZ		SZ+Stim	
	M	*SD*	*M*	*SD*
Negative	0.58	0.23	0.78	0.09
Anger	0.58	0.24	0.83	0.18
Fear	0.32	0.18	0.62	0.12

SZ=Schizophrenia alone, *N*=13; *SZ*+Stim=Schizophrenia+stimulant abuse, *N*=6.

Table 6

Comparison between schizophrenia alone and schizophrenia comorbid with cannabis abuse on emotion recognition

Emotion	SZ		SZ+Cann	
	M	*SD*	*M*	*SD*
Negative	0.58	0.23	0.74	0.08
Fear	0.32	0.18	0.45	0.18

SZ=Schizophrenia alone, *N*=13; *SZ*+Cann=Schizophrenia+cannabis abuse, *N*=10.

Table 7

Comparison between schizophrenia alone and schizophrenia comorbid with cannabis abuse on social functioning

Social functioning domaine	SZ		SZ+Cann	
	M	*SD*	*M*	*SD*
Frequency of use of capacities to interact with others	2.62	0.53	3.38	0.38
Frequency of use of capacities in social activities	2.51	0.67	3.31	0.55

SZ=Schizophrenia alone, *N*=13; *SZ*+Cann=Schizophrenia+cannabis abuse, *N*=10.

Chapter 3

Cannabis smoking in adult schizophrenia: A cognitive and functional magnetic resonance imaging perspective

Karine Paquin, Tania Lecomte & Stéphane Potvin

Chapter no. 37 published in *The Handbook of Cannabis and Related Pathologies: Biology, Pharmacology, Diagnosis and Treatments*, 2017

Paquin, K., Lecomte, T., & Potvin, S. (2017) *Cannabis smoking in adult schizophrenia: A cognitive and functional neuroimaging perspective, in Handbook of Cannabis and Related Pathologies, P. VR, Editor Academic press: London, UK*. p. 357-371.

ABSTRACT

Cognitive dysfunctions are core features in schizophrenia and they have a significant negative impact on social and occupational functioning. Highly prevalent in schizophrenia, substance use disorders can impair cognition, both in schizophrenia and in the normal population. However, in the specific case of cannabis, findings have been paradoxical, as most studies have shown that cannabis smoking impairs cognition in non-psychosis individuals while it seems to be associated with better cognitive functioning in individuals with schizophrenia. Preliminary functional magnetic resonance imaging studies have also produced results echoing these paradoxical findings. The potential reasons behind those findings include the neuro-protective effects of cannabis, the social lifestyle associated with cannabis smoking, as well as premorbid differences. Studies in the field have limitations that cannot be neglected, and methodological recommendations are made for future studies that will be performed on the topic.

Keywords

Schizophrenia, psychosis, cannabis, delta-9-tetrahydrocannabinol, comorbidity, neuro-cognition, socio-cognition, functional magnetic resonance imaging

List of abbreviations

Δ^9-THC: delta-9-tetrahydrocannabinol

fMRI= functional magnetic resonance imaging

MATRICS= Measurement And Treatment Research to Improve Cognition in Schizophrenia

Sz+Can= schizophrenia patients smoking cannabis

Sz= schizophrenia patients not smoking cannabis

SUD= substance use disorders

Cognition in schizophrenia

The lifetime prevalence of schizophrenia is lower than 1% worldwide. Schizophrenia is a severe psychiatric disorder, characterized by positive (delusions & hallucinations) and negative (flat affect, anhedonia) symptoms, as well as disorganized thinking/behaviour. A source of considerable social and economic burden, schizophrenia has been ranked by the *World Health Organization* as one of the top 10 causes of disability in developed countries (Tandon, Keshavan, & Nasrallah, 2008a). Over the years, cognitive dysfunctions have emerged as being of critical importance in schizophrenia. Given that cannabis smoking is highly prevalent in schizophrenia and that it has deleterious effects on cognition in non-psychosis individuals, the potential cognitive effects of cannabis on cognition in schizophrenia have recently attracted growing interest.

It is widely known that individuals with schizophrenia have to cope with a variety of cognitive deficits (Goldberg, David, & Gold, 2011), with close to 80% of them struggling with either socio- or neuro-cognitive deficits or both. Factor analyses have revealed that 6 neuro-cognitive domains are significantly impaired in schizophrenia, namely speed of processing, attention/vigilance, working memory, verbal and visual learning, as well as reasoning and problem solving. The socio-cognitive domains known to be impaired in schizophrenia include deficits in social knowledge, emotion recognition, Theory of Mind, attribution style as well as emotion regulation. When compared to the general population, the cognitive deficits of schizophrenia range from 1 to 1.5 standard deviations below the normal scores. Mild deficits are also present even in the prodromal phase of the disorder, indicating that they could partly be independent of duration of illness and medication intake. Furthermore, non-affected family members of individuals with schizophrenia tend to show similar though attenuated cognitive

deficits, suggesting that the cognitive impairments of schizophrenia are partially heritable. Finally, research has shown that cognitive impairments in schizophrenia are relatively stable over time, even when psychotic symptoms are in remission. Cognitive dysfunctions are therefore core features of schizophrenia, known to severely impede upon recovery and rehabilitation. Indeed, numerous studies have shown that cognition (especially social cognition) is a better predictor of social and occupational functioning and overall recovery than the negative or positive symptoms of schizophrenia. As a result, interest in investigating cognition in schizophrenia has rapidly grown over the past years, in the hopes of pinpointing where the deficits specifically lie in order to identify better treatments. As such, the *National Institute of Mental Health* created a standardized battery of test to assess cognition in clinical settings: the MATRICS Consensus Cognitive Battery, which measures 7 domains of cognition (6 neuro-cognitive, 1 socio-cognitive; Table 1) (Nuechterlein, Green, Kern, Baade, Barch, Cohen, Essock, Fenton, Frese, Gold, Goldberg, Heaton, Keefe, Kraemer, Mesholam-Gately, Seidman, Stover, Weinberger, Young, Zalcman, & Marder, 2008).

On neurobiological grounds, considerable efforts have been made in order to identify the neurobiological bases of the cognitive impairments of schizophrenia, which are considered as putative endo-phenotypes of the disorder. Thus far, functional imaging studies have mostly paid attention to deficits in working memory, executive functions, emotion processing, Theory of Mind and episodic memory in schizophrenia. This vast functional imaging literature has shown that schizophrenia is a complex psychiatric disorder characterized by impaired fronto-parietal, fronto-striatal, fronto-limbic and frontal-temporal networks (Delvecchio, Sugranyes, & Frangou 2013; Minzenberg, Laird, Thelen, Carter, & Glahn., 2009; Ragland, Laird, Ranganath,

Blumenfeld, Gonzales, & Glahn, 2009; Sugranyes, Kyriakopoulos, Corrigall, Taylor, & Frangou, 2011; Van Snellenberg, Torres, & Thornton, 2006) (Table 2).

Cannabis and psychosis outcomes

The administration of delta-9-hydrocannabinol (Δ^9-THC the main psychoactive agent of cannabis) to healthy subjects has been shown to consistently produce positive-like and negative-like symptoms, as well as disorganized thinking (D'Souza, Perry, MacDougall, Ammerman, Cooper, Wu, Braley, Gueorguieva, Krystal, 2004); therefore reproducing the complex phenomenology of schizophrenia. Similarly, in some individuals, it has also been observed that cannabis can induce a transient psychotic disorder mimicking the positive symptoms of schizophrenia. The psycho-mimetic effects of cannabis has led some authors to propose that cannabis may be a risk factor for psychosis, an idea that was first substantiated by the classic study from Andreasson, Engström, Allebeck, and Rydberg (1987) among 45 570 conscripts from the Swedish army. Since then, better controlled studies have been performed, which have provided substantial evidence that cannabis smoking is associated with a 2- to 3-fold increase in psychotic symptoms or schizophrenia-spectrum diagnoses (Moore, Zammit, Lingford-Hughes, Barnes, Jones, Burke, & Lewis, 2007). The magnitude of the relationship between cannabis smoking and psychosis outcomes seems to be dose-dependent and to be influenced by age of cannabis smoking initiation, traumatic experiences, premorbid psychosis vulnerability and genetic factors (Gage, Zammit, & Hickman, 2013).

In individuals diagnosed with schizophrenia, the risk of compulsive cannabis smoking is increased by 3 to 6, compared to the general population. A recent meta-analysis of 35 studies reported that the current rate of cannabis use disorder is 16% and the lifetime rate is 27.1% in this

population (Koskinen, Löhönen, Koponen, Isohanni, & Miettunen, 2010). Cannabis smoking negatively interferes with the course and treatment of schizophrenia, as it is associated with higher rates of hospitalizations, more severe positive symptoms, non-compliance, and more suicide attempts (Bourque, Mendrek, Durand, Lakis, Lipp, Stip, Lalonde, Grignon, & Potvin, 2013). Finally, based on 80 studies, it has been shown that cannabis smoking is associated with an earlier age of psychosis onset (~2 years), after controlling for the influence of sex, smoking chronicity and other psycho-active substances (Myles, Newall, Nielssen, & Large, 2012). Though no firm inference can be made on causality based on cross-sectional studies, these results raise the possibility that, in vulnerable people, cannabis smoking is a powerful trigger of psychosis.

The cognitive effects of cannabis in non-psychosis individuals

In non-psychiatric smokers, intoxication with cannabis or Δ^9-THC has been consistently shown to impair working memory, executive functions, attention and episodic memory (Crean, Crane, & Mason, 2011). The residual cognitive effects of cannabis use have also been studied. While the short-term abstinence from cannabis is associated with small-to-moderate deficits in episodic memory, executive functions and attention, the magnitude of the long-term residual cognitive effects of cannabis smoking remains unclear (Crean et al., 2011). Study results seem influenced by the quantities of cannabis smoked by participants as well as the length of abstinence. While some studies have shown that it usually takes about 28 days of abstinence from cannabis smoking to recover one's cognitive abilities, others have reported that certain cognitive deficits may last longer. The magnitude of the cognitive effects of cannabis may also be influenced by earlier age of smoking initiation, as shown in a 25-year cohort study involving 1037 subjects (Meier, Caspi, Ambler, Harrington, Houts, Keefe, McDonald, Ward, Poulton, & Moffitt, 2012).

Neuro-imaging studies performed on individuals without psychiatric disorders have shown that acute Δ^9-THC intoxication and chronic cannabis smoking both produce neuro-functional alterations echoing the neurophysiologic disturbances seen in schizophrenia (Bossong, Jansma, Bhattacharyya, & Ramsey, 2014). Indeed, cannabinoids have been shown to disrupt working memory-related activity in dorso-lateral prefrontal and parietal cortices; to impair amygdala reactivity during the viewing of fearful or angry faces; to alter the functioning of frontal and striatal regions during response inhibition tasks; and finally, to disrupt prefrontal and medial temporal regions during episodic memory tasks. Regardless of heterogeneity of results, cannabinoids seem to reproduce (at least, partially) the fronto-parietal, fronto-striatal, fronto-limbic and frontal-temporal alterations observed in schizophrenia (Table 2).

Cognitive performance in cannabis-using patients with schizophrenia

Considering the (mild) cognitive impairments associated with cannabis smoking, the logical expectation would be that schizophrenia patients who smoke cannabis (Sz+Can) would have more prominent cognitive deficits, compared to schizophrenia patients who do not smoke cannabis (Sz). More than 20 studies have been performed on the topic, and surprisingly, most of them have shown the opposite, namely that Sz+Can patients have *fewer* cognitive deficits than Sz patients (Table 3). It must be mentioned, however, that results have been inconsistent across studies, with a minority of studies showing that Sz+Can patients have *more* cognitive deficits than Sz patients, while others failed to show between-group differences (Table 3). Theoretically, this heterogeneity of results may reflect the heterogeneity of the recruited samples (schizophrenia, schizo-affective disorder and/or psychotic disorders), as well as the heterogeneous definitions of cannabis smoking status (use, heavy use, abuse, dependence; lifetime, current) (Table 3). However, the paradoxical cognitive performance of Sz+Can patients

has been observed in various studies, regardless of diagnosis type and of cannabis use frequency (Table 3).

In view of the diversity of results, systematic quantitative reviews have been performed (Table 4). Two of them focused solely on cannabis (Rabin, Zakzanis, George, 2011; Yücel, Bora, Lubman, Solowij, Brewer, Cotton, Conus, Takagi, Fornito, Wood, McGorry, & Pantelis, 2010), and both showed that cannabis smoking is associated with better cognitive functioning (e.g. attention, planning, speed of processing, visual memory and visuo-spatial abilities) in schizophrenia. Both reviews revealed between-group differences in the small-to-moderate range.

Interestingly, two meta-analyses examined the effects of other psycho-active substances on cognition in schizophrenia, which showed that the better cognitive performance of substance-using schizophrenia patients is mostly related to cannabis. In a meta-analysis of 23 studies, Potvin, Joyal, Pelletier, and Stip (2008) showed that substance-using patients had faster speed of processing, regardless of the substance used. Secondary analyses revealed that alcohol was associated with increased deficits in working memory; cocaine, with contradictory findings; and cannabis, with better global cognition. A subsequent meta-analysis from Donoghue and Doody (2012) showed that cannabis smoking is associated with better cognition in schizophrenia, and that cocaine use/abuse is associated with small-to-moderate impairments in verbal memory. Overall, the evidence suggests that alcohol and cocaine compromise cognition in schizophrenia, whereas cannabis is associated with better cognition. Noteworthy, a meta-regression analysis performed by Potvin et al. (2008) showed that there is a negative relationship between age and cognition in substance-using schizophrenia patients. That is, older substance-using schizophrenia patients (>30 years) have worse cognitive functioning than schizophrenia-only patients, whereas

younger substance-using schizophrenia patients have better cognition than schizophrenia-only patients. In these studies, older schizophrenia patients tended to prefer alcohol, whereas younger ones preferred cannabis. These results suggest that age X substance type interactions may explain heterogeneity in findings across studies.

Schizophrenia, cannabis and cognition: The functional imaging studies

Despite the wide interest in the psychosis-cannabis link, only six functional imaging studies have been performed in Sz+Can patients (Table 5). In the first two functional magnetic resonance imaging (fMRI) studies performed in schizophrenia patients with SUD, negative emotional stimuli were shown to patients while in the scanner (Mancini-Marië, Potvin, Fahim, Mensour, Beauregard, Roy, & Stip, 2006; Potvin, Mancini-Marië, Fahim, Mensour, & Stip, 2007). In both studies, schizophrenia patients with SUD had stronger emotional reactions than Sz patients, which translated into increased activations in the medial prefrontal cortex, which plays a critical role in self-relevancy processes. Unfortunately, both studies involved schizophrenia patients who abused both cannabis *and* alcohol. Moreover, the study lacked a control group, making it difficult to determine the exact meaning of the increased activations of the medial prefrontal cortex found in the substance-abusing group. Subsequently, Loberg, Nygard, Berle, Johnsen, Kroken, Jorgensen, and Hugdahl (2012) performed an fMRI study examining the neural correlates of attention in schizophrenia patients with and without lifetime cannabis smoking. The study showed that Sz+Can patients had increased activations in the posterior cingulate gyrus, the inferior parietal gyrus and the precentral gyrus, compared to Sz patients. Again, the lack of a control group made it difficult to determine if Sz patients had hypo-activations or if Sz+Can patients actually had hyper-activations during the task. Recently, our group performed 2 fMRI experiments in 14 Sz+Can patients, 14 Sz patients and 21 healthy volunteers. Patients with

schizo-affective or schizophreniform disorders were excluded, as well as those receiving antidepressants, and those who abused other psychoactive substances than cannabis. In a first experiment, participants performed an emotional memory task. At the cognitive level, Sz+Can patients had a better mnesic performance than Sz patients, but a poorer performance than healthy controls. Neurally, both patient groups had hypo-activations compared to controls again with Sz+Can patients showing more activation than Sz patients for both negative and positive stimuli (Figure 1 and 2). However, Sz+Can patients had increased activations in the dorso-lateral prefrontal cortex, compared to Sz patients (Bourque et al., 2013). In a second experiment, participants performed a mental rotation task, which measures visuo-spatial abilities. Although both patient groups performed worse than controls on the mental rotation task, Sz patients had decreased activations in the superior parietal gyrus, whereas the functioning of this region was normal in Sz+Can patients (Potvin, Bourque, Durand, Lipp, Lalonde, Stip, Grignon, Mendrek, 2013). Taken together, these preliminary fMRI results *tentatively* suggest that the brain functioning of Sz+Can patients is less impaired than that of Sz patients.

Explanatory models

To explain these seemingly paradoxical results, three main models have been proposed: the neuro-protection hypothesis, the social hypothesis and the hypothesis of a lower vulnerability to psychosis in Sz+Can patients. Whereas the first hypothesis postulates that the better cognition of Sz+Can patients is caused by cannabis smoking, the latter two hypotheses propose, on the contrary, that the better cognitive performance of some Sz patients is primary, not secondary, to cannabis smoking.

A. The neuro-protection hypothesis

The first model trying to explain these seemingly paradoxical findings is a neurobiological one. In pre-clinical studies, it has been shown that cannabinoids have anti-inflammatory, anti-oxydant and neuro-protective effects, and that the endo-cannabinoid system (Pertwee, 2005), which mediates the effects of cannabis in the brain, is critically involved in various neuro-developmental processes (neuronal specification, axonal elongation and synaptogenesis) (Sarne & Mechoulam, 2005). Thus, it can be hypothesized that cannabis may improve cognition in schizophrenia due to its neuro-protective properties. Although intriguing, this hypothesis seems unlikely, for 3 main reasons. First of all, cannabinoids produce cognitive impairments, not cognitive enhancement effects, in individuals who do not suffer from psychiatric disorders. Moreover, functional imaging studies have shown that cannabinoids produce brain alterations similar to those seen in schizophrenia patients performing executive or memory tasks. Finally, D'Souza et al. (2004) and D'Souza, Abi-Saab, Madonick, Forselius-Bielen, Doersch, Braley, Gueorguieva, Cooper, & Krystal, 2005 administered Δ^9-THC to healthy participants and to schizophrenia patients, and found that Δ^9-THC impaired verbal memory, attention, verbal fluency and working memory in healthy participants, and that it impaired verbal memory and attention in schizophrenia patients. More importantly, the trial showed that the amnesic effects of Δ^9-THC were more pronounced in schizophrenia patients than in controls. These results suggest that acute Δ^9-THC intoxication has more deleterious cognitive effects in schizophrenia than it does in non-psychiatric individuals. Such results are inconsistent with the notion that cannabinoids may improve cognitive performance in schizophrenia.

B. The social hypothesis

An alternative hypothesis proposes that the better cognitive performance of Sz+Can patients has to do with the set of skills required to sustain the lifestyle of substance use. In order to get substances, the user needs to be able to manage money, to make contacts with dealers and to strike deals which means that minimally, intact relational, emotional and cognitive abilities are required. According to this alterative hypothesis, first proposed by Mueser, Yarnold, Rosenberg, Swett, Miles, and Hill (2000), the better cognitive performance of Sz+patients would not be the result from the pharmacological effects of cannabis, but would rather reflect a difference *primary* to cannabis use / abuse. One of the main implications of this hypothesis is that cognitive results should vary based on the difficulty to access the substance. According to this hypothesis, Sz+Can patients should perform cognitively better than Sz patients in countries where cannabis is illegal or less common, but not in countries where cannabis smoking has been prevalent for many years. However, two main criticisms can be raised against this hypothesis. First, cannabis is now a substance easily accessible in many Western countries, regardless of its legal status (Schnell, Koethe, Daumann, & Gouzoulis-Mayfrank, 2009). Second, although cocaine is a psycho-active substance harder to access than cannabis, it is cannabis smoking which is associated with better cognition in schizophrenia, not cocaine use.

C. The lower vulnerability hypothesis

A final hypothesis proposes that the relatively better cognition of Sz+Can patients reflects a lower vulnerability to psychosis (Schnell et al., 2009). According to this hypothesis, the paradoxical performance of Sz+Can patients has to be interpreted in light of the studies showing that cannabis smoking is a risk factor for psychosis outcomes (Moore et al., 2007). As explained by Schnell et al. (2009), one of the plausible implications of the literature showing that cannabis

increases the risk for psychosis is that Sz+Can patients might have not developed schizophrenia had they not regularly smoked cannabis. From a developmental perspective, the vulnerability to psychosis, during the prodromal phase, may be lower in Sz+Can patients than it is in Sz patients, who go on to develop schizophrenia in the absence of the effects of cannabis. If so, we would expect Sz+Can patients to have milder deficits on core features of schizophrenia, such as cognitive impairments, especially during the early phase of the disorder.

As in the case of the social hypothesis, the lower vulnerability hypothesis assumes that the paradoxial cognitive performance of Sz+Can patients reflects a difference primary, not secondary, to cannabis use / abuse in schizophrenia. Obviously, only longitudinal studies performed in adolescents, before the onset of the disorder, could resolve this critical issue. Meanwhile, Ferraro, Russo, O'Connor, D.R.Wiffen, Falcone, Sideli, Gardner-Sood, Stilo, Trotta, Dazzan, Mondelli, Taylor, Friedman, Sallis, Cascia, Barbera, David, Reichenberg, Murray, & Forti, (2013) have shown that Sz+Can patients have higher premorbid IQ than Sz patients, which raises the possibility that the better cognitive performance of Sz+Can patients is explained by this premorbid difference.

Study limitations

Although the current state of the literature suggests that Sz+Can patients have better cognitive functioning than Sz patients, it is important to keep in mind that group differences are not of a large magnitude. Additionally, the literature is plagued with limitations that will need to be addressed before concluding that it is a proven fact that cannabis smoking is associated with better cognition in schizophrenia. Thus far, most studies in the field have measured a limited number of cognitive functions that do not cover the whole range of cognitive dysfunctions

associated with schizophrenia. Importantly, only a few studies have measured socio-cognitive variables in Sz+Can patients, although social cognition deficits significantly impede upon recovery and rehabilitation in schizophrenia. Similarly, only a few studies have measured inferior executive functions in Sz+Can patients, although deficits in emotional decision-making, risk-taking, response inhibition and delay discounting are core features of SUD (Potvin, Stavro, Rizkallah, Pelletier, 2014; Stavro, Pelletier, Potvin, 2013). A notable exception is the study from Mata, Rodríguez-Sánchez, Pelayo-Terán, Pérez-Iglesias, González-Blanch, Ramírez-Bonilla, Martínez-García, Vázquez-Barquero, and Crespo-Facorro (2008), which measured emotional decision-making, and found that cannabis smoking in schizophrenia was associated with poorer performance.

Another limitation of the literature is that the grouping of Sz patients into cannabis smokers and non-smokers has relied, most of the time, on self-report, and that smoking status has not been confirmed by urine drug analyses. Moreover, the quantities of cannabis smoked by patients have not been measured in most studies, and insufficient attention has been paid to the potential influence of other psychoactive substances. Deficits in attention, episodic memory, executive functions and speed of processing have been consistently observed in non-psychiatric individuals with alcohol use and cocaine use disorders (Potvin et al., 2014; Stavro et al., 2013). In addition, alcohol use disorders have been shown to exacerbate the cognitive deficits of schizophrenia, while cocaine intake has been associated with mixed findings. As a result, the unreliable measurement of those substances, in either Sz+Can or Sz patients, may significantly confound results.

Socio-demographic variables may also have influenced study outcomes. For instance, in close to 50% of studies, the Sz+Can group had an elevated male-to-female ratio compared to the Sz group (see Table 3). Theoretically, this between-group difference may explain some of the discrepancies in results, since there are subtle effects of sex-differences on cognition in schizophrenia (Mendrek & Stip, 2011). Similarly, in close to 50% of studies, Sz+Can patients were younger than Sz patients (see Table 3). Theoretically, it may be hypothesized that Sz+Can patients outperform Sz patients simply because they are younger. Although very plausible, both explanations do not necessarily rule out the presence of a real difference between Sz patients with and without cannabis smoking. Indeed, a better performance of Sz+Can patients, compared to Sz patients, has been found in studies in which the sex ratio did not differ between groups, as well as in studies in which Sz+Can patients were not younger than Sz patients (see Table 3).

Arguably, one of the main limitations of the literature on the cognitive effects of cannabis smoking in schizophrenia is that all studies have employed cross-sectional design thus far. While attempts at controlling for premorbid functioning have improved the methodological quality of studies, these attempts are not sufficient to paint a clear picture of the effect of cannabis on cognition in schizophrenia. Ideally, longitudinal studies initiated in adolescence until early adulthood in individuals with and without psychotic vulnerability, with and without cannabis smoking, would be required. However, given the low prevalence of schizophrenia, such studies would require very large sample sizes that could possibly compromise feasibility. In the meantime, it would be highly needed to perform longitudinal studies in first-episode schizophrenia patients, with and without cannabis smoking, and to measure their cognitive performance both when they are smoking cannabis and after they stop. If the better cognitive performance of Sz+Can patients is not secondary to cannabis use, then, Sz+Can patients should

have better cognition then Sz patients not only when they are actively smoking, but also after they cease.

Conclusion

Cognitive dysfunctions are core features of schizophrenia, which significantly impede upon social and occupational functioning in these patients. A significant risk factor for psychosis, cannabis smoking is highly prevalent in schizophrenia. In non-psychosis individuals, cannabis smoking has been shown to impair cognition, and to alter the functioning of brain networks known to be impaired in schizophrenia. Paradoxically however, most studies performed in Sz+Can patients have shown that cannabis smoking is associated with better, not worse, cognition in schizophrenia. Due to the cross-sectional nature of studies, it remains to be determined if the better cognitive functioning of Sz+Can patients is primary or secondary to cannabis smoking. In the future, large-scaled longitudinal studies will need to be performed in psychosis-prone and schizophrenia patients who smoke cannabis.

Mini-dictionary

- ***Comorbid***: A disorder that co-occurs with another one is said to be comorbid
- ***Endo-phenotype***: Traits that are purported as having a genetic component
- ***Mnesic***: Pertaining to memory
- ***Negative symptoms***: Deficient emotional and behavioral responses that are normally present in individuals from the general population. Example: amotivation
- ***Neuro-cognition***: Includes speed of processing, attention/vigilance, working memory, verbal and visual learning, as well as reasoning and problem solving

- ***Neuro-protection***: Refers to the preservation of functions and/or structures of the central nervous system
- ***Positive symptoms***: Ideas and perceptions that are not usually present in individuals from the general population, such as delusions and hallucinations (e.g. hearing voices)
- ***Prodromal***: Early symptoms preceding the onset of the disease
- ***Self-relevancy***: Something that has strong implications for an individual
- ***Socio-cognition***: Refers to how people apply, store and apply social information. Includes social knowledge, emotion recognition, Theory of Mind, attribution style as well as emotion regulation

Key Facts of schizophrenia

- Schizophrenia is a severe psychiatric disorder characterized by positive and negative positive symptoms as well as disorganized thinking/behavior
- Schizophrenia is associated with high rates of hospitalizations, homelessness and unemployment
- The lifetime prevalence of substance use disorder in close to 50% of in schizophrenia
- The life expectancy of schizophrenia patients is 20% shorter than that of the general population
- 7-8% of schizophrenia patients will end their life by committing suicide

Key Facts of the endocannabinoid system

- The endogenous cannabinoid system is composed of (at least) two ligands (anandamide and 2-arachidonylglycerol)
- Endocannabinoids bind to (at least) two cannabinoid receptors (CB_1 and CB_2)

- CB_1 receptors are mostly found in the prefrontal cortex, basal ganglia, hippocampus, anterior cingulate cortex and cerebellum
- These brain regions are known to be dysfunctional in schizophrenia
- Δ^9-THC, the main psychoactive ingredient in cannabis, binds to CB_1 receptors

Summary Points

- Cognitive deficits are a hallmark of schizophrenia present in close to 80% of individuals
- Cognitive deficits are present at an early stage of the disorder
- In the general population, cannabis smoking is associated with a 2- to 3-fold increase in psychosis outcomes
- Cannabis smoking can trigger first episodes of psychosis in vulnerable individuals
- Cannabis use in healthy individuals causes small-to-moderate deficits in working memory, executive functions, attention and episodic memory
- In schizophrenia, cannabis smoking seems to be paradoxically associated with better cognition
- fMRI studies using cognitive and emotional stimuli have shown that schizophrenia patients using cannabis have increased prefrontal activity, relative to non-using schizophrenia patients
- Factors that may explain these paradoxical findings include the neuro-protective properties of cannabis, social factors related to the lifestyle of cannabis smoking and uncontrolled premorbid differences.
- Limitations: Most studies did not assess all the cognitive domains known to be impaired in schizophrenia, did not confirm self-reports of cannabis smoking with urine drug analyses,

did not take into account the potential confounding influence of socio-demographic variables, and did not use longitudinal designs

Title to all Figures:

Figure 1: Brain activation corresponding to recognition of negatively valenced images.

Figure 2: Brain activation corresponding to recognition of positively valenced images.

Legend to all Figures:

(Figure 1)

SCZ=Schizophrenia group without cannabis abuse. DD=Schizophrenia group with cannabis abuse. HC=Healthy controls. Adapted from Bourque et al. (2013) with permission from the Publishers.

(Figure 2)

SCZ=Schizophrenia group without cannabis abuse. DD=Schizophrenia group with cannabis abuse. HC=Healthy controls. Adapted from Bourque et al. (2013) with permission from the Publishers.

Title to all Tables:

Table 1: MATRICS cognitive domains and associated tests.

Table 2: Neuro-functional alterations in schizophrenia.

Table 3: Studies showing intact, better or worse cognition in schizophrenia patients who smoke cannabis.

Table 4: Systematic quantitative reviews on the cognitive effects of psycho-active substances in schizophrenia patients.

Table 5: Neuro-functional alterations in cannabis-using schizophrenia patients.

Legend to all Tables:

(Table 1)

This table includes all the cognitive domains of the MATRICS battery and the associated tests used to measure them.

(Table 2)

This table shows the brain regions known to function abnormally in schizophrenia patients performing various cognitive and emotional tasks.

(Table 3)

This table summarizes the studies reporting that patients with both schizophrenia and cannabis smoking have intact, better or worse cognition. The relevant cognitive domains are cited.

(Table 4)

This table summarizes the systematic reviews that investigated the effects of psychoactive-substances on the cognitive domains known to be impaired in schizophrenia.

(Table 5)

This table summarizes the results of the functional brain imaging studies performed in schizophrenia patients using cannabis

References

Andreasson, S., Engström, A., Allebeck, P., & Rydberg, U. (1987). Cannabis and schizophrenia A longitudinal study of swedish conscripts. *The Lancet*, *330* (8574), 1483-1486.

Bossong, M. G., Jansma, J. M., Bhattacharyya, S., & Ramsey, N. F. (2014). Role of the endocannabinoid system in brain functions relevant for schizophrenia: An overview of human challenge studies with cannabis or Δ 9-tetrahydrocannabinol (THC). *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *52*, 53-69.

Bourque, J., Mendrek, A., Durand, M., Lakis, N., Lipp, O., Stip, E., Lalonde, P., Grignon, S., & Potvin, S. (2013). Cannabis abuse is associated with better emotional memory in schizophrenia: A functional magnetic resonance imaging study. *Psychiatry Research: Neuroimaging*, *214* (1), 24-32.

Crean, R. D., Crane, N. A., & Mason, B. J. (2011). An evidence based review of acute and long-term effects of cannabis use on executive cognitive functions. *Journal of addiction medicine*, *5* (1), 1-15.

Delvecchio, G., Sugranyes, G., & Frangou, S. (2013). Evidence of diagnostic specificity in the neural correlates of facial affect processing in bipolar disorder and schizophrenia: a meta-analysis of functional imaging studies. *Psychological medicine*, *43* (03), 553-569.

Donoghue, K., & Doody, G. A. (2012). Effect of illegal substance use on cognitive function in individuals with a psychotic disorder, a review and meta-analysis. *Neuropsychology*, *26* (6), 785-801.

D'Souza, D. C., Perry, E., MacDougall, L., Ammerman, Y., Cooper, T., Wu, Y. T., Braley, G., Gueorguieva, R., Krystal, J. H. (2004). The psychotomimetic effects of intravenous delta-9-tetrahydrocannabinol in healthy individuals: implications for psychosis. *Neuropsychopharmacology, 29* (8), 1558-1572.

D'Souza, D. C, Abi-Saab, W. M., Madonick, S., Forselius-Bielen, K., Doersch, A., Braley, G., Gueorguieva, R., Cooper, T. B., & Krystal, J. H. (2005). Dela-9-Tetrahydrocannabinol effects in schizophrenia: Implications for cognition, psychosis, and addiction. *Biological Psychiatry, 57*, 594-608.

Ferraro, L., Russo, M., O'Connor, J., D.R.Wiffen, B., Falcone, M. A., Sideli, L., Gardner-Sood, P., Stilo, S., Trotta, A., Dazzan, P., Mondelli, V., Taylor, H., Friedman, B., Sallis, H., Cascia, C. L., Barbera, D. L., David, A. S., Reichenberg, A., Murray, R. M., & Forti, M. D. (2013). Cannabis users have higher premorbid IQ than other patients with first onset psychosis. *Schizophrenia Research, 150*, 129-135.

Gage, S. H., Zammit, S., & Hickman, M. (2013). Stronger evidence is needed before accepting that cannabis plays an important role in the aetiology of schizophrenia in the population. *F1000 medicine reports*, *5*.

Goldberg, T. E., David, A., Gold, J. M. (2011). Schizophrenia. (3rd ed.). Neurocognitive impairments in schizophrenia: their character and role in symptom formation. (pp. 142-162). Wiley-Blackwell, Oxford, UK.

Koskinen, J., Löhönen, J., Koponen, H., Isohanni, M., & Miettunen, J. (2009). Rate of cannabis use disorders in clinical samples of patients with schizophrenia: a meta-analysis. *Schizophrenia bulletin*, *36* (6), 1115-1130.

Loberg, E. M., Nygard, M., Berle,. J. O., Johnsen, E., Kroken, R. A., Jorgensen, H. A., & Hugdahl, K. (2012). An fMRI study of neuronal activation in schizophrenia patients with and without previous cannabis use. *Frontiers in Psychiatry,* 3 (94), 1-11.

Mancini-Marië, A., Potvin, S., Fahim, C., Mensour, B., Beauregard, M., Roy, J. Y., & Stip, E. (2006). Neural correlates of the affect regulation model in schizophrenia patients with a substance use history: a functional magnetic resonance imaging study. *Journal of Clinical Psychiatry, 67* (3), 342-350.

Mata, I., Rodríguez-Sánchez, J. M., Pelayo-Terán, J. M., Pérez-Iglesias, R., González-Blanch, C., Ramírez-Bonilla, M., Martínez-García, O., Vázquez-Barquero, J. L., & Crespo-Facorro, B. (2008). Cannabis abuse is associated with decision-making impairment among first-episode patients with schizophrenia-spectrum psychosis. *Psychological Medicine, 38*, 1257-1266.

Meier, M. H., Caspi, A., Ambler, A., Harrington, H., Houts, R., Keefe, R. S., McDonald, K., Ward, A., Poulton, R. & Moffitt, T. E. (2012). Persistent cannabis users show neuropsychological decline from childhood to midlife. *Proceedings of the National Academy of Sciences*, *109* (40), E2657-E2664.

Mendrek, A., & Stip, E. (2011). Sexual dimorphism in schizophrenia: is there a need for gender-based protocols? *Expert Review of Neurotherapeutics, 11* (7), 951-959.

Minzenberg, M. J., Laird, A. R., Thelen, S., Carter, C. S., & Glahn, D. C. (2009). Meta-analysis of 41 functional neuroimaging studies of executive function in schizophrenia. *Archives of general psychiatry*, *66* (8), 811-822.

Moore, T. H. M., Zammit, S., Lingford-Hughes, A., Barnes, T. R. E., Jones, P. B., Burke, M., & Lewis, G. (2007). Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *The Lancet, 370* (9584), 319-328.

Mueser, K. T., Yarnold, P. R., Rosenberg, S. D., Swett, C., Miles, K. M., & Hill, D. (2000). Substance use disorder in hospitalized severely mentally ill psychiatric patients: Prevalence, correlates, and subgroups. *Schizophrenia Bulletin*, *26* (1), 179–192.

Myles, N., Newall, H., Nielssen, O., & Large, M. (2012). The association between cannabis use and earlier age at onset of schizophrenia and other psychoses: meta-analysis of possible confounding factors. *Current pharmaceutical design*, *18* (32), 5055-5069.

Nuechterlein, K. H., Green, M. F., Kern, R. S., Baade, L. E., Barch, D. M., Cohen, J. D., Essock, S., Fenton, W. S., Frese, F. J., Gold, J. M., Goldberg, T., Heaton, R. K., Keefe, R. S. E., Kraemer, H., Mesholam-Gately, R., Seidman, L. J., Stover, E., Weinberger, D. R., Young, A. S., Zalcman, S., & Marder, S. R. (2008). The MATRICS Consensus Cognitive Battery, Part 1: Test selection, Reliability, and Validity. *American Journal of Psychiatry, 165* (2), 203-213.

Pertwee, R. G. (2005). Pharmacological actions of cannabinoids. *In Cannabinoids* (pp. 1-51). Springer Berlin Heidelberg.

Potvin, S., Stavro, K., Rizkallah, E., & Pelletier, J. (In Press). Cocaine and cognition: a systematic quantitative review. *Journal of Addiction Medicine*.

Potvin, S., Bourque, J., Durand, M., Lipp, O., Lalonde, P., Stip, E., Grignon, S., & Mendrek, A. (2013). The neural correlates of mental rotation abilities in cannabis-abusing patients with schizophrenia: a functional magnetic resonance imaging study. *Schizophrenia Research and Treatment,* Article ID 543842.

Potvin, S., Joyal, C. C., Pelletier, J., & Stip, E. (2008). Contradictory cognitive capacities in substance-abusing schizophrenia patients: a meta-analysis. *Schizophrenia Research, 100*, 242-251.

Potvin, S., Mancini-Marië, A., Fahim, C., Mensour, B., & Stip, E. (2007). A functional magnetic resonance imaging study of social emotion in schizophrenia patients with and without comorbid substance use disorder. *Social Neuroscience, 2* (2), 1-11.

Rabin, R. A., Zakzanis, K. K., & George, T. P. (2011). The effects of cannabis use on neurocognition in schizophrenia: a meta-analysis. *Schizophrenia Research, 128* (1-3), 111-116.

Ragland, J. D., Laird, A. R., Ranganath, C., Blumenfeld, R. S., Gonzales, S. M., & Glahn, D. C. (2009). Prefrontal activation deficits during episodic memory in schizophrenia. *American Journal of Psychiatry, 166* (8), 863-874.

Sarne, Y., & Mechoulam, R. (2005). Cannabinoids: between neuroprotection and neurotoxicity. *Current Drug Targets-CNS & Neurological Disorders*, *4* (6), 677-684.

Schnell, T., Koethe, D., Daumann, J., & Gouzoulis-Mayfrank, E. (2009). The role of cannabis in cognitive functioning of patients with schizophrenia. *Psychopharmacology, 205*, 45-52.

Stavro, K., Pelletier, J., & Potvin, S. (2013). Alcoholism has widespread and sustained effects on cognition: a meta-analysis. *Addiction Biology, 18* (2), 203-213.

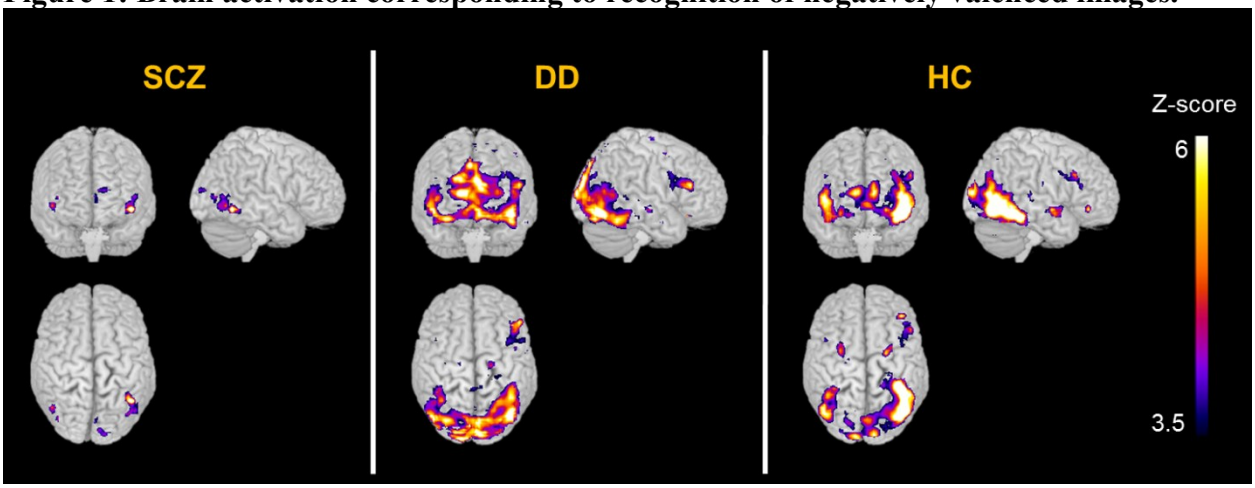
Sugranyes, G., Kyriakopoulos, M., Corrigall, R., Taylor, E., & Frangou, S. (2011). Autism spectrum disorders and schizophrenia: meta-analysis of the neural correlates of social cognition. *PloS one*, *6* (10), e25322.

Tandon, R., Keshavan, M. S., & Nasrallah, H. A. (2008a). Schizophrenia, "just the facts" what we know in 2008. Overview. *Schizophrenia Research*, *100* (1-3), 4-19.

Van Snellenberg, J. X., Torres, I. J., & Thornton, A. E. (2006). Functional neuroimaging of working memory in schizophrenia: task performance as a moderating variable. *Neuropsychology*, *20* (5), 497-510.

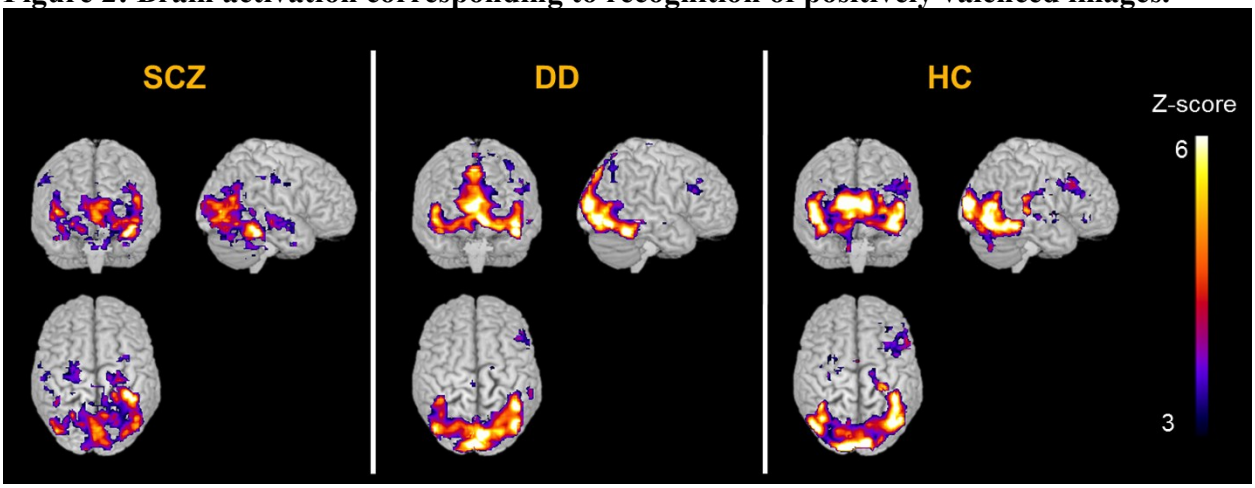
Yücel, M., Bora, E., Lubman, D. I., Solowij, N., Brewer, W. J., Cotton, S. M., Conus, P., Takagi, M. J., Fornito, A., Wood, S. J., McGorry, P. D., & Pantelis, C. (2010). The impact of cannabis use on cognitive functioning in patients with schizophrenia: A meta-analysis of existing findings and new data in a first-episode sample. *Schizophrenia Bulletin, 38* (2), 316-330.

Figure 1: Brain activation corresponding to recognition of negatively valenced images.



Legend to Figure 1. SCZ=Schizophrenia group without cannabis abuse. DD=Schizophrenia group with cannabis abuse. HC=Healthy controls. Adapted from Bourque et al. (2013) with permission from the Publishers.

Figure 2: Brain activation corresponding to recognition of positively valenced images.



Legend to Figure 2. SCZ=Schizophrenia group without cannabis abuse. DD=Schizophrenia group with cannabis abuse. HC=Healthy controls. Adapted from Bourque et al. (2013) with permission from the Publishers.

Table 1: MATRICS cognitive domains and associated tests.

Cognitive Domain	*MATRICS Test Beta-Battery*	*Most frequently used tests from 20 studies reported in Table* *
Speed of Processing	Category Fluency, animal naming	Groove Pegboard
	Trail Making Test (TMT)	CogState
	Wechsler Adult Intelligence Scale, 3rd ed. (WAIS-III), digit symbol-coding subtest	Rapid visual information processing from Cambridge Neuropsychological Test Automated Battery
	Brief Assessment of Cognition in Schizophrenia (BACS), symbol coding subtest	Forced-Choice Span of Apprehension Test
Attention/Vigilance	3–7 Continuous Performance Test, shortened version	Digit Span Test (forward version), from the WAIS-III
	Continuous Performance Test—Identical Pairs version	Spatial Span forward items of the Wechsler Memory Scale-III (WMS-III)
Working Memory	BACS, digit sequencing subtest	Bergen N-Back paradigm
	WAIS-III, letter-number sequencing Subtest	Working Memory–Mental Arithmetic test
	Letter-Number Span test	CPT Identical Pairs test
	Wechsler Memory Scale, 3rd ed.,	

	spatial span subtest	
	Spatial delayed response task	
Verbal Learning/Memory	Neuropsychological Assessment Battery, daily living memory subtest	Rey Auditory Verbal Learning Test
	Hopkins Verbal Learning Test—Revised, immediate recall	California Verbal Learning Task
		Controlled Oral Word Association Test
Visual Learning/Memory	Neuropsychological Assessment Battery, shape learning subtest	Spatial-delayed response test (SDR)
	Brief Visuospatial Memory Test—Revised	Pattern recognition memory from the Cambridge Neuropsychological Test Automated Battery
Reasoning and Problem Solving	WAIS-III, block design subtest	Wisconsin Card Sorting Test
	BACS, Tower of London subtest	Delis Kaplan Executive Functioning System
	Neuropsychological Assessment Battery, mazes subtest	Stroop Color Word Test
Social Cognition	Mayer-Salovey-Caruso Emotional Intelligence Test, perceiving emotions branch	Hinting Task for Theory of Mind
	Mayer-Salovey-Caruso Emotional	Degraded Facial Affect Recognition Task for Emotiona Recognition

	Intelligence Test, managing emotions branch	

Table 2: Neuro-functional alterations in schizophrenia

Cognitive function	Example(s) of task	Hypo-activations	Hyper-activations	References
Working memory	N-Back	*High working memory load* - dlPFC[a] - Parietal cortex	*Low working memory load* - dlPFC - Parietal cortex	Van Snellenberg et al., 2006
Executive functions	Stroop; Go/No-Go	- dl and vlPFC[b] - ACC[c] - Striatum	---	Minzenberg et al., 2009
Emotion processing	Angry / fearful faces (implicit or explicit processing)	- Amygdala - Para-hippoccampal gyrus - Fusiform gyrus - mPFC[d] - ACC - Insula	---	Delvecchio et al., 2013
Episodic memory (*encoding*)	Verbal / visual learning / memory	- dl and vlPFC	- Para-hippocampal gyrus - ACC - Medial temporal cortex	Ragland et al., 2009
Episodic memory (*retrieval*)	Verbal / visual learning / memory	- dl and vlPFC - Cortex cingulaire antérieur -Cortex temporal médian	- Para-hippocamcal gyrus	Ragland et al., 2009
Theory of mind	Judgment of mental states from pictures or eyes	- mPFC - Medial temporal cortex	---	Sugranyes et al., 2011

		- Thalamus		

[a]dlPFC= dorsolateral prefrontal cortex; [b]vlPFC = ventrolateral prefrontal cortex; [c]ACC= anterior cingulated cortex; [d]mPFC= medial prefrontal cortex;

Table 3: Studies showing intact, better or worse cognition in schizophrenia patients who smoke cannabis.

Authors	*N (cannabis only)*	*Mean age*	*Drugs assessed*	*Use Profile*	*Illness Profile*	*MATRICS Domaines*	*Main results*	*Confounding factors*
Bahorik , Newhill, & Eack, (2013)	974 (128)	39.21 (drug users)	Cannabis, cocaine and methampheta mine	Positive radioimmunoassay of hair for drug use.	SZ diagnosis according to DSM-IV criteria.	Reasoning/Problem Solving; Speed of processing; Verbal Learning/Memory; Vigilance	No between group differences (cannabis use vs. no drug use)	High male-to-female ratio in SZ+Can group
Coulston, Perdices, & Tennant, (2007)	52 (18)	26.4 (SZ)	Cannabis	DSM-IV criteria for lifetime cannabis abuse/dependence. "High" frequency: at least weekly or more frequent basis and "Medium" frequency: between two to four times per month.	Diagnosis of SZ or schizoaffective disorder according to DSM-IV criteria.	Attention; Speed of Processing; Reasoning/Problem Solving; Verbal Learning/Memory; Visual Learning/Memory	Better attention, reasoning and problem solving and speed of processing in DD patients.	
DeRosse, Kaplan, Burdick, Lencz, & Malhotra, (2010)	455 (175)	37.3	Cannabis	Cannabis use disorder (abuse/dependence).	SZ or schizoaffective disorder.	Verbal Learning/Memory; Speed of Processing;	Better speed of processing / verbal fluency and verbal memory in DD patients.	High male-to-female ratio in SZ+Can group

Authors	*N (cannabis only)*	*Mean age*	*Drugs assessed*	*Use Profile*	*Illness Profile*	*MATRICS Domaines*	*Main results*	*Confounding factors*
Ferraro et al., (2013)	119 (86)	29.6	Cannabis	Lifetime cannabis use (used at least once).	Affective psychosis and non-affective psychosis diagnosis according to ICD-10 criteria for psychosis.	Other: IQ	Higher current and premorbid IQ in psychotic patients who had smoked cannabis at least once.	High male-to-female ratio in SZ+Can group
Jockers-Scherübl et al., (2007)	39 (19)	27.7	Cannabis	Cannabis abuse defined as having consumed an average of ≥ 0.5 g/day of cannabis for a minimum of two years before the onset of the disorder. Substance use disorders, other than cannabis, were excluded.	SZ diagnosis according to DSM-IV criteria.	Verbal Learning/Memory; Attention; Visual Learning/Memory; Speed of Processing; Reasoning/Problem Solving; Other: Language abilities	Better language abilities and speed of processing in DD patients.	High male-to-female ratio in SZ+Can group Younger in SZ+Can group
Leeson, Harrison, Ron, Barnes, & Joyce, (2012)	99 (65)	23.4	Cannabis	High-frequency cannabis users (daily or almost daily use), and low-frequency cannabis users (1-2 days/ week to less than monthly). Substance misuse, other than cannabis, was excluded.	First psychotic episode.	Verbal Learning/Memory; Working Memory; Reasoning/Problem Solving	Better on all meausre for DD patients except on working memory.	Younger in SZ+Can group

Authors	*N (cannabis only)*	*Mean age*	*Drugs assessed*	*Use Profile*	*Illness Profile*	*MATRICS Domaines*	*Main results*	*Confounding factors*
Lev-Ran, Segev, Braw, & Levkovitz, (2012)	28 (12)	18-45 n/a	Cannabis	Cannabis dependence diagnosis according to DSM-IV criteria. Substance use, other than cannabis, was excluded.	SZ diagnosis according to DSM-IV criteria.	Attention; Visual Learning/Memory; Working Memory; Reasoning/Problem Solving	Worse sustained attention and speed of processing (shorter initial thinking time) in DD patients.	
Løberg et al., (2009)	29 (13)	n/a	Cannabis	Current substance use and former substance use.	Acute psychosis and SZ.	Attention; Reasoning/Problem Solving; Speed of Processing; Verbal Learning/Memory; Working Memory	Better attention, reasoning and problem solving, speed of processing, verbal memory and working memory in DD patients.	
Mata et al., (2007)	132 (61)	23.4	Cannabis	Cannabis abuse: at least weekly use of cannabis during the previous year. Drug dependence was excluded.	First episode of a schizophrenia-spectrum psychosis.	Verbal Learning/Memory; Speed of Processing; Working Memory; Reasoning/Problem Solving; Other: Decision-making & IQ	Worse decision-making in DD patients.	High male-to-female ratio in SZ+Can group Younger in SZ+Can group

Authors	*N (cannabis only)*	*Mean age*	*Drugs assessed*	*Use Profile*	*Illness Profile*	*MATRICS Domaines*	*Main results*	*Confounding factors*
Meijer et al., (2012)	956 (632)	27.3	Cannabis	Lifetime cannabis use and current use were included.	Non-affective psychosis.	Verbal Learning/Memory; Attention/Vigilance; Speed of Processing; Working Memory; Reasoning/Problem Solving; Social Cognition	Poorer performance on verbal learning, processing speed and working memory in patients with *current* cannabis use. Better performance on acquired knowledge, facial affect recognition and social cognition in patients with *lifetime* cannabis use.	High male-to-female ratio in SZ+Can group Younger in SZ+Can group
Rabin, Zakzanis, Daskalakis, & George, (2013)	58 (18)	31.6	Cannabis	Current or former cannabis dependence diagnosis according to DSM-IV criteria	SZ or schizoaffective disorder diagnosis according to DSM-IV criteria.	Attention; Speed of Processing; Visual Learning/Memory; Verbal Learning/Memory; Working Memory; Reasoning/Problem Solving	Better psychomotor speed in patients with lifetime cannabis dependence.	Younger in SZ+Can group

Authors	*N (cannabis only)*	*Mean age*	*Drugs assessed*	*Use Profile*	*Illness Profile*	*MATRICS Domaines*	*Main results*	*Confounding factors*
Ringen et al., (2010)	140 (23)	33.3	Cannabis	Cannabis abuse/dependency diagnosis according to DSM-IV criteria. Substance use other than cannabis in the previous 6 months was excluded.	SZ, schizophreniform disorder, or schizo-affective disorder diagnosis according to DSM-IV criteria.	Speed of Processing; Attention; Working Memory; Verbal Learning/Memory; Reasoning/Problem Solving	Worse reasoning and problem solving, verbal memory and working memory in DD patients.	
Ringen et al., (2013)	364 (57)	31.2	Cannabis	Lifetime DSM-IV diagnosis of cannabis abuse/addiction. Cannabis-positive urine group (n = 21) was compared to cannabis-negative urine group (n = 343).	SZ, schizophreniform disorder, and schizoaffective disorder diagnosis according to DSM-IV criteria.	Speed of Processing; Attention; Working Memory; Verbal Learning/Memory; Reasoning/Problem Solving; Other: IQ	No between-group differences after adjusting for premorbid functioning.	
Rodriguez-Sanchez et al., (2010)	104 (47)	23.6	Cannabis	Cannabis use: at least weekly use of cannabis during the previous year. Drug dependence was excluded.	First episode of non-affective psychosis.	Verbal Learning/Memory; Visual Learning/Memory; Speed of Processing; Working Memory; Attention; Reasoning/Problem Solving	Better speed of processing in DD patients.	High male-to-female ratio in SZ+Can group Younger in SZ+Can group

Authors	*N (cannabis only)*	*Mean age*	*Drugs assessed*	*Use Profile*	*Illness Profile*	*MATRICS Domaines*	*Main results*	*Confounding factors*
Sánchez-Torres et al., (2013)	42 (n/a)	37.02	Cannabis, alcohol, stimulants, other drugs (e.g. opioids) and tobacco use.	Lifetime cannabis use, excluding patients with a diagnosis of cannabis dependence.	SZ, schizoaffective disorder, psychotic mood disorder and brief psychotic disorder.	Speed of Processing; Attention/Vigilance ; Working Memory; Social Cognition; Reasoning/Problem Solving	Lifetime cannabis consumption was not associated with negative cognitive outcomes. Lifetime cannabis consumption was associated to a negative effect on performance in a social cognition task.	
Schnell, Koethe, Daumann, & Gouzoulis-Mayfrank, (2009)	69 (35)	27.1	Cannabis	Cannabis abuse/dependence diagnosis according to DSM-IV criteria. No additional substance use disorders, except for nicotine, were included.	SZ or schizoaffective disorder diagnosis according to DSM-IV criteria.	Verbal Learning/Memory; Working Memory; Visual Learning/Memory; Attention; Speed of Processing; Reasoning/Problem Solving; Other: IQ	Better speed of processing, verbal memory and working memory in DD patients.	

Authors	*N (cannabis only)*	*Mean age*	*Drugs assessed*	*Use Profile*	*Illness Profile*	*MATRICS Domaines*	*Main results*	*Confounding factors*
Scholes & Martin-Iverson, (2010)	71 (22)	35.8	Cannabis	Current use of cannabis.	SZ or schizo-affective disorder diagnosis.	Attention; Working Memory; Reasoning/Problem Solving	No between-group differences.	
Sevy et al., (2007)	27 (14)	29.0	Cannabis	Current DSM-IV diagnosis for cannabis abuse/dependence, and having cannabis as the main drug of choice.	SZ or schizoaffective disorder diagnosis according to DSM-IV criteria. Substance induced psychotic disorder was excluded.	Visual Learning/Memory; Working Memory; Attention; Verbal Learning/Memory; Speed of Processing	Better working memory in DD patients.	
Wobrock et al., (2013)	498 (115)	23.9 (drug users)	Cannabis, cocaine, amphetamine or other stimulants, heroin, XTC, LSD or other hallucinogens	Current or former substance use disorder (abuse/dependence) diagnosis according to DSM-IV criteria.	First episode of SZ, schizophreniform disorder, and schizoaffective disorder diagnosis according to DSM-IV criteria	Verbal Learning/Memory; Speed of Processing; Attention; Visual Learning/Memory; Other: Complex visual scanning	Better complex visual scanning and psychomotor speed and reasoning/problem solving (cognitive flexibility) with longer duration of cannabis use.	High male-to-female ratio in SZ+Can group Younger in SZ+Can group

Authors	*N (cannabis only)*	*Mean age*	*Drugs assessed*	*Use Profile*	*Illness Profile*	*MATRICS Domaines*	*Main results*	*Confounding factors*
Yücel et al., (2010)	85 (59)	20.7	Cannabis	Regular cannabis use (defined as >2 years of use and >2g/week).	First-episode psychosis.	Speed of Processing; Attention; Working Memory; Verbal Learning/Memory; Reasoning/Problem Solving	Better reasoning / problem solving and working memory in DD patients.	

[a] References.

Bahorik, A. L., Newhill, C. E., & Eack, S. M. (2013). Neurocognitive functioning of individuals with schizophrenia: Using and not using drugs. *Schizophrenia Bulletin*, 1-12.

Coulston, C. M., Perdices, M., & Tennant, C. C. (2007). The neuropsychological correlates of cannabis use in schizophrenia: Lifetime abuse/dependence, frequency of use, and recency of use. *Schizophrenia Research, 96*, 169-184.

DeRosse, P., Kaplan, A., Burdick, K. E., Lencz, T., & Malhotra, A. K. (2010). Cannabis use disorders in schizophrenia: Effects on cognition and symptoms. *Schizophrenia Research, 120*, 95-100.

Jockers-Scherübl, M. C., Wolf, T., Radzei, N., Schlattmann, P., Rentzsch, J., Castro, A. G.-C. d., & Kühl, K.-P. (2007). Cannabis induces different cognitive changes in schizophrenic patients and in healthy controls. *Neuro-Psychopharmacology & Biological Psychiatry, 31*, 1054-1063.

Leeson, V. C., Harrison, I., Ron, M. A., Barnes, T. R. E., & Joyce, E. M. (2012). The effect of cannabis use and cognitive reserve on age at onset and psychosis outcomes in first-episode schizophrenia. *Schizophrenia Bulletin, 38* (4), 873-880.

Lev-Ran, S., Segev, A., Braw, Y., & Levkovitz, Y. (2012). Neurocognitive functions of heavy cannabis using schizophrenia patients. *European Psychiatry, 27*, 365-368.

Løberg, E.-M., & Hugdahl, K. (2009). Cannabis use and cognition in schizophrenia *Frontiers in Human Neuroscience, 3*, 1-8.

Meijer, J. H., Dekker, N., Koeter, M. W., Quee, P. J., Beveren, N. J. M. v., & Meijer, C. J. (2012). Cannabis and cognitive performance in psychosis: a cross-sectional study in patients with non-affective psychotic illness and their unaffected siblings. *Psychological*

Medicine, 42, 705-716.

Rabin, R. A., Zakzanis, K. K., Daskalakis, Z. J., & George, T. P. (2013). Effects of cannabis use status on cognitive function, in males with schizophrenia. *Psychiatry Research, 206*, 158-165.

Ringen, P. A., Melle, I., Berg, A. O., Agartz, I., Spigset, O., Simonsen, C., Sundet, K., & Andreassen, O. A. (2013). Cannabis use and premorbid functioning as predictors of poorer neurocognition in schizophrenia spectrum disorder. *Schizophrenia Research, 143*, 84-89.

Ringen, P. A., Vaskinn, A., Sundet, K., Engh, J. A., Jónsdóttir, H., Simonsen, C., Friis, S., Opjordsmoen, S., Melle, I., & Andreassen, O. A. (2010). Opposite relationships between cannabis use and neurocognitive functioning in bipolar disorder and schizophrenia. *Psychological Medicine, 40*, 1337-1347.

Rodríguez-Sánchez, J. M., Ayesa-Arriola, R., Mata, I., Moreno-Calle, T., Perez-Iglesias, R., González-Blanch, C., Periañez, J. A., Vazquez-Barquero, J. L., & Crespo-Facorro, B. (2010). Cannabis use and cognitive functioning in first-episode schizophrenia patients. *Schizophrenia Research, 124*, 142-151.

Sánchez-Torres, A. M., Basterra, V., Rosa, A., Fañanás, L., Zarzuela, A., Ibáñez, B., Peralta, V., & Cuesta, M. J. (2013). Lifetime cannabis use and cognition in patients with schizophrenia spectrum disorders and their unaffected siblings. *European Archives of Psychiatry and Clinical Neurosciences, 263*, 643-653.

Scholes, K. E., & Martin-Iverson, M. T. (2010). Cannabis use and neuropsychological performance in healthy individuals and patients with schizophrenia. *Psychological Medicine, 40*, 1635-1646.

Sevy, S., Burdick, K. E., Visweswaraiah, H., Abdelmessih, S., Lukin, M., Yechiam, E., & Bechara, A. (2007). Iowa Gambling Task in schizophrenia: A review and new data in patients with schizophrenia and co-occurring cannabis use disorders. *Schizophrenia Research, 92*, 74-84.

Wobrock, T., Falkai, P., Schneider-Axmann, T., Hasan, A., Galderisi, S., Davidson, M., Kahn, R. S., Derks, E. M., Boter, H., Rybakowski, J. K., Libiger, J., Dollfus, S., López-Ibor, J. J., Peuskens, J., Hranov, L. G., Gaebel, W., & Fleischhacker, W. W. (2013). Comorbid substance abuse in first-episode schizophrenia: Effects on cognition and psychopathology in the EUFEST study. *Schizophrenia Research, 147*, 132-139.

Table 4: Systematic quantitative reviews on the cognitive effects of psycho-active substances in schizophrenia patients.

Authors	*Number of studies*	*Substances*	*MATRICS?*	*Main results*
Donohue & Doody, 2012	21	11 on poly-substance, 7 studies on cocaine, 3 on cannabis	No	<u>For poly-substance:</u> - Substance users performed better on verbal learning and memory, executive function, and attention and psychomotor speed, and worse on spatial working memory task than non-users <u>For cocaine:</u> - Cocaine users performed better on attention and psychomotor speed and worse on verbal learning and memory than non-users <u>For cannabis</u>: - Cannabis users performed better on executive function, attention and psychomotor speed, and verbal learning and memory than non-users
Potvin et al., 2008	28	Mixed psycho-active substances	Yes	Individuals with comorbid substance use had faster speed of processing Secondary analyses revealed significant associations with age and substance type
Rabin	8	Cannabis	No	Patients smoking cannabis were better in all domains assessed: general cognitive ability and intelligence, sustained and divided attention, executive abilities, working memory, learning, retrieval and recognition, receptive and expressive language abilities and visuo-spatial and constructional abilities
Yucel et al., 2012	10	Cannabis	Yes	Patients smoking cannabis had better processing speed, visual memory, working memory, executive functioning and sustained attention

Table 5: Neuro-functional alterations in cannabis-using schizophrenia patients.

Authors	Population	Task	Main results	Confounds / limitations
Bourque et al., 2013	21 healthy controls; 14 Sz[a] patients; 14 Sz patients with CUD[b]	Emotion recognition (positive and negative images)	- Better emotion recognition in cannabis-abusing Sz patients - Increased dlPFC[c] activations in the cannabis-abusing Sz patients, compared to non-using Sz patients	Lack of a group of non-psychosis cannabis abusers
Loberg et al., 2009	26 Sz patients; 13 cannabis users; 13 non-users	Audiroty dichotic listening task	- Increased activations of the PCC[d], the inferior parietal gyrus and the precentral gyrus in the cannabis-using group	Lack of a control group of healthy volunteers; lack of a group of non-psychosis cannabis users
Mancini-Marie et al., 2006	11 Sz patients; 12 Sz patients with SUD[e] (cannabis & alcohol)	Aversive emotional pictures	- Higher emotional ratings in substance abusing Sz patients; - Increased activations in the mPFC[f] in Sz patients with SUD	Sz patients were also abusing from alcohol; lack of a control group of healthy volunteers; lack of a group of non-psychosis cannabis users
Potvin et al., 2013	21 healthy controls; 14 Sz patients; 14 Sz patients with CUD	Mental rotation task	- Decreased activations of the superior parietal gyrus in Sc patients without CUD, compared to controls	Lack of a group of non-psychosis cannabis abusers

Potvin et al., 2007	11 Sz patients; 12 Sz patients with SUD (cannabis & alcohol)	Social emotions (sad movie clips)	- Higher emotional ratings in substance abusing Sz patients; - Increased activations in the mPFC	Sz patients were also abusing from alcohol; lack of a control group of healthy volunteers; lack of a group of non-psychosis cannabis users

[a]Sz: schizophrenia; [b]CUD: cannabis use disorder; [c]dlPFC: dorso-lateral prefrontal cortex; [d]PCC: posterior cingulate cortex; [e]SUD: substance use disorder; [f]mPFC: medial prefrontal cortex.

Chapter 4

A systematic review on improving cognition in schizophrenia: which is the more commonly used type of training, practice or strategy learning?

Karine Paquin, Alexa Larouche Wilson, Caroline Cellard, Tania Lecomte & Stéphane Potvin

Published in BMC Psychiatry, 2014

Paquin, K., Larouche Wilson, A., Cellard, C., Lecomte, T., & Potvin, S. (2014). A systematic review on improving cognition in schizophrenia: which is the more commonly used type of training, practice or strategy learning? *BMC Psychiatry,* 14(1), 139.

Abstract:

Background. The purpose of this article was to conduct a review of the type of trainings offered to people with schizophrenia in order to help them develop or compensate for neurocognitive or sociocognitive deficits. We examined the "drill and practice" type and the "drill and strategy" type to ascertain which type of trainings is more commonly used and the context of their use. **Methods.** We conducted a search of the literature using keywords such as "schizophrenia", "training", and "cognition" through the most popular databases of peer-reviewed journals. **Results.** We reviewed 99 controlled studies in total (though nine did not have a control condition). It was found that drill and practice trainings are used more often to retrain neurocognitive deficits while drill and strategy ones are used more frequently in the context of sociocognitive remediation. **Conclusions.** Hypotheses are suggested to better understand those results and future research is recommended to compare drill and strategy and drill and practice training with each other for both social and neurocognitive deficits in schizophrenia.

Keywords: schizophrenia, explicit, implicit, training, cognition, sociocognition, neurocognition

1. Introduction

About 80 % of individuals with a diagnosis of schizophrenia struggle with a variety of neuro and sociocognitive deficits (Meesters et al., 2010; Raffard, Gely-Nargeot, Capdevielle, Bayard, & Boulenger, 2009). From a neurocognitive point of view, speed of processing, attention/vigilance, working memory, verbal learning, reasoning and problem solving are the domains typically affected (Nuechterlein et al., 2008; Schaefer, Giangrande, Weinberger, & Dickinson, 2013); whereas sociocognitive domains include social cue perception, affect recognition, attribution, and theory of mind (Lecardeur et al., 2009; Wolfgang Wolwer & Nicole Frommann, 2011). Cognitive dysfunctions are considered to be core features of schizophrenia, being strongly correlated with poor functional outcome (Keefe et al., 2011; Kurtz, Seltzer, Shagan, Thime, & Wexler, 2007; Revheim et al., 2006) as well as being a better predictor of general outcome and rehabilitation than positive symptoms (Green, 1996; Lesh, Niendam, Minzenberg, & Carter, 2011). Although pharmacological and psychological treatments can effectively reduce (Susan R. McGurk, Twamley, Sitzer, McHugo, & Mueser, 2007) positive symptoms of schizophrenia, their effects are minimal on improving cognition (Keefe et al., 2011). Thus more and more attention has been directed toward using cognitive retraining or remediation, bringing about significant improvements (Franck, 2007; Keefe et al., 2011). According to Til Wykes, Huddy, Cellard, McGurk, and Czobor (2011), there are two types of trainings: 1) “drill and practice” where there is no explicit component, meaning that learning is based on repeating a task that becomes gradually more difficult and where participants learn implicitly the strategy by trial and error, and 2) “drill and strategy” where the focus is to teach an explicit use of a determined strategy (see also Susan R. McGurk et al., 2007). While explicit learning have been consistently reported in the schizophrenia literature (Aleman, Hijman, de

Haanm, & Kahn, 1999; Heinrichs & Zakzanis, 1998), there is still a great debate as to whether there are also impairments in implicit learning. For instance, some studies report that implicit learning is indeed intact where tasks like probabilistic classification learning (e.g. (Keri et al., 2000)), weather prediction (e.g. (Weickert et al., 2002)), and artificial grammar learning are concerned (e.g. (Danion, Meulemans, Kauffmann-Muller, & Vermaat, 2001)) while others report an impairment in colour pattern learning but not in letter string learning (Hsieh et al., 2004). Adding to this conundrum, there are also a variety of different training procedures (both for drill and strategy, which would refer to both explicit and implicit learning as well as for drill and practice, which would refer to implicit learning only) that are presently being tested. Furthermore, those trainings target a variety of different targets therefore, in this review, we will focus on both neurocognitive and sociocognitive domains. This means that all studies aiming solely to reduce positive or negative symptoms or to improve upon social skills, for instance, will not be included. Contrary to the recently published meta-analyses focusing on efficacy of cognitive trainings (Kurtz & Richardson, 2011; Til Wykes et al., 2011), this review aimed at analyzing and describing which training paradigms, whether it be drill and practice or drill and strategy in nature, were most utilized to improve upon neurocognitive and sociocognitive deficits.

2. Materials and methods

Selection criteria

Those were our inclusion criteria: 1) outcome: either neurocognition or sociocognition, 2) date and journal: peer-reviewed journals from 1995 up to 2013, 3) language: English or French, 4) diagnosis: majority (≥70%) of participants with a schizophrenia (others include schizoaffective

disorders and first-episode psychosis) . We excluded all that aimed solely at reducing positive or negative symptoms, improve social skills, increase metacognition etc. Nevertheless, studies that targeted sociocognition or neurocognition while also aiming to reduce symptoms or improve social skills as secondary objective, were included. We finally also removed from the selection all studies that did not use the training or remediation for treatment purposes but rather for evaluative purposes (i.e. studies that aimed at assessing the deficits at baseline with no intention of remediation or intervention) as well as meta-analyses and reviews. Indeed, our goal here was to review studies that have a therapeutic outcome. Since the main goal of our article is to provide a descriptive listing of trainings offered and not to conduct an efficacy analysis, we included studies that did not have control conditions. Given the large number of articles (e.g. 99) that were included in the end, and the fact that our definitions of the type of trainings were large, the first three authors read, classified, and compared their ratings for each article to ensure reliability of the results. Furthermore, we compared the results of our literature search with articles that are listed in the meta-analyses of Til Wykes et al. (2011), Grynszpan et al. (2011) as well as Medalia and Saperstein (2013) to ensure that we did not miss any of the relevant articles.

Article retrieval

We conducted a literature review in the following databases: PsychINFO (1995 to May 2013), MEDLINE (R) (1995 to May 2013) and MEDLINE Daily Update (R). Using the title keywords « schizophrenia and (training or remediation or intervention or practice) and (soci*[1] or neuro* or cogniti* or metacogniti* or problem-solving or visual or memory) » , we obtained 465 results in the different databases. To ensure further precision we added the following filters: a) « limit to English and French language » (to ensure the proper understanding of the content)

[1] * stands for truncation

which yielded 172 results, b) « limit to peer-reviewed journals » resulting in 164 results. The final manipulation was to remove all duplicates, which left us with a total of 121 articles to investigate. Upon final removal of all articles that did not meet our criteria, we ended up with 99 articles.

3. Results

Results are presented in Tables 1 to 3, divided according to the aim of the studies, whether it was to improve neurocognitive, sociocognitive deficits or both and also subdivided by either drill and practice or drill and strategy training methods. First, we will describe the studies that focus on a single area of cognition (i.e. Table 1 for neurocognition and Table 2 for sociocognition) as treatment targets and that used a single training type (drill and practice or drill and strategy). Then, we will describe the results of studies with multiple aims in terms of neuro and sociocognitive deficits (Table 3). There is an important distinction to be made between the targeted deficits – which is how we classified the studies between neurocognition, sociocognition, or both – and the measured variables. Indeed, it is often the case that a variable is measured to assess the impact of the training without having been specifically targeted by the training, which therefore gives a sense of the generalization of the results. As seen more explicitly in Table 2, a lot of the studies aiming at improvement of sociocognition also measure the impact of the training on more neurocognitive variables.

3.1 Neurocognitive deficits

A total of 49 studies pertaining to neurocognitive training were found. Of these, 46 included randomized controlled trials or placebo conditions, while three had no control at all. At first glance (see Table 1), it appears that drill and practice trainings are used more frequently to train

neurocognitive deficits (i.e.: drill and practice = 32 studies, 30 with controls and two without, drill and strategy = 17 studies, 16 with controls and one without) in people with schizophrenia. Examining the drill and strategy studies, a pattern rapidly emerges when the methods of training are considered. Nine of 17 studies utilize group therapy into their trainings as compared to individual computerized training with therapist assistance. However, there does not seem to be a link between the method of training (individual or in group) and the outcome measures. Though it is not the goal of our review, it is important to mention that all the articles with drill and strategy approaches to training reported between-group improvements of the targeted deficits. Furthermore, four of the 17 studies that had follow up measures at either three, four or six months also reported sustained gains in cognition (Blairy et al., 2008; Joanna M. Fiszdon, Bryson, Wexler, & Bell, 2004; Hodge et al., 2010; Poletti et al., 2010; Twamley, Savla, Zurhellen, Heaton, & Jeste, 2008).

For the drill and practice studies, computerized task done individually seem to be utilized the most. However, there seem to be more variety in the methods of training; for instance, at least five studies used pencil-and-paper procedures (Farreny et al., 2012; Kontis, Huddy, Reeder, Landau, & Wykes, 2013; Lopez-Luengo & Vazquez, 2003; Nemoto et al., 2009; R. Penades et al., 2013; though Lopez-Luengo utilized both pen-and-paper and audio) while five others used a combination of audio and visual tasks (M. Fisher, Holland, Merzenich, & Vinogradov, 2009; Melissa Fisher, Holland, Subramaniam, & Vinogradov, 2010; Popov, Rockstroch, Weisz, Elbert, & Miller, 2012; Rass et al., 2012; Surti, Corbera, Bell, & Wexler, 2011) to reduce the deficits. Furthermore, most studies using drill and practice methodologies report between-group improvements (all except Field, Galletly, Anderson, & Walker, 1997; Lopez-Luengo & Vazquez, 2003) on cognition, at least on some of the measures, between the experimental and the control

group.

Of note is the fact that a variety of neurocognitive deficits were targeted in these studies - memory, attention/vigilance, reasoning, verbal learning - and that overall, across studies, no single deficit stood out as being resistant to implicit training. Therefore, it would seem that most domains of neurocognition respond well to drill and practice training and even though only four studies had follow ups at six months (M. Bell, Bryson, & Wexler, 2003; Farreny et al., 2012; Melissa Fisher et al., 2010; Subramaniam et al., 2012), the gains were maintained.

3.2 Sociocognitive deficits

On the one hand and in contrast to studies focusing on neurocognition, those aiming to improve sociocognitive deficits use mostly drill and strategy approaches (i.e.: drill and practice = two studies with control groups; drill and strategy = 26 studies, 23 with controls and three without). Importantly, all studies included a variety of visual aids such as vignettes, Powerpoint presentations or videos of social situations. Furthermore, visual presentations and explanations by the therapist about the goal of the training were often done in group settings. This method allows modelling by the therapist but also incorporates group exercises and practice as well as role-plays. On the other hand, as was the case for studies on neurocognition, drill and strategy trainings in sociocognition seem to investigate the potential generalization of the benefits of the training on other variables that were not necessarily targeted by the training such as the improvement of social abilities and the resulting impact upon the quality of life of the participants.

Both drill and practice studies were conducted by Bell and colleagues with one study

(2005), one of their many follow-ups (others include M. Bell et al., 2003; M. Bell, Fiszdon, Greig, Wexler, & Bryson, 2007; Joanna M. Fiszdon et al., 2004; J.M. Fiszdon, Whelahan, Bryson, Wexler, & Bell, 2005) to their (2001) study which was initially aiming to improve neurocognition, furthering their research by investigating functional outcomes (i.e. work outcomes) with a neurocognitive enhancement training that had proven efficient to improve neurocognitive deficits.

3.3 Studies that aimed to improve both neuro and sociocognition

It is harder to find a pattern in the trainings when the targets deficits are broader and span across both neurocognitive domains like memory and attention to sociocognitive ones like social perception and emotion recognition. However, most use drill and strategy paradigms that generally combine computer-assisted programs for neurocognition and guided practice, modeling and role-play for sociocognition. There is also a mix of individualized and group approaches that seems again, to follow the trend that neurocognition is trained individually while sociocognition is trained in groups, and this is true for both drill and practice as well as drill and strategy.

4. Discussion

The purpose of this article was to conduct a review of the type of trainings – whether drill and practice or drill and strategy – most often offered to people with schizophrenia in the context of studies, in order to help overcome neurocognitive or sociocognitive deficits. We included articles of different scientific value – for both neurocognitive and sociocognitive trainings, i.e. three articles had no control condition and revised a total of 99 articles. However, since the main objective was not to present a thorough analysis of the efficacy or effectiveness of these trainings (see Grynszpan et al., 2011; Medalia & Saperstein, 2013; Til Wykes et al., 2011 for details), we

opted to include them for descriptive purposes. Moreover, there were a variety of training modalities offered, some more behavioral, some using computer trainings, real-life situations, indirect trainings, etc. Nevertheless, we were able to determine if a training paradigm, whether it was drill and practice or drill and strategy in nature, and which was used more frequently to improve neurocognitive or sociocognitive deficits. We also hoped to describe the patterns and modalities used to train the targeted deficits (i.e. neuro- or sociocognitive).

Upon exploration of the literature, we found that, for improving neurocognitive deficits, drill and practice training programs were used more frequently. Out of the 49 studies we reviewed, 32 of them used procedures that mostly involved errorless learning, a training involving the tasks' degree of difficulty increasing with the performance of the participant and where no conscious effort is necessary to improve. In the case of drill and strategy (i.e. 17), studies seem to be particularly interested in the impact the trainings might have on other variables outside of neurocognition, namely symptoms, quality of life and functioning for instance. This is not the case for the drill and practice approaches. Another difference is the fact that studies using drill and strategy trainings almost always have (i.e. 12) some sort of measure of executive functioning while it is not necessarily the case for drill and practice ones. However, no definite conclusions can be drawn as to whether one specific domain of neurocognition can be more easily retrained than another with drill and practice or drill and strategy procedures. Furthermore, most studies were of short duration and only a few had follow up measures (i.e. drill and strategy=4 (Blairy et al., 2008; Hodge et al., 2010; Poletti et al., 2010; Twamley et al., 2008), drill and practice=5 (M. Bell et al., 2003; Farreny et al., 2012; Melissa Fisher et al., 2010; Joanna M. Fiszdon et al., 2004; Subramaniam et al., 2012)). This could be improved upon on future

studies, since it is difficult in these circumstances to decide whether the observed effects are maintained over time or not.

When attempting to put the findings concerning neurocognitive deficits into context, we are left with a feeling of uncertainty. Why indeed, would drill and practice trainings be used more often to retrain neurocognitive deficits? Perhaps the answer lies in the way these functions come into play in our cognitive processes. Some domains like attention and speed of information processing for instance seem more implicit by nature – the bottom-up approach. We could posit that these functions are not used consciously and one might not need to inherently know 'how' to use the functions; instead one simply needs to perform the task repetitively and unconsciously. However, we need to consider that this might imply that drill and practice procedures would only work to improve upon neurocognitive deficits, which might not be the case, as judged by the results reported in recent meta-analysis (Grynszpan et al., 2011; Til Wykes et al., 2011). Furthermore, since implicit learning has been reported as being generally intact in schizophrenia (Wexler et al., 1997), some like Fisher and colleagues (2009) suggest that high levels of repetition (e.g.: more than 1,000 rehearsals) and keeping a high percentage of reward schedule (e.g.: 85%), will allow for neurological improvements. Yet, studies using drill and strategy procedures in their trainings also seem to generate consistent positive outcomes – the top-down approach. Of note, is the fact that Wykes and colleagues (2011) suggest that drill and strategy trainings include parts that are explicitly learned (through modeling, explanation or role-play for instance which refers to the strategy part) but also parts that are inevitably linked with repetition (i.e. drill part) and are considered implicit learning, which could potentially explain why they are also effective.

Tentatively, we suggest that since drill and strategy learning is described as allowing for better integration of the rules and thus greater associations between the various elements of the training (Yang & Li, 2012), changes in cognition tend to remain overtime. Indeed, Blairy and colleagues (2008) who also reported long-lasting improvements on memory and executive functions after explicit training, hypothesized that participants learned to bind different aspects of the experiment together and that it allowed for better consolidation in memory. Thus, at this point in time, no conclusion can be made regarding whether certain domains of neurocognition respond better to one training over another. Further studies need to be conducted, preferably comparing forms of trainings against each other and adding follow up measures to assess if the benefits of training remain stable through time.

Social cognition is considered by many researchers as holding a strong relationship with positive functional outcomes (Penn, Mueser, Doonan, & Nishith, 1995; Pinkham & D.L ??., 2006). Concurrently, in a meta-analysis by McGurk (2007) it was found that programs using strategy coaching (thus drill and strategy training) for sociocognitive deficits had strong effects on functional outcomes as well as on the targeted social cognition skills. Consistent with this, we found that drill and strategy training was more frequently used for sociocognitive retraining. It seems intuitive that learning and integrating a social skill would require that it be practiced in a social setting, which is what we found when analyzing the studies. Most used group settings, where participants received their training and were then allowed to actually perform and practice the learned techniques with a therapist present to correct the behavior and give feedback. Moreover, it was also reported that integrating a rehearsal portion to the trainings yields greater functional outcome improvements (Medalia & Saperstein, 2013). Indeed, sociocognitive studies tend to measure social functioning or social adjustment following training, more often then

studies aiming to improve upon neurocognitive deficits. Yet, there is a growing field around implicit learning in social cognitive psychology (Gawronski & Payne, 2010) suggesting that drill and practice or other forms of more implicit training might be useful for sociocognition as well.

As a matter of fact, Bell and colleagues work on work- and social-outcomes using drill and practice (M. Bell et al., 2005; M. D. Bell, Zito, Greig, & Wexler, 2008) hints at the importance of the generalization of the benefits of trainings to real-life situation such the ability to find and maintain work as well as to increase work productivity both in hours and in money earned. However, both those studied integrated their drill and strategy approach to a program of supported employment creating a hybrid retraining program which as been shown to be efficient in the past (Til Wykes et al., 2011). Indeed, while improving cognitive deficits in and of itself is commendable, functional outcomes are issues that should not be dismissed when considering how difficult it is for individuals suffering from schizophrenia to reintegrate the work force or create a social network.

Our review has also led us to realize that more often than not, training programs target cognitive improvements 'at large', not specifically focusing on individual deficits according to the person's profile, most likely in order to allow more people to receive the training without needing specific neuropsychological or sociocognitive evaluations. Tentatively, we suggest one might choose one training over another depending on the overall goal one is trying to achieve: drill and practice for precise deficits and drill and strategy to obtain general gains. More studies are warranted in order to determine if drill and practice could be useful for sociocognition as well.

Furthermore, it would seem that specific training methodologies benefit specific domains of social cognition. For instance, though it appears that Social Cognition and Interaction Training (even when including the family in the sessions of training) improves ToM, group practices and PowerPoint presentations detailing the concepts of ToM did not improve ToM but did improve emotion recognition. Tentatively, we propose that ToM is a more complex construct of sociocognition and it would require a more precise and detailed training than emotion recognition would. Indeed, Horan and colleagues (2009) suggest that even defining the different concepts contained within ToM such as appreciation of humour, is difficult and the training for it is this more challenging. Furthermore, a recent meta-analysis of social cognition trainings in schizophrenia (Kurtz & Richardson, 2011) also reported inconsistent effect sizes when ToM is targeted; suggesting that there is a need to better identify the key elements needed in the training for ToM .

When the objective of the trainings are broader, meaning that they are aiming to improve both neurocognitive and sociocognitive aspects through drill and strategy, measured variables are also more varied and more often than not, include a certain measure of functional or occupational outcome. Furthermore, these studies often tend to combine their trainings with other types of intervention such as cognitive-behavior therapy, supportive therapy or occupational therapy.

Overall, our review seems to give a good summary of the state of research concerning current cognitive trainings in schizophrenia. In neurocognition, drill and practice trainings seem to be used more frequently and with a variety of different formats in their procedures like auditory training (M. Fisher et al., 2009) or target discrimination (Norton, McBain, Ongur, & Chen, 2011). Tailor-fitting the trainings to aim for specific enhancements of precise deficits

might be one of the strong points of drill and practice trainings. However, from the studies we reported, drill and strategy training appears more easily generalizable to all neurocognitive deficits. Indeed, a recent meta-analysis on the benefits of cognitive remediation in schizophrenia, noted that this modality of training produces stable benefits of global cognition (Til Wykes et al., 2011). Tentatively, we suggest one might choose one training over another depending on the overall goal one is trying to achieve: drill and practice for precise deficits and drill and strategy to obtain general gains in neurocognition.

There are a few limitations to our review. First, to reflect current trends, we included only studies from 1995 until 2013 although interest in cognition remediation started as early as the end of the 1970's (Cromwell, 1975). Second, the fact that drill and practice or drill and strategy training can imply multiple strategies and training techniques (e.g.: times eye tracking, computer programs, paper-pencil tasks, errorless learning, group learning, and various modalities of feedback) did not allow us to describe them in detail and some of these specific strategies might greatly explain difference in outcomes. Our goal was to describe what was being offered, not to promote one approach in particular. We also did not include studies that were described as 'metacognitive', a term that involves cognitive biases, at times social and/or neurocognitive, that are linked to the symptoms of psychosis (Moritz, Veckenstedt, Randjbar, Vitzthum, & Woodward, 2011) – e.g. focusing on the cognitive bias of jumping to conclusions as linked to delusions. It is important to mention that trainings are not the only modalities offered to help overcome neurocognitive or sociocognitive deficits. Occupational therapy (Cook, Chambers, & Coleman, 2009), social skills training (Kopelowicz, Liberman, & Zarate, 2006), as well as certain forms of metacognitive psychotherapies (Lysaker et al., 2011) have also been documented. Future research is warranted to compare both drill and strategy and drill and practice programs

with one another in experimental conditions and against control conditions, as well as to highlight the benefits and limitations of each and help in identifying which type of deficit would benefit more from which training or in isolating participants' particular profiles that respond best to a specific training strategy. Moreover, we suggest that more effort be put in targeting specific deficits in participants and tailor-fitting the trainings to those needs in order to increase the potential impact and generalization to "real-life" situations, both in the context of neuro- and sociocognitive retraining. Finally, we propose investigating the benefits of neuro and sociocognitive trainings in the context of comorbidity. It is well know that schizophrenia is often comorbid with social anxiety (in 30% of cases; Kingsep, Nathan, & Castle, 2003) and substance abuse (in 50% of cases; Regier et al., 1990), to name only a few, and it is conceivable that the interplay of those disorders could be a substantial challenge for training. Nevertheless, few studies have examined the impact of these presentations and doing so would be of paramount importance as it could increase the ecological validity and generalizability of the results.

Table 1.

Trainings to improve neurocognitive deficits.

DRILL AND STRATEGY					
Authors	**Targeted deficits**	**Trainings**	**Measured variables**	**Results**	**Control and samples**
(Bark et al., 2003)	Memory and problems solving	CR and TAU	Psychiatric symptoms	Both CR groups improved on the Positive, negative and general psychopathology subscales but also on the Positive and Depression factors	Control group N=54
(Blairy et al., 2008)	Autobiographical memory	Group therapy and exercises to recollect specific events	Autobiographical memory, executive functioning	Improvements on the variable that were preserved after 3 months	Placebo group N = 27
(J.M. Fiszdon et al., 2005)	Psychiatric symptoms and cognition (episodic memory and attention)	NET + Work therapy and Verbal memory task based on a dichotic listening (DL) with distracter paradigm NET + Work therapy alone	Symptoms, attention and memory	Significant effect on memory but not in attention nor on symptoms	Control group N=125
(Gharaeipour & Scott, 2012)	Attention, memory and executive functioning	CR and group therapy	Verbal learning and memory, executive functioning, visual learning and memory, depression, positive and negative symptoms	Significant improvements in neuropsychological functioning, depression and negative symptoms of schizophrenia after CRT	Control group N = 42
(Hansen, Ostergaard, Nordentoft, & Hounsgaard, 2012)	Executive functioning	Cognitive Adaptation Training (CAT) applied to integrated treatment (IT) consisting of assertive community treatment (ACT)	Social functioning, symptoms and quality of life; executive functioning	Improve social functioning and compliance with IT and ACT. No solid evidence that demonstrates that IT improves when adding CAT	Control group N = 62

(Hodge et al., 2010)	Verbal and visual memory, sustained attention and executive functioning	CR with NEAR	Processing speed, executive functions, sustained attention, verbal memory, visual memory, reasoning/cognitive flexibility, social/occupational functioning, life skills, quality of life, self-esteem	Experimental group showed improvement on all variables, gains maintained after 4 months	Control group N = 40
(Ikezawa et al., 2012)	Verbal memory, working memory, motor speed, verbal fluency, attention, processing speed and executive functioning	CR with NEAR	verbalmemory,workingmemory,motor speed, verbal fluency, attention and speed of information processing executive functions	Improvement on all outcomes compared to control with CR	Control group N = 51
(Kidd, Bajwa, McKenzie, Ganguli, & Khamneh, 2012)	Neurocognition at large	Cognitive (CR) and supported education	Self-esteem, short term memory, verbal learning and memory, executive functioning, sustained attention, psychomotor speed, educational attainment	CR can be successfully integrated into an educational setting. Improvements in concentration , learning, some aspects of executive functioning, psychosis symptomatology	None N=16
(Lindenmayer et al., 2008)	Cognitive functioning in general	CR	Attention, psychomotor speed, verbal working memory, verbal learning and memory and executive functions, information processing speed, academic achievement	Cognitive remediation improvements in overall cognitive functioning, psychomotor speed, and verbal learning	Control group N=85
(Poletti et al., 2010)	Verbal and working memory, selective attention and semantic fluency	CR	Verbal and working memory, speed/coordination, selection attention, semantic and letter fluency, executive functions, sustained attention, interpersonal relations, instrumental role, self-directedness	3, 6 and months follow up: improvements in attention, psychomotor coordination, cognitive flexibility	Placebo condition N = 100
(Royer et al., 2012)	Memory and executive functioning	One program including 1) paper-and-pencil training 2) computer exercises	Visual attention, cognitive flexibility, sustained attention, inhibition, working memory, long-term verbal memory, executive function, planning	CR showed improvements in neuro- and socio-cognitive functions but not on arousal or cognitive flexibility	Placebo group N = 59
(Silverstein et al., 2005)	Attention	Attention Process Training (APT) and attention-shaping procedure after	Verbal learning, sustained attention	Dramatic improvement in attentiveness in APT but attention-shaping procedure appears to account for the change	Control group N = 31

(Spaulding, Reed, Sullivan, Richardson, & Weiler, 1999)	Social behavioral competence, neurocognition to generalize to social competence	Integrated Psychological Therapy (IPT), supportive therapy and TAU	Social competence, pre-attentional processing, attention, memory, executive functioning and symptoms	IPT improved social competence only	Control group N = 90
(Twamley et al., 2008)	Memory, attention, vigilance, executive functioning and secondary everyday functioning, level of community integration	CR alone or CR+pharmacotherapy	Attention, learning, memory, executive functioning, functional capacity, negative symptoms, subjective quality of life	CR improved verbal and visual memory at 3 months, not maintained at 6 months. Verbal learning, executive functioning and attention improved at 6 months. Quality of life improvements at 3 months, increased at 6 months	Control group N = 38
(Vauth et al., 2005)	Cognitive deficits and negative symptoms	Cognitive strategy training (CAST) and training of self-management skills for negative symptoms (TSSN)	Attention, verbal memory and planning, social withdrawal/social anhedonia, lack of drive, affect flattening	CAST=Greater improvement on attention and verbal memory but not planning ability. Higher job placement TSSN=no improvement in negative symptoms	Control group N= 138
(T. Wykes et al., 2007)	Cognitive difficulties	CR and TAU	Working Memory, cognitive flexibility, and planning, Secondary: self-esteem, positive and negative symptoms, social functioning	Improvement in working memory and cognitive flexibility, Memory improvement predicted improvement in social functioning.	Control Group N=85
(Til Wykes et al., 2007)	Memory, cognitive flexibility and planning	CR with remembering, complex planning, problem-solving and TAU	Memory, cognitive flexibility, planning, social behaviour, quality of life, self-esteem	CR improved cognitive flexibility, social functioning	Control group N = 40
DRILL AND PRACTICE					
(M. Bell et al., 2001)	Neurocognitive deficits	Neurocognitive enhancement therapy (NET) & working therapy (WT)	Cognitive flexibility, social inference, emotion recognition, abstract thought, verbal learning, memory	NET + WT greater improvements in executive functioning, working memory and affect recognition	Control group N=65
(M. Bell et al., 2003)	Working memory deficits	CR and working therapy (WT)	Attention, memory and executive function	CRT+WT yield greater improvements and effects remain over time (6 months)	Control group N = 102

(M. Bell et al., 2007)	Attention, memory and executive functioning	Neurocognitive enhancement therapy (NET) + Work therapy Work therapy alone	Working memory, verbal and nonverbal memory, thought disorder, executive function	Significant improvements on working memory and executive functioning. Both groups had a significant effect on memory (verbal and visual)	Control group N=145
(Belluci, Glaberman, & Haslam, 2002)	Neurocognition, negative symptoms, self-esteem	Computer-assisted cognitive rehabilitation (CACR)	Attentional deficit, verbal and auditory memory, general level of cognitive functioning, negative symptoms, self-esteem	CACR improved verbal/conceptual learning and memory and executive functioning	Placebo group N = 34
(Chan, Ngai, Leung, & Wong, 2009)	Repetition and memory	Virtual reality training	orientation, attention, calculations, constructions, memory, language, and reasoning	Improvement of overall cognition	Control group N = 27
(d'Amato et al., 2011)	Attention/concentration, working memory, logic, and executive functions	CR	Attention/vigilance, verbal/non-verbal working memory, verbal and visual learning and memory, speed of processing, reasoning, problem-solving, quality of life and social autonomy	Improvements in attention/vigilance, verbal memory, problem solving	Control group N = 77
(D'Souza et al., 2012)	Cognitive deficits	Pharmacotherapy and cognitive retraining (CR) together 1)drug+CR, 2) drug + control CR, 3)placebo + CR, 4) placebo+control CR	Verbal working memory, attention/vigilance Measures of tolerability and safety	CR- significant improvement in verbal working memory. Trend toward improvement in Attention/Vigilance	Control groups N = 104
(Farreny et al., 2012)	Executive functioning (and metacognition)	Problem Solving and Cognitive Flexibility training (REPYFLEC)	Verbal and visual memory. cognitive flexibility, inhibition of impulsive responses, planning and organization, working memory and time-estimation capacity, attention, processing speed and cognitive flexibility social behavior and relationships, autonomy, employment-occupation and leisure, self-care, social behavior and autonomy	Significant improvements in executive function, negative symptoms and Positive change in life skills and psychosocial functioning. Skills maintained at follow-up especially in self-care, social behavior and employment-occupation.	Control group N = 62

(Field et al., 1997)	Attentional deficit	Computer-Assisted cognitive rehabilitation or computer games	Various measures of attention suck as trail making, letter-cancellation, Stroop, seach-a-word, etc.	Both group improved on letter-cancellation task due to practice effect	Control group N = 10
(M. Fisher et al., 2009)	Verbal and global cognition	Auditory training	Global cognition, speed of processing, verbal memory/learning, problem-solving, nonverbal memory, visual learning/memory, social cognition	Strong improvement in verbal and global cognition	Placebo group N = 55
(Melissa Fisher et al., 2010)	Cognition in general	Targeted cognitive training (TCT)	Global cognition, speed of processing, verbal working and learning memory and cognitive control	TCT improvements in verbal learning/memory and cognitive control even 6 months after therapy	Control group N=32
(Joanna M. Fiszdon et al., 2004)	Cognitive deficits in memory	Computerized cognitive remediation training - digits sequenced recall and words sequenced recall (control: work therapy only)	Cognitive deficits, more specifically memory.	Significantly greater improvements on the computerized memory task (digits sequenced recall) remained at the 6 month follow up	Control group N = 94
(Habel et al., 2010)	Neural correlates of emotion identification	Training of Affect Recognition (TAR) and TAU	Emotion identification, emotion discrimination, digit symbol, digit span, symptoms, neural activation	TAR improved performance on emotion recognition and discrimination more than TAU and controls. Psychopathological status improvements for both TAR and TAU	Control group and healthy controls N = 30
(Kontis et al., 2013)	Effects of age on cognitive functioning	CR and TAU	Working memory, cognitive flexibility and planning. Groups split on age	CR improved working memory only in younger group	Control group N = 134
(Kurtz et al., 2007)	attention, memory, language and problem-solving	CR and computer-skills training	Working memory, verbal episodic memory, speed of processing, visual episodic memory, reasoning and problem-solving	CR improved working memory but both groups showed improvement on other measures	Placebo group N = 42
(Lopez-Luengo & Vazquez, 2003)	Cognitive functioning	Attention Process Training (APT)	Attention, memory and executive functioning Other: positive and negative symptoms	Neither group improved on symptoms and attention and memory measures. APT group had higher performance on executive function	Placebo group N = 24

(Medalia, Aluma, Tryon, & Merriam, 1998)	Attention and informatino processing	Continious Performance Test (CPT)	Attention and negative symptoms	CPT improved both measures	Control group N = 54
(Medalia, Revheim, & Casey, 2000)	memory	Memory remediation (MR), problem-solving remediation and TAU	Memory, verbal learning, problem-solving	MR improved memory but not verbal recall	Control group N = 54
(Medalia, Revheim, & Casey, 2001)	Problem-solving	Computer-assisted problem-solving remediation (PS), memory remediation or TAU	Problem-solving, memory, verbal knowledge, independent living	PS improved problem solving skills	Control group N = 54
(Murthy et al., 2012)	Cognitive impairment	Brain Fitness Program (BFP)	Cognitive performance (CogStat) Functional capacity, auditory processing speed for verbal and non-verbal tasks	BFP training improved auditory processing speed but no effect on cognitive impairments	None N = 55
(Nemoto et al., 2009)	Divergent thinking	Rock-paper-scissors task, calculation tiles task	Idea, design and letter fluency, digit span, social functioning	Improvements on idea fluency, functioning, and interpersonal relations	Control group N = 17
(Norton et al., 2011)	Visual motion processing	Target discrimination	Perceptual motion and direction processing	Greater perceptual improvement in schizophrenia	Healthy controls N = 27
(R. Penades et al., 2013)	Cognitive and daily functioning deficits (but concentrating on the neurobiological mechanism that underline them)	1) CR 2) Social Skills Training	Functional and structural connectivity brain changes	Brain networks activation pattern significantly changed in patients exposed to the cognitive treatment in the sense of normalizing toward the patterns observed in healthy control subjects	Control group N= 30
(Popov et al., 2011)	Dysfunctional organization of the auditory/verbal system	Targeted auditory/verbal discrimination Training (TAD) or CRT (CogPack)	Verbal learning and fluency, recall, working memory, clinical symptoms as exploratory measure	Improvement in verbal learning and memory for TAD but no effect on clinical symptoms	Control group N = 39

(Popov et al., 2012)	Brain oscillary activity, linked to dysfunctional information processing	Specific cognitive exercises (CE) fostering auditory/verbal discrimination or standard broad-range cognitive training (CP)	Verbal memory, global functioning, brain oscillary activity	CE improves brain oscillary activity and reduces information processing dysfunction	Control group and healthy controls N = 51
(Rass et al., 2012)	Verbal memory and learning, processing speed, working memory and attention	CR	Verbal memory, visual working memory, visuo-spatial memory, processing speed, psychomotor speed, working memory, verbal fluency, attention, visual-perceptual function	Patients in all groups improved on measures of information processing, verbal memory, and visuospatial memory	One placebo group and one control group N = 44
(Rauchenstein er et al., 2011)	Cognitive deficits	CR (Cogpack)	Memory functions, attention, concentration, logical abilities, verbal reasoning	Cogpack improves cognitive functioning in persons at risk. Specifically at risk group improve in long-term memory functions, attention, and concentration. Patients with schizophrenia no improvement.	Control group N =16 schizophrenia N= 10 at risk
(Rodewald et al., 2011)	Planning and problem-solving, processing speed, memory and attention	1) plan-a-day 2) training for basic cognition	Planning ability, problem-solving, global assessment, functional capacity, working memory, verbal memory, processing speed and inhibition	Both groups improved on measures of cognitive functioning and functional capacity. Plan-a-day improved planning	None N = 89
(Sartory, Zorn, Groetzinger, & Windgassen, 2005)	Verbal learning and processing speed	CR	Word fluency, memory and recall,	All outcomes improved in CR	Control group N = 42
(Subramania m et al., 2012)	Impairment in reality monitoring	CR	Reality monitoring Prefrontal cortex activity	Improvement in reality monitoring that correlated with increased medial prefrontal cortex activity (related to improvement in social functioning 6 months later)	Control group N= 31 (schizophrenia) N= 15 healthy controls
(Surti et al., 2011)	Visual and auditory learning	CR consisting of visual, auditory and cognitive control	Visual memory, visual-spatial memory, auditory verbal memory, verbal and letter learning	Visual training strongly predicts visual learning but not auditory learning	Placebo control N = 14

(Wexler et al., 1997)	Perceptual, memory and motor functions	Sustained and repeated training with no instructions, increasingly demanding tasks	Visual word, visual dot localization, motor processing	After training, most participants performed as well or better than best controls on tasks	Control group and healthy controls N = 22

Note. CR=cognitive remediation. NEAR= Neuropsychological Educational Approach to Remediation. TAU=treatment-as-usual.

Table 2.

Trainings to improve sociocognitive deficits.

DRILL AND STRATEGY					
Authors	**Targeted deficits**	**Type of trainings**	**Measured variables**	**Results**	**Control and samples**
(Choi & Kwon, 2006)	Social context appraisal	Social cognition enhancement training (SCET) and standard psychiatric rehab	Perceptual organization and sequencing in social contexts, emotion recognition	In SCET, some variables improved after 2 months, others after 6 months	Control group N = 34
(Combs et al., 2007)	Social cognition deficits	SCIT and Control: coping skills groups	Emotion and social perception, theory of mind, attributional style, cognitive flexibility, and social relationships	Improved on all socio-cogntive measures. Better self-reported social relationships	Control group N = 28
(Combs et al., 2009)	Emotion perception, attributional style, and theory of mind	SCIT and coping skills groups	Facial emotion identification and discrimination, social perception, theory of mind, attributional style and ambiguity, cognitive flexibility	Improvement on all aspects for participants in SCIT	Control group N = 18
(Corrigan, Hirschbeck, & Wolfe, 1995)	Social cue recognition	Vigilance+memory training or vigilance alone	Social cue recognition	Better recognition of social cues in vigilance+memory	Control group N = 40
(Eack, Hogarty, Greenwald, Hogarty, & Keshavan, 2007)	Emotional intelligence	Cognitive enhancement therapy (CET) and enriched supportive therapy(EST)	Emotional Intelligence	CET group improved in emotional intelligence more	Control group N=38
(Fuentes, Garcia, Ruiz, Soler, & Roder, 2007)	Learning and interpretation of social situations	Stimuli identification, interpretation of images and assignment of title	Sustained and selective attention, functional outcome, social perception	Improvement on all variables in therapy group, maintained at 6 months	Control group N = 18
(Garcia, Fuentes, Ruiz, Gallach, & Roder, 2003)	Perception and interpretation of social situations	Integrated Psychological Therapy (IPT)	Social perception, attention, psychopathology and social functioning	IPT improved social perception. No between group difference on attention or symptoms	Control group N = 20

(Hodel, Kern, & Brenner, 2004)	Emotion perception and functional outcome	Emotion Management Training (EMT) or problem-solving	Emotion perception in self and others, social adjustment, coping strategies, psychopathology	EMT improved emotion perception, social adjustment and psychopathology. At 4 month follow up, gains maintained in social adjustment and psychopathology only	Control group N = 22
(W. Horan et al., 2009)	Social cognitive skills	Presentations, group practice and training exercises	Facial emotion identification, social perception, attributional style, theory of mind, speed of processing, attention/vigilance, working memory, verbal and visual learning, reasoning, problem-solving and social cognition	Improvement in facial affect perception only	Control group N = 31
(W. P. Horan et al., 2011)	Social cognitive deficits	Socio-cognitive skills training (SCST) Other conditions 1: CR 2: standard illness management skills training, 3: Hybrid treatment that combined elements of SCST and neurocognitive remediation	Emotional processing, social perception, attributional bias, and mentalizing	The SCST group demonstrated greater improvements over time than comparison groups in the social cognitive domain of emotional processing, including improvement on measures of facial affect perception and emotion management.	Control Group N= 68
(Kayser, Sarfati, Besche, & Hardy-Bayle, 2006)	Theory of Mind (ToM)	Analyses and reasoning about social interaction scenes	ToM, symptoms, psychopathology, attribution	Slight improvement on ToM (not significant) in training group from first to second training session. No improvement on symptoms	Control group N = 14
(Kern et al., 2009)	Work outcomes	Errorless learning Conventional instruction	Work performance, job tenure, personal well-being (self-esteem, job satisfaction, work stress)	The patients in the errorless learning group performed better on work performance	Control group N=40
(Lindenmayer et al., 2012)	Emotion perception	CR and computerized Emotion Perception intervention compared with CR only	Emotion recognition, emotion discrimination, personal and social performance (also neurocognition)	Combined CR with emotion perception remediation produced greater improvements in emotion recognition, emotion discrimination, social functioning, and neurocognition	Control group N = 59

(Mazza et al., 2010)	Emotion recognition and ToM	Emotion and ToM Imitation Training and problem-solving	Psychopathology, symptoms, emotion recognition, ToM, neurocognition, flexibility, social functioning, attribution, neurophysiological activation	Training improved sociocognition (strongest was emotion recognition) and social functioning	Control group N = 32
(Marsh et al., 2013)	Social cognition	State reasoning training for social cognitive impairment (SOCog-MSRT)	Theory of mind, Social understanding, Inference of complex mental states from the eyes Working memory, IQ	Improvement in ability to reason causally about false beliefs, to infer complex mental states from the eyes, and to intuitively understand social situations However individuals with poorer working memory and lower premorbid IQ did not benefit	None N=14
(McGurk, Mueser, & Pascaris, 2005)	Work outcomes	Cognitive training (the Thinking Skills for Work Program) and supported Employment Supported employment only	Attention,psychomotor speed, information processing speed, verbal learning and memory, executive functioning, premorbid academic achievement, symptoms, Employment outcomes	Improvement on executive functioning and on a composite cognition score .They improved significantly more on Depression and Autistic preoccupation (symptoms). Client were significantly more likely to work, worked more hours, earned more wages	Control group N=44
(McGurk, Mueser, Feldman, Wolfe, & Pascaris, 2007)	Work outcomes	Cognitive training (the Thinking Skills for Work Program) and supported Employment Supported employment only	Work outcomes	Over 2–3 years, patients were more likely to work, held more jobs, worked more weeks, worked more hours, and earned more wages. Cognitive functioning and symptoms were not assessed.	Control group N=44
(D. Penn, Roberts, Combs, & Sterne, 2007)	Social cognition and social functioning impairments	SCIT	Emotion perception, attributional style and theory of mind	improved emotion perception, improved theory of mind, and a reduced tendency to attribute hostile intent to others,	None n = 17
(Roberts & Penn, 2009)	Emotion perception, Theory of mind and social skills	SCIT and TAU	Emotion perception, theory of mind, attributional style, social skills in role-play	SCIT+TAU improved emotion perception but improvements on theory of mind inconsistent	Control group N = 31
(Russell, Green, Simpson, & Coltheart, 2008)	Visual attention and facial emotion perception	CRT and repeated exposure	Emotion recognition	Improvements in pre-post- means for CRT and maintained one month post-training	Control group N = 40

(Sanz et al., 2009)	Emotion recognition and social perception	Social Cognitive Training Program and TAU	Emotion recognition, , psychopathology, social functioning, social perception	Training improved social perception between group but no improved in emotion recognition	Control group N = 14
(Silver, Goodman, Knoll, & Isakov, 2004)	Emotional communication, (Perception of facial emotional expression)	Computerized emotion training program	Identification of emotions, differentiation of facial emotions, working memory	Compared to baseline significantly better in identification of facial emotions. No changes in differentiation of facial emotions and working memory	None N = 20
(Tas, Danaci, Cubukcuoglu, & Brune, 2012)	Quality of life, social functioning and social cognition	Family-social-cognition and social stimulation (F-SCIT)	Memory, visual-spatial scanning, divided attention, inhibition, emotion perception, theory of mind, empathy, reasoning, attributional style, insight, social functioning, quality of life	F-SCIT improved social withdrawal, interpersonal communications, prosocial activities, independence/competence, theory of mind, emotion perception	Control group N = 52
(van der Gaag, Kern, van den Bosch, & Liberman, 2002)	Social and emotion perception	CR	Emotion and general perception, attention, memory, executive functioning, visual processing, cognitive flexibility and interference	Improvement of emotion perception and executive functioning, other areas of neurocognition not affected	Placebo group N = 42
(Wolwer et al., 2005)	Deficits in facial affect recognition	Training of affect recognition (TAR) Controls groups: (TAU or CRT)	Facial affect recognition, face recognition, and neurocognitive Performance	Patients under TAR (but not CRT or TAU) significantly improved in facial affect recognition. Patients under CRT improved in verbal memory functions.	Control groups N= 77
(W. Wolwer & N. Frommann, 2011)	Prosodic affect recognition, theory of mind, social competence	Training of Affect Recognition (TAR) and CRT	Facial affect recognition, prosodic affect recognition, theory of mind, social competence in role-play	Larger pre- post- improvements on TAR for all variables	Control group N = 38
DRILL AND PRACTICE					
(M. Bell et al., 2005)	Work out comes	Neurocognitive enhancement therapy (NET) + Work therapy Work therapy alone	Work productivity (hours and dollar earned)	Patients worked more hours, had more dollar earned and tend to have more competitive-wage employment	Control group N=145

(M. D. Bell et al., 2008)	Functional outcomes	Neurocognitive enhancement therapy (NET) + vocational program (VOC) VOC alone	Work hours, Employment rates	NET+VOC patients worked more hours during the 12 month follow-up period and they had higher rates of employment.	Control group N= 72

Note. SCIT=social cognition and interaction training. TAU=treatment-as-usual. CR=cognition remediation.

Table 3.

Trainings to improve both neuro- and sociocognitive deficits.

DRILL AND STRATEGY					
Authors	**Targeted deficits**	**Trainings**	**Measured variables**	**Results**	**Control and samples**
(Bowie, Grossman, Gupta, Oyewumi, & Harvey, 2013)	Everyday functioning, social and adaptive competence, neuro cognition	CR	Functional competence, information processing, verbal fluency, working memory, executive functioning, verbal memory	The early-course group had larger improvements in measures of processing speed and executive functions, adaptive competence and real-world work skills. Verbal memory, verbal fluency and social competence did not improve	None N = 39
(Bowie, McGurk, Mausbach, Patterson, & Harvey, 2012)	Cognitive deficits, and functional competence deficits	CR and Functional Adaptation skills training (FAST) Control: FAST or CR	Cognitive performance (reasoning, problem solving, processing speed, verbal memory, working memory) Social competence, functional competence, real-world functional behaviour	CR produced robust improvements in neurocognition, but not after functional skills training. Social competence improved with both trainings. Functional competence higher and more durable with combined treatment. Functional competence and real-world behavior was more likely when supplemental skills training and cognitive remediation were combined.	Control group N=107
(Cavallaro et al., 2009)	Attention, executive functioning, memory quality of life, interpersonal relations, social abilities, autonomy	CR and Standard Rehabilitation Training (SRT)	Verbal+working memory, psychomotor speed and coordination, selective and sustained attention, semantic and letter fluency, cognitive flexibility, daily functioning, interpersonal relations	CR+SRT improvements on executive function, attention and daily functioning	Control group N = 86
(Dickinson et al., 2010)	Neurocognition and sociocognitive	CR and one-on-one training and guided practice	Attention, working and episodic memory, executive functioning, processing speed, everyday community functioning	No improvements were found	Placebo group N = 69
(Eack et al., 2009)	Neurocognition, social adjustement and symptoms	Cognitive Enhancement Therapy (CET) or Enriched Supportive Therapy (EST)	Neurocognitive ability and processing speed, social cognition and cognitive style, social adjustment and symptomatology	CET improved social cognition, cognitive style, social adjustment, and symptomatology during first year and neurocognition benefits were after 2 years	Control group N = 58

(Galderisi et al., 2010)	Sociocognition: social and emotional perception neurocognition:attention, concentration, verbal memory	One program including 1) CR for neurocognition + 2)Social Skills Training for sociocognition and TAU	Verbal and non-verbal memory, attention, memory, executive functions, verbal fluency, self-care, underactivity, slowness in task execution, social withdrawal, participation in family life, functional outcome	Better efficacy on all measures for combined program compared to usual program	Placebo group N = 60
(Hadas-Lidor, Katz, Tyano, & Weizman, 2001)	Organization, comparison and organization, orientation in space, relations, social skills, integrative thinking	CR on specific areas: organization, social skills, categorization	memory, thought process and self-concept, functional outcome	Experimental group showed improvements in cognitive abilities and daily functioning, no difference on self-concept	Placebo group N = 58
(S. S. Hogarty et al., 2004)	Sociocognition and neurocognition	Cognitive enhancement therapy (CET) or enriched supported therapy (EST)	Processing speed. neurocognition, cognitive style, social cognition, social adjustment and symptoms	12 months: improvement in neurocognition, and processing speed 24 months: Same and increase in cognitive style, social cognition and social adjustment	Control group N=121
(G. E. Hogarty, Greenwald, & Eack, 2006)	Neurocognitive and social-cognitive deficits	Cognitive enhancement therapy (CET) Enriched supportive therapy (EST)	Processing speed, Neurocognition, social cognition, cognitive style, social adjustment	Significant effect of CET on measures of processing speed, cognitive style, social cognition, and social adjustment. Only the neurocogniti8ve composite is not significant at 36 months follow-up compared to the two years follow-up.	Control group N=106
(Lewandowski, Eack, Hogarty, Greenwald, & Keshavan, 2011)	Symptoms, social adjustment, social cognition, cognitive style, neurocognition processing speed	CR and enriched supportive therapy (EST)	Symptoms, social adjustment, social cognition, cognitive style, neurocognition processing speed	Improvement in all domains for schizoaffective and schizophrenia patients. Except for schizophrenia no improvement in processing speed	Control group N=58
(R. Penades et al., 2006)	Social functioning and neurocognitive deficits	CR and CBT for control	Working memory, psychomotor speed, verbal memory, nonverbal memory, and executive functioning, and social functioning	Overall improvement in neurcognition especially in verbal and nonverbal memory and executive functioning. Improvement in social functioning	Control Group N=40
(Rafael Penades et al., 2003)	Cognitive differentiation, social perception, communication, social skills, and interpersonal problem solving	Integrated Psychological Therapy (IPT)	intellectual ability, memory, verbal fluency, executive functions and psychosocial functioning	Improvement in memory and executive functioning for those with cognitive impairments	Control N = 27

(Sacks et al., 2013)	Neurocognition and sociocognition	Computerized neuroplasticity-based auditory training and Social cognition training (SCT)	Auditory perception, emotion identification, social perception, theory of mind tasks, all measures of the MATRICS	Gains in neurocognition Gains in emotion identification, social perception, and self-referential source memory.	None N = 19
(Ueland & Rund, 2004)	Cognition (attention, memory), social perception, cognitive differentiation, functioning	CR + psychoeducational programme Psychoeducational programme	Symptoms, psychosocial functioning, attention, memory, executive functioning	Improvement on psychosocial functioning, reduced symptoms (except negative symptoms), and Improvement were observed for 8 of the 10 cognitive measures. Only verbal long term memory and executive functioning (cognitive flexibility) did not improve	Control Group N=25
(Ueland & Rund, 2005)	Deficits in cognition, functioning	CR	Symptoms, psychosocial functioning, attention, memory, executive functioning	Reduce in symptoms and psychosocial functioning, only verbal long term memory and executive functioning did not improve	Control Group N=25
(Veltro et al., 2011)	Social cognition and problem solving, planning and memory	Cognitive-emotional rehabilitation (REC) and Problem Solving Training (PST)	Social and occupational functioning, working memory, psychomotor speed, verbal memory, executive functioning, verbal fluency, theory of mind	PST improved planning and memory, REC improved theory of mind and emotion recognition	None N = 24
(Vita, De Peri, Barlati, Cacciani, Cisima, et al., 2011)	Neuropsychological deficits and functional deficits	Cognitive remediation component of IPT	General attention, verbal memory, working memory, executive functions. Global functioning, positive negative symptoms	Improvements verbal and working memory, improvements in negative and total symptom severity. Functional outcome mediated by improvement in cognitive domains	Control Group N=32
(Vita, De Peri, Barlati, Cacciani, Deste, et al., 2011)	Neurocognition, psychosocial functioning	Cognitive remediation component of IPT (IPT-cog) or computer-assisted cognitive remediation (CACR) Or rehabilitative interventions	Processing speed, working memory, memory in general, executive functioning, global cognition,	IPT and CACR improvements on all variables especially speed and processing and working memory and increase in functioning	Control group N=90

(T. Wykes, Reeder, Corner, Williams, & Everitt, 1999)	Executive functioning deficits and social functioning	Neurocognitive remediation and intensive occupational therapy (control)	Cognitive flexibility, planning and working memory. Social behaviour, self-esteem	Improvements in cognitive flexibility and working memory no changes in symptoms or social functioning	Control group N=33
(T. Wykes et al., 2003)	Memory, cognitive flexibility and planning and social functioning	CR and Intensive occupational therapy	Memory, working memory, cognitive flexibility, response inhibition, planning, symptoms and functioning, self-esteem	Effects of CR at follow-up are still significant on working memory, there were no more effect on self-esteem	Control group N=33
DRILL AND PRACTICE					
(07Greig, Zito, Wexler, Fiszdon, & Bell, 2007)	Memory, attention, cognitive flexibility and social skills, emotion recognition	Vocational Program (VOC; non-cognitive intervention) alone and CR+VOC	Cognitive flexibility and executive functioning, working memory, visual and verbal memory, social cognition	VOC+CR greater improvement on all outcomes. No improvement in affect recognition after 1 year	Placebo group N = 72
(Hooker et al., 2012)	Emotion recognition deficits in the neural mechanisms involved in emotion recognition	Auditory-based cognitive training (AT) (Brain Fitness), social cognition training or non-specific computer games (CG).	Recognition of negative and positive emotions Poscentral gyrus activity (neural region known to support facial emotion recognition)	Greater pre-to-post intervention increase in postcentral gyrus activity during emotion recognition Results indicate that combined cognition and social cognition training impacts neural mechanisms that support social cognition skills.	Placebo group N = 22

Note. CRT=cognitive remediation training, CBT=cognitive behavioral therapy, TAU=treatment-as-usual, MATRICS= Measurement and Treatment Research to Improve Cognition in Schizophrenia

References.

Aleman, A., Hijman, R., de Haanm, E. H. F., & Kahn, R. S. (1999). Memory impairment in schizophrenia: A meta-analysis. *American Journal of Psychiatry, 256*, 1358-1366.

Bark, N., Revheim, N., Huq, F., Khalderov, V., Ganz, Z. W., & Medalia, A. (2003). The impact of cognitive remediation on psychiatric symptoms of schizophrenia. *Schizophrenia Research, 63*, 229-235.

Bell, M., Bryson, G., Greig, T. C., Corcoran, C., & Wexler, B. (2001). Neurocognitive enhancement therapy with work therapy. *archives of General Psychiatry, 58*, 763-768.

Bell, M., Bryson, G., Greig, T. C., Fiszdon, J. M., & Wexler, B. (2005). Neurocognitive enhancement therapy with work therapy: Productivity outcomes at 6- and 12-month follow-ups. *Journal of Rehabilitation Research & Development, 42*(6), 829-838.

Bell, M., Bryson, G., & Wexler, B. E. (2003). Cognitive remediation of working memory deficits: durability of training effects in severely impaired and less severely impaired schizophrenia. [Clinical Trial

Randomized Controlled Trial

Research Support, U.S. Gov't, Non-P.H.S.]. *Acta Psychiatrica Scandinavica, 108*(2), 101-109.

Bell, M., Fiszdon, J. M., Greig, T. C., Wexler, B., & Bryson, G. (2007). Neurocognitive enhancement therapy with work therapy in schizophrenia: 6-month follow-up of neuropsychological performance. *Journal of Rehabilitation Research & Development, 44*(5), 761-770.

Bell, M. D., Zito, W., Greig, T. C., & Wexler, B. (2008). Neurocognitive enhancement therapy with vocational services: Work outcomes at two-year follow-up. *Schizophrenia Research, 105*, 18-29.

Belluci, D. M., Glaberman, K., & Haslam, N. (2002). Computer-assisted cognitive rehabilitation reduces negative symptoms in the severely mentally ill. *Schizophrenia Research, 59*, 225-232.

Blairy, S., Neumann, A., Nutthals, F., Pierret, L., Collet, D., & Philippot, P. (2008). Improvements in autobiographical memory of schizophrenia patients after a cognitive intervention: A preliminary study. *Psychopathology, 41*(6), 388-396.

Bowie, C. R., Grossman, M., Gupta, M., Oyewumi, L. K., & Harvey, P. D. (2013). Cognitive remediation in schizophrenia: Efficacy and effectiveness in patients with early versus long-term course of illness. *Early Intervention in Psychiatry*.

Bowie, C. R., McGurk, S. R., Mausbach, B., Patterson, T. L., & Harvey, P. D. (2012). Combined cognitive remediation and functional skills training for schizophrenia: Effects on cognition, functional competence, and real-world behavior. *American Journal of Psychiatry, 169*(7), 710-718.

Cavallaro, R., Anselmetti, S., Poletti, S., Bechi, M., Ermoli, E., Cocchi, F., . . . Smeraldi, E. (2009). Computer-aided neurocognitive remediation as an enhancing strategy for schizophrenia rehabilitation. [Multicenter Study Randomized Controlled Trial Research Support, Non-U.S. Gov't]. *Psychiatry Research, 169*(3), 191-196.

Chan, C. L., Ngai, E. K., Leung, P. K., & Wong, S. (2009). Effect of the adapted virtual reality cognitive training program among Chinese older adults with chronic schizophrenia: A pilot study. *International Journal of Geriatric Psychiatry, 25*(6), 643-649.

Choi, K.-H., & Kwon, J.-H. (2006). Social Cognition Enhancement Training for Schizophrenia: A Preliminary Randomized Controlled Trial. *Community Mental Health Journal, 42*(2), 177-187.

Combs, D., Adams, S. D., Penn, D. L., Roberts, D., Tiegreen, J., & Stem, P. (2007). Social cognition and interaction training (SCIT) for inpatients with schizophrenia spectrum disorders: Preliminary findings. *Schizophrenia Research, 91*, 112-116.

Combs, D., Elerson, K., Penn, D. L., Tiegreen, J. A., Nelson, A., Ledet, S. N., & Basso, M. R. (2009). Stability and generalization of Social Cognition and Interaction Training (SCIT) for schizophrenia: six-month follow-up results. [Clinical Trial Letter]. *Schizophrenia Research, 112*(1-3), 196-197.

Cook, S., Chambers, E., & Coleman, J. H. (2009). Occupational therapy for people with psychotic conditions in community settings: a pilot randomized controlled trial. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]. *Clinical Rehabilitation, 23*(1), 40-52.

Corrigan, P. W., Hirschbeck, J. N., & Wolfe, M. (1995). Memory and vigilance training to improve social perception in schizophrenia. *Schizophrenia Research, 17*(3), 257-265.

Cromwell, R. L. (1975). Assessment or schizophrenia. [Review]. *Annual Review of Psychology, 26*, 593-619.

d'Amato, T., Bation, R., Cochet, A., Jalenques, I., Galland, F., Giraud-Baro, E., . . . Brunelin, J. (2011). A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. *Schizophrenia Research, 125*(2-3), 284-290.

D'Souza, D. C., Radhakrishnan, R., Perry, E., Bhakta, S., Singh, N. M., Yadav, R., . . . Andrada, C. (2012). Feasibility, Safety, and Efficacy of the Combination of d-Serine and Computerized Cognitive Retraining in Schizophrenia: An International Collaborative Pilot Study. *Neuropsychopharmacology*, 1-12.

Danion, J. M., Meulemans, T., Kauffmann-Muller, F., & Vermaat, H. (2001). Intact implicit learning in schizophrenia. *American Journal of Psychiatry, 158*(6), 944-948.

Dickinson, D., Tenhula, W., Morris, S., Brown, C., Peer, J., Spencer, K., . . . Bellack, A. S. (2010). A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. *The American Journal of Psychiatry, 167*(2), 170-180.

Eack, S. M., Greenwald, D. P., Hogarty, S. S., Cooley, S. J., DiBarry, A. L., Montrose, D. M., & Keshavan, M. S. (2009). Cognitive enhancement therapy for early-course schizophrenia: Effects of a two-year randomized controlled trial. *Psychiatric Services, 60*(11), 1468-1476.

Eack, S. M., Hogarty, G. E., Greenwald, D. P., Hogarty, S. S., & Keshavan, M. (2007). Cognitive enhancement therapy improves emotional intelligence in early course schizophrenia: Preliminary effects. *Schizophrenia Research, 89*, 308-311.

Farreny, A., Aguado, J., Ochoa, S., Huerta-Ramos, E., Marsa, F., Lopez-Carrilero, R., . . . Usall, J. (2012). REPYFLEC cognitive remediation group training in schizophrenai. Looking for an integrative approach. *Schizophrenia Research, 142*, 137-144.

Field, C. D., Galletly, C., Anderson, D., & Walker, P. (1997). Computer-aided cognitive rehabilitation: Possible application to the attentional deficit of schizophrenia, a report of negative results. *Perceptual and Motor Skills, 85*, 995-1002.

Fisher, M., Holland, C., Merzenich, M. M., & Vinogradov, S. (2009). Using neuroplasticity-based auditory training to improve verbal memory in schizophrenia. *American Journal of Psychiatry, 166*(7), 805-811.

Fisher, M., Holland, C., Subramaniam, K., & Vinogradov, S. (2010). Neuroplasticity-based cognitive training in schizophrenia: An interim report on the effects 6 months later. *Schizophrenia Bulletin, 36*(4), 869-879.

Fiszdon, J. M., Bryson, G. J., Wexler, B. E., & Bell, M. D. (2004). Durability of cognitive remediation training in schizophrenia: Performance on two memory tasks at 6-month and 12-month follow-up. *Psychiatry Research, 125*(1), 1-7.

Fiszdon, J. M., Whelahan, H., Bryson, G. J., Wexler, B. E., & Bell, M. D. (2005). Cognitive training of verbal memory using a dichotic listening paradigm: Impact on symptoms and cognition. *Acta Psychiatrica Scandinavica, 112*, 187-193.

Franck, N. (2007). Cognitive remediation for patients with schizophrenia. *Annales Medico-Psychologiques, 165*(3), 187-190.

Fuentes, I., Garcia, S., Ruiz, J. C., Soler, M., & Roder, V. (2007). Social perception training in schizophrenia: A pilot study. *International Journal of Psychology & Psychological Therapy, 7*(1), 1-12.

Galderisi, S., Piegari, G., Mucci, A., Acerra, A., Luciano, L., Rabasca, A. F., . . . Maj, M. (2010). Social skills and neurocognitive individualized training in schizophrenia: comparison with structured leisure activities. [Comparative Study

Randomized Controlled Trial]. *European Archives of Psychiatry & Clinical Neuroscience, 260*(4), 305-315.

Garcia, S., Fuentes, I., Ruiz, J. C., Gallach, E., & Roder, V. (2003). Application of the IPT in a Spanish sample: Evaluation of the "social perception subprogramme". *International Journal of Psychology & Psychological Therapy, 3*(2), 299-310.

Gawronski, B., & Payne, B. K. (2010). *Handbook of implicit social social cognition: Measurement, theory, and applications.*: Guilfort Press.

Gharaeipour, M., & Scott, B. J. (2012). Effects of cognitive remediation on neurocognitive functions and psychiatric symptoms in schizophrenia inpatients. *Schizophrenia Research, 142*, 165-170.

Green, M. F. (1996). What are the functional consequences of neurocognitive deficits in schizophrenia? [Review]. *American Journal of Psychiatry, 153*(3), 321-330.

Greig, T. C., Zito, W., Wexler, B. E., Fiszdon, J., & Bell, M. D. (2007). Improved cognitive function in schizophrenia after one year of cognitive training and vocational services. *Schizophrenia Research, 96*(1-3), 156-161.

Grynszpan, O., Perbal, S., Pelissolo, A., Fossati, P., Jouvent, R., Dubal, S., & Perez-Diaz, F. (2011). Efficacy and specificity of computer-assisted cognitive remediation in schizophrenia: A meta-analytical study. *Psychological Medicine, 41*(1), 163-173.

Habel, U., Koch, K., Kellerman, T., Reske, M., Frommann, N., Wolwer, W., . . . Schneider, F. (2010). Training of affect recognition in schizophrenia: Neurobiological correlates. *Social Neuroscience, 5*(1), 92-104.

Hadas-Lidor, N., Katz, N., Tyano, S., & Weizman, A. (2001). Effectiveness of dynamic cognitive intervention in rehabilitation of clients with schizophrenia. *Clinical Rehabilitation, 15*(4), 349-359.

Hansen, J. P., Ostergaard, B., Nordentoft, M., & Hounsgaard, L. (2012). The feasibility of cognitive adaptation training for outpatients with schizophrenia in integrated treatment. *Community Mental Health Journal*, 1-6.

Heinrichs, R. W., & Zakzanis, K. K. (1998). Neurocognitive deficit in schizophrenia: A quantitative review of the evidence. . *Neuropsychology, 12*, 426-445.

Hodel, B., Kern, R. S., & Brenner, H. D. (2004). Emotion Management Training (EMT) in persons with treatment-resistant schizophrenia: First results. *Schizophrenia Research, 68*, 107-108.

Hodge, M. A. R., Siciliano, D., Withey, P., Moss, B., Moore, G., Judd, G., . . . Harris, A. (2010). A randomized controlled trial of cognitive remediation in schizophrenia. [Comparative

Study Multicenter Study Randomized Controlled Trial Research Support, Non-U.S. Gov't]. *Schizophrenia Bulletin, 36*(2), 419-427.

Hogarty, G. E., Greenwald, D. P., & Eack, S. M. (2006). Durability and mechanism of effects of cognitive enhancement therapy. *Psychiatric Services, 57*(12), 1751-1757.

Hogarty, S. S., Flesher, S., Ulrich, R., Carter, M., Greenwald, D. P., Pogue-Geile, M., . . . Zoretich, R. (2004). Cognitive enhancement therapy for schizophrenia. *archives of General Psychiatry, 61*, 866-876.

Hooker, C. I., Bruce, L., Fisher, M., Verosky, S. C., Miyakawa, A., & Vinogradov, S. (2012). Neural activity during emotion recognition after combined cognitive plus social cognitive training in schizophrenia. *Schizophrenia Research, 139*, 53-59.

Horan, W., Kern, R. S., Shokat-Fadai, K., Sergi, M. J., Wynn, J. K., & Green, M. F. (2009). Social cognitive skills training in schizophrenia: An initial efficacy study of stabilized outpatients. *Schizophrenia Research, 107*(1), 47-54.

Horan, W. P., Kern, R. S., Tripp, C., Hellemann, G., Wynn, J. K., Bell, M., . . . Green, M. F. (2011). Efficacy and specificity of social cognitive skills training for outpatients with psychotic disorders. *journal of Psychiatric Research, 45*, 1113-1122.

Hsieh, M. H., Liu, K., Liu, S.-K., Chiu, M.-J., Hwu, H.-G., & Chen, A. C. N. (2004). Memory impairment and auditory evoked potential gating deficit in schizophrenia. [Research Support, Non-U.S. Gov't]. *Psychiatry Research, 130*(2), 161-169.

Ikezawa, S., Mogami, T., Hayami, Y., Sato, I., Kato, T., Kimura, I., . . . Nakagome, K. (2012). The pilot study of a Neuropsychological Educational Approach to Cognitive Remediation for patients with schizophrenia in Japan. *Psychiatry Research, 195*(3), 107-110.

Kayser, N., Sarfati, Y., Besche, C., & Hardy-Bayle, M.-C. (2006). Elaboration of a rehabilitation method based on a pathogenetic hypothesis of "theory of mind" impairment in schizophrenia. *Neuropsychological Rehabilitation, 16*(1), 83-95.

Keefe, R. S., Vinogradov, S., Medalia, A., Silverstein, S. M., Bell, M. D., Dickinson, D., . . . Stroup, T. (2011). Report from the working group conference on multisite trial design for cognitive remediation in schizophrenia. *Schizophrenia Bulletin, 37*(Suppl 5), 1057-1065.

Keri, S., Kelemen, O., Szekeres, G., Bagoczky, N., Erdelyi, R., Antal, A., . . . Janka, Z. (2000). Schizophrenics know more than they can tell: probabilistic classification learning in schizophrenia. [Research Support, Non-U.S. Gov't]. *Psychological Medicine, 30*(1), 149-155.

Kern, R. S., Liberman, R. P., Becker, D. R., Drake, R. E., Sugar, C. A., & Green, M. F. (2009). Errorless learning for training individuals with schizophrenia at a community mental health setting providing work experience. *Schizophrenia Bulletin, 35*(4), 807-815.

Kidd, S. A., Bajwa, J. K., McKenzie, K. J., Ganguli, R., & Khamneh, B. H. (2012). Cognitive remediation for individuals with psychosis in a supported education setting: A pilot study. *Rehabilitation Research and Practice, 2012*(715176), 5. doi: 10.1155/2012/715176

Kingsep, P., Nathan, P., & Castle, D. (2003). Cognitive behavioural group treatment for social anxiety in schizophrenia. *Schizophrenia Research, 63*, 121-129.

Kontis, D., Huddy, V., Reeder, C., Landau, S., & Wykes, T. (2013). Effects of age and cognitive reserve on cognitive remediation therapy. *The American Journal of Geriatric Psychiatry, 21*(3), 218-230.

Kopelowicz, A., Liberman, R. P., & Zarate, R. (2006). Recent advances in social skills training for schizophrenia. [Review]. *Schizophrenia Bulletin, 32 Suppl 1*, S12-23.

Kurtz, M., & Richardson, C. L. (2011). Social Cognitive Training for Schizophrenia: A Meta-Analytic Investigation of Controlled Research. *Schizophrenia Bulletin, 38*(5), 1092-1104.

Kurtz, M., Seltzer, J., Shagan, D., Thime, W., & Wexler, B. (2007). Computer-assisted cognitive remediation in schizophrenia: What is the active ingredient? *Schizophrenia Research, 89*(1-3), 251-260.

Lecardeur, L., Stip, E., Giguere, M., Blouin, G., Rodriguez, J.-P., & Champagne-Lavau, M. (2009). Effects of cognitive remediation therapies on psychotic symptoms and cognitive complaints in patients with schizophrenia and related disorders: a randomized study. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]. *Schizophrenia Research, 111*(1-3), 153-158.

Lesh, T. A., Niendam, T. A., Minzenberg, M. J., & Carter, C. S. (2011). Cognitive control deficits in schizophrenia: mechanisms and meaning. [Review]. *Neuropsychopharmacology, 36*(1), 316-338.

Lewandowski, K. E., Eack, S. M., Hogarty, S. S., Greenwald, D. P., & Keshavan, M. (2011). Is cognitive enhancement therapy equally effective for patients with schizophrenia and schizoaffective disorder? *Schizophrenia Research, 125*, 291-294.

Lindenmayer, J.-P., McGurk, S. R., Khan, A., Kaushik, S., Thanju, A., Hoffman, L., . . . Herrman, E. (2012). Improving social cognition in schizophrenia: A pilot intervention combining computerized social cognition training with cognitive remediation. *Schizophrenia Bulletin, 39*(3), 507-517.

Lindenmayer, J.-P., McGurk, S. R., Mueser, K. T., Khan, A., Wance, D., Hoffman, L., . . . Xie, H. (2008). A randomized controlled trial of cognitive remediation among inpatients with persistent mental illness. *Psychiatric Services, 59*(3), 241-247.

Lopez-Luengo, B., & Vazquez, C. (2003). Effects of Attention Process Training on cognitive functioning of schizophrenic patients. *Psychiatry Research, 119*, 41-53.

Lysaker, P. H., Erickson, M., Ringer, J., Buck, K. D., Semerari, A., Carcione, A., & Dimaggio, G. (2011). Metacognition in schizophrenia: the relationship of mastery to coping, insight, self-esteem, social anxiety, and various facets of neurocognition. [Comparative Study Research Support, U.S. Gov't, Non-P.H.S.]. *British Journal of Clinical Psychology, 50*(4), 412-424.

Marsh, P., Langdon, R., McGuire, J., Harris, A., Polito, V., & Coltheart, M. (2013). An open clinical trial assessing a novel training program for social cognitive impairment in schizophrenia. *Australasian Psychiatry, 21*(2), 122-126.

Mazza, M., Lucci, G., Pacitti, F., Pino, M. C., Mariano, M., Casacchia, M., & Roncone, R. (2010). Could schizophrenic subjects improve their social cognition abilities only with observation and imitation of social situations? *Neuropsychological Rehabilitation, 20*(5), 675-703.

McGurk, S. R., Mueser, K. T., Feldman, K., Wolfe, R., & Pascaris, A. (2007). Cognitive training for supported employment: 2-3 year outcomes of a randomized controlled trial. *American Journal of Psychiatry, 164*(3), 437-441.

McGurk, S. R., Mueser, K. T., & Pascaris, A. (2005). Cognitive training and supported employment for persons with severe mental illness: One-year results from a randomized controlled trial. *Schizophrenia Bulletin, 31*(4), 898-909.

McGurk, S. R., Twamley, E. W., Sitzer, D. I., McHugo, G. J., & Mueser, K. T. (2007). A meta-analysis of cognitive remediation in schizophrenia. [Comparative Study Meta-Analysis Research Support, N.I.H., Extramural]. *American Journal of Psychiatry, 164*(12), 1791-1802.

Medalia, A., Aluma, M., Tryon, W., & Merriam, A. E. (1998). Effectiveness of attention training in schizophrenia. *Schizophrenia Bulletin, 24*(1), 147-152.

Medalia, A., Revheim, N., & Casey, M. (2000). Remediation of memory disoders in schizophrenia. *Psychological Medicine, 30*, 1451-1459.

Medalia, A., Revheim, N., & Casey, M. (2001). The remediation of problem-solving skills in schizophrenia. *Schizophrenia Bulletin, 27*(2), 259-267.

Medalia, A., & Saperstein, A. M. (2013). Does cognitive remediation for schizophrenia improve functional outcomes? *Current Opinion in Psychiatry, 26*, 151-157.

Meesters, P. D., Stek, M. L., Comijs, H. C., de Haan, L., Patterson, T. L., Eikelenboom, P., & Beekman, A. T. F. (2010). Social functioning among older community-dwelling patients with schizophrenia: a review. [Review]. *American Journal of Geriatric Psychiatry, 18*(10), 862-878.

Moritz, S., Veckenstedt, R., Randjbar, S., Vitzthum, F., & Woodward, T. (2011). Antipsychotic treatment beyond antipsychotics: Metacognitive intervention for schizophrenia patients improves delusional symptoms. *Psychological Medicine, 41*(9), 1823-1832.

Murthy, N. V., Mahncke, H., Wexler, B. E., Maruff, P., Inamdar, A., Zucchetto, M., . . . Alexander, R. (2012). Computerized cognitive remediation training for schizophrenia: An open label, multi-site, multinational methodology study. *Schizophrenia Research, 139*, 87-91.

Nemoto, T., Yamazawa, R., Kobayashi, H., Fujita, N., Chino, B., Fujii, C., . . . Mizuno, M. (2009). Cognitive training for divergent thinking in schizophrenia: A pilot study. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 33*(8), 1533-1536.

Norton, D. J., McBain, R. K., Ongur, D., & Chen, Y. (2011). Perceptual training strongly improves visual motion perception in schizophrenia. *Brain and Cognition, 77*, 248-256.

Nuechterlein, K. H., Green, M. F., Kern, R. S., Baade, L. E., Barch, D. M., & Cohen, J. D. (2008). The MATRICS consensus cognitive battery, part 1: test selection, reliability, and validity. *American Journal of Psychiatry, 165*(203e13).

Penades, R., Boget, T., Catalan, R., Bernardo, M., Gasto, C., & Salamero, M. (2003). Cognitive mechanisms, psychosocial functioning, and neurocognitive rehabilitation in schizophrenia. *Schizophrenia Research, 63*(3), 219-227.

Penades, R., Catalan, R., Salamero, M., Boget, T., Puig, O., Guarch, J., & Gasto, C. (2006). Cognitive remediation therapy for outpatients with chronic schizophrenia: A controlled and randomized study. *Schizophrenia Research, 87*, 323-331.

Penades, R., Pujol, N., Catalan, R., Massana, G., Rametti, G., Garcia-Rizo, C., . . . Junque, C. (2013). Brain effects of cognitive remediation therapy in schizophrenia: A structural and functional neuroimaging study. *Biological Psychiatry, 73*, 1015-1023.

Penn, D., Roberts, D., Combs, D., & Sterne, A. (2007). The development of the Social Cognition and Interaction Training Program for schizophrenia spectrum disorders. *Psychiatric Services, 58*(4), 449-451.

Penn, D. L., Mueser, K. T., Doonan, R., & Nishith, P. (1995). Relations between social skills and ward behavior in chronic schizophrenia. *Journal of Schizophrenia Research, 16*, 225-232.

Pinkham, A. E., & D.L., P. (2006). Neurocognitive and social cognitive predictors of interpersonal skill in schizophrenia. *Psychiatry Research, 143*, 167-178.

Poletti, S., Anselmetti, S., Bechi, M., Ermoli, E., Bosia, M., Smeraldi, E., & Cavallaro, R. (2010). Computer-aided neurocognitive remediation in schizophrenia: Durability of rehabilitation outcomes in a follow-up study. *Neuropsychological Rehabilitation, 20*(5), 659-674.

Popov, T., Jordanov, T., Rockstroch, B., Elbert, T., Merzenich, M. M., & Miller, G. A. (2011). Specific cognitive training normalizes auditory sensory gating in schizophrenia: A randomized trial. *Biological Psychiatry, 69*, 465-471.

Popov, T., Rockstroch, B., Weisz, N., Elbert, T., & Miller, G. A. (2012). Adjusting Brain Dynamics in Schizophrenia by Means of Perceptual and Cognitive Training. *PLOS One, 7*(7), e39051.

Raffard, S., Gely-Nargeot, M. C., Capdevielle, D., Bayard, S., & Boulenger, J. P. (2009). [Learning potential and cognitive remediation in schizophrenia]. [Review]. *Encephale, 35*(4), 353-360.

Rass, O., Forsyth, J. K., Bolbecker, A. R., Hetrick, W. P., Breier, A., Lysaker, P. H., & O'Donnell, B. F. (2012). Computer-assisted cognitive remediation for schizophrenia: A randomized single-blind pilot study. *Schizophrenia Research, 139*(1-3), 92-98.

Rauchensteiner, S., Kawohl, W., Ozgurdal, S., Littmann, E., Gudlowski, Y., Witthaus, H., . . . Juckel, G. (2011). Test-performance after cognitive training in persons at risk mental state of schizophrenia and patients with schizophrenia. *Psychiatry Research, 185*, 334-339.

Regier, D. A., Farmer, M. E., Rae, D. S., Locke, B. Z., Keith, S. J., & Judd, L. L. (1990). Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) study. *Journal of American Medical Association, 264*, 2511-2518.

Revheim, N., Schechter, I., Kim, D., Silipo, G., Allingham, B., Butler, P., & Javitt, D. C. (2006). Neurocognitive and symptom correlates of daily problem-solving skills in schizophrenia. [Comparative Study

Research Support, N.I.H., Extramural]. *Schizophrenia Research, 83*(2-3), 237-245.

Roberts, D. L., & Penn, D. L. (2009). Social cognition and interaction training (SCIT) for outpatients with schizophrenia: a preliminary study. [Clinical Trial Comparative Study Research Support, Non-U.S. Gov't]. *Psychiatry Research, 166*(2-3), 141-147.

Rodewald, K., Rentrop, M., Holt, D. V., Roesch-Ely, D., Backenstras, M., Funke, J., . . . Kaiser, S. (2011). Planning and problem-solving training for patients with schizophrenia: A randomized controlled trial. *BMC Psychiatry, 11*, 73.

Royer, A., Grosselin, A., Bellot, C., Pellet, J., Billard, S., Lang, F., . . . Massoubre, C. (2012). Is there any impact of cognitive remediation on an ecological test in schizophrenia? *Cognitive Neuropsychiatry, 17*(1), 19-35.

Russell, T. A., Green, M. J., Simpson, I., & Coltheart, M. (2008). Remediation of facial emotion perception in schizophrenia: concomitant changes in visual attention. [Comparative Study Randomized Controlled Trial Research Support, Non-U.S. Gov't]. *Schizophrenia Research, 103*(1-3), 248-256.

Sacks, S., Fisher, M., Garrett, C., Alexander, P., Holland, C., Rose, D., . . . Vinogradov, S. (2013). Combining computerized social cognitive training with neuroplasticity-based auditory training in schizophrenia. *Clinical Schizophrenia and Related Psychoses*.

Sanz, D. G., Lorenzo, M. D., Seco, R. B., Rodriguez, M. A., Martinez, I. L., Calleja, R. S., & Soltero, A. A. (2009). Efficacy of a social cognition training program for schizophrenic patients: A pilot study. *The Spanish Journal of Psychology, 12*(1), 184-191.

Sartory, G., Zorn, C., Groetzinger, G., & Windgassen, K. (2005). Computerized cognitive remediation improves verbal learning and processing speed in schizophrenia. *Schizophrenia Research, 75*(2-3), 219-223.

Schaefer, J., Giangrande, E., Weinberger, D. R., & Dickinson, D. (2013). The global cognitive impairment in schizophrenia: Consistent over decades and around the world. *Schizophrenia Research, 150*(1), 42-50.

Silver, H., Goodman, C., Knoll, G., & Isakov, V. (2004). Brief emotion training improves recognition of facial emotions in chronic schizophrenia. A pilot Study. *Psychiatry Research, 128*, 147-154.

Silverstein, S. M., Hatashita-Wong, M., Solak, B. A., Uhlhaas, P., Landa, Y., Wilkniss, S. M., . . . Smith, T. E. (2005). Effectiveness of a two-phase cognitive rehabilitation intervention for severely impaired schizophrenia patients. *Psychological Medicine, 35*(6), 829-837.

Spaulding, W. D., Reed, D., Sullivan, M., Richardson, C., & Weiler, M. (1999). Effects of cognitive treatment in psychiatric rehabilitation. *Schizophrenia Bulletin, 25*(4), 657-676.

Subramaniam, K., Luks, T. L., Fisher, M., Simpson, G. V., Nagarajan, S., & Vinogradov, S. (2012). Computerized cognitive training restores neural activity within the reality monitoring network in schizophrenia. *Neuron, 73*, 842-853.

Surti, T. S., Corbera, S., Bell, M. D., & Wexler, B. E. (2011). Successful computer-based visual training specifically predicts visual memory enhancement over verbal memory improvement in schizophrenia. *Schizophrenia Research, 132*(2-3), 131-134.

Tas, C., Danaci, A. E., Cubukcuoglu, Z., & Brune, M. (2012). Impact of family involvement on social cognition training in clinically stable outpatients with schizophrenia - A randomized pilot study. *Psychiatry Research, 195*(1-2), 32-38.

Twamley, E. W., Savla, G. N., Zurhellen, C. H., Heaton, R. K., & Jeste, D. V. (2008). Development and pilot testing of a novel compensatory cognitive training intervention for people with psychosis. *American Journal of Psychiatric Rehabilitation, 11*(2), 144-163.

Ueland, T., & Rund, B. R. (2004). A controlled randomized treatment study: The effects of a cognitive remediation program on adolescents with early onset psychosis. *Acta Psychiatrica Scandinavica, 109*, 70-74.

Ueland, T., & Rund, B. R. (2005). Cognitive remediation for adolescents with early onset psychosis: A 1-year follow-up study. *Acta Psychiatrica Scandinavica, 111*, 193-201.

van der Gaag, M., Kern, R. S., van den Bosch, R. J., & Liberman, R. P. (2002). A controlled trial of cognitive remediation in schizophrenia. *Schizophrenia Bulletin, 28*(1), 167-176.

Vauth, R., Corrigan, P. W., Clauss, M., Dietl, M., Dreher-Rudolph, M., Stieglitz, R.-D., & Vater, R. (2005). Cognitive strategies versus self-management skills as adjunct to vocational rehabilitation. *Schizophrenia Bulletin, 31*(1), 55-66.

Veltro, F., Mazza, M., Vendittelli, N., Alberti, M., Casacchia, M., & Roncone, R. (2011). A comparison of the effectiveness of problem solving training and of cognitive-emotional rehabilitation on neurocognition, social cognition and social functioning in people with schizophrenia. *Clinical Practice and Epidemiology in Mental Health, 7*, 123-132.

Vita, A., De Peri, L., Barlati, S., Cacciani, P., Cisima, M., Deste, G., . . . Sacchetti, E. (2011). Psychopathologic, neuropsychological and functional outcome measures during cognitive rehabilitation in schizophrenia: A prospective controlled study in a real-world setting. *European Psychiatry, 26*, 276-283.

Vita, A., De Peri, L., Barlati, S., Cacciani, P., Deste, G., Poli, R., . . . Sacchetti, E. (2011). Effectiveness of different modalities of cognitive remediation on symptomatological, neuropsychological, and functional outcome domaines in schizophrenia: A prospective study in a real-world setting. *Schizophrenia Research, 133*, 223-231.

Weickert, T. W., Terrazas, A., Bigelow, L. B., Malley, J. D., Hyde, T., Egan, M. F., . . . Goldberg, T. E. (2002). Habit and skill learning in schizophrenia: evidence of normal striatal processing with abnormal cortical input. *Learning & Memory, 9*(6), 430-442.

Wexler, B. E., Hawkins, K. A., Rounsaville, B., Anderson, M., Sernyak, M. J., & Green, M. F. (1997). Normal neurocognitive performance after extended practice in patients with schizophrenia. [Clinical Trial Comparative Study Randomized Controlled Trial Research Support, Non-U.S. Gov't]. *Schizophrenia Research, 26*(2-3), 173-180.

Wolwer, W., & Frommann, N. (2011). Social-cognitive remediation in schizophrenia: generalization of effects of the Training of Affect Recognition (TAR). [Comparative Study Randomized Controlled Trial Research Support, Non-U.S. Gov't]. *Schizophrenia Bulletin, 37 Suppl 2*, S63-70.

Wolwer, W., & Frommann, N. (2011). Social-cognitive remediation in schizophrenia: Generalization of effects of the training of affect recognition (TAR). *Schizophrenia Bulletin, 37*(2), 63-70.

Wolwer, W., Frommann, N., Halfmann, S., Piaszek, A., Streit, M., & Gaebel, W. (2005). Remediation of impairments in facial affect recognition in schizophrenia: Efficacy and specificity of a new training program. *Schizophrenia Research, 80*, 295-303.

Wykes, T., Huddy, V., Cellard, C., McGurk, S. R., & Czobor, P. (2011). A meta-analysis of cognitive remediation for schizophrenia: Methodology and effect sizes. *The American Journal of Psychiatry, 168*(5), 472-485.

Wykes, T., Newton, E., Landau, S., Rice, C., Thompson, N., & Frangou, S. (2007). Cognitive remediation therapy (CRT) for young early onset patients with schizophrenia: an exploratory randomized controlled trial. [Randomized Controlled Trial Research Support, Non-U.S. Gov't]. *Schizophrenia Research, 94*(1-3), 221-230.

Wykes, T., Reeder, C., Corner, J., Williams, C., & Everitt, B. (1999). The effects of neurocognitive remediation on executive processing in patients with schizophrenia. *Schizophrenia Bulletin, 25*(2), 291-307.

Wykes, T., Reeder, C., Landau, S., Everitt, B., Knapp, M., Patel, A., & Romeo, R. (2007). Cognitive remediation therapy in schizophrenia. *British Journal of Psychiatry, 190*, 421-427.

Wykes, T., Reeder, C., Williams, C., Corner, J., Rice, C., & Everitt, B. (2003). Are the effects of cognitive remediation therapy (CRT) durable? Results from an exploratory trial in schizophrenia. *Schizophrenia Research, 61*, 163-174.

Yang, J., & Li, P. (2012). Brain networks of explicit and implicit learning. *PLOS One, 7*(8), e42993. doi: doi:10.1371/journal.pone.0042993

Chapter 5 – General discussion

Reminder of the context and of the objectives

Schizophrenia is a complex mental disorder that severely impacts the quality of life of individuals suffering from it. In this thesis, I wished to demonstrate that although positive symptoms of schizophrenia are central to the disorder, cognitive deficits need to be addressed by treatment, given their strong impact on the person's social functioning. Furthermore, the impact on social cognition and social functioning of substance abuse needs to be examined given the frequency of this presentation in individuals with schizophrenia. As is the case with many research projects, the ultimate goal is often trying to create proper interventions in order to offer relief to individuals and to improve their lives. With a complex disorder like schizophrenia, many avenues of intervention exist but have not necessarily obtained stellar results. Therefore it is essential to identify what has been done in the past to target specific deficits before any treatment is developed or implemented.

As such, our objectives were divided into three parts: firstly, we set out to explore emotion recognition deficits in a more naturalistic sample of individuals with schizophrenia, namely individuals with both schizophrenia and substance use disorder, using dynamic virtual avatars as our measuring tool. We also investigated if there could be any sort of relationship either between emotion recognition deficits and social functioning or between a comorbid substance use disorder and social functioning. Secondly, we gathered all the findings on the impact of substance use disorder on schizophrenia and particularly its impact on neurocognition, which is the area that has been studied the most over the years, in a comprehensive book chapter in order to have a clear view of the advances in that area. And lastly, in trying to put into proper context both our novel findings on emotion recognition in comorbid schizophrenia and the knowledge accumulated over the years on the impact of substance use disorder in schizophrenia

to hopefully create effective treatment protocols tailor-fitted to precise emotion recognition profiles, we explored the literature to see what had already been done in the area of cognitive remediation. Our hope was to identify the most popular types of intervention, among the many that are available in cognitive remediation, and use this information to suggest tailor-fitted interventions that could be tested out in future research. To conclude, we propose a re-definition of schizophrenia as a disorder that would allow for less stigmatisation, more prevention and treatment and above all, a thorough focus on what seems to be central to both the aetiology and the recovery from schizophrenia: social functioning.

Main findings of the two first articles

The first article hoped to shed some light on emotion recognition patterns in schizophrenia and to pinpoint if the potential deficits were for any specific emotion or at the very least, if there were linked to a certain category of emotions like negative ones or positive ones. Since social functioning is a crucial recovery outcome for this population, we also wished to explore if there was any link between emotion recognition and social functioning outcomes. Finally, given the prevalence of comorbid substance use disorder in this population, we tried to examine if the presence of that comorbidity would have an effect on the results.

While our results for global emotion recognition were similar to the results of normative samples, the deficits found for specific emotions were the most interesting. It appeared that, for our entire sample of both individuals with schizophrenia alone and some with schizophrenia and either cannabis use or stimulant use, there were marked deficits in fear recognition while sadness held the highest recognition average. Furthermore, when we examined the misinterpretation patterns – i.e. when individuals did make a mistake in recognizing an emotion, what other

emotion did they think was depicted by the avatar – our results showed that fear tended to be recognized as surprise while anger was identified as neutrality. The fear-surprise confusion has been shown to be quite common in the literature even in normal samples; however, the anger-neutral confusion could potentially be due to misuse of facial cues to recognize emotions in this population and is a novel finding.

Sadly, we were unable to support our second hypothesis that emotion recognition could predict functional outcomes. However, what remains interesting is the fact that the data showed relevant correlations between one's capacity to recognize certain emotions and specific areas of social functioning. There was a positive correlation between recognition of sadness and the frequency of positive interactions with family members and a positive correlation between the recognition of joy and one's perceived abilities to work. Taken together these findings could indicate that being better at recognizing when someone close to use is sad shows empathy and could lead to more positive interactions with these individuals and being able to recognize joy could allow for positive feedback from coworkers and employers making for increased self-esteem and better evaluation of one's abilities to work. Also, noticing that someone we care for, like a family member, is showing sorrow or distress because of the hardship we are going through, can also be perceived as a positive interaction rooted in caring. Moreover and relevant to our context, it has been suggested that family support in comorbid substance use disorder and severe mental illness such as schizophrenia, may significantly help individuals with this presentation to reduce or even eliminate completely their substance use (Cavallaro et al., 2009).

When it came to the impact of substance use on the results, we found that, with regards to emotion recognition, there are different emotion recognition profiles for individuals with

comorbid substance use disorder. Specifically, those with co-occurring cannabis use tended to be better at recognizing negative emotions, particularly fear, compared to those with schizophrenia alone. Those with stimulant use were clearly better at recognizing negative emotions as well, particularly anger and fear. At first glance, these results are surprising since we know for a fact that drug use has deleterious effects on cognition in normative samples and that cannabis use is a risk factor that increases the possibility of developing schizophrenia for vulnerable individuals. However and as mentioned before, these results are more and more common in the literature though they remain hard to put into context and to explain clearly. For now, it remains a conundrum to try and decipher the underlying mechanisms involved in these puzzling findings, since most explanations seem to indicate that the differences could be due to various aetiology trajectories. Importantly, these results are mostly reported in the evaluation of neurocognitive deficits using functional imaging technologies. Therefore, we are left with a sense that we still have more questions than answers, specifically for how this comorbid presentation affects sociocognition and therefore, emotion recognition specifically. But there are a few theoretical propositions that could help shed some light on the state of affairs and we will explore some of them in the coming paragraphs.

Cognitive remediation findings

In our review of the literature for our last article, we had two main objectives. Firstly, we wanted to see which of the more popular ways of retraining cognition was used most often - either 'drill and learning' or 'drill and practice'. Importantly, though we took a look at the results to see if the training were efficient or not in the end, this article was solely a review of the literature and not a meta-analysis of the efficacy of the trainings. Secondly, we wanted to know if the type of cognitive deficits - between neurocognitive and sociocognitive domains - mattered in

the choice of training protocols. It was our hope that given the results we found, we could find a way to integrate virtual avatars into the retraining protocol to make it more generalizable and naturalistic, given the results we found in our first article.

One of the main strengths of the findings was that more often than not, the outcome variable of cognition that was measured to insure the training was effective had not been targeted by the training specifically. For instance, sometimes the target of the training was a sociocognitive domain but the outcome focused on neurocognition domains, and still significant results were reported, allowing for greater generalization of the results. Moreover, several studies included follow-up measures that demonstrated that the benefits of the various trainings were sustained over time.

We first described the studies that targeted specific neurocognitive deficits using a single type of training protocol. The gist of the studies showed that for schizophrenia, it was the 'drill and practice' protocol that was used more often to improve neurocognitive deficits. When examining the specific methods of training, it turns out that the most commonly used one was computerized tasks that were done individually and all studies reported improvement of the targeted deficits, even at follow up. 'Drill and practice' strategy uses repetition to acquire learning, with stimuli involved in the training becoming harder and harder. There is no explicit component to it and it is solely based on getting feedback from the training trials and learning through basic trial and error procedure. Given the fact that the domains of neurocognition are mostly used implicitly, using practice to improve the deficits seems fitting. An obvious example of this is memory; to learn something by heart, one must repeat and repeat until what we wish to learn becomes stored in long term memory, not requiring any explicit component.

As for the studies conducted to improve sociocognition, they mostly utilized 'drill and strategy' approaches. The main ingredients to success in those protocols seemed to be the significant use of both visual aides like presentations, vignettes and videos but also detailed presentations and explanations on the reasons behind the training and the benefits the researchers were hoping that the participants would get from the training. All those explanations on protocols and goals of the training were done by therapists in group settings, which allowed for a 'practice' component through modelling as well as role-plays with feedback. It seems logical that learning about social interactions through practice and detailed feedback would be the appropriate way to go for individuals that lack proper and positive interpersonal relationships on which to base their interpretation of social successes or failures.

Theoretical implications

The stress-diathesis model. The stress-diathesis model of explaining schizophrenia and its onset is surely the most common used theoretical model to date. The improvements to the model over the years have allowed to include protective factors that can lead to remission from the disorder. As such, it is interesting to notice that our results are in line with these added factors. For instance, having supportive and caring relationships with family members could foster more empathy in individuals suffering from schizophrenia, making them more sensitive to the emotional expression of sadness and further improving their social interactions with family members but also potentially increasing their sense of self-esteem and social competency – which is yet another protective factor of this model – safeguarding against further stressors and relapse of the disorder (Veltro et al., 2011). However, the fact remains that this model is still lacking to consider the impact of cognitive deficits on the aetiology, course and remission from schizophrenia. It would be interesting to conduct longitudinal research while integrating the

various finding on both neuro- and sociocognition in schizophrenia to this model and see if this could lead to new methods of prevention of the onset of the disorder as well as new avenues of treatment to ensure recovery from the disorder.

Explanatory models of paradoxical findings. In order to explain the results in comorbid schizophrenia and substance abuse, it could be suggested that there is a 'neuroprotective' effect of drug use. However, data from studies evaluating neurocognitive deficits have shown opposite results, meaning that suffering from substance abuse has deleterious effects on certain neurocognitive domains, in non-psychiatric populations using cannabis. Taken together with the data showing that individuals with comorbid cannabis use perceive that they have better abilities to both interact with others and partake in social activities, we alternatively suggest that it is perhaps a more 'socioprotective' effect that is occurring (which is admittedly similar to the known explanatory model of the 'social-hypothesis'). Indeed, it could be that the need to procure drugs, has led this population to develop specific social cognitive abilities, increasing their capacity to not only interact with potential drug dealers but to also gain better abilities to recognize negative emotions of threat, that are quite common in the world of drug use. However, this model has been criticized since it would imply that the cognitive benefits would vary according to the availability of the drug of choice, and the data is not consistent with that suggestion. Furthermore, this hypothesis would imply that the absence of deficits in cognition would not be due to the pharmacological effects of the drug use itself but rather to premorbid social skills, pointing more toward aetiology explanations than explaining the neurological effects of the drug. There is also a third potential explanatory model, the 'lower vulnerability hypothesis' which is linked to findings that cannabis smoking increases the risk of developing psychosis. It has been shown by research that administration of the psychoactive ingredient found

in cannabis to healthy subjects will mimic the manifestations seen in schizophrenia like the various negative and positive symptoms. This led researchers to investigate if cannabis smoking could more readily induce psychosis and the data has shown that it is in fact associated with a 2 to 3 fold increase in psychotic symptoms and schizophrenia-like diagnoses. Of importance is that this link is affected by the dosage of cannabis consumed and is influenced by the age at which cannabis smoking actually started. What is more, and that is relevant to our objectives, is the fact that the risk of compulsive cannabis smoking in schizophrenia is 3 to 6 times higher than what is found in the general population. However the 'lower vulnerability hypothesis' states that premorbid differences such as having higher IQ or already having a lower vulnerability to psychosis before developing it for those individuals that smoke cannabis, could have an impact on interpretation. Taken together, although these three suggested hypothesis are interesting, they remain unsatisfactory since most of them point to difference in aetiology trajectories.

Regarding aetiologies. When reviewing the various possible aetiologies for the development and onset of schizophrenia, it is important to notice that most of the ones we mentioned have an impact of the social aspect of these individuals' lives. Communication deviance as well as expressed emotion in the stress-diathesis model, both leave individuals with severe interpersonal difficulties. It is challenging to expect individuals who do not have sound family relationships that are supportive and caring, to go out into the world and have appropriate social interactions with strangers. It could even be suggested that when these two constructs are present, a sense of being disconnected from one's family would severely impact one's capacity to seek out and create new, more satisfying relationships all of which would lead to social isolation. It is important to be reminded that having stressful negative family environment and therefore family interactions falls into the category of social trauma, and is therefore a vulnerability factor

to developing schizophrenia according to the stress-diathesis model.

The same can be said about individuals that suffered traumatic childhood experience, let alone those that have gone through complex trauma in early life. It has been demonstrated that early childhood traumas are not only linked the heightened risks of developing psychopathologies, but that it is associated with a myriad of negative consequences in adulthood such as low self-esteem, insecure adult attachment and a diminished capacity to deal with life-stressors (Barnum & Perron-McGovern, 2017). Therefore, most of the aetiologies proposed to explain schizophrenia's onset have an important social component that should not be neglected in the interpretation of the current findings and that should be integrated in future longitudinal research.

The social isolation hypothesis. One of the main findings that stands out the most in our initial article, is the link and impact of both emotion recognition and use of cannabis on social interactions. The importance of social functioning and functional outcome has been identified as crucial in the literature for this population; however, an important aspect of social life is often neglected in the interpretation of findings in schizophrenia but also in the general population. The concept of social isolation or of 'social disconnection', as referred to by Green and his colleagues in their recent paper on the matter (M.F. Green et al., 2017), has recently gained a lot of attention in both the media and in the scientific community. It is a social concept that has profound negative consequences on the general public as well as on clinical populations. The former surgeon general of the United States is quoted in a Harvard Business Review as reporting that, for the general public, feeling lonely and being socially isolated can lead to increased risks of premature death, several health care problems such as heart disease or obesity, depression and

anxiety as well as potentially turning to violence and drug use to alleviate loneliness. This has several implications in the context of schizophrenia. 'Social disconnection' is defined as 'long-standing lack of social/family relationships and minimal participation in social/family activities' (M.F. Green et al., 2017). The research team describes that in order to have proper social connection there are two main determinants. Firstly, one needs to have both the ability to connect - which they link to social cognition and the processes involved in being able to infer other people's thoughts and emotions (i.e. emotion recognition and Theory of Mind) - and secondly, one needs to have the motivation and see the benefits or interest in connecting with others. Noteworthy, is the fact that they specify that social cognition has the strongest association with interpersonal interactions (Fiske & Taylor, 1991; Kunda, 1999) and that reading social cues from facial expressions is impaired in schizophrenia, though they do not specify any specific deficits of emotion recognition (M.F. Green, Horan, & Lee, 2015). Though they stated that there is currently no data available on the direct consequences of social disconnection on health or mortality rate in schizophrenia, they still suggest that it could be a contributing factor. It is important to keep in mind that schizophrenia is one of the most socially stigmatized illnesses, leading to social distance from others, and social isolation. Individuals with schizophrenia also have a 10% suicidal rate, with more than 50% attempting suicide at least once in their lives (Roy, 1986). Therefore, it is a relevant research question to investigate how social disconnection impacts on areas like independent living, work or school or family interactions, which are all linked to psychological well-being and recovery in schizophrenia.

We know now, from past research and from our study, that individuals with schizophrenia have social deficits. We also now have a hint that some of those social difficulties are perhaps associated with emotion recognition dysfunctions of specific emotions. This inevitably leads to

an important theoretical question that is also linked to our findings on emotion recognition. Which comes first? The social isolation or the social cognition deficits? It is hard to decipher which leads to which because in this specific instance, we were unable to produce data that could infer causality between the two. This debate appears to be crucial, however: does having deficits in the ability to properly identify emotions in others - which is essential to social interactions - lead to social isolation because of negative experiences arising from the misinterpretation of emotions or is it rather that being socially isolated - due perhaps to the stigmatization around schizophrenia - leads individuals to lose their abilities to recognize emotions since they barely interact with anyone. Although both are possible, the latter seems to be more in line with our results. Indeed, it would help in the interpretation of the paradoxical findings in comorbid schizophrenia and substance use disorder. Our data suggests that individuals with comorbid cannabis smoking perceive that they have greater abilities to interact with others and take part in social activities. Being forced to break isolation to procure street drugs could have an impact on both social isolation and emotion recognition in the end. The lower-vulnerability hypothesis already suggests that perhaps the vulnerability profile with regard to the risk of psychosis of those that decide to engage in cannabis smoking could be different. Similarly, it appears that individuals that have schizophrenia alone (without comorbid substance use disorder) have emotion recognition profiles that differ from those that have comorbid substance use disorder. This serves to further highlight the importance of identifying sociocognitive profiles for individuals with and without various comorbid profiles. The next logical step following identification of individual patterns of impairments, will be to find the best and most efficient way to address the deficits and improve them.

The case of stigmatisation. It is a well-known fact that individuals suffering from severe mental illnesses are victims of stigmatisation. It is often linked to stereotypes that appear to be stable over time, particularly in the case of schizophrenia (Schomerus et al., 2012). Studies have shown that the general public often holds strong beliefs that individuals who have schizophrenia are unpredictable and dangerous while not necessarily realizing that it can be profoundly hurtful and distressing to be the victim of stigma and that it very often lead to social rejection (Feldman & Crandall, 2007). However, very few studies have endeavoured to examine where these stereotypes come from. Generally speaking, it is believed that informing the public about the disorder will reduce stigma. More recent studies into stigmatisation in schizophrenia have discovered that it does not uniquely stem from cognitive predictors such as stereotypes but rather that certain emotions – particularly fear – are provoked by the impression that individuals with schizophrenia display low social warmth (Cudy et al. 2007). This is interesting because it leads back to the believe that these individuals could lack the social skills to properly interact with others. Similarly and like it is suggested by Thonon and Laroi (2016), the most common behavioral reaction to perceiving fear is flight. However, what if one's has an impaired ability to detect fear in others? That individual would not notice the fear or misinterpret it and potentially stay engaged in the social interaction which would inevitably end in failure, further increasing stigmatisation stereotypes and increasing social rejection. Which is consistent with the results we found for individuals suffering from schizophrenia alone. However those with comorbid presentations were better at recognizing fear, which could lead them to adjust their social interactions accordingly or even flee potentially dangerous or negative social interactions, therefore preserving their sense of having the capacity to interaction with others successfully and explaining more positive sociocognitive results. One way of another, this serves to show that whether it is due to stigmatisation or social disconnection, sociocognition – its related deficits and

their impact on social functioning – need to be properly identified and treated with the appropriate tools.

Clinical implications

Using virtual avatars. Nowadays, the emergence of new technologies like smart phones, texting, emails and social medias are an unavoidable reality that can be considered both positive and negative in terms of their impact on social relationships. They have also allowed significant breakthroughs in scientific advancements, including for clinical research. More and more research and clinical interventions are using virtual reality for instance, which mimics real-life settings and is therefore more realistic and naturalistic in nature and furthermore, yields impressive results. Significant findings have been found in the field of physical health where virtual reality was used to help with concerns like physical rehabilitation from stroke (Laver, George, Thomas, Deutsch, & Crotty, 2012) or management of anxiety in breast cancer patients (Schneider, Ellis, Coombs, Shonkwiler, & Folsom, 2004). Furthermore, it has been shown that using virtual reality immersion to treat phobias through exposure therapy is effective (see Powers & Emmelkamp, 2008, for meta-analysis). Essentially, using this new technology for treating phobias as been shown to yield greater effect sizes for the reduction of phobias than in vivo exposure, which was always believed to be the best avenue for treatment. This stands to show that integrating new technologies for both evaluating and treating known dysfunctions can bring about new and sometimes contradicting results. Perhaps the same can be said about the results we found for emotion recognition deficits using virtual avatars. While some of our results are consistent with the current literature, some seem contradictory. This is not entirely surprising since the avatars used are much more realistic in nature and mimic almost perfectly human facial expressions, making for a very representational evaluation. Using measurement tools that are

more ecologically valid could be the reasons why we are seeing different results; perhaps the use of these avatars is yielding results that are more nuanced in nature and therefore, that could be more relevant to interventions though they need to be replicated. Static black and white images depicting only Caucasian actors, as has been used in most studies, could explain the worse deficits found in many studies compared to what we found with more realistic faces. Our results suggest that individuals with schizophrenia, with or without substance use disorder, overall perform fairly well. Although some deficits were found, these suggest that it is perhaps not the severity of the deficit that is the problem, but more the misattribution or type of mistake made and its consequences, meaning how they are interpreted in social situations. In other disorders, such as autism, facial emotion recognition is overall poor, most often because of lack of eye contact. There are however fewer misinterpretations. In schizophrenia, a misinterpretation can lead to fear, social isolation and might also feed delusions, especially when paranoia is involved.

As such, we would also suggest that virtual avatars be used not only to assess potential emotion recognition deficits but, if they are present, to create tailored and personalized training programs to improve misattribution with those same avatars. Since studies have shown that using virtual animations and virtual reality bring about similar, if not better results, than in vivo experiments, it would stand to reason that retraining emotion recognition via virtual avatars could bring a 'social' component to the treatment that could make the benefits even more significant and clinically relevant.

Furthermore, our review article revealed that the fact that 'drill and practice' protocols have proven efficient in improving targeted deficits and that the benefits remain over time, has significant implications for retraining emotion recognition with the virtual avatars. Though,

admittedly, emotion recognition is a domain of sociocognition, we suggest that it could also prove effective for this area of cognition in the next section. Therefore, using the data collected from the evaluation of specific emotion recognition profiles for each individual, we could create a computer program that would include avatars depicting specifically the emotions where identification was detected as being dysfunctional. Individuals would get feedback on the errors they made, and would continue to practice with the protocol until learning of proper identification of the emotions that are difficult for them to decipher, is acquired. Creating individual trainings for specific deficits could be both cost and time effective. All the avatars of the 6 basic emotions and of neutrality are already created. They can be manipulated with ease and in little time to change the intensity of the emotion depicted and even the angle of the face showing the emotions. It would only be a matter of adding retroactive feedback when a mistake is made to insure proper adjustment and learning. Importantly, our review has showed that, for sociocognitive domains, one of the key ingredients to success of the 'drill and practice' was explaining the reasons behind the learning process and the benefits that could be gained from the training. This can be linked to the theoretical concept of Green and his team (i.e. social disconnection), when they argue that in order to break social isolation, one needs to have motivation to engage socially that stems from understanding the benefits of social connections. Since we remain uncertain whether social isolation leads to deficits in emotion recognition or if it is having poor emotion recognition that results in more isolation, it would be ideal to integrate both aspects of the training protocols. This brings us to our main point: perhaps the best approach to improve social cognition would be to create a hybrid program targeting specifically the deficits identified in assessment but also integrating a broader social aspect to it. The 'drill and practice' part was summarized before, but we could also include a second part that would allow participants to 'put into action' their newly acquired social skills, in group exercises for instance. Importantly, these groups would be easy to

conduct and they would not necessarily require to be tailor-fitted to specific deficits. Since the emotion recognition impairments would already have been corrected by the specific and individual computerized avatars training, all the individuals could then regroup and practice social interactions using their newly acquired skills. Moreover, this would address the social isolation problem that was cited before; by having group settings for training, it would also create the potential for social interactions outside therapy. They would potentially find understanding and certainly less stigmatization from their fellow participants which could have great potential to reduce loneliness while also improving upon social skills. Online therapeutic groups, using internet teletherapy, are also being developed by our team to further help isolated people with schizophrenia connect with others with similar difficulties.

Limitations

Though our results were significant, it remains important to highlight the limitations of this thesis. While the second article is in fact a book chapter and the third one a review article, the first article is really the one with an experimentation, and thus has limitations. At first glance, it is clear that we would have preferred having a larger sample size. This was not due to lack trying – the recruitment took place over more than one year, with weekly visits to wards and clinical teams. Recruitment can be very difficult when working with people with schizophrenia, especially when no new treatment is being offered as the medical teams are less inclined to refer patients when no treatment is present. Given the interesting correlations we found in the data, having more power would perhaps have allowed us to conduct proper regression analyses in order to try and establish causality between the diagnosis and emotion recognition deficits or between emotion recognition deficits and specific social functioning impairments. Also, while a general sample size of 29 is not necessarily considered minuscule, it is rather small when

comorbid profiles are concerned -- indeed, the lack of power became more evident specifically for our group of individuals with both schizophrenia and stimulant use. Since there is very little literature on comorbid stimulant use in schizophrenia, it would be crucial to have larger groups to establish the profiles of these individuals particularly. Of greater importance, is the fact that there was no control group to run comparative analyses with, which we suggest is important to include in any future research on the matter.

Also, our sample was mainly comprised of male participants and all of them were between the ages of 18 to 35 years of age, since this thesis was part of a greater project on first psychotic episodes. Therefore, it would be interesting to see if the results can be replicated or if new emotion recognition profiles can be identified when the sample consists of individuals with longer-term schizophrenia or when more females are included.

Future research and conclusion

Although this thesis might appear to only bring a modest contribution to the current research literature, it has enabled to propose intriguing and testable new research ideas. Besides the fact that, in our project, we only explored the domain of social cognition that was identified as being the most relevant to social functioning, there remains a lot of unanswered questions with regard to other aspects of social cognition such as Theory of Mind, emotion regulation and attribution style. Including these important factors into new research projects would make for interesting contrast to what we found for emotion recognition. To reiterate, it was found that individuals in our whole sample seemed to have surprisingly intact overall emotion recognition, similar to the averages of normal individuals. This in itself it worth trying to replicate, given the argument we previously gave about obtaining novel and rather contradicting results potentially

due to the use of more naturalistic measurement tools. We also found that inclusion of substance abuse disorder brought about unexpected and controversial results; mainly that individuals with cannabis use - but also those with stimulant use - had better emotion recognition of negative emotions, precisely for fear and anger, and that they had more positive perceptions of their social abilities. Though research from our team had already hinted at the paradoxical conservation, if not improvement, of certain aspects of cognition in comorbid cannabis smoking, it is interesting to realize that we found similar results with individuals who use stimulants. Research on the impact of stimulant use in schizophrenia is scarce at best, yet our results are not entirely surprising. The initial interest of research on drug use focused mainly on the drug of choice that was more readily available at the time which was cannabis, with stimulants gaining little interest. However, the market for amphetamine production and use has been increasingly booming over the last 15 years and it is perhaps only now that we are starting the see the severe impact it can have on other disorders. Therefore, realizing that it could have the same paradoxical effect on social cognition than cannabis seems to have, certainly warrants further investigation. We could, for instance, propose a study where groups could be created to compare comorbid cannabis use with stimulant use and with schizophrenia alone to obtain more precise substance abuse sociocognitive profiles.

Furthermore, the use of virtual avatars is both cost and time effective and we hinted at the fact that their use could be yielding new and more representative results. They could be used not only for tailor-fitted emotion recognition trainings, but also when studying in more details the so-called deficits by adjusting the presentation time of the avatars as well as the delay between the presented avatars in order to assess reaction time in identification of the emotion. We suggest this avenue of future research because instead of having impaired facial recognition for certain

emotions or better recognition for others, we might realize that the results are due to either psychomotor retardation, or that a person reacts faster for emotions that are linked with his/her symptoms (attention bias). There might in fact be more to recognition deficits than what we believe we are measuring. Indeed, the lack of consensus across studies might not only be linked to measure issues or participant profiles (comorbidity present or not) but also to speed of presentation, and the presence of psychomotor retardation or of attentional biases. Knowing that it could be due to having certain pre-onset vulnerabilities, the aetiology of the disorder itself, the effect of comorbid substance abuse disorder (and if so of which type of substance), individual differences in the individuals themselves or perhaps even methodology involved in the study shows that further research is clearly needed. It would also be ideal to conduct a study that would incorporated either an eye-tracking device or the bubble technique described in (C. Clark, Gosselin, & Goghari, 2013; Gosselin & Schyns, 2001), to determine if emotion recognition deficits could be due to inappropriate use of facial cues. This would allow to answer the question if these individuals have aberrant pattern of recognition or not.

Redefining schizophrenia. Schizophrenia is often described with terms like “severe mental disorder” or “debilitating mental disorder” both of which are not necessarily inaccurate but certainly have the potential to increase stigmatisation further. Individuals suffering from this disorder are often categorized, labelled and somewhat put in a box. They are described as having serious deficits and symptoms, requiring long-term medication regimens and are overall perceived as social burdens, with important societal costs, that are better off hospitalized. This reductive and stigmatising way of conceptualising the disorder has been criticized over the years. For instance, authors such as Thomas Szasz back in 1988 argued that "schizophrenia is not a term that describes a disease but rather a term that describes what psychiatrist are allowed to do the

supposed 'schizophrenics'" (Szasz, 1988) to denounce the over-medication and internment of individuals with schizophrenia without investigation into other avenues of treatment or Mary Boyle in 2002 stated that "schizophrenia is a hypothetical construct and as such should be based on the observation of a pattern of regularities [that we are not seeing in the current research]" (Boyle, 2002) to suggest that the disorder should be understood and defined differently. Above and beyond these arguments that have been criticized over the years, when we are in contact with this population, it becomes increasingly clear that the disorder is highly heterogeneous in its presentation. Yet most researchers tend to want to find a 'one size fits all' approach to clinical treatment. This could potentially be due to looking at the disorder from a diagnostic point of view rather than from a functional point of view. Granted, investigating the impact of having a comorbidity sounds a lot like we are trying to evaluate certain diagnostic profiles. However, if the goal were to better understand functional profiles, the recognition of specific comorbid profiles could be very useful. Take the case of social awkwardness that is often seen in schizophrenia and that is briefly described at the beginning of this thesis. It is a rather vague and stereotypical term to use to refer to individuals suffering from schizophrenia but it is useful for the purpose of this discussion. Social awkwardness would come to mind individuals would tend to minimally interact during a conversation, barely making eye contact, being seemingly preoccupied more by their own thoughts than by what we are saying to them. However, if someone that could be described has 'having no filter', spilling out tons of personal information, not asking for feedback or checking in with the person they are having a monologue with, would also fit the description of being socially awkward. These two presentations are far from being equivalent and yet can be found in individuals with schizophrenia. They both suggest a deficit of some sort in social interactions, hinting at the very real possibility of deficits profiles that would be significantly different in their manifestations of the disorder. This example alone points to the problem of

having evaluation protocols and training programs that are created to measure or to improve large constructs like social interactions, without distinguishing individual differences or perhaps even the different aetiology of the manifestations. Conversely, you can have individuals that suffer from schizophrenia that appear to be highly functional, taking their medication to manage their more severe symptoms but still able to engage in a conversation in a socially appropriate manner. This could also lead us to believe that perhaps individuals that have more severe apparent difficulties socially, have specific deficit profiles, which would further support the idea of the paramount need to properly evaluate and identify specific impairments in social cognition and create trainings that are tailor-fitted to each individual's needs.

Therefore, what if we started to consider this disorder rather more a like "social disorder" than a psychiatric or brain disorder? Indeed, from aetiologies to symptoms to outcomes, it seems that the most common denominator, is social in nature. Not only does this hypothesis seem plausible when we examine the literature, but it could also significantly reduce stigmatisation around the disorder in the general public as well as change the attitude of the various professionals involved in working with individuals that have schizophrenia. However, the fact remains that suggesting such drastic changes in definition and conceptualisation – though warranted from the research and the human experience – is no easy matter. There are several implications to consider ranging from psychoeducation of the general public and the professionals involved, to the more political and financial aspects of letting go of the instant reflex of medicating these individuals and instead trying to evaluated and treat them differently. Nevertheless, the hardship of the endeavor should not be a reason for not trying, even more so if this could benefit the individuals that already suffer enough from the stigmas surrounding this disorder.

References

Addington, J., Saeedi, H., & Addington, D. (2006). Facial affect recognition: a mediator between cognitive and social functioning in psychosis? *Schizophrenia Research, 85*, 142-150.

Agosti, V., Nunes, E., & Levin, F. (2002). Rates of psychiatric comorbidity among U.S. residents with lifetime cannabis dependence. *The american journal of drug and alcohol abuse, 28*(4), 643-652.

Amminger, G. P., Schafer, M. R., Papageorgiou, K., Klier, C. M., Schlogelhofer, M., Mossaheb, N., . . . McGorry, P. D. (2012). Emotion recognition in individuals at clinical high-risk for schizophrenia. *Schizophrenia Bulletin, 38*(5), 1030-1039.

Arns, P. (1998). Canadian Version of the PSR Toolkit: Ontario Federation Community Mental Health and Addiction Programs.

Bahorik, A. L., Newhill, C. E., & Eack, S. M. (2013). Neurocognitive functioning of individuals with schizophrenia: Using and not using drugs. *Schizophrenia Bulletin, 1*(12).

Barnum, E. L., & Perron-McGovern, K. M. (2017). Attachment, self-esteem and subjective well-being among survivors of childhood sexual trauma. *Journal of Mental Health Counselling, 39*(1), 39-55.

Bayrakçi, A., Sert, E., Zorly, N., Erol, A., Sariçiçek, A., & Mete, L. (2015). Facial emotion recognition deficits in abstinent cannabis dependent patients. *Comprehensive Psychiatry, 58*, 160-164.

Bediou, B., Asri, F., Brunelin, J., Krolak-Salmon, P., D'Amato, T., Saoud, M., & Tazi, I. (2007). Emotion recognition and genetic vulnerability to schizophrenia. *British Journal of Psychiatry, 191*, 126-130.

Birchwood, M., & Chadwick, P. D. J. (1997). The omnipotence of voices: testing the validity of a cognitive model. *Psychological Medicine, 27*, 1345-1353.

Birchwood, M., Gilbert, P., Gilbert, J., Trower, P., Meaden, A., Hay, J., . . . Miles, J. N. V. (2004). Interpersonal and role-related schema influence the relationship with the dominant « voice » in schizophrenia: a comparison of three models. *Psychological Medicine, 34*, 1571-1580.

Blanchard, J. J., Brown, S. A., Horan, W. P., & Sherwood, A. R. (2000). Substance use disorders in schizophrenia: Review, integration, and a proposed model. *Clinical Psychology Review, 20*(2), 207-234.

Bossong, M. G., Jansma, J. M., Bhattacharyya, S., & Ramsey, N. F. (2014). Role of the endocannabinoid system in brain functions relevant for schizophrenia: An overview of human challenge studies with cannabis or delta-9-tetrahydrocannabinol (THC). *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 52*, 53-69.

Bourque, J., Durand, M., Lipp, O., Grignon, S., Mendreck, A., & Potvin, S. (2012). The neural correlates of positive emotion memory in cannabis-abusing patients with schizophrenia: Preliminary fMRI results. *Biological Psychiatry, 71*(267S).

Bourque, J., Mendrek, A., Durand, M., Lakis, N., Lipp, O., Stip, E., . . . Potvin, S. (2013). Cannabis abuse is associated with better emotional memory in schizophrenia: A functional magnetic resonance imaging study. *Psychiatry Research, 214*(1), 24-32.

Boyle, M. (2002). *Schizophrenia: A scientific delusion?* (2nd ed.). NY: Routledge: Taylor & Francis Inc.

Brenner, H. (2000). Psychological therapy in schizophrenia: what is the evidence? *Acta Psychiatrica Scandinavica, 102*(407), 74-77.

Brune, M., Abdel-Hamid, M., Lehmakamper, C., & Sonntag, C. (2007). Mental state attribution, neurocognitive functioning, and psychopathology: What predicts poor social competence in schizophrenia best? *Schizophrenia Research, 92*(1-3), 151-159.

Cavallaro, R., Anselmetti, S., Poletti, S., Bechi, M., Ermoli, E., Cocchi, F., . . . Smeraldi, E. (2009). Computer-aided neurocognitive remediation as an enhancing strategy for schizophrenia rehabilitation. *Psychiatry Research, 169*(3), 191-196.

Cigna, M.-H., Guay, J.-P., & Renaud, P. (2015). La reconnaissance émotionnelle faciale: validation préliminaire de stimuli virtuels dynamiques et comparaison avec les Pictures of Facial Affect (POFA). *Criminologie, 48*(2), 237-263.

Clark, C., Gosselin, F., & Goghari, V. M. (2013). Aberrant patterns of visual facial information usage in schizophrenia. *Journal of Abnormal Psychology, 122*, 513-519.

Combs, D. R., Penn, D. L., Chadwick, P., Trower, P., Michael, C. O., & Basso, M. R. (2007). Subtypes of paranoia in a nonclinical sample. *Cognitive Neuropsychiatry, 12*(6), 537-553.

Comparelli, A., Corigliano, V., De Carolis, A., Mancinelli, I., Trovini, G., Ottavi, G., . . . Girardi, P. (2013). Emotion recognition impairment is present early and is stable throughout the course of schizophrenia. *Schizophrenia Research, 143*(1), 65-69.

Comparelli, A., Corigliano, V., De Carolis, A., Mancinelli, I., Trovini, G., Ottavi, G., & Girardi, P. (2013). Emotion recognition impairment is present early and is table throughout the course of schizophrenia. *Schizophrenia Research, 143*(1), 65-69.

Corrigan, P. W., & Penn, D. L. (2001). Introduction: Framing models of social cognition and schizophrenia. In P. W. Corrigan & D. L. Penn (Eds.), *Social cognition and schizophrenia* (pp. 3-37). Washington, D.C.: American Psychological Association.

Coulston, C. M., Perdices, M., & Tennant, C. C. (2007). The neuropsychological correlates of cannabis use in schizophrenia: Lifetime abuse/dependance, frequency of use, and recency of use. *Schizophrenia Research, 96*, 169-184.

Couture, S. M., Penn, D. L., & Roberts, D. L. (2006). The functional significance of social cognition in schizophrenia: A review. *Schizophrenia Bulletin, 32*(Supp. 1), S44-S63.

Crean, R. D., Crane, N. A., & Mason, B. J. (2011). An evidence based review of acute and long-term effects of cannabis use on executive cognitive functions. *Journal of Addiction Medicine, 5*(1), 1-15.

DeRosse, P., Kaplan, A., Burdick, K. E., Lencz, T., & Malhotra, A. K. (2010). Cannabis use disorders in schizophrenia: Effects on cognition and symptoms. *Schizophrenia Research, 120*, 95-100.

Donohue, K., & Doody, G. A. (2012). Effect of illegal substance use on cognitive function in individuals with a psychotic disorder, a review and meta-analysis. *Neuropsychology, 26*(6), 785-801.

Dyck, M., Winbeck, M., Leiberg, S., Chen, Y., & Mathiak, K. (2010). Virtual faces as a tool to study emotion recognition deficits in schizophrenia. *Psychiatry Research, 179*(3), 247-252.

Edwards, J., Jackson, H. J., & Pattison, P. E. (2002). Emotion recognition via facial expression and affective prosody in schizophrenia: A methodological review. *Clinical Psychology Review, 22*(6), 789-832.

Ekman, P. (2004). Micro Expression Training Tool (METT) Online.

Ekman, P., & Friesen, W. V. (1976). *Pictures of facial affect*: Consulting Psychologists Press.

Ekman, P., Friesen, W. V., & Hager, J. C. (2002). *Facial Action Coding System: The Manual*: Consulting Psychologists Press.

Ekman, P., Sorenson, E. R., & Friesen, W. V. (1969). Pan-cultural elements in facial displays of emotion. *Science, 164*, 86-88.
Erol, A., Mete, L., Sonmez, I., & Unal, E. K. (2010). Facial emotion recognition in patients with schizophrenia and their siblings. *Nordic Journal of Psychiatry, 64*(1), 63-67.
Fernàndez-Serrano, M. J., Lozano, O., Pérez-Garcia, M., & Verdejo-Garcia, A. (2010). Impact of severity of drug use on discrete emotions recognition in polysubstance abusers. *Drug and Alcohol Dependence, 109*(1-3), 57-64.
Fernandez-Serrano, M. J., Moreno-Lopez, L., Perez-Garcia, M., & Verdejo-Garcia, A. (2012). Inteligencia emocional en individuos dependientes de cocaina. *Trastornos Adictivos, 14*(1), 27-33.
First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (2002). *Structured Clinical Interview for DSM-IV-TR Axis I Disorders - Patient edition. (SCID-I/P)*. New York.
Fiske, S. T., & Taylor, S. E. (1991). *Social cognition* (2nd edition ed.). New York, NY: McGraw-Hill Book Company.
Freeman, D., Dunn, G., Garety, P. A., Bebbington, P. E., Slater, M., & Kuipers, E. (2005). The psychology of persecutory ideation I: A questionnaire survey. *Journal of Nervous and Mental Disease, 193*, 302-308.
Fuchs, T. (2004). Neurobiology and psychotherapy: an emerging dialogue. *Current Opinion in psychiatry, 17*, 479-485.
Garety, P. A., & Freeman, D. (1999). Cognitive approaches to delusions: A critical review of theories and evidence. *British Journal of Clinical Psychology, 38*, 113-154.
Goldberg, T. E., David, A., & Gold, J. M. (2011). *Neurocognitive impairments in schizophrenia: their character and role in symptom formation*. Oxford, UK: Wiley-Blackwell.
Gosselin, F., & Schyns, P. (2001). Bubbles: a technique to reveal the use of information in recognition tasks. *Vision Research, 41*(17), 2261-2271.
Green, M. F. (1996). What are the functional consequences of neurocognitive deficits in schizophrenia? *American Journal of Psychiatry, 153*(3), 321-330.
Green, M. F., Horan, W. P., & Lee, J. (2015). Social cognition in schizophrenia. *Nature Reviews Neuroscience, 16*, 620-631.
Green, M. F., Horan, W. P., Lee, J., McCleery, A., Reddy, L. F., & Wynn, J. K. (2017). At issue: Social disconnection in schizophrenia and the general community. *Schizophrenia Bulletin*. doi:https://doi.org/10.1093/schbul/sbx082
Green, M. F., Penn, D. L., Bentall, R., Carpenter, W. T., Gaebel, W., Gur, R. C., . . . Heinssen, R. (2008). Social cognition in schizophrenia: an NIMH workshop on definitions, assessment, and research opportunities. *Schizophrenia Bulletin, 34*(6), 1211-1220.
Henry, J. D., Mazur, M., & Rendell, P. G. (2009). Social-cognitive difficulties in former users of methamphetamine. *British Journal of Clinical Psychology, 48*, 323-327.
Honig, A., Romme, M. A. J., Ensink, B., Escher, S., Pennings, M. H., & Devries, M. (1998). Auditory hallucinations: A comparison between patients and nonpatients. *Journal of Nervous and Mental Disease, 186*(10), 646-651.
Horan, W. P., Kern, R. S., Green, M. F., & Penn, D. L. (2008). Social cognition training for individuals with schizophrenia: Emerging evidence. *American Journal of Psychiatric Rehabilitation, 11*, 205-252.
Humphreys, K. (2017). A review of the impact of exclusion criteria on the generalizability of schizophrenia treatment reserach. *Clinical Schizophrenia & Related Psychoses, 11*(1), 49-57.

Jiang, Z., Rompala, G. R., Zhang, S., Cowell, R. M., & Nakazawa, K. (2013). Social isolation exacerbates schizophrenia-like phenotypes via oxidative stress in cortical interneurons. *Biological Psychiatry, 73*(10), 1024-1034.

Joyal, C. C., Jacob, L., Cigna, M.-H., Guay, J.-P., & Renaud, P. (2014). Virtual faces expressing emotions: An initial concomitant and construct validity study. *Frontiers in Human Neuroscience, 8*. doi: 10.3389/fnhum.2014.00787

Kavanagh, D. J. (1992). Recent developments in expressed emotion and schizophrenia. *British Journal of Psychiatry, 160*, 601-620.

Keefe, R. S., Vinogradov, S., Medalia, A., Silverstein, S. M., Bell, M. D., Dickinson, D., . . . Stroup, T. (2011). Report from the working group conference on multisite trial design for cognitive remediation in schizophrenia. *Schizophrenia Bulletin, 37*(Suppl 5), 1057-1065.

Kemmis, L., Hall, J. K., Kingston, R., & Morgan, M. J. (2007a). Impaired fear recognition in regular recreational cocaine users. *Psychopharmacology, 194*, 151-159.

Kemmis, L., Hall, J. K., Kingston, R., & Morgan, M. J. (2007b). Impaired fear recognition in regular recreational cocains users. *Psychopharmacology, 194*, 151-159.

Khoury, B., Lecomte, T., Comtois, N., & Nicole, L. (2013). Third-wave startegies for emotion regulation in early psychosis: a pilot study. *Early Intervention in the Real World, 9*(1), 76-83. doi:10.1111/eip.12095

Kim, Y. T., Kwon, D. H., & Chang, Y. (2011). Impairments of facial emotion recognition and theory of mind in methamphetamine abusers. *Psychiatry Research, 186*, 80-84.

Kjelby, E., Sinkeviciute, I., Gjestad, R., Kroken, R. A., Lorberg, E. M., Jorgensen, H. A., . . . Johnsen, E. (2015). Suicidality in schizophrenia spectrum disorders: the relationship to hallucinations and persecutory delusions. *European Psychiatry, 30*, 830-836.

Kohler, C. G., Turner, T. H., Bilker, W. B., Brensinger, C. M., Siegel, S. J., Kanes, S. J., . . . Gur, R. C. (2003). Facial emotion recognition in schizophrenia: Intensity effects and error pattern. *American Journal of Psychiatry, 160*(10), 1768-1774.

Kunda, Z. (1999). *Social cognition: Making sense of people*. Cambridge, MA.

Kurtz, M. (2005). Neurocognitive impairment acrosse the lifespan in schizophrenia: an update. *Schizophrenia Research, 74*(1), 15-26.

Kurtz, M. M., Seltzer, J. C., Shagan, D. S., Thime, W. R., & Wexler, B. E. (2007). Computer-assisted cognitive remediation in schizophrenia: What is the active ingredient? *Schizophrenia Research, 89*(1-3), 251-260.

Kymalainen, J. A., Weisman, A. G., Rosales, G. A., & Armesto, J. C. (2006). Ethnicity, expressed emotion, and communication deviance in family members of patients with schizophrenia. *Journal of Nervous and Mental Disease, 194*, 391-396.

Kyziridis, T. C. (2005). Notes on the history of schizophrenia. *German Journal of Psychiatry, 8*, 42-48.

Lacro, J. P., Dunn, L. B., Dolder, C. R., Leckband, S. G., & Jeste, D. V. (2002). Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. *The Journal of Clinical Psychiatry, 63*(10), 892-909.

Lally, J., & MacCabe, J. H. (2015). Antipsychothic medication in schizophrenia: a review. *British Medical Bulletin, 114*(1), 169-179.

Laver, K., George, S., Thomas, S., Deutsch, J. E., & Crotty, M. (2012). Virtual reality for stroke rehabilitation. *Stroke, 43*, e20-e21. doi:https://doi.org/10.1161/STROKEAHA.111.642439

Lecardeur, L., Stip, E., Giguère, M., Blouin, G., Rodriguez, J.-P., & Lavau-Champagne, M. (2009). Effects of cognitive remediation therapies on psychotic symptoms and cognitive complaints in patients with schizophrenia and related disorders: a randomized study. *Schizophrenia Research, 111*(1-3), 153-158.

Lecomte, T., Corbière, M., & Briand, C. (2008). *Psychosocial functioning assessment*. NY: Guildford Press.

Lecomte, T., Corbière, M., Ehmann, T., Addington, J., Abdel-Baki, A., & Macewan, B. (2014). Development and preliminary validation of the First Episode Social Functioning Scale for early psychosis. *Psychiatric Research, 216*(3), 412-417. doi:10.1016/j.psychres.2014.01.044

Lesh, T. A., Niendam, T. A., Minzenberg, M. J., & Carter, C. S. (2011). Cognitive control deficits in schizophrenia: mechanisms and meaning. *Neuropsychopharmacology, 36*(1), 316-338.

Lev-Ran, S., Harrison, I., Ron, M. A., Barnes, T. R. E., & Joyce, E. M. (2012). Neurocognitive functions of heavy cannabis using in schizophrenia patients. *European Psychiatry, 27*, 365-368.

Liberman, R. P. (1982). What is schizophrenia? *Schizophrenia Bulletin, 8*, 435-437.

Lin, A., Wood, S. J., & Yung, A. R. (2013). Measuring psychosocial outcome is good. *Current Opinion in psychiatry, 26*, 138-143.

Lysaker, P. H., Carcione, A., Dimaggio, G., Johannesen, J. K., Nicolo, G., Procacci, M., & Semerari, A. (2005). Metacognition admist narratives of self and illness in schizophrenia: Associations with neurocognition, symptoms, insight and quality of life. *Acta Psychiatrica Scandinavica, 112*, 64-71.

Malone, D. T., Kearn, C. S., Chongue, L., Mackie, K., & Taylor, D. A. (2008). Effect of social isolation on CB1 and D2 receptor and fatty acid amide hydrolase expression in rats. *Neuroscience, 152*(1), 265-272.

Mancini-Marlë, A., Potvin, S., Fahim, C., Mensour, B., Beauregard, M., Roy, J. Y., & Stip, E. (2006). Neural correlates of the affect regulation model in schizophrenia patients with a substance use history: A functional magnetic resonance imagine study. *Journal of Clinical Psychiatry, 67*(3), 342-350.

Mancuso, F., Horan, W. P., Kern, R. S., & Green, M. F. (2011). Social cognition in psychosis: Multidimensional structure, clinical correlates, and relationship with functional outcome. *Schizophrenia Research, 125*(2), 143-151.

Mandal, M. K., Pandey, R., & Prasad, A. B. (1998). Facial expressions of emotions and schizophrenia: A review. *Schizophrenia Bulletin, 24*(3), 399-412.

Mata, I., Rodriguez-Sanchez, J. M., Pelayo-Teran, J. M., Perez-Iglesias, R., Gonzalez-Blanch, C., Ramirez-Bonilla, M., . . . Crespo-Facorro, B. (2008). Cannabis abuse is associated with decision-making impairment among first-episode patients with schizophrenia-spectrum psychosis. *Psychological Medicine, 38*, 1257-1266.

Meesters, P. D., Stek, M. L., Comijs, H. C., de Haan, L., Patterson, T. L., Eikelenboom, P., & Beekman, A. T. F. (2010). Social functioning among older community-dwelling patients with schizophrenia: a review. *American Journal of Geriatric Psychiatry, 18*(10), 862-878.

Miklowitz, D. J., Strachan, A. M., Goldstein, M. J., Doane, J. A., Snyder, K. S., Hogarty, G. E., & Falloon, I. R. H. (1986). Expressed emotion and communication deviance in the families of schizophrenics. *Journal of Abnormal Psychology, 95*(1), 60-66.

Minzenberg, M. J., Laird, A. R., Thelen, S., Carter, C. S., & Glahn, D. C. (2009). Meta-analysis of 41 functional neuroimaging studies of executive function in schizophrenia. *Archives of General Psychiatry, 66*(8), 811-822.

Moore, T., Zammit, S., Lingford-Hughes, A., Barnes, T. R. E., Jones, P. B., Burke, M., & Lewis, G. (2007). Cannabis use and risk of psychosis or affective mental health outcomes: a systematic review. *The Lancet, 370*(9584), 319-328.

Morrison, R. L., Bellack, A. S., & Mueser, K. T. (1988). Deficits in facial-affect recognition and schizophrenia. *Schizophrenia Bulletin, 14*(1), 67-83.

Mueser, K. T., & Bellack, A. S. (1998). Social skills and social functionning. In E. 1998 (Ed.), *Handbook of social functionning in schizophrenia* (pp. 79-96). Needham Heights, MA: Allyn & Bacon.

Mueser, K. T., Yarnold, P. R., Rosenberg, S. D., Swett, C., Miles, K. M., & Hill, D. (2000). Substance use disorder in hospitalized severely mentally ill psychiatric patients: Prevalance, correlates, and subgroups. *Schizophrenia Bulletin, 26*(1), 179-192.

Myles, N., Newall, H., Nielssen, O., & Large, M. (2012). The association between cannabis use and earlier age at onset of schizophrenia and other psychoses: meta-analysis of possible confounding factors. *Current Pharmaceutical design, 18*(32), 5055-5069.

Nuechterlein, K. H., Green, M. F., Kern, R. S., Baade, L. E., Barch, D. M., & Cohen, J. D. (2008). The MATRICS consensus cognitive battery, part 1: test selection, reliability, and validity. *American Journal of Psychiatry, 165*(203e13).

Palmer, B., Heaton, R. K., Kuck, J., & Braff, D. (1997). Is it possible to be schizophrenic yet neuropsychologically normal? *Neuropsychology, 11*, 437-446.

Paquin, K., Lecomte, T., & Potvin, S. (2016). *Cannabis smoking in adult schizophrenia: A cognitive and functional magnetic resonance imaging perspective*. London, United Kingdom: Academic Press.

Paquin, K., Lecomte, T., & Potvin, S. (2017). Cannabis smoking in adult schizophrenia: A cognitive and functional neuroimaging perspective. In A. Press (Ed.), *Handbook of cannabis and related pathologies* (pp. 357-371). London, UK: P. VR.

Paquin, K., Wilson, A. L., Cellard, C., Lecomte, T., & Potvin, S. (2014). A systematic review on improving cognition in schizophrenia: which is the more commonly used type of training ,practice or strategy learning? *BMC Psychiatry, 14*(139).

Penk, W. E., Flannery, R. B., Irvin, E., Geller, J., Fisher, W., & Hanson, M. A. (2000). Characteristics of substance-abusing persons with schizophrenia: The paradox of the dually diagnosed. *Journal of Addictive Diseases, 19*, 23-30.

Penn, D. L., Combs, D., & Mohamed, S. (2001). Social cognition and social functionning in schizophrenia. In P. W. Corrigan & D. L. Penn (Eds.), *Social cognition and schizophrenia* (pp. 73-95). Washington, DC: American Psychological Association.

Penn, D. L., Mueser, K. T., Doonan, R., & Nishith, P. (1995). Relations between social skills and ward behavior in chronic schizophrenia. *Journal of Schizophrenia Research, 16*, 225-232.

Pinkham, A. E., & D.L., P. (2006). Neurocognitive and social cognitive predictors of interpersonal skill in schizophrenia. *Psychiatry Research, 143*, 167-178.

Pinkham, A. E., Penn, D. L., Green, M. F., Buck, B., Healey, K. M., & Harvey, P. D. (2014). The social cognition psychometric evaluation study: results of the expert survey and RAND panel. *Schizophrenia Bulletin, 40*(4), 813-823.

Poole, J. H., Tobias, F. C., & Vinogradov, S. (2000). The functional relevance of affect recognition errors in schizophrenia. *Journal of the International Neuropsychological Society, 6*(6), 649-658.

Potvin, S., Joyal, C. C., Pelletier, J., & Stip, E. (2008). Contradictory cognitive capacities in substance-abusing schizophrenia patients: a meta-analysis. *Schizophrenia Research, 100*, 242-251.

Potvin, S., Mancini-Marlë, A., Fahim, C., Mensour, B., & Stip, E. (2007). A functional magnetic resonance imaging study of social emotion in schizophrenia patients with and without comorbid substance use disorder. *Social Neuroscience, 2*(2), 1-11.

Powers, M. B., & Emmelkamp, P. M. G. (2008). Virtual reality exposure therapy for anxiety disorders: A meta-analysis. *Journal of Anxiety Disorders, 22*(3), 561-569.

Raffard, S., Gely-Nargeot, M. C., Capdevielle, D., Bayard, S., & Boulenger, J. P. (2009). [Learning potential and cognitive remediation in schizophrenia]. *Encephale, 35*(4), 353-360.

Read, J., Perry, B., Moskowitz, A., & Connolly, J. (2001). The contribution of early traumatic events to schizophrenia in some patients: a Traumagenic Neurodevelopmental model. *Psychiatry, 64*, 319-345.

Read, J., Van Os, J., Morrison, A. P., & Ross, C. A. (2005). Childhood trauma, psychosis and schizophrenia: a literature review with theoretical and clinical implications. *Acta Psychiatrica Scandinavica, 112*(5), 330-350.

Regier, D. A., Farmer, M. E., Rae, D. S., Locke, B. Z., Keith, S. J., & Judd, L. L. (1990). Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) study. *Journal of American Medical Association, 264*, 2511-2518.

Revheim, N., Schechter, I., Kim, D., Silipo, G., Allingham, B., Butler, P., & Javitt, D. C. (2006). Neurocognitive and symptom correlates of daily problem-solving skills in schizophrenia. *Schizophrenia Research, 83*(2-3), 237-245.

Ringen, P. A., Vaskinn, A., Sundet, K., Engh, J. A., Johnsdottir, H., Simonsen, C., . . . Andreassen, O. A. (2010). Opposite relationships between cannabis use and neurocognitive functioning in bipolar and schizophrenia. *Psychological Medicine, 40*, 1337-1347.

Roncone, R., Mazza, M., Frangou, I., De Risio, A., Ussorio, D., Tozzini, C., & Casacchia, M. (2004). Rehabilitation of theory of mind deficit in schizophrenia: a pilot study of metacognitive strategies in group treatment. *Neuropsychological rehabilitation, 14*(4), 421-435.

Roy, A. (1986). Depression, attempted suicide, and suicide in patients with chronic schizophrenia. *Psychiatric Clinics of North America, 9*(1), 193-206.

Rummel-Kluge, C., Komossa, K., Schwarz, S., Hunger, H., Schmid, F., Asenjo Lobos, C., . . . Leucht, S. (2010). Head-to-head comparisons of metabolic side effects of second generation antipsychotics in the treatment of schizophrenia: A systematic review and meta-analysis. *Schizophrenia Research, 123*(2-3), 225-233.

Saha, S., Chant, D., Welham, J., & McGrath, J. (2005). A systematic review of the prevalence of schizophrenia. *PLOS Medicine, 2*(5), e141. doi:10.1371/journal.pmed.0020141

Salyers, M. P., & Mueser, K. T. (2001). Social functioning, psychophathology, and medication side effects in relation to substance use and abuse in schizophrenia. *Schizophrenia Research, 48*(1), 109-123.

Schneider, S. M., Ellis, M., Coombs, W. T., Shonkwiler, E. L., & Folsom, L. C. (2004). Virtual reality intervention for older women with breast cancer. *Cyberpsychology & Behavior, 6*(3), 301-307.

Silver, H., Bilker, W. B., & Goodman, C. (2009). Impaired recognition of happy, sad and neutral expressions in schizophrenia is emotion, but no valence, specific and context dependent. *Psychiatry Research, 169*(2), 101-106.
Singer, M. T., & Wynne, L. C. (1965). Thought disorder and family relations of schizophrenics: IV. Results and implications. *Archives of General Psychiatry, 12*, 201-206.
Stopa, L., & Clark, D. M. (1993). Cognitive processes in social phobia. *Behaviour Research & Therapy, 31*(3), 255-267.
Stroup, T. S., & Geddes, J. R. (2008). Randomized controlled trials for schizophrenia: Study designs targeted to distinct goals. *Schizophrenia Bulletin, 34*(2), 266-274.
Szasz, T. (1988). *Schizophrenia: The sacred symbol of psychiatry*. Syracuse.
Thonon, B., & Laroi, F. (2016). What predicts stigmatisation about schizophrenia? Results from a general population survey examining its underlying cognitive, affective and behavioural factors. *Psychosis*. doi:http://dx.doi.org/10.1080/17522439.2016.1229361
Tiffany, S. T., Friedman, L., Greenfield, S. F., Hasin, D. S., & Jackson, R. (2011). Beyond drug use: A systematic consideration of other outcomes in evaluations of treatments for substance use disorders. *Addiction, 107*, 709-718.
Tsoi, D. T., Lee, K. H., Khokhar, W. A., Mir, N. U., Swalli, J. S., Gee, K. A., . . . Woodruff, P. W. R. (2008). Is facial emotion recognition impairment in schizophrenia identical for different emotions? A signal detection analysis. *Schizophrenia Research, 99*(1-3), 263-269.
van Os, J. (2003). Is there a continuum of psychotic experiences in the general population? *Epidemiologia e Psichiatria Sociale, 12*(4), 242-252.
van't Wout, M., Aleman, A., Kessels, R. P., Cahn, W., de Haan, E. H., & Kahn, R. S. (2007). Exploring the nature of facial affect processing deficits in schizophrenia. *Psychiatry Research, 150*(3), 227-235.
Veltro, F., Mazza, M., Vendittelli, N., Alberti, M., Casacchia, M., & Roncone, R. (2011). A comparison of the effectiveness of problem solving training and of cognitive-emotional rehabilitation on neurocognition, social cognition and social functioning in people with schizophrenia. *Clinical Practice and Epidemiology in Mental Health, 7*, 123-132.
Walker, E. F., & Diforio, D. (1997). Schizophrenia: A neural diathesis-stress model. *Psychological Review, 104*(4), 667-685.
Wells, A., Clark, D. M., Salkovskis, P., Ludgate, J., Hackman, A., & Gelder, M. (1995). Social Phobia: The role of in-situation safety behaviors in maintaining anxiety and negative beliefs. *Behavior Therapy, 26*, 153-161.
Weyers, P., Mühlberger, A., Hefele, C., & Pauli, P. (2006). Electromyographic responses to static and dynamic avatar emotional facial expressions. *Psychophysiology, 43*(5), 450-453.
Winklbaur, B., Ebner, N., Sachs, G., Thau, K., & Fischer, G. (2006). Substance abuse in patients with schizophrenia. *Dialogues in Clinical Neuroscience, 8*(1), 37-43.
Wolwer, W., & Frommann, N. (2011). Social-cognitive remediation in schizophrenia: generalization of effects of the Training of Affect Recognition (TAR). *Schizophrenia Bulletin, 37 Suppl 2*, S63-70.
Wykes, T., Huddy, V., Cellard, C., McGurk, S. R., & Czobor, P. (2011). A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. *American Journal of Psychiatry, 168*(5), 472-485.
Wynne, L. C., Singer, M. T., & Toohey, M. (1976). Communication of the adoptive parents of schizophrenics. *Schizophrenia 75: Psychotherapy, family studies, research* (pp. 413-452). Oslo: Norway.

Zubin, J., & Spring, B. (1977). Vulnerability: A New View on Schizophrenia , . *Journal of Abnormal Psychology, 86*, 103-126.

Annex A – Questionnaires and documents

Presented in alphabetical order

Sample of avatar

Brief Psychiatric Rating Scale (BPRS)
(Ventura, Green, Shaner, & Liberman, 1993)

BRIEF PSYCHIATRIC RATING SCALE

20822

Client ID | Date (dd/mm/yyyy) | Rater | Code

Indicate period (0 to 10):

0	1	2	3	4	5	6	7
Not Assessed	Not Present	Very Mild	Mild	Moderate	Moderately Severe	Severe	Extremely Severe

Rate items 1-14 on the basis of patient's self-report during interview. Mark "N" for symptoms not assessed. Note items 7, 12 and 13 are also rated on observed behavior during the interview. PROVIDE EXAMPLES

1. Somatic Concern
2. Anxiety
3. Depression
4. Suicidality
5. Guilt
6. Hostility
7. Elevated Mood
8. Grandiosity
9. Suspiciousness
10. Hallucinations
11. Unusual Thought Content
12. Bizarre Behavior
13. Self-neglect
14. Disorientation

Rate items 15-24 on the basis of observed behavior or speech of the patient during the interview.

15. Conceptual Disorganization
16. Blunted Affect
17. Emotional Withdrawal
18. Motor Retardation
19. Tension
20. Uncooperativeness
21. Excitement
22. Distractibility
23. Motor Hyperactivity
24. Mannerisms and Posturing

Sources of information (check all that apply)

— Patient
— Parents/Relatives
— Mental health professionals
— Chart

Explain here if validity of assessment is questionable:

— Underreported due to lack of rapport
— Symptoms possibly drug-induced
— Underreported due to negative symtpoms
— Patient uncoopertive
— Difficult to assess due to formal thought disorder
— Other _____

Confidence in assessment [ ] 1=Not at all 5=Very Confident

06/07/2000 BPRS 1/1

First Episode Social Functioning Scale -- Self-Report

(Lecomte, Corbière, Lehman et al., 2013)

Please answer each question honestly, using the choices suggested.
If you answer Never, or if you find a question doesn't apply to you and answer N/A, please explain why.

1. Living Skills

1.1 TRANSPORTATION

1.1.a I can get around town easily, either by taking the bus or by other means of transportation.

Totally Disagree Disagree Agree Totally Agree

1.1.b In the past 3 months, I have used public transit of other means of transportation (car, bike etc.) to get around.

Never (less than once a month) Sometimes (once a week) Often (several x's/week) Always (almost daily) N/A

If N/A or Never, please explain: (e.g. lack of resources, no need)
_____
_____

1.2 COMMUNICATION

1.2.a I am comfortable using the phone, internet or email to communicate.

Totally Disagree Disagree Agree Totally Agree

1.2.b In the past 3 months, I have used the phone, internet or email to communicate with people.

Never (less than once a month) Sometimes (once a week) Often (several x's/week) Always (almost daily) N/A

If N/A or Never, please explain: (e.g. no need)
_____
_____

1.3 BASIC HYGIENE

1.3.a I am good at taking care of my physical appearance and hygiene.

Totally Disagree Disagree Agree Totally Agree

1.3.b In the past 3 months, I have been taking care of my appearance and hygiene.

Never (shower once/week or less) Sometimes (shower every 2-3 days, clothes can be dirty) Often (shower almost daily) Always (always clean, shower daily) N/A

If N/A or Never, please explain: (e.g. lack of energy, no motivation)

_____

_____

1.4 GETTING FOOD

1.4.a I have no problem getting enough food to eat (by cooking, family, fast food, etc).

Totally Disagree Disagree Agree Totally Agree

1.4.b In the past 3 months, I have been getting enough food to eat.

Never (always hungry) Sometimes (skip meals, don't eat enough Often (usually well fed) Always (eat 2-3 good meals per day) N/A

If N/A or Never, please explain: (e.g. lack of resources, not hungry)

_____

_____

On a scale of 1 to 10, overall how important is it for you to be good in the areas of your daily living skills just mentioned (use of transportation, use of communication devices, basic hygiene, getting food)?

1 2 3 4 5 6 7 8 9 10

(not at all important) (extremely important)

Comments:_____
_____
_____

2. Interacting with people

2.1 CLERKS, COFFEE SHOP…

2.1.a I find it easy to interact with waiters, cashiers, and salespeople (e.g. small talk, asking for information, making a purchase).

Totally Disagree Disagree Agree Totally Agree

2.1.b In the past 3 months, I have been interacting with waiters, cashiers or salespeople.

Never (don't go near stores) Sometimes (once or twice/month) Often (more than once/week) Always (most days) N/A

If N/A or Never, please explain: (e.g. not interested, no need)
_____
_____

2.2 AUTHORITY/ ADULTS

2.2.a I find it easy to interact with authority figures (e.g. teacher, boss, doctor, others' parents…).

Totally Disagree Disagree Agree Totally Agree

2.2.b In the past 3 months, I have been interacting with authority figures.

Never (don't) Sometimes (less than once a week) Often (most days) Always (everyday) N/A

If N/A or Never, please explain: (e.g. no contact with authority figures)
_____
_____

2.3 ACQUAINTANCES

2.3.a I find it easy to talk with people my age I know just a little bit.

Totally Disagree Disagree Agree Totally Agree

2.3.b In the past 3 months, I have been talking to people my age I know just a little bit.

Never (don't) Sometimes (less than once a month) Often (at least once a week) Always N/A (most days)

If N/A or Never, please explain: (e.g. no interest)

_____
_____

2.4 ASSERTIVENESS

2.4.a I know how to stand up for myself when needed.

Totally Disagree Disagree Agree Totally Agree

2.4.b In the past 3 months, I have been able to stand up for myself.

Never Sometimes (less than weekly) Often (most days) Always N/A (everyday)

If N/A or Never, please explain: (e.g. no need to)

_____
_____

On a scale of 1 to 10, how important is it for you to be good the areas of interacting with people just mentioned of (interacting with waiters, authority figures and acquaintances, and being assertive)?

1 2 3 4 5 6 7 8 9 10
(not at all important) (extremely important)

Comments:_____
_____
_____

3. Friends and activities

3.1 Solo activities

3.1.a I am really good in solo activities such as going to the gym, going to the movies, chatting on the net, taking lessons (music, painting, etc). Please do not count watching TV, listening to music or playing videogames.

Totally Disagree Disagree Agree Totally Agree

3.1.b In the past 3 months, I have been doing solo activities such as going to the gym, going to the movies, chatting on the net, taking lessons (music, painting, etc).

Never (don't)	Sometimes (less than once a month)	Often (several times a month)	Always (a few times/week)	N/A

If N/A or Never, please explain: (e.g. too busy, no interest)

_____

_____

3.2 Meaningful activities

3.2.a I try to do things that are really important to me (specific hobbies, passions…).

Totally Disagree Disagree Agree Totally Agree

3.2.b In the past 3 months, I have been doing things that are really important to me.

Never (don't)	Sometimes (less than once a month)	Often (several times a month)	Always (a few times/week)	N/A

If N/A or Never, please explain: (e.g. too busy, no hobbies)

_____

_____

3.3 Balancing time alone and with others

3.3.a I am able to balance the amount of time I spend with others and by myself.

Totally Disagree Disagree Agree Totally Agree

3.3.b In the past 3 months, I have been spending most of my days alone.

Never	Sometimes (a few days a week)	Often (most days)	Always (everyday)	N/A

If N/A or Never, please explain: (e.g. live with people, too busy)

_____

_____

3.4 BEST FRIEND

3.4.a I feel I have at least one best friend with whom I can share important things that happen to me.

Totally Disagree	Disagree	Agree	Totally Agree

3.4.b In the past 3 months, I have spent time with my best friend (live or by phone).

Never	Sometimes (spoke at least once)	Often (speak or see every 2-3 weeks)	Always (speak or see weekly)	N/A

If N/A or Never, please explain: (e.g. no best friend, too busy)

_____

_____

3.5 BUDDIES

3.5.a I have friends that I can hang out with, do stuff with (shopping, movies, go out…).

Totally Disagree	Disagree	Agree	Totally Agree

3.5.b In the past 3 months, I have spent time doing activities with my friends.

Never	Sometimes (at least once a month)	Often (several times a month)	Always (weekly)	N/A

If N/A or Never, please explain: (e.g. no money, too busy)

_____

_____

3.6 ABILITIES TO DEVELOP FRIENDSHIPS

3.6.a I am able to make new friends by suggesting getting together, making invitations or phoning people up.

Totally Disagree Disagree Agree Totally Agree

3.6.b In the past 3 months, I have tried to develop a potential friendship with someone.

Never (made an invitation or accepted one) Sometimes (invited, suggested activity or did something with a new person more than once) Often (very sociable, talk to new people and open to meeting 3x's or more) Always N/A

If N/A or Never, please explain: (e.g not met anyone, no interest)

_____

_____

On a scale of 1 to 10, overall how important is it for you to be good in the areas of friendship and social activities just mentioned (solo, meaningful activities, balancing time alone and with others, develop new friendships, spending time with best friends or buddies)?

1 2 3 4 5 6 7 8 9 10

(not at all important) (extremely important)

Comments:_____

_____

_____

4. Intimacy

4.1 DATING

4.1.a I am quite comfortable dating.

Totally Disagree Disagree Agree Totally Agree

4.1.b In the past 3 months, I have been dating.

Never	Sometimes (had 2 dates or less)	Often (more than 3 dates)	Always (have been seeing someone weekly)	N/A

If N/A or Never, please explain: (e.g. no interest, too trying)

_____
_____

4.2 HAVING BOYFRIEND/GIRLFRIEND OR SPOUSE

4.2.a I enjoy having a stable boy/girlfriend or spouse.

Totally Disagree Disagree Agree Totally Agree

4.2.b In the past 3 months, I have spent time with my stable boy/girlfriend or spouse.

Never	Sometimes (every few weeks)	Often (once a week, for less than a month)	Always (weekly for more than a month)	N/A

If N/A or Never, please explain: (e.g. never had a boy/girlfriend, not interested)

_____
_____

4.3 SEXUAL RELATIONSHIP

4.3.a I am interested in sex.

Totally Disagree Disagree Agree Totally Agree

4.3.b In the past 3 months, I have had sex with someone.

Never	Sometimes (at least once)	Often (twice a month or more)	Always (weekly)	N/A

If N/A or Never, please explain: (e.g. religious beliefs, not interested)

_____
_____

4.4 EMOTIONAL CLOSENESS

4.4.a I feel I am able to share feelings, inner thoughts, and be close with my stable boy/girlfriend or spouse (when I have one).

Totally Disagree Disagree Agree Totally Agree

4.4.b In the past 3 months, I have shared my feelings, inner thoughts, and have been close with my stable boy/girlfriend or spouse.

Never Sometimes (at least once) Often **(**twice or more/month) Always N/A (weekly or more)

If N/A or Never, please explain: (e.g. no one to share with, not interested)
_____
_____

4.5 GRASPING SITUATIONS

4.5.a I can quickly understand what is going on in most situations involving other people.

Totally Disagree Disagree Agree Totally Agree

4.5.b In the past 3 months, I have been able to quickly understand most situations involving other people.

Never Sometimes (less than weekly) Often (most days) Always N/A (everyday)

If N/A or Never, please explain: (e.g. no need to)
_____
_____

On a scale of 1 to 10, overall how important is it for you to be good in the areas of intimacy just mentioned (dating, having a boy/girlfriend/spouse, sex, emotional closeness, and grasping situations)?

1 2 3 4 5 6 7 8 9 10
(not at all important) (extremely important)

Comments:_____
_____
_____

5. Family

5.1 Parents

5.1.a I can talk to my parents about things that matter to me.

Totally Disagree Disagree Agree Totally Agree

5.1.b In the past 3 months, I have talked to my parents about things that matter to me.

Never Sometimes (once a month) Often (every 2 weeks) Always (weekly) N/A

If N/A or Never, please explain: (e.g. don't have contact with parents)

_____

_____

5.2 Relationship with parents

5.2.a My parents and I typically get along.

Totally Disagree Disagree Agree Totally Agree

5.2.b In the past 3 months, I have spent time without big conflicts with one (or both) of my parents.

Never Sometimes (less than once/month) Often (at least once a month) Always (weekly) N/A

If N/A or Never, please explain: (e.g. don't have contact with parents)

_____

_____

5.3 Relationship with family

5.3.a I get along well with my family (siblings, grandparents, uncles, aunts, cousins).

Totally Disagree Disagree Agree Totally Agree

5.3.b In the past 3 months, I have spent time (live or phone or other means) with at least one member of my family.

Never Sometimes (once) Often (at least once a month) Always N/A (weekly)

If N/A or Never, please explain: (e.g. no extended family, not interested)
_____
_____

On a scale of 1 to 10, how important is it for you to be good in the areas of family just mentioned (being able to talk and not being in conflict with parents, getting along with family)?

1 2 3 4 5 6 7 8 9 10
(not at all important) (extremely important)

Comments:_____
_____
_____

6. Relationships and social activities at work (include current and jobs held in the past year)

○ I have not worked in the past year (go to rectangle on page 14).

6.1 Relationship with your supervisor

6.1.a I usually feel comfortable discussing issues related to work with my supervisor (e.g. tasks, feedback, schedules, etc.).

Totally Disagree Disagree Agree Totally Agree

6.1.b In the past 3 months, I have discussed issues related to my job with my supervisor.

Never (only once when I didn't have a choice) Sometimes (once or twice by my own initiative) Often (more than twice by my own initiative) Always N/A

If N/A or Never, please explain: (e.g. have had no problems)

_____
_____

6.2 RELATIONSHIP WITH YOUR CO-WORKERS

6.2.a I typically get along with my co-workers.

Totally Disagree Disagree Agree Totally Agree

6.2.b In the past 3 months, I have spent time with co-workers (talking about work or not).

Never Sometimes (once a month) Often (once a week) Always (most days) N/A

If N/A or Never, please explain: (e.g. no interaction with co-workers, no interest)

_____
_____

6.3 PARTICIPATION IN SOCIAL ACTIVITIES AT WORK

6.3.a I participate in social activities on the job (Christmas party, afterwork outings, etc).

Totally Disagree Disagree Agree Totally Agree

6.3.b In the past 3 months, I was able to participate in social activities on the job (Christmas party, afterwork outings, etc).

Never Sometimes (once or twice a year) Often (once or twice in 6 months) Always (once or twice in 3 months) N/A

If N/A or Never, please explain: (e.g. no planned activities, not interested)

_____
_____

On a scale of 1 to 10, overall how important is it for you to be good in the areas of work just mentioned (relationship with supervisor and co-workers, social activities at work)?

1 2 3 4 5 6 7 8 9 10
(not at all important) (extremely important)

Comments:_____
_____
_____

7. Work abilities (include current and jobs held in the past year)

7.1 PUNCTUALITY

7.1.a I always respect my work schedule (get to work on time and leave on time).

Totally Disagree Disagree Agree Totally Agree

7.1.b In the past 3 months, I have respected my work schedule.

Never Sometimes (once a week) Often (once or several times a week) Always (each day) N/A

If N/A or Never, please explain: (e.g. set my own schedule)
_____
_____

7.2 PRODUCTIVITY AND PLANNING

7.2.a I do my work tasks within the expected time-frame.

Totally Disagree Disagree Agree Totally Agree

7.2.b In the past 3 months, I was able to do work tasks within the expected time-frame.

Never Sometimes (once a month) Often (once a week) Always (several times a week) N/A

If N/A or Never, please explain: (e.g. no tasks with deadlines)
_____

_____

7.3 QUALITY OF WORK

7.3.a I consistently provide a good quality of work.

Totally Disagree Disagree Agree Totally Agree

7.3.b In the past 3 months, I was able to provide a good quality of work.

Never Sometimes (once or twice a month) Often (once or twice a week) Always (everyday) N/A

If N/A or Never, please explain: (e.g. job difficulties)

_____
_____

On a scale of 1 to 10, overall how important is it for you to be good in the areas of work just mentioned (punctuality, productivity, and quality of work)?

1 2 3 4 5 6 7 8 9 10
(not at all important) (extremely important)

Comments:_____
_____
_____

If no job or never worked:

1. Are you looking for work?	Yes	No
2. Are you enrolled in a vocational program?	Yes	No
If yes, which one? Name of the program:		
3. Are you in contact with an employment specialist/job coach?	Yes	No

8. School relationships and social activities at school **(include current and courses in the past year):**

○ I have not attended school (include college, university, or an educational program) in the past year (go to end of document).

8.1 Relationship with your teacher/professor

8.1.a I am able to talk to my teacher/professor about things at school/college/university that matter to me (classes, assignments, schedules, etc.).

Totally Disagree Disagree Agree Totally Agree

8.1.b In the past 3 months, I have talked to my teacher/professor about things at school/college/university that matter to me (classes, assignments, schedules, etc.).

Never	Sometimes (only once when I didn't have a choice)	Often (once or twice by my own initiative)	Always (more than twice by my own initiative)	N/A

If N/A or Never, please explain: (e.g. no problems with classes)

_____

_____

8.2 Relationship with students

8.2.a The other students and I typically get along.

Totally Disagree Disagree Agree Totally Agree

8.2.b In the past 3 months, I have spent time with other students (talking about classes or not).

Never	Sometimes (once a month)	Often (once a week)	Always (most days)	N/A

If N/A or Never, please explain: (e.g. no interaction with other students)

_____

_____

8.3 PARTICIPATION IN THE CLASSROOM

8.3.a I am comfortable participating in the classroom.

Totally Disagree Disagree Agree Totally Agree

8.3.b In the past 3 months, I participated in the classroom.

Never Sometimes (once or twice a month) Often (once or twice a week) Always (several times a week) N/A

If N/A or Never, please explain: (e.g. not interested)

_____
_____

On a scale of 1 to 10, overall how important is it for you to be good in the areas of school mentioned (relationship with teachers and students, participation in class)?

1 2 3 4 5 6 7 8 9 10
(not at all important) (extremely important)

Comments:_____
_____
_____

9. Educational abilities

9.1 MEETING DEADLINES

9.1.a I am always able to finish my assignments on time.

Totally Disagree Disagree Agree Totally Agree

9.1.b In the past 3 months, I was able to hand-in assignments on time.

Never Sometimes (once or twice) Often (most of the time) Always (all of the time) N/A

If N/A or Never, please explain: (e.g. arrangements made about assignment deadlines)

_____
_____

9.2 PUNCTUALITY

9.2.a I come to the school/college/university on time and rarely miss classes.

Totally Disagree Disagree Agree Totally Agree

9.2.b In the past 3 months, I have been on time for classes and not missed any.

Never Sometimes (once a week) Often (several times a week) Always (every day) N/A

If N/A or Never, please explain: (e.g. no class time)

_____
_____

9.3 QUALITY OF GRADES

9.3.a I am able to consistently get good grades.

Totally Disagree Disagree Agree Totally Agree

9.3.b In the past 3 months, I have gotten good grades for my assignments and tests/exams.

Never Sometimes (once or twice) Often (most of the time) Always (all the time) N/A

If N/A or Never, please explain: (e.g. no grading)

_____
_____

On a scale of 1 to 10, overall how important is it for you to be good in the areas of school mentioned (meeting deadlines, punctuality, quality of grades)?

1 2 3 4 5 6 7 8 9 10
(not at all important) (extremely important)

Comments:_____
_____
_____

If no school or courses:

1. **Are you looking to go back to school?** | Yes | No |
2. **Are you enrolled in an educational program?** | Yes | No |

   If yes, which one? Name of the program: | |
3. **Are you in contact with a school counselor?** | Yes | No |

PSR Toolkit for sociodemographic information

Basline Demographic Information

Date (dd/mm/yy) ☐☐ / ☐☐ / ☐☐☐☐

Birthdate (dd/mm/yy) ☐☐ / ☐☐ / ☐☐☐☐ **Age** ☐☐

Gender ○ 1 – Male ○ 2 – Female

How do you describe yourself? (Check one)

○ 1 – Aboriginal
○ 2 – African
○ 3 – Caucasian
○ 4 – East Asian
○ 5 – Latin/Hispanic
○ 6 – Middle Eastern
○ 7 – South Asian
○ 8 – West Asian
○ 9 – Mixed
○ 10 – Other
○ 11 – Do not know
○ 12 – Prefer not to answer

How do you describe your culture? (Check one)

○ 1 – Aboriginal / First Nations
○ 2 - African
○ 3 - American
○ 4 – Australian/New Zealander
○ 5 – Canadian
○ 6 – Caribbean
○ 7 – Central American
○ 8 – East Asian
○ 9 – European
○ 10 – French Canadian
○ 11 – Middle Eastern
○ 12 – South American
○ 13 – South Asian
○ 14 – West Asian or Arab
○ 15 – Other
○ 16 – Do not know
○ 17 – Prefer not to answer

Canadian Citizenship Status

○ 1 – Citizen
○ 2 – Landed immigrant
○ 3 - Refugee
○ 4 – Undocumented Resident (if not born inCanada)
○ 5 - Other **Year of Permanent Residence** ☐☐☐☐

ADDITIONAL INFORMATION

Marital Status

○ 1 – Unknown
○ 2 – Single
○ 3 – Married
○ 4 – Separated
○ 5 – Divorced
○ 6 – Widowed
○ 7 – Domestic Partner
○ 8 – Separated Domestic Partner
○ 9 – Widowed Domestic Partner

Primary Conversational Language (first language)

○ 1 – Unknow
○ 2 – English
○ 3 – French
○ 4 – Spanish
○ 5 – Japanese
○ 6 – Chinese
○ 7 – Italian
○ 8 – Russian
○ 9 – German
○ 10 – Farsi
○ 11 – Arabic
○ 12 – Other

Prefered Language

○ 1 – Unknow
○ 2 – English
○ 5 – Japanese
○ 6 – Chinese
○ 9 – German
○ 10 – Farsi

◯ 3 – French ◯ 7 – Italian ◯ 11 – Arabic
◯ 4 – Spanish ◯8 – Russian ◯ 12 – Other

Highest Level of Education

◯ 1 – No formal education ◯ 6 – Some College ◯ 10 – Graduate School
◯ 2 – Less than 7th Grade ◯ 7 – College Graduate ◯ 11 – Post Doctorate
◯ 3 – 7th-9th Grade ◯ 8 – Some University ◯ 12 – Trade School
◯ 4 – Partial High School ◯ 9 – University Graduate ◯ 13 – Unknown
◯ 5 –Completed High School or GED

Religion

◯ 1 – Tradition spirituality/First Nations ◯ 6 – Christian ◯ 11 –Sikh
◯ 2 – Agnostic (undecided) ◯ 7 – Hindou ◯ 12 –Witchcraft
◯ 3 – Atheist ◯ 8 – Jaïn ◯ 13 – Zoroastrian
◯ 4 – Bahaï ◯ 9 – Jewish ◯ 14 – Other/Unknown
◯ 5 –Bouddhist ◯ 10 –Muslim ◯ 15 – Prefers not to answer

DIAGNOSTIC & OTHER INFORMATION

Do you have a physical disability? ◯ 1-Yes ◯ 2 – No
If yes, could you please specify? _____
_____

Concurrent Disorder (Mental Illness **and** Substance Abuse) ◯ Yes ◯ No
Concurrent Disorder (Mental Illness **and** developmental disorder) ◯ Yes ◯ No

Primary Diagnostic Category (please check all that apply)

◯ 1 – Mood disorder (bipolar, depression, etc)
◯ 2 – Anxiety disorder (OCD, panic, PTSD, etc)
◯ 3 – Organic disorder (delirium, dementia)
◯ 4 – Developmental disorder (ADD, autism)
◯ 5 – Schizophrenic disorder (psychosis)
◯ 6 – Substance related disorder
◯ 7 – Personality disorder (avoidant, borderline, etc)
◯ 8 – Specific disorder of childhood/adolescence
◯ 9 – Other: _____
◯ 10 –Unknown

Age at first psychiatric hospitalization (in years) ☐☐ (Enter "98" if never)

Age at onset of Mental Illness (in year☐☐ (Enter "98" if never)

How many times have you been hospitalized during the last year (due to Mental Illness) ☐☐
(Enter "98" if never)

In the last year, have you used the following mental health services? (Please check all that apply)

◯ 1 – Psychiatric treatment ◯ 6 – Suicide prevention
◯ 2 – Clinical counseling ◯ 7 – Family / childcare counseling
◯ 3 – Assertive community treatment ◯ 8 – Substance abuse / addictions treatment
◯ 4 – Housing assistance ◯ 9 – Support group (AA, OA, Al-ANON, etc.)

○ 5 – Stress management ○ 10- Other_____

How many times have you used the above-mentioned mental health services during the last year? (Enter ☐☐ ever)

Do you take some medication for a mental illness? Yes No
If yes, could you please indicate the name of the medication(s)? (Block letters please)

1 –	2 –
3 –	4 –
5 -	6 -

Do you receive financial aid for a mental illness? ○ 1 – Yes ○ 2 – No
If yes, what kind? _____
_____

What best represents your residential status?
○ 1 – Independent
○ 2 – Assisted /Supported
○ 3 – Supervised Non-Facility
○ 4 – Supervised Facility
○ 5 – Treatment Institution
○ 6 – Homeless
○ 7 – Correctional facility
○ 8 – Unknown

Who do you live with? (Please check all that apply)
○ 1 – Spouse/partner ○ 4 – Family member ○ 7 – Roommate
○ 2 – Parents ○ 5 – Close relation (except family member) ○ 8 – Other
○ 3 – Children ○ 6 - Alone

How many times have you moved during the last year? ☐☐

Annex B – Consent form and true/false questionnaire to assess consent

Information and Consent Form

Project Title: Schizophrenia and drug use: The dual importance of cognitive style and social network

You are invited to participate in a research project led by Dr. Tania Lecomte (University of Montreal) and Stéphane Potvin (University of Montreal), in collaboration with Drs Stéphane With (University of Geneva), Amal Abdel-Baki (psychiatrist CHUM) and Luc Nicole (psychiatrist, University Institute of Mental health, Montreal) and the PEPP University Institute of mental Health Montreal.

Research Objectives

The objective of this research project is to demonstrate that drug use is associated with relative preservation of psychomotor speed and social cognition, and with more problems as related to impulse control. Qualitatively, we have a secondary objective to explore the links between changes in the social network of the individual over time, drug use and metacognition.

Participation in the research

If you agree to participate in this project, you will come in contact with a professional in the research field for three meetings to complete questionnaires, interviews and tests. You will be asked to complete various questionnaires about sociodemographic information and your mental health, answer questions in an interview format (both will be tape recorded) and to perform certain tasks on the computer. Each meeting will last approximately 2:15 and will take place at the PEPP University Institute in Mental Health of Montreal or the University of Montreal. If you consider the length of the meetings is too long, you will be able to take breaks anytime you want or continue the meeting on another day. After the first two meeting are completed, you might be contacted to find out if you are interested in participating in a third meeting. A maximum of four weeks may elapse between the first two meetings and the third.

Inclusion and exclusion criteria

- Man Or woman;
- Between 18 and 35 years old;
- Presence of psychotic disorders in the schizophrenia spectrum, with or without drug use and / or alcohol in the past 12 months;
- For drug use, we are looking in particular for use of cannabis, with or without other drugs/alcohol;

- Have a follow up as an outpatients at the PEPP University Institute of Mental Health Montreal.
- Individuals meeting the criteria for psychotic disorder induced by substances and those with a neurological disorder will be excluded from the study.

Confidentiality

Unless otherwise required by law, all information that you provide in the interviews and questionnaires will remain confidential and will only be used as part of this research. The researcher will not disclose to anyone any information about yourself and your identity will not be disclosed or published without your consent. When the results of this research will be ready to be published, your identity will be kept confidential and only data of all participants will be presented.
To ensure confidentiality, a number will be used instead of your name for the data entry of questionnaires and tests. The master list of all the participants names will be kept in a safe place, in the laboratory LESPOIR, at the University of Montreal. It will be used only by members of the research team (researchers Tania Lecomte and Stéphane Potvin, two students and the coordinator of the laboratory) for the sole purpose of linking information from various questionnaires taken at different time points to each participant in the project. Only researchers will know which name is associated with which number. All documents in our possession and the documents that displays your name will be destroyed seven years after the end of the project.

Advantages and disadvantages

Although this research may not offer you any direct benefit, it will be possible to help others
who are in the same situation as you in the future. In fact, by showing that drug use is associated with greater impulsivity in schizophrenia, the project could pave the way for interventions to improve impulse control in patients with dual diagnosis. Highlighting a relative preservation of social cognition in patients with a dual diagnosis may also have an impact on treatment, as interventions developed for these patients typically focus on reducing the harm associated drug use. Demonstrating a relative preservation of social cognition in patients with a dual diagnosis may enable the development of interventions with particular emphasis on the strengths of these patients.

This project has no known risk. Fatigue and / or boredom may result from the length of
the evaluation sessions (about 2:15 each). If you consider the length of the meetings is too long, you will be able to take breaks every time you want or continue the meeting on another day. In addition, it is possible that sharing your experience may arouse thoughts or emotional or unpleasant memories. If this happens, do not hesitate to talk with the research profesional. When appropriate, the research profesional will refer you to someone who can help you.

Right of withdrawal

Your participation is completely voluntary. You are free to withdraw at any time by verbal notice, without prejudice and without having to justify your decision. If you decide

to withdraw from the research, you may contact the principal investigator at the phone number shown on the next page.

Allowance

Financial compensation of $ 60 will be given for your participation in this study. You will receive $ 15 for the first meeting, $ 20 for the second one and $ 30 for the last meeting. If applicable, tickets transit will be refunded.

Conflicts of Interest

The objectives of the researchers on this study are not commercial in nature and do not present any conflict of interest.

Contacts

Monitoring ethical aspects of the project:

For questions about your rights as a research participant or for any ethical issues concerning the conditions under which unfolds your participation in this project, you can contact the Complaints and Service Quality.

Coordinates of Local Complaints and Service Quality:
Complaints and Service Quality
Institut universitaire en santé mentale de montréal
7401, rue Hochelaga
Montréal (Québec) H1N 3M5
Téléphone : 514-251-4000, poste 2920

Coordinates of the Research Ethics Committee:
Secretariat of the Committee of Research Ethics
Institut universitaire en santé mentale de Montréal
7401, rue Hochelaga
Unité 228 - 2e Riel - bureau RI-228-93
Montréal (Québec) H1N 3M5
Téléphone : 514-251-4015, poste 2442

The ethics research committee of the Research Centre of the University Institute of Mental Health of Montreal approved the research project and is ensuring follow up on it. In addition, it will pre-approve any revision and amendment to informed consent form and to the research protocol.

Consent

By signing below, you agree to participate in this research project. Make sure all your questions have been satisfactorily answered and that you understand your role in this project. If you wish to withdraw from the project, still have questions or feel that the information you have received is not clear enough, you can contact Dr. Tania Lecomte (details below):

Dre Tania Lecomte

Université de Montréal
Département de Psychologie
C.P. 6128, succ. Centre-Ville
Montréal (Québec) H3C 3J7
Téléphone: (514) 343-6274 Fax : (514) 343-2285 Courriel :
tania.lecomte@umontreal.ca

By agreeing to participate in this study, you do not waive any of your rights nor release the researchers namely, organizations, businesses or institutions involved in their legal and professional responsibilities.

If you decide to participate in this project, a copy of the four pages of the consent form
will be given to you. Before signing the consent form, we want to ensure that you are over 18 and have read and understand the information on this study. We also want to ensure that you understand that you participate freely in the study and you can ask questions at any time.

Therefore, I certify that I have had a sufficient period of time to read this consent form and
that all my questions were answered. I give my consent to Dr. Tania Lecomte and those who represent her to participate in this research and allows them to use the information I give for scientific purposes.

_____ _____

Participant's signature Date

_____
Participant's name

The research project was described to the participant as well as the terms of participation. A member of the research team is committed to respect what has been agreed in the consent form.

_____ _____
Member of the research team's signature Date

_____
Member of the research team's name

QUESTIONS ABOUT THE CONSENT TO PARTICIPATE IN THE PROJECT

Project Title: Schizophrenia and drug use:
The dual importance of cognitive style and social network

Please answer by True or False:

If I want to participate in the project, I expect to meet with research assistants who will ask questions and make me take tests.	**True**	**False**
If I agree to participate, I am not allowed to leave the study before the end of it.	**True**	**False**
Beside the researchers, no one will know what I responded to the questionnaires.	**True**	**False**
My doctor will be angry and may not continue to give the usual treatment and services if I refuse to participate.	**True**	**False**
Some interviews are long but I have the right to ask for breaks or to do it in more than one meeting.	**True**	**False**
If I have questions, there is someone I can contact about this project.	**True**	**False**
I will receive compensation (in money) to answer the questionnaires and tests**.**	**True**	**False**
My name might be mentioned without my permission in conferences or publications of the results of this project.	**True**	**False**

The candidate responded adequately to all the issues at the first attempt: ☐

The candidate needed _____ attempts to respond adequately to all questions. (maximum of 3 to pursue his/her participation)