The positive link between executive function and cannabis use in schizophrenia is not explained by current levels of superior social cognition

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Abstract:

Patients with schizophrenia and a history of cannabis use show better neurocognitive performance than patients with only schizophrenia. Fewer neurocognitive deficits may be a marker of the superior social cognition needed to obtain illicit substances, or cannabis use may indicate a distinct path to schizophrenia with less neurocognitive vulnerability. This study sought to determine whether the relationship of cannabis use and executive function exists independently of social cognition. Eighty-seven patients with schizophrenia were administered measures of social cognition and executive function. Social cognition was assessed using the Bell-Lysaker Emotion Recognition Test to measure affect recognition, and the Eyes and Hinting Tests to measure theory of mind. Executive function was assessed by the Mental Flexibility component of the Delis-Kaplan Executive Functioning Scale. The relations between the variables were examined with Structural equation modeling. Cannabis use positively related to executive function, negatively related to affect recognition, and had no relationship with theory of mind. There were no indirect effects of other illicit substances on duration of regular cannabis use. Alcohol use was related to worse affect recognition. The relationship between cannabis use and better executive function was supported and was not explained by superior social cognition.

Keywords: Schizophrenia, Cognition, Cannabis, Theory of Mind, Executive Function, Emotional Intelligence

1.0 INTRODUCTION

To date, both the presence and duration of cannabis use has been linked to better neurocognitive functioning in patients with schizophrenia, especially in the domain of executive functioning (Løberg and Hugdahl, 2009; Potvin et al., 2008; Rabin et al., 2011; Schnell et al., 2009; Yucel et al., 2012). Recent research has also suggested a potential dose-response, finding that moderate, as compared to little to no use or heavy use, was associated with less cognitive impairment as measured by neurocognitive and metacognitive capacity (Schnakenberg Martin et al., 2016). Of note, some studies have failed to replicate the finding of less severe cognitive impairment in individuals with schizophrenia and a history of cannabis use (Bahorik et al., 2013; Coulston et al., 2007; Mata et al., 2008), possibly due to variations in the definition of cannabis use (e.g. focus on a current or past history of use). In trying to understand why cannabis use may be related to better cognition, most authors have rejected the possibility that cannabis use directly increases cognitive functioning (Løberg et al., 2014; Power et al., 2015; Solowij and Michie, 2007). It has been suggested that better executive functioning or overall better neurocognition is a marker of a lesser degree of basic biological vulnerability for developing the disorder (Løberg et al., 2014). Cannabis users may have developed psychosis through an alternative pathway with less cognitive vulnerability and at an earlier age (Myles et al., 2016; Schnakenberg Martin et al., 2016).

An alternative explanation is that the cannabis-neurocognition relationship is merely a reflection of better overall social cognition. It is possible that the ability to obtain and maintain illicit substances is facilitated by greater capacities for social cognition and social interaction (Potvin et al., 2008; Solowij and Michie, 2007). In this model, the cannabis – neurocognition relationship is considered to be attributed to the conceptual similarity (Harvey and Penn, 2010; Penn et al., 1997), supported by moderate correlations between these functional domains in several studies (Allen et al., 2007; Ventura et al., 2013). In such a

model, social cognition could be considered a mediator of the relationship between neurocognition and general functioning (Schmidt et al., 2011), having a closer association to real life outcomes (Couture et al., 2006; Fett et al., 2011).

Social cognition involves noticing the intentions of others, as well as understanding and responding to these intentions (Green et al., 2005). It has been suggested that social cognition includes three core domains: affect recognition (emotion processing), theory of mind (ToM), and attributional style/bias (Pinkham et al., 2014). ToM can be defined as the ability to infer the intentions, dispositions, and beliefs of others (Green and Horan, 2010), while affect recognition includes ratings of affects that are displayed in faces or voices. Meta-analyses and reviews report that individuals with schizophrenia show deficits in affect recognition, social perception, and ToM (Bora et al., 2009; Green and Horan, 2010; Green et al., 2015; Kohler et al., 2010; Savla et al., 2013).

If the cannabis – neurocognition relationship is attributed to better social cognition, cannabis using patients would be expected to have higher capacities for social cognition. However, for social cognition the findings are inconclusive and scarce. Meijer et al. (2012) reported that lifetime cannabis use was associated with better performance on acquired knowledge, facial affect recognition, and facial identity recognition in schizophrenia patients (Meijer et al., 2012). Social cognition was also found to be higher in schizophrenia patients with a history of cannabis use, compared to little or no use patients (Schnakenberg Martin et al., 2016). A negative effect of cannabis use on performance in a social cognition task that involved managing emotions in patients with schizophrenia spectrum disorders has also been reported (Sanchez-Torres et al., 2013). Potvin and colleagues (2007) performed an fMRI study suggesting that social emotional processing may be less impaired in substance using patients (alcohol and/or cannabis) with schizophrenia who demonstrated activation in more

neural regions associated with social cognition, compared to patients with schizophrenia without substance use (Potvin et al., 2007).

The present study sought to test whether social cognition can explain the relationship between executive function and cannabis use. To increase the validity of the social cognition assessment both ToM and affect recognition were included, and stabilized patients were recruited since executive function and social cognition may fluctuate in the acute phase of psychosis (Balogh et al., 2014; Helle et al., 2014). ToM and affect recognition were included as these factors are most closely related to successfully interaction with other people. Duration of lifetime regular cannabis use was included to test the notion that social cognition may explain better neurocognition in cannabis using patients due to the ability to maintain substance use. A test battery examining especially complex and mentally demanding executive functioning was used to capture neurocognition. To examine the interrelationship between executive function, social cognition, and cannabis, in addition to the effects of potential confounders such as other illicit drug use, structural equation modeling was used.

2. METHODS

2.1 Design

This study had a cross-sectional design. Duration of cannabis use was the dependent variable. Executive functioning, age, and other illicit substance use were the independent variables and social cognition measures were the mediating variables.

2.2 Participants

The participants consisted of 87 patients with a schizophrenia diagnosis which was confirmed using the Structured Clinical Interview for DSM-IV (SCID) (First et al., 1995). All patients were recruited from a VA Medical Center (n = 72, 82.8 %) and a Community Mental

Health Center (n = 15, 17.2 %). Inclusion criteria were a schizophrenia diagnosis and stabilized symptoms defined as no changes in the use of antipsychotics, hospitalization or housing within the last 30 days. Exclusion criteria included current substance dependence (including cannabis and excluding nicotine) or a chart diagnosis of mental retardation. All patients gave informed consent, and received \$30 for participating in the study. The study was approved by the Institutional Review Board of Indiana University-Purdue University Indianapolis.

2.3 Clinical assessments

The clinical instruments and tests were administrated by clinically trained research staff, possessing, at minimum, a Bachelor degree in psychology. The Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) was used to rate psychotic symptoms. The PANSS five-component model of schizophrenia (Bell et al., 1994) was used, and scores for the negative, positive, cognitive, excitement and depression components were reported. Reliability was checked every second month, by blind ratings of taped PANSS interviews. The intraclass correlation coefficients ranged from .80 to .92 for PANSS components. Substance use was recorded using items from Addiction Severity Index (ASI) (McLellan et al., 1985; McLellan et al., 1980). The ASI asks participants to report the number of months of lifetime use in which they used a substance at least three times a week. Substances reported included cannabis, alcohol, heroin, methadone, other opiates/analgesics, barbiturates, other sedatives/hypnotics/tranquilizers, cocaine, amphetamines, hallucinogens, and inhalants.

2.4 Measures of executive function and social cognition

Executive functioning, was examined by use of the Delis Kaplan Executive Function System (D-KEFS) which is comprised of nine tests designed to assess higher level cognitive

functioning (Delis et al., 2001). The test battery includes Trail Making, Verbal Fluency, Design Fluency, Color-Word Interference, Sorting Test, Twenty Questions, Wording Context, Tower Test, and Proverb Test. In an exploratory factor analysis Clark et al. (2010) identified two separate components of executive functioning: inhibition/set shifting and mental flexibility by using D-KEFS in patients with schizophrenia (Clark et al., 2010). In the present study, the mental (cognitive) flexibility component was used as a measure of executive function and more specifically, was considered to reflect one's capacity to form ideas of how stimuli relate to one another (Lysaker et al., 2008). This factor is based on a synthesis of more complex executive functioning processes such as concept formation, abstraction, planning and initiation of problem-solving behavior (Clark et al., 2010). The following tests loaded on the cognitive flexibility factor: Word Context Test (total consecutively correct scaled score), Sorting Test Condition 1 (confirmed correct sorts scaled score), Twenty Questions Test (total weighted achievement scaled score), and Proverb Test Condition 1 (total achievement free inquiry scaled score). This factor would be a suitable indicator of executive function by tapping the ability to perform especially complex and demanding cognitive processes.

ToM, was examined by using the Eyes Test and Hinting Test. The Eyes Test consists of 36 photographs of pairs of men's and women's eyes (Baron-Cohen et al., 2001). Each photograph was presented one at a time to the participant whose task was to choose between four adjectives that could describe the affective or cognitive mental state of the person on the photograph. One point was given for each correct answer and it was possible to achieve a total score of 36 points. It has been suggested that the Eyes Test measures the ability to infer the mental state without drawing inferences about the content (Bora et al., 2009). The Hinting Test (Corcoran et al., 1995) consist of 10 short vignettes where two people are interacting. The scenarios are read out loud by the examiner, and each is ended by one of the characters giving a hint. The participants were required to report the real intended meaning. Each correct

answer received 2 points. If not answered correctly, the examiner gave a prompt. Participants received a score of one when answering correctly after the additional information. It was possible to obtain a total score of 20. The test that was used in the present study was a version containing items rewritten in American English (Greig et al., 2004). Both the Eyes and Hinting Tests have been administrated in stabilized outpatients with schizophrenia (Bora et al., 2006) and have been shown to distinguish between a non-clinical control group and a group of individuals with schizophrenia (Scherzer et al., 2012). However, it is useful to use two different ToM tests when aiming to target different content and contexts related to ToM (Scherzer et al., 2012).

Affect recognition was measured by the Bell-Lysaker Emotion Recognition Task (BLERT) (Bell et al., 1997; Bryson et al., 1997). The BLERT is an audio-visual affect recognition task, designed to evaluate a person's ability to discriminate between seven affect states, based on facial, voice-tonal and upper-body movement cues that are presented on video. The participant was seated three feet in front of a 21-inch monitor and shown 21 vignettes, that each lasted 10 seconds. The emotions that demonstrated by the same actor in the vignettes included: happiness, sadness, fear, disgust, surprise, anger, and no emotion. Each of the affect states were paired with three monologues, resulting in 21 combinations. An example of the first monologue is as follows:

I just received my job rating from my supervisor. He called me into his office and gave me a rating of adequate. He told me that I hadn't made any serious mistakes lately.

After each presentation of the vignettes the tape was paused and the participant selected a response from the list of seven affects options. The test included measures of the number of correct responses, number of correctly discriminated positive affects (happiness and surprise), and number of correctly discriminated negative affects (fear and sadness). It has been demonstrated that the BLERT-Total score has high categorical stability (weighed $k = 0.94$)

and strong test-retest reliability ($r = .0.76$) in a sample of patients with schizophrenia (Bryson et al., 1997) and the BLERT has demonstrated discriminant validity (Bell et al., 1997). For the purpose of this study, only the BLERT- Total score was used.

2.5 Statistical analyses

SPSS version 22 was used for the descriptive analyses (CORP, 2013). Categorical variables were presented by number and percentage and continuous variables were presented by mean and standard deviations. The analysis of the data was conducted in two phases. First, a Pearson correlation (Pearson r ; one-tailed) was used to assess bivariate associations between the measures of executive function, social cognition (ToM and affect recognition), and substance use (cannabis, illicit substance use and alcohol). An illicit substance use variable was created that included heroin, methadone, other opiates/analgesics, barbiturates, other sedatives/hypnotics/tranquilizers, cocaine, amphetamines, and hallucinogens. In addition, skewness was analyzed in order to check for normality in the outcome variable, cannabis use, before conducting structural equation modeling (SEM).

The structural model of the direct and indirect relations between predictor variables and the cannabis outcome variable was estimated with Mplus 7.3 (Muthén and Muthén, 2008). Cognitive flexibility together with covariate variables, such as alcohol and illicit substance use, were specified as exogenous variables and the social cognition variables measuring ToM (Hinting and Eyes tests) and affective recognition were specified as intermediate variables. In this way, the model consisted of both direct and indirect effects. The Maximum Likelihood Robust (MLR) was used to account and correct the model for non-normality in the outcome variable. Model fit was evaluated according to established guidelines (Kline, 2010; Wang and Wang, 2012). First, a tentative model with all parameters set free was estimated, including variables such as age and gender. Then, the model was re-

estimated after removing relations and variables that did not contribute to the model (Jöreskog, 1993).

3. RESULTS

3.1 Sample characteristic and bivariate correlations

The sample mean years of age and education were 49.47 (SD = 8.34) and 12.86 (SD = 1.72), respectively. Seventy-five (86.2%) of the participants were male. The substances that were reported with the longest period of use were alcohol (mean months duration (M) = 128.45, SD = 152.20), followed by cannabis (M = 62.09, SD = 99.36), cocaine (M = 32.40, SD = 61.05), hallucinogens (M = 8.92, SD = 46.67) and amphetamine (M = 2.31, SD = 9.19), heroin (M = 1.51, SD = 5.77), opiates (M = 1.06, SD = 6.01), methadone (M = 1.01, SD = 5.88), sedatives (M = .91, SD = 5.75), and barbiturates (M = .51, SD = 2.46). There were no reported uses of inhalants. See Table 1 for a total overview of sociodemographic, clinical, and cognitive characteristic of the sample.

[INSERT TABLE 1 HERE]

[INSERT TABLE 2 HERE]

See Table 2 for a presentation of correlations among measures of executive function (mental flexibility), social cognition (theory of mind and affect recognition), cannabis use, illicit substance use, and alcohol use. Overall, cognitive flexibility demonstrated small to moderate significant correlations with ToM tasks, affect recognition and cannabis use ($p < .05$), and cannabis use showed small to moderate correlated with ToM tasks, illicit substance use and alcohol use ($p < .05$).

3.2 Structural equation model with both direct and indirect relations

First, a tentative model with all parameters set free was estimated. A final model was estimated after removing age and gender which did not contribute to the first tentative model. The final structural model received a satisfactory fit with data ($\chi^2 = 4.11$, $df = 3$, $p = .25$, CFI = 0.99, TLI = 0.94, RMSEA = .065, RMSEA_{CI} = .000-.203, RMSEA Close fit $p < .05 = .34$) (Figure 1).

[INSERT FIGURE 1 HERE]

The results showed that cannabis use was significantly positively related to cognitive flexibility and negatively related to affect recognition. Figure 1 illustrates how cognitive flexibility was also related indirectly with cannabis use via affect recognition. Illicit substance use was not related to any of the variables in the model, and alcohol negatively correlated with affect recognition.

4. DISCUSSION

In this study, we sought to determine whether a relationship exists between cannabis use and better neurocognitive functioning independent of social cognition. As predicted, we found that better executive function, i.e. a higher cognitive flexibility score, was related to longer duration of cannabis use, when adjusting for social cognition measures. Thus, social cognition does not explain the relationship between better executive function and cannabis use. Contrarily, a higher score on the affect recognition task was associated with a shorter duration of cannabis use. As expected, executive functioning was significantly related to the social cognition measures. There were no indirect effects of other illicit substances on duration of cannabis use. Also, longer duration of alcohol use was significantly related to a lower score on the affect recognition task.

Results thus replicate previous findings (Coulston et al., 2007; Schnell et al., 2009; Wobrock et al., 2013) and are also in line with a meta-analysis that reported better executive functioning in patients with non-affective psychosis and cannabis use compared to those without (Yucel et al., 2012).

One explanation is that the present findings are not consistent with the model that the cannabis-neurocognition relationship is a reflection of relatively positive levels of social cognition which enable persons to obtain illegal substances. Hence, this study is consistent with the notion that patients with the longest duration of regular cannabis use may have a lower basic biological vulnerability and less neurocognitive deficits (see e.g. Løberg et al., 2014 for details on this model). Thus, theoretically speaking, the patients with the most severe levels of cannabis use may be those with relatively low vulnerability for psychosis, reflected by better executive functioning, or even an overall better neurocognitive functioning level, compared to patients with no or lower cannabis use.

Alternatively, it is also possible that individuals with schizophrenia and a history of cannabis use may initially have had higher levels of social cognition which was responsible for the initiation of cannabis use, but that these abilities decreased with the development of psychosis and/or continued cannabis use. This hypothesis cannot be ruled out with the current analysis. Further, this hypothesis is supported by the literature which has shown that individuals with lifetime cannabis dependence have difficulty determining and discriminating facial emotions (Bayrakçı et al., 2015), as well as neural activation patterns during ToM tasks that are similar to those at risk for psychosis (Roser et al., 2012).

Interestingly, our findings and this alternative hypothesis also align with recent findings which suggest a dose-response relationship in that moderate cannabis use was associated with the least cognitive deficits, as opposed to high and little to no use (Schnakenberg Martin et al., 2016). As per our model, when accounting for affect recognition,

a domain of social cognition, decreased executive function was associated with increased cannabis use, through indirect effects of affect recognition. Thus, our findings show support for why heavy cannabis use in schizophrenia was associated with more severe cognitive deficits compared to moderate cannabis use.

Use of other types of illicit substances did not influence the results. A longer duration of alcohol use was related to a lower score on the affect recognition test. This is in line with the finding that chronic alcohol use may have adverse effects on the ability to recognize affect for substance users without psychosis (Kornreich et al., 2003). There could be several explanations for this finding that a higher use of alcohol, and also cannabis, are related to worse performance on the affect recognition test in the present study. For example, these deficits could have been present before the initiation of substance use or may have been a result of extensive use of alcohol and cannabis. Generally, it has been reported that females have better social functioning than men (Ochoa et al., 2012). Also, male gender and younger age is often associated to substance use (Large et al., 2014); however, in the present sample, the majority were men in their late forties and gender and age were not significantly related to cannabis use or the social cognition measures.

There are some limitations in regard to the present study. The sample composition limits the generalization of the findings in regard to gender and age, as most of the patients were males in their late forties. Recording of duration of substance use were done retrospectively, however, studies have shown that self-report is able to garner accurate information regarding illicit substance use among adults with schizophrenia (Van Dorn et al., 2012). Additionally, this study evaluated the relationship of executive function to cannabis use and social cognition, and thus future work is needed to discern the relationships with other forms of neurocognition such as cognitive inhibition. Also, social cognition was assessed with

ToM and affect recognition, but future research should also include measures of social perception and attributional style/bias.

It can be concluded that there is a unique relationship between neurocognition and cannabis use in patients with schizophrenia. This could indicate better functional prognosis for the cannabis using patients, provided they cease using illicit substances (Mullin et al., 2012). Thus, clinical interventions directed at reducing cannabis use could be recommended.

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CONFLICT OF INTEREST

Authors declare that there are no conflicts of interest.

REFERENCES

- Allen, D.N., Strauss, G.P., Donohue, B., et al., 2007. Factor analytic support for social cognition as a separable cognitive domain in schizophrenia. *Schizophr. Res.* 93, 325-333.
- Bahorik, A.L., Newhill, C.E., Eack, S.M., 2013. Neurocognitive Functioning of Individuals With Schizophrenia: Using and Not Using Drugs. *Schizophr. Bull.*
- Balogh, N., Egerhazi, A., Berecz, R., et al., 2014. Investigating the state-like and trait-like characters of social cognition in schizophrenia: a short term follow-up study. *Schizophr. Res.* 159, 499-505.
- Baron-Cohen, S., Wheelwright, S., Hill, J., et al., 2001. The "Reading the Mind in the Eyes" Test revised version: a study with normal adults, and adults with Asperger syndrome or high-functioning autism. *Journal of Child Psychology and Psychiatry, and allied disciplines* 42, 241-251.
- Bayrakçı, A., Sert, E., Zorlu, N., et al., 2015. Facial emotion recognition deficits in abstinent cannabis dependent patients. *Compr. Psychiatry* 58, 160-164.
- Bell, M., Bryson, G., Lysaker, P., 1997. Positive and negative affect recognition in schizophrenia: a comparison with substance abuse and normal control subjects. *Psychiatry Res.* 73, 73-82.
- Bell, M.D., Lysaker, P.H., Beam-Goulet, J.L., et al., 1994. Five-component model of schizophrenia: assessing the factorial invariance of the positive and negative syndrome scale. *Psychiatry Res.* 52, 295-303.
- Bora, E., Eryavuz, A., Kayahan, B., et al., 2006. Social functioning, theory of mind and neurocognition in outpatients with schizophrenia; mental state decoding may be a better predictor of social functioning than mental state reasoning. *Psychiatry Res.* 145, 95-103.
- Bora, E., Yucel, M., Pantelis, C., 2009. Theory of mind impairment in schizophrenia: meta-analysis. *Schizophr. Res.* 109, 1-9.
- Bryson, G., Bell, M., Lysaker, P., 1997. Affect recognition in schizophrenia: a function of global impairment or a specific cognitive deficit. *Psychiatry Res.* 71, 105-113.
- Clark, L.K., Warman, D., Lysaker, P.H., 2010. The relationships between schizophrenia symptom dimensions and executive functioning components. *Schizophr. Res.* 124, 169-175.
- Corcoran, R., Mercer, G., Frith, C.D., 1995. Schizophrenia, symptomatology and social inference: investigating "theory of mind" in people with schizophrenia. *Schizophr. Res.* 17, 5-13.
- CORP, I., 2013. IBM SPSS Statistics for Windows. Version 22.0. IBM Corp, Armonk, NY.
- 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. *Schizophr. Res.* 96, 169-184.
- Couture, S.M., Penn, D.L., Roberts, D.L., 2006. The functional significance of social cognition in schizophrenia: a review. *Schizophr. Bull.* 32 Suppl 1, S44-63.
- D'Souza, D.C., Abi-Saab, W.M., Madonick, S., et al., 2005. Delta-9-tetrahydrocannabinol effects in schizophrenia: implications for cognition, psychosis, and addiction, *Biol. Psychiatry*, 2005/03/23 ed, pp. 594-608.
- Delis, D.C., Kaplan, E., Kramer, J.H., 2001. Delis-Kaplan Executive Function System (D-KEFS). The Psychological Corporation, San Antonio, TX.
- Fett, A.K., Viechtbauer, W., Dominguez, M.D., et al., 2011. The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: a meta-analysis. *Neurosci. Biobehav. Rev.* 35, 573-588.
- First, M., Spitzer, R., Gibbon, M., et al., 1995. Structured Clinical Interview of DSM-IV Axis I Disorders (SCID-I): Patient Edition. Version 2. New York State Psychiatric Institute, Biometrics Research Department, New York.
- Green, M.F., Horan, W.P., 2010. Social Cognition in Schizophrenia. *Curr. Dir. Psychol. Sci.* 19, 243-248.
- Green, M.F., Horan, W.P., Lee, J., 2015. Social cognition in schizophrenia. *Nat. Rev. Neurosci.* 16, 620-631.

- Green, M.F., Olivier, B., Crawley, J.N., et al., 2005. Social cognition in schizophrenia: recommendations from the measurement and treatment research to improve cognition in schizophrenia new approaches conference. *Schizophr. Bull.* 31, 882-887.
- Greig, T.C., Bryson, G.J., Bell, M.D., 2004. Theory of mind performance in schizophrenia: diagnostic, symptom, and neuropsychological correlates. *The Journal of Nervous and Mental Disease* 192, 12-18.
- Harvey, P.D., Penn, D., 2010. Social cognition: the key factor predicting social outcome in people with schizophrenia? *Psychiatry (Edgmont)* 7, 41-44.
- Helle, S., Gjestad, R., Johnsen, E., et al., 2014. Cognitive changes in patients with acute phase psychosis--effects of illicit drug use. *Psychiatry Res.* 220, 818-824.
- Jöreskog, K.G., 1993. Testing structural equation models, in: Bollen, K.A., Long, J.S. (Eds.), *Testing Structural Equation Models*. Sage, Newbury Park, CA, pp. 294-314.
- Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr. Bull.* 13, 261-276.
- Kline, R.B., 2010. *Principles and practice of structural equation modeling* (3 ed.). Guilford Press, New York.
- Kohler, C.G., Walker, J.B., Martin, E.A., et al., 2010. Facial emotion perception in schizophrenia: a meta-analytic review. *Schizophr. Bull.* 36, 1009-1019.
- Kornreich, C., Foisy, M.L., Philippot, P., et al., 2003. Impaired emotional facial expression recognition in alcoholics, opiate dependence subjects, methadone maintained subjects and mixed alcohol-opiate antecedents subjects compared with normal controls. *Psychiatry Res.* 119, 251-260.
- Large, M., Mullin, K., Gupta, P., et al., 2014. Systematic meta-analysis of outcomes associated with psychosis and co-morbid substance use. *The Australian and New Zealand Journal of Psychiatry* 48, 418-432.
- Løberg, E.M., Helle, S., Nygard, M., et al., 2014. The Cannabis Pathway to Non-Affective Psychosis may Reflect Less Neurobiological Vulnerability. *Frontiers in Psychiatry* 5, 159.
- Løberg, E.M., Hugdahl, K., 2009. Cannabis use and cognition in schizophrenia, *Front. Hum. Neurosci.*, 2009/12/04 ed, p. 53.
- Lysaker, P.H., Warman, D.M., Dimaggio, G., et al., 2008. Metacognition in schizophrenia: associations with multiple assessments of executive function. *The Journal of Nervous and Mental Disease* 196, 384-389.
- Mata, I., Rodriguez-Sanchez, J.M., Pelayo-Teran, J.M., et al., 2008. Cannabis abuse is associated with decision-making impairment among first-episode patients with schizophrenia-spectrum psychosis. *Psychol. Med.* 38, 1257-1266.
- McLellan, A.T., Luborsky, L., Cacciola, J., et al., 1985. New data from the Addiction Severity Index. Reliability and validity in three centers. *The Journal of Nervous and Mental Disease* 173, 412-423.
- McLellan, A.T., Luborsky, L., Woody, G.E., et al., 1980. An improved diagnostic evaluation instrument for substance abuse patients. The Addiction Severity Index. *The Journal of nervous and mental disease* 168, 26-33.
- Meijer, J.H., Dekker, N., Koeter, M.W., et al., 2012. Cannabis and cognitive performance in psychosis: a cross-sectional study in patients with non-affective psychotic illness and their unaffected siblings. *Psychol. Med.* 42, 705-716.
- Mullin, K., Gupta, P., Compton, M.T., et al., 2012. Does giving up substance use work for patients with psychosis? A systematic meta-analysis. *The Australian and New Zealand Journal of Psychiatry* 46, 826-839.
- Muthén, L.K., Muthén, B.O., 2008. *Mplus 7.3*. Muthén & Muthén, Los Angeles.
- Myles, H., Myles, N., Large, M., 2016. Cannabis use in first episode psychosis: Meta-analysis of prevalence, and the time course of initiation and continued use. *The Australian and New Zealand Journal of Psychiatry* 50, 208-219.

- Ochoa, S., Usall, J., Cobo, J., et al., 2012. Gender Differences in Schizophrenia and First-Episode Psychosis: A Comprehensive Literature Review. *Schizophrenia Research and Treatment* 2012, 9.
- Penn, D.L., Corrigan, P.W., Bentall, R.P., et al., 1997. Social cognition in schizophrenia. *Psychol. Bull.* 121, 114-132.
- Pinkham, A.E., Penn, D.L., Green, M.F., et al., 2014. The social cognition psychometric evaluation study: results of the expert survey and RAND panel. *Schizophr. Bull.* 40, 813-823.
- Potvin, S., Joyal, C.C., Pelletier, J., et al., 2008. Contradictory cognitive capacities among substance-abusing patients with schizophrenia: a meta-analysis, *Schizophr. Res.*, 2007/07/07 ed, pp. 242-251.
- Potvin, S., Mancini-Marie, A., Fahim, C., et al., 2007. Processing of social emotion in patients with schizophrenia and substance use disorder: an fMRI study. *Soc. Neurosci.* 2, 106-116.
- Power, B.D., Dragovic, M., Badcock, J.C., et al., 2015. No additive effect of cannabis on cognition in schizophrenia. *Schizophr. Res.* 168, 245-251.
- Rabin, R.A., Zakzanis, K.K., George, T.P., 2011. The effects of cannabis use on neurocognition in schizophrenia: a meta-analysis., *Schizophr. Res.*, pp. 111-116.
- Roser, P., Lissek, S., Tegenthoff, M., et al., 2012. Alterations of theory of mind network activation in chronic cannabis users. *Schizophr. Res.* 139, 19-26.
- Sanchez-Torres, A.M., Basterra, V., Rosa, A., et al., 2013. Lifetime cannabis use and cognition in patients with schizophrenia spectrum disorders and their unaffected siblings. *Eur. Arch. Psychiatry Clin. Neurosci.* 263, 643-653.
- Savla, G.N., Vella, L., Armstrong, C.C., et al., 2013. Deficits in domains of social cognition in schizophrenia: a meta-analysis of the empirical evidence. *Schizophr. Bull.* 39, 979-992.
- Scherzer, P., Leveille, E., Achim, A., et al., 2012. A study of theory of mind in paranoid schizophrenia: a theory or many theories? *Front. Psychol.* 3, 432.
- Schmidt, S.J., Mueller, D.R., Roder, V., 2011. Social cognition as a mediator variable between neurocognition and functional outcome in schizophrenia: empirical review and new results by structural equation modeling. *Schizophr. Bull.* 37 Suppl 2, S41-54.
- Schnakenberg Martin, A.M., Bonfils, K.A., Davis, B.J., et al., 2016. Compared to high and low cannabis use, moderate use is associated with fewer cognitive deficits in psychosis. *Schizophrenia Research: Cognition* 6, 15-21.
- Schnell, T., Koethe, D., Daumann, J., et al., 2009. The role of cannabis in cognitive functioning of patients with schizophrenia. *Psychopharmacology (Berl)* 205, 45-52.
- Solowij, N., Michie, P.T., 2007. Cannabis and cognitive dysfunction: parallels with endophenotypes of schizophrenia? *Journal of Psychiatry & Neuroscience* 32, 30-52.
- Van Dorn, R.A., Desmarais, S.L., Young, M.S., et al., 2012. Assessing illicit drug use among adults with schizophrenia. *Psychiatry Res.* 200, 228-236.
- Ventura, J., Wood, R.C., Helleman, G.S., 2013. Symptom domains and neurocognitive functioning can help differentiate social cognitive processes in schizophrenia: a meta-analysis. *Schizophr. Bull.* 39, 102-111.
- Wang, J., Wang, X., 2012. *Structural Equation Modeling: Applications Using Mplus* Wiley, A John Wiley & Sons, Ltd., Publication, West Sussex, UK.
- Wobrock, T., Falkai, P., Schneider-Axmann, T., et al., 2013. Comorbid substance abuse in first-episode schizophrenia: effects on cognition and psychopathology in the EUFEST study. *Schizophr. Res.* 147, 132-139.
- Yucel, M., Bora, E., Lubman, D.I., et al., 2012. 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, *Schizophr. Bull.*, 2010/07/28 ed, pp. 316-330.

Figure Legend

Figure 1. Structural model with beta weights describing the magnitudes between executive function, alcohol use, social cognition, and cannabis use.

Note: Cogn: Flex = Cognitive flexibility component of the Delis Kaplan Executive Function System; Soc. Cogn: Hinting = ToM (theory of mind) measured with the Hinting Test; Soc. Cogn: Eyes = ToM measured with the Eyes Test; Soc. Cogn: Aff. Recogn = Affect recognition measured with the Bell-Lysaker Emotion Recognition Task; e = error; Cannabis Use, and Alcohol Use are based on lifetime months of regular substance use.

Figure 1: Structural model with beta weights describing the magnitudes between executive function, alcohol use, social cognition, and cannabis use.

Table 1: Sociodemographic, clinical and cognitive data (N = 87)

Characteristic	n	Percent (%)
<i>Gender</i>		
Male	75	86.2
<i>Race</i>		
Caucasian	41	47.1
African American	45	51.7
Latino	1	1.1
<i>Medications</i>		
Typical antipsychotic medication	10	13.3
Atypical antipsychotic medication	52	69.3
Injectable typical antipsychotic	13	17.3
	Mean	Standard Deviation (SD)
<i>General Demographics</i>		
Age	49.47	8.34
Education (years)	12.86	1.72
Age at first hospitalization	27.31	12.21
Life hospitalizations (years)	8.30	8.26
<i>PANSS</i>		
Positive	16.56	4.42
Negative	19.62	5.55
Excitement	7.67	2.50
Depressive	12.76	3.97
Cognitive	17.72	4.43
Total	76.27	14.04
<i>Executive Function</i>		
Cognitive Flexibility	15.50	9.38
<i>Social Cognition</i>		
ToM: Hinting Test	13.06	4.22
ToM: Eyes Test	21.08	5.39
Affect Recognition	12.76	3.15
<i>Lifetime Substance Use (months)</i>		
Alcohol	128.45	152.20
Cannabis	62.09	99.36
Cocaine	32.40	61.05
Hallucinogens	8.29	46.67
Amphetamine	2.31	9.19
Heroin	1.51	5.77
Methadone	1.01	5.88
Opiate (other)	1.06	6.01
Sedatives (other)	0.91	5.75
Barbiturates	0.51	2.46

Note: PANSS = Positive and Negative Syndrome Scale; ToM = Theory of Mind

Table 2 Bivariate (one-tailed) correlations between measures of executive functioning, social cognition and substance use

Item	1	2	3	4	5	6	7
1. Cognitive Flexibility	1	0.424**	0.379**	0.578**	0.220*	0.041	0.018
2. Hinting Test		1	0.260*	0.384**	0.190*	-0.002	0.078
3. Eyes Test			1	0.494**	0.193*	0.035	0.028
4. Affect Recognition				1	.017	-0.069	-0.168
5. Cannabis Use					1	0.454**	0.372**
6. Illicit Substance Use						1	0.161
7. Alcohol Use							1

Note: * $p < .05$; ** $p < .001$.