Cognitive fusion as a candidate psychological vulnerability factor for psychosis:

An experimental study of acute Δ9-tetrahydrocannabinol (THC) intoxication

Abstract

Heavy cannabis use is associated with an increased risk of psychosis. However, the psychological mechanisms involved, and interactions with established risk factors for cannabis-related psychosis, remain unclear. This study examined the role of cognitive fusion, a candidate vulnerability factor for psychosis, during acute THC intoxication, and the interaction with key risk factors – developmental trauma and schizotypy. Twenty general population cannabis-using participants were administered THC or placebo in a within-participants, double-blinded randomised study. Developmental trauma, schizotypy and cognitive fusion were all associated with psychotic experiences during intoxication. Cognitive fusion accounted for increased psychotic experiences in those with developmental trauma and high schizotypy. Cognitive fusion may be a key mechanism by which developmental trauma and schizotypy increase risk of psychosis from cannabis use. This initial study is limited by a small sample and correlational design; a larger scale mediation study is now needed to support a causal argument. The findings have implications for psychological treatments and identifying those at risk of cannabis-related psychosis. Psychological interventions that target cognitive fusion may be more effective than generic approaches. People prone to cognitive fusion, particularly those with a history of developmental trauma and high in schizotypy, may be at higher risk for cannabis-related psychosis.

Key words: psychosis; cannabis; THC; cognitive fusion; developmental trauma; schizotypy

Introduction

Heavy cannabis use is associated with an increased risk of psychosis (Colizzi and Murray, 2018). Longitudinal studies show that cannabis use predicts subsequent psychotic experience (Gage, Hickman, & Zammit, 2016), and that earlier age of first use increases risk (Day, Goldschmidt, Day, Larkby, & Richardson, 2014). A meta-analysis found evidence for a dose-response relationship (Marconi, Di Forti, Lewis, Murray, & Vassos, 2016), and a recent European multi-site study found that daily use of high potency cannabis carried the highest risk (Di Forti et al., 2019).

The major psychoactive ingredient of cannabis, Δ^9-tetrahydrocannabinol (THC), induces psychotic experiences in healthy (Bhattacharyya et al., 2015; Morrison, Zois, McKeown, & Lee, 2009) and cannabis using (Szoke et al., 2014) samples, and in those with high levels of non-clinical paranoia (Freeman et al., 2014). THC also increases psychotic experiences in people with a diagnosis of schizophrenia (D'Souza et al., 2005; Volkow, Baler, Compton, & Weiss, 2014).

Certain risk factors strengthen the relationship further. Traumatic experiences in childhood and adolescence (developmental trauma) increase risk of cannabis-related psychosis (Harley et al., 2010; Houston, Murphy, Shevlin, & Adamson, 2011; Konings, et al., 2012; Shevlin, Murphy, Houston, & Adamson, 2009). Schizotypy also increases risk of psychosis in general population samples (Barkus, Stirling, Hopkins, & Lewis, 2006; Barkus & Lewis, 2008; Spriggens & Hides, 2015; Stirling et al., 2008) and during acute intoxication (Mason, Morgan, Dhiman, & Patel, 2009). No research to date has examined whether developmental trauma affects psychotic experiences during intoxication.

Despite strong evidence for an association between cannabis and psychotic experiences, we do not yet understand the psychobiological mechanisms by which cannabis induces vulnerability to psychosis (cf. Shrivastava, Johnston, Terpstra, & Bureau, 2014). Current treatments target symptoms rather than underlying biological or psychological processes, and this seriously limits the development of interventions for people with cannabis-related psychosis. Anti-psychotic medications operate through dopamine receptor antagonism (Kapur & Seeman, 2001), and psychological interventions typically

rely on generic cognitive behavioural and motivational interviewing approaches, with modest results (Barrowclough et al., 2014; Hjorthøj, Baker, Fohlmann, & Merete, 2014; Madigan et al., 2013). By elucidating the underlying mechanisms, treatments may be more effectively targeted and outcomes improved (c.f. Garety & Freeman, 2013; Moritz & Lysaker, 2018).

Contemporary cognitive accounts identify the ability to defuse or decentre from internal experience – for example, recognising thoughts as thoughts – as a key metacognitive process effecting psychotherapeutic change (Hayes, Strosahl, & Wilson, 2012; Bernstein, Hadash, Lichtash, Tanay, Shepherd, & Fresco, 2015). By contrast, cognitive fusion (or the inability to decentre) describes the experience of thoughts and feelings as necessarily accurate representations of self and reality which dominate the person's attention and behaviour (Gillanders et al., 2014; Teasdale, Moore, Hayhurst, Pope, Williams, & Segal, 2002), and is associated with poor outcomes across diagnoses (Plonsker, Biran, Zvielli, & Bernstein, 2017). Preliminary research shows that cognitive fusion is associated with psychotic experiences and linked distress, and mediates the impact of known risk factors – early adversity and schizotypy, in both general population cannabis-users and people with psychosis who use cannabis (Newman-Taylor, Richardson, Sood, Sopp, Perry, & Bolderston, 2020). Cognitive fusion may, therefore, be a key psychological mechanism contributing to cannabis-related psychosis, though this has not yet been tested during acute intoxication.

In the present study, we examined the impact of developmental trauma, schizotypy and cognitive fusion on psychotic experiences during acute intoxication, and secondly, the role of cognitive fusion in the impact of the two risk factors. In a cannabis-using sample, we hypothesised that (i) developmental trauma, schizotypy and cognitive fusion will be associated with increased psychotic experiences during THC intoxication, and (ii) cognitive fusion will account for the impact of developmental trauma and schizotypy on psychotic experiences during intoxication.

Materials and methods

Ethical statement

The study was approved by the University of – (reference 3325/002) and University of – (reference 25242) Research Ethics Committees[1]. Participants received a small payment for their time.

Design

We used a within-participants, double-blind, randomised cross-over design. Participants attended on two occasions and were administered either oral THC (15mg) or placebo. This dose is well tolerated and elicits transient psychotic experiences in cannabis-users, with a peak effect two hours after administration (Curran, Brignell, Fletcher, Middleton, & Henry, 2002).

Participants

Twenty participants (10 male, 10 female; age range 19-35) were recruited via electronic and paper advertisements. Our sample size of n=20 was informed by a previous study administering 15mg oral THC in the laboratory with a sample size of n=15 (Curran et al. 2002). Eligibility criteria were: cannabis use on at least one previous occasion; 18-70 years old; able to give informed consent; fluent English (to complete questionnaires); body mass index (BMI) within normal limits (18.5-24.9 kgm^{-2}) (to minimise variation in drug absorption). Exclusion criteria were: current or past mental illness; history of mental illness in first degree relatives; current use of cannabis more than once a week; current use of other recreational drugs (excluding caffeine, alcohol and nicotine); alcohol or nicotine dependency; pregnancy.

Measures

The State Cognitive Fusion Questionnaire (SCFQ; Bolderston, Gillanders, Turner, Taylor, Ní Mhaoileoin, & Coleman, 2018) is a 7-item measure of the extent to which people are currently fused

[1]The study was linked to research examining neurobiological mechanisms of the impact of THC on psychotic experiences; for full details see Bloomfield et al. (in review).

with their thoughts. Items are rated on a 7-point scale from 'completely untrue' to 'completely true.' The scale has excellent internal reliability (alpha=.95).

The Psychotomimetic States Inventory (PSI; Mason, Morgan, Stefanovic, & Curran, 2008) is a 48-item measure of current psychotic-type experiences. Items are rated on a 4-point scale from 'not at all' to 'strongly.' The scale has good internal reliability (alpha=.84).

The Positive and Negative Symptom Scale (PANSS; Kay, Fiszbein, & Doppler, 1987) is a structured clinical interview of psychotic symptoms. Thirty domains are rated from 'absent' to 'extreme' yielding three subscales: positive, negative and general psychopathology. The scale has acceptable to good internal reliability (positive alpha=.73; negative alpha=.83; general alpha=.79).

The Childhood Trauma Questionnaire-Short Form (CTQ-SF; Spinhoven, Penninx, Hickendorff, & Hemert, 2014) is a 25-item retrospective measure of five types of maltreatment: physical abuse, sexual abuse, emotional abuse, physical neglect, emotional neglect. Items are scored on a 5-point scale from 'never true' to 'very often true.' The scale has acceptable to excellent internal reliability (alphas=.61-.95).

The Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason, Linney, & Claridge, 2005) is a 104-item measure of schizotypy. Items are answered 'yes' or 'no.' The scale has acceptable to good internal reliability (alphas=.62-.80).

Procedure

Participants were screened to confirm eligibility. Medical procedures (BMI, urinary tests for substances and pregnancy, carbon monoxide test for nicotine) and Structured Clinical Interviews for DSM-V (SCID) were completed by trained researchers (RL and KP). Diagnostic interviews were included as part of the screening process to assess inclusion and exclusion criteria. These assessments were done by phone, using the DSM-V SCID for mood disorders, anxiety disorders (screen), psychosis (screen) and substance misuse (screen). Those eligible were invited to attend two sessions at least one

week apart, to complete each arm of the study. Participants were required to attend both sessions at – Hospital, starting at 9:00 am, after fasting overnight. Testing sessions lasted an average of five and a half hours, ending at 14:30 pm. At the first session, participants completed the CTQ and O-LIFE. The PSI and PANSS were completed 30 minutes before THC/placebo and again 150 minutes after administration. Blood samples were taken to determine cannabinoid concentrations (THC and metabolites OH-THC and THC-COOH) at 150 minutes post drug administration. Blood samples were collected using a heparin vacutainer and immediately centrifuged. Plasma samples were stored at -80 °C prior to analysis. Cannabinoid concentrations were determined using gas chromatography coupled with mass spectroscopy (GC/MS). Participants completed additional cognitive and Magnetic Resonance Imaging assessments for a linked study examining the neurobiological mechanisms of THC. The SCFQ was completed at the end of the session, approximately 270 minutes following drug administration. Participants were assessed as safe to leave by a qualified medic. Participants then returned to complete the second arm of the study, following exactly the same procedure, and received placebo/THC, one week later.

Pharmacokinetics

Blood samples were taken to determine cannabinoid concentrations (THC and metabolites OH-THC and THC-COOH) 150 minutes post drug administration, alongside the PSI. Blood samples were centrifuged, and plasma was frozen at -80 °C. Cannabinoid concentrations were determined using gas chromatography coupled with mass spectroscopy (GC/MS).

Data analysis

Given the sample size and preliminary nature of the study, data were analysed using correlations and partial correlations. Non-significant Shapiro-Wilk tests indicated that most variables were normally distributed. For variables with significant Shapiro-Wilk tests, skewness and kurtosis were within normal limits. The exceptions were the developmental trauma (CTQ-SF) and psychotic experiences (PANSS) change scores, with skewness within but kurtosis outside normal limits. There were outliers

only for developmental trauma (CTQ-SF) and psychotic experiences (PANSS and PSI), and none of these were extreme. We therefore conducted parametric tests. Pearson correlations (one-tailed) were calculated for developmental trauma (CTQ-SF), schizotypy (O-LIFE) and cognitive fusion (SCFQ) with change in psychotic experiences (PSI and PANSS change scores). The small sample size did not permit regression or mediation analyses. Where initial correlations were significant, partial correlations were then calculated to test associations between change in psychotic experiences with the two risk factors (developmental trauma and schizotypy), controlling for cognitive fusion.

Results

Twelve participants (60%) reported being current cannabis users. Of these, the most frequent pattern of use was once weekly (n=4), meaning that current cannabis users were occasional (once a week or less) users. No participants reported using cannabis more than once a week. No users met DSM criteria for any drug use disorders.

Table 1 shows plasma data following THC administration, demonstrating absorption of THC and its metabolism into THC-OH and THC-COOH.

Tables 1 and 2 about here

The mean concentration of THC in plasma (ng/ml) 150 minutes after THC administration was 2.27 (SD = 2.06). The mean concentration of metabolites in plasma (ng/ml) 150 minutes after administration was 7.02 for THC-OH (SD = 6.20), and 64.09 for THC-COOH (SD = 48.35).

Table 2 gives descriptive statistics and inter-correlations. Developmental trauma, schizotypy and cognitive fusion were associated with increased psychotic experiences as measured by PSI and PANSS change scores. Partial correlations show that when controlling for cognitive fusion, change in psychotic experiences was no longer associated with developmental trauma, as measured by both the

PSI (r=-.224, p=.211) and PANSS (r=.147, p=.281). This indicates that cognitive fusion accounted for the impact of developmental trauma on THC-induced psychotic experiences.

Similarly, partial correlations show that when controlling for cognitive fusion, change in psychotic experiences were no longer associated with schizotypy, as measured by both the PSI (r=-.072, p=.396) and PANSS (r=-.045, p=.427). Greater cognitive fusion accounted for the impact of schizotypy on psychotic experiences during intoxication.

Discussion

In this preliminary study, we sought to examine the role of cognitive fusion on psychotic experiences during acute intoxication, and the interaction with established risk factors – developmental trauma and schizotypy. In a cannabis-using sample, we found that developmental trauma, schizotypy and cognitive fusion were all associated with increased psychotic experiences during THC intoxication, and that cognitive fusion accounted for the impact of the risk factors.

This is the first study to demonstrate that cognitive fusion is associated with psychotic experiences during intoxication. Epidemiological studies have shown that early adversity increases risk of psychosis from cannabis use (Harley et al., 2010; Houston et al., 2011; Konings, et al., 2012; Shevlin et al., 2009); this is the first to demonstrate that developmental trauma increases risk of psychotic experiences during acute THC intoxication. The association between schizotypy and psychotic experiences during intoxication is in line with previous findings (Barkus & Lewis, 2008; Mason et al., 2009; Stirling et al., 2008).

This study is limited by a correlational design that tests associations rather than causal mechanisms, and small sample size, which limits the analyses and generalizability. While it is possible that increased psychotic experiences lead to greater cognitive fusion, the wider literature suggests the converse – that people who respond to thoughts and feelings as necessarily accurate representations of

self and reality are more vulnerable to mental health problems (Plonsker et al., 2017). A larger scale mediation study would address these limitations. Additionally, the measurement of cognitive fusion before and during intoxication would confirm whether changes during intoxication predict subsequent increases in psychotic experiences.

More speculatively, we would hypothesise (i) that an inability to decentre from internal experience is a general vulnerability factor for cannabis-related psychosis, (ii) that fusion with problematic beliefs following early trauma (e.g. "I'm vulnerable" and "Others are dangerous") and schizotypal experiences (e.g. magical thinking and social anxiety fears) contributes to psychotic experiences when intoxicated (e.g. paranoid thinking), and (iii) that there is a bidirectional relationship during intoxication, when increased cognitive fusion results in transient experiences (e.g. the thought "I'm being watched") being assumed to be accurate and dominating attention, thereby increasing paranoid thinking, which in turn increases distress and cognitive fusion further. We now need to examine these more complex, potentially causal links.

The present research suggests that the inability to defuse or decenter when using cannabis may increase psychotic experiences. This has important implications for psychological treatments and identifying those at risk of cannabis-related psychosis. Psychological interventions that target cognitive fusion may be more effective than generic approaches (c.f. Garety & Freeman, 2013; Moritz & Lysaker, 2018). People prone to cognitive fusion, particularly those with a history of developmental trauma and high in schizotypy, may be at higher risk for cannabis-related psychosis.

Disclosure of interest

Please see title page for research and fellowship funding details for specific contributors.

References

Barkus, E., & Lewis, S. (2008). Schizotypy and psychosis-like experiences form recreational cannabis in a non-clinical sample. *Psychological Medicine, 32*(9) 1267-1276.

Barkus, E. J., Stirling, J., Hopkins, R. S., & Lewis, S. (2006). Cannabis-induced psychosis-like experiences are associated with high schizotypy. *Psychopathology, 39,* 175-178.

Barrowclough, C., Marshall, M., Gregg, L., Fitzsimmons, M., Tomenson, B., Warburton, J., & Lobban, F. (2014). A phase-specific psychological therapy for people with problematic cannabis use following a first episode of psychosis: a randomized controlled trial. *Psychological Medicine, 44*(13) 2749-2761.

Bernstein, A., Hadash, Y., Lichtash, Y., Tanay, G., Shepherd, K., & Fresco, D. M. (2015). Decentering and related constructs: A critical review and metacognitive processes model. *Perspectives on Psychological Science, 10*(5) 599–617.

Bhattacharyya, S., Atakan, Z., Martin-Santos, R., Crippa, J. A., Kambeitz, J., Malhi, S., Giampietro, V., Williams, S., Brammer, M., Rubia, K., Collier, D. A., & McGuire, P. K. (2015). Impairment of inhibitory control processing related to acute psychotomimetic effects of cannabis. *European Neuropsychopharmology, 25*(1) 26-37.

Bloomfield, M. A. P., Hindocha, C., Green, S. F., Wall, M. B., Lees, R., Petrilli, K., Costello, H., Ogunbiyi, M. G., & Freeman, T. P. (2019). The neuropsychopharmacology of cannabis: A review of human imaging studies. *Pharmacology and Therapeutics, 195,* 132-161.

Bloomfield, M. A. P., Petrilli, K., Lees, R. Hindocha, C., Beck, K., Rane, N., Lythgoe, D. J., Stone, J. M., Curran, V., Howes, O. D., & Freeman, T. P. (in submission). The effects of acute Δ^9-tetrahydrocannabinol on striatal glutamatergic function: A magnetic resonance spectroscopy (1H-MRS) study at 3T.

Bolderston, H., Gillanders, D. T., Turner, G., Taylor, H. C., Ní Mhaoileoin, D., & Coleman, A., (2018). The initial validation of a state version of the Cognitive Fusion Questionnaire. *Journal of Contextual Behavioural Science.* Advance online publication. https://doi.org/10.1016/j.jcbs.2018.04.002

Colizzi, M., & Murray, R. (2018). Cannabis and psychosis: What do we know and what should we do? *British Journal of Psychiatry, 212*(4) 195-196.

Curran, V, Brignell, C., Fletcher, S., Middleton, P., & Henry, J. (2002). Cognitive and subjective dose-response effects of acute oral $\triangle^9$-tetrahydrocannabinol (THC) in infrequent cannabis-users. *Psychopharmacology, 164*(1) 61-70.

Day, N., Goldschmidt, L., Day, R., Larkby, C., & Richardson, G. (2015). Prenatal marijuana exposure, age of marijuana initiation, and the development of psychotic symptoms in young adults. *Psychological Medicine, 45*(8) 1779-1787.

Di Forti, M., Quattrone, D., Freeman, T. P., Tripoli, G., Gayer-Anderson, C., Quigley, H., ... & Murray, R. M. (2019). The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): A multicentre case-control study. *The Lancet Psychiatry, 6*(5) 427-436.

D'Souza, D. C., Abi-Saab, W. M., Madonick, S., Forselius-Bielen, K., Doersch, A., Braley, G., ... & Krystal, J. H. (2005). Delta-9-tetrahydrocannabinol effects in schizophrenia: Implications for cognition, psychosis, and addiction. *Biological Psychiatry, 57*(6), 594-608.

Freeman, D., Dunn, G., Murray, R. M., Evans, N., Lister, R., Antley, A., Slater, M., Godlewska, B., Cornish, R., Williams, J., Di Simplicio, M., Igoumenoi, A., Brenneisen, R., Tunbridge, E. M., Harrison, P. J., Harmer, C. J., Cowen, P., & Morrison, P. D. (2015). How cannabis causes paranoia: Using the intravenous administration of $\triangle^9$-tetrahydrocannabinol (THC) to identify key cognitive mechanism leading to paranoia. *Schizophrenia Bulletin, 41*(2) 391-399.

Gage, S. H., Hickman, M., & Zammit, S. (2016). Association between cannabis and psychosis: Epidemiologic evidence. *Biological Psychiatry, 79*(7) 549-556.

Gillanders, D. T., Bolderston, H., Bond, F. W., Dempster, M., Flaxman, P. E., Campbell, L., Kerr, S., Tansey, L., Noel, P., Ferenbach, C., Masley, S., Roach, L., Lloyd, J., May, L., Clarke, S., & Remington, B. (2014). The development and initial validation of the Cognitive Fusion Questionnaire. *Behavior Therapy, 45*(1) 83-101.

Garety, P. A., & Freeman, D. (2013). The past and future of delusions research: from the inexplicable to the treatable. *The British Journal of Psychiatry, 203*(5), 327-333.

Harley, M., Kelleher, I., Clarke, M., Lynch, F., Arseneault, L., Connor, D., ..., & Cannon, M. (2010). Cannabis use and childhood trauma interact additively to increase the risk of psychotic symptoms in adolescence. *Psychological Medicine, 40,* 1627-1634.

Hayes, S. C., Strosahl, K. D., & Wilson, K. G. (2012). *Acceptance and Commitment Therapy: The Process and Practice of Mindful Change. (2nd ed.)* Guildford Press.

Hjorthøj, C, R., Baker, A., Fohlmann, A., & Merete, N. (2014). Intervention efficacy in trials targeting cannabis use disorders in patients with comorbid psychosis systematic review and meta-analysis. *Current Pharmaceutical Design, 20*(13) 2205-2211.

Houston, J. E., Murphy, J., Shevlin, M., & Adamson, G. (2011). Cannabis use and psychosis: Re-visiting the role of childhood trauma. *Psychological Medicine, 41,* 2339-2348.

Kay, S. R., Fiszbein, A., & Doppler, L. A. (1987). The Positive and Negative Syndrome Scale (PANNS) for schizophrenia. *Schizophrenia Bulletin, 13*(2) 261-276.

Konings, M., Stefanis, N., Kuepper, R., De Graaf, R., Have, M. t., Van Os, J., ... & Henquet, C. (2012). Replication in two independent population-based samples that childhood maltreatment and cannabis use synergistically impact on psychosis risk. *Psychological Medicine, 42*(1) 149-159.

Madigan, K., Brennan, D., Lawlor, E., Turner, N., Kinsella, A., O'Connor, J. J., Russel, V., Waddington, J. L., & O'Callaghan, E. (2013). A multi-center, randomized controlled trial of a group psychological intervention for psychosis with comorbid cannabis dependence over the early course of illness. *Schizophrenia Research, 143*(1) 138-142.

Marconi, A., Di Forti, M., Lewis, C. M., Murray, R. M., & Vassos, E. (2016). Meta-analysis of the association between the level of cannabis use and risk of psychosis. *Schizophrenia Bulletin, 42*(5) 1262-1269.

Mason, O. J., Morgan, C. J. M., Stefanovic, A., & Curran, H, V. (2008). The Psychotomimetic States Inventory (PSI): Measuring psychotic-type experiences from ketamine and cannabis. *Schizophrenia Research, 103*(1-3) 138-142.

Mason, O., Claridge, G., & Jackson, M. (1995). New scales for the assessment of schizotypy. *Personality and Individual Differences, 18*(1) 7-13.

Mason, O., Linney, Y., & Claridge, G., 2005. Short scales for measuring schizotypy. *Schizophrenia Research, 78*(2-3), 293-296.

Mason, O., Morgan, C. J. A., Dhiman, S. K., & Patel, A. (2009). Acute cannabis use causes increased psychotomimetic experiences in individuals prone to psychosis. *Psychological Medicine, 39*(6) 951-956.

Morgan, C., & Gayer-Anderson, C. (2016). Childhood adversities and psychosis: Evidence, challenges, implications. *World Psychiatry, 15*(2) 93-102.

Moritz, S., & Lysaker, P. H. (2018). Metacognition–what did James H. Flavell really say and the implications for the conceptualization and design of metacognitive interventions. *Schizophrenia Research, 201,* 20-26.

Morrison, P. D., Zois, V., McKeown, D. A., & Lee, T. D. (2009). The acute effects of synthesis intravenous $\triangle^9$-tetrahydrocannabinol on psychosis, mood and cognitive function. *Psychological Medicine, 39*(10) 1607-1616.

Plonsker, R., Biran, D. G., Zvielli, A., & Bernstein, A. (2017). Cognitive fusion and emotion differentiation: Does getting entangled with our thoughts dysregulate the generation, experience and regulation of emotion? *Cognitive and Emotion, 31*(6) 1286-1293.

Newman-Taylor, K., Richardson, T., Sood, M., Sopp, M., Perry, E., Bolderston, H. (2020). Cognitive mechanisms in cannabis-related paranoia; Initial testing and model proposal. *Psychosis,* 1-14.

Shevlin, M., Murphy, J., Houston, J. E., & Adamson, G. (2009). Childhood sexual abuse, early cannabis use, and psychosis: Testing the effects of different temporal orderings based on the National Comorbidity Survey. *Psychosis, 1*(1) 19-28.

Shrivastava, A., Johnston, M., Terpstra, K., & Bureau, Y. (2014). Cannabis and psychosis: Neurobiology. *Indian Journal of Psychiatry, 56*(1) 8-16.

Spinhoven, P., Penninx, B. W., Hickendorff, M., & Hemert, A. M. (2014). Childhood Trauma Questionnaire: Factor structure, measurement invariance, and validity across emotional disorders. *Psychological Assessment, 26*(3) 717-729.

Spriggens, L., & Hides, L. (2015). Patterns of cannabis use, psychotic-like experiences and personality styles in young cannabis-users. *Schizophrenia Research, 165*(1) 3-8.

Stirling, J., Barkus, E., Nabosi, L., Irshad, S., Roemer, G., Schreudergoidheijt, B., & Lewis, S. (2008). Cannabis-induced psychotic-like experiences are predicted by high schizotypy: Confirmation of preliminary results in a large cohort. *Psychopathology, 41*(1) 371-378.

Szoke, A., Galliot, A. M., Richard, J. R., Ferchiou, A., Baudin, G., Leboyer, M., & Schürhoff, F. (2014). Association between cannabis use and schizotypal dimensions: A meta-analysis of cross-sectional studies. *Psychiatry Research, 219*(1) 58-66.

Teasdale, J. D., Moore, R.G., Hayhurst, H., Pope, M., Williams, S., & Segal, Z.V. (2002). Metacognitive awareness and prevention of relapse in depression: Empirical evidence. *Journal of Consulting and Clinical Psychology, 70*(2) 275-287.

Volkow, N. D., Baler, R. D., Compton, W. M., & Weiss, S. R. B. (2014). Adverse health effects of marijuana use. *The New England Journal of Medicine, 370*(23) 2219-2227.

Table 1

Mean concentrations of THC and metabolites in plasma (ng/ml) 150 minutes after THC administration

	M	*SE*
THC	2.27	0.49
THC-OH	7.03	1.46
THC-COOH	64.09	11.40

THC = Δ^9-tetrahydrocannabinol; THC-OH = 11-Hydroxy-Δ^9-tetrahydrocannabinol; 11-Nor-9-carboxy-Δ^9-tetrahydrocannabinol

Table 2

Descriptive statistics and inter-correlations (Pearson 1-tailed) for study variables

	M	*SD*	(1)	(2)	(3a)	(3b)	(3c)	(4a)	(4b)	(4c)	(5)
(1) Childhood Trauma Questionnaire	3.84	4.84	1	.469*	.457	.453	.520*	.243	.555*	.511*	.526*
(2) Oxford-Liverpool Inventory of Feelings and Experiences	7.20	4.73	.469*	1	.711**	.640**	.502*	.128	.510*	.491*	.658**
(3a) Psychotomimetic States Inventory – total (T1)	6.63	4.68	.457	.711**	1	.538*	.315	.325	.455	.376	.417
(3b) Psychotomimetic States Inventory – total (T2)	19.06	19.64	.453	.640**	.538*	1	.969***	.113	.804***	.795***	.832***
(3c) Psychotomimetic States Inventory – change (T2-T1)	10.53	16.80	.520*	.502*	.315	.969***	1	.002	.759***	.774***	.806***
(4a) Positive and Negative Symptom Scale – total (T1)	30.90	1.25	.243	.128	.325	.113	.002	1	.188	-.028	.141
(4b) Positive and Negative Symptom Scale – total (T2)	34.00	5.80	.555*	.510*	.455	.804***	.759***	.188	1	.976***	.795***
(4c) Positive and Negative Symptom Scale – change (T2-T1)	3.10	5.70	.511*	.491*	.376	.795***	.774***	-.028	.976***	1	.779***
(5) State Cognitive Fusion Questionnaire	12.15	6.64	.526*	.658**	.417	.832***	.806***	.141	.795***	.779***	1

*$p < .05$; **$p < .01$; ***$p < .001$