Schizophrenia Research xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Is there a common vulnerability in cannabis phenomenology and schizotypy? The role of the N170 ERP

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ARTICLE INFO

Article history:
Received 27 March 2017
Received in revised form 15 November 2017
Accepted 16 November 2017
Available online xxxx

Keywords:
Schizotypy
Cannabis
N170
Event-related potential
Cognition
Schizotypal personality

ABSTRACT

Cannabis use is a known risk factor for the development of psychosis, although the precise nature of this relationship is unclear. The phenomenological experiences associated with cannabis use vary dramatically, and for some resemble certain features of psychosis. We hypothesized that individuals who report particularly unusual experiences associated with cannabis use would demonstrate similar electrophysiological patterns to those who score high on schizotypal personality traits. The Cannabis Experiences Questionnaire (CEQ) and the Schizotypal Personality Questionnaire (SPQ) were used to measure these experiences and traits. A sample of 97 individuals were placed into one of three experimental or two control groups based on their questionnaire scores. These were the "High CEQ", "High SPQ", "High on Both", "Average Users" and "Control" (non-using) groups. Participants completed a visual face perception task. Electroencephalography was used to measure the neural response to the stimuli. The N170 event-related potential (ERP) was used to measure perceptual encoding of the stimulus. The experimental groups elicited significantly reduced N170 ERPs compared to the Control group. The Average User group did not significantly differ from the Control group, and approached significance with the High SPQ group. None of the high scoring groups significantly differed in N170 ERP response from each other. Replicating past research, the CEQ and SPQ scales moderately correlated with each other. The attenuated N170 ERP demonstrated by the high scoring experimental groups may reflect a manifestation of an underlying shared vulnerability.

1. Introduction

Cannabis is consistently reported as a risk factor for the development of psychosis and schizophrenia (Andreasson et al., 1987; Miettunen et al., 2008). There is an increased likelihood of 1.27 to 3.69 to experience psychosis compared to non-using adults (Häfner, 2005; Miettunen et al., 2008; Davis et al., 2013). This relationship has also persisted when possible confounding variables, such as nicotine use & psychiatric diagnosis, are controlled for (Manrique-Garcia et al., 2016). Furthermore, individuals with schizophrenia who use cannabis demonstrate greater psychotic symptoms than those who do not (Hall et al., 2004; Linszen et al., 1994). Considering that cannabis is among the most commonly used illicit substances, and that its legal status is in flux around the world, it is crucial to determine the parameters of this association.

Several groups have attempted to address the questions surrounding a causative relationship between cannabis and psychosis via longitudinal datasets. Cannabis use almost always precedes the development of psychosis (Henquet et al., 2005; Stefanis et al., 2013). Stefanis et al. (2013) detected a linear relationship between the age of first use and length of time to hospitalization for psychosis. Dose-dependent effects, where greater cannabis consumption is associated with increased risk, have been found (Häfner, 2005; Moore et al., 2007; Davis et al., 2013). A degree of specificity has also been reported, where cannabis does not seem to increase the probability of other disorders (Arseneault et al., 2002). However, these findings do not preclude associative or third variable models. Furthermore, the majority of cannabis users never experience an episode of psychosis or develop schizophrenia. Therefore, the ability to determine those users most at risk becomes crucial to their well-being.

Schizotypy can be conceptualized as a personality spectrum, where greater endorsement of schizotypal traits coincides with increased risk for disorders of psychosis, including schizophrenia (Raine, 1991). Numerous studies have found an association between schizotypy and cannabis use (Compton et al., 2009; Esterberg et al., 2009; Fridberg et al., 2011). Skosnik et al. (2001) found current cannabis use was associated with increased positive traits of schizotypy. Skosnik et al. (2006) also reported neural synchronization and sensory processing deficits in cannabis users. They interpreted these results as evidence for involvement of the endocannabinoid system, which may particularly impact the positive symptoms of the schizophrenia spectrum (Skosnik et al., 2008).

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https://doi.org/10.1016/j.schres.2017.11.019
0920-9964/

Additionally, the temporal onset of schizotypal traits may precede cannabis use, and those high in schizotypy also endorse more cannabis-related problems (Schiffman et al., 2005; Cohen et al., 2011). Thus, the literature suggests a robust relationship between cannabis use and schizotypy.

Examination of the shared phenomenological experiences between psychosis and cannabis use may be one approach to delineate a subgroup of at-risk users. The subjective experiences associated with cannabis use vary dramatically, and for many individuals do not resemble psychosis at all (Barkus et al., 2006; Stirling et al., 2008). However, a significant minority of users do report psychotic-like perceptions and sensations (Thomas, 1996; Verdoux et al., 2003). Barkus et al. (2006) created the Cannabis Experiences Questionnaire (CEQ) to capture this experiential variance. Using the CEQ, this group found that self-reports of psychotic-like experiences during cannabis use significantly correlated with the endorsement of items on the brief Schizotypal Personality Questionnaire (SPQ Brief). Mason et al. (2009) conducted an experiment that involved participants consuming cannabis prior to the measurement of psychotic-like experiences. They found significantly elevated levels of psychotic experiences after consumption for the users who scored high on the SPQ, compared to those who scored low. Bianconi et al. (2016) found individuals with a first episode of psychosis scored higher on the CEQ. Together, these studies suggest that reported experiences during cannabis use may be a viable indicator of heightened schizotypal-proneness. However, the mechanisms that underlie the association between the SPQ and CEQ remain unclear.

Electroencephalography (EEG) allows examination of the patterns of neural network activation, providing high temporal resolution of neural functioning following stimulus presentation. Attenuated early event-related potential (ERP) amplitudes are thought to reflect reduced perceptual encoding. The N170 ERP has repeatedly been found to produce the largest response in the presence of facial stimuli, and is right lateralized (Heisz et al., 2006; Luck and Kappenman, 2012). The N170 is believed to capture configuration processing of faces (Batty et al., 2014. Although varying facial emotions impact the amplitude of the N170 ERP, so can neural integrity (Almeida et al., 2014; Brenner et al., 2014; Brenner et al., 2016). As such, studies have found that individuals with schizophrenia exhibit attenuated N170 ERP responses to face stimuli (Kirihara et al., 2012; Lynn and Salisbury, 2008; Wynn et al., 2013). Tsunoda et al. (2012) demonstrated that patients with schizophrenia, compared to healthy controls, do not show the typical heightened N170 ERP toward inverted facial stimuli. Additionally, N170 deficits have also been found in biological relatives of those with schizophrenia (Ibáñez et al., 2012; Wölwer et al., 2012). This suggests that neural activity in response to face discrimination tasks may be a feasible marker of vulnerability.

To our knowledge, only one study has investigated the N170 ERP within the context of schizotypy. Batty et al. (2014) found individuals who endorsed many schizotypal traits exhibited significantly reduced N170 ERPs in response to inverted faces. However, additional event-related potential abnormalities have been associated with schizotypy. Schizotypal individuals also displayed diminished P100 ERPs in response to a non-facial visual paradigm (Koychev et al., 2010). Skosnik et al. (2008) found SPQ scores (negative symptoms) inversely correlated with affective P300 responses in a visual oddball task. Similar findings are prevalent in the literature investigating schizophrenia with EEG. Overall, this suggests the study of those high on schizotypy may also be informative about a shared underlying neurobiology with those diagnosed with schizophrenia.

Thus far, there has been no direct inquiry as to whether certain cannabis-induced phenomenological experiences and schizotypal symptoms could be the result of shared or similar neural systems. Such findings may help to delineate a subset of the cannabis using population who may be at a higher risk for the development of psychosis. The present study seeks to contribute to this issue by using electrophysiology. First, we sought to determine if particularly unusual experiences during cannabis use are predictive of schizotypy, thereby replicating the results of Barkus and Lewis (2008). Then, we employed ERP analysis to determine whether those who score high on unusual cannabis experiences and those who score high on schizotypy exhibit similar neural patterns. We hypothesized that high SPQ and CEQ scorers would show reduced N170 responses toward face-present stimuli, compared to users without unusual cannabis experiences and non-users. These findings would support the hypothesis that similar deficits in neural integrity produce both particularly unusual experiences while using cannabis and more schizotypal experiences.

2. Methods

2.1. Participants

Ninety-seven participants (62 female), between the ages of 18–55 years old were given course credit or cash for participation. All participants had vision that was 20/40 or better, and were fluent in English. Participants had no diagnosed neurological disorders, seizure disorders, or stroke. Participants who experienced a head injury or lost consciousness for more than 5 min were excluded. Individuals with complicated drug use histories were also excluded from participation. All participants provided written informed consent.

A pre-screen was completed prior to the experimental task, which included the SPQ and CEQ measures. The 75th percentile was used to separate “average” and “high” scores, and this was used to determine group allocation. Five groups were created: (1) High SPQ and average CEQ (“High SPQ” group), (2) average SPQ and high CEQ (“High CEQ” group), (3) high SPQ and high CEQ (“High Both” group), (4) average SPQ and CEQ (“Average User” group), and (5) average SPQ non-users (“Control” group; see Table 1).

2.2. Questionnaires

Schizotypal personality traits were assessed with the SPQ (Raine, 1991). The SPQ is a 74 question self-report that measures experiences, thoughts, and perceptions along the schizophrenia spectrum. The scale has moderate criterion validity (0.68) and high test-retest reliability (0.82) (Raine, 1991).

Cannabis experiences were measured with the CEQ (Barkus et al., 2006). The CEQ is a self-report scale that measures three aspects of cannabis use; the frequency of pleasurable, psychotic-like, and after-effect experiences of the drug. This is a relatively new scale, designed by Barkus et al. (2006), that has been used in prior studies investigating cannabis experiences (Barkus and Lewis, 2008; Bianconi et al., 2016; Colizzi et al., 2015). Cronbach's alpha for the total score ($\alpha = 0.914$), and for each subscale (range: $\alpha = 0.893$ to 0.918) was calculated, demonstrating a high degree of internal reliability.

Table 1
Demographics and measures.

	High CEQ	High SPQ	High Both	Avg. User	Controls
Group size	19	19	15	20	24
Gender (f/m)	10 (9)	16 (3)	8 (7)	13 (11)	15 (5)
Age, years	26.00 (*9.01*)	19.42 (*1.43*)	24.20 (*7.98*)	26.21 (*10.71*)	23.30 (*7.49*)
SPQ total score	13.79 (*7.05*)	35.68 (*7.07*)	35.80 (*8.18*)	11.71 (*5.95*)	11.05 (*7.69*)
CEQ total score	132.10 (24.77)	108.33 (*18.46*)	150.07 (*25.80*)	93.50 (*17.56*)	n/a
Median cannabis use statement endorsed	“More than once a week”	“More than once a week”	“More than once a week”	“Once or twice a mo.”	n/a

Note: Cannabis related information associated with the High SPQ group is based upon the six (31.6%) participants within that group who endorsed cannabis use.

Please cite this article as: Brooks, G.A., Brenner, C.A., Is there a common vulnerability in cannabis phenomenology and schizotypy? The role of the N170 ERP, Schizophr. Res. (2017), https://doi.org/10.1016/j.schres.2017.11.019