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Do motivation deficits in schizophrenia-spectrum disorders promote cannabis use? An investigation of behavioural response to natural rewards and drug cues

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ABSTRACT

Deficits in incentive motivation are often present in both Schizophrenia Spectrum Disorders (SSD) and substance-use disorders. The current study aims to test whether the presence of such deficits confers vulnerability to cannabis use in individuals with SSD. SSD patients ($n=35$) and healthy controls ($n=35$) were each divided into a group with ($n=20$) and a group without ($n=15$) current cannabis use disorder. Subjects performed a behavioural task designed for schizophrenia patients in which they could seek exposure to pleasant and cannabis visual stimuli on the basis of internal representations of these stimuli. Intensity of cannabis use was assessed by self-report. SSD patients were significantly less likely than controls to exert effort to try to re-view pleasant stimuli but were not significantly less likely to work to avoid unpleasant stimuli. Lack of response to re-view pleasant stimuli significantly predicted higher subsequent cannabis self-administration in patients but not controls, after controlling for degree of prior exposure to cannabis. Deficits in incentive motivation may be an aspect of SSD which promotes cannabis use in this population.

1. Introduction

1.1. Background

There are negative consequences of cannabis use for individuals with Schizophrenia-Spectrum Disorders (SSD) (Zammit et al., 2008). In order to reduce this behaviour it is necessary to understand factors promoting cannabis use in this population. Some evidence suggests individuals with SSD report similar reasons for substance use as other young people (Kolliakou et al., 2011); however, more work is needed before elements of psychotic illness or its associated morbidity can be ruled out as important factors promoting cannabis use in SSD.

One of the most striking deficits observed in many patients with schizophrenia is avolition, a negative symptom of schizophrenia consisting of lack of motivation to pursue goals or effortful activities (Foussias and Remington, 2010). There is a growing body of evidence of deficits in anticipating (Gard et al., 2007), delaying (Ahn et al., 2011), working for (Heerey and Gold, 2007), learning about (Yilmaz et al., 2012), or exploring (Strauss et al., 2011) rewards in this condition. "Wanting" and behavioural exertion to seek rewards are critically modulated by the dopamine system, which is believed to signal the motivational salience of incentive environmental stimuli and is highly implicated in both schizophrenia and addiction (Schultz et al., 1997; Howes and Kapur, 2009; Heinz and Schlagenhauf, 2010). Some have argued that the primary reward-related deficit in SSD is an inability to mentally represent the value of a reward after it ceases to be experienced (Gold et al., 2008). On the other hand, liking, the degree of pleasure while in the midst of experiencing a reward, may be relatively intact (Gard et al., 2007; Heerey and Gold, 2007).

Habitual substance use may result in behavioural disengagement as the desired substance usurps attention and motivated behaviour towards itself (Anselme, 2009). On the other hand, behavioural disengagement may be a vulnerability factor to substance use in humans and animals (Terry-McElrath et al., 2011; Nader et al., 2012; Puhl et al., 2012). Along these lines it is of note that a similar intervention, boosting dopamine receptors in the striatum, can both reduce addictive behaviours in animals (Nader and Czoty, 2005) and increase the tendency to work for rewards (Trifilieff et al., 2013). However, concerning cannabis users in the general population, there is little evidence of motivation deficits despite popular conceptions (Kaestner, 1994; Barnwell et al., 2006; Looby and Earleywine, 2007; Grant et al., 2012). In the case of cannabis users with schizophrenia there has been inconsistent evidence regarding the association between substance use and symptoms of avolition (Potvin et al., 2006; Leventhal et al., 2008; Koen et al., 2009).

1.2. Rationale and hypothesis

As the nature of the reward deficits in schizophrenia has recently become better delineated (Gold et al., 2008; Ahn et al., 2011;

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Strauss et al., 2011; Yilmaz et al., 2012), a key question should be how these deficits may promote maladaptive behaviours such as substance abuse, which has been conceptualised as pathological reward reinforcement (Di Chiara, 1995). Deficits in reward processing have been theorised to contribute to the co-morbidity of schizophrenia-spectrum and substance-use disorders (Roth et al., 2005; Krystal et al., 2006); however, research in this area has not kept pace with the recent advances concerning reward deficits in schizophrenia. We theorised that deficits in incentive motivation may be an aspect of schizophrenia which could confer vulnerability to habitual cannabis use, an immediately rewarding behaviour requiring minimal exertion, and make it harder to replace cannabis with alternative recreational activities. Although this reasoning would apply to any substance of abuse, cannabis seemed the most pertinent substance to study given that it is often the most commonly abused substance in youth with psychotic illness (Koskinen et al., 2009).

We employed a behavioural task (Heerey and Gold, 2007) which was designed for use in schizophrenia and has previously exposed incentive motivation deficits in this condition. This paradigm measures incentive motivation or "wanting", operationalised as the effort exerted in a key-press procedure to seek re-exposure to pleasant images and images of cannabis. This paradigm quantifies willingness to exert effort in the present for an uncertain reward in the future and is particularly relevant to schizophrenia because response is made based on the mental representation of the value of the reward which is no longer visible when responding. We hypothesised that patients would be less inclined to seek natural rewards (pleasant images) than controls and that deficits in reward-seeking would predict the frequency of future cannabis self-administration.

2. Methods

2.1. Subjects

The study assessed male patients who were currently or formerly treated at Prevention and Early intervention Programme for Psychoses-Montreal (PEPP-Montreal), a specialised early-intervention service in Montreal, Canada. Details of the treatment model can be found elsewhere (Malla et al., 2003). All patients were currently taking antipsychotic medication (only three (9%) were taking a first-generation antipsychotic), and met criteria for DSM diagnosis of Schizophrenia-Spectrum Disorder (SSD) using the Structured Clinical Interview for DSM-IV (First et al., 1995). Male control subjects were recruited through the websites craigslist.org and kijiji.ca. The only exclusion criteria were if they, or a first-degree family member, had psychotic illness or if they had a current mood disorder.

Thirty-five patients and 35 controls were divided into groups with a lifetime diagnosis of cannabis abuse or dependence ($n=20$ patients and 20 controls) as determined by SCID assessment all of whom had at least one use in the past month; and groups with no lifetime substance-use/addictive disorder (aside from nicotine) and no cannabis use in the past 3 months ($n=15$ patients and 15 controls). Due to the use of erotic images of women, homosexual individuals were ineligible. Subjects were asked not to consume any substances (aside from nicotine) on the test day. All patient and control subjects provided informed consent to participate in the study which was approved by the McGill University Internal Review Board.

2.2. Clinical and demographic measures

Marital status was divided into "single" or "current relationship". Educational achievement was measured as years of completed education. Positive and negative symptoms were assessed using the sum of global items (global total score) on the Scale for Assessment of Positive Symptoms (SAPS) (Andreasen, 1984) and the Scale for Assessment of Negative Symptoms (SANS) (Andreasen, 1983) within 3 months of study assessment.

2.3. Intensity of cannabis use

Cannabis use (frequency and quantity over the previous month) was assessed by a short interview on the test day and 1 month later. Subjects were asked how many days they used cannabis in the past week, how many sessions of using cannabis they had on a typical day in which they used, and what quantity of cannabis they consumed in the past week. They were asked if the past week was representative of the past month; when use fluctuated over time this was reviewed in detail. The same procedure was used to assess consumption of other substances. We did not expect this to be a highly precise measure but to separate heavy, moderate, and light users. Furthermore, as the study was carried out in a specialised early intervention programme that provides intensive and very frequent contact with patients and their families, extensive information regarding patients' cannabis use was available from clinical notes and consultation with their clinicians. Although this was not incorporated into our measure of cannabis use, had any patient's report of their cannabis use been inconsistent with clinical information their inclusion in the study would have been reassessed.

To characterise the extent of cannabis addiction in patients and controls, the Cannabis Abuse Screening Test (CAST) (Karila et al., 2007) was administered for the period of lifetime and past-year, and subjects estimated the number of years during which they had used cannabis on a near-daily basis.

2.4. Experimental procedure

Behavioural and self-reported response to stimuli were assessed using the procedures previously described (Heerey and Gold, 2007). Using a computer, subjects viewed and rated 56 slides, each containing a single image, divided equally into four categories: positive, negative, neutral, and cannabis images. Emotional images came from the International Affective Picture System (IAPS) (Lang et al., 1995), the Empathy Picture System (EPS) (Geday et al., 2003) and collaborators (Pitié-Salpêtrière Hospital, CNRS UMR 7593, France). Positive images consisted of beautiful women/erotica (seven images), extreme sports, and landscapes; negative images consisted of violent scenes, sad faces, and mild injuries; neutral images consisted of unemotional people and household objects. Cannabis images were generated by a photo shoot in which two models prepared and smoked a marijuana cigarette; these were supplemented by other publicly-available close-up photos of marijuana.

Participants rated the degree to which each image was experienced as pleasurable and/or arousing using nine-point Likert scales anchored by *extremely (unpleasant/calm)* and *extremely (pleasant/arousing)*. Slides remained on the screen until ratings of valence and arousal were complete. This procedure served as a measure of evoked hedonic response (liking). Three seconds after rating each slide for valence and arousal, "wanting" or representational responding was assayed with the image no longer visible. Participants were instructed to rapidly press the "*n*" and "*m*" keys if they wanted to have a chance to see a slide again later on during the experiment, or the "*j*" and "*k*" keys if they wanted to avoid seeing the slide again. They were told that the more presses they made, the more likely that the slide would or would not reappear later on. Participants were informed that responding would not alter the total duration of the experiment and that they had no obligation to every respond. Participants were given 2 s of rest prior to presentation of the next slide. We used the same instruction script as previously described (see Fig. 1A in Heerey and Gold, 2007). Prior to testing all subjects completed a training version of the experiment in the presence of the experimenter until it was clear to the experimenter that the subject understood the task. All subjects were queried about their reasons for not responding immediately following testing. Two subjects (both cannabis-using patients) were excluded from

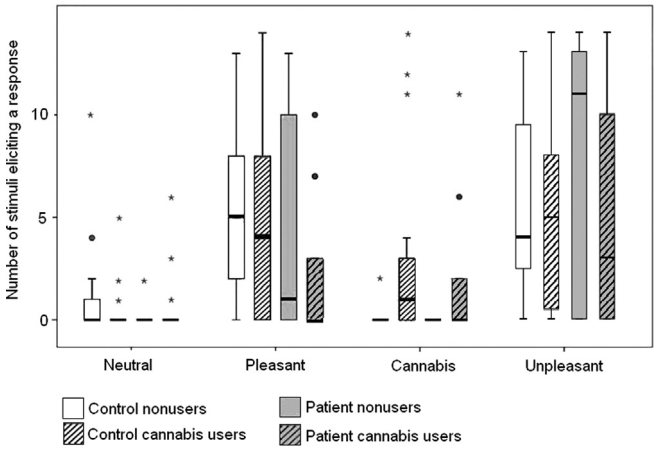

Fig. 1. Boxplot showing number of behavioural responses in patients and controls with and without cannabis use. The figure presents the number of incentive motivation responses made to re-view neutral, pleasant, and cannabis stimuli and the number of avoidant motivation responses to avoid re-viewing unpleasant stimuli. Circles represent outliers and stars extreme values.