Journal of Psychiatric Research 99 (2018) 22–32

Contents lists available at ScienceDirect

Journal of Psychiatric Research

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

Meta-analysis of neurocognition in young psychosis patients with current cannabis use

Sophia E.R. Bogaty[a], Rico S.C. Lee[a,b], Ian B. Hickie[a], Daniel F. Hermens[a,c,*]

[a] Brain and Mind Centre, University of Sydney, Sydney, NSW, Australia
[b] Brain and Mental Health Laboratory, Monash University, Melbourne, VIC, Australia
[c] Sunshine Coast Mind and Neuroscience Thompson Institute, University of the Sunshine Coast, Birtinya, QLD, Australia

ARTICLE INFO

Keywords:
Young people
Schizophrenia
Early-onset psychosis
Cognition
Marijuana
Comorbidity

ABSTRACT

Objective: Adult psychosis patients (i.e. over the age of 25 years) who are also lifetime cannabis users (CANN ±) appear to exhibit superior cognition compared to never-using patients (CANN-). The objective of this meta-analysis was to evaluate the cognitive differences between CANN- and patients who currently use cannabis (CANN +) (i.e. during the CANN ± patients' cannabis-using stage). Specifically, focusing on young patients under the age of 25 years, the typical stage of both psychosis- and cannabis-onset.

Method: Of the 308 studies identified through database searches and secondary referencing, 14 compared neurocognition of CANN + and CANN- in young people with psychotic disorders (mean age between 15 and 45 years). Effect sizes were extracted using neurocognitive test performance between CANN + and CANN- and random effects modelling was conducted on pooled ES and moderator analyses.

Results: CANN + performed worse on several cognitive domains (i.e. premorbid IQ, current IQ, verbal learning, verbal working memory, motor inhibition) compared to CANN-. The association between age and performance in CANN + cognition was varied, with older age predictive of worse performance in processing speed, sustained attention, verbal memory, and better performance in verbal learning and very fluency. Of note, CANN + outperformed CANN- in tests of conceptual set-shifting.

Conclusion: These results are consistent with previous findings indicating that CANN + demonstrate poorer neurocognition than CANN-; and that this is exacerbated with increasing age. Our findings demonstrate significant cognitive differences between patients with CANN + versus CANN- even at early-onset psychosis, which could suggest a different underlying mechanism towards psychosis for cannabis users.

1. Introduction

Cannabis remains the most prevalent illicit drug used by individuals with schizophrenia-spectrum disorders (Koskinen et al., 2010; Smucny et al., 2014; Amminger et al., 2006), and current chronic use has been shown to significantly worsen positive psychotic symptoms in patients (Talamo et al., 2006; Dubertret et al., 2006). Counterintuitively, meta-analyses and systematic reviews suggest that cognitive functioning in chronic schizophrenia patients with a history of, but not current, cannabis use (CANN ±) is superior to that of their peers who have never used cannabis (CANN-) (Yücel et al., 2012; Løberg and Hugdahl, 2009). This suggests that there may be different phenotypes among older individuals with chronic psychotic disorders. However, relatively little is known about the cognitive profiles in the context of cannabis use in younger individuals with early psychosis. Prevalence of psychoses in pre-pubertal children is relatively rare (Thomsen, 1996), although the incidence of first episode psychosis (FEP) rapidly increases after the age of 15 years (Amminger et al., 2006; Gillberg et al., 1986; Hare et al., 2010), with the highest rate of a first episode between the ages of 15 and 24 years (Amminger et al., 2006; Archie et al., 2007). Young people, aged 12–24 years, represent an important population to study psychotic disorders as such individuals represent a subgroup of patients less likely to be exposed to critical environmental factors such as chronic use of antipsychotic medication (Epstein et al., 2014). There is also evidence that the corpus callosum, the highest order, latest maturing network of the brain, continues to grow until the middle 20's (i.e. 25.45 years) (Pujol et al., 1993). This, as well as synaptic pruning, which continues until the mid-20's, suggests full brain development is incomplete until around 25 years of age (Andersen, 2003). Young people are also at a great risk of substance abuse, particularly those for whom the age of onset of drug use (alcohol and cannabis, in particular) occurs prior to around 15 years of age (Archie et al., 2007; Wells et al.,

* Corresponding author. Sunshine Coast Mind and Neuroscience - Thompson Institute, University of the Sunshine Coast, 12 Innovation Parkway, Birtinya, QLD, 4575, Australia.
E-mail address: dhermens@usc.edu.au (D.F. Hermens).

https://doi.org/10.1016/j.jpsychires.2018.01.010
Received 30 June 2017; Received in revised form 12 January 2018; Accepted 12 January 2018

2009; Palmer et al., 2009). Archie et al. (2007) stratified FEP subjects, between 15 and 50 years, into age ranges and found that those between the ages of 18–24 years accounted for the largest faction (i.e. 45%) of patients engaged in concurrent drug use (Archie et al., 2007). It would appear both psychotic episodes and substance use during a time when the brain has not fully developed could have detrimental effects for patients in the long-term, and cognition and symptomatology during this formidable time needs to be further investigated. Thus, in terms of evaluating the potential cognitive dissimilarities associated with and without concurrent cannabis use in psychotic disorders a focus on young individuals is highly warranted.

Crean et al.'s (2011) extensive review demonstrates the various effects of acute (i.e. 0–6 h after use), residual (7 h–20 days after use), and long-term (at least 21 days since use) effects of cannabis on neuropsychological functions in healthy populations (Crean et al., 2011; Broyd et al., 2016; Curran et al., 2016; Ranganathan and D'Souza, 2006). Acute effects of cannabis tend to show the greatest degree of dysfunction, with subjects demonstrating impairment across attention, decision making, impulsivity and working memory. Both residual and long-term effects appear to largely revert to near-normal functioning, specifically in attention, impulsivity and working memory, with a greater period of abstinence showing the most advanced improvement in cognition. Theoretically, cannabis using patients with a psychotic disorder would be expected to perform worse than their non-using counterparts across several cognitive domains, in keeping with studies in healthy individuals; whereby poorer cognitive performance in those who are either CANN+ or CANN ± is most pronounced in tests of executive functioning and processing speed (Meier et al., 2012). In contrast, there is evidence that chronic schizophrenia patients who have a history of cannabis use (CANN ±) outperform their CANN- peers (with schizophrenia) in general intelligence, attention, working memory, executive abilities and visuo-spatial abilities (Yücel et al., 2012; Bugra et al., 2013; Jockers-Scherübl et al., 2007; Rabin et al., 2011). Following this logic, one might assume that younger individuals with psychotic disorders (e.g. FEP) who use cannabis, but abstain later, will demonstrate improved cognitive functioning compared to their peers who never used cannabis. Given this, it is possible that the cannabis using patients' psychoses stem from an inherent gene-environment interaction partially owing to their early onset of cannabis use. Such a subgroup of patients may be diagnosed with psychosis, but may also have an atypical neurocognitive profile. This reflects Pearlson's (2015) review examining significant clinical overlap of psychoses and schizophrenia-spectrum disorders (Pearlson, 2015). Furthermore, there is evidence such as that provided by the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP) study, showing that there are clusters of individuals with shared biological features (known as 'biotypes') despite there being a commingling of their traditional clinical phenotype (i.e. schizophrenia or affective psychoses disorders) (Hill et al., 2013; Tamminga et al., 2014). Importantly, one of the three biotypes identified appears to be associated with higher cannabis use, better cognition, and lower percentage of affected relatives (Tamminga et al., 2017). This theory is supported by evidence, which shows that chronic schizophrenia patients with CANN ± who first began using cannabis before the age of 17 years exhibit some superior cognitive functioning compared to patients with later (i.e. after 16 years of age) cannabis-use onset (Yücel et al., 2012; Jockers-Scherübl et al., 2007; Hanna et al., 2016).

Yücel et al.s' (2012) meta-analysis investigated the effect of past cannabis use, typically prior to psychosis onset, on neuropsychological performance of older adults (i.e. mean age of patients was above 27 years) with a diagnosis of schizophrenia (Yücel et al., 2012). CANN ± outperformed patients with no history of use (CANN-) in tests of global cognition, processing speed, visual memory, planning, and working memory. However, they also found that patients who currently use cannabis (CANN+) did not demonstrate superior cognitive performance across a range of measures. Although, these groups differed significantly in one cognitive domain: the CANN+ showed worse performance in tests of verbal memory. Similarly, a separate study utilized biological radioimmunoassay testing rather than drug-use questionnaires to measure current drug use in schizophrenia patients, and found no significant cognitive differences between current cannabis-using patients and their non-using counterparts (Bahorik et al., 2014). However, there are several factors that may affect cognitive results, including frequency, dosage, and time since last cannabis intake. D'Souza et al. (2005) found evidence of dose-specific effects of THC on the cognition of schizophrenia patients (D'Souza et al., 2005). They demonstrated temporarily increased learning and recall deficits after 2.5 mg or 5 mg of intravenous THC, compared to 0 mg, with patients in the 5 mg group showing a pattern of worse cognitive performance compared to 2.5 mg.

On the surface, a history of moderate, (potentially regular) lifetime use of cannabis followed (importantly) by a period of abstinence in psychosis patients reveals a 'superior' cognitive profile compared to those with a psychotic disorder who never used or those who have continued to use (i.e. current use in older, more chronic stages of schizophrenia). Intriguingly, it appears that when cannabis use begins during adolescence, before the age of 17, those who later abstain (i.e. CANN ±) demonstrate better neurocognitive performance than their CANN ± peers who began using after 17 years. However only a handful of studies report any evidence of cognitive dysfunction in cannabis-using adolescents diagnosed with psychosis. Furthermore, cannabis use in the neurodevelopmental period of adolescence has been shown to confer a range of cognitive, social, and psychological harms (Meier et al., 2012; Tien and Anthony, 1990; Henquet et al., 2004; Szoke et al., 2014; Di Forti et al., 2014; Scholes-Balog et al., 2016; Meier et al., 2015; Mackie et al., 2013). In fact, Henquet et al. (2004) found that any cannabis use exacerbates psychotic symptoms in young people, particularly in those who have a predisposition for psychosis (Henquet et al., 2004).

Given the above-mentioned findings, the aim of the current study was to systematically review the potential effects of cannabis use on cognition in adolescent and young adult patients with psychosis. From previous evidence, we expected cannabis users to show significant deficits across a range of neurocognitive tests, as compared to non-using patients. However, young cannabis-using patients were expected to demonstrate superior neurocognitive performance compared to older CANN+ and CANN-, or young CANN-.

2. Methods

2.1. Search strategy and selection criteria

Studies were identified through extensive online database searches, including PubMed, Medline, and Psycinfo. Searches included keywords involving psychosis (i.e. schizophrenia, schizophreniform, psychosis, schizoaffective, schizo*, FEP, first, episode), cannabis (i.e. cannabis, marijuana, THC, tetrahydrocannabinol), and cognition (i.e. neuropsycho*, neurocognit*, cogniti*), and were limited to English-language articles with human participants. All articles up to October 2016 (i.e. the month the searches were conducted) were considered for analysis. A secondary search was conducted by reviewing the reference lists of relevant review and meta-analytic papers.

The inclusion criteria were: (1) diagnosis of a psychotic disorder according to DSM (i.e. Schizophrenia Spectrum and Other Psychotic Disorders) or ICD (i.e. Schizophrenia Spectrum and Other Primary Psychotic Disorders) criteria; (2) studies had to compare a psychotic (or schizophrenia spectrum disorder) cannabis-using group to an appropriate clinical control group (i.e. psychotic nonusers); (3) cannabis was the predominate substance used by patients, as stated by the authors in the methodology; (4) the assessment of traditional neuropsychological functions using valid and reliable tests, used routinely in clinical practice (Strauss et al., 2006); and (5) sufficient statistical data were