Schizophrenia Research xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Schizophrenia Research

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

The impact of current cannabis use on general cognitive function in people with psychotic illness

Anna Waterreus [a,*], Johanna C. Badcock [b], Patsy Di Prinzio [a], Mathew Martin-Iverson [c], Vera A. Morgan [a,b]

[a] Neuropsychiatric Epidemiology Research Unit, Division of Psychiatry, Faculty of Health and Medical Sciences, University of Western Australia, Medical Research Foundation Building, Rear 50 Murray Street, Perth 6000, Australia
[b] Centre for Clinical Research in Neuropsychiatry, Division of Psychiatry, Faculty of Health and Medical Sciences, University of Western Australia, Medical Research Foundation Building, Rear 50 Murray Street, Perth 6000, Australia
[c] Pharmacology, M510, School of Biomedical Sciences, University of Western Australia, Stirling Highway, Crawley, 6009, Australia

ARTICLE INFO

Article history:
Received 16 August 2016
Received in revised form 20 March 2017
Accepted 21 March 2017
Available online xxxx

Keywords:
Cannabis use
Cognition
Cognitive impairment
Psychosis
Affective psychosis

ABSTRACT

Background: Despite growing research, it remains unclear if cannabis use is associated with additive cognitive impairment in people with psychotic illness and whether exposure in early adolescence is associated with poorer cognitive performance in adulthood.
Methods: This cross-sectional study of a nationally representative sample of 1199 adults with psychotic illness compared current cognition (digit symbol coding) of 297 current users of cannabis (used in the past year), 460 past users (used previously but not in the past year) and 442 non-users (never used). Multiple logistic regression was used to examine whether cognitive performance of cannabis-user groups varied by exposure age and diagnosis (non-affective/affective psychoses).
Results: Unadjusted analysis showed current cannabis users had significantly higher odds of impaired cognitive function compared to non-users (odds ratio = 1.52, 95%CI = 1.04 − 2.22). After adjusting for potential confounders, differences between the three groups were not significant. Exposure age was not significant in adjusted analysis. In participants with nonaffective psychoses, cognitive ability of current cannabis users did not differ from non-users. However, in participants with affective psychoses, using cannabis in the last year was a significant predictor of impaired cognitive function (odds ratio = 2.25, 95%CI = 1.05 − 4.84).
Conclusion: Among people with psychotic illness, there was no significant difference in cognitive function between current, past and non-users of cannabis. However, when we compared cognitive performance of the three cannabis groups by diagnostic grouping, current cannabis use had a significant negative relationship with cognitive function in people with affective psychoses, but not in those with non-affective psychoses. This finding requires replication and further investigation.

1. Introduction

Cannabis use is common in people with psychotic illness (Green et al., 2005; Waterreus et al., 2016) and may contribute to greater rates of relapse and longer hospital admissions (Schoeler et al., 2016). People with psychotic illness also experience deficits across a range of cognitive domains, though the degree of impairment is generally more pronounced in schizophrenia than in bipolar disorder and major depression with psychosis (Barch and Sheffield, 2014; Krabbendam et al., 2005; Vohringer et al., 2013). There has been growing interest and research into whether cannabis use has an additive effect on the cognitive dysfunction of people with psychotic illness, mainly schizophrenia, (Curran et al., 2016; Volkow et al., 2016) and what impact cannabis exposure in early adolescence has on cognition (Levine et al., 2017; Lubman et al., 2015).

Cannabis is most commonly smoked, and the effects from its main psychoactive component - tetrahydrocannabinol (THC) (Pertwee, 2008) - occur within minutes of inhaling. (Curran et al., 2002) but most effects resolve within hours or days. Impairments may persist longer after abstinence (Broyd et al., 2016) as elimination of cannabinoids from the body can take as long as 77 days, as THC is fat soluble and can be stored and released slowly depending on the duration, frequency and THC content of the cannabis used (Ellis et al., 1985; Grotenhermen, 2003). Frequent heavy use of cannabis in early teens, as well as lengthier exposure, has been argued to affect brain development (Levine et al., 2017; Lubman et al., 2015; Yücel et al., 2008). However, it has also been suggested that cannabis-associated

* Corresponding author.
E-mail address: anna.waterreus@uwa.edu.au (A. Waterreus).

http://dx.doi.org/10.1016/j.schres.2017.03.038
0920-9964/

cognitive deficits and changes to brain structure and activity are temporary and reversible once cannabis use has ceased (Hirvonen et al., 2012; Pope et al., 2002; Schreiner and Dunn, 2012; Yücel et al., 2016).

Despite the increased focus, literature regarding an association between cannabis use and cognitive function in people with psychotic illness has been inconsistent. Some studies suggest that compared to non-use, cannabis use is associated with poorer functioning (Joyal et al., 2003; Pencer and Addington, 2003; Ringen et al., 2010), while others report better functioning (Jockers-Scherübl et al., 2007; Schnell et al., 2009; Stirling et al., 2005) or no differences (Scholes and Martin-Iverson, 2010; Sevy et al., 2007). Variations in the classification of cannabis use and non-use may go some way to account for the disparity in these findings. For example, non-users have been defined as having: never used cannabis, lifetime use five times or less, or no use in the last one, three, six or 12 months. Similarly, cannabis-using groups have included both current and past users, and those with a lifetime diagnosis of cannabis use disorder. Importantly, classifying use solely on a lifetime diagnosis of cannabis abuse/dependence, the criteria used by Power et al. (2015), is likely to mean that any effects of recent use (which may be substantial yet below the threshold for diagnosis) on current cognitive function will be obscured or missed. Interestingly, Yücel et al. (2012) concluded that patients with schizophrenia and a history of cannabis use had significantly better neuropsychological functioning only in studies defining cannabis use by lifetime exposure but not in studies using recent use criteria. Similarly, if cannabis-associated cognitive deficits are temporary, then combining past and current users may also miss any effects. Schreiner and Dunn (2012) undertook two meta-analyses to examine the residual cognitive effects of cannabis use in non-psychiatric populations: the first found a small significant negative effect, while the second including only studies where cannabis users had been abstinent for at least 25 days found that cannabis had no long-term neurocognitive effect and suggested that discrepant findings across studies may be due to variable periods of cannabis abstinence.

Finally, previous studies may have missed the negative effects of cannabis on cognition due to a number of methodological limitations including small sample sizes, polydrug use and not controlling for a range of factors known to influence cognition including: sex, level of education, premorbid IQ, psychiatric symptoms, age at illness onset, duration of illness, use of psychotropic medication, alcohol, tobacco and caffeine use and obesity.

As it remains unclear if cannabis use is associated with additional cognitive dysfunction in people with psychotic illness, using data from a large representative sample of people with psychotic illness interviewed in the second Australian national survey of psychosis – Survey of High Impact Psychosis (SHIP) we undertook to: 1) investigate whether current cannabis use is related to current cognitive performance, 2) address many of the methodological limitations highlighted in previous research (Coulston et al., 2007), 3) examine whether the cognitive performance of cannabis-user groups varied by age of exposure (16 years and under; over 16 years) and 4) whether it varied by diagnostic grouping, specifically non-affective versus affective psychoses, to enable inter-study comparison.

2. Method

SHIP was conducted within seven catchment sites across Australia, covering a population of some 1.5 million people aged 18–64 years, approximately 10% of the Australian population in this age group. Its main aims were to estimate the treated prevalence of psychosis for people aged 18–64 years and to describe the characteristics and use of services by people with psychotic illness. A two-phase design was used. In Phase 1, screening for psychosis took place in public specialised mental health services and non-government organisations supporting people with mental illness in the census month (March 2010). A psychosis screener was used to identify individuals likely to meet criteria for formal diagnosis (Jablensky et al., 2000). Administrative records were scanned to identify people with a recorded diagnosis of psychosis and in contact with public specialised mental health services in the 11 months prior to census but not in the census month. In Phase 2, people who were screened positive for psychosis were randomly selected, stratified by catchment site and age group, for interview. The Institutional Human Research Ethics Committees at all sites approved the study. Full details of the survey methodology have been published elsewhere (Morgan et al., 2014, 2012).

2.1. Participants and cannabis use

A total of 1825 participants screened positive for psychosis gave written informed consent and were interviewed. The present study used a subsample of participants who i) provided data on their cannabis use, ii) completed the assessment of current cognitive function, iii) reported not using other illicit drugs (amphetamine, heroin, cocaine, LSD/hallucinogen, ecstasy or inhalant/solvents) in the 12 months prior to interview and iv) met criteria for an ICD-10 diagnosis of affective or non-affective psychoses (see Fig. 1). Participants were classified into three groups based on self-reported lifetime and past 12-month cannabis use. Current users were those who had reported any use of cannabis in the previous 12 months and non-users had never used cannabis. Past users had used cannabis previously but not in the past 12 months: abstinence for the previous 12 months was required to be classified as a past user to minimise the possibility of any neurocognitive differences due to residual or withdrawal effects. Information was also collected on frequency of cannabis use in the past 12 months and the age of first cannabis exposure, but not on frequency or amount used at this time, nor cumulative duration of use.

2.2. Assessments

2.2.1. Demographics and physical health

Information collected included age, sex and educational status (completed highest level of schooling). Current residential postcode was used to categorise socio-economic status (SES) using Australian Bureau of Statistics Socio-Economic Indexes for Areas (Index of Relative Socio-Economic Disadvantage) (Australian Bureau of Statistics, 2008): the lower the score the greater the level of disadvantage. Height and weight were measured and body mass index (BMI) was calculated and classified using the World Health Organization (2000) reference range: obese (≥30), overweight (25–29) and underweight/normal (<25).

2.2.2. Alcohol, tobacco, caffeine, medication use

The Alcohol Use Disorders Identification Test (AUDIT) (Saunders et al., 1993) was administered and the derived AUDIT-C score (Bush et al., 1998) calculated. A score of three or more for women and four or more for men indicated hazardous drinking in the previous 12 months. The number of cigarettes smoked a day in the last four weeks was recorded as a continuous variable. Total daily caffeine intake was calculated after participants were shown a list of caffeinated drinks and asked "In the last 4 weeks how many of these would you drink on average per day?" The total daily intake was trichotomised: low (0-249 mg), moderate (250-499 mg) and high (≥500 mg). All prescribed medication taken for at least the previous four weeks was recorded (Waterreus et al., 2012).

2.2.3. Cognitive function

The National Adult Reading Test – Revised (NART-R) was used to estimate premorbid IQ (Nelson and Willison, 1991). Full-scale IQ scores were dichotomised: 'impaired' - more than one standard deviation below the population mean (107.4 (SD 17.1)) and 'intact' - within one standard deviation or above, with a third group covering those

Please cite this article as: Waterreus, A., et al., The impact of current cannabis use on general cognitive function in people with psychotic illness, Schizophr. Res. (2017), http://dx.doi.org/10.1016/j.schres.2017.03.038