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Dose–response effect between cannabis use and psychosis liability in a non-clinical population: Evidence from a snowball sample

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ABSTRACT

This study aimed to explore the associations between daily cannabis use and the specific profiles of sub-clinical symptoms in a non-clinical population obtained through snowball sampling, taking into account alcohol use, other drug use, social exclusion and age at onset of cannabis use. We included 85 daily cannabis users and 100 non-daily cannabis users. Both the case and the control populations were identified by snowball sampling. Daily cannabis use was associated with more alcohol intake and other drug use, as well as with early onset in the use of cannabis. Daily cannabis use appeared to exert a dose–response effect on first-rank symptoms, mania symptoms and auditory hallucinations, even after adjusting for sex, age, other drug use, social exclusion and age at onset of cannabis use. The paranoid dimension was only associated with the heaviest consumption of cannabis. Initial age of cannabis use modified the effects of daily cannabis use on the first-rank and voices experiences. Daily cannabis use was associated with significantly more first-rank and voices experiences among those subjects who started to use cannabis before 17 years of age.

Our study supports the association of psychotic experiences with cannabis use even among non-psychotic subjects.

1. Introduction

There is evidence that cannabis use is a moderating factor in the development of psychosis (Moore et al., 2007). In recent studies, cannabis use has been postulated as a catalytic factor for psychosis (Barrigón et al., 2010), although most cannabis users will not develop psychosis.

Researching a large sample of daily cannabis users could shed light on such questions. However, ascertaining untreated drug abuse by traditional sampling has yielded poor results to date (Lopes et al., 1996; Bromet et al., 2006). Estimates show that the prevalence of daily cannabis users in Europe is some 1% of adults and 1–3.5% among young adults (15–34 years of age) (Wiessing et al., 2009). The study by Verdoux et al. (2003) explored the association between cannabis use and psychosis in a non-clinical population of 571 females, only 17 of whom (3%) were daily cannabis users.

It is not clear whether cannabis use is associated with some specific dimension of psychosis, as studies looking into such specific associations have been contradictory (Skosnik et al., 2001; Johns et al., 2004; Stefanis et al., 2004; Hides et al., 2009; Henquet et al., 2010). Most epidemiological studies carried out in this area involve small samples of cannabis users, without taking into account other drug use, age at onset of cannabis use or social factors (Skosnik et al., 2001; Johns et al., 2004; Stefanis et al., 2004), and among clinical populations, the studies may have overrepresented

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the problem of drug users by including subjects who presented addiction (Fernández-Serrano et al., 2001).

The so-called snowball method may be a good option for such studies, overcoming the limitations of traditional cohort or case–control approaches in the research of hidden populations (Watters and Biernacki, 1989; Bromet et al., 2006). This technique is defined as "a method that yields a sample based on referrals made by people who share or know others who present the characteristics that are of research interest" (Lopes et al., 1996).

In short, three main limitations hamper studies to date about cannabis use and psychosis liability in non-clinical samples: most involve a small sample of cannabis users, they do not take into account the age at onset of cannabis use, and they do not investigate the association between cannabis use and some specific dimensions of psychosis.

The main aim of the study is to explore the associations between a given pattern of cannabis use with respect to the specific profiles of subclinical psychotic symptoms measured using the Community Assessment of Psychic Experiences (CAPE) (Stefanis et al., 2002) in a non-psychotic population gathered by snowball sampling. We adjusted for potential confounding factors such as other drug use, alcohol intake, age at onset of cannabis use and social exclusion. Finally, we aimed to determine if the age at onset of cannabis use modified the effect of daily cannabis use on the presence of psychosis liability.

2. Material and methods

2.1. Sample

The sample was identified by snowball sampling. The chain started in two areas of Andalucía (Almería and Granada), southern Spain, with three daily cannabis users (DCU) and four non-daily cannabis users (NDCU) in each area. The subjects were initially identified with the help of associations of cannabis plant growth. All of them agreed to participate in the study and each one helped to identify two friends: one DCU and another NDCU. This chain referral was continued until we reached the number of 103 subjects in each area. Four DCU and two NDCU in Almería and three DCU and one NDCU in Granada refused to participate. If, during recruitment, a given NDCU was later found to be a daily user, then the participant was accepted as a DCU and two new NDCU were recruited (Lopes et al., 1996). One psychologist in each area made the assessment (JLR, LH). Both had been trained in the use of the L section of the Composite International Diagnostic Interview (CIDI) and the Structured Clinical Interview for DSM-IV axis I disorders (SCID) (First et al., 1997).

Exclusion criteria were: 1) having a previous history of seeking help for psychosis symptoms or addiction, 2) having a previous history of head trauma with loss of consciousness for 1 h, or a history of major neurological or somatic disorder with neurological components, 3) age under 18 or over 55, and 4) having a first-degree family member with psychosis. We applied the Family Interview for Genetic Studies (FIGS) to detect family history of psychosis (Maxwell, 1992).

Thirteen participants had a previous history of taking psychotropic medication or attending a mental health service. They were evaluated with semi-structured-interview diagnostic tools (SCID) (First et al., 1997). One NDCU and two DCU were excluded because they showed a diagnosis of schizophrenia; both of them reported taking antipsychotic medication and were in Almería. In the end, the Granada group included 103 subjects and Almería 101 subjects The 10 remaining participants who attended mental health services showed a diagnosis of depression without psychosis in the past, and all reported having taken anti-depressives in the past, though none in the last year. Six of them were DCU, four were NCU and all of them were included in the study. No participants reported having sought help for drug addiction. When we re-ran the analysis without the 10 subjects with depression, the results were similar, and did not alter the main findings. Seventeen DCU and two NDCU had used cannabis in the last 2 h. In order to avoid the artifact induced by acute cannabis effects we excluded these 19 subjects.

Subjects were provided with a complete description of the study, and written informed consent was obtained. The research protocol was approved by the Ethics Committee of Jaén Hospital.

2.2. Drug and alcohol use

Lifetime drug use was recorded using the L section of the Composite International Diagnostic Interview (CIDI) (WHO, 1993). Different drugs were evaluated: cannabis, cocaine, ecstasy or MDMA (3,4 methylenedioxymethamphetamine), amphetamines, and psychodelic substances, ketamine, opium and heroin. At the end of the interview, an open question was formulated: Have you ever tried any other drugs? Four different drugs were thereby reported: Salvia divinorum, nexus (2,5-dimethoxy-4-bromophenethylamine), gamma-hydroxybutyric acid, and "poppers".

2.3. Cannabis use

The following question was used to identify cases and controls: "Have you ever smoked cannabis daily or nearly every day?" Cannabis use was broken down into daily cannabis use (lifetime) and non-daily cannabis use. In order to further analyze daily cannabis use, two groups were distinguished: 1) more than 5 cannabis cigarettes a day, 2) daily use but less than 5 cigarettes per day.

2.4. Other drugs

We created a new variable called "non-cannabis heavy drug user". This variable was dichotomized according to whether the subjects had used cocaine more than 50 times in lifetime, and/or other drugs (aside from cocaine and cannabis) more than 10 times in lifetime.

Moreover, alcohol use was dichotomized according to whether the subjects were daily alcohol drinkers in their lifetime.

2.5. Dependent variable: dimension of psychosis

Psychometric psychosis liability in lifetime was assessed through the CAPE (Stefanis et al., 2002). The CAPE covers three dimensions: positive, negative and depression dimensions; yet for this study, we used only the positive dimension. The positive dimension was further divided into the four factors reported by Stefanis et al. (2004), namely: paranoid (persecution, voodoo, references on TV and radio, conspiracy, getting odd looks, things having double meaning, things not what they seem to be); schneiderian first-rank symptoms (thought echo, thought withdrawal, thought broadcasting, thought insertion, feeling controlled, devices influencing person, telepathy), voices (hearing voices or noises) and mania experiences (being special or important). Each item explores the frequency of the experience on a four-point scale of "never", "sometimes", "often" and "nearly always." Sum scores for these four dimensions were obtained by adding the scores of the experiences in each dimension. The questions excluded times when the subjects were under acute drug effects.

Two analyses were carried out with CAPE dimensions as dependent variables. First, we used each CAPE dimension as a continuous variable; secondly, each dimension was dichotomized