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#### Full length article

## Anxiety, depression and risk of cannabis use: Examining the internalising pathway to use among Chilean adolescents

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#### ABSTRACT

*Background:* Adolescents who experience internalising symptoms may be susceptible to the use of alcohol and other substances in an attempt to alleviate or cope with these symptoms. We examined the hypothesised internalising pathway from symptoms of depression, generalised anxiety, social anxiety and panic, to incidence and frequency of cannabis use 18 months later.

*Method:* Longitudinal cohort study of participants (n = 2508; 45% female; mean age 14.5 years) recruited from the 9th grade at 22 low-income secondary schools in Santiago, Chile. Baseline internalising symptoms were assessed using the Beck Depression Inventory and the Revised Child Anxiety and Depression Scale. Frequency of cannabis was assessed at baseline, 6 month and 18 month follow-up.

Results: High rates of use were observed in this sample, with 40.3% reporting cannabis use at least once over the study period. Adjusted for baseline cannabis use, symptoms of depression, panic and generalised anxiety were associated with greater cannabis use frequency 18 months later. When all predictors were considered simultaneously, only generalised anxiety symptoms showed an independent association with subsequent cannabis use frequency (OR: 1.23, 95% CI: 1.08–1.41). Generalised anxiety symptoms were also associated with a 25% increased risk of transitioning from non-user to use of cannabis during the study (OR: 1.25, 95% CI: 1.09–1.44).

Conclusions: Internalising symptoms, and in particular symptoms of generalised anxiety, increase risk of cannabis use during adolescence. Targeted interventions that promote adaptive anxiety management among high-risk adolescents may represent a promising strategy to prevent uptake of cannabis use during adolescence.

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#### 1. Introduction

Cannabis is the most widely used illicit substance, with a peak in onset and intensity of use occurring during mid to late adolescence (Copeland and Swift, 2009). Global comparisons suggest cannabis use is less prevalent in Latin America compared to more affluent regions such as North America, Europe, Australia and New Zealand (Degenhardt et al., 2008; United Nations Office on Drugs and Crime, 2014). However, national surveys of school students in Chile suggest an upward trend in cannabis use since 2009, increasing to a 12-month prevalence of 30.6% in 2013 (Servicio Nacional para la Prevención y rehabilitación del Consumo de Droga y Alcohol, 2014).

http://dx.doi.org/10.1016/j.drugalcdep.2016.06.032 0376-8716/© 2016 Elsevier Ireland Ltd. All rights reserved. This most recent estimate places adolescent prevalence rates in Chile among the highest in the world (Castillo-Carniglia, 2015). This high prevalence is concerning given increasing evidence that adolescent cannabis use can interfere with normal brain development, leading to deficits in cognitive functioning (Bava and Tapert, 2010; Fontes et al., 2011; Squeglia et al., 2009). Furthermore, research suggests substance use patterns established in adolescence tend to predict adulthood problems such as dependence, psychosocial dysfunction, delinquency, and progression to other drug use (Copeland and Swift, 2009; Lynskey et al., 2003; Patton et al., 2007). A promising strategy for reducing these considerable harms is early intervention to prevent cannabis use during adolescence.

Understanding the risk factors that predispose adolescents to cannabis use is an important first step. Developmental models suggest an "internalising pathway" to substance use, whereby adolescents use alcohol and other substances to alleviate psychological

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symptoms, such as anxiety and depression (also known as the selfmedication hypothesis; Hussong et al., 2011; Khantzian, 1997). Evidence of the relationship between internalising symptoms and cannabis use comes predominantly from studies conducted in high-income Western regions. Systematic reviews indicate a crosssectional association between cannabis use and symptoms of depression (Degenhardt et al., 2003) and anxiety (Crippa et al., 2009; Kedzior and Laeber, 2014). Furthermore, cohort studies indicate the onset of anxiety and depressive disorders typically precedes that of cannabis use (Agosti et al., 2002; Lopez et al., 2005), lending support to the conceptualisation of internalising symptoms as important triggers for substance use initiation (Clark, 2004; Hussong et al., 2011). However, an alternative explanation is that cannabis use increases vulnerability to anxiety and depression by impairing psychosocial functioning, increasing stress reactivity or directly inducing anxiety symptoms during intoxication or withdrawal (Degenhardt et al., 2013; Wand, 2008; Zvolensky et al., 2008).

Given the potentially bidirectional relationships between cannabis use and mental health symptoms, prospective data are needed to clarify whether internalising symptoms precede cannabis use, and to date the findings have been equivocal. Several prospective studies provide evidence that frequency of cannabis use is associated with prior symptoms of depression (Feingold et al., 2014; Hooshmand et al., 2012; Wittchen et al., 2007) and anxiety (Buckner et al., 2008; Marmorstein et al., 2010b; Wittchen et al., 2007), however other studies found no evidence of an association (Bardone et al., 1998; Bovasso, 2001; Brook et al., 1998; Patton et al., 2002). The variability in results may reflect methodological differences between studies, such as age and gender differences in the sample composition. Studies with adult samples suggest these associations might be moderated by gender: one found that depression was associated with an elevated risk of cannabis use in women but not men (Butterworth et al., 2014), and another that cannabis use is more strongly associated with coping motives in women compared to men (Simons et al., 1998). An analysis of multiple cohort studies suggests there may be age-related differences in the relationship between depression and cannabis use, with the strongest association observed in mid-adolescence (Horwood et al., 2012). In addition to these methodological considerations, studies investigating the relationship between anxiety and alcohol/substance use have highlighted the importance of distinguishing between subtypes of anxiety (Kaplow et al., 2001; Marmorstein et al., 2010b; McCarty et al., 2012). While some anxiety subtypes such as generalised anxiety may promote substance use to alleviate unpleasant symptoms and tension, others manifestations such as separation or social anxiety may lead to protective behaviours such as staying close to parents and avoiding peer contexts in which substance use is likely (Buckner et al., 2016; Kaplow et al., 2001; McCarty et al., 2012).

Given the high prevalence and upward trend in cannabis use among Chilean adolescents, it is critical to understand factors associated with its use. To inform prevention strategies, an important question is whether internalising symptoms such as anxiety and depression increase risk of using cannabis during adolescence. As earlier initiation is associated with poorer longer term outcomes (Copeland and Swift, 2009), targeting vulnerability factors to delay onset of use is a promising strategy for reducing drug-related harms. Limited evidence is available about risk factors for cannabis use initiation among adolescents in Latin America, however evidence from studies conducted in Germany and the US suggests that depression, panic disorder and generalised anxiety symptoms increase risk of cannabis use (Feingold et al., 2014; Marmorstein et al., 2010a, 2010b; Wittchen et al., 2007). To our knowledge, this study is the first to examine the internalising pathway to cannabis use in a sample of adolescents in Chile. The association

between internalising symptoms and cannabis use was considered in the context of established protective factors, specifically problem-solving ability and sense of school connectedness, which are both associated with lower incidence of drug use in adolescence (Bond et al., 2007; Jaffee and D'Zurilla, 2009). In view of previous findings indicating moderating effects of age and gender, we also tested the hypothesis that associations between internalising symptoms and cannabis use would decline with age, and be most evident among females. Our study adds to existing research by disentangling the associations between specific subtypes of anxiety and adolescent cannabis use. It explores the independent contribution of depression, generalised anxiety, social anxiety and panic symptoms to predicting new cases of cannabis use and the frequency of use 18 months later. Our hypotheses, derived from review of theory and prior research, were that internalising symptoms, and in particular depression, panic and generalised anxiety, would show independent prospective associations with frequency of cannabis use and transition to use among non-users.

#### 2. Method

Data for this study were collected between 2009 and 2011 as part of a Wellcome Trust funded randomised controlled trial of a school-based prevention program for depression; the full trial protocol and analyses have been published elsewhere (Araya et al., 2013, 2011). In brief, there was no evidence of any effect of the intervention on depression or substance use outcomes. There was a suggestion of a small beneficial effect on anxiety outcomes at 6 month follow-up, but this was clinically unimportant and was absent at 18 month follow-up. In view of these null results the dataset was used for the present study; analyses were adjusted for trial arm to take into account any residual effects.

#### 2.1. Setting and participants

Twenty-two schools were randomly selected from a sampling frame comprising all municipal secondary mixed-sex schools with two or more '1° Medio' classes (equivalent to 9th grade) in Santiago, Chile. Municipal schools provide education for most low-income, secondary school students in Santiago. All students attending '1° Medio' grade in the selected schools were invited to participate; all except 4 students consented and signed a written form. In total, 2508 adolescents were enrolled in the trial at baseline. The study was approved by the Ethics Committee of the Clinical Hospital, Faculty of Medicine, Universidad de Chile. Cannabis use data were available from 2448 (97.6%) participants at baseline, and 1933 (77.1%) participants at 18-month follow-up. Table S1 in the supplementary material compares sample characteristics for participants with complete data to those with partial responses.

#### 2.2. Measures

Participants provided demographic information and completed the following self-report measures at baseline, then 6 and 18 months later.

2.2.1. Cannabis use. Participants reported frequency of cannabis use over the past month and past year on a 6-point ordinal scale. Due to small cell count for some response options, prior to analysis responses were collapsed to form a 3-category variable reflecting use in the past year classified as follows: i) No cannabis use; ii) Occasional cannabis use, defined as 9 or less times in past year; iii) Recurrent use, defined as 10 or more times in the past year. Transition from no use at baseline to use over the course of the study was determined based on responses collected at 6 and 18 month follow up. Use of past year reports from both these timepoints enabled us

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