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Age moderates the association between frequent cannabis use and negative schizotypy over time

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HIGHLIGHTS

- We examined whether age and frequent cannabis use interact to predict changes in positive and negative schizotypy over time
- Among occasional users, younger age was associated with decreasing negative schizotypy over time
- Among frequent users, younger age was associated with increasing negative schizotypy over time
- These findings suggest that cannabis use may influence psychosis risk differently depending on age and frequency of use

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ABSTRACT

The current study examined whether age and frequent cannabis use interact to influence the trajectories of positive and negative schizotypy over time. Participants were 155 cannabis users, aged 15–24 years old, assessed over a 12-month period at 6-monthly intervals. The analyses examined the influence of age, frequent use, and time on positive and negative schizotypy. The current study found that among frequent cannabis users, younger age was associated with increased negative schizotypy over time, while among occasional cannabis users, younger age was associated with decreasing negative schizotypy over time. The current findings have implications for understanding how cannabis use may influence psychosis risk differently depending on age and frequency of use, as well as bring together past mixed findings on the relationship between negative schizotypy and cannabis use.

1. Introduction

A growing proportion of adolescents are current cannabis users. For instance, in North America, 36% of 12th graders have used cannabis in the past year (UNODC 2015). These statistics are of concern in the context of animal and human research suggesting that adolescent exposure to cannabis carries a particularly high risk of psychosis-related outcomes and cognitive impairment (Arseneault et al. 2002; Ehrenreich et al. 1999; Henquet et al. 2004; Schneider & Koch 2003; Silins et al. 2014). Findings of heightened risk following adolescent exposure to cannabis, together with research suggesting that the endocannabinoid system is involved in regulating neurodevelopmental processes (Ellgren et al. 2008; Fernández-Ruiz, Gómez, Hernández, Miguel, & Ramos 2004) have led to speculation that adolescent cannabis use may result in neurodevelopmental disruption and brain changes similar to those

associated with risk for psychosis, or to psychosis itself (Bossong & Niesink 2010; Viveros et al. 2012).

The growing recognition of psychosis symptoms as dimensional in nature (as opposed to categorical, for diagnostic purposes) has seen a mounting interest in the examination of *schizotypy* to inform psychosis research (Barrantes-Vidal, Grant, & Kwapił 2015). Schizotypy refers to a collection of personality traits, including those relating to the positive symptoms of psychosis (known as positive schizotypy, and including unusual perceptions and magical thinking), disorganised thought symptoms (disorganised schizotypy, e.g., distractibility), and negative symptoms (negative schizotypy, e.g., anhedonia and avolition) (Mason, Claridge, & Jackson 1995), which are considered risk factors for psychosis (Nelson, Seal, Pantelis, & Phillips 2013). Indeed, a large number of studies have now linked cannabis use to schizotypy, with the strongest association being with positive schizotypy (Szoke et al. 2014).

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Despite converging evidence indicating that adolescent cannabis use is an important factor in risk for psychosis (e.g., [Arseneault et al. 2002](#)), very few studies ([Anglin et al. 2012](#); [Schiffman, Nakamura, Earleywine, & Labrie 2005](#); [Stefanis et al. 2004b](#)) have examined age of cannabis use in relation to schizotypy. One study ([Stefanis et al. 2004b](#)) that has examined age of use onset in relation to schizotypy dimensions found that frequent use of cannabis was associated with both higher positive and negative schizotypy, and that this effect was much larger among users who had started using cannabis in early adolescence. However, a limitation of the study by Stefanis et al. (and the majority of other studies examining the association between cannabis use and schizotypy) is that they are cross-sectional, and thus the direction of the link between cannabis use and schizotypy cannot be determined. The small number of studies that have examined schizotypy or related constructs longitudinally have done so focusing on positive symptoms only, or combining all schizotypy dimensions (e.g., [Anglin et al. 2012](#)), or have not controlled for important confounders, such as family history of schizophrenia, which has been associated both with early onset cannabis use and schizotypy ([Albertella, Le Pelley & Copeland, J. 2017](#)).

Another issue concerning past studies is that they have typically assessed schizotypy using measures that do not differentiate between current and persistent schizotypal experiences, versus any lifetime prevalence. As has been argued by others ([Cougard et al. 2007](#); [Van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam 2009](#)), transient psychosis-like experiences (which will be picked up by lifetime prevalence measures) are not only common but are also not necessarily indicative of psychosis risk. In contrast, more persistent psychosis-like experiences represent a greater risk for the development of psychotic disorder. Nonetheless, transient experiences may interact with other risk factors, such as cannabis use, to become persistent and thereby linked to progression into psychosis (for a review of these ideas and the psychosis proneness-persistence model, please refer to ([Cougard et al. 2007](#); [Kuepper et al. 2011](#); [Van Os et al. 2009](#)).

To address these gaps in the literature, the current study aimed to examine, longitudinally, whether age moderates the relationship between frequent cannabis use and current, ongoing schizotypy (both positive and negative dimensions) while controlling for important confounders such as family history of psychosis, psychological distress, and other substance use among a cohort of young Australian cannabis users.

2. Method

2.1. Participants and procedure

Participants were recruited in Australia via advertisements in national newspapers, websites, community notice boards, and email update lists. Inclusion criteria included being aged between 14 and 24 years and fluent in English. Participants who had ever received a diagnosis of schizophrenia or schizoaffective disorder were excluded from the study.

The study involved three assessments, completed at intervals of six months. Three hundred and twenty-four people completed the baseline assessment, and of these 155 reported a positive lifetime history of cannabis use and alcohol use and were included for further analyses.

The study was run online; all measures were implemented using Inquisit Millisecond Software Web version 4.0.2. Interested participants were emailed information about the study, a screening form, and a consent form. Eligible participants who consented to take part were sent a link via email to complete the online assessment. After 6 months, participants who completed the baseline assessment were sent a link to complete the 6-month follow-up assessment, and again at 12 months. Upon completion of each assessment, participants were emailed a \$20 electronics store voucher. Parental consent was not obtained for participants under 16, since this requirement may have rendered the study less accessible to drug-using adolescents, thus reducing the

generalisability and/or validity of the data. This and all other aspects of the study were approved by the UNSW Human Research Ethics Committee.

2.2. Measures

2.2.1. Demographic & substance use information

At baseline, participants completed a questionnaire asking about demographic information including sex, age, and family history of psychosis-related disorders. The questionnaire also asked participants whether they had ever used tobacco, alcohol, cannabis, and other illicit drugs. Participants who reported having ever used any drug were asked if they had used it in the past six months, frequency of use in the past six months, and use in the past month. Participants who had used cannabis on at least a weekly basis in the past 6 months were defined as 'Frequent' users, and everyone else defined as 'Occasional' users. There were 41 participants in the *Frequent* group, and 114 in the *Occasional* group. For those who had used in the past month, further measures were taken using the relevant items from the brief treatment outcome measure (BTOM; [Lawrinson, Copeland, & Indig 2005](#)), which assesses the number of days of use in the last month, quantity of use per typical day of use, and method of use.

At six and 12 months, participants were asked about use of each drug over the past year, over the past six months, and in the past month (including frequency, quantity, and method of use during that time).

2.2.2. Schizotypy

We used an adapted version of the short form of the Oxford-Liverpool Inventory of Feeling and Experiences (OLIFE; [Mason, Linney, & Claridge 2005](#)) to measure schizotypy. The OLIFE comprises four subscales: Unusual Experiences, Introverted Anhedonia, Cognitive Disorganisation, and Impulsive Non-conformity. The Unusual Experiences scale measures deviant perceptual and cognitive experiences. It is related to the positive symptoms of schizophrenia (e.g., "Have you ever thought that you had special, almost magical powers?"), and often referred to as positive schizotypy. The Introverted Anhedonia scale assesses the inability to experience pleasure, which relates to the negative symptoms of schizophrenia (e.g., "Do you like mixing with people?"). Introverted Anhedonia is often referred to as negative schizotypy. Cognitive Disorganisation items relate to disorganised thought and distractibility/inattention (e.g., "Are you easily distracted when you read or talk to someone?"), and is often referred to as disorganised schizotypy. Lastly, Impulsive Nonconformity items relate to impulsivity (e.g., "Do you often feel the impulse to spend too much money which you know you can't afford?").

We adapted the OLIFE to enable it to detect changes in symptoms over time. In its original format, the OLIFE is worded in such a way to detect lifetime prevalence of various symptoms/experiences related to schizotypy (e.g., "Have you ever..."). Though repeated administration of the OLIFE in this form might be able to detect the occurrence of new symptoms, it is unlikely to be able to detect a recent absence of symptoms in individuals with a positive lifetime prevalence (of those specific symptoms). As we wished to investigate how changes in schizotypy over time relate to cannabis use, we changed the wording and format of the OLIFE to target it more closely to changes in the occurrence (or absence of) symptoms/experiences over time. Towards this aim, for each OLIFE item in the baseline assessment we asked two questions: a) whether participants felt the item had ever been true for them, and b) whether participants felt the item had been true for them in the past six months. This allowed for both lifetime and past six-month prevalence of schizotypal symptoms and experiences to be assessed. In the follow-up assessments, participants were presented with each item and asked only whether that item had been true for them in the past 6 months.

The present study examined Unusual Experiences (positive schizotypy) and Introverted Anhedonia (negative schizotypy) as the

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