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Cannabis use in early adolescence is associated with higher negative schizotypy in females

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ABSTRACT

The current study examined the relationship between early onset cannabis use (before age 16) and different schizotypy dimensions, and whether gender moderates these associations. Participants were 162 cannabis users, aged 15–24 years, who completed an online assessment examining alcohol and other drug use, psychological distress, and schizotypy. Participants were divided according to whether or not they had started using cannabis before the age of 16 (early onset = 47; later onset = 115) and gender (males = 66; females = 96). The interaction between gender and onset group was significantly associated with the dimension of introverted anhedonia. Follow-up analyses showed that early onset cannabis use was associated with higher levels of introverted anhedonia in females only. The current findings suggest that gender is an important moderator in the association between early onset cannabis use, schizotypy, and possibly, psychosis risk.

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1. Introduction

A considerable proportion of adolescents have used cannabis recently. For instance, in Australia, up to 15% of adolescents (aged 14–19) have used cannabis in the past year, of which 30% are using it at least weekly [1]. These data are of concern in the context of animal and human research suggesting that adolescent exposure to cannabis is associated with risk of poorer psychosocial consequences, psychosis-related outcomes, and cognitive impairment [2–7]. Research showing that adolescent cannabis use is associated with a range of negative consequences, coupled with research implicating the endocannabinoid system in the regulation of neurodevelopmental processes [8,9], suggests that cannabis use in adolescence may disrupt neurodevelopmental processes and result in brain changes resembling those associated with psychosis risk [10], or even psychosis itself [11].

The growing recognition of psychosis symptoms and disorders as dimensional in nature (as opposed to categorical, for diagnostic purposes) has seen a growing interest in the examination of

schizotypy to inform psychosis research [12]. 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), those relating to disorganised thought symptoms (disorganised schizotypy), and those relating to negative symptoms (negative schizotypy, e.g., anhedonia and avolition) [13], which are considered related to psychosis risk [14]. Indeed, a large number of studies have now linked cannabis use to schizotypy, with the strongest association being with positive schizotypy [15].

Unfortunately, despite research indicating that age of first cannabis use is an important factor in determining the extent to which exposure to cannabis increases psychosis risk (e.g., [2,3]), very few studies have examined age of cannabis use onset in relation to schizotypy. One study [16] 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.

A further limitation of current studies examining the relationship between cannabis use and different schizotypy dimensions is the failure to include a number of important moderating and/or confounding variables that may impact the relationships. For instance, research suggests that sex may be an important

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54 moderator of the effects of cannabinoid exposure on psychosis-
55 related behaviour, cognitive impairments, and brain changes [17-
56 20]. Sex, however, has largely been ignored in research examining
57 the relationship between cannabis use and schizotypy. Another
58 example is the lack of consideration of various cannabis use
59 parameters. Most studies simply compare current use with never
60 use, without regard to other important variables such as quantity
61 of cannabis use. Research shows that quantity is an important
62 predictor of cannabis use problems, i.e., independently of
63 frequency [21], and further, has been associated with a number
64 of psychosis-related symptoms in cannabis-using adolescents
65 attending treatment [22].

66 The current study aims to address these gaps in the literature,
67 by investigating: (1) whether early onset cannabis use is associated
68 with different schizotypy dimensions; (2) whether sex moderates
69 the association between early onset cannabis use and schizotypy;
70 and (3) various cannabis use parameters in relation to different
71 schizotypy dimensions.

72 2. Materials and methods

73 2.1. Participants

74 Participants were 162 young people who reported having ever
75 used cannabis and had complete study data. These participants
76 were part of a longitudinal study, in which the overall sample at
77 baseline was 324 (or 327, if including 3 participants with missing
78 data, none of which were cannabis users). Participants were
79 recruited Australia-wide, via advertisements placed on websites,
80 local newspapers, community notice boards, and update lists.
81 Inclusion criteria included being aged between 14 and 24 years and
82 fluent in English. Exclusion criteria included having a past head
83 injury, history of neurological disorders, and having ever received a
84 diagnosis of schizophrenia or schizoaffective disorder.

85 2.2. Procedure

86 The study was conducted via the Internet with all measures
87 implemented using Inquisit Millisecond Software Web version
88 4.0.2. Eligible participants who consented to take part were
89 emailed a link to the study assessment. Within two weeks of
90 having completed the assessment, participants were emailed a \$20
91 electronics store voucher. Parental consent was not obtained for
92 participants under 16, since this requirement may have rendered
93 the study less accessible to drug-using adolescents, thus reducing
94 the generalisability and/or validity of the data. This and all other
95 aspects of the study were approved by the UNSW Sydney Human
96 Research Ethics Committee.

97 2.3. Measures

98 2.3.1. Demographic & substance use information.

99 The baseline assessment covered demographic information
100 including sex, age, education, and family history of psychosis-
101 related disorders. The questionnaire also asked about lifetime and
102 current tobacco, alcohol, and illicit drug use. Participants who
103 reported having ever used any drug were asked what age they first
104 used it, followed by whether they had used it in the past six
105 months. If they had used it in the past six months, they were asked
106 about the extent to which they had used it; i.e. less than once a
107 month, about once a month, once a week or more, or daily. This
108 information was used to categorize participants who had ever used
109 cannabis into two groups. One group included participants who
110 had used cannabis but had used it less than weekly (including not
111 at all) in the past six months (occasional users), while the second
112 group included participants who used cannabis once a week or

more often in the past six months (frequent users). Such a grouping
113 for frequent cannabis use has been used in previous studies, across
114 the same timeframe (6 months), and found to be associated with a
115 number of negative outcomes (e.g., [23]). Further questions
116 included items from the Brief Treatment Outcome Measure
117 (BTOM; [24]). For cannabis use, age of first use was also obtained.
118 This information was used to split participants into two groups,
119 those who used cannabis before the age of 16, and those who used
120 it for the first time after 16. This split is commonly used and
121 associated with psychosis risk and a range of other negative
122 outcomes (e.g., [2]).

123 2.3.2. Schizotypy

124 To measure schizotypy, we used the short form of the Oxford-
125 Liverpool Inventory of Feeling and Experiences (OLIFE; [25]),
126 which comprises four subscales: unusual experiences, introverted
127 anhedonia, cognitive disorganisation, and impulsive non-conform-
128 ity. The unusual experiences scale measures odd perceptual and
129 cognitive experiences related to the positive symptoms of
130 schizophrenia (e.g., "Have you ever thought that you had special,
131 almost magical powers?"). This scale is often referred to as positive
132 schizotypy. The introverted anhedonia scale assesses the inability
133 to experience pleasure and other experiences related to the
134 negative symptoms of schizophrenia (e.g., "Do you like mixing
135 with people?"), and this scale is often referred to as negative
136 schizotypy. Cognitive disorganisation items relate to disorganised
137 thought/speech and distractibility (e.g., "Are you easily distracted
138 when you read or talk to someone?"). Finally, impulsive
139 nonconformity items relate to impulsivity and emotional instabil-
140 ity (e.g., "Do you often feel the impulse to spend too much money
141 which you know you can't afford?").

142 2.3.3. Psychological distress

143 Participants completed the brief Depression Anxiety Stress
144 Scales (DASS-21; [26]). The DASS-21 contains 21 items assessing
145 depression, anxiety, and stress/tension symptoms. Total score was
146 used to control for psychological distress, as opposed to the three
147 subscales separately, due to high correlations among the latter.

148 2.4. Analyses

149 Independent samples t-tests examined differences between
150 early onset users (those who reported first use before the age of 16)
151 and later onset users (those who reported first use at age 16 years
152 or over), as well as gender, on normally distributed variables.
153 Mann-Whitney U tests were used to examine differences on non-
154 normally distributed variables, which included tobacco, alcohol,
155 and other drug use. Chi² tests examined differences between
156 groups on gender, and family history of schizophrenia.

157 Four multiple regressions were run, one for each schizotypy
158 dimension (Unusual experiences, introverted anhedonia, cogni-
159 tive disorganization, and impulsive nonconformity). Within each
160 model, the following variables were entered as predictors/
161 covariates: age, gender, family history of schizophrenia, alcohol,
162 tobacco, illicit drug use, psychological distress, various cannabis
163 use parameters (frequent use in the past 6 months, quantity of
164 use, and onset before 16 years), as well as non-dependent
165 schizotypy dimensions. These variables were selected due to
166 study aims and/or research showing their influence on schizo-
167 typy or related variables [22,27-31]. The interaction between
168 gender and early use onset was examined using mean-centered
169 values to avoid multicollinearity.

170 A significant interaction was followed up by conducting
171 linear regressions split by gender, with early onset use in the
172 model along with any other variable that was $P < .1$ in the overall
173 regression.

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