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### Motivational and control mechanisms underlying adolescent cannabis use disorders: A prospective study



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#### ABSTRACT

Cannabis use disorders (CUDs) are the most prevalent substance use disorders among adolescents in treatment. Yet, little is known about the neuropsychological mechanisms underlying adolescent CUDs. Studies in adult cannabis users suggest a significant role for cognitive control and cannabis-oriented motivational processes, such as attentional bias, approach bias, and craving in CUDs. The current 6-month prospective study investigated the relationships between attentional bias, approach bias, craving, cognitive control, and cannabis use in adolescent patients in treatment for a primary or secondary CUD. Moreover, we investigated if these motivational processes and cognitive control could predict treatment progression after 6 months. Adolescents with a CUD had an attentional but no approach bias towards cannabis. In contrast to adult findings on the role of attentional bias, approach bias and cognitive control, only cannabis and abstinence from cannabis 6 months later. These findings identify craving as a predictor of treatment outcome, thereby supporting an important role for craving in the course of adolescent cannabis use and dependence. This prospective study is among the first to investigate neuropsychological mechanisms underlying adolescent CUDs, warranting future longitudinal studies.

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#### 1. Introduction

Among adolescents in treatment for a substance use disorder (SUD), cannabis use disorders (CUDs) are the most prevalent SUDs (SAMHSA, 2010; Wisselink et al., 2014). Adolescent compared to adult onset of cannabis use is associated with greater cognitive deficits, poorer socio-economic status, poorer educational achievement and more chronic CUD trajectories (Meier et al., 2012; Perkonigg et al., 2008; Stinson et al., 2006; Swift et al., 2001). Unfortunately, only a minority of individuals with a CUD enter treatment (Agosti and Levin, 2004) and post-treatment relapse rates remain high (52–70%; Budney et al., 2008; Chauchard et al., 2013; Zumdick et al., 2006). These high relapse rates and the significant personal and societal harms associated with adolescent CUDs warrant the development of new treatment strategies. Knowledge of the neuropsychological processes asso-

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ciated with adolescent CUDs may help to identify new treatment targets, however, little is known about these mechanisms in adolescents.

The imbalance between strong drug-oriented motivational processes and compromised control processes is thought to play a significant role in the development and maintenance of SUDs (Everitt and Robbins, 2005; Koob and Volkow, 2010; Wiers et al., 2007). Strong motivational processes may develop over the course of repeated substance use through processes such as sensitization and conditioning. Encounters with cues (e.g., certain emotional states, objects, contexts) that have previously been associated with substance use may bias behaviour towards substance use in a relatively automatic way. More specifically, substance-related cues can grab attention (attentional bias), activate approach action tendencies (approach bias) and increase craving (Wiers et al., 2007). Cognitive control appears to be compromised in individuals with a SUD and has been found to moderate the relation between biased motivational processes and substance use (Grenard et al., 2008; Houben and Wiers, 2009; Peeters et al., 2012; Sharbanee et al., 2013; Thush et al., 2008). A relatively poor capacity to regulate motivational processes (pre-existent or compromised by substance

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use) may thereby further support continued substance use and relapse.

In line with previous findings on other SUDs, evidence is emerging that biased motivational processes are present in adult heavy cannabis users and individuals with a CUD. For example, cannabis cues can induce craving in adults with a CUD (Lundahl and Johanson, 2011). Moreover, an attentional bias towards cannabis cues has repeatedly been established in heavy cannabis users (Cousijn et al., 2013a; Field, 2005; Field et al., 2004, 2006) and individuals with a CUD (Asmaro et al., 2014; Cousijn et al., 2013a). Furthermore, dependent cannabis users showed a stronger attentional bias than non-dependent cannabis users (Cousijn et al., 2013a). The approach bias towards cannabis cues has been observed in heavy cannabis users (Cousijn et al., 2011; Field et al., 2006) and was found to be predictive of an increase in cannabis use six months later (Cousijn et al., 2011). Regarding cognitive control, the current literature provides preliminary evidence for a bidirectional relationship with CUDs: Long-term cannabis use may (temporarily) compromise cognitive control (Crean et al., 2011), whereas individuals with relative poor levels of cognitive control may have an increased risk of developing cannabis dependence (Cousijn et al., 2013b, 2014a,b). Cognitive control may only moderate the relationship between motivational processes and cannabis use in more severe and chronic cannabis users, not in all heavy users (Cousijn et al., 2013a,c). Despite these limited data on neuropsychological mechanisms underlying CUDs, the available studies in adult cannabis users suggest an important role for both cognitive control and motivational processes, such as attentional bias, approach bias, and craving in the development and maintenance of CUDs.

According to the literature on neurocognitive development, adolescence is marked by an increase in reward sensitivity and a not fully developed cognitive control system, putting adolescents at an increased risk to develop a SUD (Crone and Dahl, 2012; Gladwin et al., 2011). Indeed, prevalence of CUDs are highest during adolescence and young adulthood (SAMHSA, 2010; Wisselink et al., 2014). Similarly as in adults with a CUD, cannabis cues can induce craving in cannabis dependent adolescents (Gray et al., 2011; Nickerson et al., 2011). To the best of our knowledge, there are no published studies yet on attentional and approach bias in adolescent cannabis users. Cognitive control appears to be compromised in a substantial part of adolescent cannabis users (Dougherty et al., 2013; Hanson et al., 2010, 2014; Harvey et al., 2007), however, the relationship between motivational processes and cognitive control in adolescents with a CUD remains unclear. To bridge this gap and to extend adult findings on the importance of these processes in the course of CUDs, we investigated the relationships between attentional bias, approach bias, craving, cognitive control, and cannabis use in adolescent patients in treatment for a primary or secondary CUD (n = 57). Moreover, in a subset of the adolescents (n = 46) we investigated if these motivational processes and cognitive control could predict treatment progression after 6 months. Based on previous findings on motivational processes in adult heavy cannabis users (Cousijn et al., 2011, 2013a; Field, 2005; Field et al., 2004), we expected attentional bias, approach bias and craving in response to cannabis-related stimuli to covary with amount of cannabis use and severity of cannabis-related problems. Moreover, we hypothesized that individual differences in cognitive control would moderate the relationship between motivational processes (attentional bias, approach bias, craving) and amount of cannabis use and severity of cannabis-related problems. Finally, we examined whether both motivational processes and cognitive control were related to treatment progression, such that a stronger attentional bias, approach bias, and craving for cannabis, but lower levels of cognitive control would predict early dropout or lack of progress in CUD related treatment objectives.

#### 2. Materials and methods

The Ethics Committee of the University of Amsterdam approved the study.

#### 2.1. Participants

Study participants were 57 adolescent patients (15–22 years) who received outpatient treatment for CUDs at Brijder Addiction Care, a large addiction care facility in the western part of the Netherlands. See Table 1 for sample characteristics. This study combined data from (1) a test session in which motivational and control processes were assessed, (2) clinical evaluations on treatment progress by the therapist and (3) detailed information of substance use history and problems as part of baseline and 6 month follow-up Routine Outcome Monitoring (ROM) assessments of Brijder Addiction Care. For the majority of these patients data were available on drug-related motivational and control processes (n = 54) and on treatment progress at 6-month follow-up (n = 55). Data on substance use history and related problems were retrieved from ROM for 48 patients at baseline and 33 patients at 6-month follow-up. Participants either had a primary or secondary CUD diagnosis (see Table 1). One participant had no formal CUD diagnosis but a Cannabis Use Disorder Identification Test (CUDIT, see Section 2.2) score of 10, which is indicative of a cannabis use disorder (Adamson and Sellman, 2003). Participants were excluded if they had any other SUD.

All participants received cognitive behavioural treatment. The exact approach and duration of treatment highly varied between participants. A team of more than 30 therapists were involved in the treatment of this sample. Participants were not financially compensated for their participation. However, a single voucher of 50 Euros was raffled among them.

## 2.2. Questionnaires on substance use, craving and psychological functioning

As part of the ROM baseline and 6-month follow-up, the 10item CUDIT was used to measure severity of cannabis use and related problems during the past 6 months. The CUDIT contains items relating to consumption, symptoms of dependence, and other cannabis-related problems. Scores can range from 0 to 40 with a discriminant validity of 0.93 to detect a current CUD and a score of 8 or higher is considered indicative of at-risk cannabis use (Adamson and Sellman, 2003). Moreover, patients were asked on how many days in the past 30 days they had used cannabis. Due to lack of variance in the baseline assessment of this measure, only data of the follow-up assessment were used.

As part of the ROM baseline, the Alcohol Use Disorder Identification Test (AUDIT; Saunders et al., 1993), the Fagerstrom Test for Nicotine Dependence (FTND; Heatherton et al., 1991) and the Beck Depression Inventory-II (BDI-II; Beck et al., 1996) were administered. The AUDIT measures severity of alcohol use and related problems during the past 6 months and consists of 10 items assessing consumption and alcohol-related problems. Scores range between 0 and 40, with a cut-off score of 8 for hazardous drinking (Saunders et al., 1993). The FTND contains 6 items assessing severity of nicotine use and dependence during the past six months (Heatherton et al., 1991). Scores range between 0 and 10 and a score of 6 or higher is indicative of severe nicotine dependence. Moreover, the BDI contains 21 items assessing physical and psychological symptoms of depression (e.g., fatigue or suicidal thoughts). Scores range from 0 to 63 and test-retest reliability and internal consistency are high (Beck et al., 1996). A cut-off score on the BDI-II of  $\geq 12$  is suggested to be optimal to screen for depression in a clinical sample of adolescents with substance abuse problems

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