Cannabis use, cognitive functioning and behaviour problems

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1. General Introduction

Introduction

Since the 1960s, cannabis has gained enormous popularity. Nowadays, cannabis is the most widely used drug worldwide. It has been estimated that 78 million people (aged 15 – 64) have used cannabis at least once in European countries (European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2011). Also, an estimated 23 million have used cannabis in the last year, which represents 6,7 % of all 15 – 64 year olds (EMCDDA, 2011). Cannabis use has become especially prevalent among 15-24 year olds. In 1990, it was estimated that about 5 % had used cannabis in the past year. This number has increased rapidly; based on the 2011 survey reports, about 12.1 % of 15-24 year olds have used it in the past year and 6.6 % in the past month (EMCDDA, 2011). Research in countries outside Europe, including the US, New Zealand and Canada, has shown a high prevalence among young adults as well (EMCDDA, 2011). Interestingly, despite the fact that the Netherlands is the only country where possession of up to five grams of cannabis is not legally prosecuted, prevalence rates of cannabis use are higher in other countries. For example in 2009, annual prevalence within the adult population (aged 15-64 years) was far higher in the US (11%) and Australia / New Zealand (15 %) than in the Netherlands (7%) (EMCDDA, 2011; UNODC, 2012).

Along with increasing prevalence rates, the level of delta-9-tetra-hydrocannabinol (Δ^9-THC) has increased over the past years, in particular in Dutch weed (EMCDDA 2011; Pijlman et al., 2005). THC is the primary (psycho-)active ingredient of cannabis, and it has been argued that higher levels of THC may yield stronger effects. THC concentrations in imported marijuana remained stable (Pijlman et al., 2005). In 2004, Dutch marijuana contained on average 20 % THC levels, whereas THC levels in imported marijuana was around 7 %. In 2008, THC levels in European marijuana ranged between 3 – 16 %, again with especially high levels in Dutch marijuana (EMCDDA, 2011). These higher levels of THC concentrations, in combination with an increase in prevalence rates, may contribute to cannabis abuse and dependency problems (Cooper & Haney, 2009).

Whereas this is still subject to further investigations, indications for associations with (mental) health problems are strong enough to validate further research into (risk) factors associated with (the initiation of) cannabis use. It is important to study such possible (risk) factors of cannabis use as early in life as possible, as it has been shown that early initiation of cannabis use is associated with an increased risk of escalation to heavier cannabis use, and to the use of other illicit drugs (Coffey et al., 2000; Lynskey et al., 2002; Lynskey et al., 2006). Early onset of cannabis use might also mean a longer period of heavy use, and hence, an increased risk of

experiencing any adverse health effects that cannabis use may have in later adult life (e.g. Moore et al., 2007; Patton et al., 2002). According to Hawkins, Catalano & Miller's (1992) and Petraitis, Flay & Miller's (1995) risk factor taxonomy, risk factors for the initiation of cannabis use or extent of cannabis use can be summarized into four categories: (1) Socio-environmental variables (e.g. male gender, low SES, unemployment, financial situation); (2) substance-related variables (e.g. easy availability of drugs, drug-using peers, positive attitude towards drugs, prior history of tobacco, alcohol, or other illicit drug use); (3) intrapersonal variables (e.g. mental health problems) and (4) interpersonal variables (e.g. family functioning, relationship with mother, not having been brought up by both parents) (Von Sydow et al., 2002). The focus of the present thesis is on intrapersonal variables, including vulnerability for psychosis and internalizing and externalizing behaviour problems, which may be correlates of cannabis use. In addition to factors that have been more or less established as intrapersonal risk factors, there will be an emphasis on social functioning (more specifically, lack of social skills) as a risk factor for cannabis use, its initiation and its frequency. Although social functioning in general may also be considered an interpersonal risk (or protective) factor, specific social skills appear to classify more readily as intrapersonal risk (or protective factors). Lastly, we will focus on (specific) cognitive weaknesses in cannabis users, which may also classify as intrapersonal risk factors.

Cannabis Use and Mental Health

Research reveals that regular cannabis use is strongly correlated with use of alcohol, smoking, and use of other (illicit) drugs (Fergusson, Boden & Horwood, 2006, Fergusson et al., 2002a; Lynskey et al., 2003), and is related to delinquency, unemployment, risky sexual behaviour, affiliation with delinquent peers, school dropout and reduced educational achievement (Fergusson & Horwood, 1997; Fergusson et al., 2002b; Lynskey & Hall, 2000). Also, cannabis use, in particular regular use, has been associated with a wide range of mental health problems, including psychotic disorders (Arseneault et al., 2002; van Gastel et al., 2012; Malone et al., 2010; Moore et al., 2007; van Os et al., 2002), externalizing problems (aggressive and delinquent behaviour) (Monshouwer et al., 2006), depression (Degenhardt et al., 2001; Degenhardt et al., 2003; Patton et al., 2002) and anxiety (Hayatbakhsh et al., 2007; Patton et al., 2002; van Laar et al., 2007).

Associations between cannabis use and different mental health problems, including internalizing and externalizing behaviour problems and increased risk of psychosis, need to be

examined further. One important issue to investigate is the temporal order of the associations. Different hypotheses have been put forward to try to explain these associations, including the damage hypothesis, the self-medication hypothesis, the vulnerability hypothesis and the shared causes hypothesis. According to the 'damage hypothesis', the association between cannabis and mental health problems reflects cause and effect associations in which the use of cannabis leads to the development of various mental health problems (Brook, Cohen & Brook, 1998; Kandel, Yamaguchi & Chen, 1992). For example, Moore et al. (2007) concluded that cannabis use increases the risk of psychosis by 14 %. Alternatively, the 'self-medication hypothesis' proposes that cannabis use might be the result rather than the cause of mental health problems, as adolescents with mental health problems tend to resort to drug use to 'sooth painful feelings' rather than to seek pleasure (Khantzian , 1985). Previous evidence for the self-medication hypothesis stems mostly from clinical observations of patients suffering from psychiatric disorders (e.g. Klein et al., 1994; Warner et al., 1994). However, empirical studies and clinical observations have not consistently provided evidence for either the damage- or the self-medication hypothesis. Following the lack of consistency in results supporting these hypotheses, it has been suggested that cause and effect might be moderated by particular forms of vulnerability (the 'vulnerability hypothesis'), i.e. the linkage between cannabis use and mental health problems might be particularly evident in individuals who are - due to their biological, personal or familial make-up - sensitive to the damaging effects of cannabis or more likely to use drugs for their soothing effects (Caspi et al., 2005; Henquet et al., 2005; Miller et al., 2001; Verdoux et al., 2003). It should be noted that it is not entirely clear which biological, personal or familial factors might constitute particular risk enhancers for mental health problems when present together with cannabis use. A further issue is finding the best possible measures through which such moderating risk factors express themselves. For example, Caspi and colleagues (2005) showed that carriers of the catechol-O-methyltransferase (COMT) valine158 allele were most likely to exhibit psychotic symptoms if they used cannabis. Functional polymorphisms of other genes as well as several environmental factors (e.g. stress) have also been shown to moderate the effects of cannabis considering the development of different forms of psychopathology (Henquet et al., 2008). Even though a number of these interactions were replicated (Gill et al., 2010; Rijsdijk et al., 2011), the amount of variance in mental health problems explained by single gene polymorphisms or environmental factors remains limited. Thus, it may be preferable to study intermediate cognitive phenotypes, which have generally been associated with multiple gene variants and environmental factors, in association with cannabis use. It is clear, however, that

the vulnerability hypothesis may have many different faces and should be investigated more thoroughly. Moreover, it is related-, but not entirely similar to the so-called 'shared causes hypothesis'. This last type of hypothesis implies that the linkage between cannabis use and mental health problems is largely non-causal and may be the result of several factors associated with the use of cannabis and mental health problems (simultaneously), such as disadvantaged backgrounds (including low SES; low maternal education; growing up in a single parent family; poorer parental attachment) and difficult childhood circumstances (including family dysfunction, crime, depression, anxiety, suicidal behaviours, exposure to the use of (illicit) substances) (Fergusson & Horwood, 1997; Fergusson, Horwood & Swain-Cambell, 2002a). Thus, this hypothesis states that the higher rate of mental health problems found among cannabis users arises because cannabis use is more common in individuals exposed to other possible causes of mental health problems. As with the vulnerability hypothesis, there are many different (other) factors that might play a role in the development of mental health problems. The main difference between the two types of hypotheses is that the vulnerability hypotheses state that co-occurring cannabis use and other risk factors constitute supra-additive effects on mental health, whereas the shared-causes hypotheses particularly involve mediating effects of other risk factors on cannabis-mental health associations.

Although many studies have focused on cannabis use and mental health outcomes, including psychosis and both internalizing and externalizing behaviour problems, little is known about this relationship during (early) adolescence. This seems crucial, since adolescence is a life phase characterized by significant biological changes and consecutive maturation processes, especially neurologically, which might increase vulnerability to enduring effects of external influences like such as exposure to cannabis (Bossong & Nieding., 2010; Schneider, 2008). The first aim of this dissertation is to determine the temporal order of cannabis use and mental health problems, including vulnerability for psychosis, internalizing and externalizing problems, thereby testing the damage hypothesis, the self-medication hypothesis and the shared-causes hypothesis.

Cannabis use and Social Functioning

Associations between social functioning and cannabis use have not yet been extensively investigated. This is a relevant factor to study in adolescents and young adults as individuals

in this age range generally use cannabis in social contexts (e.g. at parties, dancing clubs or on the street). Indeed, some of the most frequently reported reasons for using cannabis by young adults are of a social nature, i.e. ”to bond with friends” or to “hang out” (Lee et al., 2007). Another reason for engaging in cannabis use is conformity, in other words, “under peer pressure” or “because friends do it” (Simons et al., 1998). Taken together, cannabis can be seen as a social drug, and many of the reported motives for engaging in cannabis use are socially-driven.

There has been relatively little research focusing on possible prospective associations between social parameters and cannabis use during adolescence. Cross-sectional studies have shown that adolescents who experiment with cannabis show lower levels of social self-control and higher levels of negative self-esteem compared to non-users (Sussman et al., 2003; Veselska et al., 2009). Such results appear to indicate relatively poor social adjustment among cannabis users. Also, although being under the influence of cannabis has been associated with increases in the extent of social interactive behaviour, the quality of such behaviour (e.g. of verbal exchanges during these social interactions) has been shown to be relatively low (Foltin et al., 1987, 1988). Other studies, however, showed that cannabis users displayed higher levels of social competence (e.g. assertive behaviour) compared to non-users, without apparent differences in the quality of such behaviour (e.g. Shedler & Block, 1990; Veselska et al., 2009). Such results lead to the hypothesis that socially competent adolescents may find themselves in social contexts more often, where the probability of exposure to cannabis is higher. Other studies have found similar results, namely that those who experiment with cannabis during adolescence are socially better adjusted and have better social skills than both abstainers and heavy users (Engels & Ter Bogt; 2001; Shedler & Block, 1990). Pokhrel et al. (2007) investigated the prospective relationship between cannabis use and social self-control. Lack of social self-control refers to one’s tendency to ‘act without thinking’ (Tarter, 1988), especially in a social context. Results showed a reciprocal relationship between social self-control and cannabis use. Lack of social self-control increased cannabis use, which in turn decreased social self-control.

Studies describing social functioning in cannabis users have predominantly focused on psychopathology and associated negative effects on social behaviour. Indeed, psychosis, internalizing- and externalizing behavioural problems, which are obviously characterized by social dysfunction, have been associated with cannabis use (Moore et al., 2007; Degenhardt et al., 2003; Fergusson et al., 2002a). However, cannabis is used very frequently and by many different types of people. Most of these people do not develop serious forms of

psychopathology. These individuals could, however, still experience social problems with potential impact upon everyday life. To our knowledge, there are no studies focusing specifically on social skills as predictors of cannabis use.
Therefore, another aim of the present thesis is to study cannabis use and its relation to social parameters. More specifically, the focus will be on (lack of) different social skills (cooperation, assertion and self-control) as possible risk factors of cannabis initiation and frequency of cannabis use (chapter 4).

The above research questions on mental health (Chapter 2 and 3), social functioning (Chapter 4) and cannabis use will be studied using data from a large prospective cohort study called TRAILS (Tracking Adolescents' Individual Lives Survey), which follows Dutch adolescents biennially, starting at the age of 10-12 years at the first assessment (chapter 2-3-4). Due to a lack of available data on specific possible moderating factors such as particular gene polymorphisms and their associated cognitive profiles, (variants of) the vulnerability hypothesis were not tested in this sample. In chapter 5 and 6 of this thesis moderating effects of cognitive abilities on cannabis use predicting psychological problems are tested in a different sample, consisting mainly of undergraduate students. The TRAILS-sample was used for a related research question featuring in this thesis, i.e. whether social functioning predicts (different aspects of) cannabis use. Social functioning could be regarded as another intermediate phenotype in associations between cannabis use and mental health, and might therefore also moderate such associations. It may be argued, however, that social functioning is not a very unitary concept, i.e. it contains many subcomponents and different operationalizations as well as its own broad set of determining factors. Thus, if an interaction between cannabis use and social functioning in the prediction of psychological problems would be observed, this would not yet provide very detailed information on (constellations of) risk factors for poor mental health. Moreover, social functioning has, perhaps unfortunately, not yet been extensively studied in relation to cannabis use.

Cannabis use and Cognitive Functioning

Another important factor to study in relation to cannabis use is cognitive functioning, which may be related to both initiation and continuation of drug use, as well as transition to more serious use of cannabis or other drugs. It has proven to be difficult to pinpoint specific domains of cognitive weaknesses in cannabis users (Fernández-Serrano et al., 2011). One

reason is that cognitive weaknesses generally do not appear to be specific to cannabis use: similar weaknesses can be found among users of other substances. A second reason lies in methodological issues, i.e. the means of assessment of certain cognitive constructs, the definition of those constructs, and differing sample characteristics.

Cognitive impairments that have been associated with cannabis use involve executive function (EF), implicit cognition, episodic memory, and emotional processing (Pope et al., 2001; Solowij, 1998; Solowij et al., 2002; Stacy and Wiers, 2010; Verdejo-Garcia, Lawrence & Clark, 2008). Except perhaps episodic memory, these are all broadly defined constructs. Core EF-abilities include inhibitory control and working memory, which are multi-faceted concepts themselves (cf. Christ et al., 2010; D'Esposito et al., 1999; Nigg, 2000). Core aspects of emotional processing include social perception (e.g. emotion recognition), Theory of Mind (i.e. the ability to "mentalize"), empathy, and reward/punishment sensitivity (Adolphs, 2002; Beer et al., 2004; Dodge and Rabiner, 2004; Ochsner, 2008; Pettit and Mize, 2007). Studies investigating cognitive correlates of cannabis use have often employed task paradigms addressing combinations of different (social-) cognitive skills. Examples include decision-making and implicit cognition tasks, which require working memory, and cognitive and motivational inhibitory control (Busemeyer and Stout, 2002; Stacy and Wiers, 2010; Whitlow et al., 2004).

In this thesis, the focus will be on more specific cognitive constructs that may underlie or follow cannabis use, i.e. motivational versus cognitive inhibitory control (chapter 5) and social perception (chapter 6). Contrasting cognitive and motivational inhibitory control is based on the taxonomy of executive function proposed by Zelazo and Müller (2002). Zelazo and Müller (2002) distinguish executive functions along "hot" and "cool" dimensions. Hot EF involves affect and motivation, either inherent in the task or the context in which a task has to be performed, while cool EF does not involve such components or contexts and is more related to basic abilities. This taxonomy has been supported by neuroanatomical and developmental studies (Kerr & Zelazo, 2004; Prencipe et al., 2011; Zelazo & Müller, 2002)

Results of several (recent) studies suggest that cognitive deficits in cannabis users (particularly in "non-addicted" users) may only become apparent when a task involves an affective/motivational component or has to be performed in a context containing such elements. In order to test this hypothesis, contrasting performance on tasks with and without such components is required.

The choice to investigate social perception is based on recent research findings (Platt et al., 2010), abnormalities observed in amygdala volumes and activity of cannabis users (or

following cannabis use) ((Yucel et al., 2008), thereby taking into account the evidence for amygdale-involvement in social perception (Adolphs, 2002; Ochsner, 2008), and the central role of social perception in affective/motivational information processing. Another very important argument to investigate social perception is that this aspect of cognition (similar to other aspects of cognition associated with affect and motivation) has repeatedly been associated with the types of psychological problems that have also been associated with cannabis use, including (subclinical) levels of psychosis/schizophrenia, and internalizing and externalizing behaviour problems (Demenescu et al., 2010; Germine and Hooker, 2011; Kiehl et al., 2000; Kohler et al., 2010; Marsh and Blair, 2008; Nigg et al., 1998; Raaijmakers et al., 2008; Riggs et al., 2006; Rössler et al., 2011). As for the study of cognitive versus motivational inhibitory control, a contrast will be introduced in order to allow more specific statements on the cognitive profile of cannabis users. This contrast is provided as one of the tasks that will be used involves actual emotion recognition whereas the other task does not. Moreover, the two tasks that are used differ in the amount of working memory capacity that has to be allocated to achieve optimal performance. Again similar to the cognitive versus motivational inhibition study, interrelations between possible cognitive impairments and psychological problems will be investigated, incorporating both mediating and moderating effects.

For investigation of the above research questions on cognition and cannabis use (Chapter 5 and 6), we did not make use of the TRAILS-sample. A disadvantage of this is that the self-medication and damage-hypotheses could not be investigated, as for samples that were used here (see Samples and Methods-sections below) no longitudinal data were available. We did however add to the existing literature on cannabis and cognition by adding associations with behaviour in daily life and psychological problems. Moreover, we tested the vulnerability hypothesis by examining whether cannabis users with relatively poor cognitive skills experience more psychological problems compared to those without such difficulties.

Research questions

The first aim of this dissertation is to determine the temporal order of cannabis use and mental health problems during (early) adolescence. Secondly, we will focus on social parameters in association with cannabis use. The third aim of this thesis is to investigate cognitive correlates of cannabis use, thereby specifically investigating their roles in cannabis-behaviour associations.

The main research questions of this thesis are:

1. Is there a relationship between cannabis use and both internalizing and externalizing behaviour problems in early adolescence? And if so, what is the temporal order of these relationships?
2. Is there a relationship between cannabis use and vulnerability for psychosis, as measured by social problems, thought problems and attentional problems, in adolescence? And if so, what is the temporal order of this relationship?
3. Are the social skills cooperation, assertiveness and self-control precursors of cannabis use during early adolescence? Specifically, are these social skills precursors of (early) cannabis initiation and the frequency of use?
4. Do cannabis users experience problems with motivational inhibitory control, cognitive inhibitory control or both? Also, do cannabis users experience problems in behavioural impulsivity, and is this related to motivational and/or cognitive inhibitory control?
5. Do cannabis users experience problems with respect to social perception? Also, are cannabis users with problems in social perception more likely to experience psychological problems?

Samples en Methods

For the present thesis, three different samples were used. The first 3 research questions concerning mental health and social functioning were studied in a population-based sample, the cognitive processes (research questions #4 and #5) were studied in two samples of (mostly) undergraduate students. Details of the datasets are provided below.

1. TRAILS Sample

The study described in this thesis was embedded in the Tracking Adolescents' Individual Lives Survey (TRAILS) (de Winter et al., 2005; Huisman et al., 2008). TRAILS is a large prospective cohort study of Dutch adolescents initially aged 10-12 years, who are measured biennially at least until they are 24 years old. The key objective of TRAILS is to chart and explain the development of mental health from preadolescence into adulthood, both at the level of psychopathology and the levels of underlying vulnerability and environmental risk. For the present thesis, data from the first (2001-2002), second (2003-2004), third (2005-2007) and fourth (2008-2010) assessment waves were used. The TRAILS target sample involved young adolescents living in five municipalities in the North of the Netherlands, including both urban and rural areas.

Sample selection involved two steps. First, the municipalities selected were requested to give names and addresses of all inhabitants born between 10-01-1989 and 09-30-1990 (first two municipalities) or 10-01-1990 and 09-30-1991 (last three municipalities), yielding 3483 names. Simultaneously, primary schools (including schools for special education) within these municipalities were approached with the request to participate in TRAILS; i.e., pass on students' lists, provide information about the children's behaviour and performance at school, and allow class administration of questionnaires and individual testing (neurocognitive, intelligence, and physical) at school. School participation was a prerequisite for eligible children, before parents were approached by the TRAILS staff, with the exception of children already attending secondary schools (< 1%), who were contacted without involving their schools. Of the 135 primary schools within the municipalities, 122 (90.4% of the schools accommodating 90.3% of the children) agreed to participate in the study.

If schools agreed to participate, parents (or guardians) received two brochures, one for themselves and one for their children, with information about the study; and a TRAILS staff member visited the school to inform eligible children about the study. Approximately one week later, a TRAILS interviewer contacted them by telephone to give additional

information, answer questions, and ask whether they and their son or daughter were willing to participate in the study. Respondents with an unlisted telephone number were requested by mail to pass on their number. If they reacted neither to that letter, nor to a reminder letter sent a few weeks later, staff members paid personal visits to their house. Parents who refused to participate were asked for permission to call back in about two months to minimize the number of refusals due to temporary reasons. If parents agreed to participate, an interview was scheduled, during which they were requested to sign an informed consent form. Children were excluded from the study if they were incapable to participate due to mental retardation or a serious physical illness or handicap; or if no Dutch-speaking parent or parent surrogate was available, and if it was not feasible to administer part of the measurements in the parent's language.

Of all children approached for enrollment in the study (i.e., selected by the municipalities and attending a school that was willing to participate, N = 3145), 6.7% were excluded because incapability or language problems. Of the remaining 2935 children, 76.0% (N = 2230, mean age = 11.09, SD = 0.55, 50.8% girls) were enrolled in the study (i.e., both child and parent agreed to participate). Responders and non-responders did not differ with respect to gender, parental education, proportion of single-parent families, teacher-rated problem behaviour, or school absence; but children in the non-response group needed additional help for learning difficulties more frequently. At T2, 96.4% of these participants (N=2149) were re-assessed, mean age 13.56 years; SD 0.53; 51.0% girls. T3 was completed with 81.4 % of the original number of participants (N=1816), mean age 16.27 years old; SD 0.73 and 52.3% girls. During T3, 42 subjects were unable to participate in the study, due to mental/physical health problems, death, emigration, detention or by being untraceable. With these subjects left out, response rate increases to 83.0%. T4 was completed with 84.3% of the original sample (total n = 1881, mean age 19.1 (SD 0.60), 52.3% girls) (Nederhof et al., 2012).

The number of individuals that were included in the analyses differs for the separate chapters of this thesis (specifically chapter 2-3-4), depending on the availability of complete data on the measures that were used (and the choice to use data imputation for missing data or not).

2. Leiden Samples

The two final research questions were investigated in studies using cross-sectional designs. Two samples of (mostly) undergraduate students at Leiden University were recruited. The key objectives of these studies were to obtain greater insight into the cognitive profiles of (recreational) cannabis users, to investigate associations between possible cognitive

weaknesses and psychological or behaviour problems, and to find out whether chances of psychological or behaviour problems among cannabis users were influenced by the presence of cognitive weaknesses. Participants were classified as cannabis users when they reported using cannabis at least three times a month during the past year (they had not used cannabis 24 hours prior to testing) and as non-users when they reported the use of cannabis 0 times in the past year and less than 4 times in their lifetimes. Based on these criteria, cannabis users and non-users were recruited at two points in time (2009 and 2010). In 2009 (Wave 1), 53 cannabis users (mean age of 22.6) and 48 non-users (mean age of 22.3) were recruited. In 2010 (Wave 2), 75 cannabis users (mean age 24.6 years) and 75 non-users (mean age 24.7 years) were recruited. Participants were asked to volunteer in a study into information processing and social functioning of cannabis users. All participants signed informed consent forms.

After participants agreed to enroll in the study, an appointment was made, where participants completed (social) cognitive tasks on a computer. Furthermore, they were asked to fill out several questionnaires at home. On the day of the appointment, questionnaires were handed in.

Outline of the thesis

The first focus of this thesis is on associations between cannabis use and behaviour problems. The second focus is on cannabis use and cognitive outcomes. In Chapter 2, we examine associations between cannabis use and mental health. Specifically, we focused on internalizing behaviour problems (withdrawn behaviour, somatic complaints and depression) and externalizing behaviour problems (delinquent and aggressive behaviour). First, we investigated whether cannabis use is related to both internalizing and externalizing behaviour problems in early adolescence. Next, path analysis was used to identify the temporal order of internalizing and externalizing problems and cannabis use, thereby testing the damage hypothesis, the self-medication hypothesis and the shared-causes hypothesis. In Chapter 3, we examine associations between cannabis use and vulnerability for psychosis during adolescence. Specifically, we focused on attention problems, thought problems and social problems as indicators of vulnerability for psychosis. Again, path analysis was used to identify the temporal order of cannabis use and vulnerability for psychosis, thereby testing the damage hypothesis, the self-medication hypothesis and the shared-causes hypothesis. In Chapter 4**,** we focus on social skills as possible risk factors of cannabis use. Specifically, we used multinomial regression analyses to find out whether the social skills of cooperation, assertiveness and self-control could predict cannabis use, early onset and frequency of use during early adolescence. In Chapter 5, we examine whether recreational cannabis users and non-users differed on motivational and cognitive inhibitory control. Also, we analysed possible relations between both types of inhibitory control and impulsive behaviour in everyday life. In Chapter 6**,** we examine social perception in cannabis users. We also tested whether (relatively) weak social perception would disproportionally increase the chances of cannabis users to experience psychological problems (i.e. a variant of the vulnerability hypothesis). Finally, in Chapter 7, the main findings and conclusions of chapter 2-6 are presented and discussed. This thesis concludes with some implications for clinical practice and recommendations for future research.

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