Cannabis use, cognitive functioning and behaviour problems

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7. General discussion

Discussion

Summary and Integration of main results

Cannabis use and mental health

In general, our studies confirm that cannabis use is related to different mental health problems. Firstly, we focused on the prospective relationship between cannabis and both internalizing and externalizing behaviour problems. Results showed that cannabis use during adolescence was associated with the risk for externalizing behaviour. More specifically, after controlling for potentially confounding factors, including the use of other substances, path analyses showed that level of externalizing problems (measured at age 11 and 13) predicted the risk for cannabis use a few years later (measured at age 13 and 16, respectively). Cannabis use did not predict later externalizing behaviour. These findings supported the so called 'self-medication' hypothesis, where mental health problems precede the use of cannabis (Khantzian , 1985). We also studied cannabis use and its relation to internalizing behaviour problems. Results showed however that internalizing problems were unrelated to cannabis use.

The next focus was on the prospective relationship of vulnerability for psychosis and cannabis use during adolescence. After controlling for potentially confounding factors, symptoms indicative of the risk for psychosis at age 13 and 16 predicted cannabis use at age 16 and 19, respectively. Although our earlier study indicated that externalizing behaviour did precede cannabis use, but did not increase following use of cannabis, vulnerability for psychosis followed use of cannabis (at age 16), therefore allowing the conclusion that cannabis also predicted mental health problems (i.e. psychosis vulnerability at age 19). Hereby, evidence was provided not only for the self-medication hypothesis (as for externalizing behaviour), but also for the damage hypothesis, which suggests that cannabis use induces neurobiological changes leading to different forms of psychopathology (Brook, Cohen & Brook, 1998; Kandel, Yamaguchi & Chen, 1992; Moore et al., 2007).

Both studies described above provided evidence for the self-medication hypothesis, where behaviour problems (externalizing behaviour problems and psychosis

vulnerability) preceded cannabis use during adolescence. Previous evidence supporting the self-medication hypothesis stems from clinical observations of patients suffering from psychiatric disorders (e.g. Klein et al., 1994; Warner et al., 1994). Here, those suffering from psychiatric disorders tend to self-medicate (or sooth) the associated psychiatric distress by using cannabis. Indeed, it has been hypothesized that those suffering from psychosis symptoms use cannabis to improve their mood or control their feelings, to improve sleep, and reduce anxiety and agitation (Schofield et al., 2006). However, there are also studies that indicate that individuals with symptoms of psychosis use cannabis for reasons similar to those of the general population, i.e. 'to get high', relax and have fun (Kolliakou et al., 2001). This may be particularly plausible in the present study sample, as it consists of a group of adolescents drawn from the general population. In the case of externalizing behaviour problems, previous studies have also shown that problem behaviour precedes cannabis use (Fergusson et al., 2007; King et al., 2004; Pederson et al., 2001). Possibly here, those suffering from externalizing behaviour problems use cannabis to get rid of anger and hostile feelings. Alternatively, adolescents with externalizing behaviour problems are likely to show sensation seeking behaviour, which may be expressed in a greater tendency to use substances (Huizink et al., 2006; Marsman et al., 2008; Raine, 1996).

In addition to evidence for the self-medication hypothesis, the present study also provided evidence for the damage hypothesis, where the use of cannabis leads to the development of various mental health problems, although this was only observed for vulnerability to psychosis. This result corroborated findings from earlier studies, which also showed cannabis use to precede psychosis (Ferdinand, 2005; Fergusson et al., 2003; Kuepper et al., 2011; Moore et al., 2007), and also appears to be in line with neurobiological findings indicating relatively specific effects of delta-9-tetra-hydrocannabinol (Δ^9-THC), the main psycho-active ingredient of cannabis, on systems/brain networks involved in psychosis/schizophrenia. Thus, a bidirectional relationship was observed between cannabis use and vulnerability for psychosis during adolescence. Interestingly, when cannabis use preceded psychosis vulnerability, this became apparent during late adolescence, which might indicate stronger damaging effects of cannabis when it has been used over a longer period of time. It can however not be ruled out that the developmental trajectory of psychosis

plays an important role in this context. Psychosis usually becomes evident during young adulthood, which would mean that predictors of psychosis, including cannabis use, have a greater amount of phenotypic variability to predict at later ages. Although this could also be true for the proxy variables used here to represent psychosis vulnerability, i.e. social, attention, and thought problems, it seems likely that these have a greater amount of phenotypic variability at earlier ages. Future research should address the "cascading" effect for cannabis use and psychosis vulnerability in more detail, also taking into consideration differential susceptibility to cannabis exposure based on genetic and/or environmental vulnerability.

This relates to the vulnerability hypothesis, which states that the cause and effect relationship of cannabis use and mental health problems might be moderated by particular forms of vulnerability, i.e. biological, personal or familial factors that increase chances of both substance use and mental health problems (Caspi et al., 2005; Henquet et al., 2005; Miller et al., 2001; Verdoux et al., 2003). Such factors could also render individuals more vulnerable to the effects of cannabis, which, subsequently, might increase chances to develop not only the types of mental health problems discussed above, but also substance abuse and substance dependence (Hicks et al., 2011; Kendler et al., 2003). Preliminary evidence from one of the smaller samples supported the vulnerability hypothesis (see section "Cannabis Use and Cognitive Functioning").

In the studies on temporal order of cannabis use and different mental health problems, we have controlled for several well-known confounding factors (e.g. use of other substances, parental psychopathology), when analysing associations between cannabis use and mental health problems, thereby largely ruling out the so called 'shared causes hypothesis'. This hypothesis argues 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, such as disadvantaged background and difficult childhood circumstances (Fergusson & Horwood, 1997; Fergusson, Horwood & Swain-Cambell, 2002a). However, according to Hawkins, Catalano & Miller's 1992 and Petraitis, Flay & Miller's 1995 risk factor taxonomies, confounders can be categorized into (1) socio-environmental variables, including gender and SES; (2) substance-related variables, including the use of alcohol and tobacco; (3) intrapersonal variables, including mental health problems and (4) interpersonal variables, including family functioning, and not having been

brought up by both parents (Von Sydow et al., 2002). As we could not incorporate all possible confounders (from the different categories) of cannabis – mental health associations (e.g. family functioning, relationship with mother, drug-using peers/ family), we cannot completely rule out "shared causes". Future research could address this issue by providing a more comprehensive study of potential confounders, although it should be noted that it appears impossible to include all possible factors related to both substance use and mental health problems.

Cannabis use and Social Functioning

The second aim of this dissertation was to determine the influence of difficulties in social skills as possible risk factors for cannabis use, early initiation age of cannabis use and high frequency of use during adolescence. Mental health problems are often characterized or aggravated by problems in social skills (Fergusson et al., 2002; Tarbox & Pogue-Geile, 2008). Transitions into addiction or problematic substance use do not only occur amongst those with (obvious) mental health problems. To learn more about the relation between social skills and the risk for cannabis use, we studied cannabis correlates in a non-clinical cohort of adolescents, providing a particularly suitable context for investigating social skills in relation to cannabis use. There may be much more variation in social skills in this population than in a population characterized by mental health problems. We hypothesized that associations between cannabis use and social skills may not always be straightforward in that poor social skills would be associated with higher chances of (early initiation of) substance use (which would correspond with the self-medication hypothesis for mental health problems). After all, many adolescents consider cannabis a 'social drug', which is used mainly with friends, to 'bond' and to 'hang out' (Lee et al., 2007). Therefore, we tested whether different social skills differentially predicted cannabis use. Results showed associations between social parameters and cannabis use, where both cooperation and assertive behaviours at age 11 were related to cannabis use at age 16. More specifically, higher levels of assertive behaviour were associated with higher levels of cannabis use, whereas lower levels of cooperative behaviour at age 11 predicted higher levels of cannabis use at age 16. In other words, cannabis users were less cooperative, as expressed in, for example, complying with rules and directions, than non-users but, on the other hand, they were more assertive than non-users, which

might indicate that young adolescents who more readily engage in relations with peers and others, are also more likely to use cannabis. There were no associations with the social skill "self-control", and specific predictions of early versus late onset of use or frequency of use could not be made either. Previous studies however have found associations between cannabis use and self-control (Pokhrel et al., 2007; Sussman et al., 2003). Possibly, different operationalizations of self-control could explain differences in study results. Whereas in the present study, self-control was defined as 'behaviours that emerge in conflict and non-conflict situations', and was rated by the participant's teachers (Gresham, 1990), others have defined this type of behaviour as 'one's tendency to act without thinking' and the behaviour was often judged or scored by, for example, experimenters or parents (Tarter, 1988). A lack of (involvement in) conflict situations in the classroom may have resulted in less variability in self-control scores, and subsequently a lack of associations with cannabis use. Indirect support for this suggestive explanation stems from our finding of significant associations between cannabis use and impulsive behaviour in daily life (chapter 5).

The concept of social skills or functioning in relation to substance use appears very interesting, but social functioning should be operationalized in different ways, and, as our results show, no unidirectional effects may be expected. The finding that cooperative behaviour reduced the chances of adolescents using cannabis, whereas assertive behaviour (also usually considered a social strength) increased the chances, emphasized that different aspects of social functioning may have differential relations with substance use.

Cannabis use and Cognitive Functioning

In previous sections we disucssed our findings indicating that when specific mental health problems (also at subclinical levels) were present, or when specific social skills had not developed optimally, chances of (initiating) drug use were higher. Evidence was also provided to suggest interrelations between cannabis use and poor social skills and mental health problems on the one hand, and cognitive difficulties on the other. Pre-existing mental health problems and social skills may, like particular cognitive weaknesses (e.g. in areas necessary for behaviour regulation) either predispose towards tendencies to take drugs, or serve as moderating factors in

associations between cannabis use and (further) mental health or behaviour problems. Mental health problems (including addiction and substance abuse) and poor social skills are often found to be associated to particular cognitive dysfunctions, suggesting specific underlying neurocognitive mechanisms that can help explain associations between substance use and behaviour. Consequently, development of cognitive abilities is frequently targeted in treatment of mental health problems or training of social skills. They are often found to be required in order for treatment or training programs to be effective. Therefore, investigating possible cognitive difficulties among cannabis users is highly relevant.

Cannabis use (like use of many other substances) has been associated with many different cognitive weaknesses. Previous studies did not always opt for administration of neuropsychological tasks that addressed singular cognitive domains, which we consider necessary to disentangle different contributing elements. Therefore we attempted to select cognitive tasks with clearcut measurement potentials. We compared performance of cannabis users and non-users on tasks distinguishing the following functions: inhibition (with and without an motivational aspect) and social perception (with and without the element of recognizing emotions). 53 Cannabis-users (mean age of 22.6) and 48 non-users (mean age of 22.3) were compared on inhibitory control and impulsive behaviour. Results showed that cannabis users differed from non-users on motivational inhibition. Interestingly, cannabis users did not differ from non-users on inhibitory control without a motivational component. In addition, cannabis users reported higher levels of impulsive behaviour in daily life. This behaviour was related to motivational inhibitory control, but not to inhibitory control without the motivational component.

In our other study on cognitive abilities and cannabis use, 75 cannabis users (mean age 24.6 years) and 75 non-users (mean age 24.7 years) were compared with respect to performance on two different social perception tasks, one addressing the ability to recognize faces and the other addressing the ability to match facial emotions. The second task can be distinguished from the first as it requires emotion recognition and more working memory capacity. Also, cannabis users and non-users were compared on specific psychological problems. Results show that cannabis users experience more problems on the two social perception tasks and reported more psychological problems, i.e. more insufficiency of thoughts and actions, hostility, anxiety and psychoneuroticism. In addition, quality of social perception moderated associations

between cannabis use and psychological problems. Only cannabis users with relatively poor performance in the matching emotions-task showed significantly elevated levels of psychological problems. Non-users and cannabis-users with good social perception as measured by the matching emotions task did not. Moreover, the interactions were only observed when the matching emotions task was used as a measure for social perception, not when the face recognition task was used. Thus, specific weaknesses in emotion recognition (and possibly working memory) seem to play an important role (cf. Solowij & Battisti, 2008). Moreover, the effect was dose-dependent: psychological problems were particularly experienced by heavy cannabis users with relatively poor social perception as measured by the matching emotions task.

It may be concluded from the previous TRAILS studies into social and behavioural correlates of cannabis use that the presence of symptoms of (subclinical) psychopathology, including vulnerability for psychosis and externalizing behaviour problems, may increase the risk of cannabis use. Cannabis use, in turn, may increase the risk of developing or deteriorating further (specific) mental health problems. Social functioning (regardless of the presence or absence of (subclinical) levels of psychopathology) also influences the chances that people will be inclined to use cannabis, although it should be taken into account that some aspects of social functioning increase chances of cannabis use, whereas others reduce these chances.

Whereas the previous studies on the TRAILS-sample described in this thesis focused on the temporal order of cannabis use and mental health problems, the last two studies investigated possible underlying mechanisms explaining behavioural difficulties. The study on social perception (chapter 6) could be regarded as supportive of the vulnerability hypothesis. Studies have shown that different biological or environmental factors moderate associations between cannabis use and mental health outcomes. However, rather than focusing on genetics, as a number of earlier studies have done (Caspi et al., 2005; Henquet et al., 2008, Gill et al., 2010; Rijsdijk et al., 2011), we focused on aspects of cognition (which are of course themselves influenced by genetic make-up and environmental factors) in order to examine the vulnerability hypothesis for cannabis use and psychological problems. Evidence was provided showing that (complex) social perception deficits significantly increased the chances

of psychological problems among heavy cannabis users. Future research on this issue would benefit from prospective designs, in order to find out whether (specific) cognitive weaknesses early in life predispose towards cannabis use and mental health problems later on, and to find out whether the combination of cognitive vulnerability and cannabis use disproportionately increase the risk for developing mental health problems.

Critical reflections and directions for future research

Some critical notes should be made when interpreting results of the present thesis. Throughout all studies (chapter 2-6) we made use of self-reported data to determine cannabis use (tobacco and alcohol use were also self-reported). Questions concerning initiation age and frequency of use might have led to socially desirable answers, especially for young adolescents. Although this may have been the case, there are several studies that have concluded that self-reporting of substance use is generally a valid method (e.g. Bushan et al., 2002). Also, cannabis use is generally condoned in the Netherlands, which possibly allows for more honest self-reports of cannabis use compared to studies in other countries with stricter cannabis policies. Data on mental health and behaviour (externalizing symptoms, internalizing behaviour, vulnerability for psychosis, social behaviour, impulsive behaviours) were also obtained from self-reports. Use of multiple informants would have been preferable (Offord et al., 1996).

One particular strength is the focus on temporal order of behavioural and social correlates of cannabis use within a large population based sample (n=2,230). Also, the starting point of TRAILS is early adolescence (Mean age T1: 11.1), hereby providing the opportunity to collect prospective data antedating initiation to cannabis in very early starters and to investigate multiple hypotheses on cannabis use and behaviour difficulties.

The focus on early adolescence is relevant for several different reasons. During adolescence, rapidly developing biological changes (puberty) and maturation processes take place. These developmental processes might make the human organism vulnerable for enduring effects of external influences such as exposure to cannabis (Court, 1998; Schneider 2008). Indeed, different studies have shown that cannabis use during early adolescence constitutes a risk factor for enduring negative

effects of cannabis use, including impaired reaction times (Ehrenreich et al. 1999), mental health problems and behaviour difficulties (Arsenault et al., 2002; Fergusson et al., 2002a, 2002b). Early onset delinquents, for example, not only show earlier onset of cannabis use, but also a much faster rate of increase in cannabis dependence symptoms (Lynskey et al., 2002). Thus, early adolescence seems to be characterized by a heightened risk for irreversible effects, and a heightened risk for more significant adverse outcomes as well.

A limitation of the series of studies presented in this thesis is that we were only able to select a limited amount of potential confounders to introduce to our analyses. Therefore, we may have missed a number of other factors that could also be important correlates of cannabis use and mental health problems during adolescence. For example, we have not investigated the issue of a possible heightened sensitivity for the effects of cannabis in individuals with a particular genetic make-up, or have done so only indirectly, based on the assumption that the genes of interest partly determine certain cognitive outcomes. Experimentation with cannabis use might be harmless for some, but quite harmful for other children, and patterns of cause and effect might differ accordingly. Children enter adolescence with different levels of inherited and acquired psychobiological vulnerability (or conversely, resilience) to mental disorder due to differences in a person's genetic make-up (Loehlin, 1992, Rutter et al., 1999). Although parental psychopathology may be seen as a clear marker for vulnerability in children, which we have controlled for in the present study, this does not directly investigate genetic make-up of their children.

A further recommendation for future research is to focus on a broader age span and longer follow-ups to investigate the relationships with mental health problems (including internalizing problems, externalizing behaviour and vulnerability for psychosis). There are several reasons for this. First of all, at the second measurement wave, the number of adolescents who used cannabis, but also the frequency of use, was relatively low. It is assumed that more adolescents will start using cannabis during later adolescence, around the age of 15 (Monshouwer et al., 2005). Also, the sample was quite young and had not been using cannabis for a long period of time, thereby possibly reducing the chances of finding support for the so called ‘damage hypothesis’ in relation to internalizing and externalizing behaviour problems. Studies providing evidence for damaging effects of cannabis observed these effects in young

adulthood (Fergusson et al., 2002; White et al., 1999). Possibly, such effects will also become evident in our sample at a later stage. Lastly, it can be assumed that some of those who started using at a young age, may start using it more frequently in late adolescence, which in turn forms an extra risk factor for the development of behaviour and cognitive deficits as well as addiction (Substance Use Disorders).

Another recommendation for future research is to include instruments measuring other aspects of social functioning as well, now that we have provided additional evidence for differential relations between different social skills and cannabis use. For example, in order to measure social functioning, we focused on three specific skills in relation to cannabis use. Examples of instruments which could be used in the future include the Scale for Interpersonal Behavior (Arrindell & van der Ende, 1985), to assess frequency and associated distress during social interaction, the Novotni Social Skills Checklist to assess a wider range of social skills, and the Youth Self Report (Achenbach, 1991; Verhulst and Achenbach, 1995) and the Strengths and Difficulties Questionnaire (Goodman, 1997) to assess social and peer problems next to social skills.

Clinical implications

The results of our studies may have implications for clinical and preventive practices. First and foremost, the present study has shown that prevention programs should take into consideration presenting information on associations between cannabis use and mental health problems, especially during adolescence. As described earlier, adolescence is a life phase characterized by brain maturation and growth, which might increase the risk of possible damaging effects of cannabis (Schneider et al., 2008). Prevention programs should also focus on certain vulnerable groups, such as adolescents suffering from psychosis symptoms or exhibiting externalizing behaviour problems. These individuals may tend to self-medicate by using cannabis, already during adolescence. Since these behavioural difficulties could further develop into clinical disorders with poor long-term outcomes, prevention programs should focus on these at-risk adolescents.

Considering social functioning in relation to cannabis in prevention programs, it should be considered to fine-tune the approach to different social skills, and not simply stimulate all positive social skills. Previous studies have shown different 'life skills' to be effective in prevention of cannabis use, including self-esteem (Tobler et al., 2000), focus on norms, commitment not to use and intention not to use (Cuijpers et al., 2002). Also, a 'social influence approach' seems effective in prevention, where the focus is, among others, on assertiveness (Donaldson et al., 1996; Cuijpers, 2002; Tobler et al., 2000). However, these assertive skills were mainly defined in the context of 'resistant skill training'; in other words, it seems effective to be 'assertive to say no to drugs'. Here, being assertive seems an effective preventive approach. The present study however, showed that being assertive in somewhat different contexts or situations may also serve as a risk factor of using cannabis. It may be concluded that adolescents need to show specific assertive behaviour, so it can operate as a protective factor in drug using behaviour. Also, the present study showed that prevention programs should stimulate cooperation, since higher levels of cooperation served as a protective factor in the prediction of cannabis use.

Lastly, substance use disorders have been associated with impaired decision-making and increased impulsive behaviour, which may be due to lack of motivational inhibitory control. This study showed that cannabis users also experience difficulties with social perception. Therefore, it may be considered to include training of social perception and motivational inhibitory skills in prevention and intervention programs. These aspects of cognition have not yet featured prominently in existing programs, which have focused on, for instance, management of negative thinking, problem solving skills and relaxation training. Further research is required to identify more comprehensively the range of (social) cognitive abilities that are impaired in cannabis users and may thus be targeted in prevention and intervention programs.