Cannabis use, cognitive functioning and behaviour problems

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Cannabis use and development of externalizing and internalizing behaviour problems in early adolescence
- a TRAILS study

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Abstract

Aim: To examine the prospective relationship between externalizing and internalizing problems and cannabis use in early adolescence.

Materials and Methods: Data were used from the TRAILS study, a longitudinal cohort study of (pre) adolescents (n = 1,449), with measurements at age 11.1 (T1), age 13.6 (T2) and age 16.3 (T3). Internalizing (withdrawn behaviour, somatic complaints and depression) and externalizing (delinquent and aggressive behaviour) problems were assessed at all data waves, using the Youth Self Report. Participants reported on cannabis use at the second and third wave. Path analysis was used to identify the temporal order of internalizing and externalizing problems and cannabis use.

Results: Path analysis showed no associations between cannabis use (T2-T3) and internalizing problems (T1-2-3). However, cannabis use and externalizing problems were associated (r ranged from .19–.58); path analysis showed that externalizing problems at T1 and T2 preceded cannabis use at T2 and T3, respectively. In contrast, cannabis use (T2) did not precede externalizing problems (T3).

Conclusions: These results suggest that in early adolescence, there is no association between internalizing behaviour and cannabis use. There is an association between externalizing behaviour and cannabis use, and it appears that externalizing behaviour precedes cannabis use rather than the other way around during this age period.

Introduction

Regular cannabis use has been associated with a wide range of mental health problems including psychotic disorders (Arseneault et al., 2002; Moore et al., 2007), externalizing problems (aggressive and delinquent behaviour) (Fergusson et al., 2002; Monshouwer et al., 2006) and, to a lesser extent, internalizing problems, such as depression (Degenhardt et al., 2001; Degenhardt et al., 2003; Patton et al., 2002) and anxiety (Patton et al., 2002; van Laar et al., 2007; Hayatbakhsh et al., 2007a). Several hypotheses have been put forward to explain these associations, including the "damage hypothesis", which proposes that cannabis use precedes mental health problems (Brook et al., 1998; Kandel et al., 1992) and the "self medication hypothesis", which proposes that individuals with mental health problems tend to resort to drug use to sooth their problems (Khantzian, 1985). The "shared causes hypothesis" proposes that the linkage between cannabis use and mental health problems is the result of genetic and environmental factors associated with both problem behaviour and cannabis use (Fergusson and Horwood, 1997; Fergusson et al., 2002; Shelton et al., 2007).

Shared causes are often found for externalizing behaviour and cannabis use (Fergusson and Horwood, 1997; Fergusson et al., 2002). Several studies have shown substantially weaker associations between cannabis use and externalizing behaviour after statistical control for factors such as socialeconomic status and use of other substances (e.g. Korhonen et al., 2010). However, most studies do show some residual variance in associations between externalizing behaviour and cannabis use that cannot be explained by environmental factors (Fergusson et al., 2007; Fergusson et al., 2002; Pedersen et al., 2001). The temporal order of cannabis use and both externalizing and internalizing behaviour has not yet been disentangled (Fergusson et al., 2002; Monshouwer et al., 2006). Most longitudinal evidence supports the self-medication hypothesis, which states that externalizing problems precede the use of cannabis at this age (King et al., 2004; Fergusson et al., 2007; Pedersen et al., 2001). There is also evidence to suggest that externalizing behaviour during adolescence precedes cannabis use in early adulthood (Hayatbakhsh et al., 2007b). Although it is difficult to control for all potential confounders simultaneously, some of these studies did not control for important potential confounders, such as SES, use of other substances and parental psychopathology, and therefore may have left open the

possibility of shared causes more than necessary. For internalizing behaviour, the relationship is evenmorecomplex: firstly, compared to externalizing behaviour problems, there is less evidence for an association between cannabis use and internalizing behaviour problems (Monshouwer et al., 2006). In several studies that did initially find a significant association between cannabis use and internalizing behaviour, the association became non-significant after statistical control for confounding variables (Harder et al., 2008; McGee et al., 2000). Nonetheless, there are some studies that have found evidence for the self-medication hypothesis, with internalizing behaviour problems preceding cannabis use at later age (King et al., 2004; Wittchen et al., 2007). Again, shared causes cannot be ruled out, as the associations may be explained by residual confounding (Fergusson and Horwood, 1997; Fergusson et al., 2002; Hayatbakhsh et al., 2007a). There is also (contrasting) evidence suggesting that internalizing behaviour in young adolescence is not related to substance use at a later age, including the use of cannabis (Alati et al., 2008; Hayatbakhsh et al., 2008; Ferdinand et al., 2001). Thus, in general, evidence regarding (the direction of) associations between cannabis use and internalizing/ externalizing behaviour problems in adolescence is not yet convincing, which is mainly due to the fact that most studies did not analyze temporally bi-directional associations (i.e., where cannabis use can precede but also follow behaviour problems), and which might also partly be due to the fact many studies did not control comprehensively for potentially confounding variables.

It is important to study associations between externalizing and internalizing problems on the one hand and cannabis use on the other during early adolescence for several reasons. Firstly, early adolescence is a life phase characterized by rapid biological changes and consecutive maturation processes. These developmental processes might increase vulnerability for enduring effects of external influences like use of cannabis (Schneider, 2008). Secondly, cannabis use usually starts in early adolescence (Monshouwer et al., 2005), possibly because of increases in peer-influenced risk-taking behaviours (e.g. Fergusson and Horwood, 1997). So this appears to be the best possible time to collect behavioural data antedating initiation of cannabis use. The study of associations between internalizing and externalizing behaviours and cannabis use during early adolescence may thus help identifying individuals who are at an increased risk for multiple simultaneous problems (e.g. aggression and substance use), which have been associated with the poorest long-term outcomes. At this stage it

might still help targeting one of the problems (preferably the one that occurs first in time) in order to prevent other or combined problems.

In the present study, we investigated relations between both internalizing and externalizing behaviour problems and cannabis use in a large population sample of young adolescents enrolled in the Tracking Adolescents' Individual Lives Survey (TRAILS, Huisman et al., 2008). Using path analysis, we investigated the temporal order of the association between cannabis use and internalizing and externalizing behaviour, thereby controlling for confounding factors to eliminate, to some extent, the effect of shared causes. It was expected that the link between internalizing behaviour and cannabis use would be weaker than the association between externalizing behaviour and cannabis use. In addition, based on findings to date, it was expected that internalizing and externalizing behaviour problems would precede cannabis use and not the other way around.

Method

Sample

Data were gathered from participants in the Tracking Adolescents' Individual Lives Survey (TRAILS), a prospective cohort study among adolescents in the general Dutch population. TRAILS investigates the development of mental and physical health from preadolescence into adulthood (de Winter et al., 2005). The study covers biological, psychological and sociological topics and collects data from multiple informants. Participants come from five municipalities, including both urban and rural areas, in the North of the Netherlands. So far, three data collection waves have been completed: T1 (2001–2002), T2 (2003–2004) and T3 (2005–2007). Participants will be followed until (at least) the age of 24. Of all individuals asked to participate in TRAILS (N= 2935), 76,0% agreed to participate at T1 (N= 2230; mean age 11.09 years; SD 0.55; 50.8% girls). At T2, 96.4% of these participants (N= 2149) were re-assessed. T3 was completed with 81.4% of the original number of participants (N= 1816), mean age 16.27 years; SD 0.73 (52.3% girls). At 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%. More detailed information on the selection procedures and non-response bias can be found elsewhere

(de Winter et al., 2005; Huisman et al., 2008). Analyses in the present study were based on 1.449 adolescents (53.3% girls, 46.7% boys) with non-missing data on all variables of interest (described below).

Measures

Cannabis use

Cannabis use was assessed at T2 and T3 by self-report questionnaires filled out at school, supervised by TRAILS assistants. Confidentiality of the study was emphasized so that adolescents were reassured that their parents or teachers would not have access to the information they provided. Among others, participants were asked about lifetime use and use in the last year with the following questions: 'How often have you used cannabis in your life/in the last year', with answer categories: 'I have never used', 'used it once', 'used it twice', 'three times',....., '10 times', '11–19 times', '20–39' times, '40 times or more'). Items were recoded into five categories; (1) those who had never used; (2) those who had used but not during the past year (discontinued use); (3) those who used once or twice during the past year (experimental use); (4) those who reported using cannabis between 3 and 39 times during the past year (regular use); and (5) thosewhoreported using it 40 times or more during the last year (heavy use). The construction of these categories was similar to that used in other studies investigating cannabis use and mental health in young adolescents (e.g. Monshouwer et al., 2006).

Behaviour problems

Internalizing and externalizing behaviour were assessed with the Youth Self Report (YSR), which is one of the most commonly used self report questionnaires in current child and adolescent psychiatric research (Achenbach, 1991; Verhulst and Achenbach, 1995). The YSR contains 112 items on behavioural and emotional problems in the past 6months. Participants can rate the items as being not true (0), somewhat or sometimes true (1), or very or often true (2). The YSR covers the following domains: anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention (hyperactivity) problems, aggressive behaviour, and rule-breaking behaviour. For the present study, we used two broad-band dimensions of the YSR (Achenbach, 1991): (a) internalizing problems, consisting of items measuring anxious/depressed, withdrawn/ depressed, and somatic

complaints; and (b) externalizing problems, with items measuring aggressive and rule-breaking behaviour.

Control variables

Since SES, use of other substances and parental psychopathology have been shown to be among the most important correlates of cannabis use and both internalizing and externalizing behaviour (Fergusson and Boden (2008)), it was examined whether these should be included in the path analyses.

Socioeconomic Status (SES)

Socioeconomic Status (SES) was assessed at T1 using a 5 point scale consisting of five variables: educational level (father/mother), occupation (father/mother), and family income. The internal consistency of this measure is satisfactory (Cronbach's alpha 0.84; Veenstra et al., 2006).

Parental psychopathology

Parental psychopathology (i.e. depression, anxiety, substance abuse, antisocial behaviour, and psychosis) was measured by means of the Brief TRAILS Family History Interview (Ormel et al., 2005), administered at T1. Each syndrome was introduced by a vignette describing its main symptoms and followed by a series of questions to assess lifetime occurrence, professional treatment, and medication use. The scores for substance abuse and antisocial behaviour were used to construct a familial vulnerability index for externalizing disorder. The scores for depression and anxiety disorder were used to construct an index for internalizing disorder. The construction of a familial vulnerability index was based on Kendler et al. (2003), who performed multivariate twin modelling to investigate shared genetic risk factors for psychiatric and substance use disorders. More information on the construction of familial vulnerability within TRAILS is described elsewhere (Veenstra et al., 2005). For both internalizing and externalizing disorder, parents were assigned to one of the following categories: (0) = (probably) not; (1) = (probably) yes, (2) = yes and treatment/medication (substance abuse, depression, and anxiety) or picked up by police (antisocial behaviour).

Other substances

In order to assess alcohol and tobacco use, participants filled out a questionnaire at both T2 and T3 on the frequency of use in the past month. For tobacco use reported frequency was recoded into non-weekly (0) versus weekly (1), and for alcohol use, the reported frequency was recoded into non-monthly (0) versus monthly use (1). These categories were similar to those used in other studies investigating cannabis use and mental health in young adolescents (e.g. Monshouwer et al., 2006).

Data analysis

It was first examined whether non-responders differed from responders on SES (by means of t-test) and gender (by means of Pearson χ2-test). Next, it was examined whether, among the responders, there were differences between cannabis users and non-users with respect to SES, familial vulnerability for internalizing and externalizing behaviour, use of alcohol and tobacco and gender (using Pearson Chi-square analysis for alcohol, tobacco use and gender and t-tests or GLMunivariate analysis of variance for SES and familial vulnerability). These analyses were performed in order to determine which variables should be included in the main analyses as covariates. The temporal order of occurrence of cannabis use and internalizing and externalizing behaviour was investigated using path analyses. In path analysis, an extension of the regression model, the regression weights predicted by the model are compared with the observed correlation matrix for the variables, and a goodness of fit statistic is calculated. The path coefficient is a standardized regression coefficient (beta) indicating the effect of an independent variable on a dependent variable in the path model. Thus, when the model has two or more independent variables, path coefficients are partial regression coefficients, which measure the extent of effect of one variable on another in the path model controlling for other variables, using standardized data or a correlation matrix.

Following the two step approach recommended by Anderson and Gerbing (1988), confirmatory factor analysis (CFA) was used to investigate how well our hypothesized models fit the actual data. These models were based on previous research to assess temporal order of internalizing and externalizing behaviour (T1-T2-T3) and cannabis use (T2-T3) (e.g. Fergusson et al., 2002; McGee et al., 2000).

In the path analyses, both internalizing and externalizing behaviour were introduced as latent variables with multiple indicators. The latent variable ‘internalizing’

consisted of anxious/depressed, withdrawn/ depressed and somatic complaints. The latent variable 'externalizing' consisted of the indicators aggressive and delinquency. Cannabis use was represented by one indicator (i.e., the self-report measure consisting of the following categories: (1) those who had never used; (2) those who had used but not during the past year; (3) those who used once or twice during the past year; (4) those who reported using cannabis between 3 and 39 times during the past year; and (5) those who reported using it 40 times or more during the last year (see section 2.2.1). Next, we modelled prospectively cannabis use and internalizing/ externalizing identified in the CFA. Here, we included all possible associations between latent variables. To evaluate overall model fit, the root mean square error of approximation was used (RMSEA; Steiger, 1998); a RMSEAvalue less than .05 (Browne and Cudeck, 1993) indicates good model fit. Both $\chi 2$ statistics and RMSEA are dependent on the size of the sample: as we had a relatively large sample (n = 1,449), we also used the comparative fit index (CFI; Bentler, 1990) to evaluate overall model fit. A CFI value greater than .90 (Bentler, 1990) indicates good model fit. All analyses were performed using EQS 6.1 for Windows (Bentler, 1995).

Results

Non-responders analysis

Responders (n = 1,449) and non-responders (n = 739) differed in terms of SES ($t = -9.6$, $p < .001$); responders scored higher on SES than non-responders (M= .07, SD = .78 vs. M=−.28, SD = .79). Responders also differed from non-responders in terms of gender ($\chi 2$ (1) = 10.5, p = .001: responders were more likely to be female (53.3%) than non-responders (46.1%).

Descriptives

Descriptive information regarding the frequency of cannabis use is presented in Table 1 for participants with complete data on all variables of interest. The number of cannabis users increases with age as does the frequency of use. Cannabis users did not differ from non-users with respect to SES ($t(1447) = -.9$, p = .387), gender ($\chi 2$ (1) = 1.1, p = .289), familial vulnerability for internalizing ($t(1447) = -.4$, p = .705) and externalizing behaviour ($t(1447) = -1.8$, p = .071). Cannabis users and non-users differed significantly with respect to alcohol use at T2 ($\chi 2$ (1) = 90.3, $p < .001$),

alcohol use at T3 ($\chi 2$ (1) = 95.0, p < .001), tobacco use at T2 ($\chi 2$ (1) = 137.3, p < .001) and tobacco use at T3 $\chi 2$ (1) = 346.8, p < .001), with cannabis users using alcohol and tobacco more often than non-users (57.8% vs. 31.2% reported monthly alcohol use at T2; percentages for T3: 94.0% vs. 70.7%; 19.8% vs. 2.2% reported weekly tobacco use at T2; percentages for T3: 57.4% vs. 11.1%). Tobacco and alcohol use were also related to both internalizing and externalizing behaviour and therefore included as covariates in subsequent path analysis (for detailed information, see Table 2).

Table 1: Descriptive information on cannabis use at T2 and T3 (n=1,449)

	T2	T3
Never used	93.6 % (n=1359)	69.9 % (n=1013)
Discontinued use	1.4 % (n=20)	5.9 % (n=86)
Experimental use	3.7 % (n=54)	10.9 % (n=158)
Regular use	1.2 % (n=17)	9.6 % (n=139)
Heavy use	.1 % (n=2)	3.7 % (n=53)

Table 2: *t*-statistics of significant control variables (tobacco use and alcohol use) and internalizing and externalizing behaviour

	T2 tobacco use	T3 tobacco use	T2 alcohol use	T3 alcohol use
T1 Internalizing behaviour	-3.2*	-1.6	-.2	1.0
T2 Internalizing behaviour	-3.7*	-3.3*	–.7	2.7*
T3 Internalizing behaviour	-4.2*	-3.2*	-.1	2.0
T1 Externalizing behaviour	-6.1*	-5.4*	-4.2*	-3.1*
T2 Externalizing behaviour	-11.6*	-11.3*	-9.2*	-3.4*
T3 Externalizing behaviour	-10.3*	-19.2*	-7.8*	-8.4*

* p<.05

Path analyses: Preliminary analyses

Table 3 shows the correlations between all latent variables. Factor loadings of the indicators of the latent variables of internalizing behaviour and externalizing behaviour of all three measurement waves are presented in Table 4.

Table 3: Correlations of all latent variables of the CFA

	T2 Cannabis use	T3 Cannabis use
Model 1		
T1 Internalizing behaviour	.06*	-.04*
T2 Internalizing behaviour	.06*	-.02*
T3 Internalizing behaviour	.05*	.02*
Model 2		
T1 Externalizing behaviour	.19*	.23*
T2 Externalizing behaviour	.40*	.38*
T3 Externalizing behaviour	.24*	.58*

* p<.05

Model 1. Cannabis use and internalizing behaviour problems

The independence model testing the hypothesis that all cannabis scores and internalizing behaviour scores were uncorrelated was rejected: $\chi 2$ (30, N= 1,449) = 56.4, $p < .003$. The model provided an acceptable fit to the data (CFI = .99, RMSEA = .03). However, as shown in Table 3, correlations between internalizing behaviour problems (T1-2-3) and cannabis use (T2-T3) ranged from .02 to .06 and thus are very small. Although these correlations were significant (probably due to the large sample size), they were indicative of non-relationships between cannabis use and internalizing behaviour. This was confirmed by the Wald test. Dropping parameters indicative of associations between internalizing behaviour (T1, T2 and T3) and cannabis use (T2 and T3) resulted in a non-significant change of the model [$\chi 2$ (6, N= 1,449) = 11.2, p = .081]. Path-analysis revealed that although our model represented the data well [$\chi 2$ (66,N= 1,449) = 215.2, $p < .001$; RMSEA = .04, CFI = .97], all paths between internalizing (T1-2-3) and cannabis use (T2-T3) were non-significant.

Table 4: Factor loadings of the Indicators of the Latent variables of internalizing and externalizing behaviour and cannabis use.

Variable	Factor Loadings
Internalizing behaviour and cannabis	
T1 Internalizing behaviour	
Anxious/Depressed	.24
Withdrawn/Depressed	.21*
Somatic complaints	.17*
T2 Internalizing behaviour	
Anxious/Depressed	.27*
Withdrawn/Depressed	.21*
Somatic complaints	.15*
T2 Cannabis use	
Cannabis use	1.00
T3 Internalizing behaviour	
Anxious/Depressed	.26*
Withdrawn/Depressed	.23*
Somatic complaints	.16*
T3 Cannabis use	
Cannabis use	1.00
Externalizing behaviour and cannabis	
T1 Externalizing behaviour	
Aggressive behaviour	1.00
Rule-breaking behaviour	.90*
T2 Externalizing behaviour	
Aggressive behaviour	1.00*
Rule-breaking behaviour	1.38*
T2 Cannabis use	
Cannabis use	1.00
T3 Externalizing behaviour	
Aggressive behaviour	1.00
Rule-breaking behaviour	1.67*
T3 Cannabis use	
Cannabis use	1.00

* $p<.05$

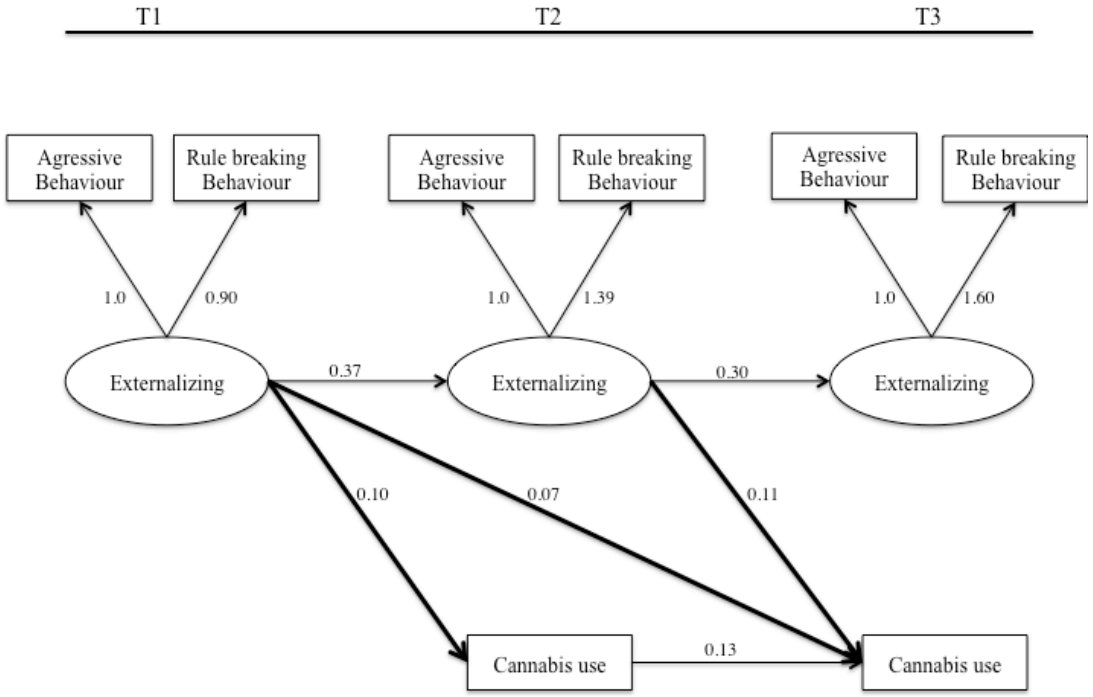
Model 2. Cannabis use and externalizing behaviour problems

The independence model that tested the hypothesis that all cannabis scores and externalizing behaviour scores were uncorrelated, was rejected: $\chi 2$ (9, N= 1,449) = 64.4, $p < .001$. Also, although RMSEA was relatively high (.07), the CFI was .99 and therefore our model provided an acceptable fit to the data. Correlations between externalizing behaviour (T1-2-3) and cannabis use (T2-T3) ranged from .19 to .58 and thus were indicative of a relationship between externalizing behaviour problems and cannabis use (see Table 4). Next, path analysis was performed to address the temporal order of cannabis use and externalizing behaviour problems (Fig. 1), hereby controlling for alcohol and tobacco use at T2 and T3.

Path analysis revealed that the model represented the data well [$\chi 2$ (34,N= 1,449) = 270.2, $p < .001$; RMSEA = .07, CFI = .96]. The paths between externalizing behaviour problems measured at T1, T2, and T3 were all significant (T1-T2; $z = 11.8$, $p < .05$; T1-T3; $z = 4.9$, $p < .05$; T2-T3; $z = 11.5$, $p < .05$). The path between cannabis use T2 and T3 was also significant ($z = 5.4$, $p < .05$). In addition, the paths between externalizing behaviour and tobacco use were all significant (T2; $z = 11.7$, $p < .05$; T3; $z = 16.9$, $p < .05$). Also, the paths between externalizing behaviour and alcohol use were all significant (T2; $z = 8.4$, $p < .05$; T3; $z = 6.6$, $p < .05$). The same occurred with cannabis use, where the paths between cannabis use and tobacco use were significant at T2 ($z = 17.8$, $p < .05$) and T3 ($z = 18.0$, $p < .05$) and also with alcohol use at T2 ($z = 2.9$, $p < .05$) and T3 ($z = 5.7$, $p < .05$). Moreover, externalizing behaviour and cannabis use significantly correlated at T2 ($r = 0.19$, $p < .05$) and T3 ($r = 0.34$, $p < .05$).

Externalizing behaviour at T1 significantly predicted cannabis use at T2 ($z = 3.8$, $p < .05$) and T3 ($z = 2.7$, $p < .05$). Externalizing behaviour at T2 also significantly predicted cannabis use at T3 ($z = 4.0$, $p < .05$). Cannabis use measured at T2 did not show significant association with externalizing behaviour problems at T3 ($z = -1.4$, $p > .05$) (Fig. 1).

Figure 1: Path analysis of externalizing behaviour, with indicators aggressive behaviour and rule breaking behaviour, and cannabis use in young adolescence after controlling for tobacco and alcohol use, measured at both T2 and T3. All non-significant paths have been removed from the full model. Latent variables are shown in ellipses, and observed variables are shown in rectangles.



Discussion

In the present longitudinal study, 1,449 respondents were followed from the age of 11 to 16 to assess the relationship between both internalizing and externalizing problems and cannabis use. Two different hypotheses, the damage hypothesis and the self-medication hypothesis, were tested using path analyses, thereby controlling for possible confounding factors.

First, our data showed that cannabis use is strongly related to externalizing behaviour problems in early adolescence, including aggressive and delinquent behaviour. This result is largely in agreement with previous studies (Fergusson et al., 2007; Fergusson et al., 2002; Khantzian, 1985; Monshouwer et al., 2006). As expected, our data supported the self-medication hypothesis, indicating that externalizing problems precede cannabis use during adolescence and not the other way around. Specifically, in our study, externalizing problems at age 11 were associated with cannabis use at age 13 and age 16. Also, externalizing behaviour at age 13 predicted cannabis use at age 16.

These results are in agreement with a number of other studies. King et al. (2004), for example, also showed that externalizing psychopathology at age 11 predicted cannabis use at age 14, although it did not take into account potential confounders, such as the use of other substances. Korhonen et al. (2010) recently showed that early onset of smoking predicts cannabis initiation, while controlling for co-occurring externalizing behaviour problems. Whereas Korhonen et al. (2010) focused specifically on whether time of smoking initiation was predictive of the onset of cannabis use, we focused on the temporal order of cannabis use and externalizing behaviour problems. Although this study therefore had a different focus compared to the present study, it does illustrate the importance of controlling for potentially confounding factors when investigating cannabis-behaviour associations (or of controlling for behaviour when studying associations between specific environmental factors and cannabis use). Another longitudinal study (spanning 25 years) that did control for confounding factors demonstrated that conduct disorders at even a younger age (7–9 years) were related to later substance use, including cannabis use (Fergusson et al., 2007). Also, Pedersen et al. (2001), confirmed that conduct disorder at a young age is strongly associated with cannabis use in young teenagers. All these studies supported results that externalizing problems precede cannabis use.

For the present study as well as earlier studies, it should be noted that externalizing behaviour explained only part of the variance of cannabis use, indicating that other factors are also important correlates of cannabis use during adolescence. Examples of such factors may be substance using peers and family functioning (e.g. Coffey et al., 2000; Fergusson and Horwood, 1997). In addition, considering the concurrent correlations of cannabis use and externalizing behaviour at different measurement points we cannot rule out reciprocal relations between the two, i.e. lagged associations remain possible (Fergusson et al., 2005). Nonetheless, some evidence is provided here that such lagged associations start with the presence of externalizing behaviour, as there was negligible cannabis use at T1, while there was externalizing behaviour at that time.

Although evidence of damaging effects of cannabis has been provided in other studies (Kandel et al., 1986; Kandel et al., 1992), our study did not support this hypothesis. This could be due to the fact that the sample was quite young and had not been using cannabis for a long period of time. Indeed, 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. For now, however, it should be concluded that externalizing problems at age of 11 and 13 predict cannabis use at later ages.

If the self-medication hypothesis is true, as the evidence suggests, it would be good to know in more detail which aspects of externalizing behaviour elicit the need for "medication". One explanation could be that those who show externalizing problems at age 11 use cannabis to get rid of feelings of hostility or anger. If the temporal order is not the consequence of some form of self-medication, a possible explanation is that cannabis use is a form of sensation seeking behaviour, which has regularly been identified as a characteristic of externalizing behaviour (Huizink et al., 2006; Marsman et al., 2008; Raine, 1996). There may be several mediating factors explaining the temporal order with externalizing problems preceding cannabis use as well. Examples include exclusion from peer groups that show less experimental behaviour and inclusion in peer groups showing increased levels of experimental behaviour among individuals characterized by externalizing behaviours (Coffey et al., 2000; Fergusson and Horwood, 1997).

With respect to internalizing behaviour problems, our study did not confirm the results of several earlier studies that did find associations with cannabis use

(Degenhardt et al., 2001; Degenhardt et al., 2003; Patton et al., 2002; Hayatbakhsh et al., 2007a). It should be noted that generally the relations between cannabis use and internalizing behaviour have been weaker than those with externalizing behaviour, and that existing associations could often be accounted for by co-occurring risk factors such as sociodemographic factors and use of other substances (Moore et al., 2007). Our results are in agreement with those studies not finding an association at all (Monshouwer et al., 2006; Harder et al., 2008; McGee et al., 2000).

A possible explanation for these mixed results might be that studies that did find significant associations focused mainly on older individuals (Brook et al., 1998; Hayatbakhsh et al., 2007a; Patton et al., 2002; van Laar et al., 2007; Wittchen et al., 2007), although there is evidence opposing this hypothesis as well (Hayatbakhsh et al., 2008). For example, Hayatbakhsh et al. (2007a) showed, using logistic regression analysis, that cannabis use at the age of 15 was associated with an increased risk for Anxiety and depression at the age of 21. One study providing compelling evidence in favor of the hypothesis was performed by Arseneault et al. (2002), who concluded that the association between cannabis use and depressive symptoms was age dependent, following findings showing that cannabis use at age 15 was not associated with depressive symptoms at age 26 while cannabis use at age 18 was. Hayatbakhsh et al. (2007a) suggested that the association is not only dependent on age, but also on duration and frequency; only those who already started cannabis use at age 15 and using it frequently until the age of 21 showed elevated levels of anxiety and depression in young adulthood. The fact that internalizing problems are more evident in late adolescence and young adulthood than in early adolescence may also play a significant role (Kessler et al., 2007).

The present study has a number of limitations. One limitation is that mental health and cannabis use data were obtained from self-reports. Use of multiple informants, particularly concerning mental health, would have been preferable (Offord et al., 1996). Despite the fact that previous studies have concluded that self-reporting on substance use is generally valid (Buchan et al., 2002) (and the fact that cannabis use in The Netherlands is not illegal, which possibly allows more honest answers), one could still argue that the nature of the questions might have led to socially-desirable answers (especially for young adolescents). Another limitation is the loss of respondents between measurement 1 and 3, especially since non-responders differed from responders in terms of SES and gender. However, it can be argued that if non-

responders would have been included in the present analysis, the present results would have strengthened, since it can be presumed that more cannabis users would be present among the non-responders. On the other hand, it can also be argued that the present results would have been weakened when non-responders (with lower SES) would have been included in the present analysis. SES could have explained a greater part of the variance of cannabis use, which in turn could have weakened the variance explained by externalizing behaviour. Lastly, despite the fact that we controlled for several important confounders, it cannot be ruled out that our results can be explained by non-observed confounding factors (thus supporting the shared causes hypothesis). For example, it has been shown that genetic factors are important determinants of both externalizing behaviour problems and cannabis use (Kendler et al., 2000; Lynskey et al., 2002; Rutter et al., 1999). Research using twin designs has also identified common genetic factors of externalizing problems and substance use behaviour during adolescence (Shelton et al., 2007; Young et al., 2000). For this study, we only had proxy variables of genetic confounding available (i.e. those constituting familial risk of internalizing and externalizing behaviour as well as substance use). There are also several environmental factors (e.g. family functioning, peer group influences) that could not be incorporated in this study.

Despite some clear limitations, it may be noted that this study is one of the few prospective studies focusing on cannabis use and both internalizing and externalizing problems that was able to incorporate data assessed before cannabis initiation, allowing testing of both the damage and the self-medication hypotheses. Whereas externalizing problems at age 11 and 13 preceded cannabis use at age 13 and 16, cannabis use did not precede externalizing problems at any age. Future research should focus on a broader age span and use longer follow-up periods to investigate relationships with mental health problems (both internalizing and externalizing) more thoroughly.

References

Achenbach, T.M. (1991). *Manual for the Youth Self-Report and 1991 Profile.* Burlington: University of Vermont

Alati, R., Kinner, S.A., Hayatbakhsh, M.R., Al Mamun, A., Najman, J.M., & Williams, G.M. (2008). Pathways to ecstacy in young adults; anxiety, depression of behavioural deviance? *Drug and Alcohol Dependence, 92,* 108–115.

Anderson, J.C., & Gerbing, D.W. (1988). Structural equation modeling in practice: A review and recommended two-step approach. *Psychological Bulletin 103,* 411–423.

Arseneault, L., Cannon, M., Poulton, R., Murray, R., Caspi, A., & Moffitt, T.E. (2002). Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *British Medical Journal, 325,* 1212–1213.

Bentler, P.M. (1990). Comparative fit indexes in structural models. *Psychological Bulletin, 107,* 238–246.

Bentler, P.M. (1995). *EQS Structural Equations Program Manual.* Encino, CA: Multivariate Software.

Brook, J.S., Cohen, P., & Brook, D.W. (1998). Longitudinal study of co-occurring psychiatric disorders and substance use. *Journal of the American Academy of Child and Adolescent Psychiatry, 37,* 322–330.

Browne, M.W., & Cudeck, R. (1993). Alternative ways of assessing model fit. In: Bollen, K.A., & Long, J.S. (Eds.), *Testing Structural Equation Models* (pp. 136–162). Newbury Park, CA: Sage.

Buchan, B.J., Dennis, M.L., Tims, F.M., & Diamond, G.S. (2002). Cannabis use: consistency and validity of self-report, on-site urine testing and laboratory testing. *Addiction, 97,* 98–108.

Coffey, C., Lynskey, M., Wolfe, R., & Patton, G.C. (2000). Initiation and progression of cannabis use in a population-based Australian adolescent longitudinal study. *Addiction, 95,* 1679–1690.

de Winter, A., Oldehinkel, A.J., Veenstra, R., Brunnekreef, J.A., Verhulst, F.C., & Ormel, J. (2005). Evaluation of non-response bias in mental health determinants and outcomes in a large sample of pre-adolescents. *European Journal of Epidemiology, 20,* 173–181.

Degenhardt, L., Hall, W., & Lynskey, M. (2001). The relationship between cannabis use, depression and anxiety among Australian adults: findings from the National Survey of Mental Health and Well-Being. *Social Psychiatry and Psychiatric Epidemiology, 36,* 219–227.

Degenhardt, L., Hall, W., & Lynskey, M. (2003). Exploring the association between cannabis use and depression. *Addiction, 98,* 1493–1504.

Ferdinand, R.F., Blum, M., & Verhulst, F.C. (2001). Psychopathology in adolescence predicts substance use in young adulthood. *Addiction, 96,* 861–870.

Fergusson, D.M., & Boden, J.M. (2008). Cannabis use and later life outcomes. *Addiction,*
103, 969–976.

Fergusson, D.M., & Horwood, L.J. (1997). Early onset cannabis use and psychosocial adjustment in young adults. *Addiction, 92,* 279–296.

Fergusson, D.M., Horwood, L.J., & Ridder, E.M. (2005). Test of causal linkages between cannabis use and psychotic symptoms. *Addiction, 100,* 354–366.

Fergusson, D.M., Horwood, L.J., & Ridder, E.M. (2007). Conduct and attentional problems in childhood and adolescence and later substance use, abuse and dependence: results of a 25-year longitudinal study. *Drug and Alcohol Dependence, 88,* 14–26.

Fergusson, D.M., Horwood, L.J., & Swain-Campbell, N. (2002). Cannabis use and psychosocial adjustment in adolescence and young adulthood. *Addiction, 97,* 1123–1135.

Hayatbakhsh, M.R., Najman, J.M., Jamrozik, K., Mamun, A.A., Bor, W., & Alati, R. (2008). Adolescent problem behaviours predicting DSM-IV diagnoses of multiple substance use disorder. *Social Psychiatry and Psychiatric Epidemiology, 43,* 356–363.

Hayatbakhsh, M.R., McGee, T.R., Bor, W., Najman, J.M., Jamrozik, K., & Mamun, A.A. (2007b). Child and adolescent externalizing behaviour and cannabis use disorders in early adulthood: an Australian prospective birth cohort study. *Addictive Behaviors, 33,* 422–438.

Hayatbakhsh, M.R., Najman, J.M., Jamrozik, K., Mamun, A.A., Alati, R., & Bor, W., (2007a). Cannabis and anxiety and depression in young adults: a large prospective study. *Journal of the American Academy of Child and Adolescent Psychiatry, 46*, 408–417.

Harder, V.S., Stuart, E.A., & Anthony, J.C. (2008). Adolescent cannabis problems and young adult depression: male-female stratified propensity score analyses. *American Journal of Epidemiology, 168,* 592–601.

Huisman, M., Oldehinkel, A.J., de Winter, A., Minderaa, R.B., de Bildt, A., Huizink, A.C, Verhulst, F.C., & Ormel, J. (2008). Cohort profile: the Dutch 'tracking adolescents' individual lives survey; trails. *International Journal of Epidemiology. 37*, 1227–1235.

Huizink, A.C., Ferdinand, R.F., Ormel, J., & Verhulst, F.C. (2006). Hypothalamicpituitaryadrenal axis activity and early onset of cannabis use. *Addiction, 101,* 1581–1588.

Kandel, D.B., Davies, M., Karus, D., & Yamaguchi, K. (1986). The consequences in young adulthood of adolescent drug involvement. An overview. *Archives of General Psychiatry, 43,* 746–754.

Kandel, D.B., Yamaguchi, K., & Chen, K. (1992). Stages of progression in drug involvement from adolescence to adulthood: further evidence for the gateway theory. *Journal of Studies on Alcohol, 53*, 447–457.

Kendler, K.S., Karkowski, L.M., Neale, M.C., & Prescott, C.A. (2000). Illicit psychoactive substance use, heavy use, abuse and dependence in a US population-based sample of male twins. *Archives of General Psychiatry, 57*, 261–269.

Kendler, K.S., Prescott, C.A., Myers, J. & Neale, M.C. (2003). The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. *Archives of General Psychiatry, 60,* 929–937.

Kessler, R.C., Amminger, G.P., Aguilar-Gaxiola, S., Alonso, J., Lee, S., & Ustun, T.B. (2007). Age of onset of mental disorders: a review of recent literature. *Current Opinion in Psychiatry, 20,* 359–364.

Khantzian, E.J. (1985). The self-medication hypothesis of addictive disorders – focus on heroin and cocaine dependence. *American Journal of Psychiatry, 142,* 1259–1264.

Korhonen, T., Prince van Leeuwen, A., Reijneveld, S.A., Ormel, J., Verhulst, F.C., & Huizink, A.C. (2010). Externalizing behaviour problems and cigarette smoking as predictors of cannabis use: the TRAILS study *Journal of the American Academy of Child and Adolescent Psychiatry, 49*, 61–69.

King, S.M., Iacono, W.G., & Mcgue, M. (2004). Childhood externalizing and internalizing psychopathology in the prediction of early substance use. *Addiction, 99,* 1548–1559.

Lynskey, M.T., Heath, A.C., Nelson, E.C., Bucholz, K.K., Madden, P.A.F., Slustke, W.S., Statham, D.J., & Martin, N.G. (2002). Genetic and environmental contributions to cannabis dependence in a national young adult twin sample. *Psychological Medicine, 32,* 195–207.

Marsman, R., Swinkels, S.H.N., Rosmalen, J.G.M., Oldehinkel, A.J., Ormel, J., & Buitelaar, J.K. (2008). HPA-axis activity and externalizing behaviour problems in early adolescents from the general population: the role of comorbidity and gender – the TRAILS study. *Psychoneuroendocrinology, 33*, 789–798.

Mcgee, R., Williams, S., Poulton, R., & Moffitt, T. (2000). A longitudinal study of cannabis use and mental health from adolescence to early adulthood. *Addiction, 95,* 491–503.

Monshouwer, K., Van Dorsselaer, S., Verdurmen, J., Ter Bogt, T., De Graaf, R., & Vollebergh, W. (2006). Cannabis use and mental health in secondary school children. Findings from a Dutch survey. *British Journal of Psychiatry, 188,* 148–153.

Monshouwer, K., Smit, F., de Graaf, R., van Os, J., & Vollebergh, W. (2005). First cannabis use: does onset shift to younger ages? Findings from 1988 to 2003 from the Dutch National School Survey on Substance Use. *Addiction, 100,* 963–970.

Moore, T.H.M., Zammit, S., Lingford-Hughes, A., Barnes, T.R.E., Jones, P.B., Burke, M., & Lewis, G. (2007). Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet, 370,* 319–328.

Offord, D.R., Boyle, M.H., Racine, Y., Szatmari, P., Fleming, J.E., Sanford, M., Lipman, E.L., 1996. Integrating assessment data from multiple informants. *Journal of the American Academy of Child and Adolescent Psychiatry, 35*, 1078–1085.

Ormel, J., Oldehinkel, A.J., Ferdinand, R.F., Hartman, C.A., De Winter, A.F., Veenstra, R., Vollebergh, W., Minderaa, R.B., Buitelaar, J.K., & Verhulst, F.C. (2005). Internalizing and externalizing problems in adolescence: general and dimension-specific effects of familial loadings and preadolescent temperament traits. *Psychological Medicine, 35*, 1825–1835.

Patton, G.C., Coffey, C., Carlin, J.B., Degenhardt, L., Lynskey, M., & Hall, W. (2002). Cannabis use and mental health in young people: cohort study. *British Medical Journal,* 325, 1195–1198.

Pedersen, W., Mastekaasa, A., & Wichstrom, L. (2001). Conduct problems and early cannabis initiation: a longitudinal study of gender differences. *Addiction, 96,* 415–431.

Raine, A., (1996). Autonomic nervous system factors underlying disinhibited, antisocial, and violent behaviour. Biosocial perspectives and treatment implications. *Annals of the New York Academic Sciences, 794*, 46–59.

Rutter, M., Silberg, J., O'Conner, T., & Simonoff, E. (1999). Genetics and child psychiatry: II empirical research findings. *Journal of Child Psychology and Psychiatry, 40,* 19–55.

Schneider, M. (2008). Puberty as a highly vulnerable developmental period for the consequences of cannabis exposure. *Addiction Biology, 13,* 253–263.

Shelton, K.H., Liffor, K., Fowler, T., Rice, F., Neale, M., Gordon, H., Thapar, A., & van den Bree, M. (2007). The association between conduct problems and the initiation and progression of marijuana use during adolescence: a genetic analysis across time. *Behavior Genetics, 37,* 314–325.

Steiger, J.H. (1998). A note on multiple sample extensions of the RMSEA fit index. *Structural Equation Modeling, 5,* 411–419.

van Laar, M., van Dorsselaer, S., Monshouwer, K., de Graaf, R., 2007. Does cannabis use predict the first incidence of mood and anxiety disorders in the adult population? *Addiction 102,* 1251–1260.

Veenstra, R., Lindenberg, S., Oldehinkel, A.J., De Winter, A.F., & Ormel, J., (2006). Temperament, environment, and antisocial behaviour in a population sample of preadolescent boys and girls. *International Journal of Behavioral Development, 30,* 422–432.

Veenstra, R., Lindenberg, S., Oldehinkel, A.J., De Winter, A.F., Verhulst, F.C., & Ormel, J. (2005). Bullying and victimization in elementary schools: a comparison of bullies, victims, bully/victims, and uninvolved preadolescents. *Developmental Psychology, 41,* 672–682.

Verhulst, F.C., & Achenbach, T.M. (1995). Empirically based assessment and taxonomy of psychopathology – cross-cultural applications – a review. *European Child and Adolescent Psychiatry, 4,* 61–76.

White, H.R., Loeber, R., Stouthamer-Loeber, M., & Farrington, D.P. (1999). Developmental associations between substance use and violence. *Developmental Psychopathology, 11*, 785–803.

Wittchen, H.U., Frohlich, C., Behrendt, S., Gunther, A., Rehm, J., Zimmermann, P., Lieb, R., & Perknigg, A. (2007). Cannabis use and cannabis use disorders and their relationship to mental disorders: a 10-year prospective-longitudinal community study in adolescents. *Drug and Alcohol Dependence, 88,* S60–S70.

Young, S.E., Stallings, M.C., Corley, R.P., Krauter, K.S., & Hewitt, J.K. (2000). Genetic and environmental influences on behavioural disinhibition. *American Journal of Medical Genetics, 96,* 684–695.