Externalizing Behavior Problems and Cigarette Smoking as Predictors of Cannabis Use: The TRAILS Study

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Objective: To examine externalizing behavior problems and cigarette smoking as predictors of subsequent cannabis use. **Method:** Dutch adolescents (N = 1,606; 854 girls and 752 boys) from the TRacking Adolescents' Individual Lives Survey (TRAILS) ongoing longitudinal study were examined at baseline (ages 10–12 [T1]) and at two follow-up assessments (ages 12–15 [T2] and 15–18 [T3]). The analysis focused on DSM-IV externalizing behavior (conduct, attention deficit hyperactivity, and oppositional) problems at T1, assessed by the Youth Self Report and the Child Behavior Check List, on self-reported ever smoking at T2, and on cannabis use at T3. **Results:** All associations of parent-rated externalizing behavior problems with cannabis were mediated by earlier smoking. Considering self-reported problems, none of these associations with cannabis were mediated by smoking, except the influence of self-reported conduct problems in girls. Interestingly, even after adjusting for externalizing problems, earlier smoking independently and consistently predicted cannabis use. The adjusted odds ratios for smoking varied in boys from 4.8 to 5.2 (ever) from 10 to 12 (daily) and from 22 to 23 (early-onset) whereas in girls from 4.9 to 5.0, 5.6 to 6.1, and 27 to 28, respectively ($p < .001$ for all). **Conclusions:** Our findings challenge the view that externalizing behavior problems directly predict cannabis initiation. Such associations were inconsistent across informants and sexes and were often mediated by earlier smoking. Early smoking onset is a powerful predictor of later cannabis initiation independent of preceding externalizing behavior problems. Although externalizing behavior problems are important as a starting point for substance use trajectories, early-onset smoking should be identified as an important marker of cannabis use risk. J. Am. Acad. Child Adolesc. Psychiatry, 2010;49(1):61–69. **Key Words:** externalizing problems, cigarette smoking, cannabis, adolescents

The harmful consequences of cannabis use have fueled researchers to elucidate vulnerabilities in adolescents who initiate and subsequently maintain cannabis use. Given that cannabis is one of the most commonly used drugs in western civilization,[1] detecting vulnerabilities is important to prevent cannabis initiation. Several studies have examined genetic and environmental predictors of cannabis use.[2] Genetic factors have a modest effect, whereas the influence of environmental factors predominates among adolescents.[3-4] Among environmental influences, several individual, family, and peer factors have been studied.[5-10]

Many researchers have focused on the influences of externalizing behaviors (ExtB), such as attention deficit hyperactivity, conduct, and oppositional problems, on the onset of substance use, including cannabis use. Literature has established that externalizing disorders are commonly comorbid with substance use disorders among adolescents.[11-13] It should be noted, however, that many studies used all-male or unbalanced-gender designs based on clinical populations.[14-16] These samples are not representative of the general population but are biased towards extreme, problematic cases of ExtB. Nonetheless, several general population studies have also shown that ExtB problems are associated with tobacco[17,18] and cannabis use.[18,19] In particular, conduct disorders predict later cannabis use.[20] Furthermore, cigarette smoking, particularly early-onset, is re-

lated to an increased risk of cannabis use.[8,21-23] For example, in a Finnish study, cigarette smoking by the age of 12 showed more than 20-fold odds for later cannabis use, whereas the ExtB-to-cannabis associations were weaker and less consistent.[8]

This study addresses the following questions: How important are ExtB problems and early smoking onset in predicting cannabis use? Do ExtB problems play an independent role after early cigarette smoking is taken into account? Comprehensive data within the TRacking Adolescents' Individual Lives Survey (TRAILS) allowed us to include DSM-IV based ExtB problem measures, instead of the personality scales used in previous studies. This study provides further understanding of the interplay between externalizing problem behaviors and cigarette smoking as predictors of cannabis use among both genders.

METHOD

Subjects and Procedures

TRAILS is a prospective population study of Dutch adolescents investigated biennially until at least the age of 25 years. This study involves data from the first, second, and third assessment waves, conducted from March 2001 to July 2002, from September 2003 to December 2004, and from September 2005 to August 2008, respectively. During the baseline measurement (T1) 2,230 subjects were enrolled (mean age 11.1 years, SD 0.55, 50.8% girls). During the first follow-up (T2) 2,149 subjects (mean 13.6, SD 0.53, 51.0% girls) participated, whereas during the second follow-up (T3) 1,816 subjects (mean 16.3, SD 0.73, 52.3% girls) participated. Previous TRAILS studies have reported more detailed descriptives.[24,25]

At T1 and T3, well-trained interviewers visited one of the parents at their homes for an interview covering a wide range of topics, including the child's developmental history and somatic health, parental psychopathology, and care use. Parents also filled out a questionnaire. Adolescents were assessed at school or other test locations, where they completed questionnaires in groups, supervised by one or more TRAILS assistants during all measurements (T1–T3). The second assessment involved only questionnaires completed by the adolescent, parents, and teachers.[24,25]

These analyses were based on 1,606 adolescents (854 girls, 752 boys) with nonmissing data on child-rated externalizing problems at T1, smoking at T2, and cannabis use at T3. The mean age at T3 was 16.3 years (SD 0.67, range 14.7–18.4). Because of missing values in parental ratings, those analyses included 1,537 adolescents (813 girls, 724 boys).

Measures

Substance use was assessed using the Youth Self-Report (YSR) and a TRAILS-developed survey.[26] Cannabis use was measured at T1, T2, and T3. The outcome variable for these analyses was self-reported ever use of cannabis at T3. Age of onset and frequency of use were also assessed.

The ExtB problems were assessed using the Child Behavior Checklist (CBCL) and the YSR.[27-29] The CBCL is a 120-item parent questionnaire designed to assess problems in 4- to 18-year-olds. The YSR,[28,30] similar to the CBCL, is a self-report questionnaire for adolescents. All items in both questionnaires ask about behavioral or emotional problems that occurred within the past 6 months before the questionnaire fill-in date. Reliability and validity of the Dutch translation of the CBCL and YSR (American version) have been confirmed.[31] The YSR and CBCL can be scored on DSM-IV scales as constructed by Achenbach et al.[32] for conduct (CD), oppositional (OD), and attention deficit/hyperactivity (ADH) problems. For this study, we used a sum score of these scales, reflecting ExtB problems in general. It is important to notice that the ExtB problems (OD, CD, and ADH) used in our study are not diagnoses but CBCL/YSR subscales that are based on questions that correspond to DSM IV criteria.

Smoking was assessed in three ways. First, ever smoking at T2 as a dichotomous variable, where the first category included those who had never smoked, whereas the second category included the smokers, i.e., those who had smoked at least one or two times. Second, ever daily smoking at T2 analyzed as a dichotomy (no/yes). Third, using data on age of onset reported retrospectively at T3, we created a variable: 0 = I have never smoked, 1 = I had my first cigarette after age of 12, 2 = I had my first cigarette at age of 12 or earlier. This variable allowed us to replicate the findings from a population-based longitudinal study among Finnish adolescent twins with three assessments at similar ages, in which smoking onset by the age of 12 was found to be a powerful predictor of cannabis use.[8]

For covariates, information about gender and age were collected via the Parent and Adolescent questionnaires. Familial loading information of psychopathology, including substance dependence at T1, was collected via the TRAILS Family History Interview, by interviewing a parent (usually the mother). Five dimensions of psychopathology were assessed: depression, anxiety, substance dependence, persistent antisocial behavior, and psychosis. Each dimension was introduced by a vignette that described the main DSM-IV characteristics, followed by a series of questions assessing lifetime occurrence, professional treatment, and medication use.[33]

Statistical Methods

In accordance with previous research suggesting gender differences,[7,31,34] and based on the means of the

TABLE 1 Means of the DSM-IV Scores (SD) Among Boys and Girls[a]: Parental Ratings (CBCL) and Child Ratings (YSR) at T1 (Age 10–12): The TRAILS Study

DSM-IV Externalizing Behavior Problems Score	CBCL Parental Ratings			YSR Child Ratings		
	Boys (n = 724) Mean (SD)	Girls (n = 813) Mean (SD)	*p*	Boys (n = 752) Mean (SD)	Girls (n = 854) Mean (SD)	*p*
Conduct Problems	2.75 (2.84)	1.65 (2.02)	<.001	4.19 (3.25)	2.72 (2.26)	<.001
Attention Deficit Hyperactivity Problems	4.37 (3.32)	3.28 (2.92)	<.001	4.21 (2.53)	4.08 (2.39)	.296
Oppositional Problems	3.07 (2.09)	2.64 (1.95)	<.001	2.36 (1.79)	2.07 (1.64)	.001
Externalizing Problems[b]	10.2 (7.08)	7.57 (5.92)	.001	10.8 (6.31)	8.86 (5.17)	.001

Note: CBCL = Child Behavior Check List; TRAILS = TRacking Adolescents' Individual Lives Survey; YSR = Youth Self Report.
[a]*Among participants with nonmissing data on smoking at T2 and cannabis use at T3.*
[b]*Sum of conduct, attention deficit hyperactivity, and oppositional problems scores.*

DSM-IV scale sum scores showing significant sex differences in behavioral problems (Table 1), we conducted all analyses by gender. To test specifically for sex differences, we also examined gender interactions. Because the sum scores tended to be skewed, we used the weighted means. Because of modest correlation between the child- and parent-reported ExtB problems sum scores ($r = 0.39$), we analyzed these ratings as separate variables. The main analyses conducted were logistic regression models using the STATA statistical package, version 9.[35]

We conducted logistic regressions to investigate ExtB problems and cigarette smoking as cannabis use predictors. We tested whether the associations of ExtB problems and cigarette smoking on cannabis use were independent of each other or whether they were mediated or moderated by each other. Considering mediation, MacKinnon et al.[36] suggest that complete mediation occurs if the direct association becomes zero. However, in psychological research it is unrealistic to show complete mediation by a single variable. Thus, in our study, mediation was considered to occur if the direct association became nonsignificant, even if there was some effect left. Regarding moderation, we tested how ExtB and smoking influence the associations of each other on cannabis. If smoking is a moderator, the association between ExtB and cannabis depends on smoking status and a significant ExtB × smoking interaction exists.[37]

We focused on cannabis use predictors. To investigate mediation, we first analyzed whether ExtB problems predict smoking. Second, we analyzed whether that smoking predicts cannabis use. Third, we analyzed whether ExtB predict cannabis use. For each ExtB measure, we examined whether the odds ratio (OR) was attenuated and whether the *p* value became nonsignificant ($p > .05$) when smoking was added to the model. To investigate moderation, we added ExtB × smoking interactions into the model. We also tested gender × ExtB × smoking interactions. We repeated all analyses regarding new onsets of cigarette smoking at T2 and cannabis use at T3 by excluding those reporting ever smoking or cannabis use at a previous measurement. All analyses were adjusted for exact assessment age at the outcome: T2 when smoking was the outcome, whereas T3 when cannabis use was the outcome. Models including ExtB problems were analyzed using the compiled externalizing score (OD+CD+ADH), as well as the individual scales (OD, CD, and ADH). However, the models analyzing the influence of smoking on cannabis use were adjusted for the compiled externalizing scores. Further adjustment included familial loading to substance use and antisocial behaviors.[33]

RESULTS

By the T3 survey 30.5% of adolescents (29.7% girls, 31.6% boys, $p = .41$) had used cannabis at least once; 10.0% had used it one to three times (11.2% girls, 8.5% boys), 6.6% had used it four to nine times (7.5%, 5.6%), 4.7% had used it 10 to 19 times (4.7%, 4.8%), and 9.2% had used it 20 times or more (6.0%, 12.8%). Of the T3 respondents 0.4% reported they had their first cannabis experiment before the age of 12 years, the lowest age of the T2 survey participants, whereas 14.1% reported experimenting by the age of 15, the highest age within that survey. Concerning cigarette smoking at T2, 34.8% (37.5% girls, 31.8% boys, $p < .05$) had ever smoked at least one cigarette, whereas 11.0% (13.6%, 8.0%) reported having ever been daily smokers. At the T3 survey, 58.7% of girls and 53.3% of boys had ever smoked a cigarette. Of the T3 respondents, 25.2% of girls and 24.1% of boys reported they had their first cigarettes by the age of 12. Among most participants, smoking was initiated first and cannabis use was initiated after smoking. There were few devi-

TABLE 2 Odds Ratio (OR) (95% CI) of Age-Adjusted Logistic Regressions on Externalizing Problems (T1) Predicting Ever Cigarette Smoking (T2): The TRAILS Study

	Boys			Girls		
Predictor at T1	**n**	**OR**	**95% CI**	**n**	**OR**	**95% CI**
DSM-IV Conduct Problems						
Parent	724	13.6	5.22, 35.4	813	30.9	8.67, 109
Child	752	7.70	3.73, 15.9	852	15.3	5.81, 40.2
DSM-IV Attention Deficit Hyperactivity Problems						
Parent	724	1.82	1.31, 2.53	812	2.42	1.71, 3.43
Child	752	1.70	1.11, 2.60	854	1.60	1.06, 2.42
DSM-IV Oppositional Problems						
Parent	724	1.89	1.30, 2.76	812	1.92	1.32, 2.78
Child	752	2.54	1.65, 3.90	851	2.34	1.53, 3.60
DSM-IV Externalizing Problems[a]						
Parent	724	1.46	1.23, 1.74	813	1.60	1.33, 1.92
Child	752	1.60	1.31, 1.95	854	1.57	1.27, 1.93

Note: CI = confidence interval; OR = odds ratio; TRAILS = TRacking Adolescents' Individual Lives Survey.
[a]*Sum of conduct, attention deficit hyperactivity, and oppositional problems scores.*

ations; 0.7% (n = 6) of girls and 1% (n = 9) of boys started to use cannabis first and then started to smoke cigarettes. Among those who had never smoked, 4.0% of girls and 5.2% of boys had used cannabis.

The first models examined whether ExtB problems predicted cigarette smoking. When adjusted for age at T2, baseline ExtB problems predicted ever smoking at T2 independent of informant and gender. Some of the DSM-IV scales, such as parent-reported CD, showed a strong association (Table 2). However, the 95% confidence intervals were very wide, probably because of relatively high standard deviations in the mean scores (Table 1). We also adjusted the ExtB-to-smoking associations for familial liability to substance dependence. Familial loading was associated with increased risk of smoking among girls (OR 2.54; $p < .001$), yet not among boys (OR 0.97; $p > .05$), but most of the ExtB-to-smoking associations were not attenuated if adjusted for familial liability (data not shown). Finally, we analyzed smoking initiation among 647 boys and 756 girls without cigarette smoking at baseline. The influence of child-rated ADH problems on new smoking onset did not remain significant among boys (OR 1.41; 95% CI 0.86, 2.31) nor among girls (OR 1.45; 95% CI 0.92, 2.29).

The second models considered cigarette smoking as a cannabis use predictor. Ever and daily smoking by T2 strongly predicted cannabis use at T3 for both sexes. Early onset of smoking (first cigarette by the age of 12 years) was a powerful predictor of cannabis use (boys: OR 25.0; girls: OR 29.1). When adjusting for ExtB problems at T1, these estimates of smoking were only slightly attenuated. Daily smoking at T2 had a strong influence on cannabis use, particularly among boys (age-adjusted OR 11.3), and this association became stronger when adjusted for parent-rated ExtB (Table 3). We also adjusted the smoking influences for familial liability, but those associations were slightly attenuated among girls only (data not shown). Furthermore, we analyzed new cannabis initiations among 797 girls and 691 boys who had no cannabis use at baseline or T2. We found a strong risk among those who had their first cigarette by the age of 12 (boys: OR 24.2; 95% CI 14.0, 42.1; girls: OR 28.6; 95% CI 15.7, 52.1). The risk for those who had their first cigarette after the age of 12 was also high (boys: OR 15.4; 95% CI 9.10, 26.1; girls: OR 18.2; 95% CI 10.1, 32.6), when compared with never smokers. Adjustment for familial loading did not attenuate these associations (data not shown).

The third models considered ExtB predicting cannabis use. In the age-adjusted logistic regressions, the baseline ExtB problem scores significantly increased the risk for cannabis use independent of the informant (parent or child him/herself), with the exception of the association of self-rated conduct problems among girls, which approached significance. However, when we added smoking at T2 into the model, the associations of parent-rated

TABLE 3 Odds Ratio (OR) (95% CI) of Logistic Regressions on Cigarette Smoking at T2 Predicting Cannabis Use at T3: The TRAILS Study

	Boys						Girls					
	Adjusted for T3 Age n = 752		Adjusted for T3 Age and Parent Rated T1 Externalizing Problems[a] n = 724		Adjusted for T3 Age and Child Rated T1 Externalizing Problems[a] n = 752		Adjusted for T3 Age n = 854		Adjusted for T3 Age and Parent Rated T1 Externalizing Problems[a] n = 813		Adjusted for T3 Age and Child Rated T1 Externalizing Problems[a] n = 854	
Predictor at T2	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Ever smoking at T2												
Never	1.00		1.00		1.00		1.00		1.00		1.00	
Ever	5.28	3.76, 7.43	5.19	3.65, 7.37	4.84	3.43, 6.84	5.11	3.71, 7.04	5.02	3.60, 6.99	4.92	3.56, 6.79
	n = 748		**n = 721**		**n = 748**		**n = 846**		**n = 807**		**n = 844**	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Daily smoking at T2												
Never	1.00		1.00		1.00		1.00		1.00		1.00	
Ever	11.3	5.69, 22.3	11.6	5.64, 23.7	10.1	5.03, 20.2	5.67	3.70, 8.68	6.07	3.87, 9.53	5.58	3.63, 8.59
	n = 761		**n = 732**		**n = 761**		**n = 864**		**n = 822**		**n = 864**	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Age of smoking onset												
Never	1.00		1.00		1.00		1.00		1.00		1.00	
Late (>12 years)	15.9	9.43, 27.0	15.3	9.01, 26.0	16.0	9.43, 27.2	18.2	10.1, 32.6	17.2	9.58, 31.0	18.1	10.1, 32.6
Early (≤12 years)	25.0	14.5, 43.2	22.7	13.0 39.5	22.0	12.7, 38.2	29.1	16.0, 53.0	27.5	15.0, 50.4	27.9	15.3, 50.8

Note: CI = confidence interval; OR = odds ratio; TRAILS = TRacking Adolescents' Individual Lives Survey.
[a]Sum of conduct, attention deficit hyperactivity, and oppositional problems scores.

problem behaviors were clearly attenuated, resulting in nonsignificant values for all behaviors. The associations of child-rated behaviors were less dramatically attenuated through cigarette smoking. Among girls the associations of CD and OD became nonsignificant, whereas the association of ADH problems remained significant. Among boys the associations of all child-rated ExtB remained significant independent of the smoking association (Table 4).

Similar results were observed when adjusting the problem behavior influences for age of smoking onset instead of ever smoking (data not shown). Further, familial loading to substance use as such increased the risk of cannabis use significantly among girls (OR 2.02; 95% CI 1.36, 3.01), but not among boys (OR 0.73; 95% CI 0.48, 1.30). However, the influences of the ExtB were not significantly attenuated if adjusted for familial liability (data not shown).

We also analyzed new cannabis use onset among those with no use at baseline or at T2. Within the parental ratings, oppositional problems among those 660 boys (OR 1.35; 95% CI 0.90, 2.04) and 758 girls (OR 1.38; 95% CI 0.91, 2.09), as well as ADH problems among girls (OR 1.41; 95% CI 0.96, 2.07) did not remain significant predictors of new onset of cannabis use. All child-rated problem behaviors remained significant, except for CD (OR 1.44; 95% CI 0.49, 4.22) and OD (OR 1.57; 95% CI 0.97, 2.53) among girls.

Finally, interactions were tested. When con-

TABLE 4 Odds Ratio (OR) (95% CI) of Logistic Regressions on DSM-IV Externalizing Problems (T1) Predicting Cannabis Use (T3): The TRAILS Study

	Boys						Girls					
Predictor at T1	**Adjusted for T3 Age**			**Adjusted for T3 Age and T2 Ever Smoking**			**Adjusted for T3 Age**			**Adjusted for T3 Age and T2 Ever Smoking**		
DSM-IV Conduct Problems	**n = 724 (parental) n = 752 (child)**						**n = 813 (parental) n = 852 (child)**					
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Parent	4.37	1.72, 11.1	.002	1.93	0.69, 5.38	.208	8.59	2.49, 29.6	.001	3.12	0.83, 11.7	.091
Child	7.87	3.77, 16.4	<.001	4.64	2.11, 10.2	<.001	2.59	0.99, 6.78	.053	0.97	0.34, 2.74	.951
DSM-IV ADH Problems	**n = 724 (parental) n = 752 (child)**						**n = 812 (parental) n = 854 (child)**					
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Parent	1.66	1.19, 2.31	.003	1.41	0.98, 2.02	.065	1.50	1.05, 2.13	.025	1.11	0.75, 1.63	.594
Child	2.18	1.42, 3.37	<.001	1.96	1.23, 3.12	.004	1.96	1.27, 3.04	.003	1.77	1.11, 2.82	.017
DSM-IV Oppositional Problems	**n = 724 (parental) n = 752 (child)**						**n = 812 (parental) n = 851 (child)**					
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Parent	1.54	1.06, 2.26	.025	1.26	0.84, 1.91	.266	1.49	1.02, 2.19	.040	1.23	0.81, 1.85	.323
Child	2.93	1.89, 4.55	.009	2.36	1.47, 3.78	<.001	1.81	1.16, 2.82	.009	1.41	0.87, 2.28	.166
DSM-IV Externalizing Problems[a]	**n = 724 (parental) n = 752 (child)**						**n = 813 (parental) n = 854 (child)**					
	OR	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Parent	1.32	1.11, 1.57	.002	1.18	0.97, 1.42	.089	1.29	1.07, 1.55	.007	1.11	0.91, 1.35	.307
Child	1.75	1.42, 2.14	<.001	1.56	1.26, 1.95	<.001	1.42	1.15, 1.77	.001	1.25	0.99, 1.57	.061

Note: ADH = Attention Deficit Hyperactivity; CI = confidence interval; OR = odds ratio; TRAILS = TRacking Adolescents' Individual Lives Survey.
[a]*Sum of conduct, attention deficit hyperactivity, and oppositional problems scores.*

sidering ever smoking moderating the influence of ExtB, we found one interaction for girls (p = .02): among the 513 girls who never smoked cigarettes, parent-rated oppositional problem score did not significantly influence cannabis use (OR 0.71; 95% CI 0.37, 1.36). In contrast, among the 299 girls who ever smoked at least one cigarette, that score significantly increased the likelihood of trying cannabis (OR 1.86; 95% CI 1.06, 3.25). No significant daily smoking × ExtB interactions existed. Concerning gender interactions, sex × conduct problem interaction approached significance (p = .07), suggesting that self-report scores predicted cannabis use more strongly among boys than girls. Also, daily smoking × sex interaction approached significance (p = .08), suggesting that daily smoking predicted cannabis more strongly among boys than among girls (data not shown).

DISCUSSION

Our findings suggest that when early-onset smoking is taken into account, ExtB problems have inconsistent associations on subsequent cannabis use initiation. A striking feature is that particularly early-onset smoking mediates the associations of parent-rated behavior problems with cannabis use, although the role of self-reported ExtB problems is relatively independent of smoking among boys.

These results somewhat differ from previous findings, mostly based on studies in the United States. A population-based twin sample[20]

showed higher odds for cannabis use/abuse for individuals with CD assessed at age 17 years. Tarter et al.[6] reported, among 224 male adolescents, that delinquency in childhood was more strongly related to marijuana than licit drug use. McGue and Iacono[38] reported that adolescent problem behavior predicted later psychopathology, including substance use disorders. In our study, smoking onset before the age of 12 was a strong independent predictor of later cannabis use. The associations of smoking on cannabis use were mostly not mediated through ExtB problems or familial liability to substance use. Such strong association of cigarette smoking may partly be explained by changing attitudes toward smoking, i.e., smoking is becoming more "deviant" for adolescents. This could partly explain why some of our findings differ from earlier studies in which more independent associations for ExtB problems existed. Further, differences in results between US and Dutch studies may also reflect differences in environmental and cultural conditions between countries in relation to cannabis. Our findings do not invalidate earlier studies showing a robust relationship of ExtB to drug use but indicate that smoking may be an essential mediating variable of this relationship.

Moreover, this study on Dutch adolescents replicates the powerful association of early-onset cigarette smoking on subsequent drug use, reported earlier in Finnish adolescents of similar age.[8] Strikingly, both studies show risk estimates exceeding 20 for adolescents who had their first cigarette by the age of 12. In both studies, this association remained significant even when adjusted for familial liability and ExtB problems. To adjust for familial influences, the Finnish twin study applied a discordant twin pair design, whereas the Dutch study adjusted for familial drug abuse risk data collected within TRAILS. The Finnish study also adjusted for peer substance use and socioeconomic status of the family. Although the findings of these two studies establish a link between early-onset smoking and subsequent cannabis use, neither of them provides exhaustive evidence for causality. Thus it remains a challenge to show whether this is a causal link reflecting the "gateway" hypothesis[39] or whether there are common genetic or environmental risk factors for both early smoking onset and cannabis use initiation.[40] Despite the replicated association between early smoking onset and subsequent cannabis use initiation, independent of ExtB problems, we should note that different scales detecting ExtB were applied in the Dutch and the Finnish studies. Although both studies used continuous measurement scales, the Finnish scale consisted of the Multidimensional Peer Nomination Inventory Teacher and Parental ratings, where the scales for hyperactivity–impulsivity, aggression, and inattention formed a factor for ExtB problems.[41] The Dutch analyses were based on separate CBCL[27] and YSR DSM-IV scales,[28,30] which clearly differentiate among ADH, CD, and OD but can also be used as a sum score of these scales reflecting ExtB problems in general.

Based on statistics in 2003, 28% of adolescents in the Netherlands and 11% in Finland reported using cannabis.[42] Part of the differences between the two countries may be related to different legislations of cannabis use. In the Netherlands, cannabis is "semi-legal," i.e., officially tolerated for both possession and sales in restricted locations and quantities.[43] Strikingly, in both studies, early-onset smoking overshadowed the predictive power of ExtB with regard to cannabis initiation.

Considering sex differences and interactions, boys scored higher in ExtB, whereas cigarette smoking was more common in girls. However, there was no significant sex difference in ever use of cannabis. Although there were no consistent sex interactions across ExtB problems, conduct problems tended to predict cannabis use more strongly among boys than among girls. Also, daily smoking predicted cannabis more strongly among boys than among girls. Interestingly, familial loading to substance use and ExtB as such increased the risk of cannabis use significantly among girls but not among boys. To understand the mechanisms underlying such sex interactions remains a challenge for further studies, but one potential explanation is that familial influences may be less important for males in this context.

Concerning moderating effects, i.e., smoking × ExtB interactions, we found only one significant interaction. Oppositional problems did not influence cannabis use when looking at girls who had never smoked, whereas for girls who had smoked there was almost a twofold increased risk for the likelihood of trying cannabis. This means that among girls the influence of oppositional problems is actually conditional on smoking status. We are not aware of similar findings in any other studies.

An important strength of our study was that

we included information from both parents and adolescents. Another strength is a longitudinal prospective design allowing assessment of children and adolescents throughout different developmental stages, even before substance use initiates. Our sample seems to be representative with regard to tobacco and cannabis use prevalence rates in the Netherlands: the national prevalence of ever smoking by the age of 16 was 57%,[42] whereas in the TRAILS sample this was 56% at T3. Those rates of ever using cannabis were 28% and 31%, respectively.

A potential limitation is the use of a DSM-IV oriented scale rather than actual DSM diagnoses. Another limitation is that we investigated substance use initiation only, and we have no information on how smoking and ExtB problems could be related to substance abuse or dependence. Moreover, we mostly included the rating of the mother instead of the father on problem behaviors. This may have limited our understanding of their adolescent's ExtB, although there is evidence for a rather strong agreement between mothers' and fathers' ratings on their children's behavior.[44] Finally, our sample did not represent the full range of ethnic diversity existing in the Netherlands, but included mostly adolescents of Dutch origin.

To conclude, several associations of ExtB problems with cannabis use were mediated through smoking. Similar to the earlier findings among Finnish adolescents, early-onset cigarette smoking was a powerful predictor of later cannabis use among Dutch adolescents as well. This early smoking influence seems to be relatively independent of ExtB problems. Such a consistent finding across two countries has implications for prevention. Although ExtB problems are important as a starting point for substance use trajectories, early-onset smoking should be identified as an important marker of cannabis use risk. Interventions to reduce ExtB may still be useful in reducing the onset of cannabis use, but the mechanism might be indirect via reducing early smoking onset. &

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