Role of individual, peer and family factors in the use of cannabis and other illicit drugs: A longitudinal analysis among Finnish adolescent twins

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Abstract

Background—Although use of illicit drugs shows varying degree of heritability, the influence of shared and unique environmental factors predominate among adolescents. We explored factors predicting use of cannabis and other illicit drugs among Finnish adolescent twins.

Methods—We used longitudinal data from the *FinnTwin12–17* study with baseline at age 11–12 and follow-up at ages 14 and 17½, including 4138 individuals. The outcome was self-reported ever use of cannabis or other illicit drugs at age 17½. The potential predictors were measures reported by the twins, their parents or teachers. As individual factors we tested smoking, alcohol use, behavioral and emotional problems; as peer factors: number of smoking friends and acquaintances with drug experience; as family factors: parental substance use, socio-economic status and prenatal exposure to nicotine. We used logistic regression models, controlling for twinship, age and sex, to compute Odds Ratios (OR) for each potential predictor. To adjust for within-family confounds, we conducted conditional logistic regressions among 246 twin pairs discordant for drug use.

Results—13.5 % of subjects had initiated use of cannabis or other illicit drugs by age of 17½. When adjusted for within-family confounds, smoking, drinking, and aggressiveness, as well as smoking and drug use among peers predicted use of illicit drugs. In the final regression model, the significant predictors were female sex, early smoking onset, drinking to intoxication, having smoking peers and acquaintances with drug experience, father's weekly drinking to intoxication, and aggressive behavior among boys. Smoking initiation by age of 12 was the most powerful predictor among individuals (OR = 26, $p < 0.001$) and within discordant pairs (OR = 22, p < 0.001).

Conclusions—Early onset smoking is a powerful predictor for subsequent use of illicit drugs among Finnish adolescents, but the causal nature of this relationship needs to be clarified.

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Introduction

Use of psychoactive substances causes a significant health and social burden worldwide. Most of the approximated 10% health burden is accounted for tobacco and alcohol, but also illicit drugs remain important for a wide variety of health and social problems (World Health Organization, 2004). In developed countries most of illicit drug use is approximated to be cannabis products (marijuana, hashish) (Compton et al., 2004; Programme on Substance Abuse, 1997).

In Finland the statistics show that 14% of men whereas 11% of women had tried any illicit drugs during lifetime. Also in Finland, like in other developed countries, most of illicit drug use is cannabis. Actually, the Finnish 2003 statistics reported in the age group of 15–16 old adolescents only on cannabis use, lifetime use being 10–11% among boys whereas 11–12% among girls (Virtanen and Sjöberg, 2006). It should be noticed, that in comparison to many other developed countries (Brook et al., 2002; Monshouwer et al., 2006) cannabis use among Finnish adolescents remains much less common. This may be because cannabis is clearly an illegal substance in Finland, while alcohol as a legal substance has played a central role in Finnish substance use and abuse culture for generations. However, the proportion having ever tried cannabis had actually doubled between 1995 and 2003 from ~5% to 10–11% among the Finnish adolescents (Virtanen and Sjöberg, 2006) and that statistic did not include experimenting with other illicit drugs.

Among illicit drugs, the numerous adverse health consequences of cannabis products have been investigated more specifically (Khalsa et al., 2002). Adolescent cannabis use poses risk for subsequent depression and substance use disorders in young adulthood (Brook et al., 2002). Further, there is consistent evidence that cannabis use increases risk of psychotic outcomes (Moore et al., 2007), doubling the risk of schizophrenia (Arseneault et al., 2004). Alarmingly, early onset of cannabis use during adolescence seems to be an even stronger risk factor for later schizophrenia (Arseneault et al., 2002), the risk being significantly higher among those with specific genetic vulnerability to the condition (Caspi et al., 2005).

Some illicit drug problems, such as opioid dependence, show very high (~70%) heritability (Tsuang et al., 2001). However, for the most common drug among adolescents, cannabis heritability varies from modest (~20%) to moderate (~30%), whereas the influence of shared and unique environmental factors predominates in this population, with most estimates varying from 60% to 100% (Agrawal and Lynskey, 2006; Shelton et al., 2007). Earlier analyses among Finnish adolescent and young adult twins indicate the presence of substantial genetic effects and shared environmental effects. Also, the gene-environment interactions need to be further explored (Kaprio, 2006a). Given that environmental influences are known to be important, it seems relevant to further analyze which specific factors predict strongest use of cannabis or other illicit drugs among Finnish adolescents.

Among individual factors, use of licit substances (Agrawal et al., 2006; Gilvarry, 2000; Guxens et al., 2007a, 2007b; Kandel and Yamaguchi, 1993; Vega and Gil, 2005; Wittchen et al., 2007) has been reported consistently as a risk factor for subsequent use of illicit drugs. Characteristics related broadly to externalizing behaviors, such as impulsivity (Conway et al., 2003), early behavior problems (Kreek et al., 2005), as well as behavioral and emotional symptoms (Brook et al., 1996; Buckner et al., 2008; Huizink et al., 2006; Jane-Llopis and

Matytsina, 2006; Monshouwer et al., 2006; White et al., 2001; Wittchen et al., 2007) have been identified as risk factors for drug use. Further, influences of peers (Agrawal et al., 2007; Guxens et al., 2007a, 2007b) and parents (Chen et al., 2005; Hayatbakhsh et al., 2007), as well as unfavorable socio-economic circumstances (Compton et al., 2005) have been documented as determinants for cannabis use. Finally, there is evidence that pre-natal exposure to marijuana may be a predictor of marijuana use in adolescence (Day et al., 2006). Also, there is evidence that prenatal nicotine exposure is related to increased risk of early onset smoking or nicotine dependence among offspring (Huizink and Mulder, 2006).

Although there is quite a rich literature available on predictors of drug use worldwide, there is only one longitudinal study published among the Finnish population (Poikolainen et al., 2001). Thus, predictors of cannabis use in Finland are not well known, and might be different from countries with easier access or higher frequency of cannabis use. Also, determinants of onset during adolescence are of particular interest because it is a strong predictor of subsequent substance use or mental health disorders (Arseneault et al., 2002; Brook et al., 2002). More importantly, studying these variables in a twin population allows one to dismiss some known within-family confounds by testing relationships in discordant twin pairs. Finnish longitudinal twin data offer a unique source for learning more about the causal nature and role of putative risk factors using multivariate models of genetic informative data. We are aware of only one other genetically informative longitudinal study of marijuana use, one conducted among female adolescent twins (Agrawal et al., 2007). That study found that among girls alcohol use and peer attitudes towards cannabis were significant predictors of cannabis use. However, although the analysis adjusted for zygosity, the study did not make use of discordant twins in a matched "case-control" design. Moreover, that analysis was done among girls only (Agrawal et al., 2007). Another twin study was a retrospective cross-sectional investigation among young adults comparing escalation of drug use among early-onset cannabis users and their co-twin controls, i.e. twin pairs discordant for early cannabis use. This study suggested that escalation of drug use cannot be solely explained by common predisposing genetic or shared environmental factors and highlighted the role of peer influences on drug use (Lynskey et al., 2003).

In summary, earlier studies suggest a wide variety of factors associated with use of illicit drugs, particularly use of cannabis. Most of them can be identified within individual, family and peer related influences. The aim of the present study was to identify factors predicting use of cannabis and other drugs among the Finnish adolescent twin population. To fulfill this aim we considered individual, peer and family factors which we selected based on earlier studies. In comparison to an earlier Finnish investigation (Poikolainen et al., 2001), and most other earlier studies, the current study used longitudinal data from adolescent female and male twins to further explore the plausible causal nature of the potential predictors of drug use while controlling for between-family confounds. In doing this, we will enrich the current knowledge on predictors of illicit drug use among adolescents.

2. Methods

2.1. Sample and participants

The longitudinal *FinnTwin12–17* study, including five consecutive birth cohorts, was started in 1994 to examine genetic and environmental determinants of precursors of health-related behaviors in initially 11–12-year-old twins (twins born 1983–1987). The study has a two-stage sampling design. The larger, first-stage study is an epidemiological investigation of five consecutive and complete birth cohorts of Finnish twin children (n = 5600 twins), including questionnaire assessments of both twins and parents at baseline, late in the year before the twins reach age 12 (87% participation rate), with follow-up of all twins at age 14 (response rate 88%; 4740 questionnaires were returned out of 5362 mailed), and again at age 17.5 years

(92% participation rate). Thus, the epidemiological first stage includes some 5600 twins and some 5000 parents. The second stage nested within this epidemiological study is an intensive assessment of a sub-sample with 1035 families. The study protocol was approved by the IRB of Indiana University and by the Ethical Committee of the University of Helsinki. The parents provided written informed consent for participation (Kaprio et al., 2002; Kaprio, 2006b).

For the current study, we used data collected within the epidemiological first stage baseline at ages 11–12 and two follow-ups at target ages of 14 and 17.5. The predictors were measured at baseline and first follow-up, except age of smoking onset reported retrospectively at age of 17.5. The outcome variable was measured at the second follow-up, which was initiated in autumn of 2000 and was completed in spring of 2005 for the five birth cohorts. The questionnaire was sent to the twins of each twin family that returned the family questionnaire. In all, 4236 questionnaires were returned out of 4594 mailed, a response rate of 92.2% for those already participating in earlier questionnaires. However, due to missing values in the outcome variable, most analyses included total of 4129 individuals (1997 boys and 2132 girls). Finally, due to missing values in some predictors, the final multivariate model of drug use predictors was based on 3118 individuals.

2.2. Definitions of variables

2.2.1. Outcome—The outcome variable was self-reported ever use of cannabis or other similar drugs at age 17 follow-up. The question was: "Have you ever tried or used drugs, such as hashish, something to sniff, or other drugs or substances that would make you feel 'intoxicated'?" The options were as follows: 1) I have never tried or used; 2) some 1–3 times; 3) some 4–9 times; 4) some 10–19 times and 5) 20 times or more. To define ever use of cannabis or other illicit drugs, we considered all who reported experimenting or using at least once.

2.2.2. Predictors—The potential predictors were chosen based on earlier research literature. These were self-reported measures at ages 11–12, 14 or 17.5, or self-reports of mother/father and behavioral ratings reported by the teacher when the twin was 12. We considered several individual, peer and family factors. When searching for relevant literature on illicit drugs we focused on cannabis, as in Finland, like in many developed countries, cannabis products (marijuana, hashish) are the most commonly used ones (Programme on Substance Abuse, 1997; Virtanen and Sjöberg, 2006).

2.2.2.1. Individual factors: Following earlier literature, we considered *other substance use*, as well as *behavioral and emotional problems*. Among licit substance use we tested *cigarette smoking* (Guxens et al., 2007a, 2007b; Kandel and Yamaguchi, 1993), especially *age of onset* (Gilvarry, 2000; Vega and Gil, 2005), *alcohol consumption* (Guxens et al., 2007a, 2007b), especially *drinking to intoxication* (Agrawal et al., 2006; Wittchen et al., 2007). Own ever smoking was asked prospectively at the age 14 survey. The question was whether she/he had ever smoked or tried smoking. Ever smoking was used as a dichotomous variable (no/yes). The age of smoking onset was asked retrospectively at the age 17 survey. The question was how old she/he was when trying smoking for the first time. Age of smoking onset was studied in three categories: no initiation, late (>12), and early (≤ 12) onset. Drinking to intoxication was based on a question at age 14 on how often she/he used alcohol to become at least slightly intoxicated. Those who reported this drinking habit occasionally, once or twice a month or more often were considered such 'binge drinkers'. Among behavioral problems we considered *externalizing behavior*, such as *aggressiveness* and symptoms of Attention Deficit Hyperactivity Disorder (ADHD), i.e. *hyperactivity – impulsivity and inattention* (Brook et al., 1996; Monshouwer et al., 2006; White et al., 2001). As *internalizing behavior* we tested *emotional problems*, such as *depressive symptoms* and *social anxiety* (Buckner et al., 2008; Henry et al., 1993; Huizink et al., 2006; Jane-Llopis and Matytsina, 2006; Wittchen et al.,

2007). The Multidimensional Peer Nomination Inventory (MPNI) Teacher ratings at age of 12 were used. The MPNI covers a wide spectrum of externalizing and internalizing behaviors consisting of scales for aggression, hyperactivity-impulsivity, and inattention, forming a factor for externalizing problem behaviors; anxiety and depression, forming a factor for internalizing problem behaviors (Pulkkinen et al., 1999). These behavioral variables were used as continuous scores in the preliminary analyses, but for the multiple adjusted models the aggressiveness score was dichotomized into low/high (median split).

2.2.2.2. Peer factors: Among peer factors we considered *substance use among friends* (Agrawal et al., 2007; Guxens et al., 2007a, 2007b). First, we used a question regarding *number of smoking friends* asked at the age 14 year follow-up. Second, we used a question regarding *number of acquaintances who had experimented with cannabis or other drugs.* The term 'acquaintances' rather than 'friends' was used here, because any illegal drug was considered and we assumed that an adolescent would be more willing to report illegal behavior if it was not too close to his or her own circle of friends. The categories for both variables ranged from no one to more than five friends/acquaintances, with 4 possible response options (Rimpelä et al., 2006).

2.2.2.3. Family factors: As family factors reported by the parents themselves at the time of the baseline survey, i.e. at age 11–12 of the twin, we analyzed *parental substance use,* where we considered current *cigarette smoking and alcohol consumption of mother and father* (Hayatbakhsh et al., 2007). Current cigarette smoking of mother and father at the time of the baseline survey was used as a dichotomous variable (no/yes). Alcohol consumption was a variable describing frequency of drinking to intoxication (drinking more than 5 beers, a bottle of wine or half a bottle of spirits or the equivalent on the one and same occasion). For mothers, the frequency categories were never, sometimes (but less often than monthly), and monthly or more often. For fathers they were never, sometimes (but less often than weekly), and weekly or more often. As there is also evidence that poor socio-economic circumstances of the family may be a risk factor for drug use (Compton et al., 2005) we used parents' socioeconomical status (SES) as an additional potential predictor. Based on the occupation reported, the SES was coded for mother and father according to the categories published by the Central Statistical Office of Finland. SES was coded into seven categories as follows: employer, self-employed, upper-level employee, lower-level employee, manual worker, pensioner, student and other. Finally, although not found in earlier literature, we considered *prenatal exposure to nicotine* as a novel predictor of subsequent use of drugs shared by the twins. There is earlier evidence that prenatal exposure to marijuana predicts marijuana use in adolescence (Day et al., 2006). We are not aware of evidence that prenatal exposure to nicotine would pose a risk of later drugs use, but we considered mother's cigarette smoking during pregnancy as a further potential prenatal predictor for drug use of the adolescent. We used prenatal nicotine exposure as a dichotomous variable (no/yes). We considered exposure to be positive if the mother reported smoking during her twin pregnancy for one month or more.

2.3. Statistical analyses

The analyses were conducted using the STATA statistical package, version 9 (StataCorp., 2005). We used logistic regression models as the main method of analysis. Although the study population consisted of twins, most analyses considered the subjects as individuals, but statistically accounted for twinship. Because observations on twins within twin pairs may be correlated, we used robust estimators of variance and the cluster option in STATA when estimating standard errors (Williams, 2000). The preliminary logistic regression models tested the strength and significance of each potential predictor. Odds Ratios (OR) with 95% Confidence Intervals (CI) were computed adjusting for age and sex. The OR is a measure of

the strength of the association between a risk factor and outcome, i.e. the ratio of the odds of outcome between those with and without the risk factor (Thomas, 2004).

Because a wide array of predictive factors in drug use, yet more specifically in cannabis use, have been found to differ largely by age and sex (Guxens et al., 2007a), we adjusted all analyses for age at follow-up and sex. Also, before dropping out non-significant predictors from the multiple logistic regression models, we first analyzed the interaction with sex of each variable. If the interaction was significant the variable was further included in the model, even if it did not show a significant direct predictive effect.

First, we analyzed the age-sex adjusted Odds Ratios (OR) of each potential predictor of drug use. If this OR was significant, we further explored the causal nature of that potential predictor. In order to control for familial factors, we utilized the fact that our population consisted of twins. Because the co-twins share their childhood environment, and all of their genes (in MZ twins) or 50% of their segregating genes (in DZ twins), an association between an explanatory factor and the outcome within such pairs would provide suggestion that the relationship between the predictor and outcome is not due to within-family confounds. We identified all twin pairs discordant for drug use (n = 246) as matched cases and controls. We conducted series of conditional logistic regression analyses where we used the McNemar Test as an unadjusted test in order to assess the risk of using drugs given the potential predictor (Thomas, 2004). If the association was found between illicit drug use and a potential predictor also within discordant pairs, that is, pairs in which one of the twins had ever used but the other twin never used cannabis or other illicit drugs then the association between the predictor and the outcome ('event' i.e. 'used drugs') could not be explained by common background predictors. Correspondingly, if a predictor is found to significantly explain drug use considering twins as individuals but not within discordant pairs, that potential predictor probably would have no direct effect on the risk of drug use. Rather, the association found in the individual-level analysis would be related to factors shared by the co-twins. However, this kind of test for within family confounds was not conducted for family factors, as the twins share these factors. Thus, only those individual and peer factors showing significant associations within families with the outcome, were taken into further consideration to be entered into the full multiple model.

When constructing the full multiple model, some potential predictors were detected with high inter-correlations (r≈0.60). Those highly correlated variables were 'ever smoking' and 'age at smoking onset', 'hyperactivity' and 'aggressiveness', as well as 'maternal smoking at the time of the survey' and 'pre-natal exposure to nicotine'. Thus, among those variable pairs, only the one showing stronger unadjusted association with the outcome was entered into the full model. Those variables were 'age at smoking onset', 'aggressiveness' and 'pre-natal exposure to nicotine'.

The full model included individual factors, such as age, sex, age at smoking onset, drinking to intoxication and aggressive behavior, peer factors, such as number of smoking friends and number of acquaintances who had experimented with drugs, as well as family factors, such as parental alcohol use and pre-natal exposure to tobacco. In backwards stepwise selection approach any non-significant variable was dropped one by one. However, before dropping a predictor, interaction with sex was tested. Thus, the final model included, in addition to sex and age, only significant predictors and those with significant sex interactions. Due to missing values in some predictors, the final model was based on 3118 individuals.

3. Results

3.1. Descriptive results

We included longitudinal data with baseline at age 11–12 and two follow-ups at ages 14 and 17, from 4138 individuals who participated in all three surveys, comprising 74% of the baseline sample. However, due to missing values in the outcome variable, most analyses included total of 4129 individuals (1997 boys and 2132 girls). The mean age at second follow-up among boys was 17.6 (SD = 0.2; range 17.2–19.3) and among girls 17.6 (SD = 0.3; range 17.2–19.5) years.

In this sample, 13.5% of adolescents had initiated use of cannabis or similar drugs by the age 17.5 follow-up. About 9% had used 1–3 times, 2% 4–9 times, 1% 10–19 times, and 2% 20 times or more. When analyzed by sex, 12% of boys whereas 15% of girls had ever used drugs, the difference being significant ($p < 0.05$; adjusted for correlated twinship). Table 1 shows the descriptive information of potential predictors and outcome, including the proportion (%) of each class for categorical variables among those who had ever used cannabis or other drugs. For continuous variables the means (*M*) with standard deviations (*S.D.*) among those who never *vs.* ever had used cannabis or other illicit drugs are given in Table 2. In both analyses the significance of differences are tested adjusting for correlated twinship.

3.2. Univariate logistic regressions

Table 3 shows the results (OR and 95% CI) of the logistic regressions, estimating the relative risk of use of cannabis or other drugs by each potential predictor, adjusted for sex and age. As seen in table 3, most variables, except depressive symptoms at age of 12, father's smoking and parental socioeconomic status (SES), had statistically significant associations with lifetime use of drugs.

3.3. Multiple logistic regressions

All relevant candidates were entered simultaneously into the full multiple logistic regression model. However, some of those significant predictor candidates were intercorrelated, i.e. the correlations being r = 0.58 for 'ever smoking measured at age 14' and 'age of smoking initiation reported retrospectively at age 17', whereas r = 0.56 for 'hyperactivity' and 'aggressiveness' scores, and r = 0.60 for 'maternal smoking at the time of the survey' and 'prenatal exposure to nicotine'. These intercorrelations were taken into account when putting together the multivariate models. Among these pairs of intercorrelated factors, the one with stronger risk estimate on outcome was taken into the full model, i.e. age of smoking initiation, aggressiveness, and prenatal exposure to nicotine. Thus, the full model included in addition to sex and age, age of smoking initiation, drinking to intoxication, number of smoking peers, number of acquaintances with drug experience, parent's 'binge drinking', and prenatal exposure to nicotine (Table 4). Further, we also conducted an 'alternative' full model with the highly correlated variables ('ever smoking at age 14', 'hyperactivity', and 'maternal smoking' instead of 'age of smoking initiation', 'aggressiveness', and 'prenatal exposure to nicotine') to see how the model would change. However, the same variables turned out to be dropped out from the final model.

After this a backwards stepwise procedure was applied to drop nonsignificant predictors until only significant ones were in the final model or those having significant interaction with sex. Actually two factors, i.e. mother's drinking to intoxication and prenatal exposure to nicotine were dropped. Thus, the final model included, in addition to sex and age, as individual predictors early onset of cigarette smoking (OR = 25.9; $p < 0.001$) and drinking to intoxication (OR = 2.61; $p < 0.001$). Aggressive behavior alone did not have a significant direct effect on cannabis use, but a significant sex interaction ($p < 0.05$). Thus, the effect of aggressiveness was included in the final model together with the aggressiveness × sex interaction term.

Analysis of the interaction showed that the effect of aggressiveness was significantly weaker among girls than boys. When the final model was run separately among boys and girls by using sex-specific cut off points, aggressiveness was significant among boys (OR = 1.59; 95%CI 1.07, 2.36 p = 0.02), but not among girls (OR = 0.92; 95%CI 0.64, 1.33; p = 0.74). As peer factors, both number of smoking friends and knowing others who have experimented with drugs remained highly significant predictors. If more than five of the adolescent's friends were smokers his/her risk of drug use was doubled (OR = 2.05; $p < 0.001$). If one acquaintance had experimented with drugs, the risk was elevated (OR = 1.64; $p = 0.005$) and if more than five had experience of drugs, the risk was almost three-fold (OR = 2.75; $p = 0.005$). The only significant family related predictor included in the final model was father's weekly 'binge drinking' (OR = 3.41; $p < 0.001$) (Table 4).

3.4. Conditional logistic regressions

The function of conditional logistic regressions conducted among 246 twin pairs discordant for drug use was to further investigate causal nature of individual an peer predictors. Only those individual and peer factors which were significant in the preliminary analyses were further investigated. The results among the discordant twin pairs (where applicable), controlling for familial factors, are shown in table 5. In general, the risk estimates were clearly attenuated after controlling for familial influences. Further, some of the variables did not remain significant, such as inattention and anxiety, suggesting that correlated within-family factors contribute to these associations. However, other variables tested, i.e. ever smoking at age 14, age of smoking onset reported retrospectively at age 17, drinking to intoxication reported at age 14, hyperactivity-impulsivity and aggressiveness reported by teacher at age 12, high number (>5) of smoking peers at age 14, and at least one acquaintance with drug experience, remained significant predictors in these within-family comparisons.

4. Discussion

In this adolescent longitudinal twin study we explored factors predicting lifetime use of cannabis or other illicit drugs in Finland. In our sample 12% of boys and 15% of girls had initiated such drug use by the average age of 17. The final model suggested that female sex, early onset of cigarette smoking, drinking to intoxication, having more than five smoking friends, and having any acquaintances who had experimented with cannabis or other drugs, as well as father's weekly 'binge drinking' were significant predictors for subsequent drug use. Aggressive behavior predicted drug use among boys only. Importantly, some of the individual predictors were replicated in analysis of co-twins discordant for lifetime use of drugs.

Methodological strengths of this study include longitudinal design, high participation rates, and analysis among discordant twin pairs as matched cases and controls. Thus, this study includes a two phased analysis, i.e. an epidemiological one of twins as individuals followed by replication of the results among discordant twins. This approach allowed us to take into account some known within-family confounds in substance use, such as family status and structure. By doing so the risk estimates for early smoking onset, drinking to intoxication, aggressiveness, smoking peers and acquaintances with drug experience were reduced but still remained significant. Because within-family factors, such as family status and structure, are major issues in substance use we consider this approach very important. Naturally, this approach was applicable for individual and peer factors only, because for family factors, reported by the parents, all twin pairs were concordant in our study.

In Finland, Poikolainen and co-authors (2001) have previously reported on cannabis use among young adults aged 21.8 on average, where some 21% reported at least having experimented with cannabis. Some 90% of life time cannabis users in their study had tried cannabis not more than once or a few times. In their sample cannabis use was related to male gender, absence of

mother, frequent lack of interest and early age at first sexual intercourse. The prevalence of lifetime cannabis use was higher, i.e. about 21%, compared to about 13% in drug use among our sample. However, our participants were younger and this age difference may explain the differences in the prevalence. For example, in data from the United States, the likelihood of trying cannabis increased from adolescence to young adulthood, being 29% at age of 14, 33% at age of 16, and 54% at age of 22 (Brook et al., 2002). We found that girls had initiated use of cannabis or other drugs more often than boys, which is not consistent with earlier Finnish findings that boys initiated more often. Also this difference may be related to age, as we have found a similar pattern for alcohol use early in adolescence, whereby girls are more likely to initiate at a younger age (Rose et al., 2001b), but there is a catch-up effect for boys later in adolescence (Rose et al., 2001a). Another explanation may be the timing of outcome data collection. In the earlier study, data collection happened in 1995, whereas in our study that data collection took place from late 2000 to early 2005. More recent data seems to show more risk taking health behaviors among girls than earlier seen. When comparing our finding to population statistics from cross-sectional surveys on cannabis use in Finland (Virtanen and Sjöberg, 2006), lifetime use both in 1995 and in 2003 among 15–16 years old girls was, indeed, slightly more common than among boys in the same age group. This may be partly because of pubertal development differences between girls and boys becoming more visible in risk taking behavior patterns than earlier. In all, however, our finding that girls initiated use of cannabis or other drugs more than boys is in contrast with most literature on this topic (e.g. Guxens et al., 2007b).

Early exposure to tobacco had a strong effect on use of cannabis or other drugs during adolescence. Moreover, even in the analysis among discordant twin pairs the effect of smoking initiation by the age of 12 was a powerful predictor for subsequent drug use. Age of first drug use at a lower stage is suggested to be a strong predictor of further progression (Kandel and Yamaguchi, 1993). Further support comes from a recent study conducted among women (Agrawal et al., 2006) where women who initiated cigarette, alcohol or cannabis use at an early age were at elevated risk for early experimentation with each subsequent drug class.

Our result raises a further question, whether this strong relationship reflects the gateway hypothesis suggested by Kandel and Yamakuchi (1993) where cigarette smoking is seen as a gateway for more serious and illegal drug use. It is also possible that shared genetic or environmental influences could explain that vulnerability for early onset of cigarette smoking is shared with vulnerability for drug use during adolescence. Further, drinking to intoxication at age 14 predicted later drug use in our sample, which is consistent with earlier longitudinal studies (Guxens et al., 2007b). However, alcohol use had much lower OR, which may suggest that smoking is a more powerful risk behavior.

Other consistently significant predictors in the current study were peer related substance use variables, i.e. number of smoking friends and acquaintances who had tried drugs. There is recent and consistent evidence suggesting that peer substance use predicts own drug use later (Agrawal et al., 2007; Guxens et al., 2007a, 2007b). More importantly, our genetically informative data allowed exploring the causal nature of these predictors. Also, Agrawal and co-authors (2007) found among a genetically informative sample of female adolescent twins that the multivariate stepwise modeling adjusted for zygosity retained only influences of peers towards substance use. Thus, it is possible that the role of peer behavior may have a causal influence on adolescent's drug use behavior. Although both cigarette smoking and drug use among peers were significant predictors in our analyses, drug use seemed to be much more powerful, as knowing at least one individual who had used drugs increased the likelihood of own drug use. The influence of smoking peers became significant only if at least five of the friends were smokers. This may be associated with the fact that smoking under the age of 18 is not illegal in Finland, although buying cigarettes is, whereas drug experimentation and use

is more clearly related to deviant behavior. Although we discovered that peer influences consistently, maybe even causally (i.e. within pairs), predicted drugs use, we should note that there is also evidence suggesting that this association may not be that simple. Influences of peers are not uniform across different families and adolescents and socialization effects of peers are more seen as processes that modulate the dispositional tendencies of adolescents. Some shared environmental effects are unique to the reciprocal interactions of siblings growing together. Moreover, adolescents tend to choose as their friends peers who are similar in terms of their behavior (Rose, 2007).

Externalizing behavior was not as important predictor of lifetime use of cannabis or other illicit drugs in our sample as in earlier literature (Brook et al., 1996; Monshouwer et al., 2006; White et al., 2001). The analyses among discordant twins suggested that the association only remained significant for hyperactivity-impulsivity and aggressiveness, but not for inattention symptoms. Thus, the association of inattention symptoms with the onset of illicit drug use is probably not causal in nature. Further, when adjusted for all other variables and significant interactions, aggressiveness was a significant predictor among boys only. However, in other countries, such as The Netherlands, cannabis use has been associated with aggression and delinquency independent of gender (Monshouwer et al., 2006). Our result that, at least some predictors of lifetime drug use differ by sex is supported by earlier literature (Guxens et al., 2007a; Hawkins et al., 1992), especially concerning aggressive behavior among boys (Kandel, 1982).

The current study did not find evidence for internalizing behavior as predictor of subsequent drug use. In previous studies early symptoms of anxiety and depression were related to illicit drug use in adolescence or in young adulthood (Buckner et al., 2008; Huizink et al., 2006; Wittchen et al., 2007). Our measures of both externalizing and internalizing behavior were based on teacher's evaluations at 12 years of age, whereas other studies collected those symptoms by parents' reports (Huizink et al., 2006), self-reports (Buckner et al., 2008) or used diagnostic assessments (Wittchen et al., 2007). It is possible that in this age group externalizing behavior is more easily observed by the teacher than internalizing behavior. Thus, internalizing behavior may be somewhat underreported. Moreover, earlier studies among Finnish adolescents have suggested that other substance use, such as alcohol drinking, and delinquent behaviour are associated with peer-oriented behaviours and aggression, but low anxiety (Pulkkinen et al., 2006). Socially anxious adolescents are not peer-oriented and do not make early experiments with substances. Perhaps self-medication aspect in substance use becomes more visible at a later age

Finally, prenatal exposure to nicotine was our novel predictor candidate for subsequent drug use. When adjusted for sex and age only, this type of exposure almost doubled the chances of later drug use. However, when adjusted for other significant predictors, this exposure did not have an independent role. Although earlier studies show that prenatal exposure to marijuana predicts marijuana use in adolescence (Day et al., 2006) and prenatal exposure to nicotine predicts smoking in adolescence (Barman et al., 2004), we were not able to demonstrate that the effect of prenatal nicotine to smoking initiation could be extended into initiation of illicit drugs. It is possible that the effect of prenatal exposure is substance specific or that other factors in our multiple model, such as early onset of own smoking mediated the effect of prenatal exposure.

Limitations

Earlier literature includes also other factors predicting use of illicit drugs. Some individual factors related to leisure time patterns have been earlier suggested as risk factors of cannabis use, such as spending time in bars and discos (Guxens et al., 2007a), delinquency (Tarter et al., 2006), and early age of first sexual intercourse (Poikolainen et al., 2001). Although we included several family factors in the current analyses, there are others which were not

considered, such as low parental involvement and higher coercive parental discipline (Chen et al., 2005), tolerance and acceptance of drugs use, poor parental monitoring and family functioning (Gilvarry, 2000). However, when testing our individual predictors among the discordant twin pairs, we actually controlled also for those potential family related factors shared by the twins. Further, although beyond the scope of our paper, some neighborhood and community factors describing unfavorable social environment, such as poverty, drug availability, acceptance of drug use, lack of community support structures, lack of social cohesion (Compton et al., 2005; Hawkins et al., 1992; Tarter et al., 2006) have been suggested as drug use determinants. Again, our analyses among discordant pairs partly accounted for these factors.

A second limitation is that the wording of the question related to outcome covered both cannabis (hashish, marijuana) and also other illicit drugs, such as "something to sniff, or other drugs or substances that would make you feel intoxicated". However, our own unpublished interview data among a subsample of 1,800 intensively assessed twins at age 14 shows that some 90% of reported illicit drug use was specifically cannabis use and less than 1% had ever used any other substance than tobacco, alcohol or marijuana (data not shown). Also the recent statistics in Finland indicate that the vast majority of illicit drug use in Finland in that age group is actually use of cannabis products (Virtanen and Sjöberg, 2006). Thus, only very few Finnish adolescents would have used any illicit drug if they had not also at least experimented with cannabis. However, we are not able to disentangle which proportion used cannabis only and which proportion both cannabis and other illicit drugs. Moreover, in order to study factors predicting cannabis use only *vs.* those predicting 'mixed' use, a larger sample is needed.

In summary, we confirmed earlier findings on importance of earlier use of other licit substances and peer influences predicting use of cannabis or other illicit drugs, even when controlling for family confounding. We conclude that initiation of cigarette smoking by the age of 12 seems to be a powerful predictor for subsequent drug use among Finnish adolescents. Also twin's own 'binge drinking' as well as smoking and drug use among peers seem to be significant predictors. These relationships were found even after adjusting for within-family confounds, which includes the influences of shared childhood effects. Further studies should investigate whether this relationship reflects the causal gateway hypothesis or whether shared genetic or environmental influences explain the co-morbidity.

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Table 1

Proportions (%) of use of illicit drugs by potential categorical predictors

		All			Boys		Girls	
		n[a]	%	P- value[b]	%	P- value[b]	%	P- value[b]
Ever smoking [c]	No	2371	5.0	<0.001	4.5	<0.001	5.5	<0.001
	Yes	1735	25.0		22.6		27.3	
Age of smoking initiation[d]	No initiation	1205	0.8	<0.001	0.5	<0.001	1.2	<0.001
	Late (> 12)	1914	14.0		12.5		15.2	
	Early (≤ 12)	960	28.8		26.1		32.1	
Drinking to intoxication[c]	No	3156	7.5	<0.001	7.1	<0.001	7.8	<0.001
	Yes	930	34.0		33.9		34.0	
Number of smoking peers[c]	None	1611	5.8	<0.001	5.8	<0.001	5.8	<0.001
	One	463	9.3		7.9		10.6	
	2–5	1106	13.8		13.9		13.8	
	More	888	29.6		25.7		32.6	
Number of acquaintances with drug experience[d]	None	3234	9.0	<0.001	9.1	<0.001	8.9	<0.001
	One	452	22.3		17.8		25.7	
	2–5	361	34.3		36.9		33.0	
	More	65	56.9		60.0		55.6	
Mother's drinking to intoxication[e]	Never	1675	9.7	<0.001	10.5	0.20	9.1	<0.001
	Less often than monthly	2046	14.7		12.4		16.9	
	Monthly or more often	321	22.7		16.1		28.1	
Father's drinking to intoxication [e]	Never	1326	9.1	<0.001	8.2	<0.01	10.0	<0.001
	Less often than weekly	2052	13.3		11.4		15.1	
	Weekly or more often	305	19.3		17.6		21.0	
Mother's[e] smoking	No	3309	12.5	<0.01	11.5	0.36	13.5	<0.01
	Yes	717	16.7		13.5		20.5	
Father's[e] smoking	No	2939	12.0	0.39	10.4	0.38	13.6	0.66
	Yes	746	13.4		12.2		14.6	
Pre-natal exposure to nicotine[e]	No	2821	11.2	<0.001	10.3	<0.01	12.1	<0.001
	Yes	1118	18.3		15.6		21.2	
Mother's SES[e]	Employer	438	11.9	0.68	11.2	0.39	12.6	0.85
	Self-employed	721	13.9		12.1		15.5	
	Upper-level employee	2096	13.8		13.3		14.3	
	Lower-level employee	683	11.7		8.5		14.5	
	Manual worker	30	6.7		5.9		7.7	
	Pensioner	0	-		-		-	
	Other	59	15.2		8.0		20.6	
Father's SES[e]	Employer	765	11.2	0.42	9.5	0.34	12.9	0.80
	Self-employed	922	13.7		12.2		15.1	
	Upper-level employee	603	13.9		12.5		15.3	
	Lower-level employee	1389	11.2		9.5		12.8	
	Manual worker	6	33.3		33.3		-	
	Pensioner	2	0		-		0	
	Other	0	-		-		-	

		All		Boys		Girls	
	n^a	%	P- value[b]	%	P- value[b]	%	P- value[b]

[a] Total numbers of observations in each predictor category

[b] Fisher's exact test for dichotomies and Chi Square test for other variables, adjusted for correlated twinship

[c] Reported at age 14

[d] Reported at age 17

[e] Reported by the parent at age 12 of the twin

Table 2

Means (*M*) with standard deviations (*S.D.*) of age as well as behavioral and emotional problems among those who had used *vs.* who had not used illicit drugs

Potential Predictor	Ever use of cannabis or other illicit drugs														
	All					Boys					Girls				
	No		Yes		P- value[a]	No		Yes		P- value[a]	No		Yes		P- value[a]
Continuous Variables	M	S.D.	M	S.D.		M	S.D.	M	S.D.		M	S.D.	M	S.D.	
Age [b]	17.62	0.26	17.65	0.26	<0.05	17.61	0.23	17.68	0.29	<0.01	17.62	0.28	17.63	0.23	0.62
Hyperactivity-Impulsivity [c]	0.63	0.69	0.82	0.77	<0.001	0.85	0.77	1.14	0.82	<0.001	0.42	0.53	0.58	0.63	<0.001
Inattention [c]	0.65	0.65	0.83	0.72	<0.001	0.86	0.71	1.06	0.79	<0.01	0.45	0.53	0.66	0.62	<0.001
Aggressiveness [c]	0.56	0.60	0.78	0.67	<0.001	0.68	0.65	0.94	0.70	<0.001	0.46	0.53	0.66	0.63	<0.001
Depressiveness [c]	0.69	0.52	0.69	0.51	0.37	0.63	0.50	0.64	0.51	0.75	0.69	0.53	0.72	0.51	0.45
Social anxiety [c]	0.89	0.74	0.77	0.72	<0.01	0.80	0.70	0.62	0.63	<0.001	0.96	0.77	0.88	0.76	0.17

[a] Wald test adjusted for correlated twin ship

[b] Exact age at the time of outcome measurement

[c] Teacher ratings at age 12 of the twin

Table 3

Age- and sex adjusted odds ratios (95%CI) of logistic regressions on each predictor for use of illicit drugs

INDIVIDUAL FACTORS		n	OR[a]	95% CI	P- value
Sex	Boys	1997	1.00		
	Girls	2132	1.23	1.01, 1.51	<0.05
Ever smoking at age 14 [b]	No	2371	1.00		
	Yes	1735	6.32	5.00, 7.98	<0.001
Age of smoking initiation reported at age 17 [b]	No initiation	1205	1.00		
	Late	1914	18.93	10.08, 35.56	<0.001
	Early	960	48.94	25.75, 93.00	<0.001
Drinking to intoxication at age 14	No	3156	1.00		
	Yes	930	6.41	5.20, 7.91	<0.001
Hyperactivity-impulsivity at age 12 [b]	Continuous	3610	1.56	1.36, 1.80	<0.001
Inattention at age 12	Continuous	3610	1.61	1.37, 1.88	<0.001
Aggressiveness at age 12 [b]	Continuous	3610	1.75	1.50, 2.04	<0.001
Depressiveness at age 12	Continuous	3610	1.09	0.89, 1.33	0.40
Social anxiety at age 12	Continuous	3610	0.79	0.67, 0.93	<0.01
PEER FACTORS					
N of smoking peers at age 14	None	1611	1.00		
	One	463	1.71	1.15, 2.53	<0.01
	2–5	1106	2.70	2.01, 3.63	<0.001
	More	888	7.08	5.32, 9.41	<0.001
N of acquaintances with drug experience at age 17	None	3234	1.00		
	One	452	2.97	2.27, 3.90	<0.001
	2–5	361	5.43	4.10, 7.19	<0.001
	More	65	13.3	7.57, 23.2	<0.001
FAMILY FACTORS [e]					
Mother's drinking to intoxication frequency	Never	1675	1.00		
	Sometimes	2046	1.62	1.27, 2.08	<0.001
	Monthly	321	2.78	1.91, 4.04	<0.001
Father's drinking to intoxication frequency	Never	1326	1.00		
	Sometimes	2052	1.59	1.21, 2.08	<0.01
	Weekly	305	3.92	2.17, 7.10	<0.001
Mother's smoking [b]	No	3309	1.00		
	Yes	717	1.50	1.14, 1.96	<0.01
Father's smoking	No	2939	1.00		
	Yes	746	1.18	0.89, 1.58	0.25
SES: Mother	Employer	438	1.00		
	Self-employed	721	1.18	0.77, 1.81	0.43
	Upper-level employee	2096	1.18	0.81, 1.71	0.39
	Lower-level employee	683	0.98	0.63, 1.52	0.92
	Manual worker	30	0.52	0.12, 2.20	0.38
	Other	59	1.21	0.45, 3.21	0.70
SES: Father	Employer	765	1.00		
	Self-employed	922	1.24	0.88, 1.76	0.22
	Upper-level employee	603	1.27	0.87, 1.85	0.22
	Lower-level employee	1389	0.99	0.72, 1.38	0.98
	Manual worker	6	4.27	0.41, 44.1	0.22
Pre-natal exposure [b]	No	2821	1.00		
	Yes	1118	1.79	1.42, 2.26	<0.001

[a]For sex adjusted for age, for all other variables adjusted for age and sex

[b,c,d]$r \approx 0.6$;

[e]Reported by parents at age 12 of the twin

Table 4

Odds Ratios (OR) (95%CI) of the multiple logistic regression models of individual, peer and family factors for use of illicit drugs [a]

INDIVIDUAL FACTORS		Full model (n = 3006)		Final model (n = 3118)	
		OR	95% CI	OR	95% CI
Sex	Boys	1.00		1.00	
	Girls	1.15	0.88, 1.51	1.57	1.03, 2.40
Smoking initiation	No initiation	1.00		1.00	
	Late	16.3	6.60, 40.2	17.13	6.95, 42.2
	Early	25.0	9.96, 62.5	25.86	10.3, 64.8
Drinking to Intoxication	No	1.00		1.00	
	Yes	2.51	1.86, 3.38	2.61	1.95, 3.49
Aggressiveness	Low score	1.00		1.00	
	High score	1.18[b]	0.90, 1.55	1.65[b]	1.09, 2.50

PEER FACTORS		Full model (n = 3006)		Final model (n = 3118)	
		OR	95% CI	OR	95% CI
N of smoking peers	None	1.00		1.00	
	One	1.38	0.85, 2.25	1.41	0.87, 2.28
	2–5	1.35	0.92, 1.99	1.38	0.95, 2.01
	More	1.95	1.30, 2.90	2.05	1.39, 3.01
N of acquaintances with drug experience	None	1.00		1.00	
	One	1.73	1.22, 2.46	1.64	1.16, 2.32
	2–5	1.95	1.34, 2.84	2.03	1.41, 2.91
	More	2.70	1.31, 5.59	2.75	2.75, 5.60

FAMILY FACTORS		Full model (n = 3006)		Final model (n = 3118)	
		OR	95% CI	OR	95% CI
Mother's drinking to Intoxication frequency	Never	1.00		Dropped	
	Sometimes	1.13	0.80, 1.60		
	Monthly	1.38	0.80, 2.38		
Father's drinking to Intoxication frequency	Never	1.00		1.00	
	Sometimes	1.09	0.76, 1.57	1.20	0.87, 1.66
	Weekly	2.87	1.39, 5.93	3.41	1.72, 6.77
Pre-natal exposure to nicotine	No	1.00		Dropped	
	Yes	1.08	0.81, 1.45		

[a] Age in model in addition to factors listed below

[b] Interaction with sex ($p<0.05$)

Table 5

Odds Ratios (95%CI) of the conditional logistic regressions on individual and peer factors among twin pairs discordant for use of illicit drugs (n = 246 pairs)

INDIVIDUAL FACTORS		OR	95% CI
Ever smoking [a]	No	1.00	
	Yes	3.37	1.93, 5.90
Smoking initiation [a]	No initiation	1.00	
	Late	14.8	3.52, 62.3
	Early	22.1	5.16, 94.9
Drinking to intoxication	No	1.00	
	Yes	4.13	2.35, 7.26
Hyperactivity-impulsivity [b]	Continuous	1.46	1.01, 2.11
Inattention	Continuous	1.10	0.77, 1.57
Aggressiveness [b]	Continuous	1.59	1.07, 2.38
Social anxiety	Continuous	0.86	0.59, 1.26
PEER FACTORS			
N of smoking peers	None	1.00	
	One	1.58	0.70, 3.54
	2–5	1.83	0.97, 3.44
	More	2.45	1.25, 4.79
N of acquaintances with drug experience	None	1.00	
	One	1.90	1.11,3.24
	2–5	2.52	1.31, 4.83
	More	13.87	2.88, 66.8

[a,b] r ≈0.6