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## Addictive Behaviors



Short Communication

## Heritability of cannabis initiation in Dutch adult twins

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## ABSTRACT

Previous studies exploring the heritability of cannabis initiation have been carried out in the United States, Australia and United Kingdom. In the present study we assess cannabis initiation in The Netherlands, where the use of cannabis in small amounts is permitted. The sample included 3115 twins with a mean age of 27.4 years (SD 4.7) who are registered with the Netherlands Twin Register (NTR). Individual differences in cannabis initiation showed moderate genetic influences (44%). The remaining variance was explained by environmental influences shared by twins (31%) and by unique environmental factors (24%). Compared to studies from other countries, these results suggest that the relative importance of genetic and environmental factors is not different in a country with a more liberal cannabis policy.

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## 1. Introduction

Cannabis is a commonly used drug worldwide. An estimated 166 million people used cannabis in 2006/7, equivalent to about 4 percent of the global population aged 15–64 (World Drug Report 2008).

Cannabis use is associated with increased risk for the subsequent use of more harmful drugs such as cocaine and heroin (Lynskey, Vink, & Boomsma, 2006) and higher risk to psychotic symptoms (Chen & Lin, 2009). Therefore it is important to know what causes people to initiate cannabis use. Twin studies can be used to disentangle the magnitude of genetic and environmental influences. Previous studies have reported both genetic and environmental factors as significant contributors to cannabis initiation. The heritability estimates ranged from 13% to 72%, while the shared environmental influences ranged from 0% to 68% (Kendler, Karkowski, Neale, & Prescott, 2000; Lynskey, Heath, & Nelson, 2002; Maes et al., 1999; McGue, Elkins, & Iacono, 2000; Miles, van den Bree, & Gupman, 2001; Rhee, Hewitt, Young, Crowley, & Stallings, 2003; Shelton, Lifford, & Fowler, 2007). These studies were mainly done in the United States, Australia and United Kingdom. In contrast to those countries, the use of cannabis in small amounts is, although not legal, permitted in the Netherlands. In the present study we use data from a sample of Dutch twins to examine the heritability of cannabis initiation in a country with a liberal cannabis policy.

## 2. Methods

## 2.1. Sample

Subjects are registered with the Netherlands Twin Register (NTR) (Boomsma et al., 2006). Most of them participate in longitudinal studies of health, lifestyle and personality. For this study we focused on the data from the 2000 survey (Vink & Boomsma, 2008; Vink, Nawijn, Boomsma, & Willemsen, 2007), which was completed by 4609 twins. We selected participants between 21 and 40 years ( $N = 3115$ ). Mean age of the subjects was 27.4 years old ( $SD = 4.7$ ). Zygosity was based on DNA tests or on questions concerning similarity.

## 2.2. Cannabis initiation

The 2000 survey included a number of questions concerning substance use. Subjects were asked at what age they initiated cannabis use with answer categories: (1) 11 years and younger, (2) 12–13, (3) 14–15, (4) 16–17, (5) 18 years or older and (6) never. The answers were recoded in the variable 'cannabis initiation', with two possible categories; 'yes' (1), when a subject initiated cannabis use at a certain age, or 'no' (0) when a subject never initiated cannabis use.

## 2.3. Data analyses

A threshold model was used (Falconer & Mackay, 1996) which assumes an underlying (latent) liability to a categorical variable such as cannabis initiation. This liability is the sum of the effects of many genetic and environmental factors. It has a normal distribution

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with standard z-scores as unit of measurement. A threshold (z-score) discriminates between the two categories (never used cannabis versus ever used cannabis).

First, we examined whether the thresholds (prevalences) differed between monozygotic (MZ) and dizygotic (DZ) twins (model 1b) and between men and women (model 1c) in a saturated model. If thresholds differ between MZ and DZ twins, this is evidence for processes of social interaction, either cooperation or competition (Carey, 1986). Tetrachoric correlations, which model the resemblance between twins for the liability to cannabis initiation, were also derived from the saturated model. MZ pairs are genetically (nearly) identical, while DZ twins share on average 50% of their segregating genes. Consequently, if the tetrachoric correlation in MZ twins is larger than in DZ twins, genetic influences play a role. If the correlations are equal (and larger than 0), the similarity between family members is not explained by genetic but by shared environmental factors.

Genetic models were fitted to the data to estimate the contribution of additive genetic variance (A), common environmental variance (C) and unique environmental variance (E) components. MZ twins share all genetic and shared environmental variance, while DZ same-sex twins share 50% of the genetic and 100% of shared environmental variance.

Initially (model 2a) the magnitude of the variance components was allowed to differ for males and females and the genetic correlation for DZ-twins of opposite sex (DOS) was allowed to be smaller than 0.5. Resemblance in opposite-sex twins may be lower than for same-sex DZ pairs if different genes influence the liability in men and women. In the second model (model 2b) the presence of qualitative sex differences was tested by constraining the genetic correlation for DOS twins 0.5, just as the genetic correlation for DZ-twins of the same sex. The third model (model 2c) tested whether there is a difference between sexes in the proportions of A, C and E. Model 2d and 2e were used to test if the influence of respectively C and A was significant. Model-fitting analyses were carried out in MX on raw data (Neale, Boker, Xie, & Maes, 1999). Significance of the parameters was tested by comparing the fit of the nested models to the fit of less restricted models. Goodness-of-fit of the sub models was assessed by likelihood-ratio test. The difference in log-likelihoods between the nested models follows a  $\chi^2$  distribution. If the difference test is significant, the constraints on the nested model cause a significant deterioration in the fit of the model to the data. If the difference test is not significant, the nested more parsimonious model is to be preferred.

### 3. Results

The prevalence in cannabis initiation did not differ for MZ or DZ twins (Table 1, model 1b), indicating that there is no process of social interaction between the co-twins. Constraining the thresholds to be the same in men and women resulted in a significant worsening of the model fit (Table 1, model 1c). The prevalence of cannabis initiation in men was 36.2% compared to 24.7% in women. The tetrachoric correlations derived from the best fitting model (model 1b), which allowed for different thresholds for men and women, are shown in Table 2. The correlations in MZ twins are higher than the correlations in DZ twins.

The lower part of Table 1 shows the genetic model fitting results. First, a full ACE model was evaluated with quantitative and qualitative sex differences. Constraining the genetic correlation in DOS pairs at 0.5 (Table 1, model 2b) did not deteriorate the fit of the model. Also, there is also no difference between sexes in the proportions of variance explained by A, C and E (Table 1, model 2c). Dropping C (Table 1, model 2d) or A (Table 1, model 2e) from the model resulted in a significant worsening of fit. Model 2c (Table 1) was the best fitting model. Of the total variance in liability to cannabis initiation 44% (95% confidence interval = 16%–74%) is explained by genes, 31% (4%–55%)

**Table 1**  
I. Model fitting results for cannabis initiation.

Model	-2 LL	Df	Vs	$\Delta$ df	$\chi^2$	P
1	<i>Saturated model</i>					
a	Full	3434.242	3060			
<b>b</b>	<b>Tmz = Tdz within sex</b>	<b>3439.098</b>	<b>3062</b>	<b>1</b>	<b>2</b>	<b>4.856</b> <b>0.088</b>
c	Tmales = Tfemales	3478.820	3063	2	1	39.722 <.001
2	<i>ACE model</i>					
a	Full ACE	3439.098	3062			
b	Rdos = 0.5	3439.153	3063	1	1	0.06 0.815
<b>c</b>	<b>ACE males = females</b>	<b>3442.387</b>	<b>3066</b>	<b>2</b>	<b>3</b>	<b>3.22</b> <b>0.359</b>
d	AE	3447.408	3067	3	1	5.02 0.025
e	CE	3451.593	3067	3	1	9.21 0.002

-2LL = -2 log likelihood; df = degrees of freedom; vs = versus model;  $\Delta$ df = difference in df;  $\chi^2$  = difference in log-likelihoods between the two models (follows a  $\chi^2$  distribution); P = p-value; T = threshold; A = additive genetic influences; C = shared environmental factors; E = unique environmental factors; Rdos = genetic correlation in DOS twin pairs.

Model 1a (Full model): different thresholds for MZ and DZ twins and for males and females. Model 1b: as 1a, but thresholds MZ males = DZ males and thresholds MZ females = DZ females. Model 1c: as model 1b, but thresholds males = females. Best fitting model is printed in bold. Model 2a: Estimation of ACE variance components in men and women and of the genetic correlation in DOS twins. Model 2b: as model 2a, but constraining the genetic correlation at 0.5 in DOS twins. Model 2c: as model 2b, but constraining ACE variance components for males and females to be the same. Model 2d: Drop C. Model 2e: Drop A. Best fitting model is printed in bold.

by shared environmental factors and the remaining variance of 24% (17%–33%) is explained by unique environmental factors.

### 4. Discussion

The prevalence of cannabis initiation was significantly higher in men than in women, which is in line with other studies (Degenhardt et al., 2008). The heritability estimates for cannabis initiation were the same in both sexes. The size of the estimate (44%) seems in line with other studies exploring the heritability of cannabis initiation. However, it should be noted that the heritability estimates in other studies ranged from 13% to 72%. This could be due to several factors, like phenotypic measures, different age cohorts, cannabis dosage/volumes used and statistical methods. All previously published articles included samples from the United States, Australia or United Kingdom. None of the studies was done in a country where small amounts of cannabis consumption are permitted, like the Netherlands. The liberal approach in the Netherlands makes cannabis more easily available. This could minimize the relative contribution of environmental factors and enlarge the relative effects of genetic factors, as a more permissive environment might allow the expression of genotypic differences between individuals. However, we did not observe a clearly larger contribution of genetic factors, as far as a comparison to other studies was possible.

Even in this adult group of twins (age range 21–40 years) we observe a significant contribution of shared environment. This result is unlikely to be explained by social interaction (e.g. imitation) between twins as this would have led to differences in prevalence among MZ and DZ twins (Carey, 1986). Still, although we cannot identify the environmental factors shared by twins, their relatively

**Table 2**  
Number of twins, complete twin pairs and tetrachoric correlations for cannabis initiation.

	Total N twins	N complete twin pairs	Tetrachoric correlation (95% CI)
MZM	435	158	0.77 (0.60–0.88)
DZM	293	98	0.70 (0.45–0.86)
MZF	1047	422	0.75 (0.63–0.83)
DZF	597	205	0.54 (0.33–0.71)
DOS	743	211	0.42 (0.18–0.61)

MZM = monozygotic male, DZM = dizygotic male, MZF = monozygotic female, DZF = dizygotic female, DOS = dizygotic opposite sex.

large contribution to variance in initiation suggests that from the perspective of prevention, it would be worthwhile to try to identify them.

Our findings suggest that both genetic factors and shared environmental factors are important in cannabis initiation regardless of cannabis policy. Cannabis initiation may represent a certain type of behavior in the Netherlands in much the same way as it does in other countries where cannabis is prohibited.

## 5. Web resources

World Drug Report: <http://www.unodc.org/unodc/en/data-and-analysis/WDR-2008.html>

Netherlands Twin Register: [www.tweelingenregister.org](http://www.tweelingenregister.org)

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## Contributors

L.W. carried out preliminary analysis and a literature search. J.V. undertook the final analyses and wrote the manuscript. D.B. and M.N. helped in the design and implementation of the study and in the interpretation of the results. All authors contributed to and have approved the final manuscript.

## Conflict of interest

All authors declare that they have no conflicts of interest.

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