BRIEF COMMUNICATION

Cannabis use in the last year in a US national sample of twin and sibling pairs

K.S. KENDLER, M.C. NEALE, L.M. THORNTON, S.H. AGGEN, S.E. GILMAN
AND R.C. KESSLER

From the Department of Psychiatry and Department of Human Genetics, Medical College of Virginia/Virginia Commonwealth University and Virginia Institute for Psychiatric and Behavioral Genetics, Richmond, VA; Department of Health and Social Behavior Harvard School of Public Health, and Department of Health Care Policy, Harvard Medical School, Boston, MA, USA

ABSTRACT

Background. Three prior population-based twin studies, none of which was nationally representative, suggested that both genetic and familial–environmental factors contribute to family resemblance for lifetime cannabis use. We seek to replicate these results in a US national probability sample of twin and sibling pairs examining only last year cannabis use.

Methods. Cannabis use in the last year was assessed by self-report questionnaire. Biometrical twin analyses were performed.

Results. Twin and sibling resemblance for last-year cannabis use was substantial, and much higher in monozygotic pairs than in dizygotic and sibling pairs, where levels of resemblance were similar. Modeling suggested that sibling resemblance was due to genetic factors – with a heritability of at least 60% – and probably family environmental factors. No evidence was found that cannabis use was influenced by a special twin environment.

Conclusions. Consistent with prior studies, use of cannabis is substantially influenced by genetic factors but family–environment is also possibly of importance.

INTRODUCTION

Our knowledge has been increasing of sources of individual differences in risk for use of cannabis, the most commonly consumed illicit psychoactive substance in the United States (SAMHSA, 1997). In particular, cannabis use has been examined in three population-based twin samples (Kendler & Prescott, 1998; Tsuang et al., 1999; Kendler et al. 2000a). Contrary to prior approaches, which emphasized the role of psychosocial factors, these studies all showed that genetic factors play an important role in the aetiology of cannabis use, with estimates of heritability ranging from 33–44%. All studies also suggested a role of family environment, accounting for between 10 to 35% of the variance in liability.

While suggestive, these studies have three potential limitations. First, none was broadly representative of the US population. Secondly, although cannabis use peaks in late adolescence, most subjects in these studies were in middle adulthood, requiring a long recall period. Thirdly, twins may share special features of their environment so that results might not extrapolate to more typical family relationships. To address these questions, we examined last year cannabis use (LYCU) in twin and sibling pairs ascertained as part of a US national probability sample.

551
METHOD

This sample has been described elsewhere (Kendler et al. 2000b). Briefly, twin-pairs were recruited as part of the MacArthur Foundation Midlife Development in the United States (MIDUS) survey, a national telephone-mail survey carried out in 1995–1996 under the auspices of the John D. and Catherine T. MacArthur Foundation Network on Successful Midlife Development. Twin ascertainment began with screening a representative national sample of approximately 50000 households for the presence of a twin. Respondents who indicated the presence of one or more twins in the household or being part of a twin-pair themselves were asked permission to be contacted by our research team for inclusion in the first national study of twins. Then, student recruiters from the University of Michigan contacted the twin households attempting to recruit twins to participate in the survey. Cooperating twins were asked to provide contact information for their co-twins, who were also recruited by the students. The final response rate for twin pairs varied depending on whether the first contact was with a relative of the twin (20–6% response rate) or the twin themselves (60–4% response rate).

Non-twin siblings were enrolled by sending a postcard asking them to provide contact information on their siblings to all MIDUS respondents (Nfl=3032). Since the family study was a secondary aim of the project, aggressive follow-up procedures were not employed. While the number of eligible MIDUS respondents who provided us with the names and addresses of their siblings was low (19–7%), the cooperation rate of these siblings was considerably higher (69–3%). The entire protocol, including obtaining informed consent via verbal assent prior to the initiation of the telephone interview, was reviewed and approved by the Human Subjects Committee of Harvard University Medical School.

The twin and sibling subjects ranged in age from 25 to 74 with mean (s.d.) of 47.2 (12.6). The majority of the sample was White (95.1%), and was diverse with respect to educational attainment. The mean age difference in the non-twin siblings was 5–8 years (4–5) years.

Using as a test sample 230 pairs of unselected genotyped adult same-sex twins from the Virginia Twin Registry, we examined the common set of eight standard zygosity self-report items that were identical or highly similar across the two datasets. We obtained a linear discriminant function from the ‘test’ sample of our 230 genotyped pairs and then applied it to the same-sex twin pairs from the MIDUS sample.

Good separation was obtained as 86% of the pairs were assigned a probability of monozygosity of <10% or >90%. We left as unassigned the 3.5% of pairs with a probability of monozygosity of between 40 and 59%.

Drug use in the last year was assessed by self-report questionnaire. The key item read ‘… did you ever use any of the following substances on your own during the past 12 months?’ Although ten classes of substances were assessed, the only substance reported with sufficient frequency to permit meaningful analysis was ‘marijuana or hashish’, which we here term cannabis.

Statistical analysis

We assess twin and sibling resemblance for LYCU by probandwise concordance (the proportion of co-twins of LYCU twins who themselves reported LYCU), odds ratio (OR) and tetrachoric correlation, which reflects the correlation in twin pairs for their underlying liability to use cannabis. We assume that four sources contribute to liability to LYCU: additive genes (abbreviated ‘a’); common/familial environmental influences that impact on the similarity of all twin/sibling pairs (c); a special twin environment that influences the similarity of twins only (t); and individual-specific environment (e). Models were fit with maximum likelihood estimation using the Mx structural modelling program (Neale, 1991). These analyses examined individual sibship families, thereby correcting for the correlations in families with more than one sibling. Because of the rarity of LYCU in this sample, we did not attempt to examine gender differences.

RESULTS

The prevalence of LYCU in the entire sample was 5.9%. The sample size and similarity for LYCU in the monozygotic and dizygotic twin pairs and sibling pairs, as assessed by proband-
DISCUSSION

Our survey of drug is comparable to the National Household Survey of Drug Abuse from 1996 (SAMHSA, 1997). Applying the age distribution of our sample to this survey, their prevalence rate for LYCU is estimated at 6.2%, very close to the 5.9% we observed. Three results of this study are noteworthy. First, consistent with prior studies of lifetime cannabis use, we found reports of LYCU – where problems of biased or selective recall are minimized – to be substantially influenced by genetic factors. Although our heritability estimate was higher than those obtained in the three prior studies (Kendler & Prescott, 1998; Tsuang et al. 1999; Kendler et al. 2000a), our wide confidence intervals for the full model included all prior estimates. Secondly, we also found evidence in our full model that aspects of the family environment impacted on LYCU. This has been a relatively consistent finding for substance use (Kendler & Prescott, 1998; Tsuang et al. 1999; Kendler et al. 2000a). While the best-fit model did not contain family environmental effects, given prior results and our low power, we feel that the full model most likely reflects the real picture in our data. Thirdly, resemblance for LYCU was very similar in DZ and sibling pairs resulting in an estimate for special twin environmental effects of zero. These results suggest that twin studies of substance use are unlikely to be biased and may be safely extrapolated to more typical non-twin family relationships.

In our full model, the CIs on our estimates were large, reflecting the inaccuracy of estimation including four parameters and a relatively uncommon trait in a medium sized twin-sibling sample. As expected, our best fit model had much tighter standard errors as it required the estimation of two versus four parameters. This sample contained the expected strong inverse relationship between age and LYCU. Since twin and sibling pairs are highly correlated for age, such effects can mimic the impact of family environment (Neale & Cardon, 1992). To address this possible bias, we re-fit our full model incorporating age effects but found only trivial changes in our parameter estimates. Our results cannot be explained by the strong age effects on the prevalence of LYCU.

These results should be interpreted in the context of at least two potential methodological limitations. First, our assessment reflected only cannabis use and cannot therefore address the more medically relevant question of the sources of individual differences for cannabis abuse or dependence. Secondly, our overall cooperation rates were only moderate for the twin sample and even lower for the sibling pairs. We cannot rule out the possibility that these results are influenced by cooperation bias. However, drug
use was a very small part of the overall MIDUS survey. Furthermore, the high correlations for LYCU in MZ twins and similar levels of resemblance in DZ and sibling pairs is not the expected pattern if the evidence for family resemblance for LYCU was due to cooperation bias. Indirectly, these results argue that our key finding of heritable influences on LYCU is substantive rather than due to methodological artefact.

The research reported here was carried out with support from the National Institutes of Drug Abuse (DA-11287) and the John D. and Catherine T. MacArthur Foundation Research Network on Successful Midlife Development. A complete list of publications and supporting documentation for the Midlife Development in the United States (MIDUS) survey appear on the MIDUS web page at http://midmac.med.harvard.edu/research.html.

REFERENCES