The negative social attributes associated with drug use and abuse/dependence may arise as a result of shared genetic or environmental factors rather than through causal pathways. To evaluate this possibility, structured interviews were conducted for 3969 male and female twins from the Mid-Atlantic Twin Registry and evaluations of their socioeconomic status (SES), social interactions, and use of drugs were obtained. Drug involvement was categorized as never used, tried, or met criteria for abuse or dependence. A co-twin control design was implemented using hierarchical linear modeling to assess whether twins who used drugs experienced lower SES and social support than non-using co-twins. Poorer social functioning in the drug-exposed twin is consistent with a causal relationship, while similar functioning in the drug exposed versus naive twins imply shared genetic or common environmental factors. Use of drugs was not significantly related to any SES measures. However, education and job status appear to share genetic influences with drug abuse/dependence. Lower income was not related to abuse/dependence of drugs. Negative interactions with friends and relatives share genetic factors with use of drugs, but the escalation from trying drugs to abusing them appears to generate discord between the abuser and friends and relatives in a causal fashion. These results indicate that presumptive causal influences of drug abuse/dependence on low SES may actually be mediated by shared genes. Drug use and social discord also appear to have shared genetic factors, but increased levels of drug involvement seem to causally influence social interactions.

Society has a vested interest in understanding the relationship between drug use and social functioning in order to effectively target prevention efforts. In 2005, 6.9 million Americans aged 12 and older met criteria for abuse or dependence of illicit drugs (Substance Abuse and Mental Health Services Administration, 2006). Clearly, illicit drug use imposes a significant social burden and has been associated with a range of adverse outcomes such as reduced educational attainment, criminality, mental health problems, and delinquency (Fergusson et al., 2002; Kandel et al., 1986; Newcomb et al., 1999). The temporal relationship between illicit drug use and numerous negative social attributes has often led to the presumption of a causal relationship. However, proof of causation is rarely possible through standard epidemiological approaches, and alternate potential relationships should not be overlooked. For instance, common predisposing factors could result in both drug use and the negative ‘outcomes.’ In order to distinguish between these possibilities, twin study designs can be employed which have greater capacity to differentiate causal, common environmental, and shared genetic relationships between behavioral variables.

Many epidemiological studies involve one group of subjects who have been exposed to a risk factor and a control group that has not. Rates of some outcome variable are then assessed between groups to determine whether the putative risk factor and outcome are correlated. The co-twin control design attempts to achieve the same design, but with ‘cases’ and ‘controls’ perfectly matched for many environmental factors and, in the case of MZ twins, genetic factors as well. In MZ twins discordant for drug exposure, an increased risk of negative social attributes in only the drug-exposed twin would provide evidence of a causal link (Figure 1). However, if negative social measures are equally likely in both drug exposed and unexposed members of a pair, some other shared factor (genetic or environmental) must be the root cause of any co-occurrences seen in a population-based sample (Kendler et al., 1993).

A growing body of research has examined the inherited biological vulnerability to substance use and abuse.
Substance abuse aggregates in families (Beirut et al., 1998; Meller et al., 1988; Merikangas et al., 1998), but since they also share many aspects of their environment, estimates of genetic influences on substance use and abuse have relied on other methods. Twin studies are commonly used to parse genetic and environmental influences for the behaviors under examination.

There is currently little doubt that drug use, abuse and dependence are to some extent genetically mediated. The heritability, or proportion of observed variance attributed to additive genetic sources, for illicit drug involvement in general has been estimated at 9 to 45% (Han et al., 1999; Maes et al., 1999; McGue et al., 2000; Tsuang et al., 2001). Heritability estimates for the use of cannabis specifically range from 31 to 40% (Kendler & Prescott, 1998; Kendler et al., 2003; Miles et al., 2001), while abuse or dependence estimates are often higher, 33 to 73% (Kendler & Prescott, 1998; True et al., 1999; Tsuang et al., 2001; Wilhelmsen & Ehlers, 2005).

Additionally, despite some resistance to the idea (Holtzman, 2002), the data support genetic influences on socioeconomic status (SES) variables as well. The proportional genetic variance in educational attainment has been estimated at 18% to 60% (Baker et al., 1996; Miller et al., 1996; Silventoinen et al., 2004; Tambs et al., 1989); 41% for occupational attainment (Tambs et al., 1989), and 40–42% for income level (Bowles & Gintis, 2002; Rowe et al., 1999).

The quality of interpersonal relationships also contains heritable aspects. A recent review incorporating measures of social support estimated heritability across available studies to be 23% for problems with friends, 38% for problems with relatives, and 17% and 31% for support from friends and relatives, respectively (Kendler & Baker, 2007).

Since the use and abuse of illicit substances as well as SES and social support all demonstrate underlying genetic influences, it seems plausible that the relationships between these measures may have some shared genetic underpinnings. To our knowledge, this idea has not been tested using methods capable of distinguishing causal versus shared genetic mechanisms. In this study, we examined the relationship between drug use or abuse and negative social outcomes.

Figure 1
Possible pathways between drug use or abuse and negative social outcomes.

Note: A. Drug involvement may causally influence negative social outcomes
B. Drug use or AD and negative social outcomes may have shared risk factors (genetic or environmental) in common.

Methods
Subjects
A total of 3969 male–male and female–female twins aged from 21 to 62.5 (mean age = 37.3, 38% female) from the population-based Virginia Twin Registry (now the Mid-Atlantic Twin Registry) were included in these analyses. Methods of ascertainment and interviews are reported in detail elsewhere (Kendler & Prescott, 2006), but briefly, Caucasian female–female twin pairs born in Virginia between 1934 and 1974 became eligible if both members responded to a mailed questionnaire in 1987–1988. The 64% of twins responding have been approached for four subsequent waves of personal interviews from 1988 to 1997.
Caucasian male–male and male–female twin pairs from birth years 1940 to 1974 were ascertained in a separate study and have now completed three waves of interviews from 1993 to 2004. After an explanation of the research protocol, informed consent was obtained prior to all interviews.

Drug Use Measures

Information about each of the illicit substances was obtained in wave three for males and wave four for females. Use of a drug was defined as ever having tried it. Abuse and dependence were defined according to DSM-IV criteria (American Psychiatric Association, 1994). These were combined because a factor analytic approach found that abuse and dependence can be accounted for by a single factor (Gillespie et al., 2007). Hereafter, the combined drug abuse and dependence variable is designated ‘AD.’ Use and frequency of use for cannabis, sedatives, stimulants, cocaine, opiates, and hallucinogens were assessed separately, but only the most commonly used, cannabis and cocaine, were analyzed independently. Among these subjects, 54% reported lifetime use of one or more drugs, and 17.5% met criteria for AD. About half of the subjects (51.7%) reported cannabis use, and 14% cannabis AD. The corresponding percentages for cocaine were 16.2% and 4.8%, respectively.

SES and Social Support Measures

Because drug use and misuse can often disrupt social bonds, we chose to examine measures of social functioning operationalized as interactions with friends and family members. Assessments of the quality of current social relationships were obtained at wave three for females and males, while socioeconomic status variables were drawn from wave four for females and wave two for males. Personal income data were obtained through selection of an income bracket, and the median reported income bracket was $27,000 to $35,000. Educational attainment was measured by self-reported years of schooling completed. Mean education level was 13.8 years ($SD = 2.5$), equivalent to approximately two years of college. Job status was assessed using an adaptation of the Hollingshead Index of Social Positions (Hollingshead & Redlich, 1958) in which professions are ranked from one (executives and highly-trained professionals) to seven (unskilled employees). The mean job status for this sample was 3.7 ($SD = 1.5$).

Statistical Methods

Confirmatory factor analysis was performed using Mplus version 4.0 (Muthen & Muthen, 2006) to examine the structure of the social support items and to construct appropriate scores from the available data. Allowing factors to correlate, three factors emerged: negativity from friends, negativity from relatives, and positivity from friends and relatives ($CFI = 0.932$, $TLI = 0.929$, $RMSEA = 0.105$). Each of the questions posed to subjects (e.g. How often do your friends criticize you?) had four response options: (1) often, (2) sometimes, (3) rarely, (4) never. Sum scores of the items found to load on each of the three factors were created to serve as predictors in the analyses.

Because the variables used in this study were scaled differently, all were standardized for convenience in interpreting the results. All variables were scored in the same direction so that higher values reflected poorer functioning. Linear regression analyses were performed using all subjects without regard to family structure to estimate the population averaged association between drug use or abuse/dependence and outcome measures. Those measures which showed significant association were further analyzed using hierarchical linear models implemented using PROC MIXED in SAS (SAS Institute Inc, 2005). Twin pairs served as the level two variable with individual twins as the level one variable. Models were constructed using the family mean at level two and individual deviations from the family mean at level one. In this parameterization, the coefficient for the individual deviation (level one) is the individual effect conditional on family mean while the coefficient for family mean (level two) is the sum of the individual effect conditional on family mean and the contextual effect of family mean (Begg & Parides, 2003). The latter is conceptually equivalent to the linear regression coefficient ignoring family structure except that it has a more appropriate standard error and confidence intervals. Age, sex, and zygosity were included as covariates in all analyses. One tailed hypothesis tests were used since our a priori assumption was that drug use would be associated with poorer outcomes for all variables.

Initially, use and abuse of any drug were separately analyzed in models with the SES and social support variables. In order to determine whether the observed patterns of regression coefficients were consistent across different classes of drugs, we examined cannabis (a popular ‘soft’ drug) and cocaine (the most commonly used ‘hard’ drug) separately. Only variables that were significant for the ‘any drug’ category were analyzed for these specific drugs.

Interpretation

If an association between drug use or AD and a social measure is seen in the general population, the causal nature of that association remains uncertain. Additional information from discordant twins can potentially be used to disentangle causal, common environmental, and shared genetic mechanisms (Figure 2). If the relationship is entirely causal, within-pair regression coefficients for MZ and DZ twins should have, within sampling error, values similar to that seen in the population averaged methods. This occurs because it is the drug use or AD which leads directly to the outcome. However, if common environment entirely mediates the relationship between these variables, regression coefficients for MZ and DZ twins will be similar to each other and lower than the population averaged regression coefficient. This is because both the drug-exposed and unexposed co-twin will have experienced the same shared environmental factors. A third possibility is that the relationships between use or AD of drugs and social measures are a
result of a shared genetic predisposition. In this case, discordant MZ twins will be equally likely to have poorer social functioning regardless of which twin actually used or abused drugs. Unrelated individuals will continue to show a strong relationship (large regression coefficient) between the measured variables. DZ twins, sharing half their genes, would be expected to fall approximately midway between.

**Results**

**Applied Interpretation**

The interpretation of the results can best be illustrated with contrasting examples as depicted in Figure 2. On the lower left of Figure 2 are the results for the association between the abuse of any drug and educational attainment. The population averaged effect (family mean) was .244 ($p < .001$). The within-pair effect (centered on family mean) was .099 for DZ twins ($p = .072$) and .026 ($p = .323$) for MZ twins. This pattern shows a significant effect of family mean (while controlling for other between family differences) but no within-pair difference between discordant MZ twins. Discordant DZ twins fall in between, as would be expected if shared genetic factors play a significant role in eliciting the two phenotypes.

On the lower right of Figure 2 are the results for the association between abuse of any drug and negativity from friends. The population averaged effect was .201 ($p < .001$) while the within-pair effect for MZ twins was .235 ($p = .018$) and .153 ($p = .076$) for DZ twins. A pattern where the magnitude of the difference between discordant twins is approximately the same as the effect due to family mean (controlling for other between family differences) suggests that the association between these variables is entirely at the individual level rather than the family level and is consistent with a causal relationship. Such a pattern would not be expected if this association arose from shared genetic risk factors.

**Any Drug**

At the population averaged level, use of any drug was significantly associated only with negativity from friends ($t = 2.79$, $p = .005$) and from relatives ($t = 4.16$, $p < .001$). AD of any drug was significantly linked to all measures examined except income (Table 1). When twin-level analyses were performed, use of any drug and negative interactions with friends as well as relatives showed a pattern most consistent with a shared genetic relationship. In contrast to drug use, AD appears to elicit negativity from friends and from relatives in a manner consistent with a causal relationship.
Positive interactions with friends and relatives, on the other hand, evinced a pattern of regression coefficients consistent with a genetic basis for the co-occurrence of low positive interactions and AD of drugs.

The regression coefficients between drug AD and educational attainment demonstrated the classic stair–step pattern predicted by the shared genetic model (Figure 2), as did the relationship between drug AD and job status. Income, on the other hand, did not show a relationship with drug use or AD of drugs.

Cannabis and Cocaine

Each of the specific drug analyses performed was significant at the population averaged level except for positive interactions with friends and relatives which was not significant for either cannabis or cocaine. Results were largely consistent with the any drug use and abuse categories, although the effect sizes were larger for cocaine use and abuse. Distinctly different patterns emerged for only two analyses. The use of cocaine and negative interactions with friends demonstrated a pattern of findings most consistent with a common environmental relationship. Also, analysis of the AD of cocaine and job status showed a pattern of regression coefficients consistent with common environmental rather than genetic underpinnings.

Discussion

The main goal of this article was to clarify the causal relationship between drug involvement and social measures using the co-twin control method. To our knowledge, this method has not been previously applied to this important question. Our data yielded a textured pattern of results in which education and job status appear to share genetic influences with drug AD, but lower income was not related to use or AD of drugs. Negative interactions with friends and relatives share genetic factors with use of drugs, but the escalation in drug involvement from trying drugs to abusing them appears to generate discord between the abuser and friends and relatives in a causal fashion.

Studies implying that low educational attainment is potentially either the cause (Annis & Watson, 1975; Henry & Huizinga, 2007) or result (Bray et al., 2000; Ellickson et al., 1998; Fergusson et al., 2003; Lynskey & Hall, 2000; Mensch & Kandel, 1988) of drug abuse have been published. These bidirectional assertions lend credence to the idea of a common factor contributing to both. One thorough review of longitudinal studies examining illicit drug use and psychosocial harm revealed consistent associations between cannabis use and low educational attainment, as well as some inconsistent associations with psychological and behavioral problems. They concluded, however, that the evidence to date can not support or refute causal relationships (Macleod et al., 2004).

It is not surprising that job status also shows a genetic relationship with drug AD considering the strong association between education and job status (McClendon, 1976). A negative relationship between drug use and employment was previously examined in a longitudinal study and interpreted as causal with the

| Table 1 |
| Results of Hierarchical Linear Model Analyses for Use of Any Drug (left) and Abuse of Any Drug (right) With the SES and Social Support Variables |

<table>
<thead>
<tr>
<th>Sample</th>
<th>Use of any drug</th>
<th>Abuse of any drug</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Regression coefficient</td>
<td>SE</td>
</tr>
<tr>
<td>SES</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>Population</td>
<td>−0.026</td>
</tr>
<tr>
<td></td>
<td>DZ</td>
<td>0.041</td>
</tr>
<tr>
<td></td>
<td>MZ</td>
<td>0.027</td>
</tr>
<tr>
<td>Job status</td>
<td>Population</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>DZ</td>
<td>0.030</td>
</tr>
<tr>
<td></td>
<td>MZ</td>
<td>0.045</td>
</tr>
<tr>
<td>Income</td>
<td>Population</td>
<td>−0.131</td>
</tr>
<tr>
<td></td>
<td>DZ</td>
<td>−0.136</td>
</tr>
<tr>
<td></td>
<td>MZ</td>
<td>0.034</td>
</tr>
<tr>
<td>Social support</td>
<td>Negativity from friends</td>
<td>Population</td>
</tr>
<tr>
<td></td>
<td>DZ</td>
<td>0.165</td>
</tr>
<tr>
<td></td>
<td>MZ</td>
<td>0.040</td>
</tr>
<tr>
<td>Negativity from relatives</td>
<td>Population</td>
<td>0.177</td>
</tr>
<tr>
<td></td>
<td>DZ</td>
<td>0.043</td>
</tr>
<tr>
<td></td>
<td>MZ</td>
<td>−0.076</td>
</tr>
<tr>
<td>Positivity from friends and relatives</td>
<td>Population</td>
<td>−0.050</td>
</tr>
<tr>
<td></td>
<td>DZ</td>
<td>−0.055</td>
</tr>
<tr>
<td></td>
<td>MZ</td>
<td>−0.011</td>
</tr>
</tbody>
</table>

Note: Asterisks mark one-tailed p-values significant at a p ≤ .05 level.
effect being larger for cocaine than for marijuana (DeSimone, 2002). Counterintuitively, reports of positive correlations between drug involvement and income have surfaced (Gill & Michaels, 1992; Kaestner, 1991; Register & Williams, 1992) amid other reports of no correlation (Kandel & Davies, 1990) or a delayed negative relationship manifesting in the mid-30s (Kandel et al., 1995). Another study explicitly examining the neuropsychological consequences of drug use in 54 male, discordant MZ twin pairs also compared measures of several other variables. No differences were seen between using and non-using twins for education level, current employment, and household income (Lyons et al., 2004), supporting our supposition that drug involvement and at least some SES variables share a common genetic relationship.

With regard to social support, merely trying drugs appears to have little long-term impact on relationships with friends and relatives, but the escalation to AD, with accompanying chemically-induced mood and personality changes, may well cause strife. Most research on this topic has focused on use alone. Negative familial relations were positively associated with substance use during adolescence and young adulthood in longitudinal studies (Johnson & Pandina, 1991; Tubman et al., 1991), and accordingly, a supportive family environment was inversely linked to substance use (Wills & Cleary, 1996). Additionally, a study examining mother–child interactions reported that stability and conventionality in both mother and child are associated with an affectionate, nonconflictual relationship conducive to limited or no drug use (Brook et al., 1986). Since experiencing the family environment necessarily predates exposure to drugs, such studies have often been interpreted as supporting a causal relationship. However, the results are also consistent with our contention that use of drugs and the quality of interpersonal relationships share genetic underpinnings. Carefully conducted longitudinal studies examining drug AD and familial interactions could potentially clarify the nature of these causal pathways.

Peer group deviance has been shown to be related to drug initiation, but the nature of peer interactions in relation to drug use or AD is not well studied. One such attempt found that first grade boys rated highly for aggressive or shy social interactions were more likely to be drug users in their teenage years (Kellam et al., 1980). Aggression against peers, rebelliousness, impulsivity, and noncompliance were some of the characteristics related to drug use in adolescents in another longitudinal study (Brook & Newcomb, 1995). Often, however, more severe behaviors such as conduct disorder, attention problems, and antisocial tendencies are examined. As our results might predict, early adolescent drug use has been found to predate disruptive disorders in young adulthood (Brook et al., 1998; Fergusson et al., 1996), but the opposite temporal relationship has also been reported (Adalbjarnardottir & Rafnsson, 2002; Lynskey & Fergusson, 1995). These seemingly contradictory reports are actually compatible with our findings since shared genetic liability to negative peer interactions and drug use may manifest in any order. Advancing to drug AD will likely generate later interpersonal problems, but studies of social interactions have rarely distinguished between levels of drug involvement.

Limitations

Despite that this design is one of the best available to distinguish causal and noncausal relationships between behavioral variables when only observational data are possible, there are still some limitations we would like to point out. For example, this type of analysis does not rule out the possibility that an event unique to one twin could result in both drug use and other unfortunate social consequences, thereby inflating estimates of causality. No evidence of this is present for the SES analyses, but this scenario could conceivably have impacted results for the social support measures.

Also, the co-twin control model is descriptive in nature, and the observed patterns of results were not subjected to additional statistical scrutiny. Furthermore, it is entirely possible that more than one mechanism may be acting to produce the observed results. For instance, a large standard error for the DZ regression coefficient may not allow genetic and shared environmental influences to be dissociated. A recent report indicated that even when genetic factors do underlie observed associations between two measures, the MZ and DZ values for the within-pair regression coefficients may not be distinct under some conditions (Gurrin et al., 2006). Reduced power due to the reliance on discordant twin pairs may also have hindered our attempts to parse the relative influences underlying differences seen in the general population.

Since the population sampled here consists of adults with a considerable age span (21–62.5), retrospective recall of drug use could be imprecise. On the other hand, most subjects are beyond the age at which they would be expected to initiate drug use, so expression of any genetic liability to do so is likely to be detected. Additionally, subject questionnaires assessed lifetime drug involvement but contemporary SES and social support measures implying that our results are relevant to long-term consequences of drug involvement but not necessarily sensitive to acute causal relationships. Potential circularity between the substance use diagnoses and putative outcome measures should also be acknowledged as the diagnosis of abuse and dependence can include interpersonal and work/school-related symptoms relevant to the social support and education measures under study (American Psychiatric Association, 1994).

Finally, this sample was limited to twins born in Virginia, and while results can likely be generalized to other populations in America, this may not be the case for populations with varying degrees of drug availability or differing societal influences.
Implications

The common genetic influences underlying the co-occurrence of drug use or AD and educational attainment in no way suggest a deterministic course of events for people predisposed to them. This simply suggests that drug use prevention efforts are unlikely to influence dropout rates, and encouraging teenagers to stay in school will probably not impact their use or abuse of drugs. Prevention efforts targeting either individually are still important since a genetic predisposition can be substantially moderated by environmental circumstances. Based on the results presented here, perhaps highlighting the negative interactions with friends and relatives that result from drug abuse could be helpful in attempts to deter people from engaging in the use of illicit substances.

Acknowledgment

This work was supported by NIH grants DA011287 and MH20030.

References


