Caffeine intake, toxicity and dependence and lifetime risk for psychiatric and substance use disorders: an epidemiologic and co-twin control analysis

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ABSTRACT

Background. Although caffeine is the most commonly used psychoactive substance and often produces symptoms of toxicity and dependence, little is known, especially in community samples, about the association between caffeine use, toxicity and dependence and risk for common psychiatric and substance use disorders.

Method. Assessments of lifetime maximal caffeine use and symptoms of caffeine toxicity and dependence were available on over 3600 adult twins ascertained from the population-based Virginia Twin Registry. Lifetime histories of major depression (MD), generalized anxiety disorder (GAD) and panic disorder, alcohol dependence, adult antisocial behavior and cannabis and cocaine abuse/depenence were obtained at personal interview. Logistic regression analyses in the entire sample and within monozygotic (MZ) twin pairs were conducted in SAS.

Results. In the entire sample, measures of maximal caffeine use, heavy caffeine use, and caffeine-related toxicity and dependence were significantly and positively associated with all seven psychiatric and substance use disorders. However, within MZ twin pairs, controlling for genetic and family environmental factors, these associations, while positive, were all non-significant. These results were similar when excluding twins who denied regular caffeine use.

Conclusions. Maximal lifetime caffeine intake and caffeine-associated toxicity and dependence are moderately associated with risk for a wide range of psychiatric and substance use disorders. Analyses of these relationships within MZ twin pairs suggest that most of the observed associations are not causal. Rather, familial factors, which are probably in part genetic, predispose to both caffeine intake, toxicity and dependence and the risk for a broad array of internalizing and externalizing disorders.

INTRODUCTION

Caffeine is the most commonly used psychoactive substance in the world, consumed daily by approximately 80% of the world’s population (James, 1997). Substantial evidence suggests that caffeine consumption can cause an acute toxicity syndrome (indicated by symptoms such as nervousness, diuresis, gastrointestinal complaints, tachycardia and insomnia) and that chronic caffeine use is sometimes associated with key features of dependence, particularly tolerance and withdrawal (Griffiths et al. 2003). However, surprisingly little research has been conducted to date, especially in community samples, about the association between caffeine consumption, toxicity and dependence, and the risk for psychiatric or other substance use disorders.

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The anxiogenic effects of caffeine have been well documented. Higher levels of caffeine intake are associated with symptoms of anxiety, nervousness, irritability and jitteriness (e.g. Veleber & Templer, 1984; James & Crosbie, 1987; Griffiths et al. 2003). Similar symptoms can accompany caffeine withdrawal (Nehlig, 1999). Caffeine has been used as a pharmacological probe in subjects without an anxiety disorder, and a sufficiently high dose can produce panic attacks in normal volunteer subjects (Uhde, 1990). Individuals with pre-existing anxiety disorders are more sensitive to the effects of caffeine (Boulenger et al. 1984; Bruce et al. 1992).

Many studies have found that caffeine has a positive effect on mood (e.g. Lieberman et al. 1987; Smith et al. 1992), but some have found either no effects or negative effects (Loke, 1988; Herz, 1999). There appears to be a dose-dependent effect, with low to moderate doses increasing positive mood states and higher doses impairing mood (Lieberman, 1992). Psychiatric patients who are higher caffeine consumers report more depressive symptoms than moderate and low consumers (Greden et al. 1978). The causal nature of the association between caffeine and depression remains unclear, but at least one study has found that psychiatric patients compared to normal volunteers used caffeine in response to depressive symptoms (Leibenluft et al. 1993).

Multiple previous reports have demonstrated a correlation between the use of caffeine and alcohol (Kozlowski et al. 1993; Swanson et al. 1994) as well as between caffeine dependence and alcohol dependence (Strain et al. 1994; Hughes et al. 2000). Genetic factors may in part underlie this association (Swan et al. 1996, 1997). Given the frequently demonstrated association between externalizing disorders such as antisocial personality and other forms of psychoactive drug use (e.g. cannabis, cocaine, tobacco and ethanol), it is of interest to determine whether these disorders are also associated with caffeine use and caffeine-related problems.

Strain et al. (1994) found that 11 of 16 persons diagnosed with “caffeine dependence” had a history of psychiatric disorders, mainly substance abuse disorders and mood disorders, which represents a higher prevalence of these disorders than in the general population.

Associations between caffeine use and psychopathology could arise from a range of possible mechanisms (Neale & Kendler, 1995), two of which are of particular relevance. The first is a direct causal model in which, for example, caffeine intake causes the development of an anxiety disorder. The second is a correlated liability model in which, for example, heavy caffeine intake is correlated with risk for an anxiety disorder because of some common set of environmental or genetic risk factors that predisposes to both conditions.

This paper has two major goals. First, we seek to quantify, in a large population-based sample of twins, the association between caffeine use, toxicity and symptoms of dependence and lifetime risk for seven common psychiatric and substance use disorders. Second, we seek to clarify the degree to which a direct causal versus correlated liability model best explains these associations. We do this by examining the relationship between caffeine use, toxicity and symptoms of dependence and psychopathology within monozygotic (MZ) twin pairs, who share all of their genes and their rearing environment.

METHOD

Sample

Our data derive from two inter-related studies in Caucasian same-sex twin pairs from the Virginia Twin Registry, a population-based register formed from a systematic review of birth certificates in the Commonwealth of Virginia. Female–female (FF) twin pairs, from birth years 1934–1974, became eligible if both members previously responded to a mailed questionnaire in 1987–1988, the response rate to which was approximately 64%. Data on caffeine were collected at the fourth wave of interviews, conducted in 1995–1997. For this wave, we succeeded in interviewing 84.7% of the entire sample and 88.5% of the eligible sample. Data on the male–male pairs came from a sample initially ascertained directly from registry records by a telephone interview to which the response rate was 72%. Data on caffeine were collected at the third wave of interviews, conducted in 1998–2004. At this wave, we succeeded in interviewing 84.7% of the entire sample and 88.5% of the eligible sample. Data on caffeine were collected at the third wave of interviews, conducted in 1998–2004. At this wave, we succeeded in interviewing 75.1% of the entire sample and 77.8% of the eligible sample. Zygosity was determined by discriminate function analyses...
using standard twin questions validated against DNA genotyping (Kendler & Prescott, 1999). At the time of the assessment of caffeine use, the mean (s.d.) age and years of education of the sample were 37·9 (8·9) and 14·1 (2·4) respectively.

This project was approved by the Committee for the Conduct of Human Research at Virginia Commonwealth University. Written informed consent was obtained prior to face-to-face interviews and verbal assent prior to telephone interviews. Interviewers had a master’s degree in a mental health-related field or a bachelor’s degree in this area plus two years of clinical experience. At each wave, members of a twin pair were interviewed by different interviewers who were blind to clinical information about the co-twin.

Assessment
The caffeine section in these interviews began by asking the respondent to define ‘a time in your life when you drank caffeine the most’. For that time period, we assessed the frequency of caffeine consumption by first asking, on average, how many days per month they consumed caffeine-containing beverages. Then, for the typical day when they consumed caffeine, we inquired about the average number of cups of caffeinated coffee, cups of caffeinated tea and servings of caffeinated soda they would consume. (Interviewers were instructed which of the typical soft drinks did and did not contain caffeine.) If they reported drinking coffee, we specifically inquired whether the coffee was largely brewed or instant. We converted these reports into daily caffeine consumption using the following estimates of caffeine content: ground coffee 125 mg/cup, instant coffee 90 mg/cup, tea 60 mg/cup and caffeinated soft drinks 40 mg/can (James, 1997). Caffeine consumption per month was then calculated by multiplying the average consumption per day by the average numbers of days per month in which caffeine was consumed. In our analyses, we used the unit of 100 mg of caffeine per average day. We defined ‘heavy use’ as individuals who, in the past year, reported consuming caffeinated beverages the most, did you ever feel ill or shaky or jittery after drinking caffeinated beverages?’ We defined caffeine dependence as the sum of endorsed items that evaluated caffeine tolerance and caffeine withdrawal. Tolerance was assessed by the response to two questions adapted from the Psychoactive Substance Abuse Section of the Structured Clinical Interview for DSM-III-R (SCID; Spitzer et al. 1987): (1) ‘During the time when you were consuming caffeinated beverages the most, did you find that you needed to drink a lot more to get the desired effect than you did when you first drank them?’ and (2) ‘What about finding out that when you drank the same amount, it had much less effect than before?’ All individuals who responded positively to the question ‘Did you ever stop or try to cut down on your consumption of caffeinated beverages?’ were asked about the four symptoms of caffeine withdrawal listed in criterion B for the Caffeine Withdrawal Syndrome in DSM-IV (APA, 1994): headaches, marked fatigue or drowsiness, marked anxiety or depression, and nausea or vomiting. For analysis, everyone was classified as having 0, 1, 2, 3 or 4 or more symptoms of tolerance or withdrawal, which we called caffeine dependence.

Short-term test–retest reliability data [and 95% confidence intervals (CIs)] were obtained on our caffeine-related measures from 334 twins interviewed a mean (s.d.) of 5·4 (6·4) weeks apart. The intraclass correlation for lifetime maximal caffeine intake was +0·74 (0·68–0·78). The unweighted $k$ values for heavy use and toxicity were 0·69 (0·57–0·80) and 0·62 (0·53–0·72) respectively. The weighted $k$ for symptoms of caffeine dependence was 0·59 (0·52–0·66).

Information on lifetime psychiatric and substance use disorders were collected at previous waves by personal interview using an adaptation of the SCID interview (Spitzer et al. 1987). The number of individuals assessed (and hence the sample size used in these analyses) varied as a function of the cooperation at that wave. The following diagnostic criteria were used: major depression (DSM-III-R; APA, 1987); alcohol dependence (DSM-IV; APA, 1994); and drug abuse/dependence (DSM-IV). We defined adult antisocial personality disorder as meeting at
least three of the DSM-III-R C criteria for antisocial personality disorder. To reduce the effects of a social desirability bias (Siemiatycki, 1979; Nederhof, 1985), adult antisocial behavior was assessed by self-report. As the low prevalence of generalized anxiety and panic disorder had been problematic in prior analyses (Hettema et al., 2001; Kendler et al., 2001), we took a broad diagnostic approach to these two disorders, reducing the minimum duration from 6 months to 1 month for the former and requiring for the latter only a history of panic attacks meeting at least two criteria within 30 min. We have shown that these broader syndromes reflect the same continuum of liability as the fully syndromal disorders (Hettema et al., 2001; Kendler et al., 2001). For some purposes, we divided our seven disorders into two groups: internalizing (major depression (MD), generalized anxiety disorder (GAD) and panic) and externalizing (alcohol dependence, cannabis and cocaine abuse/dependence and adult antisocial personality disorder). Although we collected data on conduct disorder and phobias in this sample, these were not included in these analyses because their age at onset often occurred before the onset of substantial caffeine consumption (Kessler et al., 2005). In our assessment of MD, GAD and panic disorder, we asked the subjects to rule out episodes that were a result of ‘taking drugs or medicine’. However, we cannot be certain that episodes that might have been related to caffeine use would have been detected by such questions.

Statistical analysis

A small number of twins reported very high levels of maximal monthly caffeine use. To avoid undue influence from these subjects (n = 13, 0.4% of the sample), we truncated this variable to a maximal value of 90,000 mg/month or 3000 mg/day, equal to about 24 cups of ground coffee per day.

We examined the association between our four caffeine-related variables and risk for lifetime diagnoses of seven psychiatric and substance use disorders by logistic regression. Using the SAS procedure GLIMMIX (SAS Institute, 2005), we then applied a generalized hierarchical linear model treating the twin pair as a random effect (Neuhaus & Kalbfleisch, 1998). These analyses can be understood as a quantitative and more statistically efficient version of a conditional logistic regression (i.e. a co-twin control analysis; Kendler et al., 1993). Assume, as an example, we are studying the association between caffeine use and risk for lifetime MD. Controlling for sex and age, these analyses assess the impact on risk for MD of both the mean level of caffeine consumption in the twin pair and the deviation of the caffeine use of the individual twin from that mean value. It is the latter variable that is of interest to us. We apply this model solely to MZ twins who share all their genetic and family background. This within-family effect obtained from the GLIMMIX analyses should be at least as large and possibly slightly larger than that observed from a more traditional logistic regression in the entire population if the association is truly causal (Agresti, 2002). However, the odds ratios (ORs) observed in these analyses are not exactly analogous to those obtained by standard logistic regression because the within-family effect is conditioned on the between-family effect specifically for each family whereas the ordinary logistic regression contains a between- and within-family effect averaged across the entire population. If, however, the association between caffeine intake and risk for MD was not causal but was instead due entirely to familial–environmental or genetic factors shared in common by the two constructs, then the within-family effect from the GLIMMIX procedure should produce an OR approximating unity.

RESULTS

Data on caffeine use were available on 3706 subjects (51.8% female). Of these 3706 subjects, 103 (2.8%) denied a lifetime history of any regular caffeine use. We reran these analyses excluding these individuals and no appreciable changes were seen. For our analyses between the caffeine-related variable and sex in the prediction of psychopathology.

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of caffeine toxicity and dependence, these subjects were excluded.

Controlling for age, the mean (s.d.) daily caffeine consumption during the time of maximal use was significantly greater in males [403·4 mg (431·2)] than in females [324·2 mg (345·6)] (t = 6.09, df = 3703, p < 0.0001). Heavy caffeine use was significantly more common in men (17·3%) than in women (11·4%) (x²[345·6] reported by 47.8% of men versus 1·0% of women (324·2 mg). Maximal caffeine use was significantly greater in males 0.9(1·2) than in females 0·6(1·0) (t = 6.8, df = 3608, p < 0.0001). One or more symptoms of caffeine dependence was reported by 47·8% of men versus 36·6% of women (x²[345·6] = 47·7, df = 1, p < 0.0001). The age at maximal caffeine use was 21·2 (7·9) years in women and 22·5 (8·8) in men.

The association between caffeine intake, toxicity and dependence and lifetime psychopathology

The ORs between caffeine use, heavy use, toxicity and dependence and lifetime diagnoses of seven major psychiatric and substance use syndromes were all positive and statistically significant (Table 1). In each analysis, we tested whether the association between the caffeine variable and the disorder differed significantly in men and women. Of the 28 analyses, two were statistically significant at the 5% level (the associations between caffeine consumption and MD and caffeine dependence and cannabis abuse/dependence were both significantly stronger in women than in men), which is within the range of chance effects (Feild & Armenakis, 1974).

For maximal lifetime caffeine use, where the OR was calculated per 100 mg caffeine per day, ORs were somewhat higher for externalizing disorders (range 1·07–1·08) than for internalizing disorders (range 1·05–1·06). A similar pattern was seen for lifetime heavy caffeine use, with ORs ranging from 1·50 to 1·83 for internalizing disorders and from 1·94 to 2·34 for externalizing disorders. For toxicity, the ORs were similar across all disorders (ranging only from 1·67 to 1·90) although it is perhaps noteworthy that the OR was highest for GAD.

For symptoms of caffeine dependence, ORs (per symptom) were in the narrow range of 1·15–1·22 for all disorders, with the exception of MD and GAD, where the ORs per symptom were 1·31 and 1·34 respectively.

Analyses within MZ twin pairs

To gain insight into the causal relationship between caffeine use and related symptoms and risk for psychiatric and substance use disorders, we conducted generalized hierarchical linear model analyses within MZ twin pairs (see above for details). The ORs depicted in Table 2 represent the within-family effect. For example, in examining the association between caffeine intake and risk for MD, the OR of 1·02 in Table 2 means that for each 100 mg in which the

Table 1. The association between caffeine intake, heavy caffeine use, toxicity and symptoms of dependence and risk for seven common psychiatric and substance use disorders

<table>
<thead>
<tr>
<th></th>
<th>Caffeine intake</th>
<th>Heavy caffeine use</th>
<th>Toxicity</th>
<th>Symptoms of dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>OR</td>
<td>95% CI</td>
<td>n</td>
</tr>
<tr>
<td>MD</td>
<td>3706</td>
<td>1·06*</td>
<td>1·04–1·08</td>
<td>3706</td>
</tr>
<tr>
<td>GAD</td>
<td>3485</td>
<td>1·06*</td>
<td>1·03–1·08</td>
<td>3485</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>3425</td>
<td>1·05*</td>
<td>1·02–1·07</td>
<td>3425</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>3706</td>
<td>1·08*</td>
<td>1·06–1·10</td>
<td>3706</td>
</tr>
<tr>
<td>Cannabis abuse/dependence</td>
<td>3706</td>
<td>1·07*</td>
<td>1·05–1·09</td>
<td>3706</td>
</tr>
<tr>
<td>Cocaine abuse/dependence</td>
<td>3706</td>
<td>1·08*</td>
<td>1·05–1·11</td>
<td>3706</td>
</tr>
<tr>
<td>AAPD</td>
<td>3204</td>
<td>1·08*</td>
<td>1·05–1·10</td>
<td>3204</td>
</tr>
</tbody>
</table>

MD, Major depression; GAD, generalized anxiety disorder; AAPD, adult antisocial personality disorder; OR, odds ratio; CI, confidence interval.

Levels of significance: * if p < 0·0001, † if p < 0·0010, ‡ if p < 0·0100, § if p < 0·0500.

a Odds ratio per 100 mg of caffeine/day.

b Odds ratio per symptom of caffeine dependence.
caffeine consumption in the high-using twin exceeds that of the low-using co-twin, the risk for MD in the high-caffeine-consuming twin exceeds that of the low-consuming co-twin by 2%.

Three broad patterns of results are noteworthy (Table 2). First, in marked contrast to the findings in the entire sample, within MZ twin pairs no significant associations were seen between caffeine intake, toxicity or symptoms of dependence and the risk for the seven examined disorders. As our sample size has decreased, it could be that the loss of statistical significance merely reflects less statistical power. However, second, 27 of the 28 ORs seen in Table 2 were lower than the parallel ORs observed in Table 1, the only exception being GAD and caffeine intake. Third, 27 of the 28 ORs seen in Table 2 were greater than 1, a pattern extremely unlikely to occur by chance (p < 0.001 by sign test) alone.

DISCUSSION

Despite its widespread use in most human populations, the association between caffeine consumption and adverse symptoms related to caffeine use on the one hand and psychiatric and substance use disorders on the other has been inadequately investigated. We found, in a population-based sample of adult twins from Virginia, consistent and significant positive associations between measures of maximal lifetime caffeine consumption, caffeine-induced toxicity and symptoms of caffeine dependence and risk for a broad array of common psychiatric and substance use disorders. Although men consumed more caffeine than women and had significantly more symptoms of caffeine dependence, no systematic differences were found in the association between our caffeine-related variables and psychopathology in the two sexes. These results are broadly consistent with previous reports suggesting associations between caffeine consumption and anxiety, depressive and substance use disorders (Greden et al. 1978; Veleber & Templer, 1984; James & Crosbie, 1987; Strain et al. 1994; Hughes et al. 2000; Griffiths et al. 2003). However, we were unable to find a prior comparable general population, epidemiologic study.

Associations, however, do not alone provide information about the causal relationship between the putative risk factor and the outcome variable. In particular, it is important to distinguish between direct causal and correlated liability models for the association between caffeine intake, toxicity and dependence and psychiatric and drug use disorders.

Our results suggest that both mechanisms may be operative. Most impressively, when we control for shared genes and shared rearing environment by examining the associations between our caffeine-related risk factors and our psychopathologic outcomes within MZ twin pairs, they all become non-significant. Furthermore, the ORs seen with MZ twin pairs are nearly always lower and often substantially so compared to those seen in the entire sample.

Table 2. The association within monozygotic twin pairs between caffeine intake, heavy caffeine use, toxicity and symptoms of dependence and risk for seven common psychiatric and substance use disorders

<table>
<thead>
<tr>
<th>Caffeine intake</th>
<th>Heavy caffeine use</th>
<th>Toxicity</th>
<th>Symptoms of dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>ORa</td>
<td>95% CI</td>
<td>n</td>
</tr>
<tr>
<td>MD</td>
<td>2230</td>
<td>1.02</td>
<td>0.98–1.07</td>
</tr>
<tr>
<td>GAD</td>
<td>2067</td>
<td>1.08</td>
<td>0.99–1.18</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>2039</td>
<td>1.04</td>
<td>0.97–1.12</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>2230</td>
<td>1.04</td>
<td>0.99–1.09</td>
</tr>
<tr>
<td>Cannabis abuse/dependence</td>
<td>2230</td>
<td>1.05</td>
<td>0.99–1.11</td>
</tr>
<tr>
<td>Cocaine abuse/dependence</td>
<td>2230</td>
<td>1.03</td>
<td>0.95–1.13</td>
</tr>
<tr>
<td>AAPD</td>
<td>1937</td>
<td>1.06</td>
<td>1.00–1.14</td>
</tr>
</tbody>
</table>

MD, major depression; GAD, generalized anxiety disorder; AAPD, adult antisocial personality disorder; OR, odds ratio; CI, confidence interval.

a Odds ratio per 100 mg of caffeine/day.
b Odds ratio per symptom of caffeine dependence.
These findings provide considerable support for the correlated liability model. A substantial proportion of the association between caffeine-related variables (intake, toxicity and dependence) and our seven psychiatric and substance use disorder results from familial factors that are shared by MZ twins and predispose to caffeine use, toxicity or dependence on the one hand and risk for psychiatric and substance use disorders on the other.

Our findings also provide support for direct causal models albeit in a less impressive way. Although none of the ORs found within MZ twin pairs was statistically significant, a number came close, and the overall pattern of results, with 27/28 ORs exceeding unity, its itself extremely improbable. We interpret these results as suggesting that within MZ twin pairs, the twin who consumes more caffeine or reports more caffeine-associated toxicity or dependence is at some increased risk for psychopathology. However, the magnitude of this increase is modest and too small to be detected at traditional levels of statistical significance in our sample. In this context, it is noteworthy that by far the highest OR for maximal caffeine intake in the MZ pairs was for GAD, which would be consistent with prior data supporting the anxiogenic effects of caffeine (Veleber & Templer, 1984; James & Crosbie, 1987; Griffiths et al. 2003).

Limitations
These results should be interpreted in the context of the following potential methodological limitations. First, it would be possible to clarify the causal relationship between caffeine use and psychopathology by a prospective analysis of the pattern of caffeine use over time and the age at onset of various psychiatric and substance use disorders. However, this was not possible with our data collected in adults.

Second, by examining only MZ twin pairs, we could not determine whether the correlated liability that impacts on risk for caffeine-related variables and psychopathology results from genetic and/or shared environmental factors. To do this requires the inclusion of dizygotic (DZ) twin pairs and an associated substantial increase in complexity of analysis. We completed analyses presented in Table 2 for MZ pairs on the DZ pairs in our sample. In general, the observed ORs were in between those seen in the entire sample and in the MZ pairs, with some reaching statistical significance. This is the pattern that would be expected if most of the association between caffeine intake, toxicity and symptoms of dependence and psychopathology resulted from shared genetic risk factors.

Third, while our analyses examined the ability of caffeine to predict psychopathology, some of the association between these variables could arise because psychiatrically ill individuals consume caffeine in an attempt at self-treatment (Leibenluft et al. 1993). We do not attempt to discriminate between these alternative explanations in this report. However, our analyses presented in Tables 1 and 2 would be expected to yield a similar pattern of findings if we used psychopathology to predict caffeine use and associated symptoms. That is, we would find strong associations when examining using traditional regression but much weaker and largely non-significant effects when examining within twin pairs. To illustrate this, we found, using standard linear regression (and correcting for the twin structure of the data), that a history of MD strongly predicted maximal lifetime caffeine use ($\beta = 0.12, \ z = 4.14, \ p < 0.0001$). However, when examining this relationship within MZ twin pairs, the association, while still positive, was no longer significant ($\beta = 0.07, \ t = 1.89, \ df = 971, \ p = 0.06$). Thus, our pattern of findings can be best interpreted as follows: most of the observed association between caffeine-related variables and psychiatric and drug use disorders is not a result of a direct causal effect either of caffeine use and related symptoms on psychopathology or of psychopathology on caffeine use and symptoms.

Fourth, our assessments of caffeine use and caffeine-related symptoms were all obtained retrospectively. Although we demonstrated good to excellent reliability for these assessments, we cannot rule the possibility that suffering from a psychiatric illness might systematically alter recall in a way that would bias the results presented in Tables 1 and 2. In the female twins in this sample, we assessed, at the time of the interview containing the caffeine-related questions, whether they were currently ‘in an episode’ with symptoms of depression or anxiety. Controlling for age and lifetime history of MD, being in a depressive episode did not
significantly predict their reports of caffeine intake, heavy caffeine use or toxicity (all $p > 0.10$) but did marginally predict symptoms of dependence ($p = 0.04$, OR = 1.26). A nearly identical pattern was seen with GAD and current symptoms of anxiety. A modest proportion of the observed association between MD and GAD and caffeine dependence, but not caffeine use or toxicity, could result from retrospective recall bias in which symptomatic individuals exaggerate prior dependence symptoms. Alternatively, individuals with a high vulnerability to caffeine dependence may be more prone to chronic symptoms of anxiety and depression.

Finally, this sample was made up entirely of White native-born Virginians and thus these findings may or may not extrapolate to other populations and ethnic groups.

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DECLARATION OF INTEREST

None.

REFERENCES


