

The genetics of tea and coffee drinking and preference for source of caffeine in a large community sample of Australian twins

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ABSTRACT

Aims To investigate the genetic and environmental influences on tea consumption and their commonalities with coffee consumption; and to further examine the genetic and environmental aetiology of preference for tea/coffee.

Design A classical twin design was used in which the similarity of identical and non-identical twins is compared, enabling estimates of genetic, common environmental and unique environmental influence on the trait.

Setting and participants An Australian population-based sample of 1796 identical (i.e. monozygotic) and 2013 non-identical (i.e. dizygotic) twin pairs aged 16–87 years was studied, roughly three-fifths of whom were female. The sample represented approximately 70% of those approached for study participation.

Measurements As part of a Health and Lifestyle Questionnaire, respondents were asked how many cups of each tea and coffee they consumed per day. Additional measures of 'total tea and coffee consumption' and 'preference for coffee' were calculated.

Findings Age was positively associated with tea consumption but negatively associated with coffee preference; women consumed more beverages than men, but showed a lower preference for coffee. An inverse relation between tea and coffee consumption—larger in females (−0.41) than males (−0.34)—was supported. This association was mediated entirely by the unique environment in males, and by both the unique environment (68.3%) and genes (31.7%) in females. Tea and coffee drinking were shown to have similar heritabilities (0.46) in males, but tea consumption was influenced by common environmental factors whereas coffee consumption was not. Coffee preference was shown to be influenced by genes (0.42) and the unique environment (0.58).

Conclusions As the patterns of genetic and environmental variation were shown to differ for tea and coffee consumption it may be more informative to retain them as separate measures of caffeine intake in future studies of stimulant use and taste perception.

KEYWORDS Caffeine, coffee consumption, genetic and environmental influences, tea consumption.

INTRODUCTION

Caffeine is an ingredient of tea, coffee, chocolate and cola-based drinks consumed widely in modern society

(Drewnowski 2001). While caffeine is added to drink/food products to purportedly improve their flavour, it is also known that caffeine dependency can affect taste perception through respondent and operant conditioning,

and for this reason people may report an enhanced liking (or flavour) for products containing caffeine (e.g. Rogers, Richardson & Elliman 1995; Yeomans *et al.* 2000; Yeomans, Durlach & Tinley 2005). As caffeine acts as a stimulant, its psychoactive effects and the withdrawal symptoms associated with abstinence in habitual users tends to dictate its use rather than taste alone (Hughes *et al.* 1991; Kendler & Prescott 1999; Vaugeois 2002; Juliano & Griffiths 2004). The symptoms of caffeine withdrawal have been reviewed recently by Juliano & Griffiths (2004) and include headache, fatigue, decreased energy/activeness, decreased alertness, drowsiness, decreased contentedness, depressed mood, difficulty concentrating, irritability and foggy headedness.

Positive effects of caffeine consumption have related mainly to psychomotor speed (Mitchell & Redman 1992; Jarvis 1993; Smith, Sturgess & Gallagher 1999), but accumulating evidence suggests that these improvements (and similar positive effects observed for mood state) reflect a withdrawal reversal mechanism operating in habitual caffeine users (Yeomans *et al.* 2002; Rogers *et al.* 2003; James & Gregg 2004). For instance, Yeomans *et al.* (2002) showed that the benefits of caffeine on psychomotor tasks were only apparent in (overnight) caffeine-withdrawn participants and not in participants pre-loaded with caffeine an hour earlier (i.e. not caffeine-withdrawn). Whether caffeine improves or reverses the negative effects of caffeine withdrawal on mental performance and mood state (e.g. alertness) is an unresolved issue, with a recent finding arguing against the caffeine withdrawal hypothesis (Christopher *et al.* 2005). Caffeine, however, is known to be related to sleep disturbance (Goldstein, Warren & Kaizer 1965; Heath *et al.* 1998) and a range of other adverse health effects, including raised blood pressure, palpitations and tremor (Shirlow & Mathers 1985; Hughes *et al.* 1991; James 1997). Together with the negative psychological and physiological effects of caffeine withdrawal, these reasons make the study of caffeine consumption important, with the present study focused on its genetic and environmental influences.

Early twin studies on the effects of caffeine centred on the quantification of genetic influences on coffee consumption (Partanen, Bruun & Markkanen 1966; Kaprio *et al.* 1978; Pedersen 1981; Carmelli *et al.* 1990) and a substantial range of heritability (i.e. proportion of variance in a trait due to genes) estimates was reported. More recently, focus has shifted to the consideration of caffeine as a (licit) psychoactive drug. Hettema, Corey & Kendler (1999) measured the contributions of genetic and environmental factors to variance in the use of several psychoactive substances including caffeine. Heritability for caffeine consumption in that sample was found to be 0.58 for both men and women. A moderate proportion of

both genetic and non-shared environmental factors on caffeine consumption were also found to influence alcohol and tobacco use. Research on the genetics of caffeine toxicity, tolerance, withdrawal and heavy caffeine intake in women from the same Virginia Twin Registry sample estimated the heritability of heavy caffeine use to be 77%, while broad heritabilities for the other measures ranged from 35% to 45% (Kendler & Prescott 1999).

Complicating the study of influences on caffeine consumption is the potential for genes to also influence our food choices and eating habits through taste perception (Reed *et al.* 1999; Reed 2000; Ly & Drewnowski 2001). As a result, it is important to consider any potential relationship between genetic influences on caffeine consumption and those on perception of taste, both of which may influence a person's preference for tea or coffee. In this study of adult Australian twins, we consider not only levels of consumption of caffeine in an Australian twin sample, but also subjects' preferences in terms of caffeinated drinks, namely tea or coffee.

METHOD

Sample

Twins for this study were drawn from the Australian National Health and Medical Research Council (NHMRC) Twin Register (Jardine, Martin & Henderson 1984; Kendler *et al.* 1987). This volunteer register began in 1978, and at the time of data collection for this study it was estimated that approximately 10% of all twins in Australia were enrolled. Between 1980 and 1982, a Health and Lifestyle Questionnaire was mailed to all 5967 available twin pairs born prior to 1965. Responses were received from 3809 complete pairs of twins (64%) and 570 singles (9%; only 548 of these were included in the analysis due to incomplete zygosity information). The age of the sample ranged from 16.3 to 87.3 years, with an average age of 34.1 (± 14.1) years, but note that only 1% of the sample was younger than 18 years of age.

Zygosity determination

Initially, the zygosity of twins in this sample was determined on the basis of responses to standard questions about physical similarity and the degree to which others confused them with one another. This method has been shown to give at least 95% agreement with diagnosis based on extensive blood typing (Martin & Martin 1975). Inconsistencies in the twins' responses were followed-up by telephone and asking them to send in photographs, reducing the misclassification rate still further. More recently, 10.8% of the same-sex pairs sample has been

typed for 11 independent highly polymorphic markers. The sample in this study consisted of 1231 monozygotic (MZ) female twin pairs (78 single members of a twin pair), 565 MZ male twin pairs (60 singles), 749 dizygotic (DZ) female twin pairs (102 singles), 353 DZ male twin pairs (88 singles) and 911 opposite-sex twin pairs (221 singles).

Measures of caffeine consumption

As part of the Health and Lifestyle Questionnaire, each respondent was asked: 'on average, how many cups of tea would you drink?' and 'on average, how many cups of coffee would you drink?', with the answers expressed in cups per day. Note that no distinction between regular and decaffeinated tea and coffee was made because at the time of this study decaffeinated products were not in common use. Furthermore, canned beverages (e.g. Coca-Cola) were not used widely in Australia as a source of caffeine at that time. From this information, the total number of caffeinated drinks consumed per day was calculated. While it would be ideal to quantify the caffeine content by milligrams, especially as tea is generally of a lower content than coffee, it is also known that caffeine content can vary depending on the style of coffee (e.g. brewed versus instant), and as we do not have this information we have not extrapolated our data to form such an index. An additional measure, overall preference for coffee, was obtained from the ratio of number cups of coffee consumed to the total number of caffeinated drinks consumed. A person who drank only tea would therefore score 0 on this scale, and a person who exclusively drank coffee would score 1. If neither tea nor coffee was consumed, the score on this scale would be coded as missing.

The percentage of people falling into the different response categories for tea and coffee consumption is

shown in Table 1. The trend towards greater preference for tea consumption is consistent with Australian population data from the late 1970s, which shows yearly tea consumption as slightly higher than coffee consumption (1.7 versus 1.6 kg/per person). It is important to note that in Australia today coffee consumption is double that of tea, with estimates of per capita consumption in the late 1990s rising to 2.4 kg for coffee and falling to 0.9 kg for tea (Australian Bureau of Statistics 2003).

To check how well tea and coffee consumption indexed total caffeine consumption, a subset of participants (16.2% of the full sample) for whom information on cola consumption was available was examined. This subsample ($n = 1327$ individuals) completed a Health and Lifestyle Questionnaire between 1993 and 1996 (Kirk, Hickie & Martin 1999) and were aged over 50 years; that is, the latest birth year was 1946 compared with 1964 for the entire cohort and thus does not represent the youngest approximately 40% of the sample. Seven-and-a-half per cent of the sample reported drinking cola beverages, with a median daily consumption of one drink. Only six participants reported cola use without tea/coffee consumption and of these, four drank a single cola beverage per day. Cola consumption was not associated with either tea or coffee consumption, whereas tea and coffee consumption were negatively correlated. We therefore conclude that cola consumption is not a major confounding factor in the present analysis, at least for those born before 1947.

A further analysis of the effects of body weight and body mass index (BMI) on tea and coffee was performed, as it is conceivable that more caffeine is required for heavier people to attain comparable caffeine plasma levels of lighter people (James 1991). These analyses were performed separately for males and females, and controlled for age; weight and BMI correlated 0.08 with

Table 1 Frequency (%) of tea and coffee consumption and coffee preference by sex.

Number of cups/day	0–2	3–5	6–8	9–11	12+
Tea consumption					
Women ($n = 5213$)	56.5	30.6	9.8	2.2	0.9
Men ($n = 2954$)	65.3	25.2	7.2	1.5	0.8
Coffee consumption					
Women ($n = 5213$)	61.4	28.2	8.3	1.6	0.5
Men ($n = 2954$)	65.8	25.5	6.7	1.3	0.7
Total tea and coffee					
Women ($n = 5213$)	16.7	45.7	28.8	5.9	2.9
Men ($n = 2954$)	27.5	42.9	21.6	5.8	2.2
Coffee preference*					
	0–0.20	0.21–0.40	0.41–0.60	0.61–0.80	0.81–1
Women ($n = 4951$)	22.6	23.9	11.7	19.5	22.3
Men ($n = 2828$)	21.3	23.8	12.3	19.6	23.0

*Defined as the proportion of coffee to total tea and coffee drinks consumed per day. For individuals who did not drink tea or coffee, their score would be missing on this scale.

coffee consumption in females ($P < 0.01$), and BMI correlated 0.04 with coffee consumption in males ($P < 0.05$). These effects were minor and were therefore not included in further statistical modelling.

Statistical methods

The maximum number of cups of coffee consumed per day in this sample was 23 cups, while the maximum number of cups of tea per day was 30. As the scales of the first three variables (tea, coffee and caffeinated drinks consumed) differed substantially from the fourth (coffee preference), we chose to convert the measures into categorical variables, thus avoiding problems of positive skew in the consumption measures and a multi-modal coffee preference distribution. The data were therefore analysed in terms of threshold models, which assume that underlying each variable is a continuum of liability which is normally distributed in the population, and in which thresholds are imposed to define the category boundaries (Neale & Cardon 1992).

To estimate the proportions of genetic (A), common environmental (C) and unique environmental (E) variance influencing tea and coffee consumption, the classical twin design was used. This design is based on the comparison of MZ twin pairs who share 100% of their genes with DZ twins who share roughly 50% of their segregating genes. If the causes of familial similarity are the additive effects of genes (transmissible from parent to child), the correlation in caffeine consumption of MZ co-twins is expected to be twice that of DZ co-twins. Simultaneous equations, established by the known relationship among MZ and DZ co-twins, were therefore applied to the data ($r_{MZ} = A + C$; $r_{DZ} = \frac{1}{2}A + C$). Unique (or non-shared) environmental effects—that include measurement error—are not shared by co-twins and are hence absent from the covariance equations. Genetic and environmental estimates of variance and covariance between tea and coffee measures were estimated using a maximum likelihood procedure based on raw categorical data and including data from single co-twins (while they do not contribute to estimates of covariance they do contribute to threshold estimates).

Assumptions concerning the equality of thresholds across zygosity were initially tested, also using a maximum likelihood approach. The fixed effects of age and sex were parameterized in terms of an age regression coefficient and a sex deviation which were set equal across the five zygosity groups (MZ female, MZ male, DZ female, DZ male, DZ opposite-sex). Age coefficients and sex deviations were constrained equal between thresholds if no significant deterioration in model fit was observed. The equality of co-twin correlations within MZ and within DZ groups was examined to check for potential sex

differences in the genetic and environmental variance components, known as sex limitation. Univariate analyses which decomposed the variance into genetic and environmental (common and unique) components were performed prior to bivariate modelling of tea and coffee consumption. All analysis was performed using the statistical program, Mx (Neale 1997), with model fit judged by the likelihood ratio χ^2 test (Neale & Cardon 1992). Model evaluation involves comparing a simplified model (i.e. fewer estimated parameters) to one in which it is nested, thus a non-significant χ^2 indicates acceptable fit of the simplified model to the data.

RESULTS

Sex and age both had significant effects on all variables ($P < 0.001$), with the exception of a non-significant age effect on coffee consumption. Age was positively correlated with tea consumption (unstandardized regression β of 0.02) and total consumption, but was negatively correlated with coffee preference ($\beta = 0.01$). Females consumed more tea ($\beta = 0.21$) and coffee ($\beta = 0.12$) beverages than males and showed a lower preference for coffee ($\beta = 0.05$) than males.

The preliminary data analyses of tea and coffee variables showed some differences in thresholds between zygosity groups. For tea consumption, thresholds could not be equated for males from MZ, DZ same-sex, and DZ opposite-sex groups ($\chi^2_{8\text{ df}} = 19.27$, $P < 0.05$). As the sample comprised more female than male twins, it is likely that this anomaly is due to sampling error in the male sample. Results for tea consumption suggested the presence of sex limitation because the DZ same-sex and DZ opposite-sex twin correlations (0.34 versus 0.23) differed ($\chi^2_{1\text{ df}} = 4.34$, $P < 0.05$). Similarly, this difference in correlations was found for total consumption ($\chi^2_{1\text{ df}} = 4.77$, $P < 0.05$), with the DZ opposite-sex correlation slightly lower (0.23) than the DZ same-sex correlation (0.33). Table 2 shows the maximum likelihood estimates of correlations between co-twins for each zygosity group.

Also, the correlation between tea and coffee consumption differed between sexes ($\chi^2_{2\text{ df}} = 11.83$, $P < 0.01$). The respective correlations for females and males were -0.41 and -0.34 , so that increased tea consumption was associated with decreased coffee consumption and vice-versa. There was no correlation between coffee preference and total drinks consumed.

The genetic and environmental contributions to variance in each of the measures were estimated while simultaneously removing the effects of age and sex. Where sex limitation was indicated by the co-twin correlations, a sex limitation model was tested. However, results of these tests showed that a single set of genetic and

Table 2 Maximum likelihood co-twin correlations for the measures of tea and coffee consumption.

	<i>Tea consumption</i>	<i>Coffee consumption</i>	<i>Total tea and coffee</i>	<i>Coffee preference</i>
MZ female	0.48	0.53	0.54	0.46
MZ male	0.53	0.50	0.55	0.38
DZ female	0.35	0.23	0.37	0.20
DZ male	0.33	0.20	0.24	0.18
DZ opposite-sex	0.23	0.18	0.23	0.16

MZ: monozygotic; DZ: dizygotic.

Table 3 Univariate analysis results (proportions of additive genetic, common and unique environmental variance), including 95% confidence intervals (shown in parentheses). Estimates are derived from a model which includes the regression of age and sex on consumption measures.

	<i>Additive genes</i>	<i>Common environment</i>	<i>Unique environment</i>
Tea consumption	0.26 (0.05–0.49)	0.22 (0.01–0.40)	0.52 (0.46–0.58)
Coffee consumption	0.51 (0.46–0.55)	0 (0–0.04)	0.49 (0.45–0.50)
Total consumption	0.48 (0.40–0.58)	0.06 (0.05–0.14)	0.46 (0.42–0.49)
Coffee preference	0.42 (0.32–0.46)	0 (0–0.08)	0.58 (0.53–0.62)

environmental parameters was sufficient to explain variation in males and females for all measures examined in the univariate analyses. Table 3 displays the proportions of variance explained by additive genes, common environment and unique environment for each of the measures. Genetic effects were shown to be larger than common environmental effects, but of equal or lesser magnitude to unique environmental effects.

As there was a significant negative correlation between tea and coffee consumption, a bivariate analysis of the genetic and environmental covariance between these measures was performed. Phenotypic correlations between tea and coffee consumption were shown to differ between sexes, so the equality of male and female genetic and environmental parameters was initially tested, with results supporting different covariance structures in males and females ($\chi^2_{6,df} = 14.76$, $P < 0.05$). These covariance structures are shown in the path diagrams of Fig. 1. The main difference between the models for females and males was the absence of a shared genetic factor influencing tea and coffee consumption in males.

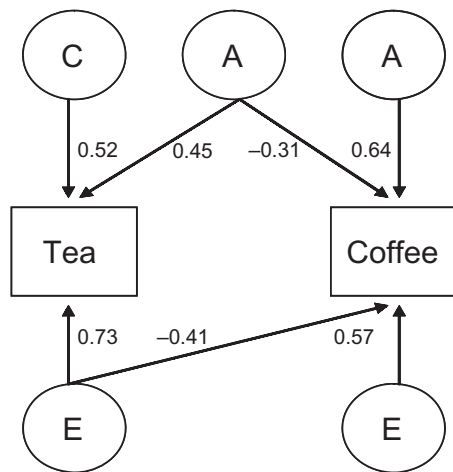
DISCUSSION

This study was focused on partitioning the environmental and genetic variance contributing to tea and coffee consumption. Due to the substantial negative dependence between tea and coffee drinking it was important to compose new measures to index overall caffeine consumption and taste preference. While reciprocal

causation modelling of tea and coffee consumption would ideally explain their observed phenotypic correlation, specification of a genetic factor loading directly on tea and coffee consumption (reflecting common genes involved in caffeine dependence) would lead to this model being statistically under-identified, and thus unsolvable. Hence, univariate analyses of tea consumption, coffee consumption, total consumption and coffee preference were performed, with further bivariate analysis of tea and coffee consumption to disentangle the genetic and environmental causes of their negative association.

As demonstrated by previous studies (Hettema *et al.* 1999; Kendler & Prescott 1999), the amount of caffeinated drinks consumed by individuals is subject to substantial genetic influences, as well as environmental influences. While we confirmed a similar proportion of genetic variance in total caffeine consumption (0.48), we further showed that tea consumption was less heritable than coffee consumption (0.26 versus 0.51). This may stem partially from the fact that tea has less caffeine content than coffee so that genetic loci influencing the common pathway of drug dependence have greater effects on coffee consumption due to its increased potential for addiction. Environmental effects were also different for tea and coffee consumption: while tea drinking was influenced by common and unique environmental factors, coffee consumption was only influenced by non-shared factors. Therefore, in addition to exposure to tea and coffee drinking from peer groups, the work-place and other unique environmental influences, exposure to tea, but not coffee, through the family (or some other common) environment is important.

a) Women



b) Men

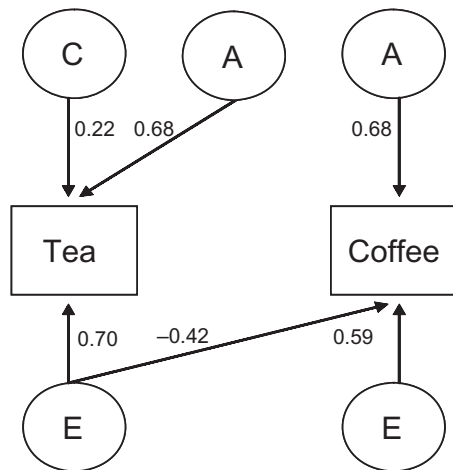


Figure 1 Path diagrams showing latent additive genetic (A), shared environmental (C) and unique environmental (E) effects (represented by circles) on the measured phenotypes of tea and coffee consumption (represented by rectangles). Standardized path coefficients are shown, and must be squared to obtain proportions of variance of the measured variable accounted for by the latent variable. Separate path parameters are shown for models representing aetiology in (a) women and (b) men. Only statistically significant paths are shown

The negative correlation between average number of drinks of tea and coffee consumed was expected—a person will only consume a certain number of drinks per day, and the consumption of one type of drink will automatically limit the consumption of other types of drinks. Our finding of a stronger negative correlation between tea and coffee consumption for women (-0.41) than men (-0.34) has been found previously in a Scottish sample, with reported female and male correlations of -0.65 and -0.58 , respectively (Woodward & Tunstall-Pedoe 1999). The stronger female correlation suggests that women are

more inclined to satisfy their drinking preference than men.

Preference for tea or coffee was shown to be 42% heritable, with the remaining variance explained by the unique environment. Part of the genetic variation may be due to genes that control the psychoactive responses to caffeine or are associated with caffeine withdrawal; those preferring coffee to tea may do so for its increased caffeine level and thus addictive properties. Coffee preference may also be influenced by genes determining taste perception, especially bitterness. There is some evidence that tasters of 6-*n*-propylthiouracil (a bitter compound) rate caffeine solutions as more bitter than people who are unable to taste this compound and report a heightened dislike for such a taste (Ly & Drewnowski 2001). These people may therefore prefer tea to coffee as it contains less caffeine, although the addition of sweeteners to caffeinated drinks will attenuate this relationship (and this has not been measured in our sample).

In men, tea and coffee intake were shown to be influenced by different genes with similar effect sizes. In women, there were no unique genetic influences on tea consumption: genes that increased tea consumption decreased coffee consumption. This trade-off of coffee for tea (and vice versa) explained the heightened negative correlation between tea and coffee consumption observed for females than males and may be explained by women's motivation to satisfy their taste preference and this could be influenced by genes and/or the unique environment. However, the larger portion of shared variance between tea and coffee consumption was from the unique environment. In men, tea and coffee consumption was only mediated by the unique environment. This common variance may reflect non-shared environmental contributors which influence taste preference and accessibility to tea and coffee in the workplace.

There was no relationship between coffee preference and number of caffeinated drinks consumed per day. Thus, an exclusive coffee drinker does not consume more cups of coffee than an exclusive tea drinker does tea, or vice versa. While one might expect that a tea drinker would drink more cups of tea to obtain comparable caffeine plasma levels of a coffee drinker, the lack of an association between coffee preference and total caffeinated drinks suggests that this is not the case. Thus, the genetic and environmental factors influencing coffee preference and caffeinated beverage consumption are completely independent.

Women consumed more caffeinated beverages than men, which may reflect differences in socialization between sexes with hot beverage drinking being more commonly a part of the social environments of women than men. Men showed a higher preference for coffee than women, although in both female and male samples

tea was preferred to coffee in this cohort in 1980–82. Age effects were such that older people drank more tea and thus total beverages, and they preferred coffee less than younger people. These patterns of age effects are consistent with those reported for the Australian population 15 years after our data were collected in the National Nutrition Survey, where more coffee than tea was consumed in the age group 19–44 years and more tea than coffee was consumed by adults above 45 years (Australian Bureau of Statistics 1999). The current coffee preference of young adults reflects the reversal to increased coffee consumption in the early 1980s by the Australian consumer market (Australian Bureau of Statistics 2003). That total tea consumption increases with age may be a result of the increased leisure time of older people. This finding has also been shown in a Dutch population-based sample aged between 24 and 81 years (Hameleers *et al.* 1999).

In conclusion, our findings confirmed an inverse relation between tea and coffee consumption that was mostly explained by unique environmental factors. Caffeine beverage consumption—regardless of tea/coffee preference—was mediated in equal proportions by genes and the unique environment. However, independent analyses of tea and coffee consumption showed the presence of common environmental variance for tea but not coffee consumption. In men, independent genes influenced tea and coffee consumption, whereas in women genes influencing tea consumption negatively affected coffee consumption in addition to the specific genes for coffee consumption. These diverse findings for tea and coffee consumption, especially between sexes (e.g. lower heritability for tea than coffee consumption in females) suggests the need to include both measures separately in studies of addiction and of related phenotypes such as sleep disturbance. Furthermore, our results highlight the need to broaden the measurement of caffeine intake to include cola soft drinks and chocolate as they may also show different patterns of heritability, and to account for the use of sweeteners and the increasing use of decaffeinated products, particularly for studies of taste. As tea and coffee consumption were both heritable and are probably both characterized to some extent by caffeine responses and taste perception, future genetic research might be able to discern the importance of each of these pathways in caffeine preference and dependence. A genetic framework may also overcome some of the limitations of epidemiological research into caffeine intake and its relationship to somatic and psychological health (James 1991); for instance, it is possible to determine the direction of causation between two variables (e.g. coffee use and cardiovascular disease) or confirm whether a third variable (e.g. socio-economic class) influences both (Duffy & Martin 1994).

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