A Genetic Analysis of Coffee Consumption in a Sample of Dutch Twins

Jaqueline M. Vink, Annemieke S. Staphorsius, and Dorret I. Boomsma

Department of Biological Psychology, VU University Amsterdam, The Netherlands

Caffeine is by far the most commonly used psycho-active substance. Caffeine is consumed regularly as an ingredient of coffee. Coffee consumption and coffee preference was explored in a sample of 4,495 twins (including 1,231 pairs) registered with the Netherlands Twin Registry. Twin resemblance was assessed by tetrachoric correlations and the influence of both genetic and environmental factors was explored with model fitting analysis in MX. Results showed moderate genetic influences (39%) on coffee consumption. The remaining variance was explained by shared environmental factors (21%) and unique environmental factors (40%). The variance in coffee preference (defined as the proportion of coffee consumption relative to the consumption of coffee and tea in total) was explained by genetic factors (62%) and unique environmental factors (38%).

Keywords: twin study, heritability, coffee

Caffeine is consumed regularly by 80 to 90% of the adults as an ingredient of coffee, tea and other products (Drewnowski, 2001). It is the most frequently used psychoactive substance in the world. The effects of caffeine on human behavior are diverse. A review including a large amount of studies concluded that caffeine influences mood. It increases alertness and reduces fatigue but high doses of caffeine can lead to increased anxiety in some individuals. Caffeine also influences mental performance and some studies suggest that caffeine has an effect on sleep (Smith, 2002). In all areas there is a difference between the effects of amounts of caffeine that are normally consumed and those observed when excessive amounts are ingested. A recent meta-analysis of the effect of coffee and caffeine on blood pressure indicated a dose response effect (Noordzij et al., 2005).

The possibility that caffeine intake adversely affects human health was explored by Nawrot et al. (2003) by reviewing published human studies obtained through a comprehensive literature search. Based on the data reviewed, it is concluded that for the healthy adult population, moderate daily caffeine intake at a dose level up to 400 mg day is not associated with adverse effects such as general toxicity, cardiovascular effects, effects on bone status and calcium balance, changes in adult behavior, increased incidence of cancer and effects on

male fertility. The data also show that reproductive-aged women and children are 'at risk' subgroups who may require specific advice on moderating their caffeine intake (Nawrot et al., 2003).

The stimulating properties of caffeine and the taste can create a caffeine dependency. Previous research has revealed that genetic effects account for a significant part of the variation in caffeine use. Table 1 shows that heritability estimates ranging from 36% to 77% have been reported for caffeine consumption, although using different phenotypes. In all studies, except one, caffeine consumption is influenced by genetic and unique environmental factors but not by shared environmental influences. The variation in perceived bitterness of caffeine is also influenced by genetic factors (30%), (Hansen et al., 2006).

In the present study we will focus on coffee consumption in a Dutch sample of twins (mean age 30 years). In the Netherlands more coffee is consumed than in many other countries, about 3.2 cups per day. It is the beverage most frequently consumed by Dutch individuals with tea being the second most consumed drink (about 2.2 cups per day) the amount of caffeine intake is relatively high (Central Bureau for Statistics of the Netherlands, 2007). We explored the heritability of coffee consumption and coffee preference (defined as the proportion of coffee consumption relative to the consumption of coffee and tea in total) in a sample of 4,495 twins (including 1,231 pairs) registered with the Netherlands Twin Registry.

Method
Subjects
A sample of (mostly) adult twins was obtained from the Netherlands Twin Register (NTR), which was established in 1987 and contains information about Dutch twins and their families voluntarily taking part in research (Boomsma et al., 2006). Since 1991, every two to three years a questionnaire is mailed to adult twins and their family members registered with the NTR. These questionnaires contain items about

Table 1

Overview Studies That Explored the Heritability of Caffeine Use — Percentages of Additive Genetic (A), Common (C) and Unique Environmental (E) Variance are Presented

Author (year)	Age	Definition caffeine	Sex[1]	A	C	E
Carmelli et al. (1990)	63–73	Daily coffee	M	36	—	—
Decastro (1993)	38.8 (±11.3)	Weekly coffee	M	67	0	55
			F	59	0	41
Hettema et al. (1999)	30.3	Daily coffee and tea	M+F	58	0	42
Kendler & Prescott (1999)	36.1 (±8.0) +35.4 (±8.6)[3]	Caffeine use	F	43[2]	0	57
		Heavy caffeine use	F	77	0	23
Luciano et al. (2005)	34.1 (±14.1)	Daily coffee	M+F	51	0	49
		Daily coffee+ tea	M+F	48	6	46
		Coffee preference	M+F	42	0	58
Teucher et al. (2007)	18–80	Weekly coffee	F	41	0	59

Note: [1] M = male, F = female; [2] including dominance; [3] mean age for respectively MZ and DZ twins

health, lifestyle and personality. In 2000 the fifth NTR survey was send out (Vink & Boomsma, 2008). The survey of 2000 was completed by 4,596 twins. Data for coffee and/or tea use or zygosity were missing for 101 subjects. A total of 4,495 twins were included in the analysis: 662 monozygotic male twins (MZM), 398 dizygotic male twins (DZM), 1,590 monozygotic female twins (MZF), 827 dizygotic female twins (DZF), 550 male–female and 468 female–male opposite sex twins (DZMF & DZFM). In total, coffee and tea data were available for 1,682 complete twin pairs and 1,231 incomplete twin pairs (the co-twin did not participate). The mean age of the sample was 30.0 (± 11.3), with 96% of the sample being older than 18 years of age. Because coffee consumption was correlated with age, the data were split in a young cohort (*n* = 3056) with a mean age of 23.9 (*SD* = 3.5, range = 14–29 years) and an older cohort (*n* = 1463) with a mean age of 42.9 (*SD* = 10.8, range = 30–90). Zygosity was based on questionnaire data, or when available, on DNA typing. Agreement between zygosity based on questionnaire data and zygosity based on DNA results was 97%.

Coffee and Tea Consumption

The 2000 survey contained the question: 'On average, how many cups of caffeinated coffee do you drink in one day?' A large part of the subjects reported drinking no coffee at all (32% reported drinking 0 cups of coffee per day) causing a skewed distribution. Therefore, the data were divided in categories: zero to two cups per day, three to five cups per day and six or more cups per day. In addition, the survey contained a question on tea use: 'On average, how many cups of tea do you drink in one day?' The variable 'coffee preference' was defined as: number of cups of coffee per day/total number of cups coffee and tea per day. Figure 1 shows the percentage of subjects in each category.

Model-Fitting Analyses

To explore the inheritance, the trait was considered to have an underlying continuous liability. The liability was assumed to be standard normally distributed with zero mean and unit variance. The variation of the liability is both genetic and environmental in origin (Falconer & Mackay, 1996). Thresholds divide this normal distribution into discrete categories. Coffee consumption was divided into three categories and therefore two thresholds were used reflecting the prevalence of the categories. Coffee preference was split into five categories: 0 – 0.2, 0.21 – 0.4, 0.41 – 0.6, 0.61 – 0.8, 0.81 – 1, i.e. with four thresholds. The categories were based on the study of Luciano et al. (2005).

Model-fitting analyses were carried out in MX (Neale et al., 1999). First, we examined whether the thresholds differed between monozygotic (MZ) and dizygotic (DZ) twins, between men and women and between young (< 30 years) and older (> = 30 years) twins. Twin correlations were derived from the most parsimonious model.

Next, univariate analyses were performed to calculate the variance components additive genetic effects (A), common environmental effects (C) and unique environmental effects (E). The total variance (A+C+E) was constrained to be 1 for males and females. Additive genetic effects are the same for MZ twins because they are 100% similar in genes. DZ twins however, share 50% of the additive genetic effects since they share only 50% of their genes. Common environmental effects are thought to be the same for MZ twins and DZ twins, based on the assumption that monozygotic twins do not share more environments with each other than DZc twins. Subsequent model fitting tests revealed whether variance components differed between males and females. This was tested by allowing the magnitude of the genetic and environmental effects to be different for males and females. In addition, the correlation between the shared environments in opposite-sex twins was allowed to be less than 1. Also, we examined whether the components A and C were significantly different from zero.

Significance of the parameters was tested by comparing the fit of the nested models to the fit of less

Coffee
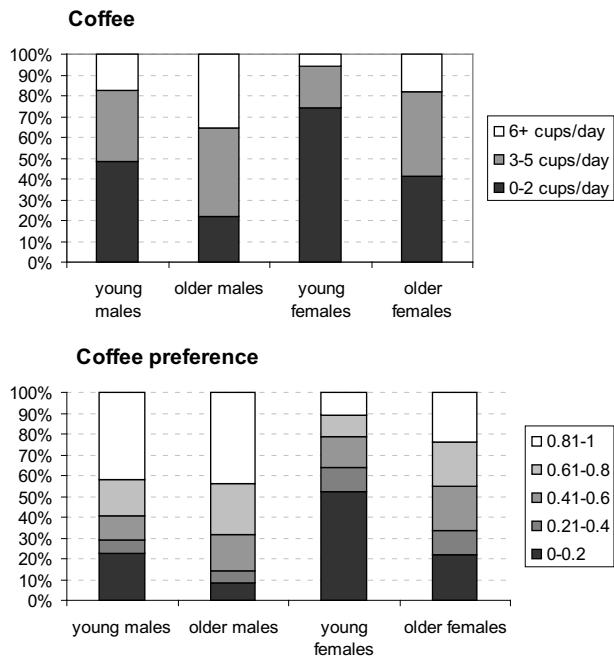
Coffee preference

Figure 1

Prevalences for coffee consumption and coffee preference in four groups: young males (< 30 years, *n* = 1074), older males (> 30 years, *n* = 420), young females (< 30 years, *n* = 1982) and older females (> 30 years, *n* = 1043).

restricted models. Goodness-of-fit of the sub models was assessed by likelihood-ration test. The difference in log-likelihoods between the nested models follow a χ^2 distribution. If the difference test is significant the constraints on the nested model cause a significant deterioration of the model. If the difference test is not significant, the nested more parsimonious model is to be preferred.

Results

The subjects reported consuming 0 to 30 cups of coffee per day. The mean amount of coffee consumed per day was 2.6 cups (SD 2.8) with a median of two cups per day. Males consumed more coffee than females, and subjects older than 30 years consumed more coffee than the younger ones (Figure 1). As one might expect a negative correlation is observed between cups of coffee and cups of tea consumed per day ($r = -0.30$), implying that the more coffee people consume the less tea they consume and vice versa. We therefore included the variable 'coffee preference': the proportion of coffee consumption relative to the consumption of coffee and tea in total. Females scored lower on coffee preference than males, especially young females (Figure 1B).

For both variables, no significant differences between zygosity groups within sex and age cohort were observed (Table 2, model 2 and 3). But constraining the thresholds in men and women (model 4) and the thresholds of the young and older cohort (model 5) resulted in a significant worsening of the model fit. The polychoric twin correlations derived from the best fitting model, with different thresholds for men and women and for the younger and the older cohort, are presented in Table 3.

Table 4 lists the genetic model fitting results. The most parsimonious models are presented in bold. First, a full ACE model was evaluated for men and women where the DZ opposite-sex correlation for shared environment was not constrained to be 1 (model 1). Next, this correlation was constrained to 1 (model 2). This did not cause a significant deterioration of the model. Next, the estimates for ACE were constrained to be equal for men and women (model 3), which also did not worsen the model fit. Finally

Table 2

Saturated Model for Coffee Consumption and Coffee Preference

Model	−2LL	df	Versus	Δdf	Δχ²	p
Coffee						
Full model	7733.145	4458				
Model 2	7750.026	4474	1	16	16.882	.393
Model 3	**7762.960**	**4482**	**2**	**8**	**12.934**	**.114**
Model 4	8080.783	4486	3	4	317.823	< .001
Model 5	8025.424	4486	3	4	262.464	< .001
Preference						
Full model	12065.140	4278				
Model 2	12096.120	4310	1	32	30.980	.518
Model 3	**12116.023**	**4326**	**2**	**16**	**19.903**	**.225**
Model 4	12373.486	4334	3	8	257.463	< .001
Model 5	12599.276	4334	3	8	483.253	< .001

Note: Full model: all parameters estimated: different tresholds for all zygosity groups, for males and females and for the young and old cohort. Model 2: as full model, but thresholds dz males = dos males and thresholds dz females = dos females. Model 3: as model 2, but thresholds mz males = dz/dos males and mz females = dz/dos females (estimating different thresholds for young males, older males, young females, older females). Model 4: as model 3, but thresholds males = females (estimating different thresholds: young and older cohort). Model 5: as model 3, but thresholds young = older (estimating different thresholds: males and females). The best fitting model is printed in bold.

Jaqueline M. Vink, Annemieke S. Staphorsius, and Dorret I. Boomsma

Table 3

Estimated Tetrachoric Correlation and 95% Confidence Intervals for Coffee Consumption and Coffee Preference Including 95% Confidence Intervals Shown in Parentheses

Variable	rMZM	rDZM	rMZF	rDZF	rDOS
Coffee consumption	.56 (.44–.67)	.44 (.25–.60)	.61 (.47–.74)	.45 (.31–.58)	.33 (.17–.46)
Coffee preference	.68 (.58–.76)	.41 (.21–.57)	.57 (.50–.63)	.39 (.26–.50)	.36 (.22–.50)

Table 4

Model Fitting Results for Coffee Consumption and Coffee Preference

Model	−2LL	df	Versus	Δdf	Δχ²	p
Coffee consumption						
1. Full ACE	7762.960	4482				
2. Rdos=1	7762.960	4483	1	1	1.606	.205
3. ACE no sex diff	**7765.309**	**4486**	**2**	**3**	**0.743**	**.863**
4. CE	7769.823	4487	3	1	4.514	.034
5. AE	7778.581	4487	3	1	13.272	< .001
Preference						
1. Full ACE	12116.023	4326				
2. Rdos=1	12116.076	4327	1	1	0.053	.818
3. ACE no sex diff	12119.283	4330	2	3	3.207	.361
4. CE	**12122.507**	**4331**	**3**	**1**	**3.224**	**.072**
5. AE	12140.557	4331	3	1	21.481	< .001

Note: A = additive genetic influences, C = shared environmental factors, E = unique environmental factors.
1. Estimating ACE for males, ACE for females and dos correlation for shared environment. 2. Constraining the dos correlation for shared environment to 1. 3. Constraining ACE for males and females to be the same. 4. Drop A. 5. Drop C. The best fitting model is printed in bold.

Table 5

Univariate Analysis Results (Proportions of Additive Genetic, Common and Unique Environmental Variance) Including 95% Confidence Intervals Shown in Parentheses

Model	A (%,95% CI)	C (%, 95% CI)	E (%, 95% CI)
Coffee	39 (18–59)	21 (5–41)	40 (34–47)
Coffee preference	62 (44–79)	0	38 (26–55)

Note: Estimates are derived from the best fitting model, printed in bold in Table 4.

the significances of A and C were tested by constraining those parameters to zero (model 4 and 5). The shared environmental factor could be dropped from the model for coffee preference but not for coffee use. Table 5 shows the proportions of genetic and environmental variance for both phenotypes. The best-fitting model is printed in bold.

Discussion

This study explored the heritability of coffee consumption and coffee preference in a Dutch twin sample. Results showed moderate genetic influences (39%) on coffee consumption and rather large genetic influences (62%) on coffee preference.

The heritability estimates for caffeine use ranged from 36% to 77% in previous studies (Table 1). Our

results fit within this range. Differences between studies could be due to the definition of the phenotype and cultural differences between countries.

Luciano et al. (2005) reported that coffee preference was influenced by both genetic and unique environmental influences which is in line with the results of the present study although the estimates for the genetic factors are slightly higher in our study (42% versus 62%). Preference for coffee over tea might be based on the level of bitterness. Hansen et al. (2006) found the perceived bitterness of caffeine to have a heritability of 30%. Tea is less bitter than coffee. The amount of caffeine could also play a role. In general, the amount of caffeine in coffee is higher than in tea. In a study in the US the caffeine content in brewed coffee was on average 85 mg per serve (Knight et al., 2004) but the amount of caffeine in coffee can vary widely. For examples, the quantity of caffeine in espresso coffee was on average 106 mg per serve but varied from 25 to 214 mg in Australia (Desbrow et al., 2007). A recent study detected that caffeine concentrations in white, green and black teas ranged from 14 to 61 mg per serving with no observable trend in caffeine concentration due to the variety of tea. The decaffeinated teas contained less than 12 mg of caffeine per serving and caffeine was not detected in the herbal tea varieties (Chin et al., 2008). In the present study we specifically asked subjects to report the

number of cups of caffeinated coffee (not deacaffeinated coffee) but still it is hard to predict the total caffeine intake because the amount of caffeine in coffee (and tea) can vary widely as described above. In addition, other beverages like carbonated soft drinks should be taken into account.

Considering that caffeine has addictive properties, genes involved in addiction could have an influence on coffee consumption. However, a recent paper reported that 91% of the heritability of caffeine use is explained by a substance-specific factor, leaving only 9% being explained by general substance factors (Kendler et al., 2007).

References

Boomsma, D. I., de Geus, E. J. C., Vink, J. M., Stubbe, J. H., Distel, M. A., Hottenga, J. J., Posthuma, D., van Beijsterveldt, T. C., Hudziak, J. J., Bartels, M., & Willemsen, G. (2006). Netherlands Twin Register: From twins to twin families. *Twin Research and Human Genetics, 9*, 849–857.

Carmelli, D., Swan, G. E., Robinette, D., & Fabitz, R. R. (1990). Heritability of substance use in the NAS-NRC twin registry. *Acta Geneticae Medicae et Gemellologiae, 39*, 91–98.

Chin, J. M., Merves, M. L., Goldberger, B. A., Sampson-Cone, A., & Cone, E. J. (2008). Caffeine content of brewed teas. *Journal of Analytical Toxicology, 32*, 702–704.

Decastro, J. M. (1993). A twin study of genetic and environmental influences on the intake of fluids and beverages. *Psychology and Behavior, 54*, 677–687.

Desbrow, B., Hughes, R., Leveritt, M., & Scheelings, P. (2007). An examination of consumer exposure to caffeine from retail coffee outlets. *Food and Chemical Toxicology, 45*, 1588–1592.

Drewnowski, A. (2001). The science and complexity of bitter taste. *Nutrition Reviews, 59*, 163–169.

Falconer, D. S., & Mackay, T. F. C. (1996). Threshold Characters. In D. S. Falconer & T. F. C. Mackay (Eds.), *Quantitative Genetics* (chapter 18). Essex: Longman Group Ltd.

Hansen, J. L., Reed, D. R., Wright, M. J., Martin, N. G., & Breslin, P. A. S. (2006). Heritability and genetic covariation of sensitivity to PROP, SOA, quinine HCL and caffeine. *Chemical Senses, 31*, 403–413.

Hettema, J. M., Corey, L. A., & Kendler, K. S. (1999). A multivariate genetic analyses of the use of tobacco, alcohol and caffeine in a population-based sample of male and female twins. *Drug and Alcohol Dependence, 57*, 69–78.

Kendler, K. S., Myers, J., & Prescott, C. A. (2007). Specificity of genetic and environmental risk factors for symptoms of cannabis, cocaine, alcohol, caffeine and nicotine dependence. *Archives of General Psychiatry, 64*, 1313–1320.

Kendler, K. S., & Prescott, C. A. (1999). Cafeine intake, tolerance and withdrawal in women: a population-based twin study. *American Journal of Psychiatry, 156*, 223–228.

Knight, C. A., Knight, I., Mitchell, D. C., & Zepp, J. E. (2004). Beverage caffeine intake in US consumers and subpopulations of interest: estimates from the Share of Intake Panel survey. *Food and Chemical Toxicology, 42*, 1923–1930.

Luciano, M., Kirk, K. M., Heath, A. C., & Martin, N. G. (2005). The gentics of tea and coffee drinking and preference for source of caffeine in a large community sample of Australian twins. *Addiction, 100*, 1510–1517.

Nawrot, P., Jordan, S., Eastwood, J., Rotstein, J., Hugenholtz, A., & Feeley, M. (2003). Effects of caffeine on human health. *Food Addit Contam, 20*, 1–30.

Neale, M. C., Boker, S. M., Xie, G., & Maes, H. H. (1999). *Mx: Statistical Modeling* (5th ed.). Richmond, VA.

Noordzij, M., Uiterwaal, C., Arends, L., Kok, F., Grobbee, D., & Geleijnse, J. (2005). Blood pressure response to chronic intake of coffee and caffeine: A meta-analysis of randomized control trials. *Journal of Hypertension, 23*, 921–928.

Smith, A. (2002). Effects of caffeine on human behavior. *Food and Chemical Toxicology, 40*, 1243–1255.

Teucher, B., Skinner, J., Skidmore, P. M. L., Cassidy, A., Fairweather-Trait, S. J., Hooper, L., Roe, M. A., Foxall, R., Oyston, S. L., Cherkas, L. F., Perks, U. C., Spector, T. D., & MacGregor, A. J. (2007). Dietary patterns and heritability of food choice in a UK female twin cohort. *Twin Research and Human Genetics, 10*, 734–748.

Vink, J. M., & Boomsma, D. I. (2008). A comparison of early and late respondents in a twin–family survey study. *Twin Research and Human Genetics, 11*, 165–173.