Interactive Effects of Genotype and Social Environment on Alcohol Consumption in Female Twins*

A.C. HEATH, R. JARDINE† AND N.G. MARTIN†

Department of Human Genetics, Box 33, Medical College of Virginia, Richmond, Virginia 23298

ABSTRACT. Information about drinking practices has been obtained by questionnaire from 1,984 monozygotic and dizygotic adult female twin pairs from the Australian twin register, including 1,690 pairs where both twins have used alcohol. Statistical analyses of these data show that marital status is an important modifier of genetic effects on drinking habits. In young twins, aged 30 years or less, genetic differences between individuals account for only 31% of the variance in alcohol consumption of married respondents, but for 60% of the variance of unmarried respondents. In twin pairs, aged 31 years or more, genetic differences account for 46-59% of the variance in married twins, but for 76% of the variance in unmarried twins. In our young sample (average age 35 years) there is no evidence that individuals genetically predisposed to heavy drinking are any less likely to be married than the rest of the population. Some alternative explanations of these findings are also rejected. (*J. Stud Alcohol* 50: 38-48, 1989)

EPIDEMIOLOGICAL SURVEYS have demonstrated the important influence of the social environment on drinking habits and alcohol abuse. In U.S. national surveys of adult drinking practices, use of alcohol and heavy drinking have been found to be more common in particular religious groups (e.g., Catholic or liberal Protestant), in particular geographic regions (e.g., Middle Atlantic States or New England), in more highly urbanized areas, and in those of particular national or ethnic origins (e.g., Irish or Hispanic). Both drinking and heavy drinking have been found to be more common in those who are better educated, who are of higher socioeconomic status or who are unmarried (Cahalan et al., 1969; Clark and Midanik, 1982; Mulford, 1964; Riley and Marden, 1947). Surveys of drinking habits in other countries (e.g., London, England—see Edwards et al., 1972a; or Sydney, Australia—see Encel et al., 1972) have found similar associations of "sociocultural" variables with drinking behavior. In those surveys where alcohol-related problems have also been reported (Cahalan and Room, 1974; Clark and Midanik, 1982; Edwards et al., 1972b, 1972c; Mulford, 1964), and in epidemiological surveys that have focused specifically on diagnosed alcoholism (e.g., Weissman et al., 1980), many (but not all—see Clark and Midanik, 1982) of these same variables have been found to be important predictors.

Studies of adoptees, of half siblings and of twins have established the important effect of genetic predisposition both on liability to alcohol abuse (e.g., Bohman et al., 1981; Cadoret et al., 1980; Cloninger, 1987; Cloninger et al., 1981; Goodwin et al., 1974; Kaij, 1960; Schuckit et al., 1972) and on individual differences in drinking practices (e.g., Cederlof et al., 1977; Clifford et al., 1981; Jardine and Martin, 1984; Kaprio et al., 1981, 1987; Partanen et al., 1966). How can these findings be reconciled with the evidence for marked cultural variation in drinking habits?

Experimental genetic studies of species other than human have shown the importance of Genotype × Environment interaction (i.e., that gene effects and environmental effects do not combine additively) and have demonstrated the variety of forms that this nonadditivity may take. The same genes may be expressed, but to differing degrees, under different environmental conditions; or, alternatively, completely

Received: December 31, 1987.

* Data collection was supported by grants from the Australian National Health and Medical Research Council and from the Australian Brewers. Data analysis was supported by Alcohol, Drug Abuse and Mental Health Administration grants AA06781 and MH40828 and National Institute of Health grants AG04954, GM30250 and GM32732.

† Dr. Jardine is now with the Alcohol and Drug Service, Australian Capital Territory Health Authority, P.O. Box 825, Canberra City 2601, Australia; and Dr. Martin is now with the Queensland Institute of Medical Research, Brisbane, Queensland 4006, Australia.

different sets of genes may be expressed under some conditions (Mather and Jinks, 1982). Quite independently of this tradition, psychiatric epidemiologists have developed the concept of "vulnerability" (e.g., Brown and Harris, 1978; Kessler et al., 1985), which recognizes that the impact of environmental events (e.g., stressful life events) may be modified or "buffered" by a variety of situational or personal factors (e.g., having a supportive, confiding relationship). It is clearly important to establish whether the effects of inherited liability on drinking behavior or alcohol abuse are likewise magnified or diminished under particular sociocultural conditions.

Despite reports of Genotype × Environment interaction for alcoholism (e.g., Cloninger et al., 1981), the effects of such an interaction on drinking patterns in clinically unselected samples have not been explored. We present here findings from a large-scale survey, conducted by mailed questionnaire, of twins in the Australian National Health and Medical Research Council (NH&MRC) Twin Register (Jardine and Martin, 1984). Results from this survey show that in female respondents there is a significant interaction of genetic effects on drinking habits with marital status. In particular, having a marriage-like relationship appears to reduce the impact of inherited liability to heavy drinking.

Method

Design

Most recent studies of alcohol use and abuse have used an adoption-based design and have focused on alcoholism (e.g., Cadoret et al., 1980; Cloninger et al., 1981; Goodwin et al., 1974). We have followed a very different research strategy of using adult twin pairs and studying differences in drinking practices in a clinically unselected sample (see Kaprio et al., 1987). Although the use of twin data has certain potential limitations (e.g., the possibility of a "special twin environment effect"), such effects are probably unimportant in adult populations (for a review of the relevant literature see e.g., Kendler, 1983) and can usually be detected and controlled for by appropriate statistical analysis of the data (see below). For our purposes the use of twin data has one major advantage: information about the importance of genetic effects and environmental effects is derived from pairs of individuals of the same age, who will have experienced very similar social conditions. Thus, by considering pairs concordant for exposure, concordant for nonexposure and discordant for exposure to one particular environmental condition, we have a very sensitive test for Genotype × Environment interaction (Eaves, 1982). An analysis of adoption data, in contrast, uses information on relatives from different generations, who will have experienced social conditions differing in many respects (Cloninger et al., 1988). Using adoption data, therefore, we would be unable to quantify the contribution of genetic differences to variability in alcohol use and abuse unless we were prepared to assume the very hypothesis that we wish to falsify (i.e., that there is no Genotype × Environment interaction). For many other purposes, the adoption design remains a more powerful method of resolving cultural and biological inheritance (Heath et al., 1985), but for our present task it is clearly inappropriate.

Sampling

Ascertainment of a representative sample of twin pairs in highly mobile societies with high immigration rates, such as Australia or the United States, raises serious practical problems. Approximately one person in 50 is a twin (Bulmer, 1970), but large sample sizes are required for the purposes of genetic analysis (Martin et al., 1978). The traditional methods of sampling used in survey research would therefore be prohibitively expensive. In Scandinavia (Cederlof et al., 1977; Kaprio et al., 1981, 1987; Magnus et al., 1983), the availability of national birth records and of centralized records of current addresses, combined with a low immigration rate, has made the development of national twin registries feasible. In some states of the U.S., too, systematic ascertainment of twin pairs from state birth records has been achieved (e.g., Virginia—see Corey et al., 1986), but in such cases the exclusion of immigrants from out of state and the difficulty of locating twin pairs who have moved out of state necessarily restrict the generalizability of findings.

To obtain as representative a sample of the population of Australia as possible, a two-stage sampling procedure was used. In the first stage, twins throughout Australia were asked to register with the Australian NH&MRC National Twin Register. Every attempt at systematic ascertainment of twins was made, although media coverage of the twin registration drive has certainly led to overrepresentation of some groups (e.g., the young, educated middle classes—see Jardine, 1985) in the register. At this first stage, the purpose of the planned survey of alcohol consumption and other health-related habits was not revealed to minimize sampling bias with respect to these variables. In the second stage, between November 1980 and March 1982, self-report questionnaires were mailed to all 5,967 twin pairs aged 18 years and older on the twin register. Responses were received from 3,810 complete pairs of adult twins. This represents a 64%

pair-wise response rate, a very high rate of return considering that separate responses from *both* members of a twin pair are needed before their data can be used for genetic analysis. Comparisons of the sample with non-twin samples drawn from the Australian population indicate that it is representative of the Australian population for measures of personality (Martin and Jardine, 1986) and symptoms of anxiety and depression (Kendler et al., 1986). Total weekly alcohol consumption of male respondents did not differ significantly from consumption figures obtained by interview from a representative sample of the Australian population (Australian Bureau of Statistics, 1978; Jardine and Martin, 1984, Table 4). Estimates of the alcohol consumption of female twin respondents actually exceeded the Australian Bureau of Statistics figures, probably reflecting a genuine increase in female drinking in the 3-5 years between the two surveys (Jardine and Martin, 1984). The two-stage sampling strategy does appear to have been effective in minimizing sampling bias, at least as far as measures of alcohol consumption, symptoms and personality are concerned.

In the present article, we focus on drinking by female same-sex twin pairs, for whom sample sizes were sufficiently large to permit detailed analysis of Genotype × Environment interaction. Completed questionnaires were received from 1,233 female monozygotic (MZ) and 751 female dizygotic (DZ) twin pairs, with average (± SD) ages 35.66 ± 14.27, and 35.33 ± 14.27,respectively. Twin pairs where one or both twins had never used alcohol were excluded from our analyses, as the determinants of abstinence may be quite different from the determinants of differences in drinking pattern (Heath and Martin, in press). Thus, our final sample size for model-fitting analyses was 1,047 female MZ pairs and 643 female DZ pairs. The overrepresentation of monozygotic twins in our sample is a familiar problem in twin research (e.g., Lykken et al., 1978) and may reflect the greater difficulty of persuading dizygotic twins that they were eligible for registration with the NH&MRC twin register. It has also been argued that overrepresentation of MZ twins may arise from selection on a latent scale of "cooperativeness", which determines registration and completion of questionnaires, and which itself has a genetic component (Martin and Wilson, 1982). Provided that cooperativeness is not correlated with the trait under study—and the good agreement of the questionnaire data with interview data (see above) suggests a relatively weak association—this selection will not influence the results of genetic analyses (Lykken et al., 1987). Statistical analyses reported below used a weighting procedure to take account of the different sample sizes for MZ versus DZ twin pairs. Because previous analyses ignoring Genotype × Environment interaction had reported heterogeneity of genetic and environmental effects as a function of age (Jardine and Martin, 1984), the female same-sex pairs were further subdivided into a young cohort, aged 30 years or younger at the time of testing, and an older cohort, aged 31+ years.

Measures

The health survey focused on current consumption of alcohol, rather than alcohol abuse. In addition to standard quantity-frequency questions (Jardine and Martin, 1984; Straus and Bacon, 1953), respondents were asked to report their consumption of beer, wine, spirits or sherry, in standard drinks (7 oz in the case of beer, 4 oz in the case of wine, 1 oz in the case of spirits), for each day of the preceding week. A measure of total weekly consumption was then derived by summing the total number of drinks reported. Estimates of total weekly alcohol consumption obtained by this 7-day retrospective diary method (Millwood and McKay, 1978; Redman et al., 1987) were consistently higher than those obtained from the quantity-frequency items. The 7-day recall method was also more reliable as assessed in a subsample of 100 twins by test-retest repeatability over an average period of 4 months (Jardine and Martin, 1984). Analyses therefore focused on this measure. Measures of total alcohol consumption based on general population samples have consistently been found to follow a log-normal distribution (Armor et al., 1976; de Lint and Schmidt, 1968; Ledermann, 1956; Malin et al., 1982). A log-transformation, log $(x + 1)$, was therefore applied to the estimate of total weekly consumption prior to statistical analysis.

In addition to the questions about alcohol consumption, respondents were asked to give their current marital status (single, widowed, married, living together, separated, divorced or remarried), and their amount of social contact with their twin (live together, almost every day, at least once a week, once or twice a month, a few times a year, less often). Because of the relative youth of the sample, to ensure adequate statistical power for genetic analysis it was necessary to recode marital status either as unmarried (single, separated, divorced or widowed) or as married (including living together).

Statistical methods

Preliminary analyses of central tendency and dispersion were computed ignoring the twin structure of the sample. Although observations on members

of a twin pair are not statistically independent, the bias that will arise when this complication is ignored will be minimal with sample sizes as large as in the present study. Alcohol consumption scores were log-transformed and then regressed on age to test for age-related differences in consumption. For the analyses of Genotype × Environment interaction, the twin pair, rather than the individual twin, was then used as the basic unit for analysis.

Testing for biases from using twins. The classical twin method has been much criticized for the "implausibility" of the assumption that the environmental correlation between members of a twin pair is identical for monozygotic and for dizygotic twins. Most of these criticisms relate to early childhood experiences of twins (e.g., wearing similar clothes or sharing the same bedroom) that have no bearing on adult drinking practices. Such special twin environment effects usually lead to differences in mean and variance as a function of zygosity, differences that are not found in this sample (Jardine and Martin, 1984). In adult twin pairs, the different amounts of social contact of MZ and of DZ twin pairs might be expected to be a problem. We know that in this sample MZ pairs reported more frequent social contact than DZ pairs (Kendler et al., 1986). Kaprio et al. (1987) have observed an association between frequency of social contact and concordance in drinking habits for male twin pairs. We therefore tested for an association between absolute intrapair differences in consumption and frequency of contact, separately for each twin group. As an additional check, covariances of young unmarried twin pairs were computed separately for those pairs who were living together and those pairs who were living apart. Too few twin pairs aged 31 years or older were still living together to permit a comparable breakdown in the older cohort.

Testing for GE correlation. If there are genetic effects on alcohol consumption and heavier drinkers are more likely to be unmarried as a consequence of their drinking habits, this is one type of genotype-environment (GE) correlation (Eaves et al., 1977; Plomin et al., 1977). The analysis of gene-environment interaction in the presence of genotype-environment correlation is a tractable problem, but requires more elaborate statistical analysis than is the case when genes and environment are acting independently. To test for GE correlation involving marital status, cross-correlations were computed between twin's alcohol consumption and co-twin's marital status, separately for each twin group. If gene-environment correlation is important, then we would expect to find a significant cross-correlation between co-twin's marital status and twin's alcohol consumption, and we would expect this cross-correlation to be higher in MZ pairs than in DZ pairs.

Testing for Genotype × Environment interaction or "vulnerability" effects. In the absence of Genotype × Environment (G×E) interaction, genetic analysis of twin data involves the attempted resolution of five competing hypotheses (Heath and Martin, in press; Martin et al., 1978; see Tables 1 and 2): (*1*) there is no twin resemblance for drinking habits (i.e., there are no genetic effects and all environmental influences on alcohol use are uncorrelated over twin pairs ["random environment" model]); (*2*) drinking habits are environmentally determined, but some important environmental influences are shared by members of a twin pair (e.g., family background, place of schooling, peer effects, etc. ["shared environment" model]); (*3*) drinking habits are influenced by both additive gene action and environment, but environmental influences are uncorrelated over twin pairs (so that twin resemblance is entirely genetic in origin ["additive genetic" model]); (*4*) twin resemblance is influenced by both additive gene action and shared environment ("genetic + shared environment" model); or (*5*) twin resemblance is due to both additive gene action and genetic dominance ("full genetic" model). The effects of genetic dominance and family background are confounded in twin data so that we cannot estimate both effects simultaneously. The effects of family background will usually mask those of dominance, unless the former are very weak (Martin et al., 1978).

In order to detect G×E interaction involving a dichotomous environmental variable (e.g., presence or absence of a marriage-like relationship), when there is no GE correlation, a very simple approach is possible (Eaves, 1982). This same approach will apply even if there is no genetic variation in drinking habits to determine whether a dichotomous environmental variable is a "vulnerability" factor which modifies the effect on drinking behavior of environmental risk-factors (e.g., family background). Instead of estimating genetic and environmental effects without regard to environmental status, we estimate these effects conditional upon environmental exposure (e.g., we estimate separate effects for those who are married and those who are unmarried). Under a simple additive model (when there is no G×E interaction or differences in vulnerability) neither genetic effects nor environmental effects should vary significantly between married and unmarried twins. Under G×E interaction, where genetic effects are modified by marital status, we would expect to find significant heterogeneity of genetic and environmental parameters between married and unmarried twins. Expectations for the variances and covariances of twin pairs,

TABLE 1. Expected variances and covariances of twin pairs, conditional upon marital status and twin cohabitation, under G × E interaction

Variance			
Unmarried twins (living together):		VA + VD + EC + EC″ + ES	
Unmarried twins (living apart):		VA + VD + EC + ES	
Married twins:		VA′ + VD′ + EC′ + ES′	
Covariance			
Concordant unmarried pairs (living together)			
Monozygotic VA	+ VD	+ EC	+ EC″
Dizygotic ½ VA	+ ¼ VD	+ EC	+ EC″
Concordant unmarried pairs (living apart)			
Monozygotic VA	+ VA	+ EC	
Dizygotic ½ VA	+ ¼ VD	+ EC	
Concordant married pairs			
Monozygotic VA′	+ VD′	+ EC′	
Dizygotic ½ VA′	+ ¼ VD′	+ EC′	
Discordant pairs			
Monozygotic g $(VA\ VA')^{½}$	+ d $(VD\ VD')^{½}$	+ r $(EC\ EC')^{½}$	
Dizygotic ½ g $(VA\ VA')^{½}$	+ ¼ d $(VD\ VD')^{½}$	+ r $(EC\ EC')^{½}$	

VA, VD, EC, ES denote the variances due to additive gene action, dominance, shared environment and random environment in unmarried twins; VA′, VD′, EC′ and ES′ denote the corresponding variances in married twins; g, d and c give the correlation between additive genetic effects, between dominance effects or between shared environmental effects, in unmarried and married twins from pairs discordant for marital status. EC″ denotes the additional shared environmental variance arising when twins are living together.

conditional upon marital status, are given for the most general model of G×E interaction in Table 1.

Even if there is significant heterogeneity of genetic and environmental effects as a function of environmental exposure (i.e., marital status), this does not necessarily imply either vulnerability or G×E interaction effects. Alternative possibilities must be eliminated (see Table 2 for a summary of the constraints on the parameters of Table 1 implied by these different alternatives):

1. *Variability differences* between groups as a function of differences in mean consumption. It is a common finding for variables such as untransformed alcohol consumption that the variance increases with the mean. This is certainly the case in our sample, although the effect is largely removed by using a log-transformation (Jardine and Martin, 1984). Differences in total variance between married and unmarried respondents will lead to corresponding differences in genetic and environmental variances. However, we would expect the genetic and environmental variances to change in the same ratio, if differences in variability were the sole cause of heterogeneity.
2. *Heteroscedasticity* (i.e., differences in random environmental [or error] variance between married

TABLE 2. Summary of hypotheses to be compared in testing for G × E interaction

CAUSES OF VARIATION

a. Random environment model: VA = VA′ = VD = VD′ = EC = EC′ = 0
b. Shared environment model: VA = VA′ = VD = VD′ = 0
c. Additive genetic model: EC = EC′ = VD = VD′ = 0
d. Genetic + shared environment model: VD = VD′ = 0
e. Full genetic model: EC = EC′ = 0
f. Cohabitation effects: EC″ ≠ 0

HETEROGENEITY OF EFFECTS

1. No heterogeneity: VA = VA′, VD = VD′, EC = EC′, ES = ES′, g = d = r = 1
2. Variability differences: VA′ = k VA, VD′ = k VD, EC′ = k EC, ES′ = k ES, g = d = r = 1
3. Heteroscedasticity: VA′ = VA, VD′ = VD, EC′ = EC, ES′ ≠ ES, g = d = r = 1
4. Spousal interaction[a]: VA′ = k VA, VD′ = k VD, EC = k EC, ES′ = k′ ES, g = d = r = 1, k′ > k > 1
5. G × E interaction: VA′ ≠ VA, VD′ ≠ VD, EC′ ≠ EC, ES′ ≠ ES, g = d = r = 1
6. G × E interaction II: VA′ ≠ VA, VD′ ≠ VD, EC′ ≠ EC, ES′ ≠ ES, g < 1, d < 1, r < 1

[a] The constraint k′ > k > 1 was not imposed in the model-fitting analyses.

and unmarried individuals). A spouse may simply introduce an extra source of random environmental or error variation. (In cross-sectional twin data, random environmental effects and error variance will have identical effects, both contributing to the dissimilarity of identical twin pairs).

3. *Social interaction between spouses (spousal interaction)*, such that heavy drinking by one spouse encourages heavy drinking by the other spouse. It is well established that spouses are highly correlated in their drinking habits (Cahalan et al., 1969), but it is not yet clear whether this occurs because 'heavy' drinkers prefer to marry other heavy drinkers (assortative mating) or because of reciprocal environmental influences of spouses. It may be shown that such reciprocal effects, when they occur, lead to an increase in estimated genetic and environmental variances in married individuals (Heath, 1987) whenever genetic effects contribute to variation in consumption. Variances due to genetic effects and to effects of shared family background will increase in the same ratio, but the variance due to unique environmental effects that make one twin differ from his co-twin will increase to an even greater extent, leading to a lower correlation in concordant married twin pairs than in unmarried twin pairs. (For full details, see Heath, 1987.)

If these alternative explanations can be excluded, then we must still distinguish between two types of G×E interaction (or "vulnerability," if there are no genetic effects on the variables of interest). The same genes and the same environmental effects may be operating under both environmental conditions (i.e., presence versus absence of a marriage-like relationship), but may have greater effects under one condition. Alternatively, some genes or some environmental effects may be expressed under only one environmental condition, so that the correlation between genetic effects or shared environmental effects across conditions will be less than unity. In the latter case, we expect to observe a reduced correlation between pairs discordant for marital status, whereas in the former case correlations between discordant pairs should be intermediate between correlations for concordant married and concordant unmarried pairs (Eaves, 1982).

Model-fitting procedure

Twin pairs of each zygosity type were subdivided into older and younger cohorts and then into concordant married pairs, discordant pairs and concordant unmarried pairs. In the younger cohort, concordant unmarried pairs were further subdivided into those pairs who were still living together and those pairs who were living apart. Variances and covariances of first and second twins were computed for log-transformed alcohol consumption. In concordant pairs, identification of a twin as the first or second member of a pair was arbitrary, but in discordant pairs, the unmarried twin was always designated the first twin from each pair, the married twin the second twin. (This reordering is important because married twins from discordant pairs are not necessarily expected to have the same mean consumption as unmarried twins from discordant pairs. We therefore wished to examine the variability of married and unmarried twins about their respective means.)

Models were fitted to the full set of twin covariance matrices for each cohort (eight matrices for the younger cohort; six matrices for the older cohort) by maximum-likelihood, using the standard methods of covariance structure analysis for multiple groups (Jöreskog, 1978; Jöreskog and Sorbom, 1986). This yielded an overall chi-square test of the goodness-of-fit of each model, which enabled us to reject models that gave a poor fit to the data. For the remaining models, the fit of different nested models was then compared by likelihood-ratio chi-square test, which provides a more powerful means of rejecting false hypotheses. On the principle of parsimony, we began by fitting the simplest possible models (shared environment model or additive genetic model, with no heterogeneity of effects). These models were progressively elaborated by allowing for heterogeneity of genetic or environmental effects and by allowing for additional sources of variation (genetic + family environment model; full genetic model). Simpler models were rejected when a more elaborate model gave a significant improvement in fit by likelihood-ratio chi-square test (Jöreskog, 1978; Jöreskog and Sorbom, 1986).

Results

Mean differences in alcohol consumption

Table 3 gives means (± SDs) of the number of

TABLE 3. Alcohol consumption (untransformed number of drinks) in past 7 days as a function of social environment

	Young cohort		Older cohort	
	n	Mean ± SD	*n*	Mean ± SD
Unmarried, living with co-twin	494	5.79 ± 7.92	19	4.74 ± 12.54
Unmarried, separated from co-twin	433	7.15 ± 8.96	291	6.87 ± 9.53
Married	731	4.17 ± 5.64	1421	6.23 ± 9.73

TABLE 4. Twin covariance matrices for log-transformed alcohol consumption, computed conditional upon marital status or cohabitation (correlations between twin pairs are given in italics as the upper element of each matrix)

	Young cohort (< 31 years old)		Older cohort (31+ years old)	
	Twin 1	Twin 2	Twin 1	Twin 2
Concordant unmarried (living together)				
Monozygotic women	(n = 147)			
Twin 1	1.280	*0.613*		
Twin 2	0.766	1.194		
Dizygotic women	(n = 85)			
Twin 1	1.077	*0.477*		
Twin 2	0.463	0.962		
Concordant unmarried (living apart)				
Monozygotic women	(n = 74)		(n = 36)	
Twin 1	1.102	*0.566*	1.080	*0.720*
Twin 2	0.642	1.146	0.771	1.061
Dizygotic women	(n = 50)		(n = 18)	
Twin 1	1.446	*0.340*	1.214	*0.074*
Twin 2	0.489	1.393	0.106	1.536
Discordant pairs				
Monozygotic women	(n = 125)		(n = 113)	
Unmarried twin	1.136	*0.349*	1.557	*0.445*
Married twin	0.363	0.968	0.642	1.348
Dizygotic women	(n = 84)		(n = 89)	
Unmarried twin	1.098	*0.265*	1.213	*0.077*
Married twin	0.266	0.975	0.088	1.081
Concordant married				
Monozygotic women	(n = 161)		(n = 391)	
Twin 1	1.019	*0.349*	1.262	*0.583*
Twin 2	0.363	1.056	0.719	1.203
Dizygotic women	(n = 100)		(n = 217)	
Twin 1	0.847	*0.243*	1.212	*0.352*
Twin 2	0.201	0.822	0.456	1.290

drinks of alcohol taken in the preceding 7 days as reported by respondents, as a function of their marital status and whether or not they reported that they were still living with their co-twin. Since there were no mean differences in alcohol consumption between zygosity groups (Jardine, 1985; Jardine and Martin, 1984), responses of monozygotic and dizygotic twin pairs were combined in these data. In the younger cohort, consumption was highest (and most variable) in unmarried twins living apart from their co-twin, intermediate in unmarried twins living with their co-twin (who in many cases would still have been living in their parents' home) and lowest (and least variable) in married twins. In the older cohort, consumption was still highest in unmarried twins living away from their co-twin, but differences in mean and variability between these and married twins were very slight. The small group of older unmarried twins still living with their co-twin had much lower consumption than the other twins, but were too small a group to use for further analysis. The linear regression of log-transformed alcohol consumption on age was not significant (F = 1.18, 1/3387 df, p = 0.28). Thus, age differences between married and unmarried twins within younger and older cohorts could not explain the heterogeneity of consumption.

Effects of twin social contact, GE correlation

There was no consistent evidence for increased twin resemblance in sisters who were living together or had frequent social contact, compared with those who had less frequent social contact. In three twin groups—young MZ women, young DZ women and older DZ women—there was no significant correlation between absolute intrapair differences in alcohol consumption and amount of social contact. In the fourth group, older MZ women, the correlation between intrapair difference and level of social contact was significant but slight (0.09).

In both cohorts, no significant correlations were found between own alcohol consumption and co-twin's marital status (married/unmarried). All correlations were less than 0.06 in absolute value. Thus,

TABLE 5. Results of model-fitting analyses: chi-square tests of goodness-of-fit

	YOUNG COHORT							
	Causes of variation							
	Shared environment		Additive genetic		Genetic + shared environment		Full genetic	
Heterogeneity of effects	*df*	χ^2	*df*	χ^2	*df*	χ^2	*df*	χ^2
No heterogeneity	22	34.09[3]	22	33.25[3]	21	29.39[3]	21	33.25[3]
Variability differences	21	31.38[3]	21	30.78[3]	20	26.94[3]	20	30.78[3]
Heteroscedasticity	21	33.96[3]	21	33.25[3]	20	29.38[3]	20	33.25[3]
Spousal interaction	20	18.91[2]	20	*14.43*	19	11.17	19	14.43
G×E, g,d,c=1	20	18.91[2]	20	*14.43*	18	9.56	18	13.59
G×E, g,d,c<1	19	17.17[1]	19	13.03	16	9.36	16	13.03
	OLDER COHORT							
No heterogeneity	16	52.32[a]	16	25.04[2]	15	25.04[2]	15	25.04[2]
Variability differences	15	49.77[a]	15	23.14[1]	14	23.13[1]	14	23.13[1]
Heteroscedasticity	15	47.21[a]	15	21.93[2]	14	21.88[2]	14	21.93[2]
Spousal interaction	14	43.87[a]	14	21.02[2]	13	20.86[2]	13	21.02[2]
G×E, $r = 1$	14	43.87[a]	14	21.02[2]	12	*10.56*	12	*7.14*
G×E, $r < 1$	13	38.38[a]	13	*9.05*	10	7.69	10	7.14

[a] Model is rejected at 0.1% significance level, by chi-square test of goodness-of-fit.
[1,2,3] Model is rejected at 5% (1), 1% (2) or 0.1% (3) significance level, by likelihood-ratio chi-square test.

for all practical purposes, we can treat GE correlation for marital status as negligible in our sample.

Genotype × Environment interaction

Twin covariance matrices are given in Table 4 and results of covariance structure analysis are presented in Table 5. Monozygotic twin pairs were highly correlated for their alcohol use, so we do not give results for a random environment model, which would predict a zero twin correlation. For ease of interpretation, results for best-fitting models are indicated in italics in Table 5. Parameter estimates under best-fitting models are given in Table 6.

In both cohorts, all shared environment models could be rejected by either chi-square test of goodness-of-fit or likelihood-ratio chi-square test. In the younger cohort, twin resemblance for alcohol consumption was adequately explained by an additive genetic model, with significant heterogeneity of additive genetic and unique environmental components of variance as a function of marital status. The additive genetic G×E interaction model with $g = 1$ and the additive genetic spousal interaction model gave equally good fits (as will always be the case when there is no familial environmental or dominance variance, unless we use constrained optimization; see Table 2, note *a*). Both models gave a significant improvement in fit over the no heterogeneity, variability differences and heteroscedasticity additive genetic models and did not give a significantly worse fit than the corresponding genetic + family environment or full genetic models. The (nonstandardized) unique environmental variance was increased in married compared with unmarried individuals (0.82 vs 0.68), but the additive genetic variance was actually decreased in married individuals (0.54 vs 0.84), so we were still able to reject the hypothesis of spousal interaction which would predict an increase in both components of variance. Under the additive genetic G×E interaction model, genetic differences were responsible for 60% of the variance in drinking habits of young unmarried individuals, but only 31% of the variance of young married respondents.

As a further test for effects of cohabitation on twin resemblance in the young cohort, the additive genetic G×E model was extended by including a shared environmental component contributing to the variance and covariance only of twin pairs living together (not tabulated). Although this model gave an excellent fit to the data ($\chi^2 = 14.17$, 19 df, $p = 0.77$), it gave a negligible improvement in fit, by likelihood-ratio test, over the simple additive genetic G×E model ($\chi^2 = 0.16$, 1 df, $p > 0.05$). There was thus no evidence for any increased environmental correlation of twin pairs who were still living together.

In the older cohort, we again found significant evidence for G×E interaction. An additive genetic G×E model (with $r < 1$, i.e., allowing for a genetic correlation less than unity in discordant pairs), a genetic plus family environment model (with $g = r = 1$) and a full genetic model (with $g = d = 1$), all gave good fits to the data. Neither the additive genetic model nor the full genetic model could be rejected by likelihood-ratio chi-square test. Under the

TABLE 6. Parameter estimates (rescaled as proportions of total variance in alcohol consumption) under best-fitting models

	Genetic variance (%)	Environmental variance (%)		Correlation of genetic effects
		Shared	Random	
Young cohort				
Unmarried respondents	60	0	40	1.00
Married respondents	31	0	69	
Older cohort				
Additive genetic model				
Unmarried respondents	76	0	24	0.59
Married respondents	59	0	41	
Full genetic model				
Unmarried respondents	77	0	23	1.00
Married respondents	59	0	41	
Additive genetic + *dominance/shared environment model*				
Unmarried respondents	77	0	23	1.00
Married respondents	46	13	41	

additive genetic + shared family environment model, our estimate of familial environmental effects (EC) was zero for older unmarried twins, and indeed from inspection of the twin correlations (Table 4) it appears that there is genetic dominance for drinking habits in the unmarried state, but a shared environmental effect in the married state. A mixed G×E model, allowing for additive gene action plus genetic dominance in unmarried twins and additive gene action plus shared environmental effects in married twins, with $g = 1$, $d = c = 0$, gave an excellent fit to the data (not tabulated: $\chi^2 = 6.37$, 12 df, $p = 0.90$). This mixed model did give a significantly better fit than the additive genetic + shared environment model with shared environmental effects restricted to married twins ($\chi^2 = 4.19$, 1 df, $p < 0.05$). Parameter estimates under this model, the additive genetic G×E model and the full genetic G×E model are all given in Table 6. Although we were unable to discriminate between these three models, they all point to the same conclusion: the importance of genetic factors, relative to environmental factors, is also increased in unmarried respondents (76-77%), compared to married respondents (46-59%), in the older cohort.

Discussion

No effects of twin cohabitation and social contact

In a study of drinking practices of male Finnish twins, Kaprio et al. (1987) found increased concordance for drinking habits in those twin pairs having more frequent social contact with each other. In our female Australian twin pairs there was no consistent evidence for such effects. Indeed, we did not find a significantly greater effect of shared environment on young female twin pairs who were still living together than on young female twin pairs living apart. It remains to be seen whether this difference is a genuine sex difference in social influences on drinking habits or a cultural difference between Finland and Australia.

No effects of GE correlation

We found no evidence that those genetic factors that predispose to heavy drinking also make it more likely that an individual will be unmarried (i.e., will either remain single or undergo divorce or marital separation). Although the association between alcoholism and marital breakdown is well-established (Paolino et al., 1977), we would not necessarily expect to find such an association with heavy drinking in our population-based sample, which is clinically unselected and also relatively young (average age 35).

Major effect of G×E interaction

Although there have been many studies documenting the important influence of either genetic or cultural factors on patterns of alcohol consumption, the interaction of genetic and cultural effects has received comparatively little attention. Our results show unambiguously that a sociodemographic variable (marital status) can be a major modifier of the effect of genotype on drinking habits. Considering unmarried and married twin pairs separately, we observed a marked increase in the total genetic variance with age—a phenomenon that had previously been noted in an analysis of these data that ignored G×E interaction (Jardine and Martin, 1984). However, the impact of inherited liability was actually decreased in those who were married or had a marriage-like relationship. Alternative explanations of the hetero-

geneity of genetic and environmental effects as a function of marital status—either as artifacts of mean differences between groups or as a consequence of marital interaction (Heath, 1987)—were rejected by our model-fitting analyses.

The observed change in the proportion of the total variation in alcohol consumption attributable to genetic effects—from 31% in young married women, to 76% in older unmarried women—is very large. This reflects the considerable heterogeneity of twin correlations as a function of marital status (Table 4). Such large differences call into question the utility of traditional "heritability" analyses (ignoring G×E interaction) when these are applied to culturally labile variables such as drinking habits. (For personality trait measures, in contrast, we have found remarkable stability of genetic effects under different environmental conditions in this same sample; see Heath and Martin, 1986.) Likewise, we must note that epidemiological analyses may seriously underestimate the importance of sociodemographic variables when their modifying impact on inherited liability is ignored. The examination of sociodemographic correlates of drinking behavior in a genetically informative design promises new insights into the determinants of variability in drinking habits.

Acknowledgments

We thank Dr. John Mathews, Dr. John Gibson and Mrs. Marilyn Olsen for assistance with the data collection phase of this project. We also thank our colleagues Drs. Lindon Eaves, John Hewitt, Kenneth Kendler and Mike Neale for their helpful comments and suggestions.

References

ARMOR, D.J., POLICH, J.M. AND STANBUL, H.B. Alcoholism and Treatment. Prepared for the National Institute on Alcohol Abuse and Alcoholism, Santa Monica, Calif.: Rand Corp., 1976.

AUSTRALIAN BUREAU OF STATISTICS. Alcohol and Tobacco Consumption Patterns, February 1977. Australian Bureau of Statistics, Catalog No. 4312.0, 1978.

BOHMAN, M., SIGVARDSSON, S. AND CLONINGER, C.R. Maternal inheritance of alcohol abuse: Cross-fostering analysis of adopted women. Arch. gen. Psychiat. 38: 965-969, 1981.

BROWN, G.W. AND HARRIS, T. Social Origins of Depression: A Study of Psychiatric Disorder in Women, New York: Free Press, 1978.

BULMER, M.G. The Biology of Twinning in Man, Oxford, England: Clarendon Press, 1970.

CADORET, R.J., CAIN, C.A. AND GROVE, W.M. Development of alcoholism in adoptees raised apart from alcoholic biologic relatives. Arch. gen. Psychiat. 37: 561-563, 1980.

CAHALAN, D., CISIN, I.H. AND CROSSLEY, H.M. American Drinking Practices: A National Study of Drinking Behavior and Attitudes. Rutgers Center of Alcohol Studies Monograph No. 6, New Brunswick, N.J., 1969.

CAHALAN, D. AND ROOM, R. Problem Drinking among American Men. Rutgers Center of Alcohol Studies Monograph No. 7, New Brunswick, N.J., 1974.

CEDERLOF, R., FRIBERG, L. AND LUNDMAN, T. The interactions of smoking, environment and heredity and their implications for disease aetiology: A report of epidemiological studies on the Swedish twin registries, Acta Med. Scand. Supplement 612, 1977, pp. 1-128.

CLARK, W.B. AND MIDANIK, L. Alcohol use and alcohol problems among U.S. adults: Results of the 1979 National Survey. In: NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM. Alcohol Consumption and Related Problems. Alcohol and Health Monograph No. 1, DHHS Publication No. (ADM) 82-1190, Washington: Government Printing Office, 1982, pp. 3-52.

CLIFFORD, C.A., FULKER, D.W., GURLING, H.M.D. AND MURRAY, R.M. Preliminary findings from a twin study of alcohol use. In: GEDDA, L., PARISI, P. AND NANCE, W.E. (Eds.) Progress in Clinical and Biological Research, Vol. 69, Part C, New York: Alan R. Liss, Inc., 1981, pp. 47-52.

CLONINGER, C.R. Neurogenetic adaptive mechanisms in alcoholism. Science 236: 410-416, 1987.

CLONINGER, C.R., BOHMAN, M. AND SIGVARDSSON, S. Inheritance of alcohol abuse: Cross-fostering analysis of adopted men. Arch. gen. Psychiat. 38: 861-867, 1981.

CLONINGER, C.R., REICH, T., SIGVARDSSON, S., VON KNORRING, A.-L. AND BOHMAN, M. Effects of changes in alcohol use between generations on the inheritance of alcohol abuse. In: ROSE, R.M. AND BENNETT, J.E. (Eds.) Alcoholism: Origins and Outcomes, New York: Raven Press Pubs., 1988, pp. 49-74.

COREY, L.A., EAVES, L.J., MELLEN, B.G. AND NANCE, W.E. Testing for developmental changes in gene expression on resemblance for quantitative traits in kinships of twins: Application to height, weight, and blood pressure. Genet. Epidemiol. 3: 73-83, 1986.

DE LINT, J. AND SCHMIDT, W. The distribution of alcohol consumption in Ontario. Q. J. Stud. Alcohol 29: 968-973, 1968.

EAVES, L.J. The utility of twins. In: ANDERSON, V.E. Genetic Basis of the Epilepsies, New York: Raven Press Pubs., 1982.

EAVES, L.J., LAST, K., MARTIN, N.G. AND JINKS, J.L. A progressive approach to non-additivity and genotype-environmental covariance in the analysis of human differences. Brit. J. math. statist. Psychol. 30: 1-42, 1977.

EDWARDS, G., CHANDLER, J. AND HENSMAN, C. Drinking in a London suburb. *I.* Correlates of normal drinking. Q. J. Stud. Alcohol, Supplement No. 6, pp. 69-93, 1972a.

EDWARDS, G., CHANDLER, J., HENSMAN, C. AND PETO, J. Drinking in a London suburb. *II.* Correlates of trouble with drinking among men. Q. J. Stud. Alcohol, Supplement No. 6, pp. 94-119, 1972b.

EDWARDS, G., HENSMAN, C. AND PETO, J. Drinking in a London suburb. *III.* Comparisons of drinking troubles among men and women. Q. J. Stud. Alcohol, Supplement No. 6, pp. 120-128, 1972c.

ENCEL, S., KOTOWICZ, K.C. AND RESLER, H.E. Drinking patterns in Sydney, Australia. Q. J. Stud. Alcohol, Supplement No. 6, pp. 1-27, 1972.

GOODWIN, D.W., SCHULSINGER, F., MOLLER, N., HERMANSEN, L., WINOKUR, G. AND GUZE, S.B. Drinking problems in adopted and nonadopted sons of alcoholics. Arch. gen. Psychiat. 31: 164-169, 1974.

HEATH, A.C. The analysis of marital interaction in cross-sectional twin data. Acta genet. med. gemellol. 36: 41-49, 1987.

HEATH, A.C., KENDLER, K.S., EAVES, L.J. AND MARKELL, D. The resolution of cultural and biological inheritance: Informativeness of different relationships. Behav. Genet. 15: 439-465, 1985.

HEATH, A.C. AND MARTIN, N.G. Detecting the effects of Genotype × Environment Interaction on personality and symptoms of anxiety and depression. (Abstract) Behav. Genet. 16: 622, 1986.

HEATH, A.C. AND MARTIN, N.G. Teenage drinking in the Austra-

lian twin register: Genetic and social determinants of starting to drink, Alcsm clin. exp. Res., in press.

JARDINE, R. A Twin Study of Personality, Social Attitudes and Drinking Behaviour, Ph.D dissertation, Australian National University, Canberra, 1985.

JARDINE, R. AND MARTIN, N.G. Causes of variation in drinking habits in a large twin sample. Acta genet. med. gemellol. 33: 435-450, 1984.

JÖRESKOG, K. Structural analysis of covariance and correlation matrices. Psychometrika 43: 443-477, 1978.

JÖRESKOG, K. AND SORBOM, D. LISREL: Analysis of linear structural relationships by the method of maximum likelihood, Chicago, International Educational Services, 1986.

KAU, L. Alcoholism in Twins: Studies on the Etiology and Sequels of Abuse of Alcohol, Stockholm: Almqvist & Wiksell International, 1960.

KAPRIO, J., KOSKENVUO, M.D., LANGINVAINIO, H., ROMANOV, K., SARNA, S. AND ROSE, R.J. Genetic influences on use and abuse of alcohol: A study of 5638 adult Finnish brothers, Alcsm clin. exp. Res. 11: 349-356, 1987.

KAPRIO, J., KOSKENVUO, M. AND SARNA, S. Cigarette smoking, use of alcohol, and leisure-time physical activity among same-sexed adult twins. In: GEDDA, L., PARISI, P. AND NANCE, W.E. (Eds.) Progress in Clinical and Biological Research, Vol. 69, Part C, New York: Alan R. Liss, Inc., 1981, pp. 37-46.

KENDLER, K.S. Overview: A current perspective on twin studies of schizophrenia. Amer. J. Psychiat. 140: 1413-1425, 1983.

KENDLER, K.S., HEATH, A., MARTIN, N.G. AND EAVES, L.J. Symptoms of anxiety and depression in a volunteer twin population: The etiologic role of genetic and environmental factors. Arch. gen. Psychiat. 43: 213-221, 1986.

KESSLER, R.C., PRICE, R. AND WORTMAN, C. Social factors in psychopathology: Stress, social support and coping processes. Annu. Rev. Psychol. 36: 531-572, 1985.

LEDERMANN, S. Alcool, Alcoolisme, Alcoolisation: Mortalité, Morbidité, Accidents du Travail, Paris: Presses Universitaires de France, 1956.

LYKKEN, D.T., MCGUE, M. AND TELLEGEN, A. Recruitment bias in twin research: The rule of two thirds reconsidered. Behav. Genet. 17: 343-362, 1987.

LYKKEN, D.T., TELLEGEN, A. AND DERUBEIS, R. Volunteer bias in twin research: The rule of two-thirds. Social Biol. 25: 1-9, 1978.

MAGNUS, P., BERG, K. AND NANCE, W.E. Predicting zygosity in Norwegian twin pairs born 1915-1960. Clin. Genet. 24: 103-112, 1983.

MALIN, H., COAKLEY, J., KAELBER, C., MUNCH, N. AND HOLLAND, W. An epidemiologic perspective on alcohol use and abuse in the United States. In: NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM. Alcohol Consumption and Related Problems. Alcohol and Health Monograph No. 1, DHHS Publication No. (ADM) 82-1190, Washington: Government Printing Office, 1982, pp. 99-153.

MARTIN, N.G., EAVES, L.J., KEARSEY, M.J. AND DAVIES, P. The power of the classical twin study. Heredity 40: 97-116, 1978.

MARTIN, N.G. AND JARDINE, R. Eysenck's contributions to behaviour genetics. In: MODGIL, S. AND MODGIL, C. (Eds.) Hans Eysenck: Consensus and Controversy, Philadelphia: Taylor & Francis, Inc., 1986, pp. 13-47.

MARTIN, N.G. AND WILSON, S.R. Bias in the estimation of heritability from truncated samples of twins. Behav. Genet. 12: 467-472, 1982.

MATHER, K. AND JINKS, J.L. Biometrical Genetics, 3d Edition, New York: Methuen, Inc., 1982.

MILLWOOD, J.E. AND MCKAY, A.M. Measurement of alcohol consumption in the Australian population. Community Hlth Stud. 2: 123-132, 1978.

MULFORD, H.A. Drinking and deviant drinking, U.S.A., 1963. Q. J. Stud. Alcohol 25: 634-650, 1964.

PAOLINO, T.J., JR. AND MCCRADY, B.S. The Alcoholic Marriage: Alternative Perspectives, New York: Grune & Stratton, 1977.

PARTANEN, J., BRUUN, K. AND MARKKANEN, T. Inheritance of Drinking Behavior: A Study on Intelligence, Personality, and Use of Alcohol of Adult Twins, Helsinki: The Finnish Foundation for Alcohol Studies (Distributed by Rutgers Center of Alcohol Studies, New Brunswick, N.J.), 1966.

PLOMIN, R., DEFRIES, J.C. AND LOEHLIN, J.C. Genotype-environment interaction and correlation in the analysis of human behavior. Psychol. Bull. 84: 309-322, 1977.

REDMAN, S., SANSON-FISHER, R.W., WILKINSON, C., FAHEY, P.P. AND GIBBERD, R.W. Agreement between two measures of alcohol consumption. J. Stud. Alcohol 48: 104-108, 1987.

RILEY, J.W., JR. AND MARDEN, C.F. The social pattern of alcoholic drinking. Q. J. Stud. Alcohol 8: 265-273, 1947.

SCHUCKIT, M.A., GOODWIN, D.W. AND WINOKUR, G. A study of alcoholism in half siblings. Amer. J. Psychiat. 128: 1132-1136, 1972.

STRAUS, R. AND BACON, S.D. Drinking in College, New Haven, Conn.: Yale Univ. Press, 1953.

WEISSMAN, M.M., MEYERS, J.K. AND HARDING, P.S. Prevalence and psychiatric heterogeneity of alcoholism in a United States urban community. J. Stud. Alcohol 41: 672-681, 1980.