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Sex and Age Effects on the Inheritance of Alcohol Problems: A Twin Study

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Male monozygotic cotwins of probands with Alcohol Abuse–Dependence ($n = 85$) were more likely than male same-sex dizygotic cotwins ($n = 96$) to report alcohol, drug, and conduct disorder problems. For women, rates of problem behavior did not differ between monozygotic ($n = 44$) and same-sex dizygotic ($n = 43$) cotwins. Opposite-sex dizygotic twin data ($n = 88$) revealed significant cross-sex transmission; alcohol problems were greatest among male cotwins of female probands. For men, proportion of liability variance associated with additive genetic factors was significantly greater when proband had an early ($h^2 = .73 \pm .18$) rather than late ($h^2 = .30 \pm .26$) age of onset. For women, heritability did not vary as a function of proband's age of onset, and the pooled estimate suggested little genetic influence ($h^2 = .00$, *SE* not computable). Findings suggest that genetic influences may be substantial only in the etiology of early-onset male alcoholism.

Alcoholism is a strongly familial trait; risk to first-degree relatives of alcoholics is approximately four to five times that of the general population (Cotton, 1979). Although in the first published adoption study of alcoholism, no evidence for a genetic effect was found (Roe, 1944), twin and adoption studies published within the past 20 years have provided evidence of a genetic influence on familial transmission (Schuckit, 1987). Indeed, in the past 20 years, an almost complete reversal of the accepted view on the causes of alcoholism has occurred. The current zeitgeist in the alcohol research field, with its emphasis on the search for biological markers and the molecular biological approaches (e.g., Devor & Cloninger, 1989), seems dominated by the view that alcoholism is a biologically determined medical disease. Nonetheless, there remain serious questions concerning the consistency of the empirical support for the existence of a genetic influence on alcoholism (Murray, Clifford, & Gurling, 1983; Peele, 1986; Searles, 1988).

Although most would, no doubt, agree that genetic factors exert *some* influence on alcoholic risk, much of the current debate centers on the strength of that influence and the extent to which it is moderated by age, sex, diagnostic subtype, and psychiatric comorbidity. In a study of Swedish male adoptees, Cloninger, Bohman, and Sigvardsson (1981) proposed two forms of alcoholism (as determined by Temperance Board registrations) and showed that one form (manifested as moderate alcohol abuse and designated male-limited, or Type II, alcoholism) was highly heritable, whereas a second form (manifested as mild or severe alcohol abuse, depending on environmental circumstances, and designated milieu-limited, or Type I alcoholism) was only moderately heritable. In a study of 114 male and 55 female twin pairs, Pickens et al. (1991) also found evidence for differential genetic heritability (h^2) of alcoholism subtypes. Alcohol dependence according to the *Diagnostic and Statistical Manual of Mental Disorders* (3rd ed; *DSM–III;* American Psychiatric Association, 1980) was found to be moderately heritable both for men ($h^2 = .595$) and for women ($h^2 = .420$), whereas alcohol abuse was shown to be less heritable in both sexes ($h^2 = .379$ in men and .000 in women). In their classic study of Danish adoptees, Goodwin, Schulsinger, Hermansen, Guze, and Winokur (1973) also reported evidence of differential heritability. The reared-away sons of alcoholics had higher rates of alcoholism, but lower rates of nonalcoholic problem drinking, than did the reared-away sons of nonalcoholics.

Women are much less likely to develop problems with alcohol than are men (Robins et al., 1984), although the sex differential appears to have decreased in recent cohorts (Reich, Cloninger, Van Eerdewegh, Rice, & Mullaney, 1988). The differential heritability of alcoholism in men and women has been the focus of much behavioral genetic research; the existing evidence suggests lower heritability in women than in men. In a recent meta-analysis of family studies, Pollock, Schneider, Gabrielli, and Goodwin (1987) concluded that the rate of alcoholism was lower among the offspring of alcoholic mothers than among the offspring of alcoholic fathers. In a study of Danish

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adoptees, an increased risk for alcoholism was observed among the adopted-away sons (Goodwin et al., 1973) but not adopted-away daughters (Goodwin, Schulsinger, Knop, Mednick, & Guze, 1977) of alcoholic biological parents. The authors of the Swedish adoption studies (Bohman, Sigvardsson, & Cloninger, 1981; Cloninger et al., 1981) did report increased risk for Temperance Board registrations in both adopted-away sons and adopted-away daughters of alcoholics, although genetic heritability was lower in daughters than in sons. Only two twin studies of alcoholics have included female samples; both have suggested less genetic influence on women than on men with regard to alcoholic risk. Gurling, Murray, and Clifford (1981) found no statistically significant differences between monozygotic (MZ) and dizygotic (DZ) twin concordance for alcoholism in either the male sample ($n = 35$ pairs) or the female sample ($n = 21$ pairs). In a larger twin study, Pickens et al. (1991) reported lower estimates of genetic heritability for female subjects than for male subjects, although the sex difference in heritabilities achieved statistical significance only for the *DSM–III* diagnosis of alcohol abuse.

Age has also been found to moderate the heritability of alcohol-related problems, albeit in an inconsistent manner. In their study of male Finnish twins, Partanen, Bruun, and Markkanen (1966) reported that the heritability of their Lack of Control measure was much lower for younger twins (aged 29–32 years; $h^2 = -.07$) than for older twins (aged 33–38 years; $h^2 = .54$). In a family study, Reich et al. (1988) reported secular significant increases in the transmissibility (a composite of genetic and environmental contributions to familial resemblance) of alcoholism for both male and female subjects. Age and cohort effects are, of course, confounded in cross-sectional comparisons. In comparison with older participants, younger participants in these studies shared a more recent birth date and, likely also, an earlier age of alcohol problem onset. Age of onset is predictive of clinical course of alcoholism and has been hypothesized to be an important moderator of genetic heritability (Cloninger, 1987).

Our article is the second in a series on the results of a twin study of alcoholism undertaken at the University of Minnesota. In the first report, Pickens et al. (1991) described the methodology and reported concordance and heritability estimates for *DSM–III*-based diagnoses of alcohol abuse and alcohol dependence in an interviewed sample of 169 twin pairs. For this second report, responses from a larger mail survey sample of 356 twin pairs were analyzed to determine whether genetic and environmental influences on alcohol problems are moderated by sex and by age of onset.

Method

Sample

The study began in 1981 when Roy W. Pickens initiated a retrospective search of records at a large private alcohol and drug abuse treatment program. Clients admitted between 1974 and 1981 (designated *probands*) who reported having a same-age sibling (later verified for twin status and designated *cotwins*) were identified. Prospective screening was initiated at that center in 1982 and at 15 additional public and private Minnesota alcohol and drug abuse treatment and follow-up programs in 1985, and it continued until 1988. The search identified 599 twin sets, of which both members of 392 sets (65.5%) agreed to participate in the study. Included in the 392 are 8 pairs of which both members had sought treatment at 1 of the 16 surveyed programs (i.e., doubly ascertained pairs) as well as four sets of triplets. As is appropriate with this method of ascertainment (see Appendix C in Slater & Cowie, 1971), we treated triplets and doubly ascertained pairs each as two independent pairs in this study; thus the total sample contained 404 pairs (305 same-sex and 99 opposite-sex). Although the majority (56.3%) of twins resided in Minnesota at the time of assessment, twins residing in 39 other states as well as in Sweden (one pair only) and Canada were included in the sample.

Procedure

Soon after recruitment, probands and their cotwins were administered a self-report questionnaire that included items assessing (a) personal background, (b) pair similarity, and (c) personal and family history of psychological disorders and of alcohol and drug use. Probands and their cotwins were each paid $25–$35 for completing the questionnaire. Later, a subsample of probands and their cotwins were personally and independently interviewed with the Diagnostic Interview Schedule (DIS) (Version III-A; Robins, Helzer, Croughan, & Ratcliff, 1981), as well as with other alcoholism, family history and personality scales.

This report is concerned with the clinical information obtained from the self-report questionnaires only. Pickens et al. (1991) reported findings that were based on the subsample of twins who completed a comprehensive interview assessment of psychopathologic disorder and alcohol and substance use and abuse. On the basis of the questionnaire responses, the proband met *DSM–III* criteria for alcohol abuse–dependence in 366 of the 404 twin pairs and qualified for inclusion in the sample.

Zygosity Determination

All 88 opposite-sex pairs were classified as DZ. For 158 of the 278 remaining pairs, blood samples had been drawn, and zygosity was determined from analyses of 12 serological factors, including 4 red blood cell antigens, 4 serum proteins, and 4 enzymes, by means of electrophoresis and isoelectric focusing. Twins were classified as MZ if all blood factors were identical (79 pairs) and DZ if one or more of these factors differed (79 pairs). Through this method, the probability of misclassifying a DZ pair as MZ is less than .001 (Lykken, 1978). For the remaining 120 pairs, zygosity was determined from answers to questions concerning similarity of the twins as children (e.g., whether the twins were as similar as "two peas in a pod" and whether even family members had difficulty telling them apart). On the basis of the questionnaire responses, 50 pairs were classified as MZ and 60 as DZ, and 10 could not be classified (because, for example, the two members of a pair disagreed about degree of similarity) and consequently were not included in the analyses. Although questionnaire methods appear simplistic, they have been shown repeatedly to yield misclassification error rates of less than 5% (e.g., Cederlof, Friberg, Jonsson, & Kaij, 1961; Cohen, Dibble, Grawe, & Pollin, 1973). For the twins in this study for whom both blood zygosity and questionnaire information were available, only 4.6% would have been misclassified by the questionnaire method. Because only 110 of the 356 pairs were classified through the questionnaire method, the overall error rate for zygosity misclassification in this study was likely to be substantially less than the 5% typical of questionnaire-based methods.

Measures

Alcohol symptoms. The 19 alcohol symptoms included in the questionnaire were developed to parallel the DIS and allow for *DSM–III*

diagnoses of alcohol abuse, alcohol dependence, or both (American Psychiatric Association, 1980). Participants indicated whether each symptom had ever characterized their drinking behavior. Consequently, all assessments refer to lifetime, rather than current, prevalence. The symptoms were organized into four alcohol symptom scales: Social Impairment (4 items; alpha reliability of .78 in men and .79 in women), Pathological Use (7 items; alpha reliability of .81 in men and .78 in women), Dependence (3 items; alpha reliability of .67 in men and .60 in women), and Total Alcohol Symptoms (19 items; alpha reliability of .92 in men and .91 in women; see the Appendix). In addition, respondents were asked about the ages at which they first became intoxicated and, for those who had ever experienced a problem with alcohol, the age at which they first experienced any of the alcohol-related symptoms (designated as *age at first symptom*) and the total length of time in which they had experienced any symptom (designated as *illness length*).

Diagnoses. *DSM–III* diagnoses (the study was designed and undertaken at a time when *DSM–III* was considered the standard for psychiatric diagnoses) of alcohol abuse, alcohol dependence, or both were made on the basis of responses to the questionnaire items. A subject received a diagnosis of alcohol abuse if he or she demonstrated at least one symptom each of social impairment and pathological use, alcohol dependence if he or she demonstrated at least one symptom of dependence and at least one symptom of either social impairment or pathological use, and for alcohol abuse–dependence if he or she met criteria for either disorder. Bacon, Pickens, Svikis, and McGue (1991) reported the agreement between the questionnaire responses and the DIS interview for the sample that completed both forms of assessment. For the composite diagnosis of alcohol abuse–dependence, the predictive values, both positive (.923 for men and .839 for women) and negative (.638 for men and .860 for women), and the kappa coefficients (.576 for men and .674 for women) were judged to be sufficiently large to justify use of the questionnaire-based diagnoses as reliable indicators of diagnoses obtained by interview. Because the kappa statistics were somewhat less for the alcohol dependence diagnoses (.358 for men and .585 for women), differential diagnosis of alcohol abuse and alcohol dependence from the questionnaires is somewhat uncertain and thus not reported here. The composite diagnosis that we used is best viewed as an accurate indicator of severe and persistent alcohol problems but not necessarily of alcoholism per se. Nonetheless, the diagnosis used here is designated alcohol abuse–dependence to reflect the *DSM–III* rationale that underlies its development, as well as its substantial correlation with interview-derived diagnoses.

Other measures. Three additional measures were derived from the questionnaire: drug use (regular use of illegal street drugs or regular and illicit use of prescription drugs); treatment for depression (whether the respondent reported ever consulting a mental health professional for depression); and conduct disorder (a four-item scale of conduct disorder symptoms).

Statistical Methods

Prediction of cotwin risk. The primary analyses involved comparison of cotwin risk (also termed *concordance*) as a function of zygosity. For each sex, two comparisons were made: (a) MZ versus same-sex DZ cotwins, and (b) same-sex versus opposite-sex DZ cotwins. For quantitative variables, the hypothesis of equal means was tested by means of a Student's t statistic. For qualitative outcome variables, hypotheses were tested with the Pearson chi-square statistic. Effect sizes were estimated as the difference in means divided by the pooled standard deviation for quantitative variables and through the use of probit transformation for qualitative variables (Glass, McGaw, & Smith, 1981).

Because most of the outcome variables were significantly associated with age, and because cotwin ages were not homogeneous across groups, key comparisons were determined both with and without a statistical adjustment for age. Age-adjusted comparisons and effect sizes were determined through use of analysis of covariance for quantitative variables and logistic regression for qualitative outcomes. For none of the outcome variables was there statistical evidence of an interaction between the covariate of age and the relevant independent variable. The logistic regression adjusted effect sizes are reported for age 35 years (approximately the mean age for the entire sample). Effect sizes were considered large if greater than .50 standard deviations, moderate if in the range .25–.50 standard deviations, and small otherwise. Because both the size of the effect and its statistical significance are emphasized here, and because readers can easily apply the conservative Bonferroni correction by multiplying the reported p value by the number of relevant comparisons, we did not explicitly attempt to adjust for the number of comparisons made.

Results

Sample Characteristics

Twin pairs in which the proband did not meet *DSM–III* criteria for alcohol abuse–dependence and pairs in which zygosity could not be reliably determined were disqualified from the study; 356 pairs remained. Table 1 summarizes demographic characteristics of the sample. The sample was primarily in early to middle adulthood; the age differences between probands and their cotwins reflect slightly different assessment dates. The sample is predominantly White, which reflects the Minnesota state population from which most subjects were drawn. Although a large proportion of the sample was ascertained through private treatment centers, there was heterogeneity in socioeconomic background, as reflected in a high school graduation rate of less than 80%. As is typical of alcoholism treatment samples in both the United States (e.g., Ross, 1989) and other industrialized countries (e.g., Blankfield, 1990), only a minority of the probands were in a marriagelike living situation when assessed (most never having been married). The MZ and DZ probands were comparable in respect to both demographic background and clinical status (not reported in the table), with one significant exception: For reasons that are not clear, the MZ male probands and their cotwins were significantly younger than the DZ male probands and their cotwins ($p < .05$). Given the substantial association between age and most of the outcome variables, this age difference represented a possible confound that required statistical adjustment.

Table 2 provides a comparison of the clinical characteristics of the male and female probands. For the alcohol-related symptom scales, the effect sizes were generally small, and the male–female comparisons were nonsignificant. Both proband groups comprised persons who had serious and long-standing problems with alcohol. Probands had a relatively early age of first problem onset, displayed a large number of alcohol symptoms, and had suffered problems with alcohol for a significant portion of their adult lives. On average, male and female probands displayed virtually the same number of symptoms on the Total Alcohol, Pathological Use, and Dependence scales. Only for Social Impairment was there a significant sex difference, but even there the effect size was moderate, and the significant result can be attributed almost entirely to a difference in the rate of display of a single item. Sixty-eight percent of male pro-

Table 1
Sample Demographic Characteristics

Characteristic	Male		Female		Opposite sex	
	MZ	DZ	MZ	DZ	Male proband	Female proband
No. pairs	85	96	44	43	65	23
Age at assessment (years)						
Proband						
M	32.3	37.9	34.0	31.1	35.7	32.3
SD	11.9	12.6	12.9	9.9	12.5	10.0
Cotwin						
M	32.5	37.8	34.3	31.3	35.7	32.6
SD	12.0	12.7	12.9	9.8	12.4	10.1
% White						
Proband	89	94	93	93	90	91
Cotwin	91	93	95	95	91	91
At least a high school education (%)						
Proband	72	82	80	77	73	83
Cotwin	68	76	77	79	81	91
Married or living together as married (%)						
Proband	33	42	43	23	39	22
Cotwin	41	62	57	51	64	52

Note. Ethnicity was obtained by self-report, and members of a twin pair did not always agree on their report of ethnic background. MZ = monozygotic; DZ = dizygotic.

bands, but only 38% of female probands, affirmatively answered Item 11 ("Did you ever experience legal problems [such as traffic arrests or other police problems] as a result of alcohol use?").

Moderate to large effect sizes and significant differences were, however, observed on some of the other clinical measures. Male probands had an earlier age at first intoxication than did female probands. The mean ages at first symptom were comparable for male and female probands. Nonetheless, because of the relative chronicity of their clinical course, male probands reported a longer mean length of illness than did female probands. Rates of self-reported treatment for depression and illegal use of street or prescription drugs were substantially higher for female probands than for male probands. For illegal drug use, female probands were more likely than male probands to report use of sedatives and stimulants, but not of hallucinogens or marijuana.

Cotwin Risk

Status of the male cotwins of probands is summarized in Table 3. Three of the MZ male cotwins (3.5%), 9 of the same-sex DZ cotwins (10.6%), and 5 of the opposite-sex DZ cotwins (21.7%) either never drank or never became intoxicated as a result of drinking, and so they never occasioned the possibility of an alcohol-related symptom or diagnosis. These cotwins were, however, included in samples compared in Table 3. In comparison with male same-sex DZ cotwins, male MZ cotwins were more likely (a) to receive a positive alcohol abuse–dependence diagnosis, (b) to display alcohol-related symptoms (large and significant differences on all four symptom scales and on 14 of the 19 individual symptoms), (c) to illicitly use drugs other than alcohol, and (d) to have exhibited symptoms of adolescent conduct disorder. After adjustment for age, effect sizes were moderate, and differences between MZ and same-sex DZ cotwins remained statistically significant.

Although the sample was small, the male cotwins of female DZ probands exhibited more problems with alcohol than did the male cotwins of male DZ probands. The effect sizes were moderate to large, and group differences were statistically significant for two of the alcohol symptom scales: the overall diagnosis of alcohol abuse–dependence and age at first intoxication. Indeed, on most relevant measures, the risk pattern exhibited by the male cotwins of female DZ probands was virtually identical to that observed among the male cotwins of male MZ probands.

Table 4 presents results for the female cotwins of affected probands. Only 4 female cotwins reported never having been intoxicated; all were same-sex DZ cotwins. For female cotwins, the pattern of risk was markedly different from that observed for male cotwins. There were no significant differences between the MZ and same-sex DZ cotwins or between the same- and opposite-sex DZ cotwins. Although this failure to observe statistically significant differences may, in a few cases, be ascribed to the modest size of the female sample, the effect sizes for the alcohol-related measures were uniformly low and suggested few if any meaningful differences among the groups. Nonetheless, it is of some interest to note the variables that show the largest, albeit nonstatistically significant, differences between the MZ and same-sex DZ cotwins: In comparison with the same-sex DZ cotwins, the MZ cotwins were more likely to report illicit drug use and treatment for depression.

It is, of course, possible that our findings would have differed qualitatively had an alternative diagnostic scheme (Feighner, *DSM–III–R*, etc.) been used. Unfortunately, the available clinical information does not allow direct evaluation of this possibility. Nonetheless, further analysis of the data strongly suggests that the essential findings just described (i.e., significant and

Table 2
Comparison of Male and Female Probands with Alcohol Abuse–Dependence

Characteristic	Male (246 probands)	Female (110 probands)	Effect size
Symptom scales			
Total alcohol symptoms (maximum = 19)			.03
M	11.5	11.4	
SD	3.9	4.0	
Pathological use (maximum = 7)			.05
M	4.7	4.6	
SD	1.8	2.0	
Social impairment (maximum = 4)			.27*
M	2.8	2.5	
SD	1.1	1.2	
Dependence (maximum = 3)			.00
SD	1.4	1.4	
SD	0.7	0.6	
Temporal characteristics			
Age at first intoxication			−.30**
M	15.2	16.5	
SD	3.8	5.2	
Age at first symptom			−.06
M	23.4	24.0	
SD	10.1	10.4	
Length of illness			.39***
M	9.3	6.7	
SD	7.2	5.3	
Other clinical characteristics			
Treated depression (%)	27.4	65.5	−1.00***
Conduct disorder			.14
M	1.4	1.2	
SD	1.4	1.4	
Drug use (%)	46.3	60.9	−.37*

Note. Effect sizes are calculated as mean of first designated group minus mean of second divided by the pooled standard deviation for quantitative variables, and the difference in probits for qualitative variables. Significance levels are of difference in means (*t* test) or proportions (Pearson chi-square).
* $p < .05$. ** $p < .01$. *** $p < .001$, two-tailed.

moderate-sized MZ–DZ differences for male twins but nonsignificant and small MZ–DZ differences for female twins) would have resulted under alternative schemes. Figure 1 depicts the distribution of total alcohol symptoms for the male and female cotwins of affected probands. Under any diagnostic scheme, a positive diagnosis requires the display of at least two, but usually more, symptoms. The male MZ and same-sex DZ difference in risk for alcohol abuse–dependence reported in Table 3, is seen in Figure 1 to be attributable almost entirely to a difference in the proportion of cotwins reporting fewer than two symptoms (i.e., those who would receive a negative diagnosis under any scheme). Only 19.3% of the MZ but 39.6% of the same-sex DZ male cotwins displayed none or one of the alcohol-related symptoms. This 20.3% difference is virtually equivalent to the 22.3% difference in risk for the overall diagnosis. Put another way, if attention were restricted to cotwins who reported at least two symptoms, the MZ–DZ difference in rate of alcohol-related problems would be nonsignificant. For female cotwins, the distributions of Total Alcohol Symptom scores were nearly identical for the MZ and same-sex DZ cotwins, which suggests that alternative diagnostic schemes would not have yielded substantial MZ–DZ differences in the female sample.

Heritability Analysis

Heritability calculations were made for the diagnosis of alcohol abuse–dependence from data of same-sex twins only.[1] In these analyses, we assumed that the diagnosis could be modeled as a threshold character (Falconer, 1965; McGue, Gottesman, & Rao, 1985); that is, underlying the qualitative phenotype of alcohol abuse–dependence was an assumed, normally distributed, quantitative liability. Persons achieve a positive diagnosis whenever their combined quantitative liability exceeds a fixed threshold value along the liability continuum. Three factors were assumed to contribute to liability: additive genetic effects, shared environmental effects, and nonshared environmental effects. We further assumed that there was no assortative mating for alcoholism among the parents of the twins, so that the genetic correlations were 1.0 between MZ twins and 0.5 between DZ twins. Shared environmental effects are environmental factors shared by both members of a twin pair regardless of zygosity (rearing social class, parental child-rearing practices, exposure to parental alcoholism, etc.). Nonshared environmental effects refer to environmental factors that are not shared by both members of the twin pair (developmental accidents, differential peer pressure, differential parental treatment, etc.). Shared environmental factors contribute to pair similarity; nonshared environmental factors do not.

Models were fitted and parameters were estimated by means of the maximum likelihood method; that is, we estimated parameters by numerically minimizing the quantity

$$F = 2 \sum n_{ij} \ln (n_{ij}/e_{ij}),$$

where n_{ij} is the observed number and e_{ij} the expected number of cotwins of zygosity i ($i = 1$ for MZ and 2 for DZ) in diagnostic class j ($j = 1$ for unaffected and 2 for affected), and the summation is over both zygosities and both diagnostic classes. The e_{ij}s were derived under the assumptions (a) that diagnosis occurred whenever a subject's combined liability exceeded a fixed threshold value and (b) that twin pair liability followed a bivariate

[1] Behavioral geneticists typically restrict heritability calculations to comparisons between monozygotic (MZ) and same-sex dizygotic (DZ) twins. There are two justifications for this practice. First, in comparison with opposite-sex DZ twins, the environmental similarity of same-sex DZ twins is likely to be more comparable with that of MZ twins. Second, correlations between opposite-sex family members reflect not only shared genes and shared environments but also the male–female correlation in liability. This latter correlation cannot be assumed to equal one because the factors contributing to male and female liability may not be identical. With our design, the male–female liability correlation cannot be independently estimated.

Table 3
Characteristics of the Male Cotwins of Probands with Alcohol Abuse–Dependence

Characteristic	MZ (n = 85)	SS DZ (n = 96)	OS DZ (n = 23)	MZ vs. SS DZ		SS DZ vs. OS DZ	
				Effect size	Age-corrected effect size	Effect size	Age-corrected effect size
Diagnosis							
Alcohol abuse–dependence (%)	76.5	53.6	78.3	0.63***	0.49**	−0.70**	−0.47
Symptom scales							
Total alcohol symptoms				0.54***	0.47**	−0.47*	−0.39
M	7.3	4.6	6.9				
SD	5.1	4.9	5.1				
Pathological use				0.57***	0.50***	−0.30	−0.25
M	3.2	2.0	2.6				
SD	2.2	2.0	2.0				
Social impairment				0.55**	0.38*	−0.42	−0.37
M	1.8	1.1	1.7				
SD	1.1	1.4	1.5				
Dependence				0.53**	0.33*	−0.69**	−0.55*
M	0.9	0.5	1.0				
SD	0.8	0.7	0.8				
Temporal characteristics							
Age at first intoxication				0.27	0.10	0.53**	0.41
M	15.9	16.9	14.7				
SD	3.3	4.0	4.6				
Age at first symptom				−0.12	−0.19	0.14	0.06
M	21.0	21.9	20.9				
SD	7.9	6.7	8.2				
Other clinical characteristics							
Treated depression (%)	14.3	16.5	19.0	−0.09	0.09	−0.10	0.06
Conduct disorder				0.52**	0.36*	−0.39	−0.26
M	1.4	0.7	1.2				
SD	1.5	1.2	1.6				
Drug use (%)	36.5	19.6	26.1	0.51**	0.40*	−0.22	0.23

Note. SS = same-sex, OS = opposite-sex twin pairs; MZ = monozygotic, DZ = dizygotic. Effect sizes are calculated as mean of first designated group minus mean of second divided by the pooled standard deviation for quantitative variables and the difference in probits for qualitative variables. Significance levels are of difference in means or proportions for both uncorrected and age-corrected data.
* $p < 0.05$. ** $p < .01$. *** $p < .001$, two tailed.

normal distribution. The tetrachoric correlation in liability was expressed in terms of two variance component parameters: the proportion of liability variance associated with additive genetic factors, designated h^2, and the proportion of liability variance associated with shared environmental factors, designated c^2. The tetrachoric correlation was parameterized as $h^2 + c^2$ for MZ twins and $0.5h^2 + c^2$ for DZ twins. The remaining variance component, the proportion of variance associated with nonshared environmental factors, designated e^2, was derived from estimates of the other two components with the constraint $h^2 + c^2 + e^2 = 1.0$. For detailed discussion of the maximum likelihood procedure as applied to qualitative family data, see Rice and Reich (1985).

We estimated standard errors for the three estimated parameters by inverting the information matrix at the maximum likelihood solution. Under the null hypothesis that the fitted model is the true model, the minimized value of F is distributed as a chi-square random variable with degrees of freedom equal to the number of independent observations minus the number of independently estimated parameters. The minimized value of F thus provides a vehicle for testing specific parametric hypotheses. In particular, if a reduced model is derived from a more general model by the setting of one or more parameters to their null values (e.g., $h^2 = 0$), the difference in minimized F values between the reduced and general models is, under the null hypothesis implied by the constraints, distributed as a chi-square random variable with degrees of freedom equal to the number of independent constraints.

The heritability analyses required information on population base rates (McGue, 1988), which were derived from the Epidemiologic Catchment Area study (ECA; Eaton & Kessler, 1985). Population base rates for *DSM–III* diagnoses of alcohol abuse–dependence were determined by analysis of data from the two sites (St. Louis and Los Angeles) in the ECA study in which the DIS alcohol section was administered with the same skipout procedures used in the interview portion of this study. The

Table 4
Characteristics of the Female Cotwins of Probands with Alcohol Abuse–Dependence

Characteristic	MZ (n = 44)	SS DZ (n = 43)	OS DZ (n = 65)	MZ vs. SS DZ		SS DZ vs. OS DZ	
				Effect size	Age corrected effect size	Effect size	Age corrected effect size
			Diagnosis				
Alcohol abuse–dependence (%)	38.6	41.9	30.7	−0.09	0.05	0.29	0.11
			Symptom scales				
Total alcohol symptoms				0.09	0.21	0.25	0.13
M	3.8	3.4	2.3				
SD	4.8	4.3	4.2				
Pathological use				0.05	0.16	0.27	0.14
M	1.6	1.5	1.0				
SD	1.9	1.9	1.8				
Social impairment				0.38	0.30	0.26	0.14
M	0.8	0.8	0.5				
SD	1.3	1.2	1.1				
Dependence				0.00	0.14	0.16	0.03
M	0.4	0.4	0.3				
SD	0.8	0.7	0.6				
			Temporal characteristics				
Age at first intoxication				0.09	0.20	−0.14	0.12
M	18.6	18.1	18.9				
SD	6.0	5.0	6.2				
Age at first symptom				0.45	0.03	−0.38	0.07
M	22.6	19.4	22.2				
SD	8.3	5.6	8.8				
			Other clinical characteristics				
Treated depression (%)	47.7	32.6	25.4	0.39	0.47	0.21	−0.08
Conduct disorder				0.08	0.33	0.18	−0.03
M	0.8	0.7	0.5				
SD	1.3	1.1	1.1				
Drug use (%)	25.0	16.3	15.6	0.30	−0.31	0.03	0.14

Note. SS = same-sex, OS = opposite-sex twin pairs; MZ = monozygotic, DZ = dizygotic. Effect sizes are calculated as mean of first designated group minus mean of second divided by the pooled standard deviation for quantitative variables, and the difference in probits for qualitative variables. Significance levels are of difference in means or proportions for both uncorrected and age-corrected data.

ECA study was a series of five epidemiologic research studies performed by five independent research teams in collaboration with the National Institute of Mental Health, Division of Biometry and Epidemiology. Population base rates were computed separately by sex and zygosity as the proportion of Whites (92% of our study's probands were White) within the relevant age range who met lifetime criteria for *DSM–III* alcohol abuse–dependence. These base rates were .298 for the MZ men, .281 for the same-sex DZ men, .090 for the MZ women, and .092 for the same-sex DZ women.[2]

Table 5 summarizes results from the heritability analyses. The first set of fitted models involved direct comparison of the total sample of male and female twin data. When estimated separately, the variance components estimates differed markedly for male and female twins. For male twins, estimates of genetic heritability (h^2 = .543 ± .138) and proportion of variance associated with shared environmental effects (c^2 = .331 ± .125) were both moderate and statistically significant (i.e., more than twice their standard errors). In contrast, for female twins, h^2 was estimated at a boundary value of zero (standard error not computable), whereas the estimate of c^2, .633 ± .049, was substantial and statistically significant. Constraining the variance components estimates to be equal in the two sexes resulted in a significant increase in chi-square, $\chi^2(2, N = 268) = 6.2$, $p < .05$, which indicated that variance components were not homogeneous across sex.

Recall that of the male twins, the MZ twins were, on average, significantly younger than the same-sex DZ twins. Age was also a significant predictor of risk for alcohol abuse–dependence.

[2] The ECA lifetime prevalence rates of alcohol abuse, dependence, or both are higher than rates of alcoholism reported in other epidemiological surveys. Although our method is comparable with that of the ECA, it is reasonable to wonder how lower prevalence estimates might affect the heritability calculations. If the actual prevalence rates were lower than those reported by the ECA, genetic heritability would be overestimated, and the proportion of variance associated with shared environmental factors would be underestimated in our analyses.

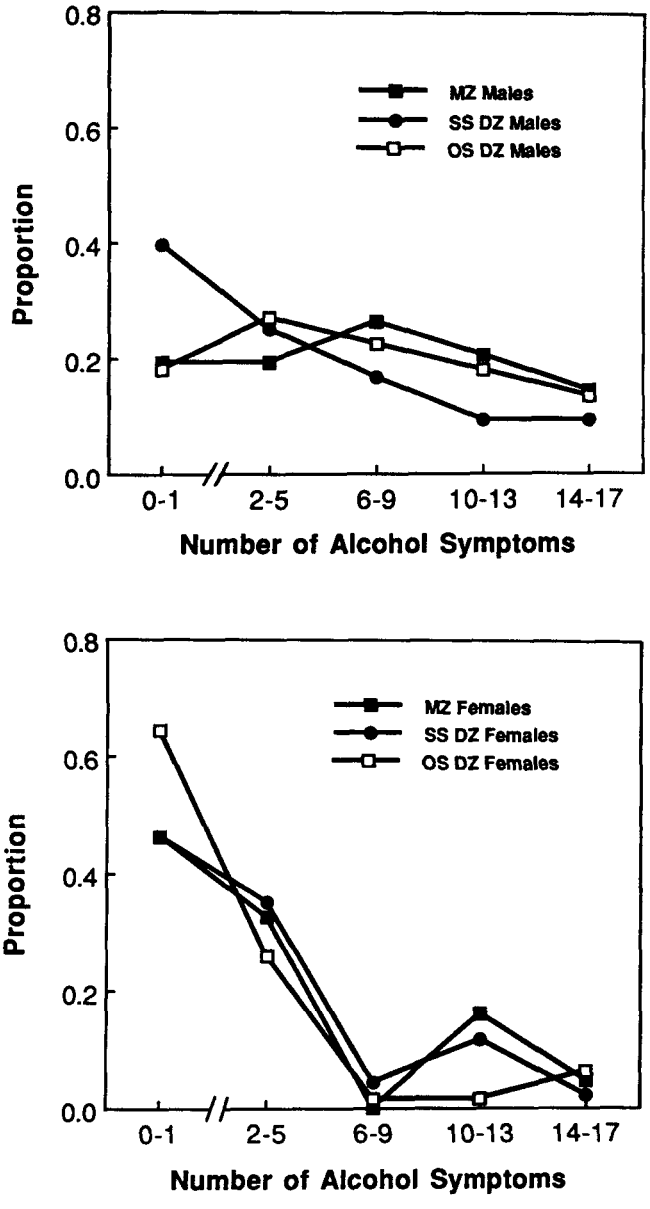

Figure 1. Distribution of Total Alcohol Symptoms among the male (top) and female (bottom) cotwins of probands with alcohol abuse–dependence. (Note the discontinuity along the horizontal axis that is introduced to distinguish subjects who would not qualify for a positive diagnosis, under any scheme, from those who might.)

When cotwin risk was predicted as a logistic function of zygosity and cotwin age, the regression coefficient for age was significantly negative in both the male sample (logistic regression weight equal to $-.053 \pm .014$) and the female sample (logistic regression weight equal to $-.074 \pm .024$); that is, with increasing age came decreasing pair concordance. A finding that is somewhat paradoxical is that, all other things being equal, one would expect that older twins, having lived through more of the relevant risk period, would more likely be concordant than would younger twins. But all other things were not equal: Younger twins also had a relatively early age of onset. The correlation between proband's age and proband's age at first symptom was large and significant in both sexes ($r = .77$ for male probands and .84 for female probands). The age effect on cotwin risk appears to be a result of this correlation; when proband's age at first symptom is included in the logistic regression equation, age is no longer significantly related to cotwin risk.

Age differences between MZ and same-sex DZ males may, then, have biased the heritability calculations reported earlier; that is, the MZ male sample included proportionately more of the highly concordant early-onset pairs than did the same-sex DZ male sample. When cotwin risk was predicted from a logistic regression of zygosity and proband's age at first symptom, the latter was statistically significant for both the male probands (logistic regression weight of $-.073 \pm .019$) and female probands (logistic regression weight of $-.059 \pm .025$) samples. Regressions fitted separately by zygosity indicated that although there was some tendency for the cotwin's risk to decline more rapidly with proband's increasing age at first symptom in MZ male twins (logistic regression weight of $-.101 \pm .030$) than in same-sex DZ male twins (logistic regression weight of $-.052 \pm .023$), the difference in regression weights was not statistically significant, $\chi^2(1, N = 181) = 1.67$, $p > .05$. The relation between proband's age at first symptom and cotwin's risk was also statistically homogeneous in the female sample (MZ logistic regression weight of $-.052 \pm .023$, DZ logistic regression weight of $-.071 \pm .041$), $\chi^2(1, N = 87) = 0.15$, $p > .05$.

To correct for possible bias, variance components were reestimated after the sample was divided according to proband's age at first symptom. For both male and female twins, pairs were designated *early onset* if proband's age at first symptom was less than or equal to 20 years and *late onset* otherwise.[3] Twenty years approximated probands' median age at first symptom in both the male and female samples, and so dividing the sample at this point maximized the stability of statistical results. As demonstrated by the logistic regression analyses, the decrease in cotwins' risk with increasing probands' age of onset was not an arbitrary result of dividing the sample at this particular point. For male twins, heritability was large and statistically significant for the early-onset pairs ($h^2 = .725 \pm .175$) but not the late-onset pairs ($h^2 = .295 \pm .264$). For both male samples, the proportion of variance associated with shared environmental effects was modest and nonsignificant. Constraining the variance components estimates to be equal in the early- and late-onset male samples resulted in a significant increase in chi-square, $\chi^2(2, N = 181) = 7.05$, $p < .05$. For both early- and late-onset female pairs, heritability was estimated at a boundary value of 0.0, whereas estimates of c^2 were large and statistically significant. Constraining the variance components estimates to be equal in the early- and late-onset female samples did not result in a significant increase in chi-square, $\chi^2(2, N = 87) = 2.27$, $p > .05$. Finally, male–female differences in vari-

[3] Although a cutoff score of 25 years has been widely used in other studies to determine early- versus late-onset cases (e.g., Irwin, Schuckit, & Smith, 1990), these other studies have been concerned with the onset of alcoholism and not the onset of the first problem with alcohol. Our use of a cutoff score of less than 25 years is warranted by this distinction.

Table 5
Twin Pair Concordances, Tetrachoric Correlations, and Variance Component Estimates

Group	Monozygotic			Same-sex dizygotic			Variance component					
							Genetic		Shared environmental		Nonshared environmental	
	n	Concordance	*r*	*n*	Concordance	*r*	*M*	*SE*	*M*	*SE*	*M*	*SE*
Males												
Early onset	52	.865	.957	44	.568	.595	.725	.175	.232	.174	.043	.022
Late onset	33	.606	.666	52	.509	.475	.295	.264	.372	.203	.333	.097
Total	85	.765	.874	96	.536	.563	.543	.138	.331	.125	.126	.034
Females												
Early onset	20	.500	.729	22	.500	.736	.000[a]		.732	.061	.268	.061
Late onset	24	.292	.501	21	.333	.558	.000[a]		.525	.076	.475	.076
Total	44	.386	.617	43	.419	.660	.000[a]		.633	.049	.367	.049

Note. Early versus late onset was determined by proband's age at first symptom (≤ vs. >20 years).
[a] Boundary solution estimate; standard error not calculable.

ance component estimates were not statistically significant for early-onset pairs, $\chi^2(2, N = 138) = 0.59$, $p > .05$, but approached statistical significance for late-onset cases, $\chi^2(2, N = 130) = 5.53$, $.06 < p < .05$.

Concordant Versus Discordant MZ Twins

Table 6 provides a comparison of probands from concordant and discordant MZ twin pairs. Such a comparison may help identify factors contributing to the likely heterogeneity underlying the causes of alcohol-related problems. Environmental factors necessarily account for any differences between genetically identical individuals, whereas for a multifactorial characteristic, concordance is likely to be associated with a high genetic loading (Reich, Cloninger, & Guze, 1975). Because the sample sizes are small, statistical power is low so that these comparisons are best viewed in the context of discovery rather than as providing rigorous tests of a priori specified hypotheses. Consequently, we focused on effect sizes rather than on the results of the statistical tests; caution was of course warranted. For male MZ twins, probands from concordant pairs were more likely than those of discordant pairs to display a large number of alcohol symptoms, to have experienced first intoxication and first symptom expression at an early age, and to report illicit drug use and symptoms of conduct disorder. The probands from the concordant pairs were also younger than the probands from the discordant pairs. Nonetheless, the age-corrected effect sizes remained moderate to large.

In contrast to the male probands differences between the female probands from concordant and discordant MZ twin pairs were minimal. With respect to the alcohol-related measures, the effect sizes were all near zero. With respect to other variables, a younger age, higher rate of illicit drug use, and increased rates of reported treatment for depression were all more characteristic of probands from concordant pairs than of those from discordant twin pairs. Nonetheless, except for illicit drug use, the effect sizes were all modest, and none of the results of the statistical tests even approached statistical significance.

Discussion

Sex Differences in the Inheritance of Alcohol-Related Problems

Our results constitute evidence of the existence of a sex difference in the inheritance of alcohol-related problems. Among male twins, there was a zygosity effect on the overall diagnosis of alcohol abuse–dependence, as well as on all four alcohol symptom scales. Heritability analysis of the male same-sex twin data revealed a moderate and significant heritability. For female twins, there were no significant differences in cotwin risk as a function of pair zygosity, and genetic heritability was estimated at a boundary value of zero, a value significantly less than the estimate for the male twins. Although the female sample was not large, failure to find statistically significant zygosity effects may be attributable more to lack of substantial differences than to lack of statistical power. The effect sizes associated with the comparison of the female MZ and same-sex DZ

Table 6
Comparison of Probands from Monozygotic Twin Pairs Concordant or Discordant for Alcohol Abuse–Dependence

Characteristic	Male				Female			
	Concordant (n = 65)	Discordant (n = 20)	Effect size	Age-corrected effect size	Concordant (n = 17)	Discordant (n = 27)	Effect size	Age-corrected effect size
Symptom scales								
Total alcohol symptoms			0.43	0.63*			0.11	0.10
M	11.4	9.7			11.6	11.1		
SD	3.8	4.4			4.4	4.3		
Pathological use			0.16	0.45			0.00	0.09
M	4.5	4.2			4.5	4.5		
SD	1.8	2.1			2.1	2.1		
Social impairment			0.62*	0.48			0.15	−0.06
M	2.8	2.1			2.6	2.4		
SD	1.1	1.2			1.5	1.2		
Dependence			0.44	0.50			0.27	0.16
M	1.4	1.1			1.5	1.3		
SD	0.6	0.9			0.6	0.8		
Temporal characteristics								
Age at first intoxication			−0.76**	−0.34			−0.16	0.26
M	14.7	17.7			16.5	17.6		
SD	3.8	4.5			8.2	6.0		
Age at first symptom			−1.09***	−0.47			−0.48	−0.08
M	19.4	28.7			21.6	27.2		
SD	6.9	12.6			9.9	12.6		
Illness length			0.14	0.63*			−0.35	−0.20
M	8.3	7.5			5.6	7.4		
SD	5.6	6.5			4.9	5.3		
Other clinical characteristics								
Treated depression (%)	17.2	15.0	0.09	0.32	70.6	55.6	0.40	0.33
Conduct disorder			0.62	0.31			0.21	−0.29
M	1.7	0.8			1.4	1.1		
SD	1.5	1.3			1.2	1.6		
Drug use (%)	66.2	30.0	0.94**	0.36	70.6	59.3	0.31	0.58
Age			−1.07***	—			−0.58	—
M	29.8	41.6			29.8	37.1		
SD	10.6	12.4			9.0	14.3		

Note. Effect sizes are calculated as mean of first designated group minus mean of second divided by the pooled standard deviation for quantitative variables, and the difference in probits for qualitative variables. Significance levels are of difference in means or proportions for both uncorrected and age-corrected data.
* $p < .05$. ** $p < .01$. *** $p < .001$, two-tailed.

cotwins on the alcohol-related measures were uniformly low and suggested few meaningful differences between the two groups on these variables. The sex difference in inheritance was further confirmed by comparison of probands from discordant and concordant MZ twin pairs. If genetic factors are important, differences between probands from concordant pairs (high genetic loading and similarity of exposure to relevant environmental factors) and those from discordant pairs (low genetic loading and discordance for environmental factors) would be expected. For male twins, for whom zygosity comparisons yielded evidence of the existence of a genetic influence, numerous large and significant differences between probands from the two types of twin pairs were observed. For female twins, for whom zygosity comparisons provided no evidence of a genetic effect apart from age, there were few differences between these two groups.

Because women are less likely than men to suffer problems with alcohol, one might speculate that a genetic influence in the female sample was not observed because women have a less severe form of the disorder than do men. Our data strongly suggest, however, that severity per se cannot account for the sex differences in heritability that we did observe. Male and female probands had similar numbers and similar patterns of alcohol-related symptoms; this finding is consistent with those of other research in which large differences in the drinking-related behavior of male and female *alcoholics* are not found (e.g., Ross, 1989). Furthermore, severity, as indicated by a large number of symptoms, was predictive of concordance in the male MZ sample but not the female MZ sample. Finally, at least one group of cotwins of female probands (males from the opposite-sex pairs) did exhibit high rates of alcohol abuse–dependence.

The explanation for the sex difference in transmission of alcohol problems may lie not in differences in drinking behavior but in differences in other clinical characteristics. Female twins were much more likely than male twins to report treatment for depression and illicit drug use. The increased use of drugs among female twins was attributable to increased illegal use of prescription drugs (sedatives and stimulants) but not of street drugs (hallucinogens or marijuana), which suggests that motivations for drinking may also differ between the two sexes. Alcohol and other drugs are used by some people to control symptoms of psychological distress, particularly dysphoria and anxiety (Bibb & Chambless, 1986; Blane & Leonard, 1987). The propensity to self-medicate may be environmentally mediated. It is interesting in this regard that the characteristic that best, albeit not significantly, differentiated the female MZ cotwins from the female cotwins of same-sex DZ pairs was rate of reported treatment for depression. Larger samples with more sensitive indicators of depression and affect are needed in order to better understand how personality and temperament moderate the inheritance of alcoholism, especially in women.

Alternatively, excessive drinking and alcohol abuse may be associated with a general pattern of undersocialized behavior that includes delinquency and sociopathy, abuse of street drugs, and an early age of alcohol problem onset. This pattern of alcohol abuse may be more prevalent among men (Cloninger, 1987), who are also at greater risk for antisocial personality (Robins et al., 1984). Consistent with this explanation is the finding among men, but not women, that symptoms of conduct disorder and rate of illicit drug use varied in the cotwins as a function of pair zygosity and were predictive of MZ pair concordance.

The distinction between these two patterns of drinking behavior has been made before. Thus, for example, cluster-analytic studies of the Minnesota Multiphasic Personality Inventory (MMPI) responses of alcoholics (Morey & Blashfield, 1981) usually identify two broad clusters: one associated with a primary elevation on MMPI Scale 4 (Psychopathic Deviance) and described as a psychopathic personality with emotional instability, and another associated with elevations on Scales 2 (Depression), 7 (Psychasthenia), and 8 (Schizophrenia) and described as a neurotic depressive–anxiety pattern. Cloninger (1987) distinguished between Type I alcoholism (low heritability, associated with anxiety and rigidity, a form of alcoholism that affects both men and women) and Type II (high heritability, associated with antisocial behavior, a form of alcoholism that affects men almost exclusively). Schuckit (1985) and Hesselbrock, Hesselbrock, and Stabenau (1985) also emphasized the importance of differentiating alcoholism from the antisocial personality in etiological research. Finally, Zucker (1987) detailed a model that describes alternative developmental pathways to alcoholism. The two most prominent pathways, antisocial and negative-affect alcoholism, are clearly consistent with the distinction made here. Our results underscore the need to consider preexisting behavior disorders as well as personality factors to resolve heterogeneity in the inheritance of alcoholism; these factors were not considered in earlier twin studies of alcoholism.

Transmission of Alcohol-Related Problems in Opposite-Sex Twin Pairs

This study is the first published twin study of severe alcohol-related problems to include a sample of opposite-sex twins. Use of this sample allowed us to address two questions concerning sex differences in the transmission of alcohol problems: Is there significant cross-sex transmission, and is there an effect of sex of proband? In relation to population base rates, the rates of alcohol abuse–dependence were elevated among both the female cotwins of male probands and the male cotwins of female probands. The rate of alcohol abuse–dependence was more than 30% among female cotwins of male probands, in comparison with an age-appropriate base rate among women of 6.3% derived from the ECA study. Similarly, the rate of alcohol abuse and dependence was 78.3% among the male cotwins of female probands, in comparison with an ECA-derived base rate of only 26.3%. The elevated cross-sex rates suggest that although the magnitude of the underlying variance components may differ, there are significant communalities to the development of the disorder in the two sexes. The association between alcohol problems of men and women is further supported by the finding that among the risk factors considered here, having an affected female cotwin was the most powerful predictor of male risk for alcohol abuse–dependence. In view of the failure to find a genetic influence on female risk, it seems likely that the familial association between alcohol problems of men and women is attributable largely to shared environmental factors.

The question of what those environmental factors are remains unanswered in our research.

For multifactorial disorders in which there is a substantial sex difference in prevalence, a distinctive pattern of inheritance is often observed: Risk is largest among relatives of the less frequently affected sex (Cloninger, Christiansen, Reich, & Gottesman, 1978). This pattern is expected whenever the sex difference in prevalence is attributable to a difference in threshold —that is, a difference in the magnitude of loading required before the disorder is expressed. A higher loading among probands from the less frequently affected sex is transmitted as increased risk to their relatives. This pattern has been observed with mental retardation (Pauls, 1979), sociopathy (Cloninger, Reich, & Guze, 1978), and pyloric stenosis (Emery & Rimoin, 1983) but has not been observed with depression (Merikangas, Leckman, Prusoff, Pauls, & Weissman, 1985). A sex-of-proband effect was observed in our study; all other things being equal (e.g., cotwin's sex), cotwins of female probands were at greater risk than cotwins of male probands. Although this effect was statistically significant among male cotwins only (Table 3), the pattern was still evident among female cotwins (Table 4). It is interesting to note that Pollock et al. (1987) failed to observe a sex-of-parent effect in their meta-analysis of parent–offspring studies of alcoholism. The inconsistency between our results and Pollock et al.'s (1987) summary may be caused by the confounding influence of cohort effects. If so, sibling studies of alcoholism would be expected to replicate the sex-of-proband effect that we observed here.

Age and Age of Onset as Moderators of the Transmission of Alcohol Problems

For both male and female subjects, twin concordance decreased with increasing age. If the alcohol reports of older and younger twins were equally veridical (and we have no reason to expect that they were not), this decrease in *lifetime* concordance with increasing age must have resulted from differences between the older and younger problem drinkers. The age of onset of alcohol problems for younger problem drinkers was earlier than that of their older counterparts. The younger probands were also more likely to abuse drugs other than alcohol and to commit, as adolescences, minor delinquent acts. Both adoption studies (Cloninger et al., 1981) and family studies (Gilligan, Reich, & Cloninger, 1987) have shown age of onset to be a powerful moderator of familial risk, an observation that was replicated in our study with twins. For male probands, genetic heritability was large and statistically significant in the early-onset sample but small and nonsignificant in the late-onset sample. For female probands in both the early- and late-onset samples, genetic heritability was estimated at a boundary value of zero, whereas shared environmental factors were estimated to be large and statistically significant. Although recent reports have been critical of Cloninger's (1987) alcoholism typology (e.g., Irwin, Schuckit, & Smith, 1990), this formulation provides the most parsimonious explanation of these findings. Early-onset male probands with concomitant antisocial behavior manifested a highly heritable form of alcoholism, whereas late-onset male and all female probands manifested another form with low to negligible heritability.

Environmental Influences

One of our more surprising findings was the significance of shared environmental factors, especially for female and late-onset male probands. Reviews of behavioral genetic research have led to the conclusion that environmental influences on individual differences in personality and psychopathology are likely *not* shared by family members (e.g., Plomin & Daniels, 1987). However, for alcohol problems, we consistently found the effect of shared environmental factors to be greater than the effect of nonshared environmental factors. Shared environmental effects may reflect the operation of one or more factors. First, cohort effects are substantial for alcohol abuse (Reich et al., 1988) and were evident in our sample. Cohort effects, which are of course shared equally by MZ and DZ twins, increase twin pair similarity and also the proportion of variance associated with shared environmental factors (see McGue & Bouchard, 1984). Second, social interaction between the twins may influence similarity in their alcohol-related behavior. A significant social contact effect on twin similarity for self-reported alcohol consumption has been reported in both cross-sectional studies (Kaprio et al., 1987) and longitudinal studies (Kaprio, Koshkenvuo, & Rose, 1990) of male Finnish twins. Quantity and frequency of alcohol consumption are also much higher among cohabitating than noncohabitating family members (Clifford, Hopper, Fulker, & Murray, 1984). However, these studies have been concerned with social and not problem drinking, and the former may be more influenced by social modeling than is the latter. Indeed, preliminary analyses of results from our study revealed no relation between social contact and pair concordance (Huber, 1991).

Although the shared environmental effects that we observed may not be attributable to direct social modeling between the twins, other forms of social learning may be important. Many authors have speculated that the increased risk of alcoholism among the offspring of alcoholics is a result, at least in part, of offspring modeling of parental behavior. Adoption studies provide some support for this hypothesis (e.g., Cadoret, O'Gorman, Troughton, & Heywood, 1985), and we hope to explore it further in future publications. A major source of shared environmental influences may be shared cognitions about the effects of alcohol. Alcohol-related expectancies begin to develop before alcohol exposure (Christiansen, Goldman, & Inn, 1982) and are predictive of subsequent alcohol-related behavior (Brown, 1985). It is remarkable that no behavioral genetic studies to date have included a systematic assessment of the possible moderating role of alcohol expectancies. It is hoped that with a reassessment of the biological model of alcoholism will come a renewed interest in how social environments interact with genetic constitution in the origins of alcoholism.

Limitations

Several features of our design potentially limit its generalizability. The probands were all ascertained as such because they sought treatment for an alcohol or a drug problem. Alcoholics who seek treatment are more likely to be severely affected and to suffer from concomitant psychopathology than are those who do not seek treatment (Helzer & Pryzbeck, 1988). More

problematic is the role that family background might play in treatment-seeking behavior. Concordant pairs may be more likely to seek treatment than are discordant pairs. Although this possibility was difficult to directly assess in our study, we believe that it did not greatly bias the results. In only 8 twin pairs had both members sought treatment at one of the surveyed clinics. Furthermore, for other mental disorders, this form of ascertainment bias appears to be minimal. For example, with schizophrenia, similar findings have been reported in twin studies of treatment and nontreatment samples (Gottesman & Shields, 1982). The generalizability of our study is also limited by its restricted ethnic composition; more than 90% of the twins were White. Although caution is warranted in attempts to extrapolate our results to other populations, it is not clear that sampling bias alone affected the results. Svikis and Pickens (in press) showed that the twin probands in our study did not differ clinically or demographically from nontwin clients at the surveyed treatment centers.

Our results depend heavily on the accuracy of self-report assessments of alcohol abuse. Although it would have been preferable to personally interview all study participants, it was neither feasible nor economical. The availability of interview data allowed Goodwin et al. (1973) to distinguish severe problem drinking from alcoholism, which led them to the conclusion that alcoholism but not problem drinking was heritable. In the interview portion of this study, Pickens et al. (1991) found a pattern similar to that reported by Goodwin et al. (1973): *DSM–III*-diagnosed alcohol dependence was found to be more heritable than *DSM–III*-diagnosed alcohol abuse in both the male and the female samples. Our failure to find significant heritability within the female sample, may reflect an inability, with the use of survey information only, to identify a severely affected subgroup in the female sample.

Finally, the key comparisons in our sample depended on the validity of the assumptions underlying the classical twin study. One assumption is especially critical: Can the higher risk among the MZ cotwins than among DZ cotwins be attributed to greater environmental, rather than genetic, similarity? The validity of the assumption of equal environmental similarity has long been debated in the behavioral genetic literature. MZ twins show more environmental similarity than do DZ twins, but this greater environmental similarity does not appear to affect phenotypic similarity (Scarr & Carter-Saltzman, 1979). This key assumption should, nonetheless, be considered in the interpretation of the results of any twin study. This is especially true for alcohol-related behavior, in which similarity in quantity and frequency of alcohol consumption is related to increased environmental similarity in nonclinical samples (e.g., Clifford et al., 1984; Kaprio et al., 1987). The heritability analysis required the assumption of no genetic similarity between spouses. Failure to meet this assumption results in an underestimation of genetic heritability and an overestimation of the proportion of variance associated with shared environmental factors. There certainly is marital resemblance for alcohol-related phenotypes, and it appears that some of that resemblance exists before marriage (i.e., is attributable to assortative mating; Hall, Hesselbrock, & Stabenau, 1983). Nonetheless, it is not clear whether the assortative mating induced a genetic correlation between spouses, nor do we know whether spouse similarity varied among the parents of early- and late-onset probands and of male and female probands. The variance component estimates reported here should be considered approximate.

Concluding Remarks

Perhaps the single most remarkable finding in this research is the modest genetic influence on alcohol problems in women and late-onset men. Although this result may appear to run counter to current opinion in the alcohol research field, results of other behavioral genetic studies have suggested modest or weak genetic effects. Both the adoption study by Roe (1944) and the twin study by Gurling et al. (1981) revealed no evidence for a genetic influence, whereas the Finnish twin study by Partanen et al. (1966) yielded modest and nonstatistically significant heritabilities for the quantitative scales Lack of Control and Social Complications From Alcohol. Although there is, no doubt, some genetic influence on alcoholic risk, especially for early-onset men, the magnitude of this influence may be more modest and age–gender specific than is currently and widely believed. In any case, our findings suggest that in the headlong rush to identify molecular genetic processes, researchers may be ignoring the significant influence that the environment has in the origins of alcoholism.

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Appendix

Alcohol Questionnaire Items and Derived Scales

Pathological Use (7 Items, All Scored for Lifetime Prevalence)

1. Intoxicated throughout the day on at least two separate occasions.
2. Occasional consumption of a fifth of hard liquor during a drinking session (or its equivalent in beer or wine).
3. Attempts to control drinking by trying to drink only under certain circumstances (at certain times of the day, or in certain places).
4. Necessity for use of alcohol on a daily basis for adequate functioning.
5. Continued use of alcohol despite knowing that a serious physical disorder was being made worse by its use.
6. Two or more blackouts resulting from alcohol (a blackout is an inability to remember events occurring for a period of one half-hour or more during intoxication).
7. Inability to stop once drinking had begun.

Social Impairment (4 Items, All Scored for Lifetime Prevalence)

8. Did you ever experience family problems (such as arguments or difficulties with spouse or relatives) as a result of alcohol use?
9. Did you ever experience social problems (such as arguments or difficulties with friends or others with whom you are acquainted) as a result of alcohol use?
10. Did you ever experience occupational or school problems (such as arguments, poor job performance, missed work or school classes, being fired) as a result of alcohol use?
11. Did you ever experience occupational or legal problems (such as traffic arrests or other police problems) as a result of alcohol use?

Dependence (3 Items, All Scored for Lifetime Prevalence)

12. Use of alcohol in the morning.
13. Withdrawal symptoms when use of alcohol was stopped or reduced (such as, convulsions, hallucinations, anxiety, depression, the "shakes," D.T.'s).
14. Heavy drinking as indicated by consumption of at least 5–8 drinks every day (1/2 pint of hard liquor) for an extended period of time.

Total Alcohol Symptoms (19 Items, Including the Preceding 14 and the Following 5, All Scored for Lifetime Prevalence)

15. Did you ever experience health problems (such as liver impairment, irritation of the stomach, heart or blood pressure problems) as a result of alcohol use?
16. During the period of your most extensive use of alcohol, did you ever experience emotional or psychological problems (such as feeling crazy, paranoid, depressed, or uninterested in things) as a result of alcohol use?
17. Drinking of nonbeverage alcohol (such as rubbing alcohol, food flavoring, mouth wash).
18. Inability to reduce or control use of alcohol.
19. Tolerance to the effects of alcohol (more alcohol needed to achieve the same effect, or lessened effect from regular use of alcohol).

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