Inheritance of Alcohol Consumption Patterns in the Australian Twin Survey, 1981

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OVERVIEW
We review published data from the 1981 survey of alcohol consumption patterns in the Australian Twin Register and present results from new analyses. Both genetic and shared environmental effects have a substantial influence on whether or not teenage drinking occurs (as indicated by the results of parametric model fitting); however, the timing of the onset of drinking is under purely environmental control in males though also subject to genetic influence in females. Results from both multidimensional scaling (MDS) and model-fitting analyses indicate that adult alcohol consumption patterns are determined by separate abstinence, quantity, and frequency dimensions. Twin correlations for abstinence are uniformly high across all twin groups and are consistent with nongenetic determination of this dimension. For both quantity and frequency dimensions, there are substantial genetic effects in females and, at least, moderate genetic (and, possibly, also shared environmental) influences in males. The implications of this evidence for genetic effects on alcohol exposure are considered.

INTRODUCTION
Studies of adoptees (Goodwin et al. 1974; Cadoret et al. 1980; Cloninger et al. 1981), half-siblings (Schuckit et al. 1972), and twins (Kaij 1960; Hrubec and Omenn 1981; McGue et al. 1989) indicate a significant genetic influence on alcoholism in males (although evidence for genetic influence on female alcoholism is more equivocal [Goodwin et al. 1977; Bohman et al. 1981; McGue et al. 1989]). Despite criticism of the shortcomings of individual studies (Searles 1988), the broad consistency of findings from different studies, using different sampling strategies, makes theories of alcoholism that
ignore heredity untenable. Apparent negative findings (e.g., Gurling et al. 1981; Murray et al. 1983) are easily explained when one considers the low resolving power of the twin study in the presence of assortative mating (Martin et al. 1978; Heath et al. 1985), which is observed to a high degree for alcoholism (Reich et al. 1988).

Most research on the genetics of alcoholism has treated the evidence for a strong genetic influence on alcohol consumption patterns as irrelevant (Par­tanen et al. 1966; Cederlof et al. 1977; Clifford et al. 1981; Kaprio et al. 1981, 1987; Jardine and Martin 1984). However, exposure to alcohol is a necessary prerequisite for the development of alcoholism; and insofar as exposure is partly under genetic influence, it should be taken into account in any genetic analysis of alcoholism. Application of both nonmetric MDS (Heath et al. 1990a) and parametric model-fitting methods (Heath and Martin 1988; Heath et al. 1989, 1990b) to twin data has provided some new insights into the genetic and environmental determination of alcohol exposure.

RESULTS

Onset of Teenage Drinking

Questionnaires were mailed to 5967 adult twin pairs, aged 18–88, enrolled on the Australian National Health and Medical Research Council volunteer twin panel, between November 1980 and March 1982. Completed questionnaires were returned by 3810 pairs, including 1233 female monozygotic (MZ), 567 male MZ, 751 female dizygotic (DZ), 352 male DZ, and 907 unlike-sex DZ pairs. The questionnaire requested information both about current alcohol use and age of first use (Jardine and Martin 1984). Because assessment of onset of drinking necessarily relied on the retrospective recall of the respondents, data about onset must be interpreted with some caution. For this reason, we have published genetic analyses of age of onset of drinking only for the young cohort, aged 18–30 years at the time of the Australian survey (Heath and Martin 1988), whose memories might be expected to be less fallible.

We have computed two-way contingency tables for age of onset of alcohol use (or abstinence from alcohol use as a teenager) for the entire sample, broken down into the five sex/zygosity groups, and used these as the basis for nonmetric MDS. We have discussed the application of MDS to twin data elsewhere (Heath et al. 1990a; J. Meyer et al., unpubl.). In brief, MDS is used to determine relative locations of variables in multidimensional space and the dimensionality of that space from a matrix of distances between such variables. Thus, in one textbook example (Kruskal and Wish 1978), a matrix of distances between major airports is used to generate a two-dimensional
map of the United States. In applications to twin data, we cannot use the raw
cell frequencies as a distance metric, because differences in
marginal frequency between response categories will yield spurious results.
Instead, we divide the raw cell frequencies by the product of the correspond­
ing row and column marginal frequencies to yield a proximity measure that
would be the reciprocal of the conventional distance metric. No exact statisti­
cal test is available to compare the goodness of fit of MDS solutions of
different dimensionality; however, Kruskal (1964) has proposed a stress
measure, which is given by

\[ S = \left( \sum \left| d_{i,j} - d'_{i,j} \right|^2 \right) \left( \sum d_{i,j}^2 \right)^{-0.5} \]

where \( d_{i,j} \) is the estimated distance between variables \( i \) and \( j \), and \( d'_{i,j} \) is a
monotonic transformation of the observed distance between variables. Stress
values \( > 0.20 \), by convention, are interpreted as showing a poor fit.

When applied to twin data, MDS uses differences within pairs to scale
response categories. In MZ twin pairs, such differences will reflect only
within-family environmental effects. In DZ twin pairs, such differences will
also be the result of genetic segregation within families. Separate MDS
analyses were therefore performed for each twin group. Unlike-sex twin pairs
were excluded from these analyses, as it was not considered appropriate to
assume the equivalence of onsets at the same age in the two sexes.

Table 1 gives the stress values obtained for each twin group, for solutions of
differing dimensionality. In all cases, the one-dimensional solution, which
posits that teenage abstainers lie on the same dimension as drinkers with
differing ages of onset, gives a very poor fit. In the two MZ groups, the
two-dimensional solution gives an adequate fit and identifies a teenage age-of­
onset dimension, discriminating between onset at different ages, and a late
onset or abstinence dimension, discriminating between teenage drinkers and
those who remained abstinent or only began drinking at age 19 or 20. In the
DZ like-sex groups, however, the two-dimensional solution still gives a

<table>
<thead>
<tr>
<th>Twin group</th>
<th>one dimensional</th>
<th>two dimensional</th>
<th>three dimensional</th>
</tr>
</thead>
<tbody>
<tr>
<td>MZ male pairs</td>
<td>0.23</td>
<td>0.12</td>
<td>0.10</td>
</tr>
<tr>
<td>DZ male pairs</td>
<td>0.48</td>
<td>0.27</td>
<td>0.19</td>
</tr>
<tr>
<td>MZ female pairs</td>
<td>0.31</td>
<td>0.14</td>
<td>0.10</td>
</tr>
<tr>
<td>DZ female pairs</td>
<td>0.37</td>
<td>0.24</td>
<td>0.17</td>
</tr>
</tbody>
</table>
relatively poor fit, and a third dimension must be added to give an adequate fit to the data. In each case, this third dimension was found to discriminate very early onset drinkers (≤12 years) from other drinkers or abstainers. Because this dimension was observed in the DZ, but not the MZ, groups, this raises the possibility that this is a genetically determined dimension, with no corresponding environmental dimension.

Table 2 gives item weights derived from the MDS analyses for the MZ female pairs (two-dimensional solution) and the DZ female pairs (three-dimensional solution). Results for male like-sex pairs were comparable and are not shown here. Even with the very large sample sizes obtained by pooling older and younger cohorts, these solutions are far from perfect. Nonetheless, the interpretation of the first factor as an age-of-onset dimension and the second factor as a teenage drinking versus late onset or abstinence dimension is broadly consistent across the two groups.

The results of fitting genetic and environmental models to the twin age-of-onset data have been published elsewhere (Heath and Martin 1988). These analyses, which used only data from the younger cohort, give support to the notion that the determinants of teenage abstinence are quite different from the determinants of timing of onset of drinking in those who become teenage drinkers. Specifically, when onset of teenage drinking was treated as a dichotomous variable and analyzed under the assumption of an underlying normal liability distribution (Olsson 1979), additive genetic effects and shared environmental effects accounted for 35% and 32% of the variance in liability in females and 47% and 48% of the variance in liability in males. Environmental effects shared by members of like-sex pairs were largely uncorrelated over unlike-sex pairs, suggesting that peer influences or other sex-specific environmental influences were important. The age of first alcohol use, however, was purely determined by shared and nonshared environmental effects in males but was also influenced by genetic effects, and influenced only weakly by shared environmental effects, in females.

In subsequent analyses motivated by the MDS results, we have attempted to explore genetic influence on very early onset of drinking, treating onset of drinking by age 12 as a dichotomous variable. However, the number of twins reporting this early onset was very low in this general community sample, and the power of our test for genetic effects was correspondingly slight. In male twin pairs, tetrachoric correlations were consistent with a simple genetic model, but the standard errors of these correlations were so large as to make it impossible to exclude a nongenetic model (MZ males, \( r = 0.77 + 0.10 \); DZ males, \( r = 0.39 + 0.26 \)). In female like-sex pairs, data were consistent with a nongenetic model (MZ females, \( r = 0.71 + 0.10 \); DZ females, \( r = 0.79 + 0.11 \)). Only when data are available on larger samples will it be possible to resolve this issue.
<table>
<thead>
<tr>
<th>Age-of-onset category</th>
<th>≤12</th>
<th>13–14</th>
<th>15</th>
<th>16</th>
<th>17</th>
<th>18</th>
<th>19–20</th>
<th>abstinent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monozygotic female pairs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dimension 1</td>
<td>-0.43</td>
<td>-0.49</td>
<td>-0.22</td>
<td>-0.05</td>
<td>0.41</td>
<td>0.61</td>
<td>0.23</td>
<td>-0.07</td>
</tr>
<tr>
<td>Dimension 2</td>
<td>-0.08</td>
<td>-0.28</td>
<td>-0.41</td>
<td>-0.39</td>
<td>-0.32</td>
<td>0.10</td>
<td>0.61</td>
<td>0.77</td>
</tr>
<tr>
<td><strong>Dizygotic female pairs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dimension 1</td>
<td>-0.12</td>
<td>0.14</td>
<td>0.54</td>
<td>0.33</td>
<td>0.31</td>
<td>0.65</td>
<td>0.41</td>
<td>0.06</td>
</tr>
<tr>
<td>Dimension 2</td>
<td>0.10</td>
<td>0.74</td>
<td>0.08</td>
<td>0.21</td>
<td>-0.52</td>
<td>-0.08</td>
<td>0.53</td>
<td>0.76</td>
</tr>
<tr>
<td>Dimension 3</td>
<td>0.76</td>
<td>-0.00</td>
<td>-0.12</td>
<td>0.36</td>
<td>-0.05</td>
<td>0.09</td>
<td>0.35</td>
<td>0.32</td>
</tr>
</tbody>
</table>
Adult Consumption Patterns

The first publication on the inheritance of alcohol consumption patterns in the Australian Twin Survey was that of Jardine and Martin (1984). This focused on total weekly alcohol consumption, both as derived from a 7-day retrospective diary (Redman et al. 1987) and as assessed using standard quantity and frequency questions (Straus and Bacon 1953). That study reported a significant and substantial genetic influence on level of alcohol consumption in female twins and young male twins but no genetic effect in the cohort of male twins aged 31 years and older. However, the data analysis included abstainers and twins who were infrequent users of alcohol, as well as those who were more regular drinkers, and thus may have confounded the inheritance of two different characters, abstinence and level of consumption by drinkers.

When we applied nonmetric MDS to an alcohol consumption scale derived from the items about abstinence, quantity, and frequency of consumption (Heath et al. 1990a), separate abstinence, frequency, and quantity dimensions emerged. Subsequent model-fitting analyses of the quantity/abstinence and frequency/abstinence data confirmed that there were separate dimensions controlling abstinence from alcohol use and level of alcohol consumption (Heath et al. 1990b). Neither a single liability dimension (SLD) model (Eaves et al. 1978) nor a conventional two-dimensional model that postulated independent abstinence and quantity (or frequency) dimensions—the latter influencing level of consumption in those who were not abstainers on the first dimension (Eaves and Eysenck 1980)—gave an adequate fit to the data. It was necessary to fit a combined model (CM), which recognized that those who were not abstainers on the first abstinence dimension could nonetheless be abstainers by virtue of their position on the second dimension, i.e., that some people were so low in liability on the consumption dimension that they were effectively abstainers (Heath et al. 1990b).

Model fitting revealed substantial twin correlations for all twin groups for the abstinence dimension and no evidence for genetic effects on this dimension, but strong genetic effects on the second, frequency (or quantity) dimension. In females, genetic effects accounted for 57–66% of the variance in consumption level on the second dimension. In males, a purely genetic model for twin resemblance and a model allowing for both genetic and shared environmental effects gave equally good fits to the data. Under the former model, genetic effects explained as much as 61–75% of the variance, comparable to the heritability observed in females; however, under the latter model heritability was no higher than 24–42% with shared environmental effects explaining an additional 32–35% of the variance on the second frequency (or quantity) dimension. No significant evidence for an interaction of genetic and environmental effects with cohort was found in either sex ($\chi^2_{10} = 5.95$, $P =$...
Table 3
Comparison of Polychoric Correlations Under SLD, ILD, and CM Models for Quantity of Alcohol Consumed When Drinking

<table>
<thead>
<tr>
<th></th>
<th>SLD</th>
<th>ILD</th>
<th>CM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>abstinence</td>
<td>quantity</td>
<td>abstinence</td>
</tr>
<tr>
<td><strong>Young cohort</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MZ female pairs</td>
<td>0.57</td>
<td>0.71</td>
<td>0.56</td>
</tr>
<tr>
<td>MZ male pairs</td>
<td>0.61</td>
<td>0.72</td>
<td>0.69</td>
</tr>
<tr>
<td>DZ female pairs</td>
<td>0.43</td>
<td>0.51</td>
<td>0.21</td>
</tr>
<tr>
<td>DZ male pairs</td>
<td>0.51</td>
<td>0.63</td>
<td>0.47</td>
</tr>
<tr>
<td>Unlike-sex DZ pairs</td>
<td>0.24</td>
<td>0.40</td>
<td>0.22</td>
</tr>
<tr>
<td><strong>Older cohort</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MZ female pairs</td>
<td>0.59</td>
<td>0.63</td>
<td>0.46</td>
</tr>
<tr>
<td>MZ male pairs</td>
<td>0.60</td>
<td>0.73</td>
<td>0.46</td>
</tr>
<tr>
<td>DZ female pairs</td>
<td>0.34</td>
<td>0.41</td>
<td>0.05</td>
</tr>
<tr>
<td>DZ male pairs</td>
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<td>0.68</td>
<td>0.23</td>
</tr>
<tr>
<td>Unlike-sex DZ pairs</td>
<td>0.33</td>
<td>0.47</td>
<td>0.14</td>
</tr>
</tbody>
</table>
0.82 for the frequency/abstinence data; $\chi^2_{10} = 5.98$ for the quantity/abstinence data). However, because the standard errors of parameter estimates under the two-dimensional CM were somewhat large, this may reflect a lack of statistical power for detecting heterogeneity of twin correlations across cohorts.

Table 3 summarizes the correlations estimated under the SLD, independent liability dimension (ILD), and CM models for the young and the older Australian cohorts, for the quantity/abstinence data (correlations for the frequency/abstinence data were comparable). Comparison of the estimates of correlations under the general model and the two submodels that were rejected by goodness-of-fit or likelihood-ratio Chi-square test gives some indication of the biases that can arise when incorrect assumptions about the dimensionality of the determinants of alcohol consumption patterns are made.

The SLD correlations suggest a relatively weak genetic influence on male consumption and consumption by younger female twins. A much more pronounced genetic effect is apparent for the quantity dimension under the CM. This suggests that it is the confounding of abstinence and quantity traits, having very different modes of inheritance, that explains the SLD results and supports our interpretation that such confounding was also the cause of the failure of Jardine and Martin (1984) to find significant heritability for total consumption in the older male cohort. The ILD quantity correlations underestimate those obtained under the CM, particularly in the older cohort. We would expect this because the ILD model truncates the second dimension by not allowing for any individuals who are abstainers because of their position on this second dimension.

**DISCUSSION**

Onset of drinking emerges from our analyses as at least a two-stage process. Both genetic and shared environmental effects influence whether or not an individual is at risk of becoming a teenage drinker. The timing of onset of drinking in those at risk, in males at least, appears to be environmentally determined, although there appears to be some genetic influence in females. From the analyses of quantity/abstinence and frequency/abstinence data, it also appears that there are two types of abstainers: those who abstain for familial environmental reasons, probably related to religious and similar beliefs; and those who abstain because of factors relating to personality or intolerance of alcohol, which are, in part, under genetic control.

Model-fitting analyses have indicated substantial genetic influence on frequency and quantity dimensions of alcohol consumption in females and, at least, moderate genetic influence in males. Because alcoholism cannot de-
velop without exposure to alcohol, total abstainers have no risk of alcoholism. It has yet to be determined whether there are levels of alcohol use that are the equivalent of total abstinence, i.e., that involve no increased risk of alcoholism even for the first-degree relatives of alcoholics, and what such levels might be. The methods of model fitting and MDS that have been reviewed in this paper and elsewhere (Heath et al. 1990a,b), when applied to twin or other family data on both alcoholism and alcohol consumption patterns, can be used to address this question with considerable power.

If there are “safe” levels of alcohol consumption, even for those at high genetic risk of alcoholism, then the fact that alcohol exposure, itself, is partly under genetic control has important implications for genetic studies of alcoholism. It will be necessary to analyze jointly the inheritance of alcoholism and the inheritance of alcohol consumption patterns. Only in this fashion will it be possible to separate out the contributions to alcoholism of genes that influence level of exposure and genes that determine differences in risk of developing symptoms of alcohol abuse or dependence in response to a given degree of exposure.

ACKNOWLEDGMENTS

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REFERENCES


