Acta Genet Med Gemellol 33: 333-339 (1984)

TWIN RESEARCH 4 - Part B: Twin Psychology and Behavior Genetics
Proceedings of the Fourth International Congress on Twin Studies (London 1983)

Depression, Criminality and Psychopathology Associated with Alcoholism: Evidence from a Twin Study

H.M.D. Gurling, B.E. Oppenheim R.M. Murray
Genetics Section, Institute of Psychiatry, University of London

Abstract. A study of 74 twin pairs with alcoholic probands from the Maudsley Hospital is reported. Pairwise concordance for alcoholism as categorised by the SADS-L Research Diagnostic Criteria is similar in MZ twins (29%, 8/22) and DZ twins (33%, 13/39). Concordance for all diagnoses other than alcoholism is however significantly greater in MZ twins (48%, 13/27) than DZ twins (21%, 8/39, $P < 0.001$). Concordance in MZ and DZ twins for all diagnoses other than alcoholism, inlcuding depression, did not coincide with concordance for alcoholism. Data on criminality revealed that 21% (32/148) of the twin sample had non-alcohol, non-traffic offences on record at the UK Home Office. Of the 32 with criminal records, 28 were alcoholic probands and pairwise concordance for criminality was found in only 1 MZ and 2 DZ pairs.

Key words: Alcoholism, Depression, Criminality, Twins

INTRODUCTION

The possible genetic transmission of alcoholism has been examined by studies using the adoption [7], twin [11] and half-sib [14] strategies. The adoption approach has suggested some degree of genetic predisposition. The Danish-American study of Goodwin et al [7] defines alcoholism for both adopted away offspring and their alcoholic biological parent in terms of hospital admission and alcohol related problems, rather then by clinical criteria. If the category of alcoholism as defined by Goodwin et al is combined with their problem-drinking category, then the genetic predisposition disappears [12]. Perhaps the explanation of this lies in the fact that a rather abitrary definition of alcoholism was used on data not adequate for close clinical appraisal.

Similar criticisms can be made of the extensive genetic and environmental correlations observed by Cloninger et al [4] in a Swedish adoptive sample, in which a genetic predisposition was found to be most prominent for the moderate, less severe, type of alcoholism.

This latter study does have the advantage that criminality and demographic data were included, thus making it possible to detect the presence of an underlying predisposition such as the inheritance of an antisocial personality. In fact, a subtype of severe alcoholism with a considerable heritability was found that was strongly associated with criminal behaviour. This study is now being extended to include clinical interview data of the biological parents and their adopted away offspring, so that underlying psychiatric abnormality, such as depression or neurosis, can be examined in the analysis. Bohman et al [1] also studied the maternal transmission of alcoholism in Danish adoptees and found evidence of a maternal influence which could possibly be attributed to the effect of alcohol on the unborn foetus; a finding termed "pseudogenetic" transmission.

Some of the problems of definition noted above were avoided in a Swedish twin study by Kaij [11] where chronic alcoholism was defined by medical rather than social criteria, eg, pathological desire for alcohol, blackouts and physical dependence. Kaij found that the pairwise concordance for chronic alcoholism in MZ twins (71.4%) was higher than the pairwise rate in DZ twins (32.3%). Kaij obtained his sample by matching Swedish Temperance Board registrations with the Swedish twin register. Thus, he may have biased his sample towards a type of alcoholism associated with antisocial behaviour [12], because registration with the Temperance Board is often the result of action by the police or other agencies after some antisocial behaviour has occurred. The twin study based on the US Veterans Administration twin register [10] is less well clinically documented than that of Kaij but it does report concordance, not only for alcoholics ascertained through hospital admission, but also for alcoholic psychosis and liver cirrhosis, two complications of severe alcoholism. The pairwise concordance rates in this study are higher in MZ (26.3%) than DZ (11.9%) twins but the rates are much lower than would be expected on the basis of the generally accepted familial rates of alcoholism. The predicted pairwise concordance rate for DZ twins should be in the range of 15% to 45% ie, the rate for sibs reared together in the same family [5]. If any genetic effect for alcoholism exists, then the MZ concordance should be considerably higher than the observed 26.3%. It may be that cotwins were inadequately investigated in this computer based study or an intrapair mutual effect may have operated thus preventing the development of alcoholism in the cotwins. The explanation which we favour is that investigation and diagnosis of alcoholism in the cotwins was inadequate, particularly in the DZ pairs, because MZ twins are more likely to have both been included on the veterans' register.

We report here a twin study using the Maudsley Hospital Twin Register [15], which is unique, in that it relies on the systematic ascertainment of twins attending a single hospital from 1948 to the present day. This, of course, may introduce another set of biases to be taken into consideration and therefore its value will depend on comparison with other twin studies of alcoholism. A further aspect of our work is the extensive clinical information collected, which makes it possible to examine underlying psychiatric abnormalities that might predispose to alcoholism. In addition to the likelihood of personality and psychiatric disorder contributing to the development of alcoholism, it is also possible that a psychopharmacogenetic or biochemical effect is operating. In a Japanese sample of alcoholics with cirrhosis of the liver a very strong association has been found with aldehyde dehydrogenase isoenzymes [9]. Such an effect has so far been identified in oriental populations with a high incidence of the alcohol flushing response. It is possible that in caucasians as well, isoenzymes of alcohol dehydrogenase

and aldehyde dehydrogenase also contribute towards becoming alcoholic as could a tendency to produce addictive tetrahydroisoquinolines [13]. The twin method can detect the general influence of such biochemical variation but cannot specify the mechanism itself unless specific tests are carried out. We have concentrated on psychiatric disorder and criminality as possible predisposing factors.

METHODS

Ascertainment of Twins

The sample of alcoholic probands was extracted from the Maudsley Twin Register. The Register contains about 1,000 twin probands who have attended the Maudsley Hospital with a variety of psychiatric disorders as outpatients or have been admitted for assessment or treatment. The register was started in 1948 and uses diagnostic criteria according to the various revisions of the International Classification of Diseases (ICD). All twins with an ICD diagnosis of alcohol addiction, alcoholic psychosis or habitual excessive use of alcohol were included in the sample. A number of probands who had unrecognised alcoholism but who had been included on the twin register under other diagnoses were detected amongst the twins on the twin register files, but these were discarded in order to avoid any bias which could have led to ascertainment of concordant or discordant pairs.

Tracing and Investigation

Probands and their cotwins were systematically traced by means of the UK National Health Service Register, which provided the names and adresses of family practitioners with whom the twins were currently registered. This was an effective tracing method because all UK citizens are registered with a primary care physician as part of the National Health Service. Data on psychiatric admission anywhere in the UK over the previous 20 years were also obtained from the Department of Health and Social Security Mental Health Enquiry which records admissions by name and diagnoses. In addition, the UK Home Office made available any criminal records for all twins in the sample.

Zygosity was determined by the use of a physical resemblance questionnaire (27%), fingerprints (4%), and bloodgroups (54%): at least 12 blood protein markers were utilised for zygosity by courtesy of the MRC Blood Group Unit (Dr R. Sanger) at University College, London. In 12% of pairs, zygosity was based only on case notes and interview reports.

Follow up and interviewing success for probands and cotwins is tabulated in Table 1. All tracing failed for 2 MZ and 3 DZ cotwins, so these pairs were excluded from the study. Fortunately, some pairs who could not be interviewed specifically for the project had already been interviewed by members of the old MRC Genetics Unit 30 years ago, and this constituted a valuable reservoir of longitudinal data that could be corroborated at follow up.

A seventeen-page twin-adapted version of the Clinical Alcohol Interview Schedule devised by Caetano et al [2] permitted collection of occupational, personal, family and marital history, as well as a detailed drinking history including Jellinek's criteria. Interviewing was undertaken using the Schedule for Affective Disorders and Schizophrenia – Lifetime Version [16] (SADS-L), which yielded the Research Diagnostic Criteria of Spitzer et al [16]. We also used the WHO definition of alcoholism – the Alcohol Dependence Syndrome [6].

TABLE 1 - Follow-up

No information/no trace	
2/31	MZ cotwins
3/34	cotwins
No study interview but probands traced	
7/29	MZ probands all previously interviewed
14/40	DZ probands all previously interviewed
Cotwins	
12/29	MZ cotwins, 4/12 not previously interviewed but information gathered
18/40	DZ cotwins, 8/18 not previously interviewed but information gathered

RESULTS

The question as to whether twinning itself may be associated with alcoholism was investigated by determining the incidence of hospital diagnosed (ICD) alcoholism amongst all twins on the twin register (6.2%) and comparing it with the cumulative incidence of alcoholism in the hospital population of patients as a whole. This latter rate was 5.9%, very similar to the rate amongst twins. A strong secular effect was in evidence for rates of alcoholism almost certainly due to the sharply rising per capita consumption of alcohol in the British population as a whole. This rise is indeed a testimony to the strong cultural component in the development of alcoholism.

Table 2 shows the pairwise concordance rates for the Alcohol Dependence Syndrome and for the whole sample subdivided by sex. The concordance rates are all pairwise because no double proband pairs were found in the sample. These concordance rates, which are preliminary [8], showed no evidence for a genetic predisposition in the development of alcoholism. Analysis by sex showed a similar lack of genetic effect and also the expected preponderance of male alcoholics. Further analysis of concordance rates incorporating independent diagnosis by blind raters is currently being undertaken and will be published together with concordance rates for other classification systems such as the Research Diagnostic Criteria [16].

TABLE 2

Pairwise Concordance for the Alcohol Dependence Syndrome

	MZ	DZ
	6/28 (21.0%)	7/28 (25.0%)

Sex Differences in Concordance for the Alcohol Dependence Syndrome

	MZ	DZ
Males	5/15 (33.0%)	6/20 (30.0%)
Females	1/13 (8.0%)	1/8 (13.0%)

PSYCHIATRIC DISORDERS IN ALCOHOLIC PROBANDS AND THEIR COTWINS

Table 3 reveals the distribution of present and past RDC defined psychiatric disorder in the alcoholic twins, whether they are probands or cotwins, compared to the nonalcoholic cotwins. Of note is the higher rate of disorder, especially depression (67%), in the alcoholics compared to non alcoholics (26.9% depressed). Nevertheless, neurosis and depression were also common in the nonalcoholic cotwins. We then divided the depressed cotwins into those who were and were not alcoholic themselves. Eleven out 17 (65%) of cotwins who were also alcoholic were depressed, compared with 20 out of 39 (51%) of those cotwins who were not alcoholic (Table 4). The high rate of depression in the nonalcoholic cotwins is explicable by either a genetic or common environmental, ie, nongenetic familial, effect. We can conclude that a considerable amount of depression exists in the alcoholic probands, and also in their cotwins whether alcoholic or not, and at least in some cases this is primary to alcoholism. Nevertheless, the presence of depression in both members of a twin pairs is insufficient to explain concordance for alcoholism because not all concordant alcoholic pairs were concordant for depression

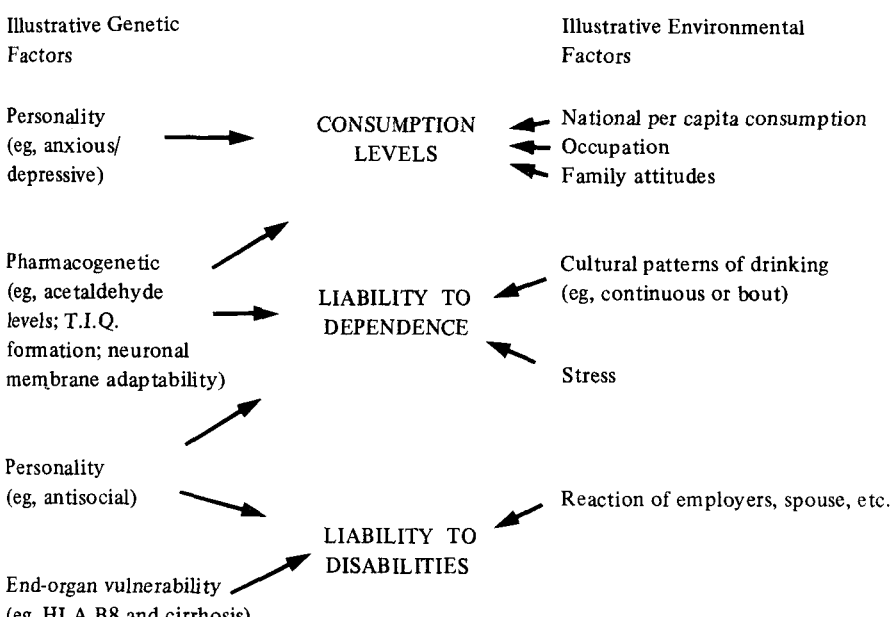
TABLE 3 - Psychiatric Diagnosis in Alcoholic Probands and Cotwins

	Alcoholic probands + alcoholic cotwins (N = 96)		Nonalcoholic cotwins (N = 52)	
Bipolar disorder	1	(0.1 %)	0	(0.0 %)
Major depressive disorder	45	(47.0 %)	12	(23.0 %)
Intermittent depressive disorder	6	(6.3 %)	0	(0.0 %)
Minor depressive disorder	8	(8.3 %)	2	(3.9 %)
Panic disorder	5	(5.2 %)	0	(0.0 %)
Generalised anxiety disorder	15	(15.6 %)	6	(11.5 %)
Obsessive compulsive disorder	2	(2.0 %)	3	(5.8 %)
Phobic disorder	7	(7.3 %)	2	(3.9 %)
Antisocial personality	10	(10.0 %)	0	(0.0 %)
Labile personality	8	(8.3 %)	1	(1.9 %)
Cyclothymia	8	(8.3 %)	0	(0.0 %)
Somatisation disorder	0	(0.0 %)	2	(3.9 %)
Schizophrenia	3	(3.0 %)	1	(1.9 %)
Alcoholic hallucinosis	3	(3.0 %)	0	(0.0 %)
Schizoaffective disorder	1	(1.0 %)	0	(0.0 %)
No diagnosis	8	(8.0 %)	21	(40.0 %)
No. of diagnoses per twin	1.37		0.58	

TABLE 4 - Proportion of Cotwins of Alcoholics Diagnosed as Depressed

All cotwins	Cotwins also alcoholic	Cotwins nonalcoholic
55 %	65 %	51 %
22/56	11/17	20/39

TABLE 5 - Model of Genetic and Environmental Effects in the Development of Alcoholism



as well. The presence of depression and the other neuroses in the alcoholics must be secondary in other cases because if it were not, the frequency of psychopathology would be the same amongst alcoholics as in their nonalcoholic cotwins.

CRIMINALITY

The criminal records we obtained were confined to nonalcohol related offences and excluded prosecutions and arrests for being drunk and disorderly or for being convicted of drink and driving offences. The data related to theft, criminal damage, deception and all other crimes. Twenty-eight MZ and DZ alcoholic probands (41%) had nonalcohol criminal convictions, but amongst their cotwins only one DZ cotwin and no MZ cotwins had such a criminal conviction. In this particular sample of twins the evidence is, therefore, strongly in favour of the argument that nonalcohol criminal behaviour was secondary to alcoholism. Table 3 also indicates that antisocial personality was not common as a diagnosis. This may have been either because the diagnosis of antisocial personality is a stringent one, which we believe it is, or because our sample was biased away from this type of alcoholic and that the Maudsely Hospital tends to admit or treat as outpatients the more depressed and neurotic type of alcoholic.

CONCLUSIONS

A suitable model for the development of alcoholism has been proposed by Murray et al [12], and this is shown in Table 5. It will be readily appreciated that such a multifaceted disorder as alcoholism cannot easily be partitioned into genetic and environmental causes. The genetic component itself, on prima facie grounds alone, must consist of psychiatric abnormality, personality, and a metabolic component including genetic susceptibility to physical damage. We found no evidence that any of these were operating, yet we do not discount the possible existence of such a genetic effect. An explanation might be found in the subtle intrapair effects that could exist between twins reared together. Thus, in our study a genetic effect could have been masked by a mutual pair effect reducing concordance for alcoholism in MZ pairs. One such mechanism might be that development of alcoholism in one member of an MZ pair could act as a strong disincentive for alcoholism in the cotwin. In the case of the Swedish twin study by Kaij we suspect that the genetic effect that was observed may reflect the greater antisocial nature of twins ascertained from the Temperance Board register. We hypothesise that twins with antisocial personality characteristics might be more prone to disregard the deleterious effect of alcohol on their cotwins.

The joint effects of genetic and environmental influences in alcoholism have been studied very little with the exception of the work of Cloninger and Bohman [4]. However, alcohol consumption in normal twins has been studied by Clifford [3] using biometrical genetic methodology and evidence for both nongenetic familial and specific environmental effects have been found. We conclude that further twin studies on different samples of twins are needed before any consensus can be reached and that the twin evidence should be considered alongside all other human behaviour genetic approaches. Eventually, a more reliable picture of the role of genetic effects will emerge. The much less culturally malleable phenomenon of schizophrenia needed to be examined in more

than a dozen twin and adoption studies before a genetic effect became reasonably well established.

Aknowledgments: Dr. Gurling was supported by grants from the Maudsely Hospital Research Fund and the Wellcome Trust. The U.K. Home Office and the Department of Health and Social Security provided very valuable help.

REFERENCES

1. Bohman M, Sigvardsson S, Cloninger R (1981): Maternal inheritance of alcohol abuse. Cross fostering analysis of adopted women. Arch. Gen. Psychiatry 38:965-969.
2. Caetano R, Edwards G, Oppenheim AN, Taylor C (1978): Building a standardised alcoholism interview schedule. Drug and Alcohol Dependence, 3:185-197.
3. Clifford CA (1982): Twin Studies of Drinking Behaviour and Obsessionality. PhD. Thesis, Institute of Psychiatry, University of London.
4. Cloninger CR, Bohman M, Sigvardsson S (1981): Inheritance of alcohol abuse. Cross fostering of adopted men. Arch Gen Psychiatry 8:861-868.
5. Cotton NS (1979): The familial incidence of alcoholism. A review. Journal of Studies on Alcohol 40:89-115.
6. Ewards G, Gross MM, Keller M, Moser J, Room R (1977): Alchol-related disabilities. World Health Organisation, Geneva.
7. Goodwin DW, Schulsinger F, Hermansen L, Guze SB, Winokur G (1973): Alcohol problems in adoptees raised apart from alcoholic biological parents. Arch Gen Psychiatry 28:238-243.
8. Gurling HMD, Murray RM, Clifford CA (1981): Investigations into the genetics of alcohol dependence and into its effects on brain function. In Gedda L, Parisi P, Nance WE (eds): Twin Research 3: Part C, Epidemiological and Clinical Studies. New York: Alan R Liss, p 77-87.
9. Harada S, Misawa S, Agarwal DP, Goedde HW (1980): Liver alcohol dehydrogenase and aldehyde dehydrogenase in the Japanese: Isozyme variation and its possible role in alcohol intoxication. Am J Hum Genet 32:8-15.
10. Hrubec Z, Omenn GS (1981): Evidence of genetic predisposition to alcoholic cirrhosis and psychosis: Twin concordances for alcoholism and its biological end points by zygosity among male veterans. Alcoholism: Clinical and Experimental Research 5:207-212.
11. Kaij L (1960): Alcoholism in Twins. Stockholm: Almqvist and Wiksell.
12. Murray RM, Clifford CA, Gurling HMD (1983): Twin and adoption studies: how good is the evidence for a genetic role? In Galanter E (ed): Current Research in Alcholism. New York: Academic Press.
13. Murray RM, Clifford CA, Gurling HMD, Topham A, Clow A, Bernadt M (1983): Current genetic and biological approaches to alcoholism. Psychiatric Develoopments 2:179-192.
14. Schuckit MA, Goodwin DA, Winokur G (1972): A study of alcoholism in half siblings. Am J Psychiatry 128:1132-6.
15. Slater E, Shields J (1969): Genetical aspects of anxiety in studies of anxiety. In Lader M (ed): Br J Psychiatry Special Publication No. 3. Headley Bros.
16. Spitzer RL (1978): Critical Issues in Psychiatric Diagnosis. New York: Raven Press.

Correspondence: Dr. H.M.D. Gurling, Genetics Section, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, U.K.