

Family History and Other Characteristics of Heroin-Dependent Jewish Males in Israel: Results of a Case-Control Study

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Abstract

Background: Various studies support the concept of an inherited vulnerability to drug dependency, while emphasizing the importance of social and environmental influences and their interactions.

Objectives: To compare the characteristics of heroin-dependent Jewish men in Israel with those of the general population, focusing on the nature of family history of substance abuse.

Method: This case-control study compares 64 heroin-dependent Jewish male residents of Jerusalem with a community sample of 131 randomly selected Jerusalem residents with no drug use disorder. Univariate and multivariate models were employed to appraise the independent associations between heroin dependence and exposure variables such as family history of substance misuse and exposure to legal psychoactive substances.

Results: The case group is characterized by heavy tobacco and alcohol involvement. Nearly 70% of the cases report an alcohol and/or drug problem in at least one first-degree relative compared with 10% of controls (odds ratio 14.5, adjusted for sociodemographic and other potential confounders). Cases with a positive family history have, on average, higher alcohol consumption levels and higher heroin-use severity scores, as compared with cases with no such history.

Conclusions: Familial aggregation of drug and alcohol problems, along with smoking at a young age, is the strongest predictor of heroin dependence in this population. Better understanding of the components underlying this familial aggregation can lead to improved prevention and treatment strategies.

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It is widely accepted today that the predisposition to drug-taking behavior and vulnerability to established and maintained use are outcomes of both environmental and genetic factors [1]. A high degree of familial aggregation has been noted in the few recent case-control and family studies of non-alcoholic drug dependence [2–5]. Although evidence of familial clustering does not necessarily implicate a genetic underpinning in the development of drug dependence, it suggests that heredity cannot be dismissed as a putative risk factor. Although few in number, most of the published twin studies indeed revealed significantly greater concordance for drug abuse and dependence among monozygotic twin pairs than among dizygotic twins, suggesting the presence of genetic influences [6–8]. Results of another study of nearly 300 twin pairs were inconclusive regarding the relative importance of genetic and environmental influences on the liability to use non-alcoholic drugs [9]. Finally, the only adoption study on non-alcoholic drugs found some evidence for heritability of illicit drug abuse (with transmission seemingly occurring via different genetic pathways), although evidence for non-genetic transmission was also found [10].

Little, other than anecdotal evidence, has been reported about the characteristics of the population of treatment-enrolled drug misusers in Israel. Even less is known about the relative importance of familial/genetic and other factors in the development of drug abuse in the country. The extent to which drug abuse manifests a familial aggregation has direct implications on the provision of services and treatments. The aim of the present study was to compare the characteristics of heroin-dependent Jewish men in Israel with those of the general population, with a focus on the nature of family history of substance abuse.

Methods

Study population

The study population comprised 195 unrelated Jewish males, who participated in a broader case-control investigation of genetic and environmental determinants of drug and alcohol use and misuse. Details of the sampling and recruitment procedures have previously been described in detail [11] and will be reviewed here briefly.

- **Cases.** The case group comprised 64 unrelated Jewish male residents of Jerusalem, aged 25–64, actively enrolled at the time of interview in a drug treatment program in any of the three non-private treatment centers in Jerusalem. Inclusion required that cases had been using heroin regularly for a minimum of 3 years and met DSM-III-R criteria for opiate dependence [12]. The average age at which members of this group began using any illicit drug was 15.8 years (range 5–43), and 22.1 years for first heroin use (range 13–43). The average duration of heroin use at the time of interview was 11.3 years (range 3–27). The sociodemographic characteristics of these individuals and their drug-taking behaviors were reflective of the male Jewish clientele who received treatment at the three facilities during the data collection period.
- **Controls.** The 131 individuals who served as controls comprised a random sample of the non-institutionalized population of Jewish male residents of Jerusalem. At the time of initial contact, nine potential controls reported a serious medical condition (including three with a drug-dependence problem) and were therefore not interviewed. The 23 interviewed controls (15%) who classified themselves as ultra-Orthodox were excluded from the present analyses as none of the cases classified themselves as such, and the demographic characteristics of these ultra-Orthodox individuals differed significantly from those of the remaining 131 controls. Fifty-three potential controls refused to participate (16.6% of the total sample and 24.5% of those

contacted), of whom nearly half (40%) described themselves as ultra-Orthodox. Fifteen of the interviewed controls had experimented with marijuana and/or hashish in the past, although none of these self-reports provided any indication of regular use and hence these controls were not excluded.

The ethnic and age composition of the interviewed control group did not differ significantly from that of the 25–64 year old non-ultra-Orthodox Jewish population of Jerusalem [13].

Interview

All subjects were interviewed by trained lay interviewers, using a standard closed questionnaire developed for the purposes of this study. Cases were interviewed at the treatment center in which they were enrolled, and controls were interviewed at a location of their preference, usually in their home. Interviews were conducted in private after assuring the respondent that all information reported by him would be anonymous. An Institutional Review Board-approved letter of informed consent was read and explained, and was signed by all participants prior to the interview.

The interview included sociodemographic information, and a detailed quantity-frequency history was obtained about the use of tobacco, alcohol, and six classes of illicit drugs: marijuana, opiates (heroin, opium and methadone), cocaine/crack, hallucinogens, amphetamines, and benzodiazepines/barbiturates. This information included age at first use, duration of use, quantity and frequency of use over time, and routes of administration of each of these illicit substances. Questions were also posed about DSM-III-R criteria for dependence (i.e., attempts to limit or stop use, and feelings of tolerance) [12]. A composite score of heroin severity was calculated based on average daily heroin intake (in grams) multiplied by the duration of heroin use (in years). All participants who reported current smoking completed the six-item Fagerstrom scale that measures current degree of nicotine dependence on a 0–10 scale [14]. Pedigree information was requested from all respondents regarding first-degree relatives in accordance with developed techniques [15]. The presence of a current or past alcohol and/or drug problem was reported for each family member without the application of formal diagnostic criteria [16]. Age of onset was not ascertained. Familial patterns of substance abuse-related problems were assessed using a conventional dichotomous classification of present/absent in any first-degree relative, as well as a continuous classification that calculated the proportion of known first-degree relatives with a problem.

Refusal to provide any or all of this information did not constitute disqualification from the study; only one case and 13 controls refused to do so. No significant differences were noted between controls who did and did not provide family data regarding basic demographic variables (age, education, ethnic background, marital status, level of religiosity) and alcohol/drug consumption patterns.

Analysis

Univariate comparisons of mean values between cases and controls were examined using the *t*-test statistic. Differences between the

cases and the controls with respect to categorical independent variables were assessed by odds ratio point estimates together with their 95% confidence intervals. Excess risk associated with exposure to legal addictive substances (cigarettes and alcohol) was similarly estimated by the odds ratio measure.

Multiple logistic regression was employed to appraise independent associations between heroin dependence and exposure variables (such as family history of substance abuse) while adjusting for potential confounders. These models also adjust for residual age effects due to incomplete matching. Interaction effects were tested through the introduction of multiplicative terms into these models. Comparison of the goodness of fit of various models was based on the difference of the -2 log likelihood values between two hierarchical models being compared (which is asymptotically distributed as χ^2), with the degrees of freedom being the difference in the number of parameters estimated in the models being compared.

Results

Demographic characteristics

As seen in Table 1, which presents demographic characteristics of the 64 cases and 131 controls, cases are significantly younger than controls by an average of 5 years. Cases had received considerably less schooling: only six had completed high school, of whom three received a high school diploma (data not shown). Of the controls, nearly three-quarters (73%) had completed high school, and just over half (52%) had matriculated.

The ethnic composition of the cases and controls differed significantly. All but six of the cases classified themselves as non-Ashkenazi (i.e., non-European), 41% of whom are of North African origin (not shown), compared with slightly more than half of the controls who classified themselves in this category (19% with a North African origin).

Sixty percent of the cases considered themselves 'traditional' in their religious observance, while only five cases declared themselves to be 'Orthodox'. Among the controls, just under one-quarter (23%) considered themselves 'traditional', with the remaining 80% equally distributed between 'secular' and 'Orthodox'. Compared to those who classified themselves as Orthodox, the likelihood of being a case was fivefold higher (odds ratio 4.7) among those who are traditional.

Half of the cases were married at the time of the interview [Table 1] and an additional 16% were divorced (not shown). This is compared to a much higher proportion (85%) of the control group who were currently married.

There was no significant difference between the cases and controls regarding the marital status of their parents. On the whole, the cases came from significantly larger families than the controls [Table 1], although the average birth rank of the cases and controls was similar. Average birth rank was calculated as the sum of the ratios of birth rank to sibship size divided by the number of sibships: $(\sum(\text{birth rank}/N_{\text{sibs}})/N_{\text{sibships}})$, for each of the two groups. These values are 0.59 and 0.62 for the cases and controls, respectively.

Table 1. Selected demographic characteristics of 64 heroin-dependent Jewish males and 131 male controls from Jerusalem

	Cases		Controls		OR*	95% CI	P
	No.	%	No.	%			
Age (yr)							
<35	33	51.6	45	34.4	5.3	1.7–16.6	0.004
35–44	27	42.2	57	43.5	3.4	1.1–10.7	0.034
45+	4	6.2	29	22.1	1.0		
Education (yr)							
0–7	17	26.6	6	4.6	45.3	13.1–157.1	< 0.000
8–11	41	64.0	29	22.1	22.6	8.7– 58.6	< 0.000
12+	6	9.4	96	73.3	1.0		
Current employment							
Unemployed	50	78.1	13	10.0	32.4	14.2–73.9	< 0.000
Employed	14	21.9	118	90.0	1.0		
Ethnic origin							
Non-Ashkenazi	58	90.6	74	57.8	7.1	3.0–16.2	< 0.000
Ashkenazi	6	9.4	54	42.2	1.0		
(Unknown)			3				
Religiosity							
Secular	21	32.8	52	39.7	2.4	0.8– 7.1	> 0.05
Traditional	38	59.4	49	37.4	4.7	1.6–13.1	0.004
Orthodox	5	7.8	30	22.9	1.0		
Marital status							
Not married	32	50.0	20	15.3	5.6	2.8–11.0	< 0.000
Married	32	50.0	111	84.7	1.0		
Parental marital status							
Not married	5	8.9	5	6.0	1.5	0.4–5.5	> 0.05
Married	51	91.1	78	94.0	1.0		
(Unknown)** ^a	8		48				
					<i>t</i> -test		
Mean age (SD)	34.4 (6.8)		39.3 (10.1)		-4.01		0.0009
Mean education (SD)	8.5 (3.3)		13.6 (4.7)		-8.86		< 0.000
Mean no. of siblings (SD)	5.8 (3.2)		3.8 (2.7)		4.28		< 0.000

* OR: 1.0 = reference category. ** Parental marital status at the time of death of a parent was not obtained, accounting for the missing information

Table 2. Smoking habits of opiate-dependent cases and controls

	Cases (n=64)	Controls (n=131)	<i>t</i> -test	P
Current regular smokers	64 (100.0%)	45 (34.4%)		0.000*
Mean initiation age (SD)	14.4 (4.2)	19.2 (6.0)**	-5.62	0.000
Mean no. of cigarettes/ day (SD)				
Currently	33.3 (15.1)	18.7 (13.7)***	5.15	0.000
Peak period	47.0 (20.7)	25.7 (15.7)**	5.83	0.000

* As determined by the Fisher exact test. ** Among the 76 ever-smokers.
*** Among the 45 current smokers

Tobacco smoking

All of the heroin-dependent cases were current tobacco smokers, smoking an average of one and a half packs of cigarettes (33 cigarettes) a day [Table 2]. The average maximum number of daily cigarettes smoked during the course of at least one year was nearly 50. They began smoking at the mean age of 14, with 20% having begun before the age of 13, which was the youngest age at which any case began using opiates (not shown in the table). For all cases,

cigarette smoking preceded their first use of illicit drugs.

Among the controls, 38% never smoked tobacco and 24% smoked in the past but not currently; 38% were current smokers, of whom 45 (34% of all controls) smoked regularly (i.e., minimum of one cigarette per day). The controls on the whole smoked significantly fewer cigarettes daily and began smoking at an older age as compared to the cases [Table 2]. Only 4% of the controls who smoked currently or in the past began smoking before the age of 13. The odds in favor of initiating smoking prior to 13 years of age were 5.8 times higher among cases than controls (95% confidence interval 1.6–21.2). Among the controls, the mean score on the Fagerstrom scale was significantly lower than that of the cases.

Alcohol consumption

Besides the differences described above between the cases and controls regarding their illicit drug-taking behaviors, sociocultural characteristics, and smoking habits, they also differed considerably in terms of their alcohol consumption patterns.

Sixty-six percent of the cases had consumed some alcohol during the year prior to the interview [Table 3]. All but 14 of them (including 7 who claimed never to have drunk alcohol) had experienced a period of at least one year in which they drank more than during the year preceding the interview. The large difference between mean weekly intake during the past year and during the peak consumption period (which on average persisted for slightly more than 5 years) reflected the sizable proportion of cases who had consumed alcohol heavily before becoming involved with other drugs, primarily heroin. Indeed, 36 cases reported having experienced their period of heaviest alcohol consumption prior to the onset of drug use, and 17 others prior to first opiate use. This was also evident when comparing the 44 cases who reported having drunk alcohol on a daily (or near daily) basis for at least 12 consecutive months sometime in the past, compared with only 4 cases who reported current daily drinking (data not shown). The relatively moderate level of current drinking among this sample of heroin-dependent individuals was commensurate with the feelings described by many of them that "heroin and alcohol don't mix."

Total abstinence from alcohol was reported by 10% of the controls [Table 3], half currently drank alcohol at least once a week (data not shown), and 11 controls (8%) drank on a daily basis or did so in the past. Twenty-five controls (21% of drinkers) reported having experienced a period of at least one year during which they consumed more alcohol than at the time of interview. The mean peak weekly consumption level among the controls was twice as

Table 3. Alcohol consumption patterns in opiate-dependent cases and controls

	Cases (n=64)	Controls (n=131)	Odds ratio	95% CI	P-
Ever consumed alcohol (%)	56 (87.5)	118 (90.1)	1.3	0.5–3.3	NS*
Drank alcohol in past year (%)	42 (65.6)	117 (89.3)	4.4	2.1– 9.3	0.000
Daily drinking for ≥ 1 year (%)	44 (68.8)	11 (8.4)	24.0	10.6–54.1	0.000
Mean weekly intake in last year (ml) (SD)			t-test		
Among current drinkers** ^b	160.5 (353.3)	36.2 (67.4)	2.27		0.029
Among total group	105.3 (295.2)	32.3 (64.6)	1.96		0.055
Peak weekly intake in ml (SD)					
Among drinkers*** ^c	1537.4 (1,414.2)	66.6 (127.5)	7.77		0.000
Among total group	1345.3 (1,417.3)	60.0 (122.6)	7.24		0.000

* Not significant ($P > 0.05$). ** $n = 42$ cases, 117 controls. *** $n = 56$ cases, 118 controls.

Table 4. Prevalence of a positive family history for drug or alcohol problems among opiate-dependent cases and controls: crude and adjusted odds ratios

Familial problem	Cases (n=63)	Controls (n=118)	Odds ratio	95% CI
Drugs or alcohol (%)				
Crude	43 (68.3)	12 (10.2)	19.0	8.5–42.2
Adjusted*			15.7	6.9–35.8
Adjusted**			14.5	4.8–43.7
Drugs (%)				
Crude	28 (44.4)	2 (1.7)	46.4	10.5–204.5
Adjusted*			36.7	8.2–163.7
Adjusted**			39.5	6.6–236.0
Alcohol (%)				
Crude	33 (52.4)	10 (8.5)	11.9	5.3–26.8
Adjusted*			9.3	4.0–21.4
Adjusted**			7.2	2.4–21.0

* Odds ratio from a multiple logistic model adjusting for family size.

** Odds ratio from a multiple logistic model adjusting for family size, age, education, ethnic origin, level of religious observance, and smoking at a young age.

high as their current weekly drinking level (compared to the cases whose average peak weekly level was 10 times higher than the current level).

Family history

Just less than 70% of the cases reported a past or current history of alcohol and/or drug problems in at least one first-degree relative [Table 4]. Half reported a positive family history of alcoholism (of whom 18 classified their father as a present or past alcoholic, not shown in the table), and slightly under half (44%) reported a current or past familial illicit drug problem. Seventeen cases (27%) reported an alcohol or drug problem among their brothers and 6 (9%) among their sisters (data not shown). Of the 118 controls who provided information about their families, 10 reported an alcohol problem among first-degree relatives and two reported a drug problem.

As the differences between the cases and controls with regard to family history may be due, at least in part, to the larger families from which the cases are derived (as reported above), the odds ratios adjusted for family size are also presented in Table 4. Even after accounting for the confounding effect of family size, the

increased likelihood of a positive family history of drug or alcohol problems among cases of heroin dependence was maintained.

Family history was also calculated as the percentage of relatives with a drug and/or alcohol problem. On average, 9.1% of the cases' relatives were classified as positive for drug problems compared with 0.5% of the controls' relatives ($P < 0.0001$). An alcohol problem was reported for 11.5% and 1.3% of relatives of cases and controls respectively ($P < 0.0001$).

Among the heroin-dependent cases, a positive family history of drug or alcohol problems was not significantly associated with ethnic background ($P=0.31$), level of religious observance ($P=0.68$), or marital status ($P=0.65$). The average age of cases

with a positive family history of substance abuse (35.7 years) was significantly older than that of cases with no such family history (31.5 years, $P=0.02$). On average, family history-positive cases had fewer years of schooling (7.8 years) than cases with no family history (9.8 years, $P=0.03$). A family history of drug and alcohol problems was also significantly associated with family size ($P=0.02$). Peak weekly alcohol intake level was higher among family history-positive cases (1,589.7 ml) compared with cases with a negative family history (817.8 ml, $P=0.04$).

The prevalence of a positive family history was also compared between cases whose heroin-taking history was more severe or less severe. The proportion of cases who reported a positive family history of drug and/or alcohol problems was significantly higher among those who scored above the median heroin severity score (83.3%) than among those with a score below the median (54.8%) (OR 4.12, $P=0.0200$).

Multiple logistic regression models were developed to assess the association between a family history of substance abuse and heroin dependence independent of the effects of the various sociocultural variables (i.e., family size, age, education, ethnic origin, level of religious observance, and smoking at a young age). Alcohol consumption was not included in these models since alcohol consumption, particularly heavy consumption, did not necessarily precede the use of heroin or other illicit drugs. The association between heroin dependence and a positive family history for drug or alcohol problems remained extremely robust after adjusting for the effects of these other factors, and family history remained the strongest correlate of proband status (OR 14.52), together with young smoking (OR 17.00). The association between heroin dependence and age also remained significant ($P=0.003$), as did the association with education ($P=0.018$). Inclusion of interaction terms between family history and each of the other independent variables included in the model (as listed above) did not significantly improve the fit of the model (χ^2 difference between the log likelihood values of the two models = 1.90, $df=6$, $P = 0.929$). A family history of drug problems revealed an

OR = odds ratio

adjusted odds ratio of 39.5 (95% CI 6.6–236.0), although this estimate was somewhat unstable (as evidenced by the wide confidence interval) due to the limited number of reported cases of familial drug problems.

Discussion

While much has been written about the psychosocial determinants of drug involvement, investigation into the role of inherited factors is less developed [17,18]. The present case-control study set out to examine characteristics of a heroin-dependent sample of Israeli Jewish males in Jerusalem and compare them to those of a randomly chosen community sample of Jewish males living in the same city.

The data revealed a 14-fold greater likelihood of familial drug or alcohol problems in the sample of heroin-dependent individuals compared with the control sample. A positive family history of drug and/or alcohol problems, together with cigarette smoking at an early age, remains the strongest correlate of opiate dependence in this population, independent of the significant effects of age and education. The prevalence rates of these disorders among male and female relatives of the cases and among the different types of relatives are in keeping with published reports [2–4,19]. Among cases, family history was positively associated with heroin severity and with alcohol consumption levels.

While the observed strong familial aggregation of these traits may point to the possible role of genetic factors, studies of this type cannot provide conclusive evidence as to the mechanism(s) that produce such aggregation. Common predisposing environmental conditions, particularly those that are familial, may produce similar patterns, as do genetic factors. Furthermore, investigations into the genetic basis of susceptibility to complex multi-factorial conditions are difficult due to the heterogeneity of the phenomena, and the likely role of multiple genes – each with varying levels of penetrance and differing interactions with the environment. This may explain the somewhat ambivalent conclusions of the twin and adoption studies cited above regarding the relative contribution of genetic and environmental influences on the risk of drug misuse and dependence. Complex segregation analysis of alcohol consumption patterns in the families of these heroin-dependent Jewish males could not rule out the possibility of a genetic influence alongside the strong environmental influences [20].

All cases reported having begun smoking (nicotine) cigarettes prior to taking illicit drugs, so that early cigarette smoking may be seen as a precursor to illicit drug use in this population. Patterns of tobacco use have previously been shown to predict the use of other psychoactive substances [21]. Indeed, together with alcohol drinking, cigarette smoking – particularly at an early age – is the strongest predictor of marijuana use in both males and females [22].

Several issues warrant consideration in relation to these results, including the degree to which the cases and controls are representative of the larger populations from which they were drawn and the degree of accuracy of the information provided.

The ethnic composition of the Jerusalem case group in the present study is virtually identical to another sample of nearly 200 heroin-dependent males selected from an ambulatory treatment center in Jerusalem (from which 12 of the current cases were recruited) [23]. In that sample, 92% were of non-Ashkenazi origin, of whom 40% were of North African descent. Ascertainment bias is not likely to be a major source of bias in the current study with regard to the Jerusalem group of heroin-dependent males receiving treatment. Indeed, a review of the records of the clinic from which the bulk of the cases was recruited confirms that the ethnic and age distribution of the present sample is representative of the male Jewish clients attending the clinic.

Generally, treated drug-dependent individuals may be affected more severely, and if severity of abuse is associated with the familial prevalence of the disorder, as we have shown, the selected families may not be representative of all families with a drug-dependent member. The decision by each case to seek treatment may itself be determined in part by the number or proportion of family members who are similarly affected. There is no systematic information available to estimate the number and characteristics of persons in Israel who do not seek treatment for their drug problem.

The control group comprised 131 randomly selected male Jewish residents of Jerusalem between the ages of 25 and 64. This number represents 71% of those with whom contact was established subsequent to the initial mailed invitation. Only limited information is available regarding the sociodemographic characteristics of the general population of Jerusalem upon which a comparison with these controls can be made. As described above, the ethnic composition and age distribution of the controls resemble those of the Jerusalem population. This would suggest that no substantial bias was introduced into the present findings as a result of the selection process.

The main potential source of information bias concerns sensitive items of information, such as the self-reporting of personal drug use and substance abuse among family members. Although the present study did not assess the validity and reliability of the reported drug-use information, the heroin-dependent cases who participated in this study had previously disclosed their drug-taking behavior to staff members of the facilities where they were receiving treatment. This, together with the repeated assurances of confidentiality on the part of the interviewer, likely reduced or eliminated any feelings of the need to conceal information. Reported patterns of drug use among the cases fit the known drug habits of Israeli heroin abusers [24]. Also, a high rate of alcoholism among opiate-dependent individuals has been observed in other populations as well, and, as in our sample, alcohol use generally precedes the use of heroin and typically decreases as regular heroin use is established [25].

As to the validity of data regarding drug-taking behaviors among the controls, while some under-reporting of drug use may have occurred, the study's inclusion criteria for controls did not exclude one-time or even occasional users. Given the extensive probing of current and past drug use, the likelihood that drug dependence would be successfully hidden from the interviewer is remote. Any such misclassification, if it did occur, would only serve to diminish differences between the two groups.

CI = confidence interval

Permission to approach some, or all, family members was denied by some respondents, and other relatives were not available or refused to participate. The present study therefore relied largely on the family history method for determining the prevalence of substance abuse in first-degree relatives. While direct interviews are possibly a more accurate source of information, they are more costly, less efficient, and must be supplemented with family history data for deceased relatives and those who cannot or will not be interviewed. There is a fair amount of evidence suggesting that results obtained from information provided through the family history approach do not differ significantly from those based on direct interview of relatives [8]. The respondents' reports of family history were compared with the self-reports of those male relatives who were interviewed directly in our study, in order to assess the reliability of these reports. There was a high degree of agreement, as evidenced by a kappa value of 0.94, between respondent-reported and self-reported presence and absence of a drug problem in the case group. Nonetheless, the possibility of under-reporting of substance abuse among family members, particularly by the controls, cannot be entirely ruled out. Despite assurances of confidentiality, controls may seek to present their families as "normative" and thus provide information that they consider to be socially acceptable. However, given what we know of the prevalence of substance abuse in the general population of Israel, this potential bias would not explain away the observed 14-fold increased likelihood of drug/alcohol problems in the cases' relatives. Overall, the cases and controls included in the above analyses likely represent, to a large extent, the populations from which they were drawn. So too, the information that they provided seems to be reliable and valid.

Results of the study show a strong familial clustering of drug and alcohol problems and lend further support to a small but growing body of literature suggesting the contribution of familial, and thus possibly inherited, influences in the development of drug misuse and dependence. Furthermore, the major factors associated with and influencing the development of heroin dependence in Israel are similar to those found in other populations and cultures. Continued investigation into the nature and role of familial aggregation of drug misuse in this and other population groups is warranted from an etiologic viewpoint and as a treatment consideration. Appropriate recognition of genetic and environmental vulnerabilities can lead to improved targeting of prevention programs and better treatment strategies for heroin dependence.

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