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Personality and the Inheritance of Smoking Behavior: A Genetic Perspective

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In contrast to the extensive research effort to understand the genetic contribution to alcoholism risk, there has been little research directed at understanding genetic influences on smoking behavior. Data from large twin studies in Scandinavia and Australia are consistent with a major genetic influence on the probability that an individual will become a smoker ("initiation") and will persist in the smoking habit once smoking has started ("persistence"). We use data from the 1988/1989 follow-up survey of the Australian NH&MRC twin panel to determine to what degree personality measures (Tridimensional Personality Questionnaire, Eysenck Personality Questionnaire—Revised) and attitudinal and sociodemographic variables (social and political conservatism, education, religious involvement) might account for genetic or environmental influences on smoking. While we find significant phenotypic associations between these variables and smoking, these are too modest to account for much of the genetic variance. Possible mechanisms by which this genetic variance may arise are discussed.

KEY WORDS: Personality; smoking behavior; inheritance; Australian NH&MRC twin panel; attitudinal variables; sociodemographic variables.

INTRODUCTION

An extensive body of behavioral genetic data supports a major genetic contribution to alcoholism in men and in women also (reviewed by Heath *et al.*, 1994c). The 95% confidence limits to estimates of the heritability of alcoholism derived from individual twin or adoption studies are extremely broad; however, most studies using epidemiologic or community-based samples have yielded results consistent with an overall heritability of alcoholism in men and women of 45–60% (see Table I below). [While estimates derived from clinically ascertained samples have been more variable, these estimates have depended upon strong and arguably unjustifiable assumptions about how to correct for sample ascertainment (Heath *et al.*, 1994c), a complication that has not always been fully appreciated (Plomin *et al.*, 1994).] These findings have stimulated a variety of research strategies to clarify the mechanisms by which genetic influences on alcoholism risk may arise, ranging from theories of the mediating role of personality or temperament variables (Tarter *et al.*, 1984; Cloninger, 1987) to attempts to map individual genetic loci that may account for alcoholism risk (Begleiter, 1993). High-risk studies, comparing the offspring of alcoholic parents and controls, have attempted to determine, using an alcohol challenge paradigm, whether innate differences in initial sensitivity or rate of acquisition of acute tolerance to alcohol may mediate the genetic influence on alcoholism risk (e.g., Schuckit, 1994). Selective breeding experiments using rats or mice have been used to develop animal models of alcoholism (Li, 1990; Crabbe *et al.*, 1994).

By way of contrast, we may consider research on genetic influences on smoking behavior. Like

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Table I. Estimates of the Genetic Contribution to Alcoholism Risk, and to Smoking Behaviors, Derived from Community Samples of Twins or Adoptees[a]

Country	Study	Gender	Design	Phenotype	Assessment	Heritability (%)	95% confidence interval
Alcoholism							
Sweden	Kaij (1960)	M	T	2+ temperance board registrations	R	46	14–76
	Cloninger *et al.* (1981, 1988, 1990)	M,F	A	1+ temperance board registrations	R	32	15–50
	Cloninger *et al.* (1981, 1988, 1990)	M	A	2+ temperance board registrations	R	41	10–70
	Allgulander *et al.* (1991, 1992)	M,F	T	ICD-8 alcoholism	R	57	0–67
Finland	Koskenvuo *et al.* (1984)	M	T	ICD-8 alcoholism	R	63	0–74
	Romanov *et al.* (1991)	M	T	ICD-8 alcoholism or alcohol abuse related	R	60	0–72
U.S.A.	Hrubec & Omenn (1981)	M	T	ICD-8 alcoholism/ alcoholic psychosis	R	63	31–69
	Kendler *et al.* (1992)	F	T	DSM-III-R dependence	I	55	0–69
	Kendler *et al.* (1992)	F	T	Problem drinking	I	61	21–71
Smoking							
Sweden	Medlund *et al.* (1977)	M	T	Smoking initiation	Q	52	43–60
	Medlund *et al.* (1977)	M	T	Smoking persistence	Q	35	10–57
	Medlund *et al.* (1977)	F	T	Smoking initiation	Q	43	35–51
	Medlund *et al.* (1977)	F	T	Smoking persistence	Q	55	31–66
Finland	Kaprio *et al.* (1978)	M	T	Smoking initiation	Q	50	39–61
	Kaprio *et al.* (1978)	M	T	Smoking persistence	Q	52	29–66
	Kaprio *et al.* (1978)	F	T	Smoking initiation	Q	37	28–46
	Kaprio *et al.* (1978)	F	T	Smoking persistence	Q	53	5–67
Australia	Heath and Martin (1993a)	M	T	Smoking initiation	Q	22	0–54
	Heath and Martin (1993a)	F	T	Smoking initiation	Q	79	59–85
	Heath and Martin (1993a)	M, F	T	Smoking persistence	Q	44	11–62

[a] Alcoholism data are adapted from Heath *et al.* (1994c), which should be consulted for further details. Smoking data are adapted from Heath and Madden (1994).

Questionnaire measures of alcoholism were not considered here. Gender: M, males; F, females. Assessment: R, official records; I, personal interview; Q, mailed questionnaire. Design: T, twin; A, adoption.

alcoholism, smoking is associated with serious health consequences, not only to the smoker (USDHEW, 1979), but also to others in the smoker's environment (USDHHS, 1986), and hence with enormous economic costs to society. In the United States alone, as many as 400,000 lives are lost each year to smoking (USDHHS, 1989; Peto *et al.*, 1992). In contrast to alcoholism and illicit drug use, which are more prevalent in men than in women (e.g., Robins and Regier, 1991), levels of smoking by women have approached or surpassed those by men in many societies (Grunberg *et al.*, 1991), so that annual smoking-related deaths in women are expected to reach 250,000 in the near future (Peto *et al.*, 1992).

Such data as do exist on the genetics of smoking have typically been collected as part of general health surveys of twin panels in Scandinavia, the United States, and elsewhere (e.g., Raaschou-Nielsen, 1960; Cederlof *et al.*, 1971; Medlund *et al.*, 1977; Hrubec and Neel, 1978; Kaprio *et al.*, 1978; Carmelli *et al.*, 1992; Jardine and Martin, 1984). In consequence, assessments of smoking have been limited to gross measures of whether an individual ever smoked, whether he/she still smokes, and how much he/she smokes (or used to smoke), with no attempt made to assess nicotine dependence. In some studies, not all data have been presented in a form that will permit meaningful genetic analysis of important aspects of smoking behavior (e.g.,

Carmelli *et al.*, 1992). Nonetheless, from a reanalysis of the existing data (Heath and Madden, 1994), we have found support for a major genetic influence on the risk of becoming a smoker and probability of persisting in the smoking habit once smoking has started. When we consider the three largest studies in which data were published in a form that would permit secondary data analysis [the Swedish survey reported by Medlund *et al.* (1977), the Finnish survey reported by Kaprio *et al.* (1978), and the Australian twin panel 1981 survey reported by Heath and Martin (1993a) and Heath Cates *et al.* (1993)], the magnitude of the genetic influence is seen to be comparable to that reported for alcoholism (Heath and Madden, 1994; see Table I).

When we consider the question of how genetic influences on smoking may arise, only limited progress has been made in studies on humans, although the potential now exists for important advances to be made. To some extent this lack of progress is explained by the very limited assessments used in the large-scale genetic surveys, which do not permit us to determine with any confidence what role differences in the development of nicotine dependence may play in determining persistence in the smoking habit, or what role differences in initial sensitivity to nicotine may play in determining which individuals become nonsmokers after experimenting only once or twice. With the exception of the early work of Eaves and Eysenck (1980), little progress had been made in determining the role of heritable personality differences (e.g., Eaves *et al.*, 1989; Loehlin, 1992) or other behavioral or sociodemographic variables [e.g., educational level (Vogler and Fulker, 1983)] in the inheritance of smoking behavior.

In this paper, we use data from the 1988–1989 survey of the Australian NH&MRC twin panel (Heath *et al.*, 1994a) to test whether there is an important mediational role of personality variables in the inheritance of smoking behavior. In particular, we examine whether a theory advanced by Cloninger (1987) for the role of temperament in the inheritance of alcoholism can be applied to the inheritance of smoking. According to Cloninger's theory, alcoholism is a heterogeneous disorder in which one subtype ("type II"), found predominantly in men, is associated with the early onset of alcohol problems, a strong genetic influence, and a personality profile characterized by high impulsivity ("novelty seeking") and low trait anxiety ("harm avoidance") and low reward dependence; the second subtype (type I) is characterized by a later onset and a weaker genetic influence and is associated with low impulsivity, high anxiety, and high reward dependence (Cloninger, 1987). While the specific details of this theory remain controversial, the basic division into a subtype associated with behavioral undercontrol/impulsivity more commonly seen in men and a subtype associated with negative affect/anxiety and more commonly seen in women has been a recurrent theme in many classifications of alcoholism (e.g., Sher, 1991). The possibility that a similar subclassification of smokers might be appropriate has long been recognized (e.g., Eysenck, 1980).

METHODS

Sample

Twins from the Australian National Health and Medical Research Council volunteer twin panel, who had been surveyed initially as adults by mailed questionnaire in 1980–1981 (Jardine and Martin, 1984; Hannah *et al.*, 1985), were followed up by mail in 1988–1989 (Heath *et al.*, 1994a). Table II summarizes the estimated number of twin pairs, by zygosity group, in the original target sample for the 1981 questionnaire mailing, as well as the number of complete pairs and single twins returning questionnaires in the 1981 and 1989 mailings. The zygosity breakdown for the 5967 pairs to whom questionnaires were mailed in 1980–1981 is only approximate, since provisional zygosity assignments had to be used for pairs where neither twin returned a questionnaire in the 1981 survey, and since it has not been possible to reconstruct with complete certainty which twins on the twin panel at this period were not included in the questionnaire mailing (currently we have identified 6386 pairs as potential targets for the mailing). In projecting the zygosity breakdown, we have assumed that the zygosity distribution for pairs assigned as of unknown zygosity in the target sample was the same as for those unknown zygosity pairs who responded to the 1981 questionnaire mailing (for whom zygosity could be assigned on the basis of responses to zygosity questions in that survey). We have also assumed that the zygosity distribution in the target sample who received mailed ques-

Table II. Breakdown by Zygosity Group of (a) Number of Twin Pairs in the Target Sample for the 1981 Questionnaire Mailing, (b) Number of Complete Pairs and Single Twins Returning Questionnaires in the 1980/1981 Mailing, and (c) Number of Complete Pairs and Single Twins Returning Questionnaires in the 1988/1989 Mailing

		1981 questionnaire			1989 questionnaire	
	Target sample (estimated)	Complete pairs		Single twins	Complete pairs[a]	Single twins[a]
MZ female pairs	1706	1232		77	946	104
MZ male pairs	901	567		61	401	75
DZ female pairs	1113	747		119	541	100
DZ male pairs	630	350		100	223	72
DZ unlike-sex pairs	1617	912	Male	56	569	192
			Female	154		
Total	5967 pairs	3808 pairs		567 twins	2680 pairs	543 twins

[a] Excludes twins who completed an abbreviated telephone interview.

tionnaires was the same as that in the 6386 pairs who were potential targets of mailings. The number of complete pairs reported in the 1981 survey is two fewer than reported in some early publications on this sample (Jardine and Martin, 1984), since by the follow-up of this sample two pairs had been identified who had been doubly ascertained, and who had returned two sets of questionnaires. The total of 3808 pairs who both returned questionnaires in the 1981 survey, and who formed the target sample for the 1989 mailing, excluded 3 pairs where both twins returned questionnaires but at least one twin returned a questionnaire after data entry on the original study had been completed. The number of single twins reported for the 1981 survey likewise excludes single twins who had responded after the original study had been completed. Pairwise response rates for the 1981 survey were 70.2% for female like-sex pairs [72.2% for MZ female (MZF), 67.1% for DZ female (DZF), assuming that our target sample zygosity projections are correct], 59.9% for male like-sex pairs [62.9% for MZ male pairs (MZM), 55.6% for DZ male (DZM) pairs] and 56.4% for unlike-sex (DZFM) pairs. Corresponding individual response rates were 74.5% for MZF, 72.5% for DZF, 66.3% for MZM, 63.5% for DZM, 61.2% for DZFM female twins, and 58.1% for DZFM male twins.

For the 1989 survey, we report only numbers for those twins who completed and returned a mailed questionnaire. Twins who did not return a mailed questionnaire were given the option of an abbreviated telephone interview, which included assessments of smoking, but not of the personality measures that are the primary focus of this paper. Including both questionnaire and telephone respondents, follow-up data were obtained from both members of 2997 twin pairs (79% pairwise response rate) and from one twin only from an additional 334 pairs (83% individual response rate). Treloar (1993) has reported that for the female like-sex pairs, once cases of nonresponse due to death, illness, work overseas, or inability to locate the twins were excluded, the pairwise response rate in the 1989 follow-up survey increased to 90%.

Important information about potential sample biases may be obtained by comparing characteristics of complete pairs (i.e., where both responded to the questionnaire mailing) versus singleton twins in the 1981 survey and of those participating in the 1989 survey versus those lost to follow-up. A higher proportion of current or former smokers was found among singleton twins in the 1981 survey (54.4% in women, 64.0% in men) than among complete pairs (40.6 and 51.8%, respectively). Since smoking is strongly familial, the noncooperative cotwins of these twins would also be more likely to be smokers, implying that undersampling of smokers in the original sample had occurred. However, the increase in the proportion of smokers among single twins was not higher in dizygotic than in monozygotic pairs (e.g., a 12.0% increase in MZ females versus 14.9% increase in DZ females, but a 21.4% increase in MZ males versus a 15.7% increase in DZ males). This is an important conclusion, since if there were a substantially

higher rate of loss of smokers from concordant smoking pairs in DZ than in MZ pairs, this would mimic evidence for a genetic influence on smoking. In men, smokers from complete pairs did not differ significantly from single twin smokers on any smoking variable, i.e., there were no differences in the proportion who were heavy or committed or persistent smokers (defined below). In women, smokers from complete pairs were more likely to be current smokers (63.2 versus 53.9%), or had a later age of quitting if they were exsmokers (27.1 versus 24.7 years), although it should be noted that each of these associations was only marginally significant at the 5% level, making no correction for the nonindependence of observations on twin pairs.

Smoking in mean, assessed in 1981, did predict nonresponse in 1989, the attrition rate being 22.9% for males who were current or former smokers in 1981, compared to 16% for those who had never smoked. This association may perhaps be explained at least in part by differential mortality. Neither smoking persistence nor quantity smoked in 1981 was predictive of nonresponse at follow-up. No significant association between smoking in 1981 and nonresponse in 1989 was observed in women.

Measures

The 1989 survey included a short-form 54-item version of the Tridimensional Personality Questionnaire of Cloninger (Cloninger *et al.*, 1991), as well as the short-form of the EPQ-R (Eysenck *et al.*, 1985). Psychometric properties of these instruments based on results from the Australian twin panel, which demonstrate acceptable internal consistency and test–retest reliability, are presented elsewhere (Heath *et al.*, 1994a). The TPQ assesses hypothesized personality dimensions of Novelty Seeking, Harm Avoidance, and Reward Dependence. Novelty Seeking is assessed by items relating to thrill-seeking, impulsive behavior, and low self-control; Harm Avoidance, by items concerning anticipatory anxiety, tension, social shyness, and fatigability; and Reward Dependence, by items relating to sensibility, drive, social extraversion, and dependency. The EPQ-R assesses Extraversion, Neuroticism, Social Conformity (''lie'' scale) and Toughmindedness (Psychoticism or ''P'' scale). These Eysenckian scales have been used very extensively in behavioral genetic research (see, e.g., Eaves *et al.*, 1989; Loehlin, 1992). However, it should be noted that the P scale of the EPQ-R represents a very extensive revision of the P scale used in the EPQ and earlier instruments, so that continuity of the core construct cannot be assumed. All personality scores were rescaled by dividing by the maximum possible score on the scale, so that scores lie between zero and unity. Evidence for substantial heritability of both EPQ-R and TPQ personality measures has been presented elsewhere (Heath *et al.*, 1994a,b). There are strong correlations between some of the TPQ and EPQ-R subscales, e.g., 0.63 between Harm Avoidance and Neuroticism, −0.55 between Harm Avoidance and Extraversion, 0.4 between Novelty Seeking and Extraversion, and also between Reward Dependence and Extraversion, and −0.28 between Novelty Seeking and Social Conformity (Heath *et al.*, 1994), and so for this reason we examined the prediction of smoking behavior by the two sets of personality variables separately as well as jointly.

Assessment of smoking behavior was by the following five items: (i) Write in the number which best describes (your) smoking habits—(1) never smoked, (2) exsmoker, (3) current smoker; (ii) Which expresses your best estimate of (your) average daily cigarette consumption—(1) never smoked cigarettes, (2) smoked 1–4 per day, (3) 5–10 per day, (4) 11–20 per day, (5) 21–40 per day, (6) more than 40 per day; (iii) At what age did you start smoking? (iv) If you have stopped smoking, how old were you when you stopped? (v) For how many years all together have you smoked? In addition to self-report data, items (i) and (ii) were also asked about the respondent's cotwin, mother, father, and spouse (if any), and items (iii), (iv), and (v) about the cotwin, to provide a check on the validity of self-reports and informant ratings. These items clearly provide a very incomplete assessment of smoking behavior, as is to be expected from a study in which smoking was not a primary focus. For the purposes of this paper, smoking initiation—whether or not the respondent had ever smoked cigarettes—was operationalized by defining as lifetime smokers those individuals who reported that they were current or exsmokers and who did not report that they had never smoked cigarettes and as never smokers those who reported that they had never smoked or that they had never smoked cigarettes. Thus some individuals who had used other tobacco products but had never smoked cig-

arettes would have been classified as never smokers. Smoking persistence—whether or not a lifetime smoker was still smoking—was defined for cigarette smokers only, according to whether they reported that they were ex- or current smokers. It is theoretically possible, therefore, that some individuals who had quit smoking cigarettes but who continued to use other forms of tobacco were classified as exsmokers. Following Hannah *et al.* (1985), we also defined a "committed" smoking trait, operationalized for the purposes of this paper as whether or not a smoker reported smoking for at least 10 years. Finally, heavy smoking, again defined for lifetime smokers only, was operationalized as smoking at least 21 cigarettes per day. We note that the common practice of including never smokers as a zero point on measures of daily cigarette consumption (e.g., Carmelli *et al.*, 1992) may give quite misleading results if quite different social or genetic factors determine initiation of smoking versus amount smoked by those who become smokers (for further discussion of this issue, see Heath and Madden, 1994).

In addition to personality variables, we also examined the role of attitudinal and sociodemographic variables as mediators of shared environmental (or possibly genetic) influences on smoking behavior. Variables assessed included (i) year of birth (1900–1964 in this sample), which was recoded by subtracting 1900 and dividing by 10; (ii) educational level (Baker *et al.*, 1994), coded as a dichotomous variable, with low education corresponding to 10 or fewer years of schooling and high education to 11 or more years of schooling, apprenticeship or diploma, technical or teachers' college, or university first degree or higher; (iii) religious involvement, also operationalized as a dichotomous variable according to whether or not the respondent reported attending church or other observances at least once a month; (iv) social conservatism, assessed by a 14-item scale (Heath and Martin, 1993b) with high social conservatism being indicated by endorsement of such items as "bible truth," "church authority," and (anti-) "legalized abortion"; (v) political conservatism, assessed by a 16-item scale (Heath and Martin, 1993b), with high political conservatism being indicated by endorsement of such items as "death penalty," "Royalty," (anti-)"Trade Unions," and (anti-) "Medicare." Social conservatism was included as a measure of religious beliefs that might prohibit or discourage smoking. Political conservation was included as a measure of political beliefs that might be associated with resentment at public health policy efforts to regulate individual health-related habits and, therefore, with greater resistance to quitting smoking. Both attitudinal measures were scaled to take values between zero and one; all other sociodemographic variables were binary.

Data Analysis

Age-adjusted personality and attitude scores were compared as a function of smoking status by analysis of covariance, without adjusting for the nonindependence of observations on twin pairs. This approach will yield unbiased estimates of the means but will underestimate their sampling variance, so that statistical tests at the conventional 5% significance level will have an inflated type I error rate. Since the sample sizes in this study are very large and will detect as significant effects that are of no substantive interest, we focused chiefly on results significant at the 1% significance level, unless otherwise noted. Response surface regressions were used to predict age at onset of smoking as a function of the linear and quadratic effects, and interaction terms, for the TPQ and EPQ-R personality variables. In addition, we compared smoking variables for those meeting a "narrow type II" or "narrow type I" profile (type II—scoring in the top quartile on Novelty Seeking and the bottom quartiles on Harm Avoidance and Reward Dependence; type I—scoring in the top quartiles on Harm Avoidance and Reward Dependence and the bottom quartile on Novelty Seeking) and all other respondents, and for those meeting a "broad type II" or "broad type I" personality profiles (defined by using a median split on each variable, rather than the top and bottom 25%). The joint effects of sociodemographic, personality, and attitudinal variables were tested in multiple logistic regression analyses. The 95% confidence limits reported for the adjusted odds ratios are not corrected for nonindependence of observations on twin pairs, but we discuss only results significant at the 1% significance level, unless otherwise noted. For continuous personality and attitude variables, adjusted odds ratios were computed for a difference in score equal in magnitude to the interquartile range for that variable. All these analyses were computed using SAS 6.09 (SAS Institute, Inc., 1989). To put into per-

spective these phenotypic associations, we also computed adjusted odds ratios when cotwin's smoking status (initiation, for analyses of the respondent's smoking initiation; persistence, for analyses of the respondent's smoking persistence) was included in the multiple logistic regression analysis. Finally, polychoric and polyserial correlations were computed between smoking initiation and persistence and the predictor variables using PRELIS 2 (Joreskog and Sorbom, 1993a), and a multiple regression model was fitted to these correlations by maximum likelihood using LISREL 8 (Joreskog and Sorbom, 1993b), to provide estimates of the variance in smoking behavior accounted for by the observed personality, attitudinal, and sociodemographic variables that could be more readily compared to estimates of the total genetic and shared environmental variance derived by model-fitting.

RESULTS

Smoking and Personality

Figure 1 summarizes age-adjusted personality and attitude scores of never smokers, former smokers, and current smokers. Among women (N=3135), compared to never smokers, current or former smokers had higher scores on Novelty Seeking (NS) and Extraversion (E) and lower scores on Social Conformity (L) and Social Conservatism (SocCon). Other differences were more modest, though still significant at the 0.1% significance level [except in the case of Reward Dependence (RD) and Political Conservatism (Pol-Con)] because of the very large sample sizes. However, among women who became smokers (N=1703), personality differences were only weakly predictive of persistence in the smoking habit, persistent smokers having modestly higher scores on Toughmindedness (P: p=.04), and lower scores on L (p=.01). Among men (N=1722), lifetime smokers (N=853) had significantly elevated scores on NS, Neuroticism (N), P, and PolCon and significantly lower scores on L and SocCon. Compared to former smokers, men who were current smokers had significantly elevated scores on NS and significantly lower scores on L.

Among lifetime smokers, personality differences were only weakly predictive of whether or not an individual smoked more than 20 cigarettes a day (heavy smoking) or smoked for 10 years or more (committed smoking) (not shown). Women heavy smokers had higher N scores than light smokers (0.47 vs 0.42, $p<.01$), while men heavy smokers had higher NS scores (0.47 vs 0.42, $p<.001$), lower RD scores (0.53 vs 0.55, $p<.05$), lower L scores (0.42 vs 0.46, $p<.05$), and lower SocCon scores (0.34 vs 0.38, $p<.01$). Women committed smokers had higher scores on NS (0.46 vs 0.41, $p<.001$), but all other personality differences were either nonsignificant or only marginally significant at the 5% level. Men committed smokers had lower RD scores (0.54 vs 0.57, $p=.01$), but other personality differences were again minimal.

Estimated polychoric and polyserial correlations between smoking and personality variables were uniformly low. In women, smoking initiation correlated 0.22 with E, −0.21 with L, 0.28 with NS, and −0.23 with SocCon, but correlations of smoking persistence, heavy smoking, and committed smoking variables with personality or attitudinal variables were less than 0.15 in absolute value in all instances. In men, smoking initiation correlated 0.18 with NS and smoking persistence exhibited modest correlations with L (−0.18), P (0.15), NS (0.27), and SocCon (−0.18). PolCon correlated 0.16 with committed smoking. Other correlations were again uniformly low. When a multiple regression model was fitted to the polychoric and polyserial correlations for either smoking initiation or smoking persistence and personality variables, the above personality predictors accounted for only 11.8% of the variance in risk of smoking initiation in women and 3.8% of the variance in men; and for 1.2% of the variance in risk of smoking persistence in women and 8.8% of the variance in men. Inclusion of SocCon and PolCon as predictors (SocCon only in the case of smoking persistence) increased these R^2 values modestly but significantly, to 14.7, 5.9, 1.2, and 8.8%, respectively.

Attempts to predict age at onset of smoking from the personality variables in a multiple regression analysis were also disappointing. Earlier onset of smoking was significantly associated with higher Novelty Seeking scores in both genders, and with lower Harm Avoidance scores in men only, but with very modest R^2 values (0.03 for women, 0.04 for men).

Smoking and the Type I/Type II Classification

Some support was found for an association of a type II personality profile with smoking behavior.

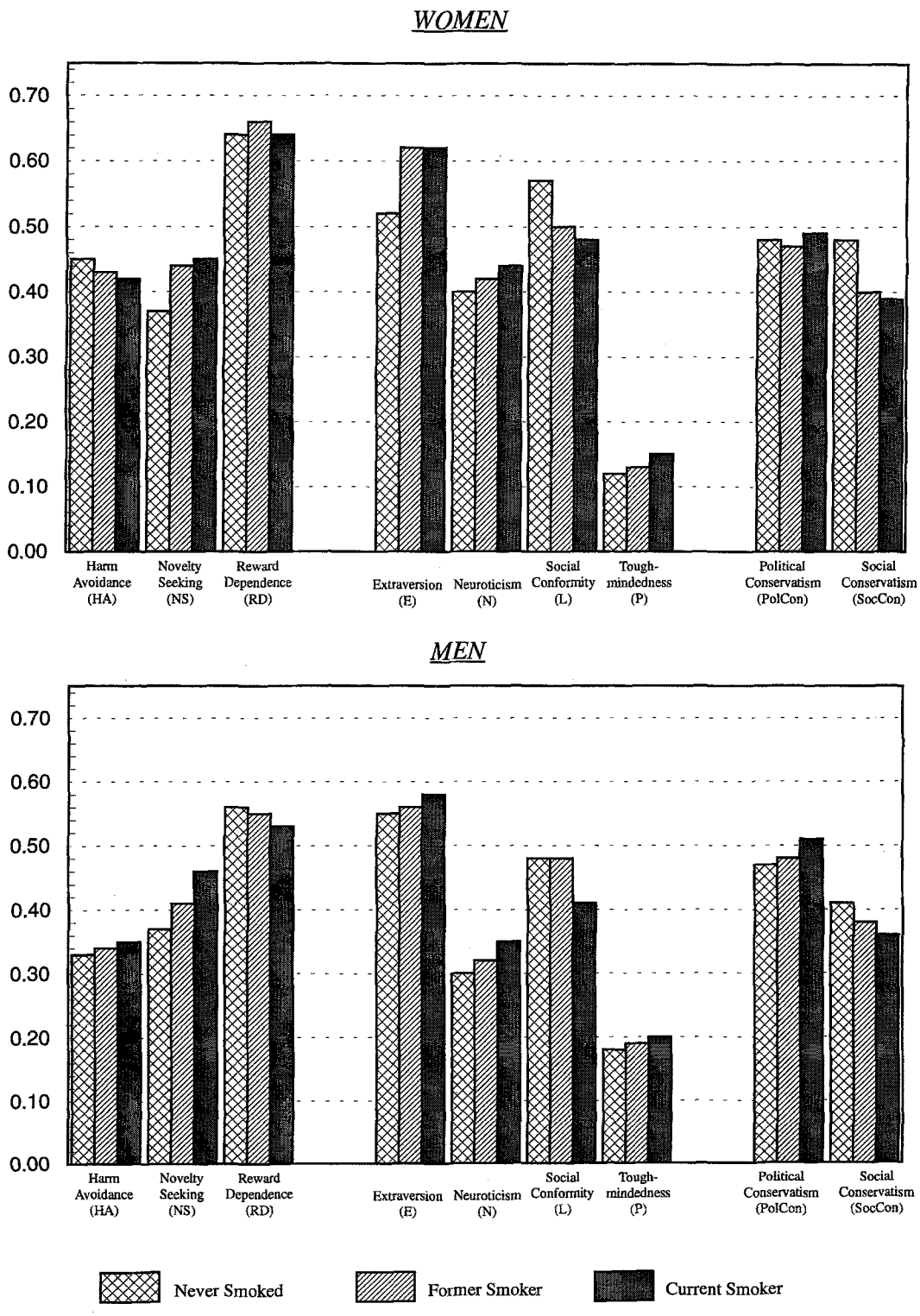

Fig. 1. Age-adjusted personality and attitude scores of never smokers, exsmokers, and current smokers.

Using the narrow operationalization (see Methods), 63.8% of type II women compared to 39.9% of non-type II's were smokers ($p<.001$), and 67.6% of type II men compared to 48.5% of non-type II's were smokers ($p=.02$). There were no significant differences in age at onset of smoking, but a trend for earlier onset among type II versus non-type II men (15.4 vs 16.8, $p=.07$). There were no significant differences in heavy smoking or committed smoking by type II compared to non-type II smokers, but type II male smokers (but not female smokers) were more likely to be persistent smokers (64.0 vs 40.6%, $p=.02$). However, despite the significant findings, it should be noted that because of the small number of respondents in the sample fitting the narrow type II definition that we have used [58 women (1.8%), 37 men (2.1%)], the type II profile accounts for only 2.9% of lifetime smokers in women and 3.0% of lifetime smokers in men. Using the broad type II profile [which classified 228 women (7.2%) and 102 men (5.9%) as type II's], type II women were more likely to be lifetime smokers than the rest of the sample (48.0% versus 39.6%, with 8.0% of smokers identified with the type II profile: $p=.01$), but there was no significant association in men. The broad type I personality profile in women was associated with a significantly reduced probability of becoming a smoker, compared to the rest of the sample (28.1 vs 42.1%, with 16.1% of nonsmokers having the type I profile: $p<.001$), and there was a trend in the same direction in men (44.4 vs 49.6%, $p=.12$). Women type I smokers were significantly less likely to smoke for 10 years or longer (62.9 vs 71.8%, $p=.04$) than non-type I smokers, and men type I smokers were significantly less likely to be persistent smokers (31.7 vs 42.6%, $p=.02$).

Other Predictors of Smoking

Table III summarizes adjusted odds ratios for predicting smoking measures from the sociodemographic as well as attitudinal and personality variables, estimated from the multiple logistic regression analyses. Initiation of smoking was predicted by low religious involvement in both genders and by low educational level and early decade of birth in men. Low religious involvement also predicted smoking persistence and committed smoking in women but not in men. Low educational level was significantly associated with persistence, heavy smoking, and committed smoking in women and with persistence and committed smoking in men. Early decade of birth predicted heavy smoking in men and committed smoking in both genders; recent decade of birth predicted persistence in both genders.

As was the case for the personality and attitudinal variables, polyserial and polychoric correlations between the sociodemographic and the smoking behaviors were quite modest: low religious involvement correlated 0.31 with smoking initiation, 0.25 with smoking persistence, and 0.19 with heavy smoking in women and 0.26, 0.25, and 0.16 with these variables in men; low educational level in women correlated 0.22 with heavy smoking and 0.32 with committed smoking and in men correlated 0.32 with smoking initiation and 0.37 with committed smoking. Early decade of birth was negatively correlated with smoking persistence (-0.41 in men, -0.17 in women) and positively correlated with committed smoking (0.37 in men, 0.35 in women). Results of fitting multiple regression models to the polychoric and polyserial correlations for these data are summarized in Figs. 2a–c. Estimated R^2 values were 19.8 and 29.5% for smoking initiation in women and men and 13.3 and 25.5% for smoking persistence.

Genetics and Smoking

We have presented elsewhere analyses of these data showing substantial heritability of smoking initiation and smoking persistence, even when differences in similarity of early experience between monozygotic and dizygotic twin paris (e.g., probability of sharing the same peers) are controlled for (Madden *et al.*, 1993). Heritability estimates obtained were 47–76% for smoking initiation (varying as a function of concordance or discordance for early environmental experiences) and 62% for smoking persistence. The phenotypic correlations that we have observed suggest that these are the two aspects of smoking behavior for which the influence of genetic factors is most likely to be at least partially mediated by personality variables (especially in women, in the case of smoking initiation, and in men, in the case of smoking persistence). But as we have seen above, even the proportion of the total phenotypic variance accounted for by these variables is low compared to the amount of genetic variance to be explained.

Table III. Partial Odds Ratios (and 95% Confidence Interval) for Predicting Smoking Variables from Personality, Attitudinal, and Sociodemographic Measures (Only Significant Effects Are Shown)[a]

	Initiation		Persistence		Heavy smoking		Committed smoking	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Women								
Decade of birth			1.37[b]	1.21–1.54			2.09[b]	1.76–2.49
Low education	1.17	0.97–1.41	1.79	1.36–2.35	2.12	1.54–2.91	1.89	1.35–2.65
Low religious involvement	1.82	1.42–2.33	1.87	1.23–2.84			2.17	1.36–3.45
Low social conservatism	1.27	1.09–1.47						
Political conservatism							1.24	1.02–1.50
Extraversion	1.53	1.27–1.85						
Neuroticism	1.23	1.04–1.45	1.41	1.09–1.82	1.44	1.06–1.96	1.37	1.02–1.84
Low social conformity	1.41	1.21–1.65						
Harm Avoidance			0.74	0.57–0.97				
Novelty Seeking	1.39	1.21–1.59					1.30	1.02–1.64
Men								
Decade of birth	1.41	1.27–1.55	1.79[b]	1.51–2.11	1.30	1.11–1.51	2.13[b]	1.71–2.66
Low education	1.78	1.29–2.46	1.95	1.26–3.02			2.32	1.24–4.33
Low religious involvement	1.89	1.34–2.68						
Political conservatism	1.17	1.00–1.38						
Extraversion					1.51	1.03–2.21	2.24	1.46–3.44
Low social conformity							1.43	1.01–2.02
Harm Avoidance							1.94	1.28–2.92
Novelty Seeking	1.66	1.38–1.99	1.62	1.24–2.11	1.57	1.18–2.09		
Low Reward dependence					1.30	1.01–1.66	1.52	1.16–1.99

[a] For continuous personality and attitude variables, odds ratios were computed for a change in score equal in magnitude to the interquartile range for the variable.
[b] Association with recent decade of birth.

To give some perspective to the adjusted odds ratio in Table III, without relying upon the strong assumptions associated with genetic model-fitting (e.g., Neale and Cardon, 1992) it is instructive to consider the odds ratio for smoking initiation (or persistence, or heavy or committed smoking), given that the cotwin is a lifetime (or current or heavy or present or former committed) smoker. The adjusted odds ratios in Table IV were estimated, separately for each zygosity group, from multiple logistic regression analyses which included the same predictor variables as those used in Table III, with the sole addition of the cotwin's smoking status. In women, for whom sample sizes were largest, odds ratios for cotwin's smoking status were significantly higher for MZ than for like-sex DZ cotwins for all smoking variables; and this was also true for smoking initiation, smoking persistence, and committed smoking in male like-sex pairs. For monozygotic pairs, the odds ratio estimated for cotwin's smoking status was, in every instance, higher than the ratios estimated for other predictor variables and, in many instances, very substantial (e.g., for MZ female pairs, odds ratios given cotwin's smoking status range from 5.71 to 17.62; and those for MZ male pairs, from 2.60 to 8.34). Furthermore, once the effect of cotwin's smoking status was allowed for, other variables did not predict smoking status consistently across zygosity groups, with the exception of decade of birth in the case of smoking persistence and committed smoking measures.

DISCUSSION

Behavioral genetic methods have been applied with considerable success to further our understanding of the joint effects of genes and environment in the inheritance of psychiatric disorders including major depression and the anxiety disorders (Kendler, 1993) and alcoholism (Kendler *et al.*, 1992, 1994). They are being increasingly applied to study such phenotypes as obesity or cardiac reactivity to stress in the field of behavioral medi-

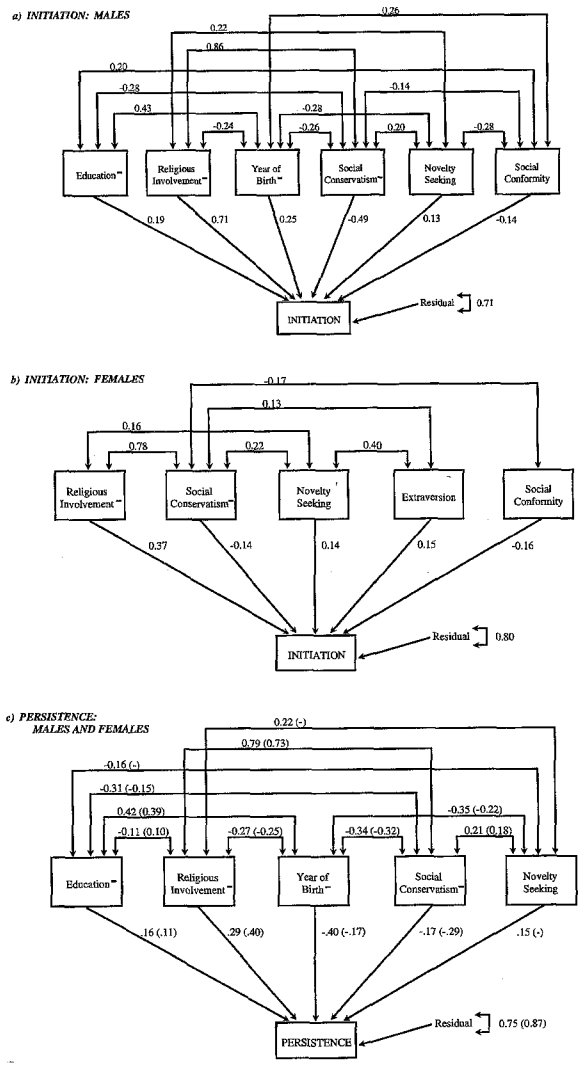

Fig. 2. Associations between smoking status (initiation or persistence) and personality, attitudinal, and sociodemographic variables estimated under a multiple-regression model. Only correlations or paths with values greater than ± 0.10 are shown. In c, estimates for women are given in parentheses.

cine (e.g., Turner *et al.*, 1994). Data from major twin studies in Scandinavia, the United States, and Australia (reviewed by Heath and Madden, 1994) are consistent with a very important role of genetic factors in risk of initiation of smoking and progression of the smoking habit once smoking has begun (quantity smoked, persistence in smoking versus successful quitting). In this paper, we have examined the phenotypic associations between these variables and smoking, to assess the extent to which such genetic influences may be mediated by personality or sociodemographic variables.

Phenotypic associations between smoking variables and personality, attitudinal, and sociodemographic variables in this sample, though in many cases statistically significant, were nonetheless quite modest. The Novelty Seeking scale of the Tridimensional Personality Questionnaire proved to be the most predictive personality measure, exhibiting correlations of 0.28 with smoking initiation in women and 0.27 with smoking persistence in men and a correlation of 0.18 with smoking initiation in men. The Social Conformity ("Lie") scale of the EPQ-R was also a useful predictor, with low Social Conformity having correlations of the order of 0.2 with smoking initiation in women and with smoking persistence in men. Sociodemographic variables such as low religious involvement and low educational level had somewhat higher, but still modest, correlations with smoking measures (e.g., 0.37 between low education and committed smoking in men, 0.31 between low religious involvement and smoking initiation in women). The strongest associations for both smoking persistence and committed smoking were with year of birth, consistent with the interpretation that there is a "censoring" problem in these data, with younger individuals being less likely to have smoked for 10 years or longer and more likely not yet to have quit smoking. A more sophisticated approach to data analysis than we have used here, using a survival analysis framework (Meyer *et al.*, 1991), would be needed to address this issue further.

Our results suggest that most of the genetic variance in our smoking variables cannot be accounted for by mediational effects of personality, attitudinal, or sociodemographic variables. How then can this residual genetic variance be explained? For smoking initiation, because we have only very gross self-report questionnaire measures, we cannot tell whether the group of self-report never smokers includes a substantial number of individuals who have smoked only once or twice, so that individuals who report themselves as smokers are in fact those who became regular smokers. If this is the case, as seems plausible, then it is possible that innate differences in initial sensitivity to nicotine may play an important role, with many individuals who experience a strong adverse reaction giving up smoking after the first or second attempt. Evidence for genetic control of initial sen-

Table IV. Adjusted Odds Ratios (and 95% Confidence Interval) When Cotwin's Smoking status Is Included as a Predictor Variable[a]

	MZF pairs		MZM pairs		DZF pairs		DZM pairs		Females from unlike-sex pairs		Males from unlike-sex pairs	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
	Smoking initiation											
	(*N*=1471)		(*N*=659)		(*N*=839)		(*N*=391)		(*N*=477)		(*N*=466)	
Cotwin has smoked	**17.62**	**13.34–23.27**	**8.34**	**5.78–12.06**	**4.28**	**3.13–5.86**	**2.75**	**1.75–4.32**	**2.63**	**1.73–4.03**	**2.61**	**1.72–3.97**
Extraversion	1.44	1.03–1.99										
Novelty seeking			1.66	1.21–2.29			1.72	1.18–2.50	1.49	1.04–2.14		
Low social conformity					1.86	1.35–2.56						
Low religious involvement					2.55	1.53–4.24	2.38	1.08–5.23			2.20	1.10–4.38
Year of birth											1.40	1.14–1.72
Low education											2.68	1.42–5.07
	Smoking persistence											
	(*N*=454)		(*N*=220)		(*N*=215)		(*N*=110)		(*N*=136)		(*N*=140)	
Cotwin still smokes	**5.71**	**3.70–8.81**	**5.70**	**2.77–11.72**	**2.64**	**1.49–4.67**	**1.20**	**0.50–2.89**	**1.28**	**0.61–2.68**	**1.13**	**0.55–2.32**
Decade of birth[b]	1.55	1.22–1.97	2.47	1.58–3.86							1.49	1.02–2.16
Political conservatism			1.91	1.04–3.52								
Low social conformity			1.95	1.13–3.35			2.35	1.02–5.37				
Low education									2.76	1.12–6.80		
	Heavy smoking											
	(*N*=447)		(*N*=214)		(*N*=210)		(*N*=107)		(*N*=133)		(*N*=136)	
Cotwin is/was heavy smoker	**6.90**	**4.12–11.54**	**4.27**	**2.01–9.08**	**3.15**	**1.57–6.34**	**5.40**	**1.92–15.19**	**1.99**	**0.70–5.65**	**1.91**	**0.74–4.95**
Low education	1.76	1.02–3.02							4.41	1.38–14.11		
Neuroticism	1.85	1.11–3.09										
Novelty Seeking			2.06	1.12–3.76								
Low social conformity					2.32	1.27–4.24					3.24	1.43–7.34
	Committed smoking											
	(*N*=446)		(*N*=206)		(*N*=207)		(*N*=104)		(*N*=133)		(*N*=136)	
Cotwin's committed smoking	**6.76**	**3.98–11.45**	**2.60**	**1.17–5.79**	**3.84**	**1.60–9.24**	**0.92**	**0.16–5.25**	**1.51**	**0.59–3.86**	**1.24**	**0.45–3.38**
Decade[b]	1.40	1.40–1.87	1.86	1.22–2.85	1.75	1.07–2.85	2.04	1.04–4.01	2.18	1.25–3.81	2.04	1.11–3.77
Political conservatism	1.45	1.01–2.08										
Low Neuroticism							4.64	2.63–8.21				
Low educational level											9.12	1.00–82.95
Low Reward Dependence											2.37	1.04–5.39

[a] With the exception of cotwin's smoking status, only significant effects are shown. Odds ratios for continuous variables are for a change in score equal in magnitude to the interquartile range for the variable.

[b] Recent decade of birth.

sitivity to nicotine is provided by studies of other species, with differences among inbred mouse lines in response to an acute dose of nicotine being a consistent finding (reviewed by Collins and Marks, 1989). As we suggest elsewhere (Heath and Madden, 1994), recent refinements of methods of nicotine administration to allow nicotine challenge research with nicotine-naive human subjects (Pomerleau *et al.*, 1993b) now offer the possibility of studying the genetic control of nicotine sensitivity in humans.

How can genetic differences in the risk that a smoker will become a persistent smoker be explained? There are few, if any, published data on the genetic contribution to nicotine dependence in humans. In mice, genetic differences in level of development of tolerance to nicotine have been demonstrated using strains of mice differing in sensitivity to nicotine (Collins and Marks, 1989; Marks *et al.*, 1986). Pomerleau has argued that greater initial sensitivity to nicotine leads to increased capacity to develop tolerance, which we might expect to be associated with greater smoking persistence (Pomerleau *et al.*, 1993a). It is unlikely that genetic differences in initial sensitivity to nicotine can account for a substantial proportion of the genetic variance in risk of smoking initiation *and* smoking persistence, since analyses of twin data suggest that there are genetic influences on persistence that are independent of effects on initiation (Heath and Martin, 1993a; Madden *et al.*, 1993; Heath and Madden, 1994). Nonetheless, as we have argued elsewhere (Heath and Madden, 1994), it is possible that use of nicotine challenge with nicotine-naive twins from smoking discordant pairs will help clarify the relationship between genetic differences in nicotine sensitivity and risk of smoking initiation or persistence. Certainly the accumulation of evidence pointing to a major genetic influence on smoking behavior and the relatively poor prediction of smoking behaviors by heritable personality measures [in both our own analyses and those of Eaves and Eysenck (1980)] suggest that such research into the mechanisms by which genetic influences on smoking arise would be timely.

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