Behavior Genetics, Vol. 29, No. 6, 1999

The Genetics of Smoking Persistence in Men and Women: A Multicultural Study

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Received 31 Mar. 1999—Final 9 Nov. 1999

Using a correlated liability dimensions model, we examined the extent to which the same genetic and environmental factors influence both initiation of regular cigarette smoking and maintenance of the smoking habit in men and women. We analyzed questionnaire survey data obtained from large samples of male and female like-sexed twins from three countries, Australia (N = 1535 pairs), Sweden (N = 5916 pairs), and Finland (N = 4438 pairs), subdivided into three age bands (18–25, 26–35, and 36–46 years of age). We found that familial influences on risk for persistence in smoking cannot be entirely explained by the same factors responsible for risk of smoking initiation. Total genetic variance for smoking persistence varied little by age band and sex (range, 39–49% in women and 42–45% in men); however, even among twins in the youngest group (18–25 years of age), who on average have the fewest years of cigarette use, less than 40% of the total genetic variance in smoking persistence was accounted for by the same genetic factors that increased risk of smoking initiation, and this percentage decreased to less than 10% in the 36–46 year olds.

KEY WORDS: Smoking persistence; smoking initiation; cross-cultural; twins.

INTRODUCTION

Cigarette smoking is an important risk factor for morbidity and mortality from disorders such as lung cancer, heart disease, emphysema, and bronchitis (Doll *et al.*, 1980; Doll and Peto, 1976; Risch *et al.*, 1993) in both industrialized and developing countries [World Health Organization (WHO), 1997]. In most, but not all (Kaprio *et al.*, 1984), twin studies on the etiology of smoking behavior, evidence has been found for genetic influence on risk of cigarette use in women (Crumpacker *et al.*, 1979; Edwards *et al.*, 1995; Hughes, 1986; Kaprio *et al.*, 1982; Pedersen, 1981; Raascho-Nielsen, 1960), men (Crumpacker *et al*, 1979; Carmelli *et al.*, 1990, 1992; True *et al.*, 1997; Raaschou-Nielson, 1960; Eaves and Eysenck, 1980; Kaprio, 1978; Heath *et al.*, 1993; Hannah *et al.*, 1985; Hughes, 1986; Swan *et al.*, 1990; Kaprio *et al.*, 1982), and adolescent boys and girls (Kaprio *et al.*, 1995; Boomsma *et al.*, 1997).

Motivated by this literature, we began a set of reanalyses of mailed questionnaire data obtained from surveys of large numbers of Swedish, Finnish, and Australian same-sex adult male and female twins who were in early or middle adulthood at the time of survey, to address questions about consistency in the relative importance of genes and experiences shared by family members to smoking behavior across country, age and sex.

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0001-8244/99/1100-0423$16.00/0

Despite substantial differences in prevalence, in previous analyses of these data (Madden *et al.,* 1999), we found the magnitude of genetic influences for lifetime regular smoking to be consistent across country and age, with small but statistically significant differences between men and women. The contribution from environmental experiences shared by cotwins to becoming a regular smoker was found to increase from the oldest to the youngest twins (who had also begun smoking at younger ages) and to play a larger role in the onset of regular smoking in women (26, 35, and 45% for twins aged 18–25, 26–35, and 36–46 years, respectively) than men. Shared environmental effects were also observed in men to be greater in the Scandinavian (19, 29, and 33%) than the Australian (11, 9, and 26%) twins. We did not find significant cross-cultural differences in the magnitude of genetic influence on risk of becoming a smoker. An earlier study that did report such differences (Heath *et al.,* 1993) compared only the Australian and Virginian twins, and their U.S. sample included a large proportion of older twins (who were recruited from the American Association of Retired Persons).

Twin studies have consistently reported a strong genetic contribution to risk of persistent smoking [i.e., long-term continuation in the smoking habit by those who have become smokers (Heath and Martin, 1993; Heath and Madden, 1995; True *et al.,* 1997)]. Unlike initiation of regular smoking, there has been little evidence reported to support the hypothesis that environmental experiences shared by cotwins as adults play an important role in the maintenance of cigarette use. Consistent with the findings of others (Heath and Martin, 1993; Heath and Madden, 1995; True *et al.,* 1997), we found familial sources of risk for persistence in smoking to be entirely due to genetic factors. In addition, we found that the relative contribution of genetic factors for smoking persistence to be similar across country, across sex, and in early and later adulthood.

Findings from some (Heath and Madden, 1995; True *et al.,* 1997; Heath and Martin, 1993), but not all (Heath, 1990), twin studies on smoking behavior suggest that familial factors that increase risk for smoking initiation are substantially different from factors influencing whether or not a smoker quits cigarettes. Therefore, in our previous cross-cultural analyses, we used the simplifying assumption of independence of genetic and of environmental effects on smoking initiation versus persistence (Madden *et al.,* 1999).

Here we reanalyze data on smoking behavior obtained from large samples of twins assessed at similar ages from Australia, Finland, and Sweden under a model that allows for correlated genetic and environmental influences on smoking initiation and persistence. We address the following questions: (1) Controlling for genetic influences on the initiation of smoking, are there additional genetic factors influencing persistence in smoking? and, if so, (2) Is the relative importance of genetic and environmental sources of risk on continued smoking consistent in men and women?

METHODS

Samples

The samples for this study were drawn from three nationwide adult twin registries maintained for research purposes in three different countries; the Australian National Health and Medical Research Council, the Finnish Twin Cohort, and the New Swedish Twin Registry (see Madden *et al.,* 1999). Almost all subjects were of European descent, and in all cases, zygosity was determined by questionnaire. The accuracy of ascertaining zygosity using this method has been estimated to be at least 95% (Cederlof *et al.,* 1961; Sarna *et al.,* 1978; Eaves *et al.,* 1989).

The Finnish and Swedish twins were both ascertained from population citizen registries, while enrollment in the Australian registry was dependent on volunteerism, with twins recruited throughout Australia using newspapers and other forms of advertising media.

The New Swedish Data. These data were obtained by a mailed questionnaire survey conducted in 1973 with Swedish male and female like-sex twin pairs born between 1926 and 1958 [about 14,000 like-sex pairs (Medlund et al., 1977)]. For purposes of this project, only twins aged 18–46 years (born 1926–1954) were included in the Swedish sample, and the deletion of cases with missing data left for analysis 2332 MZ and 3584 DZ female and 1923 MZ and 3109 DZ male like-sex twins, and 1 twin only from an additional 2514 pairs, with a mean age of 31 years (SD = 8 years) in women and of 30 years (SD = 8 years) in men.

The Finnish Data. The Finnish data used in this study were obtained by a mailed questionnaire survey conducted in 1975 that was completed by 4936 male like-sex and 5545 female like-sex pairs born before 1958 and alive in 1967 (the overall rate of response was 89%) (Kaprio and Koskenvuo, 1988; Kaprio et al., 1978). For comparability with the Swedish and the Australian samples, only twins aged 18–46 years (born 1929–1957) were included in the Finnish sample, and

the deletion of cases with missing data left 1473 MZ and 2965 DZ female and 1258 MZ and 2955 DZ male like-sex twins, and 1 twin only from an additional 1636 pairs, with a mean age in both men and women of 29 years (SD = 8 years).

The Australian Data. The Australian data used in this study were obtained by a mailed questionnaire survey conducted in 1980–1981 which was returned by 1232 complete MZ female pairs, 747 DZ female like-sex pairs, 567 MZ male pairs, and 350 DZ male like-sex pairs (respectively, 72, 67, 63, and 63% pairwise response rates) (Jardine and Martin, 1984; Heath et al., 1995). For the purposes of this study, only same-sex twins aged 18 to 46 years (born 1935 to 1963) in the Australian sample were analyzed here, and the deletion of cases with missing data left 958 MZ and 577 DZ female and 456 MZ and 293 DZ male Australian like-sex pairs, and 1 twin only from an additional 292 pairs, with a mean age of 29 years (SD = 8 years) in women and of 28 years (SD = 7 years) in men.

Measures

Respondents from all three countries completed mailed questionnaires which obtained self-report measures of smoking status and history, and other aspects of lifestyle, as well as measures of personality, attitudes, and sociodemographic variables (e.g., education, marital status, and religious affiliation). The Finnish and Swedish questionnaires were designed to be used together in research, and many survey questions, including those on cigarette use, had equivalent wording. Regular smoking in Scandinavians was defined as smoking at least 5–10 packs of cigarettes in their lifetime and responding positively to the item, "Do you smoke or have you at some time smoked regularly, in other words, daily or almost-daily?" In the Australian survey it was defined by a positive response to the question, "Have you EVER been a smoker?" Lifetime regular smoking was coded as a two-level variable, never vs. ever a regular smoker, by combining current and ex-smokers into a single category.

Among the lifetime regular smokers, persistent smoking in the Scandinavian twins was measured by the question, "Do you still smoke regularly?" and for the Australian twins it was indicated by the absence of an age for quitting cigarette use among those who had endorsed ever smoking. From these data a three-level measure of smoking status was derived, with the categories (i) never smoked (regularly), (ii) ex-smoker, and (iii) continuing smokers.

Genetic Analysis

The contributions of genetic, shared environmental, and nonshared environmental effects to risk of smoking behavior (i.e., risk of becoming a regular smoker and of continued smoking) were evaluated under a multifactorial threshold model, which assumes a continuous normal distribution of liability, with distinct thresholds superimposed. These are standard assumptions used in the genetic analysis of categorical data under a polygenic model and are also used in the estimation of tetrachoric or polychoric correlations (Joreskog and Sorbom, 1993).

Our approach to determining the extent to which the same genetic or environmental factors are responsible both for initiation and for later stages of smoking behavior involved fitting correlated liability models with two liability dimensions ("initiation" and "persistence") using the structural equation modeling program MX (Neale, 1997). The initiation dimension determines the unconditional probabilities of lifetime smoking status for each twin (i.e., never smoked regularly versus current/former smoker), while the persistence dimension determines the conditional probability of persistence in smoking and, therefore, has no effect in those who have never smoked (cf. Eaves and Eysenck, 1980; Heath and Martin, 1993). Rather than estimating twin pair polychoric correlations for initiation and for persistence directly, these were expressed as functions of genetic and environmental parameters, and the latter parameters were estimated directly from the observed data [see, e.g., Heath *et al.* (1998) for technical details of estimation procedures]. In previous analyses of these data (Madden *et al.*, 1999), the results suggested that risk of becoming a smoker was modified by experiences shared by twins that differed by age band (AB); therefore, three sets of analyses were conducted, one for data obtained from twins 18–25 years of age, a second from those 26–35 years of age, and a third from those who were 36–46 years of age at the time of survey. Since we found no evidence for an important role for nonadditive genetic factors for either the initiation or the persistence of smoking in our earlier work, the variance here was decomposed into three sources of liability: additive genetic effects, shared environmental effects, and nonshared environmental effects.

The correlated liability dimensions model that we fitted (see Fig. 1) is a special case of a bivariate direction-of-causation model (Neale and Cardon, 1992; Heath *et al.*, 1993; Kendler *et al.*, 1999), in which a

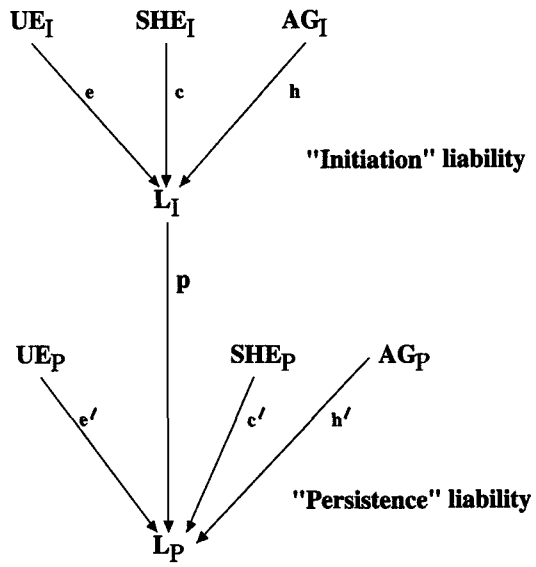

Fig. 1. Correlated liability dimensions model for smoking initiation and persistence. AG, SHE, and UE denote additive genetic, shared environmental, and unshared environmental effects: L denotes the latent liability dimensions; and *p*, the regression of persistence liability on initiation liability. Subscripts I and P denote direct effects on Initiation and on Persistence.

causal influence of initiation liability on persistence liability is assumed. A full bivariate genetic model, in contrast, would be underidentified, since we cannot estimate a nonshared environmental correlation between "initiation" and "persistence"; this would require the availability of nonsmokers who were also persistent smokers. The correlated liability dimensions model imposes the constraint that the genetic and environmental common factor loadings for the persistence dimension are a constant multiple parameter *p* of the loadings for the initiation dimension, where *p* (the regression coefficient in Fig. 1) is the expression of persistence liability on initiation liability. Models were fitted to sets of 12 3 × 3 contingency tables (3 countries × 2 sexes × 2 zygosity groups = 12 contingency tables), by the method of maximum likelihood, yielding a chi-square test of goodness of fit (Neale, 1997). The parameter constraints used in these models were guided by the results of previous univariate genetic analyses of these data: genetic and environmental effects on initiation of smoking were estimated separately by sex and equated across all three countries, except for the shared environmental parameters in men, which were estimated separately in data obtained from Scandinavia (i.e., Finland and Sweden combined) and Australia (Madden *et al.*, 1999). The regression of "persistence" liability on "initiation" liability, and the additive genetic, shared environmental, and unshared environmental parameters used to estimate effects specific to liability for persistence in smoking were equated across country but were allowed to vary by gender.

To test for sex differences in genetic and environmental effects on liability for smoking persistence, the goodness of fit of the full models (one for each AB) was compared by likelihood-ratio chi-square test to submodels in which the regression coefficient and the genetic and environmental components specific to smoking persistence were constrained to be equivalent in men and women. In our earlier work with these data, models where thresholds in MZ and DZ twins were constrained to be equivalent provided a significantly worse fit to data on smoking initiation in men and women, and for smoking persistence in men, than did a model where thresholds were estimated separately; therefore, in these analyses, separate thresholds were estimated for each zygosity group.

RESULTS

Genetic Influences on Persistence in Smoking

Correlated liability dimension models allowing for separate estimates in men and women for the regression of persistence liability on initiation liability, and for genetic and environmental effects specific for smoking persistence, gave good fits to data from all age bands by chi-square goodness-of-fit criteria (ages 18–25 years, $\chi^2 = 33.52$, df = 35, $p = 0.54$; ages 26–35 years, $\chi^2 = 33.73$, df = 35, $p = 0.53$; and ages 36–46 years, $\chi^2 = 23.92$, df = 35, $p = 0.92$). Compared with the full model, constraining the regression coefficient and the parameters specific to smoking persistence to be equal across sex did not provide a significantly worse fit to data obtained from twins in the youngest and the oldest age bands (ages 18–25 years, $\chi^2 = 1.56$, df = 7, $p = 0.98$; ages 36–46 years, $\chi^2 = 2.33$, df = 7, $p = 0.94$) but did provide a significantly worse fit to data obtained from twins 26–35 years of age ($\chi^2 = 20.27$, df = 7, $p < 0.01$).

Table I presents genetic and environmental parameter estimates for smoking initiation and for smoking persistence under the best-fitting models, including estimates of risk specific for continued smoking and for risk shared with the initiation of regular cigarette use, by sex and age band. For example, for women aged 18–25 years, the first row and second column in Table I show that 43% of the variance in liability to smoking initiation was explained by additive genetic

Table I. Genetic and Environmental Variance Component Estimates (and 95% CIs) Associated with Initiation of Lifetime Regular Smoking and Specific to Smoking Persistence, in Women and Men (Unless Indicated Otherwise, Parameters Could Be Constrained to Be Equal Across Societies)

	Women						Men							
	Initiation			Specific to persistence			Initiation					Specific to persistence		
								Australian		Scandinavian				
	AG	SHE	UE	AG	SHE	UE	AG	SHE	UE	SHE	UE	AG	SHE	UE
Initiation														
18–25 years[a]	43	48	10				54	28	18	35	11			
	(34–52)	(39–55)	(8–12)				(43–65)	(15–41)	(10–28)	(26–44)	(8–14)			
26–35 years	46	35	19				68	0	32	19	13			
	(35–58)	(25–44)	(15–22)				(56–77)	(0–15)	(21–42)	(11–30)	(10–16)			
36–46 years	59	16	25				46	21	33	28	27			
	(42–75)	(3–30)	(20–31)				(28–63)	(0–45)	(17–54)	(13–41)	(21–33)			
Persistence														
18–25 years	12	13	3	27	9	36	15	8	5	10	3	27	9	36
	(10–15)	(11–15)	(2–3)	(9–45)	(0–23)	(27–44)	(12–18)	(4–11)	(3–8)	(7–12)	(2–4)	(9–45)	(0–23)	(27–44)
26–35 years	21	16	9	28	4	21	5	0	2	1	1	37	0	56
	(16–27)	(12–20)	(7–10)	(7–47)	(0–21)	(11–33)	(4–5)	(0–1)	(1–3)	(1–2)	(1–1)	(24–47)	(0–8)	(45–67)
36–46 years	4	1	2	42	0	51	3	1	2	2	2	42	0	51
	(3–5)	(0–2)	(1–2)	(24–51)	(0–13)	(41–62)	(2–4)	(0–3)	(1–4)	(1–3)	(1–2)	(24–51)	(0–13)	(41–62)

Note. AG represents the percentage of the total variance due to additive genetic factors; SHE, shared environmental factors; UE, unshared environmental factors.
[a] Age at assessment.

effects (95% confidence interval, 34–52%). Additive genetic influences on the initiation dimension also explained 12% of the variance in smoking persistence (row 4, column 2), but additive genetic effects specific to persistence explained an additional 27% of the variance. Consistent with our previous analyses, we confirmed substantial additive genetic effects on the initiation of smoking, with the effects of genes significantly stronger in men than in women among twins 18 to 35 years of age. The importance of environmental experiences shared by twin and cotwin for risk of becoming a smoker was found to decrease with age at survey and was observed to be of greater importance for women of all ages and for Scandianvian compared with Australian men. Total genetic variance for smoking persistence varied little by AB and sex (range, 39–49% in women and 42–45% in men). As summarized in Table I, our data suggest that, in both men and women, familial factors that increase risk for persistence in smoking cannot be entirely explained by the same factors responsible for risk of initiation of regular smoking.

In men, the greatest overlap in sources of liability for the initiation and the persistence of smoking occurred in the youngest adults (see Table II), 18–25 years of age, who on average had the fewest years of cigarette use (Madden *et al.*, 1999). A modest 28% of the total variance in persistent smoking among men from this age band was found due to factors also responsible for risk of onset of regular smoking. These factors account for a substantial portion of the total genetic variance (36%) and shared environmental variance (Australian, 47%; Scandinavian, 53%) and a more modest proportion of the total unshared environmental variance (Australian, 12%; Scandianvian, 8%) in risk for continued cigarette use. A similar story was observed in women surveyed at 18–25 years of age. However, in contrast to findings in the women, the percentage of overlap in liability between these smoking behaviors dropped to a minimal 7% in men who were 26–35 years at the time of the survey and remained at 7% in men from the oldest age band. Our findings in men surveyed at from 26 to 46 years of age suggest that, once we account for factors responsible for increased risk of becoming a regular smoker, there is *no* evidence that experiences shared by cotwins contribute to liability for continued smoking, and this is also true for women surveyed at 36 to 46 years of age.

Findings under the best-fitting models in women suggest an increase, rather than a decrease, in the proportion of overlap in risk between the onset and the persistence of regular cigarette use between those in the youngest age band and those 26–35 years of age. Some 46% of the total variance in risk for smoking persistence in women from this age band was observed to be shared with risk for the initiation of smoking, and this overlap in risk accounted for about 43% of the total genetic, 80% of the total shared environmental, and 30% of the total unshared environmental variance. It was only in women surveyed at 36–46 years of age that we observed, as in men, minimal evidence for overlap in risk between these two stages in smoking (i.e., 7%), indicating that a marked separation in genetic risk for the onset versus persistence of smoking in these women occurred only in later adulthood.

DISCUSSION

The purpose of this study was to examine the extent to which the same genetic and environmental factors influence initiation and continuation of cigarette use ("persistence") and whether additional genetic influences on risk for continued smoking may be modified by differences in age or sex. Genetic analyses using a correlated liability dimensions model were conducted on smoking data obtained from mailed questionnaire surveys of large numbers of Swedish, Finnish, and Australian same-sex adult male and female twins. Consistent with our previous analyses, we confirmed substantial additive genetic effects on the initiation of smoking, with the effects of genes stronger in men than in women among twins 18 to 35 years of age. The importance of environmental experiences shared by twins for risk of becoming a smoker was found to decrease with age at survey and was observed to be of greater importance for women of all ages and for Scandinavian compared with Australian men. In agreement with the findings from some (Heath and Madden, 1995; True *et al.*, 1997; Heath and Martin, 1993), but not all (Heath, 1990), twin studies on smoking behavior, our present findings suggest that there are important differences between factors that increase risk for smoking initiation and factors that influence whether or not a smoker quits cigarettes (Heath and Martin, 1993; Heath and Madden, 1995; True *et al.*, 1997). We also find that the magnitude and the sources of overlap between early and later stages of smoking may vary by age and gender.

Genetic Influences on Persistence In Smoking

In early adulthood, many of the same familial factors that increase risk of becoming a regular smoker also increase liability for persistent smoking. Our re-

Table II. Estimates (and 95% Confidence Intervals) for the Regression Coefficient of Smoking Persistence on Initiation, and the Percentage of Variance in Liability in Persistent Smoking Shared with Liability for the Initiation of Regular Smoking in Women and Men

			% of total genetic or environmental variance in persistence shared with initiation				
				Australian		Scandinavian	
Age group	Regression coefficient	% of total variance shared[a]	% of AG	% of SHE	% of UE	% of SHE	% of UE
Men							
18–25 years[b]	0.53 (0.40–0.65)	28 (16–42)	36	47	12	53	8
26–25 years	0.27 (0.06–0.46)	7 (0–21)	12	100	3	100	7
36–46 years	0.26 (0.04–0.46)	7 (0–21)	7	100	4	100	4
Women							
18–25 years	0.53 (0.40–0.65)	28 (16–42)	31	59	8	59	8
26–35 years	0.68 (0.51–0.81)	46 (26–66)	43	80	30	80	30
36–46 years	0.26 (0.04–0.46)	7 (0–21)	9	100	4	100	4

Note. AG represents additive genetic factors; SHE, shared environmental factors: UE, unshared environmental factors.
[a] Regression coefficient squared × 100.
[b] Age at assessment.

sults suggest that up to 35% of the genetic variance for smoking persistence in men and 30% in women aged 18 to 25 years may be accounted for by the same genes that contribute to liability for becoming a regular smoker. However, we found a less pronounced overlap in variance for the onset and later stages of smoking in men over age 25 or for women in the oldest age band. In contrast with the men, in women surveyed at from 26 to 35 years of age, we found a clear and significant increase in the percentage of variance shared between the onset and the persistence of smoking (from 28 to 46%), which was accounted for in part by a significant increase in the amount of shared genetic variance (from 31 to 43%).

How do we explain this difference between men and women? There is much that remains unknown about factors driving smoking behavior; however, the disparity in our findings may be due in part to some genetically influenced factor with a larger impact in women than men, that is associated with both early and later stages in smoking. For example, smokers with both current and lifetime histories of mood disturbance have been reported to be less likely to quit the use of cigarettes. A strong genetic correlation has been observed by Kendler and his colleagues (1993) between average lifetime cigarette consumption and 1-year prevalence of major depression in a follow-up of female twins. We may speculate that, if depression increases risk for both initiation and persistence in smoking, there would be substantially larger overlaps for genetic sources of liability for these smoking behaviors in women, who are more likely to suffer from depression than men. Why the importance of such a shared risk factor should decline earlier in men than in women remains to be determined.

Environmental Influences on Persistence in Smoking

Once we account for the risk factors for becoming a smoker, there is little evidence for an important role for experiences shared by cotwins in determining risk of persistence in smoking in men or in women from any age band (all 95% CIs include 0). In contrast, except in women 26 to 35 years of age, there was only a small amount of risk from environmental events experienced separately by cotwins (range: 4–8%) that increased liability for both onset and continuation of smoking behavior. Environmental effects contributing to maintenance of the smoking habit appear to be due mostly to life events specific to the individual and to be separate from events that increase the likelihood of becoming a smoker. These findings suggest that once someone has become a regular smoker, it may be genetic factors, plus life events specific to the individual, that have the largest effect on maintenance of the smoking habit.

The Interpretation of Age Effects

Although we subdivided the data presented by age at the time of assessment, it should be noted that, for

smoking initiation, "age" is really a proxy for birth cohort, with differences between age cohorts most probably reflecting sociocultural differences at the time these individuals were starting to smoke. In contrast, for smoking persistence, because of the issue of censoring, it seems plausible that it is age rather than birth cohort that is the critical variable. Under this hypothesis, the declining overlap in older age groups between genetic or environmental risk factors for initiation and for persistence would be explained if the percentage of persistent smokers who are unable to quit, rather than smokers who have not yet seriously made a quit attempt, is increasing with age. Data from other birth cohorts, assessed at the same age, would be needed to address this hypothesis.

Limitations

When interpreting the results of this study, several potential limitations must be borne in mind. The assessments of smoking behavior were obtained by retrospective self-report, and our findings are limited by the reliability of these data, which may be affected by the subject's ability to recall past events. Also, in the Australian survey, information on both the initiation and the persistence of regular smoking were determined using somewhat more ambiguous measures than in the Scandinavian surveys. A lifetime history of regular smoking was obtained in Australia using the questionnaire item, "Have you EVER been a smoker?" which may confound liability for experimentation with cigarettes with liability for lifetime regular smoking. However, even among Australian male and female twins 18–25 years of age, over 90% reported having smoked for more than 1 year, suggesting that most subjects who endorsed this item had done more than just experiment with cigarettes. Among the Australian twins, persistence in smoking was determined by the absence of a reported age for quitting, among those who had endorsed ever smoking, so respondents who overlooked that item may have been incorrectly classified as nonsmokers. However, our finding that heritability estimates could be constrained across Australian and Scandinavian samples suggests that any reduction in reliability must have been slight.

As reported by Madden *et al.* (1999), across all three societies the prevalences of lifetime and persistent smoking in men and women were higher in twins whose cotwin chose not to participate than in pairs where both twins responded to the questionnaire survey. Since smoking is familial, the nonresponding cotwins were more likely to have a history of smoking then the randomly chosen twin, indicating that smokers may have been undersampled. As in many previous studies on substance use measures (e.g., Heath and Madden, 1995), significant zygosity differences in prevalence were observed, which necessitated the estimation of separate thresholds for MZ and DZ pairs. There is also a problem with censoring of data for smoking persistence, i.e., some younger smokers currently labeled as "persistent" will not have been smoking for many years and might be identified as ex-smokers if they were assessed at an older age.

Conclusion

In conclusion, we find evidence for substantial specificity of genetic influences on liability for smoking persistence, and this is especially true in later adulthood. Given the high economic and public health costs of persistent smoking, this suggests that gene-mapping studies focused on identifying genes that predict long-term persistent smoking should be a high priority.

ACKNOWLEDGMENTS

This work was supported by NIH Grants DA00272, DA12540 (to P.A.F.M.), AA07535, AA11998, and AA07728 (to A.C.H.), a grant from the Alcohol Beverage and Medical Research Foundation (to P.A.F.M.), Swedish Council for Planning and Coordination of Research Grant 970763:4 (to N.L.P.), Australian NH & MRC Grant 941177 (to N.G.M.), support from the Academy of Finland, and Grants 38332 and 42044 (to J.K. and M.J.K.). The authors would like to acknowledge the Australian Twin Registry maintained by the Australian National Health and Medical Research Council; the Finnish Twin Cohort Study managed through the Department of Public Health, Helsinki University; and the Swedish Twin Registry administered through the Division of Epidemiology, Institutet of Environmental Medicine, Karolinska Institutet.

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Edited by Richard J. Rose