Psychological Medicine, 2004, **34**, 1263–1269. © 2004 Cambridge University Press
DOI: 10.1017/S0033291704002417 Printed in the United Kingdom

Level of family dysfunction and genetic influences on smoking in women

KENNETH S. KENDLER*, STEVEN H. AGGEN, CAROL A. PRESCOTT, KRISTEN C. JACOBSON AND MICHAEL C. NEALE

Department of Psychiatry, Medical College of Virginia/Virginia Commonwealth University, Richmond, VA, USA; Department of Human Genetics, Medical College of Virginia/Virginia Commonwealth University, Richmond, VA, USA; Virginia Institute for Psychiatric and Behavioral Genetics, Richmond, VA, USA

ABSTRACT

Background. An adoption study of alcoholism suggests that in women, the impact of genetic risk factors become greater in the presence of conflict in the family of origin. Is the same true for cigarette smoking (CS)?

Method. We obtained, in a sample of 1676 twins from female–female twin pairs from a population-based register, a measure of maximum lifetime CS (divided into six ordinal categories) and family dysfunction (FD) assessed as the mean report of up to four informants (twin, co-twin, mother, father). Statistical analysis was conducted by traditional regression analysis and a moderator structural equation twin model using the computer program Mx.

Results. With increasing levels of FD, maximum CS increased substantially while correlations for CS in monozygotic (MZ) and dizygotic (DZ) twins decreased modestly. Regression analyses demonstrated reduced twin-pair resemblance for CS with increasing levels of FD. The best-fit structural equation model found high levels of heritability for CS and no evidence for a role of shared environment. With increasing levels of FD, the proportion of variance in CS due to genetic factors (i.e. heritability) decreased while that due to unique environmental effects increased.

Conclusions. Several different statistical methods suggested that, contrary to prediction, heritability of CS decreased rather than increased with higher levels of dysfunction in the family of origin. The hypothesis that genetic effects for psychiatric and drug-use disorders become stronger in more adverse environments is not universally true.

INTRODUCTION

A disrupted home environment is associated with an increased risk for smoking (Tyas & Pederson, 1998). In this report, we examine a different mechanism by which the home environment may impact on smoking behavior – *by moderating the effects of genetic influences*.

Various aspects of the family environment have been proposed as modifying the effect of genetic risk factors for several psychiatric and substance-use disorders including conduct disorder (Cadoret *et al.* 1995), antisocial personality (Cadoret *et al.* 1983), schizophrenia (Tienari, 1991) and alcoholism (Cutrona *et al.* 1994). For all these disorders, the difference in risk for those with and without a genetic predisposition is greatest in those exposed to a pathogenic rearing environment. In particular, Cutrona *et al.* found in an adoption design that in women, the impact of genetic risk factors for alcoholism become greater in the presence of conflict in the adoptive family. We are unaware of any study of this form of genotype × environment interaction on any other form of psychoactive substance use.

* Address for correspondence: Dr K. Kendler, Medical College of Virginia, Box 980126, Richmond, VA 23298-0126, USA.

In this report, we examine whether the level of family dysfunction (FD) influences the heritability of cigarette smoking (CS). CS is a useful model for psychoactive substance use because it is a common, highly heritable (Sullivan & Kendler, 1998; Kendler *et al.* 1999; Li *et al.* 2003) and public behavior about which relatively accurate self-report measures can be obtained (Luepker *et al.* 1989; Slattery *et al.* 1989).

In accord with the prior results with alcoholism, our *a priori* hypothesis was that FD would moderate the impact of genes on CS, such that the heritability of CS (that is, the proportion of variance in liability to CS that was due to genetic factors) would increase with increasing levels of FD in the home of origin.

METHOD

Sample

The twins in this study were sampled from the population-based Virginia Twin Registry (Kendler & Prescott, 1999) which now constitutes part of the Mid-Atlantic Twin Registry. These female–female twin pairs, from birth years 1934–1974, became eligible if both members previously responded to a mailed questionnaire, the response rate to which was ~64%. They have been approached for four subsequent waves of personal interviews from 1988 to 1997, with cross-wave cooperation rates ranging from 85 to 92%. During 1990–1991, all cooperative parents (90% of those available) were personally interviewed. Zygosity was determined by a combination of standard questions (Eaves *et al.* 1989), photographs and DNA analysis (Spence *et al.* 1988; Kendler & Prescott, 1999). For these analyses, from the fourth interview wave, ~2400 twins were potentially eligible of whom complete data were available on 1676 (~70%). This sample included 435 complete monozygotic (MZ), 300 complete dizygotic (DZ) pairs and 204 unpaired twins (103 from MZ and 101 from DZ pairs).

Measures

In our fourth wave of personal interviews, we first asked twins 'Have you ever smoked cigarettes?' If the answer to that question was yes, we later asked 'What is the greatest number of cigarettes you've ever smoked during a week?' We coded the responses to these two items into six categories reflecting maximum weekly cigarette intake: (i) zero (34·5% of the sample), (ii) $\leqslant 2$ (16·2%), (iii) >2 and $\leqslant 20$ (15·7%), (iv) >20 and $\leqslant 120$ (11·1%), (v) >120 and $\leqslant 200$ (14·7%) and (vi) >200 (7·8%).

FD was measured using 14 items chosen from the Family Environment Scale (Moos & Moos, 1986) which reflected the general emotional tone of the home when 'the twins were growing up', that is up to age 16. Data were collected from the twins and their parents during 1990–1991 and rated on a 4-point-scale (often to never). Two sample items are:

> Family members really helped and supported one another.
> Family members would get so angry sometimes that they would throw things or hit each other.

A categorical variable factor analyses on these 14 items, carried out in the program Mplus (Muthen & Muthen, 1998), produced eigenvalues for the first four factors of 5·56, 1·73, 0·91 and 0·83 respectively. The first unrotated principal factor had loadings in excess of +0·40 for 12 of the 14 items. In the interest of parsimony, our analyses treated these 14 items as a single dimension, reverse-coding certain items so that increasing scores reflected higher levels of FD. Scores obtained from the mother, father and twins were separately standardized. The number of reporters for the measures of FD were as follows: 4 (twin, co-twin, mother, father) – 50%, 3 (most typically, twin, co-twin and mother) – 32%, 2 (usually twin and co-twin) – 13% and 1 (self) – 5%. The inter-informant correlations for FD scores ranged from +0·35 to +0·58 with a mean (S.D.) of +0·41 (0·08). We then took the within-family average of Z scores for FD from all available reporters and re-scaled it to range between 0 and 1. This variable – which was always the same for both members of a twin pair – served as the moderator variable for the interaction model.

Model-fitting

Our major goal was to determine whether the heritability of CS was influenced by the level of reported FD. In these analyses, while FD was continuously distributed, CS was treated as a polychotomous variables. As in typical twin modeling, we divided the sources of individual

https://doi.org/10.1017/S0033291704002417 Published online by Cambridge University Press

differences into those due to additive genetic effects (A or a^2), shared or 'common' environment (C or c^2) and individual-specific or 'unique' environment (E or e^2). This model allows for the direct regression of FD onto the liability to CS, the 'basal' or unmoderated effect of A, C and E on CS and an effect of A, C and E on CS that is moderated by the level of FD. (When – as in these analyses – the environmental effects are perfectly correlated within twin pairs, the model cannot estimate the correlation between the genetic or shared environmental factors that impact on the basal *versus* moderated levels of CS.)

We are particularly interested in three models. We present the models here from simplest to most complex. The simplest is the *standard* model – in which the moderated pathways to CS are set to zero. The model estimates a single value for the proportion of variance in CS that is due to a^2, c^2 and e^2 and this value is independent of the level of FD. In this model, the total variance in liability to CS is independent of the level of FD. The *scalar* model predicts that the variance in liability to CS changes as a function of FD. However, across the range of FD, the scalar model assumes that the proportion of variance in liability to CS that is due to a^2, c^2 and e^2 is invariant. Since genetic variance changes proportionally with total variance in this model, heritability remains constant. The key assumption of the *moderator* model is that the proportion of variance in liability that is due to a^2, c^2 and e^2 changes as a function of the level of FD. The moderator model used in these analyses also predicts that the total variance in liability to CS changes as a function of FD.

In our previous application of this model (Kendler *et al.* 2003), the dependent variable was continuous and therefore had a measurable variance. In the present application, the variance in liability is latent. However, changes in the variance of liability to CS are manifested as changes in the prevalence of our CS categories. An increase in variance effectively moves the thresholds towards the mean; it predicts greater frequencies in the more extreme categories. Conversely, a decrease in variance reduces the proportion of the sample expected to fall in the extremes, while increasing the representation of those categories closer to the mean. For binary data, changes in variance and changes in mean are typically indistinguishable, but for ordinal data with at least three categories it is possible to distinguish between changes in variance and changes in mean. This multiple threshold model therefore equals the informativess of continuous data qualitatively, in that changes in both mean and variance may be assessed. In terms of quantity, the precision of these estimates will be less than those obtained using continuous data from a similar sample.

The full model, in these analyses, is the moderator model including the scalar and standard models as nested submodels. However, before we fit these submodels, we try to simplify the full model by constraining A or C paths to be zero. Mx fits these models to the raw data by maximum likelihood. While taking into account missing patterns of data, we compare the fits of these models by both the χ^2 difference test [where $\Delta\chi^2 = -2(\ln L_i - \ln L_j)$, where L_i and L_j are -2 times the likelihoods of alternative models i and j] and Akaike's Information Criterion (AIC) (Akaike, 1987), where lower values indicate a more favorable balance of parsimony and explanatory power (Williams & Holahan, 1994). Our polychotomous logistic regression analyses used general estimating equations (Liang & Scott, 1986) to correct for the correlational structure of the twin pairs.

RESULTS

Preliminary analyses

The level of FD strongly and positively predicted the category of maximum weekly CS ($\chi^2_1 = 62{\cdot}3$, $p < 0{\cdot}0001$). Because of this, we allowed FD to directly influence threshold levels of CS in all of our twin models.

Our *a priori* hypothesis – that FD and genetic risk factors for CS positively interact in the etiology of CS – predicts that the similarity in twin pairs for level of maximum CS should increase as the level of FD increases. Prior to formal model-fitting, we explored the support for this prediction in our data in three different ways. First, we divided our sample into quartiles based on FD scores and examined, in each quartile, the mean category level of CS and the polychoric correlation for CS in MZ and DZ pairs (Fig. 1). The mean level of maximum CS increased substantially with increasing levels of FD (although this increase was pronounced only in the upper two quartiles of FD). The

https://doi.org/10.1017/S0033291704002417 Published online by Cambridge University Press

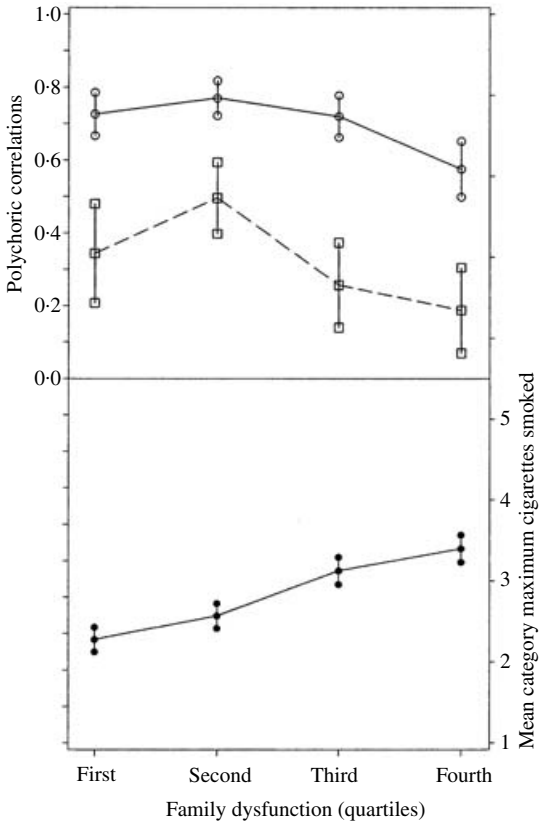

FIG. 1. Changes (±95% CI) in the MZ and DZ twin polychoric correlations for a six-category classification of maximum lifetime weekly cigarette smoking and the mean smoking category (±95% CI) as a function of the quartiles of family dysfunction. Open circles (○) indicate MZ twins and open squares (□) indicate DZ twins. Solid circles (●) indicate the mean of the following smoking categories reflecting maximum weekly cigarette intake: (1) zero, (2) less than 2, (3) between 2 and 20, (4) between 20 and 120, (5) between 120 and 200 and (6) greater than 200.

pattern of twin correlations did not resemble that predicted by our hypothesis. The correlation in MZ twins is similar at the two lower quartiles of FD and then decreases with increasing FD scores. The pattern in DZ twins is similar except that twin resemblance for CS is greater in the 2nd than the 1st quartile of FD.

Second, in individual twins, we predicted the category of CS in twin2 from the category of CS in twin1, level of FD and the interaction between them. The main effects of twin1 CS ($\chi^2_1 = 52{\cdot}6$, $p < 0{\cdot}0001$) and FD ($\chi^2_1 = 15{\cdot}0$, $p < 0{\cdot}0001$) were both significant. More importantly, the interaction between FD and CS in twin1 was negative and significant in the prediction of CS in twin2 ($\chi^2_1 = 5{\cdot}10$, $p = 0{\cdot}02$). This means that, as levels of FD increased, CS in one twin became a progressively poorer predictor of CS in her co-twin.

Third, we predicted, from FD scores, the absolute value of the difference in categories of maximum CS between the twins. In all twin pairs, FD was positively and significantly related to the difference in CS in the twin pairs ($\chi^2_1 = 7{\cdot}87$, $p = 0{\cdot}006$). That is, as FD increased, the between-twin difference in maximum CS significantly increased.

Model-fitting

The results of model-fitting are presented in Table 1 with parameters estimated for two conditions. In the first or unmoderated condition, FD – the moderator variable – is set at its minimal value of zero. Thus, this condition gives a picture of results for very well functioning families where FD is effectively absent. The second condition is where FD is set at its maximal value of unity. This gives us a picture of the results for families with very high levels of dysfunction.

Our full or moderator model produced a fit of $-2 \ln L = 5022{\cdot}3$ with 1574 df. We set the AIC for this model at zero so its fit could be used as a baseline against which to compare the fit of subsequent submodels. As seen in Table 1, this model estimated that the variance of CS increases with increasing levels of FD. The heritability of CS is *higher* when FD levels are at a minimum ($a^2 = 0{\cdot}79$) than when they are at a maximum ($a^2 = 0{\cdot}57$). Individual-specific environment has the reverse pattern – being more important at maximum ($e^2 = 0{\cdot}43$) than minimum ($e^2 = 0{\cdot}21$) levels of FD. The effect of shared family environment is estimated to be zero in all conditions.

These results arise because the magnitude of the genetic variance in liability to CS is estimated to be stable across levels of FD while individual-specific environmental variance increases with increasing dysfunction. Therefore, it follows that, as FD increases, heritability (which is just the ratio of genetic to total variance in liability) declines because of increasing environmental variance not decreasing genetic variance.

Before going on to further model-fitting, we simplify the model by constraining the shared

https://doi.org/10.1017/S0033291704002417 Published online by Cambridge University Press

Table 1. *Parameter estimates for the sources of variation in liability to maximal weekly cigarette smoking as a function of level of family dysfunction*

	Parameter	Full moderator	Reduced moderator	Scalar	Standard
Unmoderated (when moderator at minimum)	a^2	0·79	0·79	0·70	0·70
	CI	0·58–0·90	0·64–0·90	0·64–0·75	0·64–0·75
	c^2	0·00	—	—	—
	CI	0·00–0·19	—	—	—
	e^2	0·21	0·21	0·30	0·30
	CI	0·10–0·32	0·10–0·32	0·25–0·36	0·25–0·36
	Variance	1·00	1·00	1·00	1·00
	CI	—	—	—	—
When moderator at maximum	a^2	0·57	0·57	0·70	0·70
	CI	0·40–0·71	0·46–0·70	0·64–0·75	0·64–0·75
	c^2	0·00	—	—	—
	CI		—	—	—
	e^2	0·43	0·43	0·30	0·30
	CI	0·29–0·54	0·30–0·54	0·25–0·34	0·25–0·36
	Variance	1·39	1·39	1·36	1·00
	CI	1·02–2·12	1·02–2·12	1·00–2·50	—
$\Delta\chi^2$		—	0	3·6	4·6
Δdf		—	2	3	4
ΔAIC		—	−4·0	−2·4	−3·4

CI, 95% Confidence interval.
a^2, Additive genetic effects; c^2, shared environmental effects; e^2, individual-specific environmental effects.
df, Degree of freedom.
AIC, Akaike's Information Criterion.
Variance, variance in latent liability to cigarette smoking.

environmental parameters to zero. This produces the reduced moderator model. The fit of the model does not change and the AIC improves to −4. By constraining the proportion of variance in liability to CS due to a^2 and e^2 to be constant across values of FD, we produced the scalar model. Compared to the reduced moderator model, the fit of this model increases by 3·6 χ^2 units and the AIC deteriorates to −2·4. This model, as required by its constraints, estimates that the heritability of CS is constant but the variance in liability to CS increases with increasing levels of FD.

By constraining the variance of liability to CS to be constant across all values of FD, we then produce the standard model which fits slightly better than the scalar model (AIC = −3·3). As expected, the heritability estimates for CS were identical for the scalar and standard models and equal to 0·70.

COMMENT

The goal of this report was to determine if a broad measure of dysfunction in the family of origin – averaged across reports by twins and their parents – modified the impact of genetic risk factors on maximum weekly CS. Consistent with other reports (Sullivan & Kendler, 1998; Li *et al*. 2003), we found CS to be highly heritable. Two recent reviews (Sullivan & Kendler, 1998; Li *et al*. 2003) have both noted that the role of shared environmental factors are more pronounced in studies that examine smoking initiation than in studies that examine either nicotine dependence or traits, such as smoking persistence or quantity of cigarettes smoked, that are proxies for the level of dependence. Our results, which detect no evidence for shared environmental influences on maximum weekly cigarette consumption, are consistent with these prior trends in the literature.

In accord with prior studies of psychiatric and alcohol-use disorders (Cadoret *et al*. 1983, 1995; Tienari, 1991; Cutrona *et al*. 1994), we predicted that heritable factors for CS would be more important in twin pairs exposed to high *versus* low levels of FD. More specifically, we predicted that the moderator model would fit the data best and this model would show increasing heritability with increasing level of FD. However, while the moderator model did indeed

https://doi.org/10.1017/S0033291704002417 Published online by Cambridge University Press

provide the best fit, the parameter estimates indicated results opposite to those predicted. With increasing levels of FD, the variance due to individual-specific environmental effects on CS increased while the heritability declined. Our confidence in these findings is augmented by parallel findings from two simpler regression-based analyses, both of which suggested that twin similarity for maximum CS decreased as levels of FD increased as well as the raw pattern of the twin correlations when divided into quartiles of FD scores (Fig. 1).

We are aware of only one study which explored the interaction between genetic risk and FD in the prediction of a psychoactive substance-use-related phenotype. In an adoption cohort ascertained in Iowa, Cutrona *et al.* (1994) found that adoptive women with an alcoholic biological background were at increased risk for alcoholism only in the presence of high levels of adoptive family conflict, as assessed by the same instrument used in this study (Moos & Moos, 1986). They found no such interactive effect in males. Two other adoption studies of alcoholism, both performed in Sweden (Cloninger *et al.* 1981; Cutrona *et al.* 1994) also provide relevant results. Both studies found that an increased risk for 'severe' alcohol abuse was found only in adopted sons who had both a genetic predisposition and a set of post-natal environmental risk factors including longer contact with biological mother and low occupational status of the adoptive father.

Two other studies are of possible relevance in the interpretation of the current findings. First, in a prior analysis of this twin sample, using similar methods, we found no evidence that increasing levels of FD moderated the effect of genes on the personality trait of neuroticism (Kendler *et al.* 2003). Second, in an analysis of regular tobacco use in Swedish female twins born in the first half of the 20th century, we found evidence that heritability of tobacco use could be modified by environmental effects in that as prevalence increased in more recent cohorts, heritability increased as well (Kendler *et al.* 2000).

Our knowledge about the role of gene–environment interactions in drug-use-related phenotypes is too limited to support any detailed speculation about the differences between our present results and those of prior relevant studies. With respect to the most similar study by Cutrona *et al.* (1994), smoking differs in many ways from alcoholism and our twin-based method of assessing interactions between genes and aspects of the family environment was quite different from that used in this adoption study. Nonetheless, given our state of comparative ignorance, our findings in this report and our prior study of genotype × environment interactions in this sample (Kendler *et al.* 2003) suggest caution in the articulation of broad laws about the nature of these interactions such as 'heritability will increase in the presence of environmental adversity'. The reality is likely to be far more complex.

Limitations

These results should be interpreted in the context of five potential methodological limitations. First, the sample was restricted to Caucasian female twins born in Virginia and it is unknown whether these results would extrapolate to other ethnic or geographical populations or males. Second, this paper reports the first application of a recently developed structural model for genotype × environment interaction to an ordinal variable modeled as a multiple-threshold trait rather than continuous dependent variable. A recent series of power analyses assuming a continuous dependent variable suggests that the method has reasonable power for sample sizes on the order of those studied in this report (Purcell, 2002). However, the use of a multiple-threshold model, where changes in variance of the underlying latent liability cannot be directly measured but must be inferred from changes in prevalence, poses additional interpretative questions.

Third, the observed increase in individual-specific environmental variance for CS with higher levels of FD could result from 'true' environmental effects or from increased errors of measurement, as in standard twin studies based on only one time of assessment, these two sources of variance are entirely confounded. Because the mean level of CS was so strongly linked with the level of FD, this pattern could occur from heteroscedasticity – in which the error variance of our measure of CS increased with the mean. We examined the test–retest reliability of our categories of maximum CS in 192 twins interviewed twice with a mean (±S.D.)

https://doi.org/10.1017/S0033291704002417 Published online by Cambridge University Press

inter-interview interval of 30 (±9) days apart. The reliability of our CS measure was very high (weighted $k = +0{\cdot}87$; 95% CI +0·83–0·90) with no evidence that degree of agreement was related to the level of CS. We also tested whether the level of FD impacted on the stability of cross-time CS measures. It did not ($\chi^2_1 = 0{\cdot}19$, $p = 0{\cdot}66$). These results suggest that increasing error variance for our measure of CS with increasing levels of FD is an unlikely explanation for the observed results.

Fourth, the differences in fit between our reduced moderator, scalar and standard models were modest and it was not possible to chose one model over another with a high degree of certainty. However, it was possible, with more confidence, to reject our prior hypothesis of increasing genetic variance and heritability for CS with increasing levels of FD. Neither the model-fitting nor the two simpler regression-based models provided any support for this hypothesis.

ACKNOWLEDGMENTS

This work was supported by NIH grants MH-40828, MH/AA/DA-49492, MH-65322, DA-11287 and AA-09095 and the Virginia Tobacco Settlement Foundation (Contract no. 8520012) through the Virginia Youth Tobacco Project, Virginia Commonwealth University. Mx was developed with funding from RR-08123 and MH-01458. We acknowledge the contribution of the Virginia Twin Registry, now part of the Mid-Atlantic Twin Registry (MATR), to ascertainment of subjects for this study. The MATR, directed by Dr L. Corey, has received support from the National Institutes of Health, the Carman Trust and the WM Keck, John Templeton and Robert Wood Johnson Foundations.

DECLARATION OF INTEREST

None.

REFERENCES

Akaike, H. (1987). Factor analysis and AIC. *Psychometrika* **52**, 317–332.

Cadoret, R. J., Cain, C. A. & Crowe, R. R. (1983). Evidence for gene–environment interaction in the development of adolescent antisocial behavior. *Behavior Genetics* **13**, 301–310.

Cadoret, R. J., Yates, W. R., Troughton, E., Woodworth, G. & Stewart, M. A. (1995). Gene–environment interaction in genesis of aggressivity and conduct disorders. *Archives of General Psychiatry* **52**, 916–924.

Cloninger, C. R., Bohman, M. & Sigvardsson, S. (1981). Inheritance of alcohol abuse: cross-fostering analysis of adopted men. *Archives of General Psychiatry* **38**, 861–868.

Cutrona, C. E., Cadoret, R. J., Suhr, J. A., Richards, C. C., Troughton, E., Schutte, K. & Woodworth, G. (1994). Interpersonal variables in the prediction of alcoholism among adoptees: evidence for gene–environment interactions. *Comprehensive Psychiatry* **35**, 171–179.

Eaves, L. J., Eysenck, H. J., Martin, N. G., Jardine, R., Heath, A. C., Feingold, L., Young, P. A. & Kendler, K. S. (1989). *Genes, Culture and Personality: An Empirical Approach.* Academic Press: London.

Kendler, K. S., Aggen, S. H., Jacobson, K. C. & Neale, J. M. (2003). Does the level of family dysfunction moderate the impact of genetic factors on the personality trait of neuroticism? *Psychological Medicine* **33**, 817–825.

Kendler, K. S., Karkowski, L. M. & Pedersen, N. C. (2000). Tobacco consumption in Swedish twins reared-apart and reared-together. *Archives of General Psychiatry* **57**, 886–892.

Kendler, K. S., Neale, M. C., Sullivan P. F., Corey, L. A., Gardner, C. O. & Prescott, C. A. (1999). A population-based twin study in women of smoking initiation and nicotine dependence. *Psychological Medicine* **29**, 299–308.

Kendler, K. S. & Prescott, C. A. (1999). A population-based twin study of lifetime major depression in men and women. *Archives of General Psychiatry* **56**, 39–44.

Li, M. D., Ching, R., Ma, J. Z. & Swan, G. E. (2003). A meta-analysis of estimated genetic and environmental effects on smoking behavior in male and female adult twins. *Addiction* **98**, 23–31.

Liang, K.-Y. & Scott, L. Z. (1986). Longitudinal data analysis using generalized linear models. *Biometrika* **73**, 13–22.

Luepker, R. V., Pallonen, U. E., Murray, D. M. & Pirie, P. L. (1989). Validity of telephone surveys in assessing cigarette smoking in young adults. *American Journal of Public Health* **79**, 202–204.

Moos, R. & Moos, B. (1986). *Family Environment Scale Manual* (2nd edn). Consulting Psychologists Press: Palo Alto, CA.

Muthen, L. K. & Muthen, B. O. (1998). *Mplus: The Comprehensive Modeling Program for Applied Researchers; User's Guide*. Muthen & Muthen: Los Angeles, CA.

Purcell, S. (2002). Variance components models for gene-environment interaction in twin analysis. *Twin Research* **5**, 554–571.

Slattery, M. L., Hunt, S. C., French, T. K., Ford, M. H. & Williams, R. R. (1989). Validity of cigarette smoking habits in three epidemiologic studies in Utah. *Preventive Medicine* **18**, 11–19.

Spence, J. E., Corey, L. A., Nance, W. E., Marazita, M. L., Kendler, K. S. & Schieken, R. M. (1988). Molecular analysis of twin zygosity using VNTR DNA probes [Abstract]. *American Journal of Human Genetics* **43**, A159.

Sullivan, P. F. & Kendler, K. S. (1998). The genetic epidemiology of smoking. *Nicotine and Tobacco Research* **1**, S51–S57.

Tienari, P. (1991). Interaction between genetic vulnerability and family environment: the Finnish adoptive family study of schizophrenia. *Acta Psychiatrica Scandinavica* **84**, 460–465.

Tyas, S. L. & Pederson, L. L. (1998). Psychosocial factors related to adolescent smoking: a critical review of the literature. *Tobacco Control* **7**, 409–420.

Williams, L. J. & Holahan, P. J. (1994). Parsimony-based fit indices for multiple-indicator models: do they work? *Structural Equation Modeling* **1**, 161–189.