Correlates of regular cigarette smoking in a population-based sample of Australian twins

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Submitted 14 December 2004;
initial review completed 4 February 2005;
final version accepted 29 April 2005

ABSTRACT

Aims To investigate the role of measured risk factors and the influence of genetic and environmental factors on regular cigarette smoking.

Design Members of monozygotic and dizygotic, including unlike-sex twin pairs ($n = 6257$) from a young adult cohort from the Australian Twin Registry.

Methods Cox proportional hazards models were used to determine whether putative risk factors were significantly associated with regular cigarette smoking. Risk factors were classified into four tiers: tier 1 (parental history, including parental education, alcoholism and cigarette smoking), tier 2 (early home and family influences), tier 3 (early life events, e.g. trauma) and tier 4 (psychiatric symptoms/disorders with onset prior to 14 years), after controlling for gender, zygosity and their interactions. Genetic models were fitted to examine the heritability of smoking behavior before and after controlling for significant covariates from the four tiers.

Findings Parental history of cigarette smoking and alcoholism, parental closeness and home environment, as well as incidence of childhood sexual abuse or other trauma, a history of early onset panic attacks and conduct problems were associated with regular cigarette smoking. Important age interactions were found, particularly for family background risk factors. Regular cigarette smoking was moderately heritable, even after accounting for significant covariates.

Conclusions Several measured risk factors are associated with regular smoking. While some of the genetic influences on regular smoking may be shared with these risk factors, a significant proportion of the genetic vulnerability to regular smoking is phenotype-specific.

KEYWORDS Cigarette smoking, early onset, risk factors, survival model.

INTRODUCTION

Nearly 3.1 million US adolescents smoke cigarettes on a weekly basis [1]. Regular cigarette smoking, which is a necessary precursor to nicotine dependence, has become a significant source of morbidity and mortality, claiming multiple lives due to a variety of lung diseases and cancers associated with extended smoking [2]. Regular cigarette smoking (commonly defined as smoking 100 or more cigarettes and/or smoking as often as twice a week) is also correlated with a number of putative risk factors. These risk factors may be measured (e.g. parental monitoring, conduct problems) or latent (e.g. a genetic predisposition). In the present study, we sought to identify significant measured correlates of regular cigarette smoking and to examine the role of genetic, shared and unique environmental influences on regular cigarette smoking before and after controlling for these covariates.

Several twin studies have explored the genetic etiology of smoking behavior. Reviews of the literature suggest

 doi:10.1111/j.1360-0443.2005.01217.x

that regular cigarette smoking is moderately heritable (46–56%). Shared environmental influences or the environmental factors shared by members of a twin pair also account for a modest proportion of the variance, although their influence appears to attenuate with age [3–5]. None of these studies have accounted for measured risk factors or covariates in their twin models. The presence of the confounding influence of covariates may result in higher rates of concordance in identical (MZ) versus fraternal (DZ) twins. Consequently, the heritability estimates [2*(Rmz-Rdz)] from such studies may have been somewhat biased. By using retrospectively reported data, we can isolate a number of measured risk factors that are correlated with regular smoking and control for their phenotypic influence on the twin model. The resulting model would be better equipped to provide estimates of variance due to genetic and environmental factors on regular smoking.

A vast and rich literature suggests that a number of risk factors may be associated with regular smoking. Our selection placed emphasis on those factors that may have had an early age of manifestation and may have exerted a greater influence in adolescence rather than adulthood.

First, we selected risk factors that assessed a family history of smoking and drinking. Parental attitudes and beliefs regarding smoking play a pivotal role in the smoking habits of the offspring [6–8]. Parental alcohol consumption and heavy drinking have also been implicated as a potential risk factor for smoking in adolescence.

Secondly, we considered familial influences such as family connectedness and bonding, authoritative parenting style and disruptive home environment as putative correlates of regular cigarette smoking. Numerous studies have verified the robust associations between parental bonding, parenting style and drug use [9]. Chilcoat & Anthony showed a positive correlation between low parental monitoring and initiation of alcohol, tobacco and drug use [10]. Measures of poor academic achievement, conflicts with parents and risk-taking behavior (e.g. early sexual intercourse) may also be correlated with regular smoking. Using data from two national samples, Bryant *et al*. showed a positive association between school misbehavior and escalation in cigarette use [11]. Storr and colleagues also noted increased rates of smoking in children with higher scores for teacher-rated misbehavior [12]. Disobedience and misbehavior may be inextricably bound to the home environment (e.g. resulting from harsh parenting or poor family cohesion) and may also be symptomatic of more severe and non-normative behavior with smoking as one aspect. Early indices of conduct disorder or antisocial personality disorder may include conduct problems, early sexual initiation, general deviancy and early-onset alcohol and tobacco use, making these factors essential in a survey of risk factors for regular cigarette smoking [13].

Finally, we also included psychiatric conditions, such as depression, social anxiety disorder and panic disorder. Several studies have demonstrated that these measures of psychiatric illness may be associated with regular cigarette smoking [14–17].

The present study has three goals: (i) to investigate the extent of association between 44 risk factors (classified into four tiers) and regular cigarette smoking; (ii) to test whether any of these associations were punctuated by age of onset for regular cigarette smoking; and (iii) to examine the genetic etiology of regular cigarette smoking after accounting for significant covariates identified from (i) and (ii).

MATERIALS AND METHODS

Participants

The Australian Twin Registry (ATR) is a volunteer panel of same-sex monozygotic (MZ) and dizygotic (DZ) twins and opposite-sex dizygotic (DZOS) twin pairs. Founded in 1978, the ATR consists of two cohorts of twins. Twins born before 1964 are members of the older cohort (or cohort 1) [18], while twins born between 1964 and 1971 constitute the young adult cohort (cohort 2) [19] used for this study. Cohort 2 was ascertained through the school systems and via media invitations. All consenting twins in cohort 2 were administered a semistructured interview via telephone, during the period of 1996–2000 (Semi-Structured Assessment for the Genetics of Alcoholism: SSAGA) [20]. The interview included assessments of smoking and nicotine dependence as well as pertinent psychiatric diagnoses and information on putative risk factors. Of the 8536 twins targeted for participation in cohort 2, 6257 individual twins were interviewed telephonically. The male compliance rate was 77.7% and the female compliance rate was 68.6% Further details regarding data collection and ascertainment are available elsewhere [21].

Sample characteristics

The sample consists of 3454 Caucasian females with an average age of 30.1 years (SD 2.5) and 2803 Caucasian males with an average age of 30.0 years (SD 2.5). Half the sample reported being currently married, 43% reported having never been married and the remainder reported being divorced, widowed or separated at the time of the interviews. About 10% of the sample reported having 10 years or less of schooling while 10% of the sample reported having earned a university postgraduate

diploma. The remaining 80% included individuals with 11–12 years of schooling or 8–10 years of schooling plus an apprenticeship or diploma or both and 25% of the sample had studied in a teacher's or technical college or received a university degree. Also, 66% of the participants had full-time jobs while 30% were either students, homemakers or employed on a part-time basis (4% unemployed). Approximately 90% of sample reported life-time tobacco use and 50% met the criteria for life-time regular cigarette smoking with a mean age of onset of 16.2 years (SD 3.7) for life-time regular cigarette smoking.

Measures

Dependent measure

For all statistical analyses, the dependent measure was self-reported history of regular cigarette smoking operationalized as smoking between 20 and 100 times in their life-time and as often as 1 or 2 days a week (or daily) for a period of 3 weeks or longer. Individuals who reported having smoked 100 or more cigarettes in their life-time but did not report daily or weekly smoking were also included. Age of onset for regular cigarette smoking was defined as the age at which the participant reported smoking at least 1 day a week for 3 weeks or longer. Individuals who did not report having ever tried a cigarette even once in their life-time were not queried regarding their smoking habits. For the purposes of these analyses, non-smokers are coded as non-regular smokers (i.e. 0 for the binary phenotype).

Putative risk factors

Guided by the literature and based on the available data, 44 putative risk factors and three control variables were selected for the analyses. To simplify the survival analysis models, risk factors were classified, a priori, by the developmental period in which they were most likely to manifest and associate with regular cigarette smoking. We established a control tier (gender, zygosity, member of an opposite-sex DZ twin pair and interactions between (a) gender and zygosity and (b) between gender and DZOS membership) and the following four tiers for risk factor classification:

Tier 1. We hypothesized that the earliest developmental influences that may be related to regular cigarette smoking would include parental history measures. The family background measures in our data comprised twin reports on biological parents. Consequently, four measures were selected for this tier: (i) parental education level coded as 0 (neither parent had tertiary education = education after high school), 1 (either parent had tertiary education) and 2 (both parents had tertiary education); (ii) parental smoking status coded as 0 (neither parent smoked cigarettes = life-time ever-smoked), 1 (either parent smoked) and 2 (both parents smoked); (iii) parental heavy drinking coded as a dichotomous outcome (0 = no, 1 = yes) based on the twin's perception of their parent's excessive drinking; and (iv) parental problem drinking coded as a dichotomous outcome (0 = no, 1 = yes) based on twin's perception of their parent's drinking being a source of health, work, legal or family problems. Separate maternal and paternal drinking variables (heavy drinking and problem drinking) were used because we found evidence for a significant interaction of these two variables (but not for the parental smoking or parental education measures) with gender of parent.

Tier 2. Measures in the second tier were comprised of early family influences, including relationships with parents, presence of a step-parent and religious background. The following 31 putative risk and protective factors were selected for this tier. (A) Family structure: (i) presence of a step-parent (stepmother or stepfather); (ii) separation from the biological parent (mother and father); (iii) smoking status of the step-parent; (iv) interaction between smoking-status of step-parent and separation from the biological parent. (B) Family–child relationship: (i) frequency of unpleasant disagreements with parents (ages 6–13), coded on a 1–4 scale where 1 = never and 4 = often; (ii) closeness of relationship with parents (ages 6–13), coded as 1–4 scale where 1 = very close and 4 = not at all close; (iii) closeness to another adult; (iv) two items assessing frequency of parental arguments and conflicts in the household (ages 6–13), coded on a 1–4 scale where 1 = often and 4 = never. (C) Parental attitudes: (i) relative lack of importance of school performance (ages 6–13); (ii) parental denial of permission to allow twins to bring friends over to play (ages 6–13); (iii) relative lack of rules regarding chores and three items assessing strictness, frequent disobedience and fairness in scolding; (D) Parental discipline: (i) four items assessing punishment and severity of punishment (frequency of being smacked, being hit with a stick or belt on a 1–4 scale where 4 = often, physical punishment that hurt the next day on a 1–4 scale where 4 = often and harsh punishment); (ii) physical injury or being hurt as a child (hurt intentionally by parent or other adult). (E) Other: (i) below average grades in primary school; (ii) parental heavy alcohol consumption when respondent was aged 6–13 years; (iii) incidence of sexual contact, before the age of 16, with someone outside the family; (iv) incidence of sexual contact, before the age of 16, with a family member; (v) religious affiliation (1 = non-catholic,

0 = catholic). Unless otherwise specified, items in tier 2 were dichotomous.

Tier 3. We used three variables: consensual intercourse by 13 years (dichotomous); traumatic events, such as injury, life-threatening accidents, molestation or physical abuse, scored on a scale ranging from 0 to 5 events and occurring before the age of 13 years; and early maturation coded dichotomously as the twin's response to a question on whether they considered themselves to have matured earlier than their peers.

Tier 4. In tier 4, we included psychiatric disorders or symptoms that were indicative of psychiatric disorders. All diagnoses and symptoms were adjusted by their ages of onset to reflect only early onset cases. All variables in tier 4 were dichotomous. We used the following five measures: (i) history of Diagnostic and Statistical Manual version IV (DSM-IV) major depressive disorder before 13 years; (ii) history of social anxiety before 13 years; (iii) panic attacks before 13 years; (iv) DSM-IV conduct disorder with onset before 13 years; and (v) two or more conduct problems (but not meeting full criteria for conduct disorder) with onset before 13 years.

Statistical analyses

Cox proportional hazards models were fitted in STATA [22] using the robust variance estimator to correct for clustering of data (familial correlations for twin pairs). The event of interest for the survival analysis was regular cigarette smoking and age of onset of regular cigarette smoking was the time to event (age at interview for non-regular smokers). Variables from tiers 1–4 were individually added to the equation that always included the control variables. Each risk factor was tested for a statistically significant association with regular cigarette smoking (P-value < 0.05). For each variable that was significantly associated with regular cigarette smoking, a test of the proportional hazards (PH) assumption was performed using Schoenfeld residuals [23]. We defined separate variables (age-ranges 0–11, 12–16, 17–21 and 22 + years) for variables with significant interactions with age. Equality across adjacent age-ranges was tested, *post-hoc*, using a Wald χ^2 test. Variables from each subsequent tier were always added to an equation that retained significant variables from the preceding tier. We also fitted a summary model where risk factors from all tiers were added in the same equation. Significant variable selection was performed using a backward stepwise selection process.

Genetic model

In the classical twin model, three sources contribute to the total variance in a phenotype: additive genetic (A) factors, shared environmental (C) factors and non-shared environmental (E) factors. Additionally, when data from DZOS twin pairs are available, quantitative (equating the magnitude of A, C, E across sexes) and qualitative (constraining the nature of A or C to be equal across sexes), gender differences can be examined. Gender difference models were fitted to the data using the software package Mx [24,25] and compared using the difference in χ^2. The DZ twin correlation was greater than half the MZ twin correlation (Rmz = 0.82 and 0.85, Rdz = 0.50 and 0.61 in females and males, respectively), suggesting that C rather than dominant (D) genetic influences should be considered. The uniqueness of the model-fitting in our study arises from our inclusion of all significant covariates (as fixed covariates) from the survival model. Model-fitting was performed initially without controlling for any covariates, followed by models that controlled for all significant covariates from Table 1 (summary model).

RESULTS

Rates of onset of regular smoking

Figure 1 depicts the Nelson–Aalen cumulative incidence survival plots for regular cigarette smoking for males and females. The plots indicate that there were no significant gender differences in the rates of onset of regular cigarette smoking.

Tier 1

Family history: descriptive statistics and results from the Cox proportional hazards models (hazard ratios (HR), SD and 95% confidence limits) for variables in tier 1 are presented in Table 2. Parental education was negatively associated with early onset regular cigarette smoking (0–11 years). Parental smoking and paternal heavy and problem drinking were positively associated with regular cigarette smoking. *Post-hoc* tests revealed the association between these risk factors and regular cigarette smoking was strongest (greatest effect size and significantly different from the HR for the other age groups) for the age-group of 0–11 years.

Tier 2

Early family influences: overall, separation from the biological parent and the presence of a stepmother were positively associated with regular cigarette smoking. These associations could not be explained by the introduction of a step-parent figure who smoked. However, a plausible reason for the lack of statistical significance may be low

Table 1 Hazards ratios (HR) and 95% confidence intervals for summary model.

Risk factor	*Hazard ratio*	*95% CI*
Control variables		
Gender	1.07	0.91–1.26
Zygosity	1.20	1.03–1.39
Member of a dizygotic opposite-sex (DZOS) pair	1.00	0.85–1.17
Interaction: zygosity and gender	0.93	0.74–1.17
Interaction: DZOS and gender	1.06	0.85–1.31
Tier 1: family history		
Parental education	0.91	0.84–0.97
Parental smoking	1.29	1.17–1.43
Paternal heavy drinking	1.23	0.64–1.18
Tier 2: home environment/familial influences		
Unpleasant conflicts with parents	1.27	1.19–1.42
Frequent disobedience	1.62	1.43–1.84
Hit hard to hurt the next day	1.33	1.22–1.49
Sexual contact: non-family	1.58	1.34–1.85
Religiosity	0.74	0.67–0.83
Below average grades	1.33	1.15–1.58
Tier 3: early life events		
Early intercourse	2.06	1.49–2.86
Tier 4: psychiatric diagnoses/symptoms		
Panic attacks	1.45	1.11–1.89
Conduct problems (2+)	1.53	1.36–1.72

Only significant *P*-values (<0.05) are depicted in Table 1 for a reduced model with control variables and risk factors from all tiers added together. The results reflect control variables and statistically significant results from tiers 1–4 (full model reduced by a backward stepwise process).

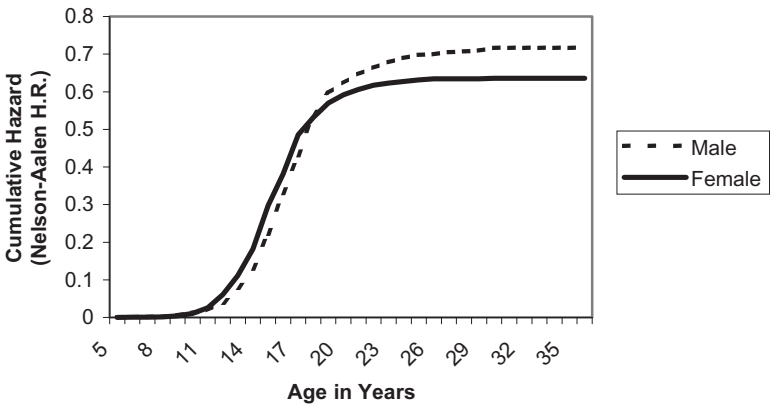

Figure 1 Nelson–Aalen cumulative hazard plot of regular cigarette smoking with age of onset of regular cigarette smoking

power, as only 2% of the females and 6% of the males reported having a step-parent and of those that had step-parents, about 50% were smokers. The 95% confidence intervals for the main-effect of step-parent smoking and the interaction are fairly wide, suggesting imprecision in the estimation of the HR. An interesting finding from tier 2 was the positive association between parental heavy drinking (when the twin was between the ages of 6–13) and regular cigarette smoking. The association between parental drinking behavior during the twin's childhood and regular cigarette smoking was significant even after controlling for overall parental heavy and problem drinking.

Conflicts with parents, parental strictness regarding schoolwork, chores, having friends over to play and disobedience were positively associated with regular cigarette smoking. Scolding that did not seem fair and harsh punishment including punching or hitting were also associated with onset of regular cigarette smoking. A large effect size was also observed for the association between regular cigarette smoking and reported sexual contact with a family member or a non-family member

Table 2 Hazard ratios and 95% confidence intervals for correlates of regular smoking.

Risk factor	*HR*	*95% CI*	*PH no.*	*Interaction with age: HR*
Parental education	0.82*	0.80–0.87	Yes	0–11 years: 0.73*
Parental smoking	1.38*	1.26–1.50	Yes	0–11, 11–16 years: 1.35,* 1.29*
Paternal heavy drinking	1.24*	1.08–1.41	No	–
Maternal heavy drinking	0.96	0.80–1.15	No	–
Paternal problem drinking	1.32*	1.20–1.45	Yes	0–11 years: 1.31*
Maternal problem drinking	1.09	0.90–1.33	No	–
Stepmother	1.50*	1.14–2.02	No	–
Stepfather	1.18*	1.03–1.40	No	–
Separation: mother	1.53*	1.06–2.18	No	–
Separation: father	1.08	0.78–1.22	No	–
Stepmother smoking	1.12	0.90–1.40	No	–
Stepfather smoking	1.35	0.90–2.02	No	–
Interaction: separation from mother/stepmother smoking	1.14	0.47–2.79	No	–
Interaction: separation from father/stepfather smoking	0.93	0.55–1.56	No	–
Unpleasant conflicts with parents	1.19*	1.13–1.26	Yes	0–11 years: 1.27*
Lack of parental closeness	1.12*	1.06–1.19	Yes	0–11 years: 1.23*
Confiding adult	1.07	0.97–1.18	Yes	11–16 years: 1.22*
Parental arguments	1.00	0.95–1.06	No	–
Inter-parent conflict	0.99	0.94–1.04	Yes	0–11 years: 1.08*
Importance of school performance	0.84*	0.73–0.96	Yes	0–11 years: 0.84*
Friends not allowed home to play	1.16*	1.02–1.33	No	–
Lack of rules for chores	0.93	0.84–1.05	No	–
Consistency of rules	1.05	0.96–1.15	No	–
Strictness	1.29*	1.10–1.52	No	–
Frequent disobedience	1.95*	1.75–2.19	Yes	0–11, 11–16 years: 2.13,* 1.50
Fairness in scolding	1.16*	1.10–1.22	Yes	11–16 years: 1.26*
Smacked by parents	1.09	1.00–1.18	Yes	0–11 years: 1.13*
Hit (belt, stick)	1.13*	1.07–1.18	Yes	0–11, 16–21 years: 1.15,* 1.35*
Hit hard to hurt next day	1.31*	1.23–1.41	Yes	0–11, 11–16 years: 1.32,* 1.15*
Harsh physical punishment	1.06*	1.03–1.10	No	–
Physical injury	1.58*	1.36–1.83	Yes	0–11 years: 1.08*
Below average grades	1.31*	1.12–1.54	Yes	0–11 years: 1.44*
Parental heavy drinking	1.15*	1.02–1.30	Yes	0–11 years: 1.23*
Sexual contact: family	1.85*	1.60–2.10	Yes	0–11, 11–16 years. 2.03,* 1.58*
Sexual contact: non-family	1.28*	1.07–1.54	Yes	0–11 years: 1.34*
Religiosity	0.75*	0.68–0.83	No	–
Early Intercourse	3.38*	2.59–4.41	Yes	0–11 years: 3.58*
Early maturation	1.20*	1.08–1.32	No	–
Traumatic events	1.15*	1.09–1.23	Yes	0–11 years: 1.16*
DSM-IV major depression	1.14	0.85–1.54	Yes	0–11 years: 1.56*
Social anxiety	1.01	0.91–1.26	No	–
Panic attacks	1.57*	1.24–1.98	No	–
Conduct disorder	1.43*	0.84–2.43	No	–
2 + conduct problems	1.62	1.47–1.80	No	–

*P-value <0.05.

before the age of 13 years. Finally, religious involvement was negatively associated with regular cigarette smoking while reporting below average grades in primary school was positively associated with regular cigarette smoking.

A large proportion of the family influence variables showed a significant interaction with age. The association between the risk factors and regular cigarette smoking was stronger, in most cases, at younger rather than older ages but the difference in effect sizes across the age groups was not as pronounced as those observed in tier 1.

Tier 3

Early life events: early consensual intercourse, early maturation and traumatic events before 13 years of age were

Table 3 Parameter estimates and 95% confidence intervals for genetic models of regular smoking.

		Males			*Females*				
Model no.	*Model*	a^2 *(95% CI)*	c^2 *(95% CI)*	e^2 *(95% CI)*	a^2 *(95% CI)*	c^2 *(95% CI)*	e^2 *(95% CI)*	*Rg** (95% CI)*	*Model fit* χ^2 (Δdf)*
Model *without* significant covariates from Table 1									
I	ACE/ACE	0.47	0.18	0.35	0.57	0.04	0.39	0.27	–
	Unequal	(0.30–0.65)	(0.02–0.33)	(0.30–0.40)	(0.41–0.65)	(0.00–0.19)	(0.35–0.44)	(0.24–0.35)	
II	ACE/ACE	0.53	0.10	0.37	0.53	0.10	0.37	0.50	5.05
	Equal	(0.41–0.65)	(0.00–0.21)	(0.34–0.40)	(0.41–0.65)	(0.00–0.21)	(0.34–0.40)		(3)
III	AE/AE	0.63	–	0.37	0.63	–	0.37	0.50	3.12
	Equal	(0.58–0.67)		(0.34–0.42)	(0.58–0.67)		(0.34–0.42)		(1)
Model *with* significant covariates from Table 1									
I	ACE/ACE	0.48	0.14	0.38	0.56	0.02	0.44	0.33	–
	Unequal	(0.29–0.65)	(0.00–0.30)	(0.34–0.45)	(0.41–0.60)	(0.00–0.12)	(0.40–0.50)	(0.27–0.39)	
II	ACE/ACE	0.54	0.04	0.42	0.54	0.04	0.42	0.50	5.52
	Equal	(0.41–0.62)	(0.00–0.16)	(0.38–0.46)	(0.41–0.62)	(0.00–0.16)	(0.38–0.46)		(3)
III	AE/AE	0.58	–	0.42	0.58	–	0.42	0.50	0.49
	Equal	(0.49–0.62)		(0.38–0.51)	(0.49–0.62)		(0.38–0.51)		(1)

*Model-fitting results and parameter estimates for twin models that examine quantitative (same magnitude of A, C and E in both sexes) and qualitative (same genes or environment, also called gender interaction) sex differences for regular cigarette smoking using same and opposite sex male and female twin pairs. Individual differences are partitioned into three sources: additive genetic (A), shared environment (C) and non-shared environment (E).
**In a separate model, constraining Rg = 0.5 did not result in a significant deterioration of fit suggesting absence of qualitative sex differences/gender interactions.

positively associated with regular smoking. Early sexual intercourse was a particularly potent predictor of regular cigarette smoking.

Tier 4

Psychiatric disorders: in tier 4, panic attacks and having two or more conduct problems was positively associated with regular cigarette smoking. We did not find statistically significant associations between regular cigarette smoking and social anxiety or conduct disorder (onset prior to 13 years). Both variables satisfied the PH assumption, suggesting that the association between regular cigarette smoking and panic attacks or conduct problems had been correctly specified. On the other hand, major depression was associated only with early onset regular smoking (0–11 years).

The results of the model in which all risk factors were jointly modeled and then selected using a stepwise process are presented in Table 1. Parental smoking and drinking were associated with regular cigarette smoking. Several risk factors from tier 2 dropped out of the model. Early intercourse, conduct problems and panic attacks were associated with regular cigarette smoking. We no longer found a violation of the PH assumption, which implies that variables from each consequent tier account for the age interactions observed when variables from earlier tiers were individually assessed.

Twin modeling

Data from 1496 MZ females, 1136 MZ males, 1140 DZ females, 941 DZ males and 1544 DZ opposite-sex twins were available to us for model-fitting. Results, including parameter estimates and fitted statistics, are presented in Table 3. Sex-difference models were first fitted without accounting for covariates and then repeated to include significant covariates from Table 1. We found no evidence for quantitative sex differences (magnitude of A, C, E equal across sexes). Also, we could drop the effects of C (but not A or A and C) from this constrained model. Furthermore, we were able to exclude the role qualitative sex differences (gender interaction) because constraining the additive genetic correlation across DZ opposite-sex twins to 0.5 did not result in a significant deterioration of model fit. The total variance in regular cigarette smoking was accounted for by additive genetic [58% (95% CI 49–62%) with covariates; 63% (95% CI 58–67%) without covariates] and unique environmental influences (remainder of variance). Also, the heritability of regular cigarette smoking was somewhat higher in the model where significant covariates were not accounted for (0.63 versus 0.58).

DISCUSSION

Regular cigarette smoking is still a pervasive habit across the world, despite aggressive antismoking campaigns and

scientific verification of the life-threatening health hazards of cigarette smoking [9]. In this study, we sought to examine the association between regular cigarette smoking and the risk factors that are most likely to be influential in childhood and early teen years and then, controlling for these significant covariates, to investigate the role of genetic and environmental influences on regular cigarette smoking. Based on prior literature and availability of data, we included 4 tiers of risk variables.

Tier 1

Family history: parental drinking and smoking behavior is a strong index of childhood disruptive behaviors as well as adolescent smoking and drinking. Numerous studies have made a similar observation [6,8,26,27]. This association may be due to direct or indirect effects. Parental smoking and drinking may influence regular cigarette smoking in the offspring via genetic predisposition [5] or disruptive home environment [28,29]. Most probably, an interaction of diathesis (genetic vulnerability from parent) and stress (disruptive home environment) is responsible for progression to regular smoking in adolescence.

In our study, parental education was negatively associated with regular cigarette smoking in the offspring. Some studies substantiate this finding [30–33] and propose that the effect of parental occupation or education is indirect and mainly mediates either parental smoking or the offspring's education, which in turn impacts the offspring's smoking.

Tier 2

Early family and home influences: adults who reported a healthy relationship with their parents and fewer conflicts between the ages of 6–13 were less likely to be regular smokers. Furthermore, children separated from a biological parent were also more likely to report regular cigarette smoking as adults. Studies on smoking phenotypes often report a protective relationship between high levels of parental bonding and smoking habits [1,26,34]. Tucker *et al*. reported that non-intactness of family structure (OR = 0.65 for intactness of family) and poor parental support (OR = 1.32) are risk factors for regular cigarette smoking [34]. Covey and colleagues showed a positive association between living in a single-parent home and smoking among 11th graders [35].

Our study also revealed an association between parental attitudes and disciplining variables and regular cigarette smoking in the offspring. Complete lack of supervision and extreme strictness were positively associated with regular cigarette smoking. Furthermore, harsh punishment, especially punishment resulting in severe physical pain, was positively associated with regular cigarette smoking. Several independent studies report an association between authoritative parenting styles and adolescent smoking [36–39]. Most interestingly, similar to our findings, Chilcoat & Anthony observed that poor parental monitoring leads to an escalation in drug use, especially before 11 years of age [10].

Tier 3

Early life events: early intercourse and its association with regular cigarette smoking may suggest risk-taking behavior. Risk-taking behavior may also indirectly be responsible for early maturing adolescents starting to smoke on a regular basis [40]. For instance, early maturing females are more likely to keep the company of older males and indulge in non-normative behavior [41]. Alternatively, early maturing adolescents may have greater rates of early consensual sex.

Tier 4

Psychiatric symptoms and disorders: our finding of the association between early onset panic attacks and regular cigarette smoking has been reported previously [42–46]. Due to the bidirectional nature of the causal hypotheses that govern this relationship, it is difficult to ascertain whether regular cigarette smoking increases rates of panic attacks or whether smoking is used as a coping mechanism for panic attacks. Using data from two independent epidemiological samples, Breslau & Klein reported a greater likelihood that prior smoking may have a causal impact on initiation of panic attacks [42]. Isensee *et al*. also supported this unidirectional smoking-to-panic pathway but could not rule out the reverse path [43].

Our sample did not have adequate power to detect a significant relationship between DSM diagnoses and regular cigarette smoking. Moolchan, Aung & Henningfield pointed to the interrelationship between anxiety, depression and smoking in their review [47,48]. However, we did note an association between regular cigarette smoking and conduct problems. Problem Behavior Theory (PBT) [49] provides one explanation for this clustering. According to PBT, the comorbid occurrence of smoking and conduct problems is due to a general and shared predisposition to deviant behavior [13,50]. Therefore, smoking and conduct problems may be components of a spectrum of disordered behaviors.

Genetic etiology of regular cigarette smoking

In conjunction with reports from other twin studies, we found evidence for the role of additive genetic influences on regular cigarette smoking [3–5]. None of these studies

accounted for potential covariates when calculating heritability of regular smoking behavior. Overall, even after accounting for measured risk factors that significantly associated with it, regular cigarette smoking was highly heritable. Confounding covariates may result in upward or downward biasing of heritability estimates. For instance, delinquent behavior is highly heritable [51] and correlated with early onset regular cigarette smoking. Therefore, the heritability estimates for smoking may include genetic factors that predispose individuals to smoking or delinquent behavior or both. It is important to eliminate the effect of confounding covariates and examine a 'refined' phenotype in twin analyses. Our study found that refining the phenotype resulted in substantial genetic variation in regular cigarette smoking. We found that a model that did not account for significant covariates (similar to previously published reports) allowed for a greater heritability of regular cigarette smoking than the model that accounted for significant covariates, suggesting that MZ correlations may have been upwardly biased in previous studies of regular smoking due to confounding risk factors that were not partitioned out of the twin model.

Limitations

Despite the richness of the current data set, our findings may be viewed with certain limitations in mind. First, all data used in our study are derived from retrospective reports from adult participants. Recall bias and intentional denial of certain events or incidents may have biased some results. Furthermore, we were unable to infer causal directionality from our findings. Therefore, all results reported in this study mark associations and not causation between regular cigarette smoking and putative risk measures. Secondly, this is a sample of Australian Caucasian twins and results may not be extrapolated to other ethnicities or cultures. With regard to the use of twin data as an epidemiologically representative sample, we accounted for twin clustering in all our analyses. Also, findings from the literature suggest that twins behave no differently than unrelated individuals, when the presence of the cotwin in the sample is accounted for [52,53]. Thirdly, our data does not include measures of peer behavior, which is an important correlate for regular cigarette smoking. We also did not have access to direct reports from parents regarding their own behavior.

CONCLUSIONS

Regular cigarette smoking, especially in those who have an early age of onset, is strongly associated with a gamut of risk and protective factors. Findings from our study add to a growing body of literature that posits a robust relationship between regular smoking and parental smoking, disruptive home environments, parent–child conflicts, risk-taking behavior and conduct problems. Most importantly, our study underscores the influence of the confounding effects of measured correlates on estimates of genetic and environmental variance in regular smoking. Whether the influence of covariates is genetic or purely phenotypic, genetic models should account for measured covariates when estimating heritability. The resulting estimates are more likely to capture influences that are specific to smoking behavior instead of a composite phenotype that includes smoking and other correlated heritable factors.

Acknowledgements

Funded by grants AA13221 and AA07728 (to Dr Heath) and DA12854 (to Dr Madden). We would also like to thank our interviewers and administrative staff (QIMR) and our twins.

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