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Transmission of second-hand smoke sensitivity and smoking attitude in a family

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Abstract

Introduction and objective. The role of genetic factors in nicotine dependence is well understood, but no information is available on the inheritability of second-hand smoke (SHS) exposure sensitivity and their co-variance.

Materials and methods. 186 adult same-gender pairs of twin (146 monozygotic, 40 dizygotic; 44±17 years±SD) completed a questionnaire.

Results. The model showed a significant role of unshared environmental factors influencing the co-variance between smoking habit and SHS sensitivity (r_e=–0.191, 95% CI, –0.316 to –0.056, or the total phenotypic correlation of r_{ph}=–0.406, p<0.001) without evidence for genetic covariation. Age, gender and country-adjusted analysis indicated 51.5% heritability for smoking habit (95% confidence interval/CI/, 6.2 to 89.8%), 49.7% for SHS sensitivity (95%CI, 19.1–72.0%), 35.5% for general opinions on SHS exposure in restaurants/cafés (95%CI, 10.7–58.6%), and 16.9% in pubs/bars (95%CI, 0.0–49.0%).

Conclusions. The co-variance between SHS sensitivity and smoking habits is driven mainly by the unshared environment. SHS sensitivity is moderately inheritable. The considerable influence of environmental factors on general opinions on SHS exposure in designated indoor public venues emphasizes the importance of smoking bans and health behaviour interventions at the individual level in developing an anti-smoking attitude.

Key words

tobacco smoking, heritability, genetics, smoking habits, environmental exposure

INTRODUCTION

Second-hand smoke (SHS) is a complex mixture of the gases and particles emitted by the burning end of a cigarette, pipe or cigar, and also the smoke exhaled from the lungs of smokers. These particles are in the fine to ultrafine particle size range (< 2 μm), have been shown to be inhaled deep into the lungs and cause an array of adverse health effects, e.g. tumour genesis, and cardiovascular and respiratory diseases [1, 2, 3, 4, 5, 6]. SHS contains over 3,000 chemicals with at least 50 of them known to be or suspected of being carcinogenic, while over 200 are regarded as poisonous [7]. Their adverse effects on human health have been well-documented and it is generally accepted that there is no safe level of exposure to cigarette smoke [8]. There is no lower threshold for tobacco carcinogenesis, either regarding lung cancer or tumours in other tissues that are indirectly exposed [9]. Carcinogens absorbed in the lung are distributed throughout the body and have been shown to create and/or aggravate tumour genesis [9]. Adverse reactions, such as dizziness, unpleasant or grossly high heart frequency, headache, coughing or choking, characterize an individual sensitivity to tobacco smoke.

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Several twin studies investigated the possible role of genetic factors on nicotine dependence and withdrawal. These compare identical twins with non-identical twins, providing information on the relative contribution and interaction of genes and environment. Nicotine dependence for cigarette smoking or snuff use has a moderate genetic determination (30–39%) [10, 11] which shows a weak genetic association with the intelligence quotient [10]. In addition, nicotine withdrawal symptoms were reported to be moderately inheritable (49%) in adult and adolescent smokers [12], similar to smoking withdrawal [13]. A Chinese twin study reported a moderate genetic variance on the influence on smoking initiation [14]. An Australian study demonstrated the significant influence of both genetic and environmental factors in the liability to smoking initiation, and significant effects of primarily non-parental shared environment on smoking initiation [15]. The inheritability of age at first cigarette was 60% for males and 39% for females in a Danish twin study [16]. The D1A dopamine receptor gene is suggested to be partially responsible for smoking behaviour [16].

OBJECTIVES

Even though moderate inheritability of smoking habits, smoking initiation and quitting is well described, to-date there is no information regarding the genetic influence on

second-hand smoke sensitivity which would be essential for understanding the development of anti-tobacco behaviour. Since it is affected by smoking habit, the main goal of the presented study was to investigate whether the co-variance of second-hand smoke sensibility and smoking habits is influenced by shared genetic or environmental factors. An additional aim was to comprehensively investigate the genetic and environmental factors on second-hand smoke sensitivity in a relatively large multi-national twin cohort. Assessment of the difference in the state of respondents' general opinions on exposure to tobacco smoke in designated indoor public venues was additionally attempted. It was hypothesized that a decreasing genetic influence exists in general opinions on exposure to tobacco smoke related to indoor public places polluted by tobacco smoke. This finding would confirm the scientific evidence of environmental protective interventions (eg., smoking ban, health behaviour changes) in countries where indoor public venues are polluted by harmful, ultrafine particles.

MATERIALS AND METHODS

Subjects and study design. 138 Hungarian and 48 American adult same-gender twin pairs (146 monozygotic, MZ and 40 same-sex dizygotic DZ pairs; age 44±17 years±standard deviation) were recruited in this classical twin study. The volunteer healthy subjects recruited via the Hungarian Twin Registry [17] completed a questionnaire separately from one another in the research venues: on the spot at 2 twin festivals held in Agfalva and Szigethalom, in Hungary, or at two large hospitals in Budapest, the Semmelweis University Department of Radiology and Oncotherapy and the Military Hospital Department of Cardiology, in 2009 and 2010. American healthy twins were involved in a Twins' Days Festival in Twinsburg, Ohio, in the USA in 2009.

In the absence of genotyping, and in order to maximize the accuracy of zygosity classification, zygosity was assigned according to a 7-part self-reported response [18]. All study subjects gave informed consent prior to entering the study, which was conducted in full compliance with regulations of the local Ethical Committees. Present or past smoking habit was asked with the following question: What type of smoker are you? – where 'current', 'former' and 'never' were given as response categories. Twins were also asked: Does second-hand smoke bother you? Four ordinal response categories were offered: 'A lot', 'Somewhat', 'A little' and 'Not at all'. If one of the first 3 choices was reported, the individual was considered to be sensitive to second-hand smoke and the phenotype was called the SHS attitude. This question was a part of the validated Western New York Adult Tobacco Survey questionnaire, a cross-sectional survey designed to measure smoking habits in the population [19]. In addition, the following questions were assessed: How do you rate the general smoke pollution in *restaurants and cafés* on a scale between one and seven? – where the degree of pollution worsens with increasing the value. The same question was also asked replacing *restaurants and cafes* with *drinking establishments, bars and pubs,* which are considered to be venues more polluted with tobacco smoke (scientifically confirmed by our study team). These questions asked of the respondents concerning general opinion on passive exposure to tobacco smoke in public places, also included outside factors, e.g. the twins' general opinions pertaining to the situation in these places (newspaper reports, opinions of family members and others, including own siblings participating in the study), rather than their actual attitudes towards exposure to tobacco smoke in this environment.

Statistical analysis

Participant characteristics. Initially, a descriptive analysis was made for smoking habits in MZ and DZ twins. Between-gender, between-zygosity and between-country differences were calculated using independent-samples t-tests by SPSS Statistics 17.

Estimating genetic influence on smoking habits and second-hand smoke sensitivity characteristics. A descriptive estimate of the genetic influence was calculated using the bi-variate co-twin correlation in MZ (*r*MZ) and DZ (*r*DZ) pairs. The corresponding 95% confidence intervals (CI) for *r*MZ and *r*DZ were boot-strapped. If the within pair similarity for a phenotype is greater in MZ than DZ pairs, this provides evidence of genetic influence.

To estimate inheritability, an ACE structural equation model was used [20, 21]. The ACE model decomposes phenotypic variance into additive genetic (A), common environmental (C) and unique environmental (E) effects. The additive genetic component measures the effects due to genes at multiple loci or multiple alleles at one locus. The common environmental component estimates the contribution of the shared family environment by both twins, whereas the unique environmental component estimates the effects that apply only to each individual twin, and also includes measurement error. More formally, the variance-co-variance matrix of the MZ co-twins is modeled to be equal to $a^2+c^2+e^2$ (or the total phenotypic variance), and the off-diagonal as a^2+c^2 (the components that the co-twin co-variance consists of). For DZ twins, the diagonal restrictions are the same for MZ twins, but the off-diagonals are restricted to $0.5*a^2+c^2$ (since genetic co-twin co-variance, on average, is 0.5 for non-identical twins while their shared environmental correlation is the same as for MZ twins). With these restrictions in place, a multi-group structural equation model obtains the estimates for a, c and e. Model fitting was carried out with Mplus Version 6 [22] with a mean and variance corrected weighted least squares for the ordinal phenotypes (second-hand smoke sensitivity and smoking habits), and full information maximum likelihood for the continuous smoke pollution ratings. Chi-Square model fit p-values are presented where the desired results show insignificant model misfit. Instead of a variance – co-variance matrix, the estimation procedure uses the raw data matrix. Given the small sample size, no component was fixed to 0 in the model.

Since the main interest of the presented study was the genetic and environmental factors of the co-variation between smoking habits and second-hand smoke sensitivity, the first model uses a multi-variate extension of the ACE model that estimates what proportion of this correlation is attributable to common underlying genetic and environmental factors in addition to the proportions of the variance. In order to estimate the amount of overlap between genes or environment that influences the 2 parameters, genetic and environmental correlations between those phenotypes were calculated.

RESULTS

Table 1 presents clinical characteristics of the sample by gender and country. 78% of the involved twins were monozygotic. 76% of the respondents were females. Dizygotic twins were significantly older than MZ twins (p<0.01) and had smoked longer (p<0.001). Significant differences were observed in second-hand smoke sensitivity across nationality (p<0.05). Parental smoking habit and self-reported smoke pollution also differed across zygosity and nationality (p<0.05).

Genetic influence on smoking habits and second-hand smoke sensitivity and their co-variance. Since it was hypothesized that second-hand smoke sensitivity is influenced by past or active smoking, a bi-variate Cholesky decomposition model was estimated in order to investigate a common genetic background of these traits. The correlation between smoking habits and general second-hand smoke sensitivity was negative and significant (r_{ph}=–0.406; p<0.001). Table 2 shows the standardized genetic, common and unique environmental components of the co-variance, and consequently, the variances as well. In the ACE genetic decomposition model, unshared environmental factors accounted for the co-variance significantly (–0.191, 95% CI, –0.316, –0.056). No significant role of genetic or shared environmental covariance was noted. Furthermore, age-, gender- and country-adjusted inheritability was 51.5% for smoking habit (95% confidence interval /CI/, 6.2 to 89.8%), and 49.7% for general second-hand smoke sensitivity (95% CI, 19.1 to 72.0%) (Tab. 2). Second-hand smoke sensitivity is certainly moderately influenced by genetic factors, as demonstrated by the fact that the presented results replicate past studies on smoking habit which reported moderate inheritability [10, 11].

Table 2. Genetic and environmental variance components (in percentage in the overall sample), and covariance (A, C, E) of smoking habits and secondhand smoke sensitivity with phenotypic correlation (r_{ph}) and model fit as estimated under the best bivariate ACE Cholesky model

Measure	Genetic decomposition model between second-hand smoke sensitivity and smoking habits	Variance components		
		A	C	E
Second-hand smoke sensitivity	r_{ph}=-0.406 (p<0.001) A: -0.082 (-0.391; 0.251) C: -0.133 (-0.471; 0.069) E: -0.191 (-0.316; -0.056) Chi-Square Test of Model Fit (p-value): 0.9321	49.7% (19.1, 72.0)	5.7% (0.0, 36.4)	44.6% (28.5, 65.1)
Smoking habits (former, active or never smoker)		51.5% (6.2, 89.8)	30.7% (0.0, 74.0)	17.8% (8.8, 31.4)

A – additive genetic factors; C – shared environmental variance component; E – unique environmental variance component; MZ – monozygotic; DZ – dizygotic
Numbers in parentheses – lower and upper limits of 95% confidence interval.
AE – similarly good fit; CE model – worse fit; AE model – accompanied by significant, low genetic covariance.

Genetic and environmental effects on the state of respondents' general opinions on exposure to tobacco smoke in various venues. As general second-hand smoke sensitivity was moderately inheritable, a univariate analysis was performed on special venue-related attitudes concerning general opinions on second-hand smoke exposure (places for eating out: restaurants and cafés; drinking establishments: bars and pubs) in order to investigate whether there is a difference in genetic influences of general opinions on SHS exposure related to these special indoor public places differently polluted by tobacco smoke. Age-, gender- and country-adjusted inheritability was 35.5% for the general opinions on second-hand smoke exposure in restaurants and cafés (95% CI; 10.7–58.6%), and 16.9% in pubs and bars (95% CI; 0.0–49.0%) in the total sample (Tab. 3). Shared

Table 1. Clinical characteristics and measures according to zygosity and nationality

	Total	Zygosity		Nationality	
		Monozygotic	Dizygotic	Hungarian	American
Subjects, n	372	292	80	276	96
Monozygotic:dizygotic, n	292:80	N/A	N/A	202:74	90:6
Male:Female, n	88:284	68:224	20:60	72:204	16:80
Age, years	44±17	43±17†	49±15†	43±16	47±18
Never smokers, n (%)	254 (68.3)	202 (69.9)	52 (65.8)	189 (69.0)	65 (68.4)
Ex-smokers, n (%)	61 (16.4)	47 (16.3)	14 (17.7)	35 (12.8)	26 (27.4)
Current smokers, n (%)	53 (14.2)	40 (13.8)	13 (16.5)	49 (17.9)	4 (4.2)
Regular smoking at least one year, n (%)	83 (22.3)	59 (20.4)	24 (30.4)	79 (28.8)$	4 (4.2)$
Smoking duration, years	15.1±12.0	11.5±9.8‡	12.9±13.0‡	15.5±12.0	9.5±13.8
Second-hand smoke sensitivity, n (%)					
very much (high)	193 (56.8)	151 (57.4)	42 (54.5)	152 (55.7)II	41 (61.2)II
somewhat (moderate)	76 (22.4)	61 (23.2)	15 (19.5)	56 (20.5)II	20 (29.9)II
a bit (little)	41 (12.1)	31 (11.8)	10 (13.0)	35 (12.8)II	6 (9.0)II
not at all (none)	30 (8.8)	20 (7.6)	10 (13.0)	30 (11.0)II	0 (0.0)II
Parental smoking in childhood, n (%)	139 (37.7)	98 (33.8)†	41 (51.9)†	88 (32.1)$	51 (53.7)$
General opinion on smoke pollution in bars (scale 1–7)*, average	4.3±2.0	4.2±2.1§	4.9±1.8§	4.8±1.8$	2.7±2.1$
General opinion on smoke pollution in restaurants and cafés (scale 1–7)*, average	2.7±1.7	2.6±1.7§	3.1±1.7§	3.0±1.7$	1.8±1.5$

Values are shown as mean ± standard deviation or n (%) where appropriate.
† – Monozygotic *vs.* dizygotic p<0.01
‡ – Monozygotic *vs.* dizygotic p<0.001
II – Hungarian *vs.* American p<0.05
$ – Hungarian *vs.* American p<0.001
• The exact question pertaining to the general opinion on SHS exposure in public places: 'How do you rate the general smoke pollution in *restaurants and cafés / drinking establishments, bars and pubs* on a scale between one and seven?' – where the degree of pollution worsens with increasing the value.
AE model had a similarly good fit, but CE model had a worse fit, and AE model accompanied by significant, low genetic covariance

Table 3. Co-twin correlations, genetic and environmental variance components as estimated by the univariate ACE models in percentage

Measure	Twin correlations		Variance components			Chi-Square Test of Model Fit (p value)
	rMZ	rDZ	A	C	E	
General opinion on second-hand smoke exposure in restaurants and cafés	0.394 (0.154, 0.599)	-0.078 (-0.371, 0.298)	35.5% (10.7, 58.6)	0.0% (0.0, 36.9)	64.5% (41.9, 87.5)	0.5710
General opinion on second-hand smoke exposure in bars and pubs	0.321 (0.137, 0.498)	0.236 (-0.220, 0.690)	16.9% (0.0, 49.0)	15.1% (0.0, 45.5)	67.9% (51.0, 86.5)	0.0284

A – heritability; C – shared environmental variance component; E – unique environmental variance component; MZ – monozygotic; DZ – dizygotic
Results according to age, gender, and country, adjusted in the total sample (146 monozygotic, 40 dizygotic twin pairs).
Numbers in parentheses – 95% confidence intervals.

environmental factors were responsible for 0–15% of the variance (non-significant). Unshared environmental effects were always significant, accounting for 64–68% of the variance (Tab. 3). In the second model, results were adjusted for age and gender in the Hungarian sub-sample only (101 monozygotic, 37 dizygotic twin pairs), but the results did not change in magnitude, direction or significance.

DISCUSSION

The presented study is the first to investigate genetic effects on second-hand smoke sensitivity. The findings indicate a common unshared environmental background between second-hand smoke sensitivity and smoking attitude, and a moderate genetic influence on smoking habits and second-hand smoke sensitivity.

Since second-hand smoke sensitivity attitude is influenced by smoking habit, the main aim of the study was to investigate whether the co-variance of second-hand smoke sensibility and smoking habits is influenced by shared genetic or environmental factors. Unsurprisingly, an inverse relationship was found between tobacco smoking and second-hand smoke sensitivity, indicating that active and ex-smokers are less likely to be sensitive to tobacco smoke, a relationship which is mainly determined by an unshared environment. A recent study found that SHS (as 'unpleasant or gross') is a phenotype for mechanisms associated with protection against smoking susceptibility, and second-hand smoke sensitive individuals are protected against smoking susceptibility and smoking initiation [23]. The current study highlights that this association could be influenced mainly by unshared environmental factors. This implies that we are dealing with factors that are more suitable for targeted interventions to keep susceptibility low, and to decrease smoking initiation risk. Only a weak indication of genetic covariation between tobacco smoking and secondhand smoke sensitivity was found. In spite of this finding, the presented study shows that the great majority of the co-variation between tobacco smoking and second-hand smoke sensitivity is governed by environmental factors.

The current findings on the moderate inheritability of smoking habits (51%) corroborate the inheritable theory of smoking habits, as reported by previous studies [10, 11, 24]. Since smoking behavior, including nicotine dependence and withdrawal, smoking initiation, age at first cigarette, and smoking behaviour shows a complex genetic background [10, 11, 12, 13, 14, 15, 16]. The aim of this was to clarify whether genetic effects also influence second-hand smoke sensitivity. It was found that there is 50% inheritability for second-hand smoke sensitivity without a considerable role of shared environmental influence (eg., familiar socialization). Unique environmental factors showed that 47% share in determining second-hand smoke sensitivity. Those individuals who are more sensitive to second-hand smoke avoid smoky environments, are less likely enter a smoky indoor public venue, and therefore they are less affected by the ultra-fine < 2 μm particles associated with tumour genesis, cardiovascular and respiratory diseases [1–6]. Accordingly, second-hand smoke sensitive persons are genetically protected at a moderate level against these adverse health effects and related disorders. On the other hand, less sensitive individuals are more likely to be influenced by unshared environmental effects, and have a higher risk of suffering from the debilitating health consequences of second-hand smoke exposure.

Data was also collected on special venue-related general opinions on second-hand smoke exposure attitudes (e.g., restaurants and cafés; drinking establishments: bars and pubs) and with the univariate ACE-models environmental effects were found, but that inheritability have a significant influence in venues with increasing smoking pollution, namely, in restaurants and cafés, and have an even larger effect in designated smoking areas of pubs and bars. None of the second-hand smoke sensitivity or related opinion features (general vs. venue-specific) is notably influenced by shared environmental factors, such as family socialization or air pollution, but modified by individual habits. Taking these into consideration, the current results indicate that second-hand smoke sensitivity is a habit considerably influenced by the environment, and health behaviour changes in order to develop an anti-smoking behavior, and can be intervened at the individual level. These findings emphasize the role of smoking bans in these types of special venues (restaurants and cafés; and more importantly, bars and pubs), since in these types of venues environmental interventions will be more effective for the population. Consequently, smoke pollution could be more disturbing, and venues polluted by ultrafine particles might be less visited.

At the time of the study, different smoking laws were in place in the 2 sampled countries. It is a challenging task to review the various laws and regulations in force in the United States as member states and municipalities have their own jurisdiction over smoking. In some places smoking is permitted, in others it is banned. In general, American laws at that time were stricter than those in Hungary. However, in the study years (2009 and 2010) smoking was banned in Hungary in government buildings, private worksites, educational and health care facilities, on buses and in taxis. However, smoking was still permitted, but restricted to (not very well segregated) designated smoking areas in restaurants, cafés, bars, nightclubs, and on trains and ferries; therefore, studying second-hand smoke exposure was possible at these facilities.

In a previous work, the authors of the presented study reported that the levels of indoor fine particle air pollution measured in smoking public locations in Hungary were 18 times higher than the levels in non-smoking places, and exceeded the harmful levels stipulated by the World Health Organization and US Environmental Protection Agency [25]. The possible influence of diverse regulations in the 2 countries must be noted; nevertheless, no significant difference was found in the results of the ACE-models according to different sample size by excluding the American sub-population, and the shared environmental effects (C) were found to have a negligible role.

An additional limitation might be that sensitivity to SHS was assessed only by a questionnaire and not by a personal interview based on standard questions, such as in the study by Lessov-Schlaggar et al, published recently and could not be used in the presented study [23]. There were additionally some differences in the clinical characteristics among the respondents. Women who smoked tobacco more rarely, but were more frequently exposed to passive smoking (especially at home), showed a preponderance. A difference in age between mono- and dizygotic twins and country-specific variations were also observed. However, statistical analysis was performed on data adjusted for gender, age and country, which attenuated these confounding effects.

CONCLUSIONS

In summary, the presented study was the first twin study to investigate the genetic variance on second-hand smoke exposure sensitivity and its co-variance with smoking habits. A moderate genetic influence on second-hand smoke sensitivity is revealed, which shows a mainly unshared environmental background with smoking attitude. An increasing influence of environmental factors on general opinions on second-hand smoke exposure in polluted special indoor public venues is shown, which emphasizes the importance of smoking bans and health behaviour interventions at the individual level in developing an anti-smoking behaviour.

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