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Maternal smoking during pregnancy and offspring's tobacco dependence. A study of exposure-discordant sibling pairs

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ABSTRACT

Background: Prenatal exposure to maternal smoking has previously been linked to tobacco dependence, but confounding from genetic and early-environmental factors is of concern. The aim of this study was to clarify if maternal smoking during pregnancy may affect the onset and manifestations of tobacco dependence after taking such factors into account.
Methods: The study is based on a matched cohort of 1538 siblings discordant for prenatal exposure to maternal smoking, who participated in a survey conducted in 2010 in Sweden. Analyses were based on pairs where both siblings had been daily smokers (193 pairs) or snus users (173 pairs) at some time in their life. Participants were 19–27 years old at the time of participation. Outcomes were tobacco dependence measured with the Cigarette Dependence Scale (CDS-12) in smokers and with the adapted Smokeless Tobacco Dependence Scale (STDS-12) in snus users, and previous quit attempts. Exposure to maternal smoking during pregnancy was retrieved from the Swedish Medical Birth Register.
Results: There was no difference in dependence scores in exposure-discordant siblings (mean difference 0.36 on CDS-12 [95% confidence interval: −1.23 to 1.95] and 0.61 on STDS-12 [95% confidence interval: −1.20 to 2.43]). Neither did the siblings differ with regard to previous quit attempts.
Conclusions: Maternal smoking during pregnancy does not appear to influence tobacco dependence in adult offspring. A potential effect of heavy maternal smoking during pregnancy cannot be excluded, but genetic and environmental influences seem to be more influential for the onset of tobacco dependence.

1. Introduction

Prenatal exposure to maternal smoking during pregnancy has been linked to tobacco dependence in offspring (Buka et al., 2003; Cornelius et al., 2012; Lieb et al., 2003; O'Callaghan et al., 2009; Rydell et al., 2012). Nicotine crosses the placental barrier, reaches the fetus in relatively high concentrations (Hellstrom-Lindahl and Nordberg, 2002) and can activate and desensitize nicotinic acetylcholine receptors (Smith et al., 2010). This may alter the development of neurotransmitter systems in the fetus, in particular, concerning pathways mediating the rewarding effects of nicotine (Smith et al., 2010). Hence, prenatal exposure to maternal smoking may have a brain priming effect, causing a vulnerability to tobacco dependence that lasts into adulthood.

It is difficult to disentangle the intra-uterine effect of maternal smoking during pregnancy on later tobacco dependence as both genetic and environmental factors are likely to influence the association (Kendler et al., 2012). Therefore, previous studies of the association between maternal smoking during pregnancy and risk of tobacco dependence in the offspring (Buka et al., 2003; Cornelius et al., 2012; Lieb et al., 2003; O'Callaghan et al., 2009; Rydell et al., 2012), are likely confounded by unmeasured environmental or genetic factors. Sibling studies would ideally provide control for confounding by shared genetic and environmental familial factors, since full siblings are usually brought up together and share approximately 50% of their segregating genes (Lahey and D'Onofrio, 2010). However, to date only one such study investigating the effect of maternal smoking during pregnancy on offspring nicotine dependence, has been published (Shenassa et al., 2015). Shenassa et al.

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found that maternal smoking during pregnancy was associated with a three-fold increased risk of progression from weekly smoking to nicotine dependence among 40 year old offspring (Shenassa et al., 2015). On the other hand, the authors found no such association for lifetime smoking, lifetime nicotine dependence or for progression from ever smoking to nicotine dependence. This is in line with findings from two other recent sibling studies, where no association was found between prenatal smoking exposure and initial (D'Onofrio et al., 2012) or regular (Rydell et al., 2014) tobacco use. However, to become a smoker and to develop tobacco dependence are two different processes, influenced by different mechanisms. For instance, uptake of tobacco use is mostly influenced by social and environmental factors, whereas dependence is more likely influenced by biologic factors (Kendler et al., 2008). Therefore, the mechanism linking smoking during pregnancy to offspring tobacco use on the one side and to dependence on the other side might also differ. Furthermore, the study by Shenassa et al. is also based on a relatively small sample compared to the other two sibling studies (i.e., the analysis on progression to nicotine dependence was based on 70 discordant sibling pairs), resulting in imprecise estimates. Thus, more studies are needed to clarify if prenatal smoking exposure is associated with subsequent risk of tobacco dependence, possibly also including measures of dependence from tobacco products other than cigarettes. If prenatal exposure to nicotine from maternal smoking would induce a potential for dependence later in life, this should manifest with increased risk not only for smoking, but also for the use of other types of tobacco, such as smokeless tobacco. Only one previous study of adolescents included symptoms of tobacco dependence from use of other tobacco products than cigarettes (Rydell et al., 2012), and found two- to three-fold increased odds of experiencing withdrawal symptoms and craving in girls prenatally exposed to maternal tobacco use, compared with prenatally unexposed girls.

In this study, we investigated the association between prenatal exposure to maternal smoking and tobacco dependence following use of cigarettes and/or snus in young adults with a lifetime history of daily tobacco use. We used a matched cohort study of full siblings whose mothers smoked cigarettes in one, but not in the other pregnancy.

2. Material and methods

2.1. Study population and data collection

The study is based on the Swedish Sibling Health Cohort, described in detail elsewhere (Rydell et al., 2014). The cohort was recruited in order to study the influence of prenatal exposure to maternal smoking on health in adult life, taking genetic and early environmental factors into account. Briefly, a random sample of 5000 same-sex sibling pairs (10,000 individuals), discordant for maternal smoking exposure during pregnancy, was drawn among all sibling pairs born in Sweden 1983–1991. Of the original sample, 4368 individuals (44%) responded to a survey and 4253 of these consented to linkage with population-based registries. In total, 1538 complete sibling pairs participated, yielding a response rate of 32% at the level of sibling pairs. Participants were 19–27 years old at time of participation. This study is based on subgroups where both siblings reported having smoked daily for at least 6 months in their life (193 pairs) or having a corresponding history of daily snus use (173 pairs) (Fig. 1).

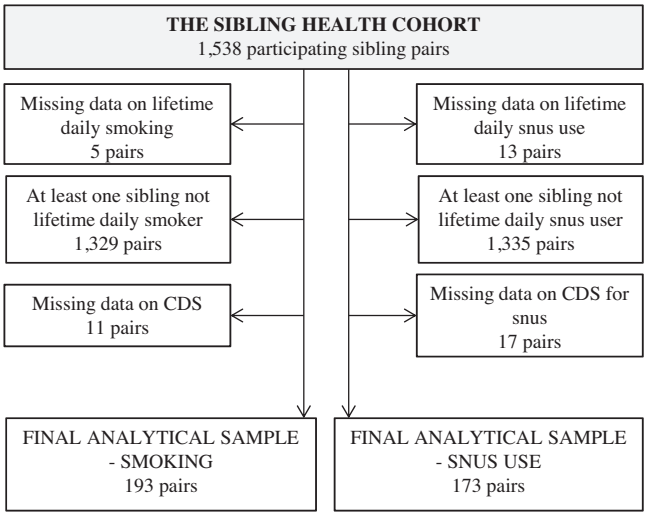

Fig. 1. Derivation of analytical samples of cigarette smokers and snus users. The Swedish Sibling Health Cohort 2010–2011.

2.2. Measures

Prenatal exposure to smoking was retrieved from the Medical Birth Register, which comprises information on 98% of all births in Sweden (The National Board of Health and Welfare, 2003). From 1983 and onwards, the registry contains information about smoking during pregnancy as reported by mothers at the first antenatal visit (usually between the 8th and12th gestational weeks). In the registry, smoking is categorized as: no daily smoking; smoking 1–9 cigarettes per day; or smoking ≥10 cigarettes per day. In this study, maternal smoking was categorized as daily smoking versus no daily smoking, since exposure to ten or more cigarettes per day occurred in few pregnancies (44 smokers and 38 snus users).

Tobacco dependence was assessed among participants who had smoked/used snus daily for at least six months ever in life. The Cigarette Dependence Scale (CDS-12; Etter et al., 2003; Rydell et al., 2015) and the Smokeless Tobacco Dependence Scale (STDS-12; Rydell et al., 2015) were used to assess tobacco dependence in smokers and snus users, respectively. The CDS-12 is a self-administered instrument, developed to capture DSM-IV and ICD-10 criteria of dependence, with high reliability (Etter et al., 2009, 2003). The scale consists of 12 items (Table S1), where each item is given a value from 1 to 5. Items' scores are summed up to a total CDS-12 score (range 12–60). The STDS-12 (Table S1) was adapted from CDS-12 and field-tested for the assessment of tobacco dependence among Swedish snus users (Rydell et al., 2015). In this study, CDS-12 and STDS-12 were treated as continuous variables as well as dichotomized at a score of ≥43 versus less (recommended for identification of dependent smokers (Etter, 2008; Etter et al., 2009)).

Lifetime daily tobacco users with at least one quit attempt of one week or longer were asked about the number of previous quit attempts, as well as duration of the longest attempt (less than 2 weeks, 2 to <4 weeks, 1 to <3 months, 3 to < 6 months, 6 months to <1 year, 1 to <2 years, 2 years or more), separately for smoking and snus use. Previous quit attempts were categorized as more than one versus one, since a majority of former smokers included attempts to quit at least once (John et al., 2004). Duration of the longest quit attempt was categorized as two weeks or shorter versus more than two weeks, as most relapses occur within 8 days from a quit attempt (Hughes et al., 2004).

Probands' birth order (first born versus other) and year of birth was retrieved from the Medical Birth Register. Sibling order was dichotomized as being the older or younger sibling in a pair. Information about maternal country of birth was retrieved from the Medical Birth Register, and categorized as: Sweden; other Nordic country, i.e., Finland, Denmark, Norway or Iceland; or any other country. Information about maternal education (highest achieved