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Short Communication

New methods shed light on age of onset as a risk factor for nicotine dependence

Stephanie T. Lanza [a,b,*], Sara A. Vasilenko [a,c]

[a] The Methodology Center, The Pennsylvania State University, University Park, PA, USA
[b] Department of Biobehavioral Health, The Pennsylvania State University, University Park, PA, USA
[c] College of Health and Human Development, The Pennsylvania State University, University Park, PA, USA

HIGHLIGHTS

- We examine the rate of nicotine dependence as flexible function of age of onset
- Peak risk coincides with onset at age 10, with an elevated risk through age 20
- Risk of dependence is higher for females than males for onset between ages 9 and 18
- Early onset is a relatively stronger risk factor for adolescent females than males
- Time-varying effect modeling provides more nuanced understanding of risk factors

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ABSTRACT

Introduction: Early onset of substance use is a risk factor for later drug use, abuse, and dependence. This study examines how the rate of nicotine dependence differs as a function of age of onset of regular smoking in continuous time, in order to identify critical age periods that are most predictive of later dependence for males and females.
Methods: Time-varying effect modeling (TVEM) can reveal specific ages of onset that confer greatest risk for adult nicotine dependence. The rate of dependence in adulthood is modeled as a flexible function of age of onset using a subset of adults ($N = 15{,}748$) from the National Epidemiologic Survey on Alcohol and Related Conditions who ever smoked regularly.
Results: The peak risk of adult nicotine dependence coincides with onset of regular use at approximately 10 years old, with an elevated risk persisting to 20 years. The risk of dependence is significantly higher for females compared to males for onset of regular use between ages 9 and 18.
Conclusions: Results suggest that the risk of adult nicotine dependence is highest when onset of regular smoking occurs at around 10 years, though the associated risk is high for ages of onset into young adulthood. Early onset of regular use is a relatively stronger risk factor for adolescent females than males. Smoking prevention programs should focus on late childhood through early adolescence, particularly among females. TVEM provides a more nuanced understanding of the risk associated with different ages of onset of health risk behaviors.

1. Introduction

Smoking is the leading cause of preventable death in the United States and worldwide (Centers for Disease Control & Prevention (CDC), 2004; World Health Organization (WHO), 2009). One reason for the high rates of smoking-related problems is the highly addictive nature of nicotine, which makes quitting smoking difficult once regular smoking has begun (Stolerman & Jarvis, 1995); only about 5% of smokers who attempt to quit are successful (CDC, 2004). About 17% of all adults meet lifetime criteria for nicotine dependence (Goodwin, Pagura, Spiwak, Lemeshow, & Sareen, 2011), with about half of adults who had ever engaged in regular smoking progressing to nicotine dependence (Breslau, Johnson, Hiripi & Kessler, 2001).

The progression to nicotine dependence is understood as an outcome of a series of milestones, including contemplating cigarette use, first cigarette, experimental smoking, regular smoking, and then ultimately dependence (Mayhew, Flay, & Mott, 2000). The age at

* Corresponding author at: The Methodology Center, The Pennsylvania State University, 404 Health and Human Development Building, University Park, PA 16802, USA. Tel.: +1 814 865 7095; fax: +1 814 86 0000.
E-mail address: SLanza@psu.edu (S.T. Lanza).

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which individuals reach particular smoking milestones has been implicated as a risk factor for nicotine dependence (Dierker et al., 2008). Early initiation is related to factors such as smoking susceptibility (Pierce, Choi, Gilpin, Farkas, & Merritt, 1996), neurobehavioral disinhibition (Tarter et al., 2003), and cigarette availability (Roberts, Colby, & Jackson, 2015). Early exposure to nicotine predicts higher rates of nicotine dependence in both animals (e.g., Brielmaier, McDonald, & Smith, 2007; Kota, Robinson, & Imad Damaj, 2009) and humans (e.g., Kendler, Myers, Damaj, & Chen, 2013). Several studies have found that initiation of smoking before age 14 (Behrendt, Wittchen, Höfler, Lieb, & Beesdo, 2009), before age 16 (Breslau, Fenn, & Peterson, 1993), and before age 20 (Storr, Zhou, Liang, & Anthony, 2004) is associated with increased odds of nicotine dependence compared to initiation at later ages. However, as these studies compared different age groups rather than examining age continuously, it is not clear exactly which ages are associated with greater odds of dependence. In addition, most studies of the impact of smoking milestones on nicotine dependence focus on smoking initiation rather than regular smoking, and thus less is known about the effect of onset of regular smoking at different ages on later nicotine dependence (CDC, 2010).

The progression to nicotine dependence differs by sex. Although the mean age of first cigarette is slightly older for females (12.5 years) than males (12.0 years), mean age of onset of regular cigarette use is similar across sex (Dierker et al., 2012). Overall rates of adult nicotine dependence are slightly higher for men than women (14.1% v. 11.5%; Grant, Hasin, Chou, Stinson, & Dawson, 2004), but women may have a more difficult time quitting smoking than men once they are nicotine dependent (Cepeda-Benito, Reynoso, & Erath, 2004; Piper et al., 2010).

To derive more nuanced information about the association between age of onset and subsequent nicotine dependence and how this complex association varies across sex, we use the time-varying effect model (TVEM; Tan, Shiyko, Li, Li, & Dierker, 2012) to estimate regression coefficients as a flexible function of continuous age of onset. Previous applications of TVEM in tobacco research have used ecological momentary assessments to shed light on the dynamic associations between negative affect and craving (Lanza, Vasilenko, Liu, Li, & Piper, 2014), and between craving and cessation fatigue (Liu, Li, Lanza, Vasilenko & Piper, 2013) and between negative affect and smoking lapse (Vasilenko et al., 2014). A recent study (Selya et al., 2015) used TVEM to examine the mood between smoking and mood across continuous levels of dependence.

This study is the first to use TVEM to model the nuanced association between age of onset of a behavior and a later outcome. The rate of nicotine dependence in adulthood is modeled as a flexible function of age of first regular cigarette use; sex is examined as a moderator.

2. Methods

2.1. Participants and procedure

This study used data from Wave 1 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; National Institutes of Health, 2006), a national sample of the non-institutionalized U.S. population 18 years of age and older. The Wave 1 sample of $N = 43{,}093$ adults was drawn from a survey administered by the National Institute on Alcohol Abuse and Alcoholism in 2001–2002. Participants in the overall sample were 43.0% male with mean age of 46.4 ($SD = 19.1$); the racial/ethnic composition was 56.9% non-Hispanic White, 19.1% non-Hispanic Black, 19.3% Hispanic, 3.1% Asian/Native Hawaiian/Pacific Islander, and 1.6% American Indian/Alaska Native. Because of our focus on timing of first regular smoking, we limited our sample to those adults who reported ever having smoked cigarettes regularly by age 40. This resulted in a sample of 15,748 individuals (50.5% male; M age = 48.7, $SD = 17.3$; 66.9% non-Hispanic White, 16.5% non-Hispanic Black, 12.5% Hispanic, 1.9% Asian/Native Hawaiian/Pacific Islander, and 2.3% American Indian/Alaska Native).

2.1. Measures

Sex was measured by self-report. *Age of onset of regular cigarette use* was assessed by a self-report item about the age at which participants first started smoking cigarettes every day. *Nicotine dependence*, a binary indicator of whether the individual met the symptom criteria in the past 12 months, was assessed by the tobacco module of the Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV; Grant, Dawson, & Hasin, 2001). Diagnosis required respondents to satisfy at least 3 of 7 DSM-IV (American Psychiatric Association, 1994) criteria in the past year. Of the overall NESARC sample of adults, 11.5% met this definition; 29.5% of the analysis sample (adults who reported ever having smoked cigarettes regularly by age 40) met this definition. Among those with past-year nicotine dependence, past-year rates of tobacco product use were 95.3% cigarettes, 7.1% cigars, 1.2% pipe, 6.0% snuff, and 3.4% chew tobacco.

2.2. Analytic approach

Models were run using intercept-only logistic TVEM, a semi-parametric model that estimates regression coefficients as functions of continuous time (Vasilenko et al., 2014). Intercept-only models estimating the rate of adult dependence as a function of age of regular smoking onset were run for the full analysis sample, and then separately for male and female participants to allow sex to fully moderate the complex association. All models were run in SAS 9.3 using the %TVEM_logistic macro (Li et al., 2014).

3. Results

The mean age of onset of regular smoking was 18.6 ($SD = 4.7$), and was significantly younger for males than females (18.2 and 19.1, respectively; $t = 12.5$; $p < .0001$). The rate of past-year nicotine dependence differed significantly across sex, with 27.4% of males and 31.7% of females meeting this definition (chi-square = 35.1, $df = 1$, $p < .0001$).

3.1. Complex association between age of onset and nicotine dependence

Fig. 1 shows the exponentiated intercept coefficient function for the full sample, reflecting the rate of nicotine dependence in adulthood as a function of age at first regular cigarette use. The rate of adult dependence is highest for individuals who experienced onset of regular use in middle childhood to early adolescence, with peak risk of adult dependence (43%) corresponding to regular smoking onset at approximately 10 years old. For ages of onset between 10 and 18, the rate of nicotine dependence in adulthood decreased steadily and steeply to about half the original rate, and then leveled off at about 25% for ages of onset from about 18 to 35; thereafter the rate decreased to around 15% for age of onset at age 40.

3.2. Sex differences in the role of age of onset

Fig. 2 shows prevalence of adult dependence as a function of age of onset separately for men and women. Ages where the confidence bands do not overlap indicate significantly different rates of nicotine dependence in adulthood for the two groups. There are significant sex differences at ages 9 to 18: females who first smoked regularly during those ages having higher rates of dependence in adulthood compared to males. Females' rates of adult dependence peaked at more than 50% for an age of onset of approximately 10 years; this rate was double that for females with an age-of-onset of age 20 or older. For males, the rate of adult dependence peaked at 36% for an age of onset of around 10 years and was approximately 25% for an age of onset of 20 or older.