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### Drug and Alcohol Dependence



# Recalled first reactions to inhaling nicotine predict the level of physical dependence



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#### ABSTRACT

**Background**: The level of physical dependence is a measure of addiction that correlates highly with addiction-associated changes in brain structure. We sought to determine whether age at first inhalation and initial reactions to inhaling nicotine are related to level of physical dependence in early adulthood. **Methods**: Young adults (n=312; mean age=24 years; 51% female) from the Nicotine Dependence in Teens study who had smoked at least once in the preceding three months completed self-report questionnaires in 2011–12. We assessed level of physical dependence with three validated self-report items assessing 'wanting,' 'craving' and 'needing' triggered by nicotine deprivation. Survey items assessed smoking behavior, including age at first inhalation, and recalled first reactions to inhaling nicotine. **Results**: After adjusting for covariates, experiencing relaxation, heart racing/pounding, rush or "buzz"

(OR = 1.45; 95% CI: 1.08, 1.94) and dizziness (OR = 1.58; 95% CI: 1.15, 2.18) at first nicotine inhalation were associated with an increased odds of being at a higher level of physical dependence in young adulthood; the association for experiencing relaxation (OR = 1.78; 95% CI: 1.20, 2.64) and heart racing/pounding (OR = 1.51; 95% CI: 1.00, 2.28) persisted after additionally controlling for all other first reactions. Neither age at first inhalation nor unpleasant first reactions predicted level of physical dependence.

**Conclusions**: In accordance with prior research, our findings suggest that smokers who are particularly sensitive to the pleasant, "buzz-related" and generally arousing effects of nicotine may be more likely to attain higher levels of physical dependence.

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#### 1. Introduction

Prior to the onset of addiction, novice smokers usually experience no symptoms when abstinent, even for long periods of time (DiFranza and Wellman, 2005). Physical dependence on tobacco is typically heralded by the development of both withdrawal symptoms and craving (Gervais et al., 2006; O'Loughlin et al., 2009) during prolonged abstinence from nicotine (Hughes, 2007). Clinical case studies revealed that, as smokers continue to use, withdrawal symptoms intensify through a predictable progression from 'wanting,' a mild desire to smoke that is transitory and easily ignored, to 'craving,' a strong, persistent and intrusive urge to smoke, to 'needing,' an unremitting urgency to smoke to restore "normal" function

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http://dx.doi.org/10.1016/j.drugalcdep.2014.07.021 0376-8716/© 2014 Elsevier Ireland Ltd. All rights reserved. and emotional wellbeing (DiFranza et al., 2010). Based on these findings, we validated a self-report measure for determining the level of physical dependence (DiFranza et al., 2011a). Level of physical dependence is diagnosed based on the most advanced symptom reported, so smokers are diagnosed at level 3 if they experience needing, at level 2 if they experience craving but not needing, at level 1 if they experience only wanting, and at level 0 if they experience none of these symptoms (DiFranza et al., 2011b). Progression to higher levels of physical dependence is associated with measures of tobacco addiction such as higher scores on the Hooked on Nicotine Checklist (HONC; DiFranza and Wellman, 2007), and the Fagerström Test of Nicotine Dependence (FTND; DiFranza et al., 2012), and is strongly correlated with changes in the anterior cingulate bundle, the superior and medial frontal areas and the precuneus (Huang et al., 2013, 2014). The medial prefrontal and orbital frontal cortex have been implicated in resistance to craving (Hartwell et al., 2011) while the precuneus seems to be involved in reactivity to smoking cues (Engelmann et al., 2012).

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Two factors that appear to robustly predict both increased risk of future smoking and nicotine dependence are age of smoking initiation and symptoms associated with the first smoking experience. The earlier in life one initiates smoking, the more likely one is to become a "regular smoker" (Everett et al., 1999; Reidpath et al., 2014, 2013), to smoke more heavily in early adulthood (Chen and Millar, 1998; Taoli and Wynder, 1991), to have difficulty quitting (Chen and Millar, 1998) and to become nicotine dependent (Hu et al., 2006, 2012). However, the operational definition of smoking initiation differs from study to study including the first time a smoker smoked "part of a cigarette" or "a whole cigarette" or took "one or two puffs on a cigarette." The resulting lack of a consistent benchmark for initiation makes interpretation of the findings difficult (Reidpath et al., 2013). Indeed, the two most important population-based surveys of youth smoking use different definitions, with the Global Youth Tobacco Survey (Centers for Disease Control and Prevention, 2012) using the lowest threshold of one or two puffs, and the Youth Risk Behavior Survey (Centers for Disease Control and Prevention, 2013) using the more stringent threshold of a whole cigarette. Given that inhaling a cigarette ensures exposure to nicotine while puffing may not, it is likely more useful to consider the age at which a smoker first takes smoke into her/his lungs as a meaningful indicator.

First reactions to inhaling nicotine are also associated with the likelihood that smokers progress to heavier smoking and develop symptoms of dependence. The role played by specific first reactions, however, is unclear. Richardson et al. (2010) found evidence for three separate dimensions of initial reaction: pleasurable sensations (relaxation or feeling "good"), unpleasant sensations (feeling sick, feeling nervous, coughing), and "buzz"-related sensations (feeling dizzy or high). Generally, pleasurable sensations are risk factors (Blitstein et al., 2003; Chen et al., 2003; DiFranza et al., 2004; Hu et al., 2006, 2012; Kandel et al., 2007; Pomerleau et al., 1998, 1999; Richardson et al., 2010; Rodriguez and Audrain-McGovern, 2004; Urbán, 2010), while unpleasant sensations have been found to be both protective (Hu et al., 2006; Richardson et al., 2010; Rodriguez and Audrain-McGovern, 2004; Urbán, 2010) and risk factors (DiFranza et al., 2004). Dizziness on first inhaling nicotine also seems to be an independent predictor of progression to heavy smoking and dependence (DiFranza et al., 2004; Hu et al., 2006; Pomerleau et al., 1998, 1999; Richardson et al., 2010). The sensitivity model (Pomerleau et al., 1993) proposes that individuals who are especially sensitive to the effects of nicotine and who report more intense reactions, both pleasurable and aversive, to initial inhalation are most likely to progress to heavy, dependent smoking.

Our objective in the current study was to determine whether age at first inhalation or first reactions to inhaling nicotine predict level of physical dependence in young adulthood.

#### 2. Methods

#### 2.1. Data collection

We drew data from the 2011–12 survey cycle of the Nicotine Dependence in Teens (NDIT) study, a prospective longitudinal investigation conducted in Montréal, Canada since 1999. The baseline cohort of seventh graders (n=1294; average age 12.5 years) was recruited in a convenience sample of 10 secondary schools. Participants completed self-report questionnaires, in English or French, at school every three months for a total of 20 survey cycles over the five years of secondary school (O'Loughlin et al., 2014), followed by two postsecondary school cycles in 2007–08 and 2011–12. Parental consent was obtained for the secondary school survey cycles, while participants provided consent for the postsecondary school cycles. The study was approved by the McGill University Institutional Review Board and the Ethics Research Committee of the Centre de Recherche du Centre Hospitalier de l'Université de Montréal.

For the current study, data on demographics, smoking behaviors and first reactions to inhaling nicotine were drawn from the survey cycle completed in 2011–12, while data on age at first inhalation were collected in the survey cycle at which the participant first reported having inhaled. Thus, the study design was longitudinal for the objective related to age at first inhalation and cross-sectional for the objective related to first reactions to nicotine.

#### 2.2. Study sample

The 2011–12 survey was completed by 859 young adults, representing 66% of the baseline NDIT cohort and 82% of the 1052 participants who are currently eligible for continued participation in future survey cycles. During the 13 years of follow-up since 1999, 241 NDIT participants (19% of the baseline cohort) refused to continue follow-up. At baseline, those lost to follow-up were heavier smokers than continuing participants; they consumed an average of 24 cigarettes in the three months preceding baseline data collection, vs. eight cigarettes for continuers (O'Loughlin et al., 2014).

*2.2.1. Participants.* Eligible participants for the current study were current smokers who indicated in 2011–12 that they had smoked at least one cigarette in the preceding three months.

#### 2.3. Measures

2.3.1. Outcome: level of dependence. We assessed each participant's level of physical dependence with three items that measure the response to nicotine deprivation. 'Needing' was assessed with: "If I go too long without smoking I just can't function right, and I know I will have to smoke just to feel normal again." 'Craving' was assessed with: "If I go too long without smoking, the desire for a cigarette becomes so strong that it is hard to ignore and it interrupts my thinking," and 'wanting' was assessed with: "If I go too long without smoking the first thing I will notice is a mild desire to smoke that I can ignore." Each statement offered response options: describes me not at all (0), describes me a little (1), describes me well (2), and describes me very well(3). Smokers are assigned to a level of dependence according to the most severe symptom endorsed (i.e., with a score  $\geq$ 1: needing=level 3, craving=level 2, wanting=level 1, no symptoms=level 0.

#### 2.3.2. Predictors.

2.3.2.1. Age at first inhalation. Participants were asked at each of the 22 survey cycles whether they had ever taken cigarette smoke into their lungs; those who indicated that they had were asked the age at which this first occurred. The age provided in the first survey cycle in which a participant reported having inhaled was used as the measure of age at first inhalation.

2.3.2.2. Initial reactions to inhaling nicotine. In 2011–12 participants who had ever inhaled were asked: "The first few times you took cigarette smoke into your lungs, did you experience ...relaxation?" ...rush or buzz?" ... dizziness?" ...nausea?" ...coughing?" ...burning in the throat?" ...upset stomach?" or ...heart racing or pounding?" Response options were not at all, a bit, a lot, scored 1–3.

2.3.3. Data analysis. Predictors were tested in ordinal logistic regression analyses using a proportional odds model (Norusis, 2012), which determines the odds of being at a higher level of physical dependence (i.e., level 0 vs. all others; level 1 vs. levels 2 and

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