Cigarette smoking duration mediates the association between future thinking and norepinephrine level

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HIGHLIGHTS

* Future thinking is associated with smoking cigarettes for longer durations.
* Smoking cigarettes for longer durations is associated with higher norepinephrine.
* Smoking duration significantly mediated the future thinking-norepinephrine link.

ARTICLE INFO

Keywords: Future thinking, Impulsivity, Norepinephrine, Smoking duration, Smoking cessation

ABSTRACT

Fixating on the present moment rather than considering future consequences of behavior is considered to be a hallmark of drug addiction. As an example, cigarette smokers devalue delayed consequences to a greater extent than nonsmokers, and former smokers devalue delayed consequences more than nonsmokers, but less than current smokers. Further, cigarette smokers have higher norepinephrine levels than nonsmokers, which is indicative of poor future health outcomes. It is unclear how duration of cigarette smoking may impact these associations. The current secondary analysis of publicly available data investigated whether extent of future thinking is associated with smoking duration, as well as norepinephrine level, in a large national US sample (N = 985) of current, former, and never smokers. Individuals scoring lower on future thinking tended to smoke for longer durations and had higher norepinephrine levels relative to individuals scoring higher on future thinking. In addition, duration of cigarette abstinence interacted significantly with future thinking and smoking duration for former smokers. Specifically, the mediation relationship between future thinking, smoking duration, and norepinephrine level for former smokers was strongest at shorter durations of cigarette abstinence and decreased as a function of increasing duration of cigarette abstinence. Overall, results from this study suggest the potential importance of implementing smoking cessation treatments as early as possible for smokers and support future thinking as a potential therapeutic target for smoking cessation treatment.

1. Introduction

Duration of cigarette smoking plays a role in several health outcomes, in which longer durations are associated with worsening health (e.g., chronic obstructive pulmonary disease, lung cancer; U.S. Department of Health and Human Services, 2014). One potential underlying mechanism for smokers’ increased risk for poor health is associated with elevated central and peripheral NE levels relative to nonsmokers (see reviews by Maas, 1984; Bruijnzeel, 2012). High urinary NE levels are indicative of amplified sympathetic nervous system activity (Reuben, Talvi, Rowe, & Seeman, 2000; Supiano, Hogikyan, Sidani, Galecki, & Krueger, 1999), and are related to the development of cardiovascular disease, obesity, inflammatory disorders, and other conditions often seen in cigarette smokers (see Bayles, Dawood, Lambert, Schlaich, & Lambert, 2008 and Puzserova & Bernatova, 2016 for reviews). High urinary NE levels also predict a greater incidence of premature mortality (Reuben et al., 2000). However, to our knowledge, no work exists that examines whether urinary NE levels increase gradually with increasing smoking duration or if levels increase following smoking initiation and then reach a plateau, with no further increases occurring during smoking maintenance.

In addition to effects of smoking duration on NE levels, only a few studies to date have examined the relation between smoking cessation and NE (West, Russell, Jarvis, Pizzey, & Kadam, 1984; Ward, Garvey, & Bliss, 1991; Zuspan & Davis, 1979). In one study (Zuspan & Davis, 1979), urinary NE levels were not only reduced significantly from pre-
to post-smoking cessation, but post-cessation NE levels were comparable to those for nonsmokers. Given that inclusion criteria for most studies specify a minimum number of years smoking to be classified as a current cigarette smoker (e.g., at least one year; West et al., 1984; Zuspan & Davis, 1979), smoking duration may vary widely between participants in a given sample. It therefore remains unclear whether NE levels will recover for individuals that smoke for 10 years in a similar manner to those that smoke for 20 years.

In addition to characterizing effects of smoking duration and cessation on NE dysregulation, recent attention has been directed towards understanding psychological factors that may be associated with behaviors such as smoking and physiological biomarkers of health such as NE (Powell, Pickering, Dawkins, West, & Powell, 2004; Schwartz & Portnoy, 2017), with the long-term goal of developing better treatments for cessation. One such factor is future thinking, because those who are fixated on the present moment and seek immediate rewards may engage in a variety of unhealthy behaviors, including smoking (e.g., Adams, 2012; Beenstock, Lindson-Hawley, Aveyard, & Adams, 2014; Bickel, Odum, & Madden, 1999). Indeed, relative to never cigarette smokers, current smokers tend to score lower across a variety of measures that arguably assess future thinking: Considerations of Future Consequences Scale (Adams, 2012; Beenstock et al., 2014), delay-discounting assessments (Bickel et al., 1999; Mitchell & Wilson, 2012; Reynolds, Richards, Horn, & Karraker, 2004), and the Barratt Impulsiveness Scale (Chang, Lim, Lau, & Alicata, 2017). Current smokers have also shown to devalue delayed rewards more heavily than former smokers (Bickel et al., 1999; Odum, Maddgen, & Bickel, 2002; Skinner, Aubin, & Berlin, 2004), suggesting that higher future thinking promotes successful cessation (Sheffer et al., 2014) and/or that future thinking increases following smoking cessation (Bickel et al., 1999; Odum et al., 2002; Skinner et al., 2004).

1.1. Current study

The current secondary data analysis tested whether future thinking predicted urinary NE levels in a large national U.S. sample of adults, aged 28–84. Based on prior research, we predicted that lower future thinking would be associated with longer smoking durations and in turn, higher levels of NE. We also hypothesized that the strength of the mediation for former smokers would decline with a longer duration of smoking abstinence.

2. Material and methods

2.1. Sample

The national survey of Midlife Development in the United States (MIDUS) is a publicly available, longitudinal survey aimed at understanding developmental differences in physical and mental health based on psychological, social, and behavioral factors. The first wave of MIDUS data collection (1995–1996; MIDUS 1) included 7108 non-institutionalized participants, aged 28 to 84 years, selected via random-digit telephone dialing. The second MIDUS wave (2004–2006; MIDUS 2) involved re-contacting 4963 participants from MIDUS 1 to participate in additional survey measures. Detailed information regarding attrition between waves is available elsewhere (Radler & Ryff, 2010). The current study drew from participants that completed the MIDUS 2 assessment (n = 4963), which included a 30-min telephone questionnaire followed by an ~2-h questionnaire that participants received via mail and sent back upon completion.

All MIDUS 2 respondents were eligible for further participation in biomarker assessments, given their willingness to stay overnight at a study-affiliated center: University of California Los Angeles, University of Wisconsin, or Georgetown University. Biomarker data were collected from 2004 and 2009 from n = 1097, with an average of 2.80 years (SD = 1.33) between MIDUS 2 completion and biomarker assessment. Samples taken included blood, urine, and saliva for analysis of biomarkers reflecting functioning of the autonomic nervous system, immune system, and others (see Love, Seeman, Weinstein, & Ryff, 2010 for full description).

To be included in the current analysis, participants had to have completed the following measures at MIDUS 2: phone and self-administered questionnaires; demographic information; future thinking assessments (i.e., Live for Today (LFT) scale); and questions related to current and/or past cigarette smoking and other drug use. Respondents were also required to have provided medication use information and a 12-h urine sample for analysis of NE level during the biomarker sub-project. Respondents missing any of these items, including the urine sample (n = 38), were removed from analyses. Comparing respondents with complete versus incomplete data at MIDUS 2, participants with complete data were significantly older (t(4960) = 9.57, p < .001), more likely to be white/Caucasian (X2 = 47.23, p < .001), and male (X2 = 37.54, p < .001). Attrition analyses also revealed that those who did not complete the biomarker subproject scored lower on future thinking (assessed via the LFT scale; t(3968) = −6.64, p < .001; CI = −0.21 to −0.12) and to have smoked longer (t(4916) = −4.61, p < .001; CI = −3.59 to −1.45) than those that completed the biomarker assessment. Of the 1097 participants who completed the biomarker subproject and the MIDUS 2 questionnaires, 985 were included in the final sample.

2.2. Measures

2.2.1. Covariates

All models were adjusted for potential confounds of age, sex, race, education, and medication use. Participants were aged 28 to 84 years (M = 55.43, SD = 12.45), and were primarily female (53.5%) and Caucasian (90.2%). Educational attainment was scored on a scale from 1 (no school/some grade school) to 12 (graduate or professional degree) with mean level of education being some college/college graduate (M = 7.20, SD = 2.52). Dichotomous variables were created for sex, race (white/Caucasian coded 0, all other races coded 1, including black/African American, Native American/Alaskan, Native Aleutian Islander/Eskimo, Native Hawaiian/Pacific Islander), and medication use that can be linked to NE levels (blood pressure, cholesterol, depression, corticosteroids; Annane, Sebille, Charpentier, et al., 2002; Chistiakov, Ashwell, Orekhov, & Bobryshev, 2015; Chrousos, 2009; Vaughn, Murphy, & Buckley, 1996). All models were also adjusted for time lag between completion of the self-administered questionnaire at MIDUS 2 and completion of the biomarker assessment (M = 25.32 months, SD = 14.22, range 0 to 62).

2.2.2. Future thinking

Future thinking was evaluated using a scale contained in the MIDUS 2 self-administered questionnaire, “Live for Today” (LFT; Prenda & Lachman, 2001). LFT is a subscale of the Planning and Making Sense of the Past questionnaire in MIDUS 2. LFT items assess the extent to which participants think about the future, and the scale includes four items (i.e., “I live one day at a time”; “I have too many things to think about today to think about tomorrow”; “I believe there is no sense planning too far ahead because so many things can change”; “There is no use in thinking about the past because there is nothing you can do about it”). Each item was presented on a 4-point Likert scale ranging from 1 (strongly agree) to 4 (strongly disagree). The LFT scale was created by reverse-coding and computing the average of the four items. Higher scores reflect lower future thinking (Cronbach’s alpha = 0.65, M = 2.28, SD = 0.68). Validation of the LFT scale is indicated by significant correlations with alternative measures of future thinking (e.g., Consideration of Future Consequences Scale; r range = 0.31 to 0.33, p’s < 0.01; Basile & Toplak, 2015; Strathman, Gleicher, Boninger, & Edwards, 1994).
2.2.3. Smoking variables

Respondents were stratified into three groups based on smoking status: never (n = 549; 55.7%), current (n = 105; 10.7%), and former (n = 331; 33.6%) smokers. These groups were constructed based on self-reported answers to questionnaires administered via telephone at MIDUS 2. Respondents were asked, “Have you ever smoked cigarettes regularly—that is, at least a few cigarettes every day?” If respondents answered “no,” they were designated as a never smoker. Respondents that answered “yes” to this question were prompted further by asking, “Do you smoking cigarettes regularly NOW?” If respondents answered “yes” to this follow-up question, they were designated as a current smoker. If respondents answered “no” to the follow-up question, they were designated as a former smoker. Smoking status was then used to construct additional variables. These included smoking duration for former smokers when tested separately. Importantly, none of the covariates altered the parameter estimates or indirect effects in any models.

2.2.4. Urinary norepinephrine

Participants were instructed to void urine at approximately 7:00 p.m. on the first day of their overnight visit, which is standard practice to ensure that all urine collected during the 12-h period was urine produced during that period (e.g., Laskar, Iwamoto, Nakamoto, Koshiyama, & Harada, 2004). Following disposal of this initial void, participants were instructed to collect all urine samples until approximately 7:00 a.m. on the second day of their visit. They were also instructed to notify a nurse immediately following each void, whether day or night. To prevent missing voids, participants were given reminders between 9 and 10 p.m. (for nighttime voids), upon awakening, and also during blood draws that occurred prior to 7 a.m. Following the 12-h collection period, nurses were instructed to indicate any missed voids as well as the reason for the missing void(s). Because an incomplete collection period may influence results of NE levels, we excluded participants that were missing one or more voids during this period (n = 38). Current cigarette smokers were permitted to continue smoking ad libitum during the overnight study visit. All voids were combined into a single sample along with 25 mL acetic acid and stored in a −60 to 80 °C freezer before shipment to MIDUS Biocore laboratories. Catecholamine analyses were performed at the Mayo Medical Laboratory (Rochester, MN).

According to a method described previously (e.g., Moyer, Jiang, Tyce, & Sheps, 1979), high-pressure liquid chromatography was used to extract catecholamines from urine. First, acidic metabolites were removed using ethyl acetate. Then, 1.0 mL of non-acidic urine was absorbed on aluminum oxide at an alkaline pH and eluted with acid. For further purification, the specimen was then complexed with boric acid gel. By washing with boric acid, free catecholamines were removed from the specimen. Finally, an aliquot of boric acid eluate was injected onto a high-performance reverse-phase paired ion-chromatography column where the catecholamines were resolved into individual components. Catecholamines were then oxidized electronically to an O-quinone. Current generated at the detector was converted by an amplifier to a voltage signal and an XY recording was generated to detect NE concentrations. The mean NE value was 18.18 μg/12 h (SD = 9.52, Range 0.54 to 102.20).

2.3. Data analysis

All analyses were conducted using SPSS version 24.0. Using the SPSS macro PROCESS, mediation models were tested by creating 1000 bootstrap samples through random sampling with replacement (Preacher & Hayes, 2008). Separate mediation models were tested using NE level as the outcome, smoking duration for different smoking groups as mediators, and the LFT scale as the predictor. We then tested whether the duration of smoking abstinence (“years quit”) significantly moderated the mediation relationship for former smokers between LFT scores, smoking duration, and NE level. Indirect effects were considered significant if 95% confidence intervals did not include zero. Also conducted was a one-way analysis of variance to assess potential differences in LFT scores and NE levels as a function of smoking status. For all analyses, statistical significance was defined as p < .05.

3. Results

Table 1 displays descriptive statistics and correlations for all measures. Fig. 1 shows that when all smoking groups were included in the model, those scoring higher on the LFT scale (i.e., indicative of lower future thinking) smoked longer and had higher levels of urinary NE relative to those scoring lower on the LFT scale. Calculation of the indirect effect for mediation revealed that smoking duration significantly mediated the LFT-NE association. That is, those scoring higher on the LFT scale were more likely to smoke longer, and smoking longer was predictive of higher NE levels. However, no significant differences between groups were observed for LFT scores, F(2, 2845) = 0.524, p = .592, or NE levels, F(2, 866) = 0.135, p = .874.

When never smokers were removed from the mediation model (n = 549) (Fig. 2), and when only former smokers were included in the model (Fig. 3), the mediation relationship described above persisted. However, when only current smokers were included in the model (Fig. 4), LFT scores were not associated with smoking duration or NE levels. Thus, the relationship between LFT scores, smoking duration, and NE levels in the first two models (Figs. 1 and 2) was driven by the current sample of former smokers. When duration of cigarette abstinence was included in the model for former smokers as a moderator (Fig. 5), there was a significant interaction between LFT scores and duration of cigarette abstinence, as well as the presence of a conditional indirect effect. The mediation relationship between LFT scores, smoking duration, and NE level was strongest for former smokers at shorter durations of cigarette abstinence, and weakened as duration of cigarette abstinence increased.1

1 Given that alternative drug use often covaries with tobacco use, models were subsequently adjusted for use of illicit drugs, alcohol, and caffeine. At MIDUS 2, participants reported their use of drugs taken without a prescription, in larger amounts than prescribed, and/or for longer than prescribed in the past 12 months (e.g., sedatives/barbiturates, amphetamines/stimulants, painkillers, marijuana). Only 9.89% of the sample had used any of these drugs, with marijuana (4.45%) and sedatives (3.5%) being the most common. Thus, a binary variable was created that indexed use or no use of any of these drugs. Those who participated in the biomarker project were asked to report on their alcohol and caffeine use. For alcohol, participants reported consuming an average of 1.19 (SEM = 0.04) drinks on days when they drank in the past month. One alcoholic drink was defined per the following: 12-oz can/bottle of beer, one wine cooler, 5-oz glass of wine, and 1.5-oz liquor in a shot or mixed drink. For caffeine, participants reported consuming an average of 3.96 (SEM = 0.11) drinks per day. One caffeine-containing drink was defined as an 8-oz serving. Caffeine use was the only drug use covariate to predict significantly years smoked when all smoking groups were included in the mediation model; however, this covariate failed to predict any outcome measure for former or current smokers when tested separately. Importantly, none of the covariates altered the parameter estimates or indirect effects in any models.
4. Discussion

Among the present sample of former smokers, the relationship between future thinking and NE was mediated by smoking duration. Lower future thinking (i.e., higher scores on LFT) was associated with smoking cigarettes for longer durations, which was associated with increased NE levels. However, this mediation effect was moderated by duration of smoking abstinence. Specifically, the association between future thinking and years smoking was weaker among those who had been abstinent for a longer duration. Such a pattern might suggest that individuals differ in future thinking prior to smoking initiation, and these differences affect success of quit attempts. Indeed, future thinking as assessed via delay-discounting measures has shown to predict smoking initiation during adolescence (Audrain-McGovern et al., 2009),

Table 1

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<th>Predictor Variable</th>
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<td>Blood Pressure Med</td>
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<td>Steroid Med</td>
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<td>Time lag (in months)</td>
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<td>Live for today</td>
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<td>Years smoked (all)</td>
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<td>Years smoked (smokers)</td>
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<td>Years smoked (former)</td>
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<td>Years smoked (current)</td>
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<td>Years quit</td>
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<td>NE</td>
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Note: Bolded values denote statistical significance, *p < .05; **p < .01; ***p < .001.

Fig. 1. Mediation model used to test the association between future thinking, smoking duration, and NE level for all smoking groups (never, current, and former). Asterisks denote statistical significance, *p < .05; **p < .01; ***p < .001.

Fig. 2. Mediation model used to test the association between future thinking, smoking duration, and NE level for current and former smokers. Asterisks denote statistical significance, *p < .05; **p < .01; ***p < .001.

Fig. 3. Mediation model used to test the association between future thinking, smoking duration, and NE level for former smokers. Asterisks denote statistical significance, *p < .05; **p < .01.

Fig. 4. Mediation model used to test the association between future thinking, smoking duration, and NE level for current smokers.
and also to predict smoking abstinence (Sheffer et al., 2014). Alternatively, future thinking may increase with duration of cigarette abstinence (Secades-Villa, Weidberg, Garcia-Rodriguez, Fernandez-Hermida, & Yoon, 2014). In this case, the former smokers may have scores that indicate higher future thinking, relative to the current smokers, as a consequence of quitting cigarettes. A bi-directional association may also be present such that smoking may lead to lower future thinking, just as lower future thinking may lead to smoking initiation. Unfortunately, a temporal pathway cannot be discerned in the present study due to the retrospective nature of the data. This pathway will be important to investigate given work that has shown behavior can influence personality characteristics (Hampson, 2012; Smith, 2006).

Longer smoking durations among former smokers were also associated significantly with higher NE levels. Given that illicit drug, alcohol, or caffeine use may also contribute to elevated NE levels (e.g., Markianos & Vakis, 1984), we re-ran all of our mediation analyses with these items as covariates and they did not affect the overall pattern of results (data not shown, but see footnote), suggesting that cigarette smoking was the primary driver of elevated NE levels for participants in the current study. However, given that elevated NE may serve as an etiological factor in smoking initiation (Fitzgerald, 2013), future work should examine NE levels before smoking onset, during, and following cessation. The latter assessment will be key in understanding whether NE levels decrease after smoking cessation and whether levels become normative. Given the increased risk of adverse health outcomes for individuals with high NE levels (Bayles et al., 2008; Puzserova & Bernatova, 2016), results provide further support for quitting smoking as early as possible. This finding also highlights the utility of understanding how future thinking impacts other biological markers indicative of negative health outcomes, such as allostatic load and inflammation, which are elevated for smokers compared to nonsmokers (e.g., Korani, Hassan, Tony, & Abdou, 2016; Wiggert, Wilhelm, Nakajima, & Al’Absi, M., 2016).

Understanding how future thinking impacts biomarkers of health specifically may lead to improved therapeutic treatments. One treatment developed recently for increasing future thinking in an effort to change behavior is that of “episodic future thinking” (EFT; Atance & O’Neill, 2001; Benoit, Gilbert, & Burgess, 2013; Peters & Buchel, 2010; Stein et al., 2016). EFT involves prospective thinking, such as asking individuals to imagine or simulate events that may occur in the future, in order to increase the value of delayed consequences (Atance & O’Neill, 2001). EFT has been effective in increasing the value of future consequences in adults and children with obesity (Daniel, Stanton, & Epstein, 2013), alcohol-dependent individuals (Snider, Laconte, & Bickel, 2016), and current cigarette smokers (Stein et al., 2016). Further, EFT has been successful in reducing alcohol (Snider et al., 2016) and cigarette (Stein et al., 2016) consumption acutely. It is therefore possible that EFT would increase the likelihood of successful cigarette quit attempts, which may lead to reductions in smoking duration and ultimately NE level.

Smoking groups failed to differ on future thinking, which is consistent with work using the Consideration of Future Consequences Scale (Beenstock et al., 2014) but in contrast to work using delay-discounting assessments (Bickel et al., 1999; Odum et al., 2002; Skinner et al., 2004). While these measures are highly correlated (Cosenza & Nigro, 2015; Epstein et al., 2014), they may represent different constructs. That is, delay discounting may not serve as a proxy for future thinking. Further work is needed to dissociate the similarities and differences between these common assessments.

Importantly, results must be considered in light of some important limitations. In addition to the cross-sectional nature of the data, participants in the current sample were primarily White/Caucasian, older, and college-educated. Results may not generalize to other racial, ethnic, age, or education groups. NE levels may have been influenced by design features such as self-reports that were unable to be verified biochemically (e.g., medication and illicit drug use) (Markianos & Vakis, 1984), and stress precipitated by staying overnight in a new environment for the biomarker project (Laskar et al., 2004). Unfortunately, assessments that allow for examining the potential influence of stress on NE levels are not available. Another limitation involves the relatively small sample of current smokers, which may have resulted in reduced power or lack of variability in future thinking. Finally, questions related to cigarette smoking and future thinking were arguably limited, and thus future work would benefit from inclusion of more detailed assessments.

5. Conclusions

Results suggest additional clinical implications for targeting future thinking in therapeutic treatments for substance-use disorders, specifically cigarette smoking. Because reduced future thinking predicts higher rates of smoking initiation (Dallery & Raiff, 2007), longer smoking durations (current study), and higher relapse rates following a quit attempt (Sheffer et al., 2014), understanding individual differences in future thinking may facilitate personalized prevention and/or treatment strategies for nicotine/tobacco addiction. Ultimately, our results suggest an important role for future thinking in duration of cigarette smoking and NE level, and open several avenues for future research.

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Contributors

Author JEO and NAT designed the study and conducted statistical analyses. Author JEO wrote the first draft of the manuscript and all authors contributed to literature, editing, and have approved the final manuscript.

Conflict of interest

All authors declare that they have no conflicts of interest.

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