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Brief report

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Sex Differences in Time Perception During Smoking Abstinence

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Abstract

Introduction: Nicotine withdrawal leads to impulsive decision-making, which reflects a preference for smaller, immediate rewards and often prompts a relapse to smoking. The mechanism by which nicotine withdrawal leads to impulsive decision-making is not well known. An essential dimension of decision-making is time perception. Impulsive decisions reflect intolerance of temporal delays and the perception that time is passing more slowly. Sex may be an important factor in impulsive decision-making and time perception, but no studies have investigated whether sex moderates the effects of nicotine withdrawal on impulsive decision-making and time perception.

Methods: Thirty-three (12 female) adult smokers completed 2 laboratory sessions: following 24-hr abstinence and once smoking-as-usual (order counterbalanced, abstinence biochemically verified). Participants completed 2 time perception tasks, a decision-making task, and self-report measures of craving, withdrawal, and mood.

Results: During time reproduction, males overestimated time during abstinence compared to smoking, whereas there was no session effect for females. On the time discrimination task, smokers were less accurate during abstinence, and this effect tended to be stronger among females. In general, males had higher discounting rates compared with females, but there was no effect of abstinence.

Conclusions: The current data suggest that the effect of abstinence on time perception may be stronger in males and that males generally exhibit steeper delay discounting rates. Time perception may be an important mechanism in smoking abstinence. Our future work will investigate the role of time perception in smoking relapse and whether this is moderated by sex.

Introduction

Delay discounting refers to an individual's preference for smaller, immediate rewards versus larger, delayed rewards.[1,2] In the context of smoking behavior, for example, a smoker must choose between smoking a cigarette now to relieve withdrawal symptoms versus resisting temptation to avoid health problems in the future. Steeper delay discounting, a type of impulsive decision-making, is associated with smoking. Individual differences in discounting rates are positively correlated with number of cigarettes smoked per day[3–5] and severity of nicotine dependence.[6–8] Importantly, impulsive decision-making predicts smoking relapse.[9–12] However, the psychological mechanisms that contribute to the discounting of delayed rewards are not well understood.

One potentially important contributor is time perception. Timing functions are a critical component of impulsive decision-making.[13–15] The perception that time is passing slower or faster, or an inability to distinguish between short and long delays, may have an important influence on decision-making.[13,15,16] More impulsive individuals tend to overestimate time[17] and shifting time perspective decreases delay

discounting.[18] At the neurobiological level, time perception[19–21] and impulsive decision-making[22–25] engage similar neural circuits (e.g., ventral striatum and prefrontal cortices). Neural responses during time perception predict discounting rates, such that steeper discounting rates are associated with increased neural activity when judging short, compared to long, delays.[26] The ability to delay gratification and maintain goal-directed behavior in the face of cravings to smoke is critical to maintain smoking abstinence. These higher order cognitive functions rely on accurate time perception.[27,28] Thus, deficits in time perception may prompt behaviors to alleviate short-term discomfort (i.e., relapse) rather than behaviors focused on long-term goals (i.e., maintaining abstinence).

Nicotine withdrawal produces unpleasant physiological, affective, and cognitive symptoms that are related to relapse,[29,30] and affects delay discounting and time perception. Abstinence increases delay discounting[31,32] and causes smokers to overestimate time.[33,34] Although sex may be an important factor in impulsive decision-making and time perception, no study has investigated whether sex moderates abstinence effects on impulsive decision-making and time perception. Some studies have found that men discount future rewards more steeply than women[35,36] and we predict that this effect will be more pronounced during abstinence, compared to smoking. Based on evidence that females are less accurate when determining the duration of a stimulus and underestimate duration when reproducing intervals,[37,38] we predict that females will exhibit greater abstinence effects on time perception, compared to males. The current study tested the hypothesis that nicotine withdrawal increases the subjective passage of time and impulsive decision-making and that this relationship would be moderated by sex.

Methods

Participants

Eligible smokers between 18 and 65 years old who smoked at least 10 cigarettes/day for at least 6 months were recruited through print fliers and internet advertisements (e.g., Craigslist). Exclusion criteria included: enrolled in a smoking cessation program; history of *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)* Axis I disorders (except nicotine dependence); use of psychotropic or smoking cessation medications; pregnancy; low or borderline intelligence (<90 score on Shipley's IQ test); and any impairment that would prevent cognitive task performance (e.g., color blindness). Of the 217 participants who completed the initial telephone screen, 108 were eligible, 75 attended the screening visit, and 45 met final eligibility criteria. Reasons for exclusion included: Shipley IQ score<90 (n = 13), positive breath alcohol or urine drug screen (n = 8), carbon monoxide (CO) sample <10 ppm (n = 6), or failure to adhere to protocol (n = 3). Thus, 33 smokers (12 female) completed the study.

Procedures

All procedures were approved by the University of Pennsylvania Institutional Review Board and all participants provided written informed consent. This study included two laboratory sessions separated by approximately one week: once following 24 hr of abstinence and once smoking-as-usual (order counterbalanced). Participants completed an eligibility screening including, a urine drug screen, breath alcohol test, and pregnancy test. Psychiatric or substance abuse disorders were assessed using the Mini International Neuropsychiatric Interview.[39] The Shipley Institute of Living Scale[40] and Fagerström Test for Nicotine Dependence[41] were also administered.

At each laboratory session, those with a positive drug screen, a breath alcohol >0.01, or a CO > 9 ppm (for the abstinent session) were excluded. Participants completed measures of withdrawal (Minnesota Withdrawal Scale),[42] craving (questionnaire on smoking urges-brief),[43] and mood (positive and negative affect schedule).[44]

Assessments

Time Discrimination Task

The time discrimination task (TDT) is based on prior research.[45] Participants are presented with two intervals and asked to press a key to indicate which was longer. On half the trials, the longer interval is presented first and the difference between comparison intervals (duration difference) is 250 ms, 500 ms, or 750 ms (randomly determined). Durations of comparison intervals are multiples of 250 ms up to 2,750 ms. The first interval is followed by a blank screen (500 ms) and a crosshair (250 ms). After the second interval, participants indicate which was longer. The 108 trials are randomly intermixed so that any duration difference and any pair of comparison intervals can occur on a given trial. The primary outcome is the discrimination index, d'. Correct responses ("hits") and errors ("false alarms") were used to calculate d' using the following equation: $\left(\frac{1}{\sqrt{2}}\right)\times\left(z(\text{Hit})-z(\text{False Alarm})\right)$.[46] Higher d' indicates greater sensitivity to distinguish between stimuli.

Time Reproduction Task

The time reproduction task (TRT) is a measure of retrospective time perception based on prior research.[47,48] The TRT consists of two phases: encoding and reproduction. During the encoding phase participants must retain the duration of a visual stimulus (red cross), which is followed by a 5-s inter-stimulus interval (gray cross). The reproduction phase begins with the presentation of a green cross displayed for 1.5 times the duration of the encoding interval. Participants must reproduce the duration by clicking the computer mouse. For the 16 trials, the duration of the encoding interval is selected pseudo-randomly out of eight durations: 5.00, 5.95, 7.07, 8.41, 10.00, 11.89, 14.14, and 16.82 s (i.e., a geometric sequence $x_{i+1} = x_i 2^{1/4}$) so that each interval is used twice. Participants are instructed to avoid mental counting. The primary outcome is the accuracy coefficient, "theta" (i.e., θ), which is the ratio of the estimated duration to the actual duration.[49,50] Values greater than 1 indicate overestimation and lower than 1 indicate underestimation.

Delay Discounting Task

In this hypothetical delay discounting task, participants choose between a smaller reward available immediately (e.g., $20 today) and a larger reward available after a longer delay (e.g., $40 in a month). The magnitude of the immediate reward and the magnitude and delay of the larger, later reward vary from trial to trial. Participants make 60 choices. The primary outcome is the discount rate. Keeping with standard behavioral findings,[23,51,52] we assume that subjective value (SV) is a hyperbolic function of the reward amount (A) and delay (D): $SV = A/(1+kD)$, where k is the participant's discount rate. Larger values of k indicate a greater degree of discounting future rewards. An R^2 value was calculated for each subject's discounting curve and a minimum cutoff of 0.3 was used to screen out random responding.[3,53,54] Two subjects (one female) were excluded using these criteria. Six additional participants (2 females) chose all immediate or all delayed rewards. Estimates for these subjects were constrained to the lowest and highest discount

rates that could reliably be estimated. Three participants (1 female) had discount rates at the lowest extreme and three (1 female) were at the highest extreme. Results were consistent when analyses were conducted with and without these six participants and they were included in subsequent analyses.

Data Analysis

Mixed linear regression models were used to test the hypothesis that abstinence would result in over-estimation of time during the TRT (i.e., $\theta > 1$), less sensitivity to the difference between short and long intervals on the TDT (i.e., lower d'), and steeper discounting rates (i.e., higher k values). Session (abstinence vs. smoking-as-usual) was a within-subject term and sex was a between-subjects factor and the session by sex interaction was tested. Models included session order as a between-subjects factor to control for practice effects and relevant covariates (e.g., age, Shipley). Cohen's d effect sizes are included in Table 1.

Results

Participants

Demographic and smoking characteristics by sex are presented in Table 1. On average, participants were 38.5 years old (SE = 12.5). There were no significant differences by sex, except that males tended to have a higher CO during abstinence (p = .05). As expected, CO levels during abstinence (3.9 ppm, SD = 2.5) were significantly lower than during smoking (19.4 ppm, SD = 7.8, $p < .0001$), but this did not vary by sex.

Subjective Measures

Craving and withdrawal scores were higher during abstinence (means = 45 and 15.5, SDs = 14.0 and 8.5, respectively) compared to smoking (means = 30.9 and 7.8, SDs = 13.9 and 5.9, respectively; ps < .0001). Likewise, positive affect was lower and negative affect was higher during abstinence (means = 28.8 and 19.1, SDs = 9.0 and 7.6, respectively), compared to smoking (means = 32.5 and 13.8, SDs = 7.7 and 4.2, respectively; ps < .02). There were no significant main or interacting effects of sex (ps > .18; Table 2).

Time Perception

As shown in Table 2, there was a significant sex by session interaction on theta (p = .01; main effect of session, p = .001). Males overestimated time during abstinence, compared to smoking ($p < .001$), whereas there was no session effect for females (p = .27).

For the TDT, d' was significantly lower during abstinence compared to smoking (p = .005), but the sex by session interaction was not significant (p = .14). As shown in Table 2, the pattern of means suggested that females were less accurate during abstinence (p = .005), whereas there was no session effect for males (p = .10).

Delay Discounting

There was a main effect of sex on delay discounting indicating that males had higher discount rates (i.e., more impulsive decision-making; p = .02, d = 0.81). There were no main or interacting effects of session on discounting rate (ps > .7).

Discussion

Our study provides preliminary evidence of sex differences in abstinence effects on time perception. Previous studies have found that abstinence leads smokers to overestimate time intervals.[33,34] We find that this effect is stronger in males than in females. Abstinence also led to poorer time discrimination, and this effect was significant in females alone but not males alone. These data are partially consistent with previous research demonstrating that females are less accurate and tend to underestimate time intervals, relative to males.[37,38,55] This pattern was only evident following 24 hr of smoking abstinence.

There are plausible mechanisms by which sex could moderate effects on time perception during abstinence. Preclinical and clinical studies have demonstrated sex differences in dopamine function following chronic exposure to nicotine[56–58] and in cholinergic function during abstinence.[59] Dopaminergic and cholinergic function are critical for accurate time perception.[60,61] Furthermore, estrogen may modulate the effects of nicotine on dopamine release,[62] which may contribute to sex-specific cognitive deficits.[63] Indeed, estrogen has been shown to modulate time perception differently for males and females.[64] Future work could explore whether pharmacological agents that modify time perception via dopaminergic, cholinergic, or estrogen pathways attenuate nicotine withdrawal or promote abstinence in a sex-specific manner.

Consistent with some previous studies,[36,65] we found that men discounted more steeply than women. However, we did not find that smoking abstinence increased discounting rates. Though this is inconsistent with previous studies, it is consistent with the view that impulsive decision-making may represent a trait-like characteristic.[66,67]

Several limitations warrant mention. Our sample size was small and we may not have been sufficiently powered to detect an interaction effect. Indeed, a post-hoc power analysis suggested that power ranged from 25%–45% for the primary outcomes. Nevertheless, these results provide preliminary evidence that require further investigation and replication in a larger sample. Although more males completed the study than females, we examined a subset of equal numbers of males and females and results were not substantially different. We did not find strong correlations between time perception and impulsive decision-making, which may be partially explained by the fact that our measures assessed different time domains. The time perception tasks assessed intervals in millisecond and seconds range whereas the intervals in the delay discounting task were in the days to months range. Nevertheless, the fact that we assessed

Table 1. Demographic and Smoking Characteristics by Sex

Measure	Male (n = 21)	Female (n = 12)	p
Age (years)	37.1 (12.2)	40.2 (15.4)	.38
Race (n, % Caucasian)	10, 48%	6, 50%	.91
Nicotine dependence	4.6 (1.6)	4.8 (1.6)	.58
Baseline cigarettes per day	18.6 (18)	14.3 (4.1)	.30
Shipley Institute of Living Scale	103 (7.6)	101.1 (6.3)	.26
CO during smoking session (ppm)	19.9 (8.0)	182 (7.4)	.55
CO during abstinent session (ppm)	4.4 (2.6)	2.7 (1.8)	.05

Values are mean (standard deviation). p values are unadjusted for multiple comparison. CO = carbon monoxide; ppm = parts per million.

Table 2. Subjective Measures and Behavioral Performance by Session and Sex (Males [$n = 21$] and Females [$n = 12$])

Measure	Males				Females				
	Smoking	Abstinent	p	Cohen's d	Smoking	Abstinent	p	Cohen's d	Interaction p
Subjective measures									
Craving	31.6 (2.9)	45.3 (2.8)	<.001	0.89	29.4 (4.2)	43.8 (4.2)	.001	1.01	.88
Withdrawal	7.2 (1.5)	15.5 (1.5)	<.001	1.01	8.9 (2.2)	15.2 (2.2)	.02	0.67	.54
Positive affect	31.7 (1.7)	29.3 (1.17)	.14	0.28	34.2 (2.6)	27.7 (2.5)	.01	0.87	.18
Negative affect	14.1 (1.2)	19.3 (1.2)	<.001	0.82	13.1 (1.8)	18.4 (1.8)	.01	0.41	.98
Behavioral measures									
Time reproduction (θ)	0.87 (0.11)	1.04 (0.10)	<.001	1.13	0.93 (0.08)	0.99 (0.11)	.44	0.06	.01
Time discrimination (d')	0.58 (0.18)	0.53 (0.19)	.1	0.31	0.54 (0.22)	0.38 (0.31)	.005	0.57	.14
Delay discounting (log k)	−3.79 (1.0)	−3.71 (1.18)	.75	0.04	−4.6 (0.87)	−4.6 (0.88)	.93	0.03	.89

Unless otherwise noted, values are mean (standard deviation) and adjusted for relevant covariates. Effect sizes represent the effect of abstinence separately for males and females. θ = theta (ratio of perceived duration to actual duration); d' = discrimination index (accuracy); k = discounting rate (natural log scale).

perception of multiple interval durations builds on prior research and is a strength of the current study. A follow-up study is currently underway to explore whether abstinence effects on time perception predict relapse. Understanding these underlying mechanisms and the degree to which they differ between males and females may help identify more targeted treatment strategies to help more smokers successfully quit smoking.

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Declaration of Interests

None declared.

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