

### Original investigation

## Withdrawal-Related Changes in Delay **Discounting Predict Short-Term Smoking Abstinence**

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#### **Abstract**

Introduction: Impulsive decision making is associated with smoking behavior and reflects preferences for smaller, immediate rewards and intolerance of temporal delays. Nicotine withdrawal may alter impulsive decision making and time perception. However, little is known about whether withdrawal-related changes in decision making and time perception predict smoking relapse.

Methods: Forty-five smokers (14 female) completed two laboratory sessions, one following 24-hour abstinence and one smoking-as-usual (order counterbalanced; biochemically verified abstinence). During each visit, participants completed measures of time perception, decision making (ie, discount rates), craving, and withdrawal. Following the second laboratory session, subjects underwent a well-validated model of short-term abstinence (quit week) with small monetary incentives for each day of biochemically confirmed abstinence.

Results: Smokers significantly overestimated time during abstinence, compared to smokingas-usual (p = .021), but there were no abstinence effects on discount rates (p = .6). During the quit week, subjects were abstinent for 3.5 days (SD = 2.15) and smoked a total of 12.9 cigarettes (SD = 15.8). Importantly, higher discount rates (ie, preferences for immediate rewards) during abstinence (abstinence minus smoking difference score) predicted greater number of days abstinent (p = .01) and fewer cigarettes smoked during the quit week (p = .02). Withdrawal-related change in time reproduction did not predict relapse (p = .2).

Conclusions: These data suggest that individuals who have a greater preference for immediate rewards during abstinence (vs. smoking-as-usual) may be more successful at maintaining shortterm abstinence when provided with frequent (eg, daily) versus less frequent incentive schedules (eg, 1 month). Abstinence-induced changes in decision making may be important for identifying smokers who may benefit from interventions that incentivize abstinence such as contingency management (CM).

Implications: The present results suggest that smokers who place greater subjective value on immediate rewards during withdrawal (compared to smoking-as-usual) may be less likely to relapse if offered small, frequent monetary incentives to maintain abstinence. Thus, the current findings may have important implications for identifying smokers most likely to benefit from

particular interventions such as CM. Future research might evaluate whether withdrawal-related changes in delay discounting moderate treatment response to different incentive schedules with the goal of optimizing CM effectiveness to improve abstinence rates.

#### Introduction

Cigarette smoking continues to be the greatest preventable cause of morbidity and mortality,<sup>1</sup> yet the majority of smokers relapse within the first week after a quit attempt.<sup>2,3</sup> Moreover, the number of days abstinent during the first week of a quit attempt is highly predictive of long-term success. Each additional day of abstinence nearly doubles the odds of success.<sup>4</sup> Thus, there is a clear need to elucidate the processes underlying withdrawal symptoms during this vulnerable period of nicotine deprivation. The development of clinically valid procedures for laboratory models of short-term smoking cessation permits evaluation of putative mechanisms that underlie smoking relapse.<sup>5-7</sup>

One psychological process that may play a critical role in relapse is impulsive decision making, or delay discounting. Delay discounting is defined by an individual's preference for smaller, immediate rewards versus larger, delayed rewards. Pypically, these preferences are assessed by presenting an individual with a series of choices for a small amount of money now (eg, \$5 now) versus a larger amount of money at some point in the future (eg, \$30 in 1 month). A higher discounting rate reflects a preference for smaller, immediate rewards and indicates an inability to wait or insensitivity to delayed consequences. 10,11 In the context of smoking behavior, a smoker must choose between smoking a cigarette now to relieve withdrawal symptoms versus resisting temptation to avoid health problems in the future.

Higher delay discounting rates have been associated with cigarette smoking at the initiation, maintenance, and relapse phases. For example, there is evidence that delay discounting promotes smoking acquisition<sup>12</sup> and current smokers discount the value of money significantly more than never- and ex-smokers.<sup>13</sup> Among smokers, individual differences in discounting rates are positively correlated with number of cigarettes smoked per day<sup>14-16</sup> and severity of nicotine dependence.<sup>17,18</sup> Acute withdrawal from nicotine increases delay discounting rates in some studies,<sup>19,20</sup> but not in others.<sup>21,22</sup> Importantly, greater discounting of delayed rewards predicts smoking relapse.<sup>23-26</sup> Indeed, recent evidence suggests that delay discounting is independently associated with relapse, above and beyond the role of nicotine dependence and stress in predicting relapse.<sup>27</sup>

Although the neural substrates of delay discounting have been well characterized, <sup>28-30</sup> the psychological processes that underlie evaluation of delayed rewards are not well understood. Impulsive decision making is often described as an "inability to wait" or "acting on the spur of the moment," implying that timing functions are a critical component.31,32 Steeper discounting could reflect not only intolerance of temporal delays but also a subjective overestimation of time (ie, time appears to pass more slowly). Thus, the perception that time is passing slower or faster, or a lack of sensitivity for distinguishing between short and long delays, may have an important influence on decision making.31,32 For example, it is possible that the perception that time is passing too slowly may prompt behaviors to alleviate short-term discomfort (ie, relapse) at the expense of behaviors focused on long-term goals (ie, maintaining abstinence). Indeed, a stronger orientation toward the present, relative to the future, has been associated with impulsive behavior and drug use.33

Specifically, substance abuse (eg, amphetamine, cocaine, and heroin) is associated with impaired time perception and shorter temporal horizons due to overestimation of delay lengths, and a perception that time is "speeded up". 34-36 This altered perception of time may partially explain why substance abusers display difficulty in delaying gratification. 37,38

Convergent evidence suggests that time perception may also account for the association between nicotine withdrawal and impulsive decision making. Preliminary evidence from our lab<sup>21</sup> and other labs<sup>39,40</sup> suggests that, during acute abstinence, smokers overestimate time. However, no study that we know of has examined whether changes in time perception were related to the ability to quit smoking. There is also evidence that withdrawal-related changes in neural activity during cognitively demanding tasks are strongly associated with smoking relapse,41 suggesting that withdrawal "reactivity" may be an important predictor of the ability to quit. Using a wellvalidated model of short-term smoking abstinence, 5,7,42 the current study sought to (1) test whether acute nicotine withdrawal increases delay discounting and the subjective passage of time and (2) evaluate whether withdrawal-related changes (abstinence minus smoking-asusual) in time perception and delay discounting predict short-term quitting success. Elucidating the mechanisms that underlie withdrawal-related impulsive decision making and their association to the ability to quit smoking may lead to novel approaches that target time perception and decision making to treat nicotine dependence.

#### **Methods**

#### **Participants**

The study protocol was approved by the University of Pennsylvania Institutional Review Board. Male and female treatment-seeking smokers aged 18-65 y who smoked at least 10 cigarettes per day for the past 6 months were recruited from the community through Craigslist and newspaper advertisements. Smokers had to report an interest in quitting smoking in the next 6 months and rate their confidence of making a quit attempt in the next 6 months 50% or greater (eg, "On a scale from 0 to 100, what is your confidence of making a quit attempt in the next 6 months?"). Exclusion criteria included current daily use of noncigarette tobacco products (eg, cigars or e-cigarettes) or smoking cessation medications; a history of DSM-IV Axis 1 disorders (except nicotine dependence); current use of antipsychotics, antidepressants, anxiolytics, prescription stimulants, or opiate-containing medications; a history of substance abuse in the past 6 months or consuming more than 25 alcoholic drinks per week; colorblindness; any impairment (physical and/or neurological) that would affect cognitive task performance; low or borderline intelligence (estimated IQ < 90 Shipley Institute of Living Scale)43; lack of fluency in English; and pregnancy or breast feeding.

Participants provided written informed consent and completed an in-person eligibility screen including a urine drug screen, a breath alcohol test, and an expired breath carbon monoxide (CO) reading to confirm smoking status (at least 10 ppm.); women completed a urine pregnancy test. Participants also completed a medical history, a psychiatric interview (Mini International Neuropsychiatric

Interview [MINI]<sup>44</sup>), and a brief intelligence test (Shipley Institute of Living Scale [SILS]<sup>43</sup>). Standardized questionnaires to collect demographics (age, gender, income, and education) and smoking history (eg, age at smoking initiation and current smoking rate) were collected. The Fagerström Test for Nicotine Dependence (FTND)<sup>45</sup> was also administered. Additionally, participants completed the Delay Discounting Task (see *Measures and Outcomes*), and those whose decision preferences were extreme at intake (ie, analogous to floor or ceiling effect) were excluded so as not to bias the direction of abstinence effects.

#### **Procedures**

#### Laboratory Sessions (Days 1 and 8)

Participants completed two laboratory sessions separated by approximately 1 week: once following 24 hours of smoking abstinence and once smoking-as-usual (order counterbalanced). Smoking status was confirmed by a breath CO test of ≥10 ppm (smoking-as-usual session) and less than 5 ppm (abstinent session).46 At each laboratory session, participants provided urine specimens for drug and (if applicable) pregnancy tests. Participants who had positive urine drug or pregnancy screens or positive breath alcohol tests were withdrawn from the study. Participants completed measures of withdrawal (Minnesota Withdrawal Scale; MNWS),47 craving (Questionnaire on Smoking Urges-Brief; QSU-B),48 and mood (Positive and Negative Affect Schedule; PANAS),49 as well as smoking rate using a standard self-report timeline follow-back (TLFB) method.<sup>50</sup> Participants then completed a 45-minute cognitive task battery via E-Prime 2.0 (Psychology Software Software Tools, Inc) that included two time perception tasks and a delay discounting task (see Measures and Outcomes). Tasks were completed in the following order: (1) time discrimination task (TDT), (2) time reproduction task (TRT), and (3) delay discounting task.

#### 7-Day Monitored Abstinence Period (Days 10-16)

Following completion of the second laboratory session, participants received a brief 20-minute counseling phone call (day 9) and were instructed to try their best to abstain from smoking for 7 days, beginning 10 PM on day 9. During this period, participants came to the center for four brief visits (days 10, 12, 14, and 16) to monitor their smoking status. Abstinence was verified with a CO assessment and smoking data were collected with TLFB assessments. To increase abstinence motivation, participants received a \$15 bonus per visit (maximum of \$60) for self-reported abstinence (not even a single puff of a cigarette) that was biochemically confirmed via CO (see *Measures and Outcomes* for abstinence criteria).

#### Measures and Outcomes

#### Abstinence Outcomes

During the monitored abstinence period, abstinence was assessed at each visit by self-report of no smoking at all and an expired-air CO less than 5 ppm. <sup>46</sup> The primary outcome is the total number of days abstinent via self-report and biochemically verified (out of 6). This measure has been shown to be highly predictive of long-term cessation outcomes <sup>4</sup> and has demonstrated sensitivity to efficacious treatments for smoking cessation and specificity for nonefficacious medications. <sup>5,7,51</sup> Thus, this paradigm is thought to reflect an efficient model for evaluating mechanisms associated with smoking relapse. <sup>52</sup> The secondary outcome was the total number of cigarettes smoked (via timeline followback) during the monitored abstinence period.

#### Time Discrimination Task

The TDT was based on prior research.<sup>53</sup> Participants were presented with two intervals and asked to press a key to indicate which was longer. On half the trials, the longer interval was presented first and the difference between comparison intervals (duration difference) was 250, 500, or 750 ms (randomly determined). Durations of comparison intervals were multiples of 250 up to 2750 ms. The first interval was followed by a blank screen (500 ms) and a crosshair (250 ms). After the second interval, participants indicated which was longer. The 108 trials were randomly intermixed so that any duration difference and any pair of comparison intervals can occur on a given trial. Responses from one participant were considered outliers (ie, less than 2.5 SD below the mean). Results were consistent with or without this participant in the model and therefore the data were retained. The primary outcome was the discrimination index, d'. Correct responses ("hits") and errors ("false alarms") were used to calculate d' using the following equation:  $(1/\sqrt{2}) \times (z(\text{Hit}) - z(\text{False alarm}))$ . Higher d' indicated greater sensitivity to distinguish between temporal durations.

#### Time Reproduction Task

The TRT was a measure of retrospective time perception based on prior research.55,56 The TRT consists of two phases: encoding and reproduction. During the encoding phase, participants were instructed to retain the duration of a visual stimulus (red cross), which was followed by a 5-s interstimulus interval (gray cross). The reproduction phase began with the presentation of a green cross, which was displayed for 1.5-times the duration of the encoding interval. Participants reproduced the duration by clicking the computer mouse. For the 16 trials, the duration of the encoding interval was selected pseudorandomly out of eight durations: 5.00, 5.95, 7.07, 8.41, 10.00, 11.89, 14.14, and 16.82 s (ie, a geometric sequence  $x_{i,j} = x_i 2^{1/4}$ ) so that each interval was used twice. Participants were instructed to avoid mental counting. Responses from three participants were considered outliers (ie, less than 2.5 SD below the mean). Two of these sessions were smoking-as-usual sessions and one was the abstinent session. Data from these participants were retained in subsequent analyses because their removal did not impact the findings. The primary outcome was the accuracy coefficient, "theta" (ie,  $\theta$ ), which was the ratio of the reproduced duration to the actual duration.57,58 Values greater than 1 indicate overestimation and lower than 1 indicate underestimation.

#### **Delay Discounting Task**

In this computer-administered delay discounting task, participants chose between hypothetical monetary rewards. Each trial was a forced choice between two options: a smaller reward available immediately and a larger reward available after a longer delay (eg, "Would you prefer \$20 today or \$85 in 43 days?"). The magnitude of the immediate reward and the magnitude and delay of the larger, later reward varied from trial to trial. Monetary rewards ranged from \$15 to \$85 and the longest delay was 174 days. There were a total of 60 choices and participants had 6 s to respond after which the trial was marked as missing if no choice was made (fewer than 1% of trials).<sup>59</sup> Five participants chose all immediate or all delayed rewards during at least one session. Estimates for these subjects were constrained to the highest and lowest discount rates that could reliably be estimated. Three participants had discount rates at the lowest extreme and two were at the high extreme. Analyses were conducted with and without these five participants and results were consistent. Thus,

subsequent analyses included all participants. The primary outcome was the discount rate (k). Keeping with standard behavioral findings, the estimated subjective value (SV) of choices was assumed to follow a hyperbolic function of the reward amount (A) and delay (D): SV = A / (1 + kD). <sup>28,30,60</sup> Choices were predicted with the logistic function,  $p(\text{delayed}) = 1 / [1 + \beta e^{(SVimm-SVdel)}]$ , where SVdel denotes the delayed option's subjective value, SVimm represents the immediate offer,  $\beta$  models the slope of the logistic curve, and p(delayed) returns the probability of delayed option choice. The optimization process, implemented in MATLAB, converged upon the pair of k and  $\beta$  values associated with the maximum log likelihood of observing the actual choices that the participant made. 59,61,62 Since discount rates are not normally distributed, the estimated k values were log-transformed prior to submission to statistical analysis. Larger values of k indicated a greater degree of discounting future rewards. An R<sup>2</sup> value was calculated for each subject's discounting curve as an estimate of model fit. The median  $R^2$  value was 0.60 and ranged from 0.17 to 0.89, suggesting that the model fits the data well. A minimum  $R^2$  of 0.3 was used to screen out random responding,  $^{14,63,64}$  which resulted in excluding two subjects (one female).

#### Statistical Analysis

To evaluate abstinence effects on time perception ( $\theta$  and d') and decision making ( $\log k$ ), mixed linear regression models were estimated with session (abstinence vs. smoking-as-usual) as a within-subject term and session order as a between-subjects factor to control for practice effects (Stata xtreg; Stata Corp, College Station, TX). Next, we tested the hypothesis that abstinence-induced changes in time perception and decision making predicted the ability to maintain short-term abstinence. Because the distribution of number of days abstinent (out of 6) was overdispersed (ie, the variance was greater than the mean), separate beta-binomial regression models (Stata nbreg) were conducted with change scores (abstinence minus smoking-as-usual) for time perception and decision making as predictors. An additional model included abstinence effects on both time perception and decision making to examine the unique effects of each variable on short-term quitting success. Parallel models were then conducted using baseline measures of time perception and delay discounting as predictors of short-term abstinence. All models included relevant covariates (sex, nicotine dependence, education, and income). Session order was evaluated as a potential betweensubjects moderator, but was not significantly related to any outcome and was therefore removed from subsequent models.

#### Results

#### Sample Characteristics

The majority of the sample was male (n = 31, 69%) and African American (n = 32, 71%). Most participants completed at least some college or technical school (n = 25, 56%), but nearly half the sample reported an annual income less than \$20 000 (n = 20, 45%). On average, the sample was 45.1 years old  $(SD\ 10.9)$ , smoked 13.7 cigarettes per day  $(SD\ 4.3)$ , was moderately nicotine dependent (mean FTND 4.9,  $SD\ 1.6$ ), had a body mass index of 28.9  $(SD\ 5.5)$ , had Shipley IQ scores of 101.7  $(SD\ 7.5)$ , and reported being 78%  $(SD\ 17.4)$  confident of making a quit attempt in next 6 months. Approximately half the sample (n = 24) was randomly assigned to undergo the abstinence condition first and there were no differences between those who were abstinent first compared to those who were

abstinent in the second session in terms of demographic or smoking characteristics (ps > .15). During the monitored abstinence period, participants were abstinent 3.3 days ( $SD \ 2.1$ ) and smoked a total of 12.89 cigarettes ( $SD \ 15.8$ ).

Self-reported craving, withdrawal, and CO breath readings all exhibited expected abstinence effects confirming compliance with the abstinence requirement during the laboratory sessions. Specifically, craving and withdrawal symptoms were significantly higher during the abstinent session (means = 41.4 and 10.5, SDs = 14.6 and 6.0, respectively) compared to the smoking-as-usual session (means = 29 and 7.7, SDs = 1.8 and 0.9, respectively; ps < .001). CO readings were lower during the abstinent session (mean = 2.8, SD = 1.2) compared to the smoking-as-usual session (mean = 19.6, SD = 8.0, p < .001). However, there were no session effects on positive or negative affect (ps > .19).

## Abstinence Effects on Time Perception and Delay Discounting

For the TRT, there was a significant session effect on  $\theta$  (p = .02), with participants underestimating time more during smoking-asusual (mean = 0.87, SD = 0.12) relative to abstinence (mean = 0.92, SD = 0.11; Table 1). For the TDT, there was no session effect on d' (abstinent mean = 0.37, SD = 0.25; smoking mean = 0.39, SD = 0.26; p = .66). Likewise, there was no effect of abstinence on delay discounting (log k values: abstinent mean = -1.59, SD = 0.46; smoking mean = -1.64, SD = 0.44; p = .37).

# Abstinence-Induced Changes in Time Perception and Delay Discounting and Short-Term Smoking Cessation

As shown in Table 2, individuals who exhibited greater increases in discounting (eg,  $\log k$ ) during abstinence (vs. smoking-as-usual) were abstinent for more days (p = .002) and smoked fewer cigarettes  $(\beta = -3.17, 95\% \text{ CI } -5.78 \text{ to } -0.57, p = .015)$  during the monitored abstinence period (Figure 1). In a supplemental analysis, we evaluated only the days during the quit week for which biochemical verification was available (maximum number of days was 4). This measure was highly correlated with the total number of days abstinent (r = 0.62, p = .0001). Importantly, the model predicting number of days abstinent from the change in delay discounting remained significant (p = .03). Neither the abstinence effect on  $\theta$  nor on d'was significantly related to number of days abstinent (p = .2 and p =.8, respectively) or number of cigarettes smoked (p = .9 and p = .8, respectively). When the change scores for all three outcomes  $(k, \theta)$ , and d') were included in models predicting number of days abstinent and cigarettes smoked, the abstinence effect on delay discounting remained a significant predictor (p = .015; p = .002) (Table 2).

## Baseline Time Perception and Delay Discounting and Short-Term Smoking Cessation

Because previous studies have found baseline delay discounting (eg,  $\log k$ ) to be predictive of relapse,  $^{24,26,27}$  we also evaluated whether discount rates and time perception at baseline (ie, the first laboratory session) were related to short-term smoking cessation. Using the same models employed for the change scores, none of these baseline measures predicted number of days abstinent or cigarettes smoked during the quit week (ps > .15).

Table 1. Multivariate Regression Models for Abstinence Effects on Task Performance

	Coefficient	SE	z	p	95% CI
Model 1: Delay discounting (log <i>k</i> )					
Session (Reference = Smoking)	0.05	0.06	0.90	.37	0.06 to 0.165
FTND score	0.03	0.04	0.89	.37	-0.04 to 0.11
Education (Reference = High school/GED or less)	-0.27	0.13	-2.10	.04	-0.52 to -0.02
Income (Reference = <\$20000)	-0.24	-0.13	-6.62	<.01	-2.00 to -1.09
Model 2: Time reproduction task $(\theta)$					
Session (Reference = Smoking)	0.04	0.02	2.31	.02	0.01 to 0.08
FTND score	0.00	0.01	0.39	.70	-0.01 to 0.02
Education (Reference = High school/GED or less)	0.01	0.03	0.46	.65	-0.05 to 0.07
Income (Reference = <\$20000)	0.02	0.03	0.74	.46	-0.04 to0.08
Model 3: Time discrimination task (d')					
Session (Reference = Smoking)	-0.01	0.03	-0.43	.66	-0.07 to 0.05
FTND score	-0.00	0.02	-0.09	93	-0.05 to 0.04
Education (Reference = High school/GED or less)	0.04	0.07	0.58	.56	-0.10 to 0.19
Income (Reference = <\$20 000)	0.03	0.07	0.38	.70	-0.12 to 0.17

FTND = Fagerström Test for Nicotine Dependence.

Table 2. Multivariate Regression Models of Abstinence Effects on Task Performance Predicting Quit Outcomes

	Coefficient	SE	z	p	95% CI
Model 1: Total cigarettes smoked during quit weel	ζ				
Delay discounting $(\log k)^a$	-40.50	11.74	-3.45	.015	-64.64 to -16.37
Time reproduction task (θ) <sup>a</sup>	8.42	20.2	0.42	.68	-33.13 to 49.97
Time discrimination task (d') <sup>a</sup>	12.82	12.63	1.02	.32	-13.14 to 38.79
FTND score	2.18	1.44	1.52	.14	-0.78 to 5.13
Education (Reference = High school/GED or less)	-14.08	5.42	-2.6	.02	-25.23 to -2.93
Income (Reference = <\$20000)	11.58	5.04	2.30	.03	1.21 to 21.95
Sex (Reference = Male)	-1.35	6.29	-0.22	.83	-16.15 to 25.50
Model 2: Total number of days abstinent					
Delay discounting $(\log k)^a$	1.60	0.51	3.12	.002	0.59 to 2.60
Time reproduction task (θ) <sup>a</sup>	-1.24	0.96	-1.30	.19	-3.12 to 0.63
Time discrimination task $(d')^a$	-0.42	0.52	-0.80	.42	-1.44 to 0.60
FTND score	-0.05	0.06	-0.75	.46	-0.17 to 0.08
Education (Reference = High school/GED or less)	0.52	0.24	2.20	.03	0.06 to 0.99
Income (Reference = <\$20000)	-0.35	0.22	-1.60	.11	-0.78 to 0.08
Sex (Reference = Male)	-0.36	0.26	-1.37	.17	-0.88 to 0.15

<sup>&</sup>lt;sup>a</sup>Represent change score (abstinent minus smoking).

#### **Discussion**

The current study evaluated the effects of 24 hours of smoking abstinence on the perception of time and delay discounting and whether these measures were predictive of short-term smoking cessation. We found that smokers' ability to reproduce time intervals was significantly impaired (eg, time was overestimated) during abstinence, relative to smoking-as-usual. This may be related to findings of previous studies that demonstrate abstinence effects on time perception accuracy, 39,40 There was no evidence of acute abstinence effects on temporal interval discrimination or delay discounting. Somewhat surprisingly, however, our data suggest that individuals whose preference for immediate rewards increases the most during abstinence (vs. smoking-as-usual) may be more successful at maintaining short-term abstinence. Thus, our study provides new evidence that individual differences in withdrawal-related delay discounting may be an important predictor of short-term smoking abstinence.

The significant abstinence effects on the TRT were in the predicted direction and are consistent with our previous study.<sup>21</sup> Moreover, this finding corresponded to a medium-sized effect (d = 0.43), similar to a previous study of time perception during abstinence.40 The fact that abstinence significantly affected time reproduction, but had no effect on discounting, combined with the result that withdrawal-related changes in delay discounting, but not time reproduction or time discrimination, was predictive of shortterm cessation indicates that time perception and decision making may not be related psychological processes. This may be due, in part, to differences in the temporal durations used across tasks. The TRT and TDT assess the perception of time in seconds, whereas the delay discounting task considers temporal intervals on the order of days, which may be more relevant as a predictor of abstinence. In addition, the forced-choice nature of the TDT, compared to the open-ended response on the TRT, may have reduced the sensitivity of this task to detect abstinence effects. Nevertheless, the fact that we observed significant changes in time reproduction during abstinence suggests that strategies that target time perception may be useful adjuncts to behavioral treatments for smoking cessation.

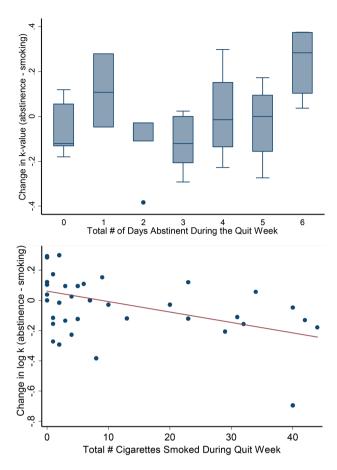


Figure 1. Association of changes in delay discounting during abstinence (vs. smoking) with total number of days abstinent (top) and the total number of cigarettes smoked (bottom) during the monitored abstinence period. The line represents the predicted values for number of cigarettes smoked based on the regression model (bottom).

For instance, in addition to poor sustained attention and greater impulsivity, individuals with ADHD also exhibit deficits in time perception <sup>32,65</sup> and effective treatments for ADHD attenuate deficits in time perception. <sup>66</sup> Importantly, behavioral strategies to improve time perception may attenuate ADHD symptoms. <sup>67,68</sup> Therefore, incorporating similar strategies into behavioral treatments for smoking cessation may have downstream effects on decision making and ultimately improve abstinence rates.

The finding that abstinence did not produce overall changes in delay discounting contributes to a mixed literature on abstinence effects. One possibility is that methodological differences across delay discounting tasks could partially account for the discrepancies across studies. For example, while some tasks utilize amounts ranging from \$1 to \$1000 and delays ranging from 1 day to 25 years, 13,23 others (including the current study) utilize smaller amounts (eg, up to \$85) and shorter delays (eg, up to 186 days). 69,70 In addition, some tasks (including the current one) offer a standard set of choices, whereas others employ algorithms to adjust the amounts offered based on participant choices which may yield differences in discount rates.<sup>71</sup> It has been suggested that differing procedures across delay discounting tasks may be measuring unique processes.<sup>71–73</sup> In future studies, it would be interesting to evaluate whether the association of delay discounting with smoking cessation depends on the delays used in the task. Perhaps, shorter delays might be more relevant for

studies with shorter outcomes (as in the current study), whereas tasks with longer delays might be more sensitive in studies with long-term follow-up (eg, 1 year).

Previous studies have found that baseline delay discounting predicts relapse.<sup>24,26,27</sup> In contrast, our data suggest that withdrawalinduced changes in delay discounting, but not baseline delay discounting, predicts number of days abstinent during the quit week. Likewise, baseline measures of time perception were unrelated to short-term smoking cessation. The current finding is consistent with evidence that abstinence-induced decreases in neural activity during working memory predicts smoking relapse. 41 The ability to delay gratification and maintain goal-directed behavior in the face of cravings to smoke is critical to maintain smoking abstinence. However, nicotine withdrawal reduces the ability to engage brain regions important for regulating cognitive control.74,75 Although the magnitude of the current findings is small, prior work from our lab and other labs suggests that each additional day of abstinence during the first week of a quit attempt nearly doubles the odds of long-term abstinence. 4,76 Likewise, for every 1% reduction in daily cigarettes smoked over 6 weeks, the odds of achieving abstinence at 24 weeks increased by 3%.77 Thus, even small changes in smoking behavior may be clinically relevant and our data suggest that withdrawal "reactivity"-or the degree to which an individual changes during acute abstinence—is related to changes in smoking behavior and may be an important indicator of the ability to quit smoking.

Furthermore, the direction of this association was surprising, as individuals whose preference for immediate rewards increased more during abstinence (vs. smoking-as-usual) were more successful at maintaining short-term abstinence. Our incentive structure may have contributed to this surprising finding. Similar to a contingency management (CM) model, we provided small monetary incentives for each day of biochemically verified abstinence during the quit week. CM interventions are effective approaches for reinforcing stable periods of abstinence from drug use, including cigarette smoking in adults<sup>78-81</sup> and adolescents.<sup>82,83</sup> Perhaps among individuals who experienced an increased preference for immediate rewards during abstinence, the prospect of earning the immediate \$15 for each test of abstinence was a strong enough incentive to forgo smoking during this short period. Thus, those who exhibited greater withdrawalrelated changes in delay discounting may have been more successful in maintaining abstinence during the quit week due to enhanced valuation of immediate monetary rewards over smoking cigarettes. Alternatively, it is possible that the financial incentives encouraged individuals to falsify their self-reported smoking behavior. However, when we restricted our analysis to only the days on which visits occurred (permitting stringent biochemical verification of abstinence), withdrawal-related delay discounting remained a significant predictor. Although we cannot test the role of incentives in maintaining abstinence in the current study (since all participants were provided financial incentives), there is evidence that delay discounting predicts response to CM interventions. 84-86 Thus, future research might consider evaluating the influence of withdrawal-related changes in discounting on the effectiveness of various schedules of reinforcement when offering financial incentives for abstinence.

Several limitations of the present study are important to take into consideration. Our sample was relatively small, especially with respect to the number of female participants. In our previous study,<sup>21</sup> we found sex differences in time perception during abstinence, but we were not able to replicate that in the current study. Although the delay discounting task was completed last and it is possible that

participants felt some fatigue after completing the time perception tasks, evidence suggests that hours, rather than minutes, of cognitive work are required before there are measurable effects on delay discounting. Lastly, the duration of abstinence was only 1 week. Without a long-term follow-up, we have no way to evaluate whether withdrawal-related changes in delay discounting are predictive of long-term abstinence. Nevertheless, there is strong evidence to suggest that the primary outcome used in our study (ie, the number of days abstinent during the first week of a quit attempt) is highly predictive of long-term success and that the current paradigm represents an efficient model for evaluating mechanisms associated with smoking relapse. Leave that the current paradigm represents an efficient model for evaluating mechanisms associated with smoking relapse.

In spite of these limitations, our study provides important new evidence that furthers our understanding of how smokers' delay discounting may impact their ability to maintain periods of abstinence when offered monetary rewards. Our results suggest that smokers whose motivation for immediate rewards increases the most during withdrawal (compared to smoking-as-usual) may experience greater success if offered small, frequent monetary incentives. This is in contrast to CM paradigms which may wait at least 1 month before providing incentives for abstinence. So,81 Thus, the current findings may have important implications for identifying smokers most likely to benefit from a particular treatment. Future research might evaluate whether withdrawal-related changes in delay discounting moderate treatment response to different incentive schedules with the goal of optimizing CM effectiveness to improve abstinence rates.

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#### **Declaration of Interests**

None declared.

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