Nicotine Deprivation Influences P300 Markers of Cognitive Control

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Studies suggest that reduced cognitive control due to nicotine withdrawal may have a critical role in promoting tobacco use. The P3 family of event-related brain potential (ERP) components is thought to serve as markers of cognitive control processes. Unfortunately, existing research that examines the effects of nicotine deprivation on P3 amplitude has been marred by small sample sizes and other design limitations. The present study sought to determine the effects of nicotine deprivation on P3b and P3a amplitudes, which index task relevant target detection and orienting responses to novelty, respectively. A secondary aim was to examine self-reported trait cognitive control as a moderator of nicotine deprivation-induced reductions in P3b and P3a amplitudes. In all, 121 nicotine-dependent smokers attended two experimental sessions following 12-h smoking/nicotine deprivation. In a counterbalanced manner, participants smoked nicotine cigarettes during one session and placebo cigarettes during the other session. Findings indicated that nicotine deprivation reduced P3b amplitude ($p < 0.00001$) during a three-stimulus oddball task independent of trait cognitive control. In contrast, nicotine deprivation reduced P3a only among participants who scored lower on measures of trait cognitive control. Implications for conceptualizing risk for nicotine dependence, and its treatment, are discussed.

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INTRODUCTION

Nicotine-dependent smokers show deleterious symptoms of withdrawal within 30 min of smoking abstinence (Hendricks *et al*, 2006), including difficulty in paying attention and remembering things relevant to the task at hand. Smoking rapidly reverses these symptoms, a function that is believed to contribute to the development and maintenance of nicotine dependence (Evans and Drobes, 2009; Newhouse *et al*, 2004; Singh *et al*, 2004). Cognitive control deficits may have a central role in driving the aversive effects of nicotine withdrawal. Reduced cognitive control may contribute to other prominent withdrawal symptoms (eg, negative effect). For instance, the capacity to shift attention away from negative effect-related ideation and/or the capacity to maintain focus on alternative ideation may be compromised by reductions in cognitive control, resulting in a greater distress (see Evans and Rothbart, 2007, 2009). Research is needed to better under-

stand the specific aspects of cognitive control that are disrupted during nicotine abstinence, and whether certain individuals are more likely to experience these disruptions.

Understanding nicotine deprivation effects on cognitive control may be advanced by the research examining the neural substrates of these effects. Behavioral performance amid both laboratory and naturalistic tasks may have multiple neural substrates that contribute to observed withdrawal-related deficits. Identifying these substrates may improve the capacity to pinpoint specific cognitive functions that are affected by nicotine deprivation. In turn, this may assist with the development of targeted behavioral and/or pharmaceutical treatments for nicotine dependence, as well as with identifying people whose motivation to smoke is derived from its cognitive effects, thereby enabling the targeting of individuals who may be the most likely to benefit from these interventions.

One of the most frequently tested and robust neurophysiological markers of cognitive control-related processing is the 'P3/P300' event-related potential (ERP) component (see Dien *et al*, 2004 and Polich, 2007). While most rapid response reaction time tasks evoke P3-like activity, different P3 components can be elicited depending on task design. The most commonly referenced P3 component (often labeled 'P3b') is evoked by the traditional oddball task, which involves infrequently presented target (eg, 15%)

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relative to standard (eg, 85%) stimuli. Thus, the P3b is associated with identification of task-relevant target stimuli. P3b amplitude is negatively associated with a wide range of maladaptive traits and behaviors (Iacono *et al*, 2003), including substance abuse (Iacono *et al*, 1999) and other disinhibitory disorders (Iacono *et al*, 2002). Research has also shown that smokers have reduced P3b amplitude compared with non-smokers, lighter smokers, and former smokers (Anokhin *et al*, 2000; Mobascher *et al*, 2010). In addition, another important P3 component is the P3a, which is an orienting response to unexpected task-irrelevant stimuli (see Polich, 2007 and Hagen *et al*, 2006). P3a has also been negatively associated with disinhibitory disorders (eg, Iwanami *et al*, 1998). Together, these P3 indices assay the maintenance of focused target pursuit (P3b) and the capacity for attention to be flexibly shifted by unexpected stimuli not relevant to immediate goals (P3a).

Several prior studies have specifically examined the nicotine deprivation effects on P3b and P3a ERP components, but with mixed and inconclusive findings. Domino and Kishimoto (2002) reported that nicotine deprivation was associated with reduced auditory oddball P3b in a sample of 10 smokers. However, smoking/nicotine deprivation was not blinded so results are difficult to interpret. In contrast, Houlihan *et al* (1996) did not find nicotine deprivation-induced reduction in P3b amplitude as measured across multiple oddball tasks (two auditory and one visual). Evans *et al* (2009) also failed to find an overall effect of smoking/nicotine deprivation on P3 activity during a go-nogo task. Yet deprived individuals experiencing a greater negative effect exhibited reduced P3, suggesting that nicotine withdrawal does indeed reduce P3 among vulnerable individuals. Knott *et al* (1995) did not find a nicotine deprivation effect on auditory-evoked P3a amplitude. Each of these studies is relatively small, and therefore may lack statistical power for detecting small to moderate effects that may still be clinically significant.

A large-scale ERP study using the three-stimulus oddball task that evokes both P3a and P3b components may provide a more definitive answer regarding the effects of nicotine deprivation on P3-related neural activity. A sufficient sample size also enables exploration of potential moderators of nicotine deprivation effects. In particular, individuals with diminished cognitive reserve may be more vulnerable to conditions that reduce cognitive control (Stern, 2009). For this reason, nicotine deprivation may result in greater decrements among individuals lower in trait cognitive control, and nicotine self-medication of cognitive control may therefore result in nicotine being more reinforcing among these individuals (see Evans and Drobles, 2009 and Newhouse *et al*, 2004). The capacity to identify individuals who find smoking more reinforcing for cognitive reasons may inform the field with respect to the development of tailored treatment programs that match the needs of this subgroup of smokers.

Hypotheses

It was hypothesized that nicotine deprivation will result in reduced P3b and P3a amplitudes. Trait cognitive control and nicotine dependence were also examined as moderators of these hypotheses.

METHODS

Participants

In all, 137 (A subset of the overall sample ($N=52$) was recruited separately. This subset of participants was in the 21–40 and 51–70 year age ranges. For these participants, medical screening was performed at the baseline session for the sake of older participant safety. The experimental sessions were identical.) smokers were recruited from the Greater Tampa Bay region. Eligible participants were between the ages of 18 and 70 years, and smoked an average of 15 cigarettes or more per day for the past 2 years. Smoking status was confirmed via an expired air carbon monoxide (CO) sample of at least 10 parts per million (p.p.m.) and a cotinine level of ≥ 100 ng/ml. Additional eligibility criteria included being able to read and understand the consent form and questionnaires, and not actively trying to quit or reduce smoking.

Participants were excluded if they were reported using nicotine products other than smoking (eg, chewing tobacco) within the past 3 months, were diagnosed with a neurological condition, were taking medication that could affect physiological responding (eg, beta blockers and tricyclic antidepressants), had sustained a significant head injury/concussion, had any other serious medical conditions (cardiopulmonary problems) or respiratory-related illness exacerbated by smoking (eg, bronchitis, emphysema, and asthma), were currently using psychoactive substances (eg, cocaine, amphetamines, barbiturates, and benzodiazepines) as assessed by a urine drug test, had vision problems, were pregnant or breast feeding, or presented with current psychosis, mood disorders, or non-nicotine substance-dependent disorders as assessed by the Structured Clinical Interview for DSM disorders (SCID; First *et al*, 1994).

Procedure

Informed consent was obtained at the beginning of an initial screening session. During this session, eligibility was established according to the above criteria. Eligible participants completed a self-report measure of nicotine dependence (Fagerström Test for Nicotine Dependence (FTND); Heatherton *et al*, 1991). To assess trait differences in cognitive control, participants completed a variety of personality measures, including the Cognitive Failures Questionnaire (CFQ; Broadbent *et al*, 1982), the Adult Temperament Questionnaire (ATQ; Evans and Rothbart, 2007), and the conscientiousness scale of the Ortho-40 measure (Saucier, 2002). Each of the CFQ (eg, Smilek *et al*, 2010), ATQ attentional control (eg, Claes *et al*, 2010; Lin *et al*, 2013; Schwebel *et al*, 2009), and Big Five conscientiousness (eg, Mathews and Zeidner, 2012) scales have documented associations with cognitive control-related performance indices.

Eligible participants attended two 2.5-h experimental sessions following the overnight nicotine deprivation. First, deprivation was confirmed biochemically by the CO level either less than or equal to 10 p.p.m., or less than or equal to half of the CO level obtained during the screening session. Next, participants completed a modified version of the Wisconsin Smoking Withdrawal Scale (WSWS; Welsch *et al*, 1999), with two subscales (sleep and diet) that are

irrelevant to overnight deprivation omitted. At each of these double-blind counterbalanced sessions, participants smoked either four moderate nicotine (0.60 mg nicotine yield) or placebo (<0.05 mg nicotine yield) cigarettes (Quest, Vector Tobacco). Instead of being told that nicotine cigarettes were given during one session and placebo cigarettes during the other session, participants were only told that cigarettes contained varying amounts of nicotine. Sessions were scheduled between 3 and 14 days apart. After smoking the first cigarette, participants were fitted with a 64-channel Neuroscan electroencephalogram (EEG) cap. A second cigarette was smoked 40 min after the first cigarette. Participants then completed the three-stimulus oddball task reported herein. The final two cigarettes were smoked subsequent to this task (~ 40 min apart) and additional cognitive tasks were administered (findings to be reported elsewhere). The WSWS was again completed by participants at the end of the experiment. Participants were compensated $\sim \$200$ for completing the study.

Cognitive tasks. E-prime software (Psychology Software Tools) was used to administer an established version of the three-stimulus oddball task (Hagen *et al*, 2006). Visual stimuli were presented every 1000 ms, each for 100 ms duration, for a total of 400 trials (divided into two 200 trial blocks, separated by a 30-s break). The target stimulus was a 3.5-cm diameter blue circle (presented 15% of trials), the standard stimulus was a 3.0-cm diameter blue circle (presented 70% of trials), and the distracter stimulus was an 18-cm² black and white checkerboard (presented 15% of trials). Participants were instructed to respond via button press as quickly as possible to target stimuli using the index finger of their dominant hand.

EEG recording. The 64-channel electrode array included the 10–20 montage and additional electrodes. Impedance values were kept below 50 k Ω . The Neuroscan Synamps 2 system and its accompanying SCAN 4.3 software system were used to record the EEG data. EEG was digitally sampled at a rate of 250 Hz, with online low-pass filtering at a corner frequency of 100 Hz. EEG was referenced online to a midline vertex electrode. Electro-oculogram (EOG) data were also recorded from bipolar-reference electrodes placed above and below the left eye and lateral to each eye for measuring vertical and horizontal eye movements, respectively.

Data Processing and Analysis

Incorrect responses were omitted before EEG data processing. To ensure that artifacts were removed from the leading and trailing edges of the stimulus-locked epochs (-100 to 1000 ms), we began with an extended epoch interval spanning of 300 ms pre-stimulus to 1200 ms after stimulus onset. Blink artifact was corrected using an Independent Component Analysis-based approach (see Glass *et al*, 2004) implemented in Matlab (MathWorks). Next, spherical spline interpolation, also implemented in Matlab (Nunez and Srinivasan, 2006, see Appendices J1–J3), was used to correct noisy electrodes detected for each trial (ie, excessive amplitude, excessive fast wave activity, and drift). A trial

was discarded if more than four channels were tagged as bad.

Participants who had fewer than 30 trials remaining after artifact correction for any trial type (standards, distracters, and targets) across either session were removed. The remaining data were filtered with a low pass 40-Hz filter, re-referenced to the average of mastoid sites, epoch length truncated to 100 ms pre-stimulus to 1000 ms after initial presentation of stimulus, and baseline corrected to a 100-ms pre-stimulus baseline.

A temporal-spatial principal component analysis (PCA) was used to score amplitude of ERP components. Recent work by Dien (2010) suggests that this approach is optimal for identifying and parsing the variance associated with specific ERP components. Averaged subject ERP waveforms for each of the three trial types across both sessions were submitted to a covariance-based temporal-spatial PCA. That is, PCA (Promax oblique rotations) of time points was first conducted to identify distinct time windows of ERP activation across the ERP waveform. Next, using the factor scores from this first step as an input, spatial PCAs with Infomax oblique rotations were applied to temporal factor data indicative of P3a and P3b components to examine spatial factors (ie, virtual electrodes). Included as part of this latter step, P3a- and P3b-related temporal-spatial factor scores were computed for each participant by filtering the averaged ERPs by a temporal factor, and then by a spatial factor.

Repeated measures analysis of variance (ANOVA) was used to test hypotheses, which focused on trial type $\times$ cigarette type (nicotine *vs* placebo) interactions. Trial type included standards *vs* targets for P3b, and standards *vs* distracters for P3a. Covariates included with repeated measures ANOVA can be used to generate within subject factor $\times$ covariate interaction predictors, thereby enabling examination of continuous variables as moderators of nicotine influence on ERP components (eg, cigarette condition $\times$ trial type $\times$ covariate). This latter approach was used to test moderation effects indicating that individuals lower in trait cognitive control would exhibit a greater nicotine deprivation-induced reduction in P3a/P3b amplitudes. FTND and age were included as covariates in the trait cognitive control moderator models. All tests were two-sided and the alpha value was set at 0.05.

RESULTS

Of the 137 participants who completed both experimental sessions, 2 were excluded due to EEG recording problems in one of the sessions, 5 were excluded because of poor task compliance (ie, markedly reduced accuracy), and 9 were excluded for low-quality EEG data from at least one of the experimental sessions. This resulted in analyses of data from 121 (90 men and 31 women) participants. The age range was 19–61 years (mean age = 38.6, SD = 12.2). Education level ranged from 6 to 18 years (mean = 12.7, SD = 2.0). The racial makeup of the sample included 99 White, 19 Black, 1 Pacific Islander, 1 Native American, and 1 participant who did not report race. In all, 103 participants reported non-Hispanic ethnicity, 13 reported Hispanic ethnicity, and 5 participants did not report

Figure 1 ERP waveforms of averaged trials by trial type at midline electrode sites. Black = nicotine condition, gray = placebo condition. Dotted, solid, and dashed lines correspond to standard, distracter, and target trial types, respectively. Time is plotted on the x axis from 0 to 1000 ms.

ethnicity. Mean score on the FTND was 5.68 (SD = 1.87), which reflects a moderate-to-high level of nicotine dependence. Mean CO levels at the preliminary session were 30.06 (SD = 13.27) p.p.m., before nicotine session 9.77 (SD = 9.00) p.p.m., and before the satiation session 9.90 (SD = 9.00) p.p.m. There were no significant baseline differences in CO as measured at the beginning of the nicotine and placebo cigarette sessions. CO from both the nicotine and placebo smoking sessions was significantly different from baseline, $t(120) = 19.70$, $p < 0.00001$ and $t(120) = 20.05$, $p < 0.00001$, respectively.

ERP Waveform

Figure 1 shows grand average waveforms for midline Fz (frontal), Cz (central), and Pz (parietal) electrodes independently for trial type and nicotine condition. Visual inspection reveals that P3a preceded P3b in peak latency (~ 380 ms vs ~ 520 ms), and P3a shows greatest peak amplitude at anterior sites (electrodes Cz and Fz), whereas P3b peaks relatively posteriorly (Pz).

Figure 2 Temporal factor loadings. Time is from 0 to 1000 ms. Gray line is temporal factor 2 loadings indicative of P3b amplitude, and black line is temporal factor 3 loadings indicative of P3a amplitude.

Withdrawal State Effects

Participants did not differ in self-reported withdrawal (WSWS) at the beginning of nicotine vs placebo cigarette sessions. Significant reductions in self-reported withdrawal were observed over the course of the session ($F(1,120) = 84.35$, $p < 0.00001$). However, the nicotine deprivation $\times$ time (pre vs post) interaction was not significant, suggesting that smoking but not nicotine influenced subjective measurement of withdrawal.

Oddball Task Behavioral Data

Overall task accuracy was close to 100%, with slightly greater accuracy during the nicotine satiation (99.17%) vs deprivation (98.62%) session, $t(120) = 4.10$, $p = 0.0001$. Reaction time to accurate trials was significantly reduced in the satiated condition (433 ms satiated vs 443 ms deprived), $t(120) = 3.67$, $p < 0.001$.

Temporal-Spatial PCA of ERP Waveform

Rule M (Preisendorfer and Mobley, 1988) was used to determine the optimal number of PCA components (hereafter referred to as factors to avoid confusion with ERP components) to extract for temporal and subsequent spatial PCAs. This procedure estimates the point at which factors have eigenvalues that account for no more variance than would be expected by chance. Rule M indicated extraction of 11 temporal factors.

Variance scaled loadings for temporal factors 2 and 3 are presented in Figure 2. Temporal factor 2 peaks at 528 ms and temporal factor 3 peaks at 380 ms. On the basis of previous data (eg, Polich, 2007) and the raw data presented in Figure 1, these factors clearly map onto the time windows of the P3b and P3a, respectively. Temporal factor scores derived from this step were then separately subjected to spatial PCAs (ie, separate spatial PCAs for temporal factor 2/P3b and temporal factor 3/P3a). Rule M indicated the extraction of four spatial factors from PCA of temporal factor 2 factor scores. Spatial factor 1 derived from temporal factor 2 (P3b) shows high loadings from parietal (eg, Pz) and central (Cz) sites (see Figure 3B). Thus, spatial factor 1 was selected for generating temporal-spatial factor scores

Figure 3 Spatial factor loadings.

Figure 4 Nicotine deprivation effects on P3b. Gray bars = mean factor scores in response to standard stimuli, and black bars = mean factor scores to target stimuli. Error bars indicate standard error.

indicative of P3b. Rule M suggested the extraction of two spatial factors for temporal factor 3. Central sites (eg, electrodes Cz and Fcz) are common sites for measuring P3a (ie, without conducting PCA of ERP data). Cz, Fcz, and adjacent sites loaded highest on spatial factor 1 (see Figure 3A) derived from temporal factor 3. Factor scores generated by temporal factor 3 spatial factor 1 were therefore selected for generating temporal-spatial factor scores indicative of P3a. Note that the spatial factor 1 map associated with temporal factor 3 includes noticeably greater weights at anterior sites relative to spatial factor 1 associated with temporal factor 2 (see Figure 3), which is consistent with grand average waveforms ranging from parietal to frontal sites (see Figure 1). Distributions of these temporal-spatial factor scores representing P3b and P3a amplitudes were normal, and no influential outliers were observed.

P3b

The main effect for trial type was significant, $F(1,120) = 132.47$, $p < 0.00001$. As expected, target stimuli evoked greater P3b amplitude. The nicotine deprivation $\times$ trial type interaction was also significant in predicting P3b amplitude, $F(1,120) = 21.59$, $p < 0.00001$. Partial η^2 was 132, indicating a large effect size. As hypothesized, P3b amplitude to targets relative to standards was reduced in the deprived condition compared with the satiated condition (see Figure 4). Additionally, FTND significantly moderated the effect of nicotine deprivation on P3b amplitude ($F(1,119) = 4.36$, $p = 0.039$), with higher levels of dependence resulting in greater nicotine deprivation-induced reductions in P3b amplitude. Gender and age did not significantly moderate

Figure 5 Nicotine deprivation P3a effects (nicotine satiation (distracter – standard scores) – nicotine deprivation (distracter – standard scores)). Low ATQ = below median and High ATQ = at or above median. Error bars indicate standard error.

nicotine deprivation effects on P3b. Tests of Ortho-40 conscientiousness, CFQ, and ATQ attentional control as trait moderators of nicotine deprivation influence on P3b amplitude did not approach significance. No changes in effects were observed when FTND and age were entered as covariates in the trait cognitive control models.

P3a

The main effect for trial type (standard vs distracter) was significant, $F(1,120) = 831.96$, $p < 0.00001$. As expected, distracter (relative to standard) stimuli evoked greater amplitude. However, the hypothesized nicotine deprivation $\times$ trial type interaction did not approach significance, nor did FTND, gender, or age significantly moderate nicotine deprivation effects on P3b. Yet a nicotine deprivation $\times$ trial type $\times$ ATQ attentional control (continuous measure) interaction was significant, $F(1,17) = 8.76$, $p = 0.004$ (partial $\eta^2 = 0.070$, indicating a medium effect size). Big Five conscientiousness also moderated the influence of nicotine on P3a amplitude in a similar pattern ($F(1,119) = 4.30$, $p = 0.041$), but this latter effect did not survive Bonferroni correction for the three separate trait cognitive control moderators. The CFQ interaction was not significant.

As seen in Figure 5, nicotine deprivation reduced P3a to a greater extent among individuals lower in attentional control relative to individuals higher in attentional control. Follow-up analyses show that individuals scoring below the median on ATQ attentional control experienced nicotine deprivation-induced reductions in P3a ($F(1,58) = 5.52$, $p = 0.022$), whereas those scoring above the median did not. No changes in effects were observed when FTND and age were entered as covariates in the trait cognitive control models.

DISCUSSION

This study provides the strongest support to date for the detrimental effects of nicotine deprivation on P3b amplitude. The effect size is large, and the factor score differences across conditions indicate an 18.5% decrease in amplitude.

Further, as would be expected, higher levels of nicotine dependence were associated with increased nicotine deprivation-induced reduction in P3b. In contrast, nicotine deprivation reduced P3a only among individuals lower in trait cognitive control. Specifically, individuals lower in ATQ attentional control exhibited greater nicotine deprivation-induced reductions in P3a amplitude.

Objective and Subjective Measures of Nicotine Deprivation

The effects for P3b and P3a amplitudes reveal nicotine deprivation effects that were not detected with subjective measures. As is common across a number of double-blind nicotine *vs* placebo cigarette studies, nicotine deprivation did not impact self-reported withdrawal (eg, Perkins *et al*, 2010). This may be because expectancy effects overwhelm the more subtle withdrawal symptoms that result from short-term deprivation, particularly on self-report measures. Reductions in P3a (ie, among those lower in trait cognitive control) and P3b amplitudes (across all participants) appear to serve as objective and robust cognitive markers of nicotine deprivation that are independent from the act of smoking. It remains an issue for further research to determine whether these objective measures of withdrawal predict smoking behaviors better than self-report.

Nicotine Self-Medication of P3b and P3a Substrates

To the best of our knowledge, this is the first study to find that nicotine deprivation reduces a neural index of cognitive control (ie, P3a amplitude) to a greater extent among individuals with lower trait levels of cognitive control. This finding is consistent with a nicotine cognitive self-medication hypothesis, which posits that nicotine deprivation is especially deleterious to cognitive activity among individuals with premorbid reductions in cognitive control (see Evans and Drobles, 2009; Newhouse *et al*, 2004, and Singh *et al*, 2004). The effects of nicotine deprivation may be more disruptive among individuals with lowered trait cognitive control because of this diminished processing of novel stimuli as indexed by P3a. Although the self-medication-related P3a findings are intriguing, it is important to note that the current study relied on self-report and did not utilize objective baseline performance measures of cognitive control. Second, smoke exposure was not controlled in this study. Additional research is also needed to establish that nicotine self-medication of cognition is actually occurring (ie, establishing that reduced cognitive control actually motivates smoking).

Further research should examine trait cognitive control moderation of the effects of nicotine deprivation on specific brain areas using more spatially resolute imaging methods (eg, functional magnetic resonance imaging (fMRI)). For example, convergent evidence suggests that the anterior cingulate cortex (ACC) is one principle source generator of P3a activity (Polich and Criado, 2006) and thus may be compromised by nicotine deprivation. Another avenue via which to examine the nicotine self-medication of cognitive control hypothesis involves genetic moderation of nicotine deprivation effects. For example, Evans *et al* (2009) found that A1 carriers at the Taq1a polymorphism on the

dopamine receptor D2 gene is associated with reduced P3 amplitude during a go-nogo task. Future research might examine genetic moderation of nicotine effects on P3b and P3a. Nicotine is an agonist of norepinephrine and dopamine, which in turn are believed to be the major neurotransmitters involved in generating P3b and P3a, respectively (Polich, 2007). Genetic variants related to the functioning of these three neurotransmitters may therefore be examined as moderators of nicotine effects on P3b and P3a.

Treatment Implications

Future studies may utilize alternative methods such as fMRI and genetic analysis to further refine our understanding of the biological underpinnings of nicotine self-medication of cognition. Smokers might then be targeted with specific behavioral and/or pharmaceutical treatments that match unique cognitive deficits, which may reduce their motivation to smoke via several pathways (eg, elimination of need for self-medication and mitigate withdrawal symptoms). For example, some individuals may have perturbations in dopaminergic functioning that result in cognitive deficits. Treatment with specific dopamine agonists may ameliorate related cognitive deficits. Other individuals might profit from use of alpha-7 nicotinic receptor agonists to address deficits in hippocampal function and concomitant working memory (see Evans and Drobles, 2009). Similarly, more refined behavioral interventions may also help to reduce these deficits.

Conclusion

This study has demonstrated that nicotine deprivation reduces P3b amplitude. In addition, P3a is reduced by nicotine deprivation among individuals lower in trait cognitive control. P3b and P3a as objective measures were more sensitive to the effects of nicotine deprivation than subjective measures. Future research may examine P3b and P3a indices in relation to other smoking/addiction-related characteristics and outcomes, such as craving, cessation, and relapse.

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