HHS Public Access

Author manuscript

*Addict Res Theory*. Author manuscript; available in PMC 2015 June 04.

Published in final edited form as:

*Addict Res Theory*. 2015 ; 23(3): 205–212. doi:10.3109/16066359.2014.953940.

# Time dependency of craving and response inhibition during nicotine abstinence

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## Abstract

**Background—**Nicotine withdrawal produces increased craving for cigarettes and deficits in response inhibition, and these withdrawal symptoms are predictive of relapse. Although it is well-established that these symptoms emerge early during abstinence, there is mixed evidence regarding whether they occur simultaneously. Given the importance of the early withdrawal period, this study examined craving and response inhibition at 24h and 72h abstinence.

**Methods—**Twenty-one non-treatment seeking adult smokers were evaluated at baseline, 24h, and 72h abstinence for craving (Questionnaire on Smoking Urges – Brief) and response inhibition (Stop Signal Task, Stroop Task, Continuous Performance Task). Generalized linear regression models were used for primary outcomes, and Pearson correlations for examining the association between craving and response inhibition.

**Results—**Factor 2 craving (anticipated relief of negative affect) increased from baseline to 24h abstinent ($p$=0.004), which subsided by 72h ($p$=0.08). Deficits in response inhibition measured by the Stop Signal Task were observed at 72h ($p$=0.046), but not 24h ($p$=0.318). No correlation was found between response inhibition and craving at any time point ($p$-values>0.19), except between the Stroop Task and factor 1 craving at baseline ($p$=0.025).

**Conclusions—**Factor 2 craving peaked at 24h, whereas deficits in response inhibition did not emerge until 72h, indicating that need to target craving and cognitive function during early abstinence may not occur simultaneously. Further characterizing the time course of withdrawal symptoms may guide development of targeted treatments for smoking cessation.

### Keywords

smoking; withdrawal; cessation; craving; response inhibition

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**DECLARATION OF INTERESTS**

The authors report no conflict of interest.

## INTRODUCTION

Tobacco use remains the greatest preventable cause of mortality in the United States. In fact, one in five Americans is a current smoker despite the behavioral and pharmacotherapies available to treat nicotine addiction (Ray, Schnoll, & Lerman, 2009). Of the smokers who do utilize the currently recommended smoking cessation aids such as nicotine replacement therapy (NRT), antidepressants (bupropion), and nicotinic receptor agonists (varenicline), most do not achieve long-term abstinence (Schnoll & Lerman, 2006). In order to understand why successful quit attempts are so rare, much work has been done to understand the time course of smoking abstinence. Importantly, the majority of smokers relapse within their first week of abstinence (Garvey, Bliss, Hitchcock, Heinold, & Rosner, 1992). Therefore, it is imperative that we improve our understanding of the first few days of a quit attempt in order to develop effective strategies for maintaining long-term smoking abstinence.

Although the nicotine withdrawal syndrome is complex, craving and cognitive deficits, such as response inhibition have been identified as reliable predictors of short (one week) and long term (one and three month) abstinence (Powell, Dawkins, West, & Pickering, 2010). Craving is a frequently reported affective withdrawal symptom that is typically measured via self-report questionnaires such as the Questionnaire on Smoking Urges (Tiffany & Drobes, 1991) and Mood and Physical Symptoms Scale (West & Hajek, 2004). Quitting smoking is associated with increased craving, which in turn, serves as a barrier to successful abstinence (Javitz, Swan, & Lerman, 2011; Killen & Fortmann, 1997; Orleans, Rimer, Cristinzio, Keintz, & Fleisher, 1991; Van Zundert, Boogerd, Vermulst, & Engels, 2009). Post-quit craving has been shown to be a negative predictor of abstinence in clinical studies of cessation treatment (Cappelleri et al., 2007; Doherty, Kinnunen, Militello, & Garvey, 1995; Killen & Fortmann, 1997; Powell et al., 2010; Swan, Ward, & Jack, 1996). Further evidence of the clinical relevance of craving is shown in nicotine cessation studies where treatment (varenicline and nicotine replacement therapy) is shown to reverse the symptoms of cravings (Patterson et al., 2009; Waters et al., 2004).

Nicotine withdrawal is also associated with cognitive deficits, including response inhibition, which play an important role in the ability to maintain abstinence. Response inhibition is an executive function that describes an individual's ability to suppress an inappropriate action that interferes with a goal-driven behavior (Logan, 1994; Logan, Schachar, & Tannock, 1997). In the context of smoking cessation, the inappropriate action would be succumbing to a craving for a cigarette during the goal-driven behavior of a quit attempt. Response inhibition is typically measured by conditioning a response to the default stimulus, the "go" stimulus, and measuring the subject's ability to inhibit the default response during exposure to a "stop" or "no-go" stimulus (Logan, 1994). Short periods of abstinence (18–24h) have shown to impair response inhibition on the Stop Signal task (Ashare & Hawk, 2012) and go-no-go task (Harrison, Coppola, & McKee, 2009). Declines in response inhibition have also been shown using other measures including the Stroop task (Dawkins, Powell, Pickering, Powell, & West, 2009) and false positives on a continuous performance task (CPT) (Harrison et al., 2009; Kozink, Kollins, & McClernon, 2010). Furthermore, abstinence-induced deficits in response inhibition are reversed after nicotine exposure (Myers, Taylor, Moolchan, & Heishman, 2008), and following treatment with smoking cessation medication,

such as varenicline (Patterson et al., 2009). Greater response inhibition is also predictive of the ability to maintain abstinence in adolescents (Krishnan-Sarin et al., 2007) and in adults at one and three months (Powell et al., 2010).

There is mounting evidence that both craving and response inhibition are crucial factors of a successful nicotine quit attempt. However, few studies have systematically examined whether specific cognitive deficits are sensitive to shorter or longer abstinence periods. The present study evaluated craving and response inhibition in a cohort of non-treatment seeking smokers. These measures were evaluated during smoking as usual (baseline) and following 24h and 72h abstinence. We hypothesized that craving would be intensified and response inhibition deteriorated during abstinence compared to baseline. Furthermore, we hypothesized that these changes would be more pronounced following 72h abstinence compared to 24h and that there would be a positive association between abstinence-induced craving and response inhibition. Based on evidence that different response inhibition tasks may represent separate components of response inhibition (Swick, Ashley, & Turken, 2011), we incorporated performance on the Stroop task and false positives on a CPT as additional indices of response inhibition. Understanding the course of craving and response inhibition over time will help identify the most vulnerable periods during a quit attempt, helping to guide more effective therapies for nicotine cessation.

## METHODS

### Participants

Study participants were adult non-treatment seeking smokers between the ages of 18 and 65 who reported smoking at least 10 cigarettes per day for the past year. Study participants were recruited over a 9-month period between November 2011 and August 2012. A baseline carbon monoxide (CO) breath test of greater than 10 parts per million (ppm) was used to confirm smoking status. Exclusionary criteria included the current use of chewing tobacco, snuff, or snus, or the anticipated use (within the next 3 months) of nicotine substitutes or smoking cessation medications; history or current diagnosis/treatment for substance abuse (alcohol, opioids, cocaine, marijuana, stimulants, or benzodiazepines); alcohol use of more than 25 drinks/week; positive urine drug screen (opioids, cocaine, benzodiazepines, amphetamine, or methamphetamine); pregnant or lactating; contraindicated medical condition (cancer, insulin dependent diabetes, uncontrolled hypertension); history of or present diagnosis of a psychiatric condition (major depression, schizophrenia, psychosis, bipolar disorder, hypomanic/manic episodes, or ADHD); any condition that may preclude participants from performing cognitive tasks including prohibitive physical or neurological impairment, history of brain injury, color blindness, and low or borderline intellectual functioning, evaluated by a score of less than 90 on the Shipley Institute of Living Scale (SILS; Zachary, Zilberman, Tavares, & el-Guebaly, 2000). Participants received a total remuneration of up to $235 for completing all study sessions. Initial phone screens were conducted with 135 people, of which 66 were deemed initially eligible. Of the 69 who were ineligible at phone screen, 37 reported smoking fewer than 10 cigarettes per day, 11 reported current or past history of substance abuse (other than nicotine), 8 were taking contraindicated medications (e.g., antidepressants), 9 reported comorbid medical conditions

(e.g., uncontrolled hypertension), and 4 were currently participating in other smoking-related research. Forty four people attended a screening/baseline session, 26 were eligible and 25 enrolled. Of the 18 who were ineligible at baseline/screening, 3 had low breath CO (<10ppm), 4 had a positive drug screen, 7 had a Shipley score < 90, 1 was taking a contraindicated medication, and 3 had uncontrolled hypertension. Three participants missed mandatory sessions, and were removed from the study. One participant was deemed ineligible during neurocognitive testing session 1 after providing a positive urine drug screen. In total, 21 participants completed the study (5 female). Demographics and smoking behavior are listed in Table 1.

## Procedure

**Screening/Baseline—**All procedures were approved by the University of Pennsylvania Institutional Review Board. Participants were recruited from previous studies conducted at the University of Pennsylvania, as well as through local media outlets (newspaper and internet). At the initial screening session, participants reviewed eligibility requirements, and complete written informed consent, and HIPAA forms. Eligibility measurements were obtained including urine drug and pregnancy screens, smoking confirmation/baseline through breath CO, and intellectual functioning via the SILS. If eligible, participants completed baseline assessments including standard measures of smoking history and other relevant self-report measures including the Fagerstrom Test for Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991) and craving (Questionnaire on Smoking Urges - described below). Response inhibition was assessed via the Stop Signal task, Stroop task, and Continuous Performance Task (described below).

**Neurocognitive Testing Session 1 – 24 hours abstinent—**Participants received a reminder call to stop smoking 24h prior to the first testing session. A trained smoking cessation counselor provided brief (10 minute) counseling support to help participants maintain abstinence for the duration of the 72h period. Participants arrived at the same time of the day for each testing session (between 8am and noon). Upon arrival, participants confirmed abstinence through breath CO test (less than 10ppm or at least a 75% reduction from baseline). If a participant failed an abstinence test at any point during the 72h abstinence period, he or she was removed from the study (n=1). The participants then completed craving and response inhibition assessments.

**Brief Laboratory Visit – 48 hours abstinent—**The day following the first testing session, participants came for a brief visit to provide a CO breath sample to confirm abstinence. Coping strategies for withdrawal symptoms were reviewed.

**Neurocognitive Testing Session 2 – 72 hours abstinent—**The second testing session (after 72h abstinence) was scheduled for the same time of day as the first. A breath CO test was taken and a value of less than 10ppm was as abstinence verification. Participants then completed craving and response inhibition assessments.

## Measurements

### Primary

**Questionnaire on Smoking Urges- Nicotine Craving:** The 10-item brief questionnaire on smoking urges (QSU-brief) was used to assess craving for cigarettes. The QSU-brief has been shown to be consistent with expressions of craving found in the 32-item version of the QSU (Cox, Tiffany, & Christen, 2001). In addition, the QSU is found to be sensitive to other measures of craving including cue induced craving (Morgan, Davies, & Willner, 1999). We chose to measure general craving rather than cue-induced craving because it is generally more intense and longer lasting in nature during a quit attempt, and may be a stronger predictor of cessation outcome (Wray, Gass, & Tiffany, 2013). The QSU-brief contains 2 subscales: craving in anticipation of increased positive affect (factor 1), and craving in anticipation of relief from negative affect (factor 2). Previous work (Cox et al., 2001) has shown excellent internal consistency for the QSU-brief (Cronbach's alpha = 0.97) as well as internal consistency within factor 1 (Cronbach's alpha = 0.95) and factor 2 (Cronbach's alpha = 0.93). The current study confirms the internal consistency of the QSU-brief, and factor 1 and factor 2 subscales with Cronbach's alpha values of 0.91, 0.90, and 0.83 respectively. Craving has also been related to long-term cessation outcome in many, but not all, clinical studies (Killen & Fortmann, 1997).

**Stop Signal Task - Response Inhibition:** The Stop Signal task (SST) is a measure of response inhibition, or the ability to inhibit a prepotent response. The task was presented on a monitor attached to a desktop running E-Prime software (Psychology Software Tools, Pittsburgh, PA). In this task, participants are instructed to press labeled keyboard keys as quickly and as accurately as possible to indicate the direction an arrow is facing ("z" for left; "/" for right). Following a 32-trial practice, stop signals (800-Hz, 100-ms, 70-dB tone) are presented on 25% of trials for a 32-trial practice, followed by three task blocks of 64 trials each. For each block, the initial stop delay between the stop signals and appearance of the arrows is 250ms. The stop delay adjusts by 50ms increments depending on whether the participant is able to successfully inhibit a response (Logan et al., 1997). The algorithm determines the stop delay at which inhibition of response occurs on approximately 50% of trials. Each trial consists of a 500ms warning stimulus followed by a 1000ms go signal (left and right facing arrows) and 1000ms blank screen intertrial interval. Mean reaction time for each block is calculated based on valid responses. Only blocks with 20–80% inhibition and at least 80% accuracy are included in analysis. Stop signal reaction time (SSRT) is the primary dependent variable and is calculated by subtracting the mean stop delay from the mean reaction time on go-trials. A higher SSRT value therefore indicates relatively impaired response inhibition.

### Secondary

**Stroop Task – Response Inhibition:** The Stroop test is a measure of interference control, or the ability to screen out distracting stimuli (Stroop, 1935) and has demonstrated sensitivity to the effects of cigarette smoking on response inhibition (Domier et al., 2007). In this task, participants view a series of words on a computer monitor and using the keyboard, are asked to press the key associated with the color of the word rather than the word itself. Congruent

trials are trials in which the word and color match (e.g., the word “green” appears in the color green). Incongruent trials are trials in which, the words are printed in colors that do not match the colors of the words (e.g., the word "red" might appear in green). An interference score, or Stroop Effect, is calculated as the difference between the reaction time of incongruent trials and reaction time of congruent trials and measures the ability to suppress a habitual response in favor of an unusual one.

**Penn Continuous Performance Task – Number/Letter Version (CPT) – Response Inhibition:** The Penn Continuous Performance Task – Number/Letter Version (CPT) is a measure of visual attention and vigilance based on the Penn CPT (Kurtz, Ragland, Bilker, Gur, & Gur, 2001). In this task, a series of red vertical and horizontal lines (7-segment displays) flash in a digital numeric frame (resembling a digital clock). The participant must press the spacebar whenever these lines form complete numbers or complete letters. The task is divided in two parts, each lasting three minutes: in the first part the participant is requested to respond to numbers and in the second part the response is to letters. Three different measures are calculated which response to different cognitive domains. False positives (errors of commission) are a measure of response inhibition, true positives are a measure of sustained attention, and reaction time is a measure of speed of processing.

### Data analysis

The primary outcome measures (QSU craving and SSRT) were analyzed using generalized linear regression models (xtreg, Stata). Abstinence condition was a within-subject term (smoking as usual/baseline, 24h abstinent and 72h abstinent). Sex was a between-subjects factor and other relevant covariates were included (e.g., nicotine dependence, age, and Shipley IQ score). Block (1, 2, and 3) was included as a covariate in the model for stop signal time. Secondary outcome measures were analyzed as described above. Relationships between craving and response inhibition were also examined using Pearson correlations. The significance level was set at $p$=0.05.

## RESULTS

### Craving

For the QSU factor 2 subscale, there was an increase from baseline to 24h abstinent, β=3.5, $p$=0.004, which subsided by 72h abstinent, β=2.14, $p$=0.08 (See Figure 1). There were no significant increases in the QSU factor 1 subscale at either time point, $p$-values>0.3. As expected, FTND was positively related to both subscales, β=1.14, $p$=0.03 and β=2.7, $p$<0.001.

### Stop Signal Reaction Time

For the stop signal reaction time, there was no significant increase from baseline to 24h abstinent, β=9.7, $p$=0.315 (See Figure 2). However, there was a significant increase from baseline to 72h abstinent, β=18.8, $p$=0.046. The median “go” reaction time increased from baseline to 72h ($p$=0.016), but not at 24h ($p$=0.107).

### Continuous Performance Task and Stroop task

The median correct reaction time on the CPT significantly increased from baseline at both 24 and 72h, *p*-values<0.001 (see Table 2). The number of true positives on the CPT significantly increased from baseline at both 24 and 72h (*p*-values<0.001). A decrease in false positives on the CPT at 24h approached statistical significance (*p*=0.054), an effect which subsided by 72h (*p*=0.135; see Figure 3a). There was no statistically significant effect of abstinence on the Stroop Effect (*p*>0.10, see Figure 3b).

### Relationship between Craving and Stop Signal Reaction Time

There was no apparent relationship between either craving subscale and any of the measures of response inhibition (SSRT, false positives on CPT, Stroop task) at baseline (*p*-values>0.19), 24h abstinent (*p*-values>0.21), or 72h abstinent (*p*-values>0.41) with one notable exception. At baseline, the Stroop task interference score showed a negative correlation with factor 1 craving (r=−0.499, *p*=0.025).

## DISCUSSION

### Summary of results

The current study sought to describe the time dependent nature of craving and response inhibition during the first 72h of smoking abstinence. We hypothesized that craving would be increased and response inhibition impaired during abstinence, with these changes being more pronounced at 72h than at 24h. Our hypotheses were partially supported. Specifically, although we found no changes in cravings to smoke in anticipation of increased positive affect (factor 1) over 72h of abstinence, increased craving to smoke to relieve negative affect (factor 2) was found at 24h abstinence, but subsided by 72h. Response inhibition, as measured by Stop Signal reaction time, was impaired at 72h but not at 24h abstinence, compared to baseline. In contrast, other indices of response inhibition, as measured by CPT false positives and Stroop Effect, showed no impairment at 24h or 72h and may have actually shown improvement over the period of abstinence. We found little evidence to support our hypothesis that changes in craving and response inhibition during abstinence would be positively correlated.

### Craving

Previous work has shown that craving can start to increase within the first hours of abstinence (Brown et al., 2013; Hendricks, Ditre, Drobes, & Brandon, 2006), may peak within the first few days, and then approaches baseline levels around 4 weeks (Shiffman, West, & Gilbert, 2004). Our finding that factor 2 craving increased at 24h, and subsided by 72h is partially consistent with evidence that among adolescent smokers, craving increases in the 24h following a quit attempt and decreases over the course of three weeks (Van Zundert et al., 2009). However, our data suggest that among healthy adult smokers, changes in craving were specific to urges to smoke to relieve withdrawal-related negative affect. Interestingly, one study found that after one week of abstinence, factor 1 responses on the QSU-brief decreased more than factor 2 responses and this trend continued over the course of the 7-week trial (Cappelleri et al., 2007). These seemingly incongruous results may

actually support the bidimensional model of drug addiction, integrating both positive and negative reinforcement (Baker, Morse, & Sherman, 1986; Koob & Le Moal, 1997; Solomon & Corbit, 1973). Perhaps abstinence-induced craving shifts from a predominantly a negatively reinforced phenomenon (24–72h) to a positively reinforced one at longer time points. The shift in the nature of craving might be explained by the time course of other withdrawal symptoms such as affect, cognitive performance, irritability, and restlessness (Gritz, Carr, & Marcus, 1991; Hatsukami, Hughes, Pickens, & Svikis, 1984; Mooney & Sofuoglu, 2006; Shiffman et al., 2006). In the current study, the peak in withdrawal symptoms soon after abstinence may have resulted in negative affect, causing the observed elevation in factor 2 craving at 24h, but not at 72h. This conclusion fits with the bidimensional affective model of addiction which associates negative affective reinforcement with withdrawal symptoms (Baker et al., 1986). While recent models have espoused a more unidimensional reinforcement model (Baker, Piper, McCarthy, Majeskie, & Fiore, 2004), or have abandoned the positive and negative affective reinforcement model altogether (Robinson & Berridge, 2003; Stewart & Wise, 1992), the evidence points towards the relevance of continued exploration of both positive and negative affective reinforcement during drug cessation.

## Response Inhibition and Practice Effects

Previous work has shown deficits in response inhibition performance (Ashare & Hawk, 2012; Dawkins et al., 2009; Harrison et al., 2009) and in the neural correlates of response inhibition (Kozink et al., 2010) following 24h of smoking abstinence. However, we observed a decrease in response inhibition (i.e., an increase in SSRT) at 72h abstinence, but not 24h, suggesting that there may be a temporal effect of abstinence on the ability to inhibit a prepotent response. Indeed, others have shown time dependent changes in response inhibition over shorter durations (17 vs. 5h) (Harrison et al., 2009). It is important to note that abstinence effects may have been obscured by practice effects on other tasks. In fact, there was a marginally significant improvement in CPT false positives at 24h. There was also an improvement in CPT true positives and median correct reaction time suggesting that there may be significant practice effects on the CPT task overall. However, we felt that our study design was critical to address the question of the time course of abstinence symptoms during the first 72h of a quit attempt. Thus, we can hypothesize that the observed improvement in the CPT and lack of change on the Stroop task can be attributed to learning effects. The fact that we did not observe practice effects on the Stop Signal task is consistent with prior research demonstrating that the Stop Signal task requires controlled (or top-down) inhibition, rather than automatic (or bottom-up) inhibition (Verbruggen & Logan, 2008). These findings should be taken into consideration in future work examining cognitive function during smoking abstinence.

## Response Inhibition and Craving

Based on evidence that impulsive individuals may experience more craving due to the reduced ability to exert cognitive control over the urge to smoke (Doran, Spring, & McChargue, 2007; Zilberman, Tavares, & el-Guebaly, 2003), we explored the relationship between one facet of impulsivity, response inhibition, and craving. Although some have found that, among non-abstinent smokers, higher trait impulsivity (Doran et al., 2007; Litvin

& Brandon, 2010) and behavioral impulsivity, measured via delay discounting, (Litvin & Brandon, 2010) are associated with increased craving, others have found no such relationship (Doran, McChargue, & Spring, 2008; Doran, Spring, McChargue, Pergadia, & Richmond, 2004). With the exception of a positive relationship between factor 1 craving and the Stroop effect at baseline, we found no other significant correlations between measures of response inhibition and craving at any time point. The heterogeneity of results across studies may be partially due to the differences in the assessment of impulsivity and further support the idea that impulsivity is a multifactorial construct (Bloom, Matsko, & Cimino; Verdejo-Garcia, Lawrence, & Clark, 2008; Whiteside, Lynam, Wilkinson, & Gould, 2001). Differences in participant smoking status (abstinent vs. satiated) may also contribute to heterogeneity of results (Doran et al., 2004). Thus, there may be a complex relationship between impulsivity and craving that warrants deeper exploration.

## Limitations of Study Design

The study design places some limitations on these conclusions. Although our within-subject design provides increased power, some effects may not have been adequately captured due to the limited sample size. In addition, gender balance in the study sample was skewed towards men (16 of 21 participants), which precluded examination of gender as a potential moderator of abstinence effects. Several studies have shown that women may experience more craving during abstinence (Xu et al., 2008) and may experience greater cue-induced craving (Knott et al., 2008; Saladin et al., 2012). Therefore, the predominantly male sample may have decreased the observed effect of abstinence on craving. Moreover, there is evidence of sex differences from neuroimaging studies during response inhibition tasks (Li, Huang, Constable, & Sinha, 2006; Rubia et al., 2013). Thus, future studies should balance the sample according to gender and examine whether it moderates the relationship between response inhibition and craving during abstinence.

Although the observed increase in median “go” reaction time during the Stop Signal task across sessions may have contributed to changes seen in the SSRT over time, the task is designed to account for varying “go” times by adjusting the stop delay to ensure participants can only inhibit 50% of responses (Logan, 1994). Therefore, the observed increase in “go” reaction times likely did not significantly affect the results. As mentioned before, learning effects of neurocognitive testing may have blunted abstinence effects on response inhibition. Although counterbalancing abstinence order across participants would have limited practice effects, we felt it was important to examine these abstinence effects throughout a 72h abstinence period. Furthermore, we did not correct for multiple testing which may increase the likelihood of committing a type-1 error. Because the participants in the study were not treatment-seeking smokers, our results may not be generalizable to the population of smokers during an actual quit attempt. Lastly, a clinical measure of relapse to smoking will be critical for future studies to determine the clinical significance of abstinence-induced cognitive deficits on ability to quit smoking.

## Conclusions and Future Work

Because the ability to remain abstinent during the first week of a quit attempt is predictive of long term abstinence (Ashare, Wileyto, Perkins, & Schnoll, 2013), understanding and

managing withdrawal symptoms early in a cessation attempt is crucial. The current study has shed light on two critical withdrawal symptoms during a period of smoking abstinence: craving and response inhibition. Craving associated with withdrawal relief appeared to peak during early abstinence, and decreased by 72h. On the other hand, deficits in response inhibition increased over the course of 72h. Importantly, the neurocognitive effects of abstinence may be a target for smoking cessation. For instance, the smoking cessation medication, varenicline, has been shown to alleviate cognitive deficits following 72h of abstinence (Patterson et al., 2009). Other cognitive enhancing drugs, such as galantamine, an acetylcholinesterase inhibitor and allosteric modulator of nicotinic acetylcholine receptors, may also be a target for alleviating cognitive symptoms during withdrawal (Wilkinson & Gould, 2011). Further testing is necessary to determine whether reducing withdrawal-related cognitive deficits enhances quit rates among treatment-seeking smokers. The fact that we did not observe a relationship between craving and response inhibition suggests that they may contribute independently to the likelihood of relapse and adds to the evidence that smokers form a heterogeneous group that may benefit from individualized treatment (Bierut, Johnson, & Saccone, 2014; Patterson et al., 2008). With this in mind, future work is warranted to characterize specific groups of smokers and develop more targeted treatments to improve the likelihood of successful quit attempts.

## ACKNOWLEDGMENTS

The funding for this study was supported by P50 CA143187 and by the Clinical Neurosciences Training Program (CNST) at the University of Pennsylvania. The NIH had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

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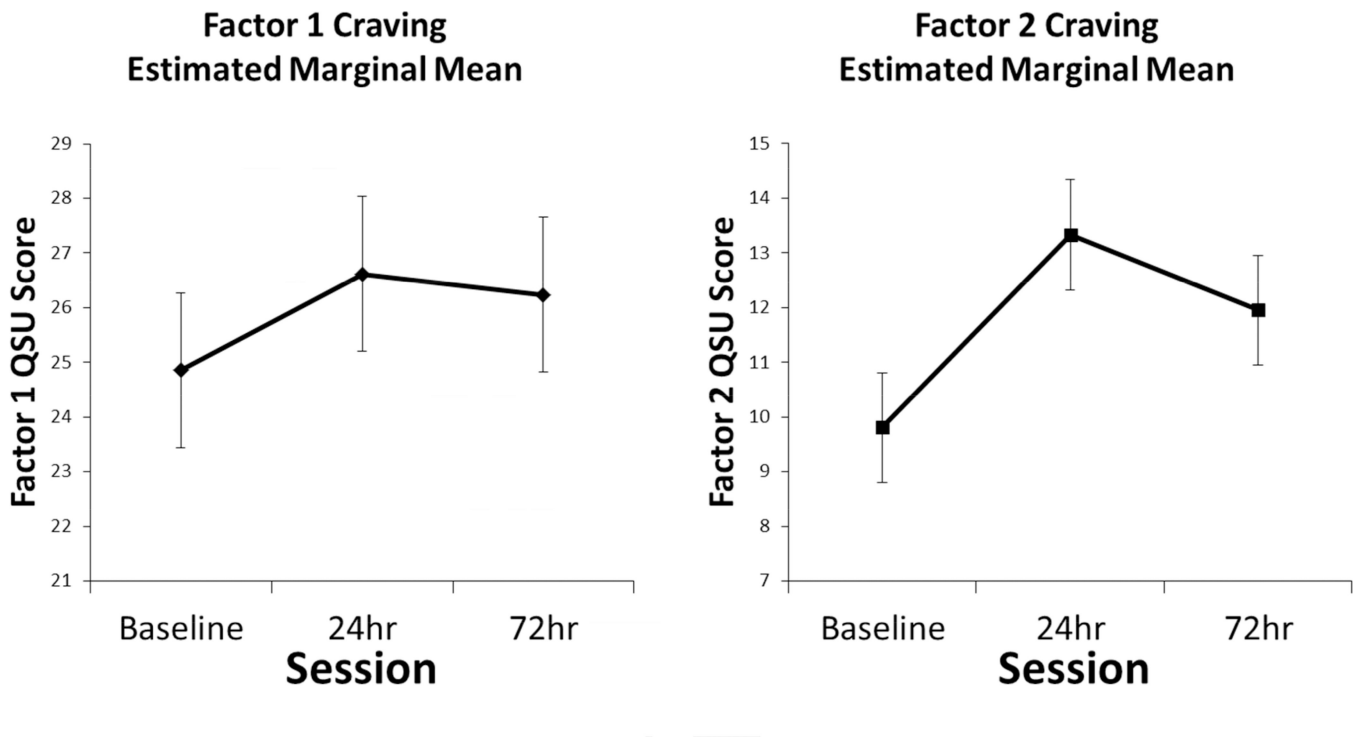


**Figure 1. Questionnaire on Smoking Urges – Brief Scores across Sessions**

QSU scores for factor 1 (anticipated increase in positive affect) and factor 2 (anticipated relief of negative affect) craving across the three testing sessions. Factor 2 increased from baseline to 24h abstinent, β=3.5, *p*=0.004, which subsided by 72h abstinent, β=2.14, *p*=0.08. There were no significant increases in the QSU factor 1 subscale relative to baseline at either time point, *p-values*>0.3.

Note. * p<0.05; error bars are standard error of the mean

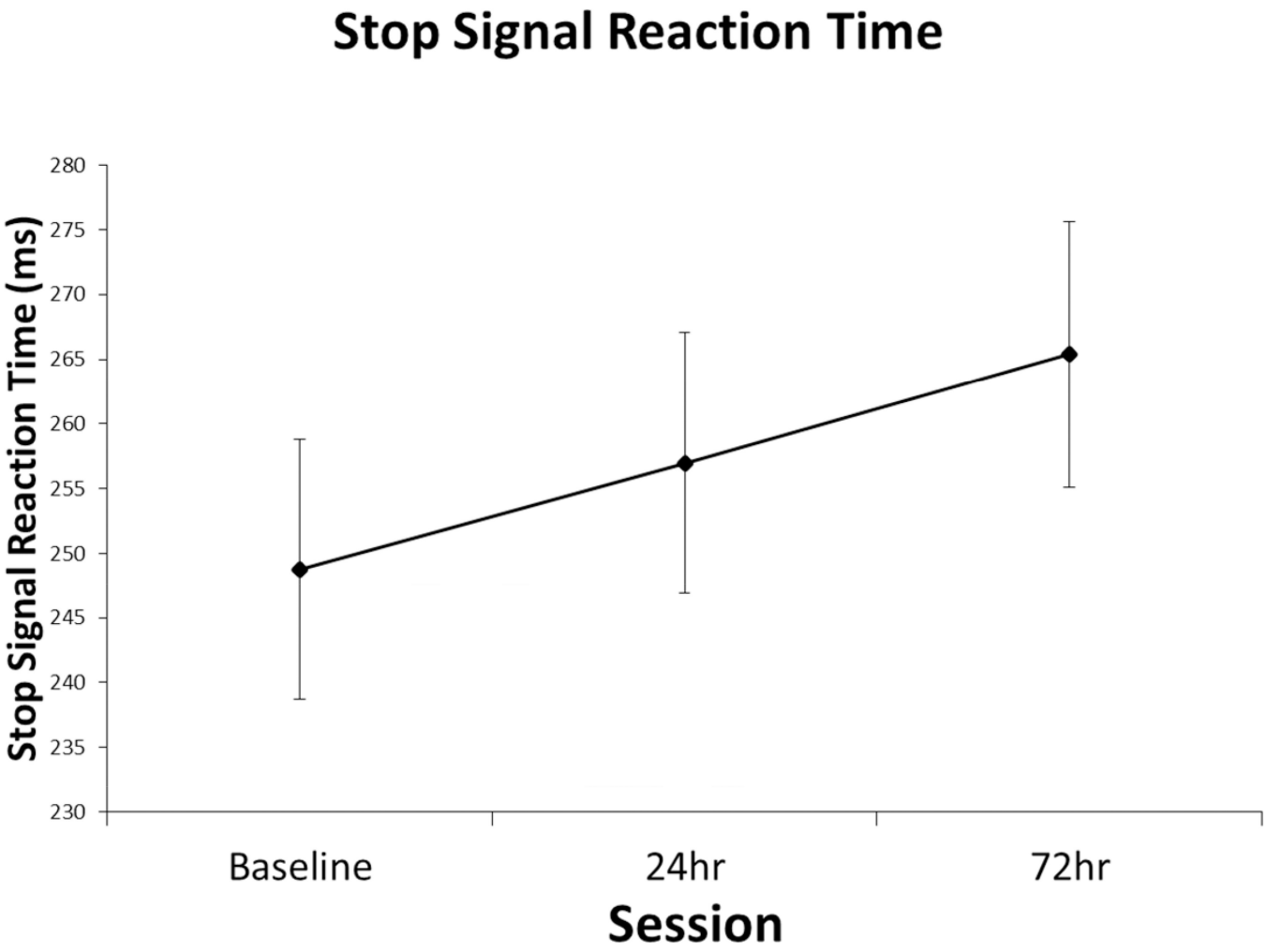


**Figure 2. Stop Signal Reaction Time across Sessions**

Stop signal reaction time across the three testing session. There was no significant increase from baseline to 24h abstinent, β=9.7, *p*=0.315. However, there was a significant increase from baseline to 72h abstinent, β=18.8, *p*=0.046.

Note. * p<0.05; error bars are standard error of the mean

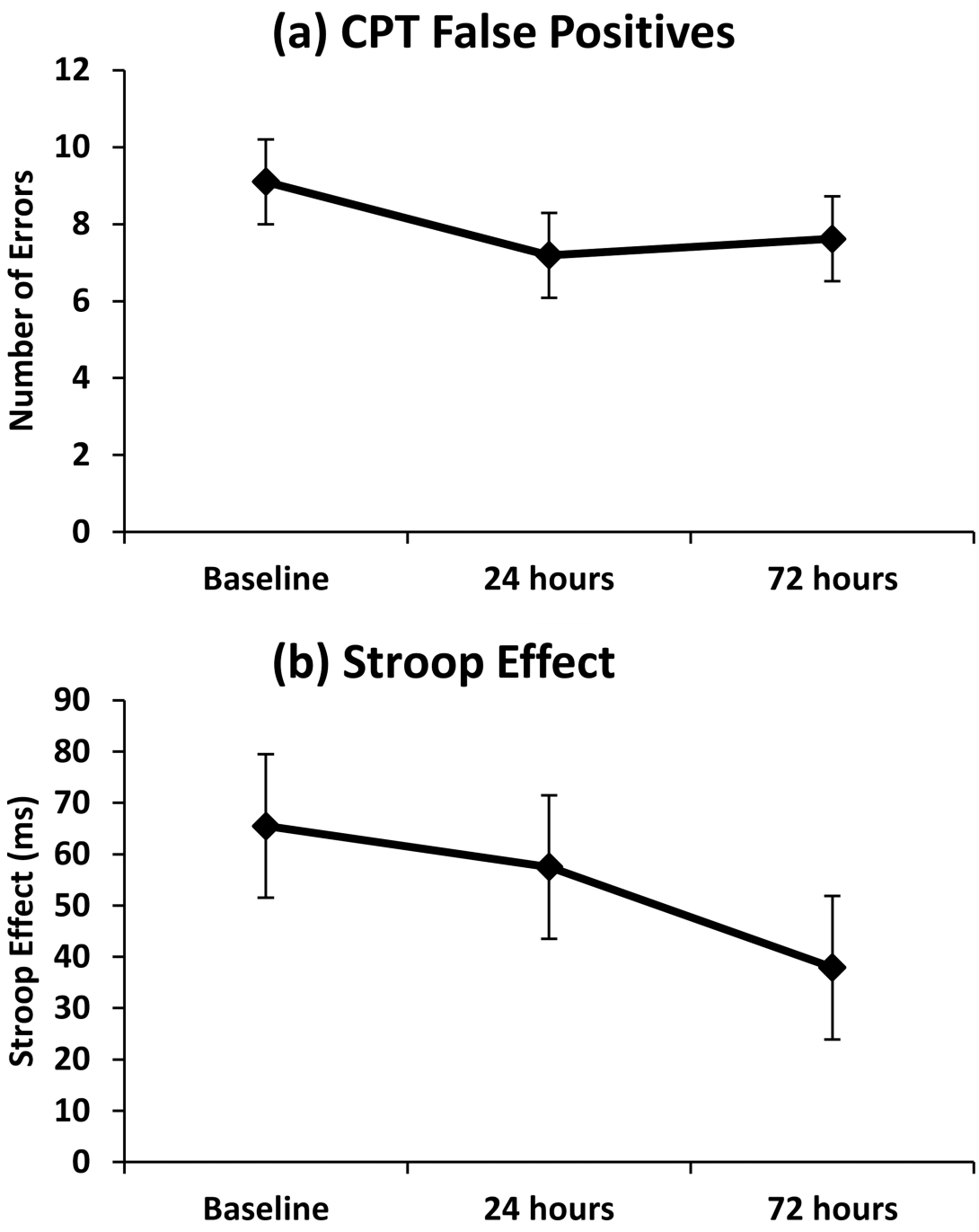


**Figure 3.**

Secondary measures of response inhibition at Baseline, 24h, and 72h. (a) A decrease in false positives (errors of commission) on the CPT at 24h approached statistical significance ($p$=0.054), an effect which subsided by 72h ($p$=0.135). (b) Stroop effect reflects the difference in reaction time to incongruent vs. congruent trials (all *p-value*s>0.1).

## Table 1

Demographic and smoking characteristics for full sample.

| Characteristic | *N*=21 |
|---|---|
| Age (years) | 34.7 (12.5) |
| Age started smoking (years) | 19.0 (6.9) |
| Sex (female:male) | 5:16 |
| Race (#) | |
| Asian | 1 |
| Black or African American | 7 |
| White | 13 |
| Fagerström test for nicotine dependence | 4.8 (1.6) |
| Cigarettes per day (#) | 15.9 (3.6) |
| Shipley institute of living scale | 105.3 (9.0) |
| Carbon monoxide (ppm) | |
| Initial | 20.0 (8.6) |
| 24hr abstinence | 3.1 (1.6) |
| 72hr abstinence | 3.1 (2.1) |

*Note*. ppm, parts per million; Values are mean (standard deviation) unless otherwise specified.

**Table 2**

CPT measures of attention at Baseline, 24 hours, and 72 hours

| Session | CPT Median Correct Reaction Time (ms) | CPT True Positives |
|---|---|---|
| **Baseline** | 454 (6.4) | 110 (1.4) |
| **24 hours** | 437 (6.4) | 115 (1.4) |
| **72 hours** | 429 (6.4) | 117 (1.4) |

***Note***. CPT, Continuous Performance Task; Values are mean (standard error)