Behavioral and electrophysiological responses to smoking-related words in a Smoking Stroop task discriminate between relapse and abstinence following a one-month quit attempt

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Abstract

Cigarette smoking is still quite prevalent despite public education campaigns, and more understanding about the processes that relate to relapse and abstinence is still needed. In the current study, recent abstinent smokers who were later deemed to be relapers or abstainers responded to the color of smoking-related and neutral words in a Smoking Stroop Task while high-density EEG was recorded. One-month Abstinent smokers responded more slowly to smoking words relative to control participants who had never smoked, while Relapsers did not show this effect. Cigarette-related word colors evoked greater voltage of the late positive potential (400-600 ms, aLPP) over the left frontal scalp relative to both one-month abstinent smokers and never smokers. Our findings suggest that smoking cues are more salient for abstinent smokers who are prone to relapse, and this ERP activity evoked by cigarette cues may be a potential biomarker for relapse susceptibility. In contrast, successful abstainers may respond to smoking cues by engaging top-down cognitive control mechanisms leading to less aLPP voltage but greater RT interference. This appears to be the first ERP study to use a Smoking Stroop Task and a high-density electrode array to characterize the spatiotemporal dynamics of smoking-related cue reactivity in abstinent smokers who successfully abstained for one month and those who later relapsed within the same period.

Keywords: ERPs; Cigarette; Relapse; LPP; Abstinence

Introduction

Nicotine dependence is a global issue that has created a health burden for human beings across the world. Smokers’ attempts at abstinence are frequently met with failure, and studies have reported relapse rates approaching 50% less than 2 months after the initial attempt at quitting is made [1]. Given the great difficulty cigarette smokers have when trying to achieve long term abstinence and because of the human and economic costs associated with this habit [2], a great deal of research has been conducted in order to increase abstinence success rates and understand the neural correlates of smoking cue-reactivity.

One method that has considerable utility in addressing this area of research is the event-related potential (ERP) technique. ERPs are extracted from the scalp EEG and have excellent temporal resolution (up to 1 msec) [3], and can detect biological markers in addicted individuals that may be useful for identifying groups that are at high risk for relapse. ERP research has revealed that pictures of substances that people chronically use or crave (i.e., marijuana, chocolate, cigarettes, or cocaine) elicit reliable increases in amplitude in various ERP components relative to neutral pictures, and these are usually absent in control groups that are not composed of chronic substance users or cravers [4-7]. These ERP changes include an early positive going potential over the frontal scalp occurring about 200-350 msec after stimulus presentation (EAP effect), as well as a late occurring positive potential in the 400-2000 msec range reported over posterior or anterior scalp (LPP effect).

One commonly used paradigm that produces reliable behavioral effects in substance dependent groups relative to non-users is the drug Stroop task (dStroop), which is related to the emotional Stroop (eStroop) task that was developed to assess attentional bias towards concern or symptom-specific words in individuals with high anxiety or depression [8]. A subtype of the dStroop task is the smoking Stroop (sStroop task). The consistent finding in these paradigms is that the meaning of concern-specific words (such as cigarette-related words) captures attention and causes slower RT while responding to task-relevant word colors for smokers relative to never smokers (particularly after periods of abstinence) [9-12]. Canamar and London [10] found that resumption of smoking in abstinent smokers reduced the RT interference, indicating that attentional bias to cigarette cues may subside when cigarette craving is eliminated. However, inconsistent results in sStroop studies are not uncommon. For instance, [13] found that there was no indication of attentional bias across groups of smokers that either did not intend to quit or among those who participated in therapy.

Despite its promise, only a single study has been published employing the sStroop task in combination with EEG recording as of the current date. In this study, [14] reported that a frontal positivity (300-400 msec time range) was greater for both smoking-related and neutral words in smokers relative to non-smoking controls. However, the study failed to identify any significant RT interference among groups. Additionally, no studies have employed the sStroop task in combination with EEG recordings in attempts to identify predictors of smoking recurrence or protracted abstinence in abstinent smokers during quitting attempts.

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In order to address the aforementioned limitations, the aim of the present study was to investigate whether behavioral interference in the sStroop task and ERP responses to smoking and neutral words would distinguish future relapers from abstainers at one month follow-up. A group of matched never-smoking controls were also included as a comparison cohort.

Based on previous literature, we hypothesized that baseline differences in the amount of RT interference in the sStroop would differentiate one-month relapers from abstainers relative to never-smoking controls. Furthermore, we hypothesized that frontal positive modulations associated with smoking-related words would be greater in recently abstinent smokers who later relapsed.

Methods

The Simon Fraser University Research Ethics Board approved this study’s procedures. All participants gave their written informed consent before participating and received either course credit or a monetary incentive for their involvement.

Participants

40 nicotine dependent participants willing to make a serious attempt at quitting smoking participated in the study. The success or failure of their quit attempts was assessed over the course of a 31 day period, and the group was subsequently divided into an “Abstinent” group and a “Relapse” group based on whether they were able to refrain from relapsing for one month. Due to technical issues with the EEG and computer equipment, five smokers were dropped from the analysis. The final sample consisted of 19 relapers (10 males) and 16 successful Abstainers (8 males). A group of 20 participants who had never smoked before were also included as a control group. One participant from this group was dropped due to technical issues during data collection, leaving a final sample size of 19 never-smokers (7 males). All participants were between 18-45 years old, and the three groups were well matched in terms of education level and alcohol/substance use. All participants were recruited through word of mouth, the Research Participation System used in the Psychology department at SFU, and through advertisements in and around the university community. Participants were pre-screened in order to ensure that the inclusion criteria for the study were met using the Fagerstrom Test for Nicotine Dependence (FTND) and a medical history/demographic questionnaire. Inclusion criteria included having nicotine dependence or having never smoked, and having normal or corrected to normal visual acuity. Exclusion criteria were admittance of current or past neurological or psychiatric disorder, learning disability, or comorbid illicit substance use and color blindness.

Materials

Questionnaires. The FTND [15] was administered at the time of screening. It is a six-item questionnaire that assesses the severity of a person’s dependence on nicotine. This questionnaire is currently the most widely used measure of nicotine addiction [16]. Participants needed to have scores of 3 or higher to be included in our sample of smokers, as research has shown that this score is a strong indicator of at least a low level of dependence [17,18].

Current depression symptoms were assessed with the Beck Depression Inventory Version II (BDI-II; [19]. State- and Trait-Anxiety were assessed using the State-Trait Anxiety Inventory [20]. Participants also completed the Behavioral Inhibition System/Behavioral Activation System scales (BIS/BAS, Carver & White, 1994) [21]. The questionnaire includes 4 subscales relevant to addiction (BIS, BAS Drive, BAS Reward Responsiveness, and BAS Fun Seeking). They are deemed to measure anticipation of punishment (BIS), goal persistence (BAS Drive), positive responses to reward anticipation (BAS Reward Responsiveness), and desire for new rewards (BAS Fun Seeking).

Quit Smoking Follow-Up Survey. In order to determine whether the abstinent smokers were able to successfully abstain from smoking for at least 1 month (31 days), a survey instrument that could be completed during a phone-call interview or over email was created in collaboration with a tobacco addiction expert at the MD Anderson Cancer Center in Houston, Texas. The survey required participants to note whether they had even one puff of a cigarette in the last 24 hours, last 7 days, and last 31 days. If any cigarette smoking occurred, they were also required to report how many cigarettes they had per day and in total for each of the periods. Participants were also required to report whether they used nicotine replacement therapies (e.g. nicotine patches, nicotine gum) for each of the aforementioned periods. Once data had been acquired for all participants, determinations for instances of relapse were made based on a definition provided by the Society for Research on Nicotine and Tobacco (SRNT) where relapse was defined as a return to regular smoking after an initial abstinence period [22].

Procedure

After meeting inclusion criteria at screening, participants were invited to the EEG session, during which they sat 60 cm from a computer screen in a sound-attenuated booth performing the smoking Stroop task (sStroop) while EEG was recorded from the scalp. After EEG data collection was completed, participants then completed the BIS/BAS, STAI, and BDI questionnaires, were debriefed, and the abstinent smokers were informed that they would be contacted in 1 month for a follow-up to determine whether they were able to successfully abstain.

Stimuli

Two categories of word stimuli were presented during the sStroop task. There were a total of 198 randomly presented stimuli, with half being smoking-related words and half being neutral words. The paradigm utilized a block format, with each of six blocks consisting of 33 neutral or smoking stimuli, with short breaks after each block. There were three “smoking” and 3 “neutral” blocks, in random order. All stimuli were randomly presented using the E-Prime (version 2.0) program. All smoking-related words as well as their neutral counterparts were selected based on a previously published study that assessed cue-reactivity in a sample of smokers using a sStroop task [12].

Participants were required to respond to each color (red, yellow or blue) on a black background with three designated keys of a keyboard using their dominant hand. A fixation cross was present on the screen at all times. Each word was presented for 500 msec, followed by a randomly jittered ISI (500-1000 msec). Examples of the stimulus sequence are shown in Figure 1 below.

Apparatus

The Active Two BioSemi electrode system (BioSemi; Amsterdam, Netherlands) was used to record continuous EEG from 70 Ag/AgCl electrodes; 64 electrodes embedded in an elastic cap with a conventional 10-20 layout, two skin electrodes placed on the left and right mastoids, and four extra electrodes placed at the corner of each eye and below the left and right eye, to monitor eye movements and blinks. DC offset was kept between +/- 25 millivolts. EEG signals were digitized at 512
nificant scores on the FTND relative to Control participants (for both, p<.0001). While Relapsers had slightly higher FTND scores, they did not differ significantly from Abstainers (T\textsubscript{rel}=1.43, p=.15). Importantly, Relapsers and Abstainers did not differ from each other for any other demographic or psychological variable examined (for all, T<1.000, p>.17).

Some differences emerged when each smoker group was individually compared to the Never Smokers. First, Abstainers were older than Controls (on average 3.5 ys older, T\textsubscript{rel}=2.74, p=.011), but they did not differ from Never Smokers for any psychological variable, with only trait-anxiety scores (STAI-T) approaching significance (T\textsubscript{rel}=1.90, p=.067). In contrast, Relapsers reported significantly higher trait-anxiety (STAI-T) than Controls, t(36)=2.62, p=.013, and significantly higher trait-depression (BDI-II scores) than Controls, t(36)=2.14, p=.039. Details of the Demographic data are shown in Table 1 below.

**Behavioral effects**

**RT Effects:** In the global ANOVA, the main effect of Group was significant, F(2,51)=3.47, p=.039. The main effect of Stimulus, F(1,51)=2.62, p=.11, and the Group x Stimulus interaction, F(2,51)=1.39, p=.26, did not approach significance. Overall, Abstainer RTs were significantly slower than Never Smokers (Abstainers: 607.37 ± 92.92; Never Smokers: 535.29 ± 70.25; difference: 72.08 msec) while Relapsers and Never Smokers were not dissimilar (Relapsers: 560.10 ± 80.52; Never Smokers: 535.29 ± 70.25; difference: 24.81 msec). Following the a-priori hypothesis that group differences would be specific to Smoking stimuli, and may vary with relapse status, we proceeded with planned independent samples t-tests comparing Relapsers and Abstainers to Never Smokers for Smoking and Neutral Stimuli (two-tailed, Bonferroni correction for 4 comparisons, p<0.0125). Abstainers’ responses to Smoking stimuli were significantly slower than Never Smokers, T\textsubscript{rel}=2.81, p=.006, Cohen’s d=.74, while the corresponding contrast for Neutral stimuli was not significant, T\textsubscript{rel}=2.11, p=.047. Relapsers’ responses to both Smoking and Neutral words were not dissimilar to those of Never Smokers (for both, p>.10; Table 2 for more details on the RT analysis).

While the between-group contrasts were the ones suggested by previous literature on the sStroop, we also conducted (on an exploratory basis), other contrasts to determine whether within group effects existed for RTs between smoking and neutral words. None of these paired-samples comparisons came close to reaching significance (for all, p>.11).

**Smoking stroop accuracy:** Accuracy data was entered into a similar ANOVA to the one used for the RT analysis. No significant main effects or interactions were observed (for all, p>.2). All groups had high accuracy rates for our Smoking Stroop task (Table 1).

**ERP effects**

Figure 2 top illustrates the grand average waveforms to Smoking related stimuli.
and parietal sites (similar effects were present for Neutral word presentations, but are not shown). Note how traces diverge around 400 ms over frontolateral sites, particularly on the left scalp. Figure 2 (bottom) reports the results of the omnibus F-Statistics performed on all scalp sensors for the relevant Group contrasts (across Smoking and Neutral trials) in the 400-600 ms time window. Note how Relapsers vs. both Abstainers and Controls are distinguished by greater voltage LPP centered over left frontal scalp (with a maximum over left anterior lateral scalp sites), while no difference is present over posterior scalp sites.

**Anterior LPP Effect (400-600 ms, aLPP):**

The repeated measures ANOVA returned a significant main effect of Group, $F(2,52)=5.83, p=.005$, partial $\eta^2=.19$. The main effect of Stimulus, $F(1,53)=.023$, $p=.88$ and the interaction of Stimulus x Group did not approach significance, $F(2,52)=1.0, p=.37$. On average, Relapsers had a significantly more positive amplitude aLPP than Abstainers (Relapsers: $2.40 \pm 1.14 \mu V$; Abstainers: $0.39 \pm 1.54 \mu V$; $T_{17}=3.75$, $p=.001$), and Never Smokers ($1.19 \pm 1.43 \mu V$; $T_{17}=2.25$, $p=.030$). No difference was present between Never Smokers and Abstainers, $T_{17}=1.18$, $p=.25$. The exact scalp topography of the aLPP effect is illustrated with the F-Maps of the group contrasts shown in Figure 2 (bottom) illustrating how the effect is maximal over left anterior-lateral frontal sites, is more pronounced in the contrast between Relapsers and Abstainers, but is still significant in the contrast between Relapsers and Never Smokers.

**Posterior LPP effect (300-600 ms)**

The mixed effects ANOVA on the pLPP yielded no significant Group nor Stimulus main effects, $F(2,52)=1.08, p=.35$ and $F(1,53)=.093$, $p=.76$, respectively. Similarly, the Group x Stimulus interaction failed to approach significance, $F(2,52)=.27$, $p=.76$. Unlike the frontal LPP, voltage of the posterior LPP did not vary as a function of Group. These results confirm those of the omnibus F-statistics in Figure 2, showing no significant group differences over posterior scalp in the 400-600 ms time period.

**Discussion**

The present study investigated whether baseline behavioral performance and ERP activity in response to smoking-related words...
in the smoking Stroop task in recent abstinent smokers attempting to quit could provide possible markers of one-month smoking recurrence or further abstinence. We hypothesized that RT slowing in Smokers vs. Never-Smokers and amplitude of the frontal LPP may index vulnerability to Relapse, possibly differentiating between Relapsers and Abstainers at one-month after their initial quit attempts were made. The two samples of Smokers were well matched for all demographic and psychological measures, and their level of nicotine dependence measured by the FTND was comparable. Relative to the Never-Smoking controls, the Relapser group had greater trait-anxiety and depression symptoms suggesting slightly greater emotional dysregulation. It is not clear whether this slight emotional unbalance is part of the vulnerability diathesis in Relapsers or whether it is due to greater levels of chronic dependence or acute abstinence in this sample (although withdrawal time and FTND scores were also comparable).

### Behavioral effects

Our first hypothesis (that RT slowing to smoking words would differentiate between one-month Relapsers and Abstainers) was supported. While a significant group difference was found, the direction of change was not the one originally expected. It was the Abstainer group that experienced a significant degree of interference while responding to Smoking words relative to the Never Smokers (on average 84.9 msec). On the other hand, interference caused by smoking-related words in the Relapser group relative to Controls was reduced and not significant (on average 38.31 msec) in the face of similar levels of accuracy in the sStroop task. Based on other ERP studies employing the emotional Stroop task and the dStroop task by our group and others (see below) we believe this finding suggests that Abstinent Smokers experienced more cognitive conflict in response to smoking cues when attempting to restrain their urge to use nicotine and sustain their quit attempt. In contrast, Relapsers may have responded to the motivational salience of the smoking cues and likely experienced a hedonic, appetitive response which did not yield the same cost in terms of response speed because it did not tax working memory and attentional resources to the same extent. It is also possible that a motivational component was present for members of this group, and this may have affected their decision making processes (see below for more support of this interpretation).

### ERP effects (aLPP 400-600 ms)

Undoubtedly, the most interesting and novel result of the present study is the finding that frontal LPP amplitudes elicited by words in the sStroop task distinguished Relapsers from Abstinent Smokers attempting to quit, potentially providing a new marker of vulnerability for relapse. This result extends previous findings of posterior LPP and P3 results found in past studies that looked at responses to smoking cues in smokers and never smokers [23-25]. Similar left frontal positivities (albeit slightly earlier in time) have been reported in ERP studies of cue-reactivity to drug-related images in abstinent marijuana [5] and cocaine users [26], chocolate images in high chocolate cravers [4] and in obese people watching words related to high caloric vs. neutral food [27]. These effects have been interpreted as reflecting an exaggerated attentional bias to the sight of a substance having high motivational value to the individual and likely reflecting the desire/urge to consume. Such frontal effects have also been discussed in relation to fMRI studies showing prefrontal cortex activation in response to drug cues associated with craving experiences [28].

In our study, the left aLPP effect was strongest in the contrast between Relapsers and Abstainers. A look at the scatterplots in Figure 3 shows how all Relapsers had a positive going wave in the 400-600 ms range, while Abstainers had more negative values in this time window (with several being quite negative). Similar findings of an increased sustained frontal Negativity (300-700 msec) have been found in restrained relative to unrestrained eaters to the sight of food made available at the end of the study relative to unavailable food [29], and in chocolate Non-Cravers to the sight of chocolate [4]. A process shared by our Abstainer group and by restrained eaters could be the engagement of top-down cognitive control over the desire to consume available substances. The timing and scalp topography of the ERP effect is reminiscent of the Conflict Negativity (or N450) observed in the classical Stroop Task [30], which requires cognitively overriding...
slowing in the Stroop task may represent a predictor of abstinence of Abstainers and Relapsers to confirm the intriguing result that RT findings. Future studies should be conducted using larger samples additional power would help provide support for the legitimacy of our size. Although a number of ERP studies use samples similar to our own, were noted. Perhaps the most obvious of these pertains to the sample settings where intervention and prevention approaches are utilized. An important initial step towards bringing laboratory techniques into clinical environment first. It may also be more fruitful to use psychological effects that distinguish across groups when attempting to predict vulnerability to relapse perhaps fail to modulate the motivational significance, but this had a cost in terms of cognitive performance (hence the RT interference effect). Those who are prone to relapse perhaps fail to modulate the motivational significance of smoking cues, which may ultimately lead to relapses following abstinence attempts.

Clinical significance

Clinicians may be able to use this knowledge to their advantage when assessing relapse vulnerability and when providing treatment to those seeking to quit smoking. For example, our findings may guide those who are conducting interventions to teach patients a set of skills that allow them to effectively regulate themselves in real-world settings, perhaps by diminishing smoking cue reactivity within a controlled clinical environment first. It may also be more fruitful to use psychological effects that distinguish across groups when attempting to predict vulnerability to relapse (as opposed to paper and pencil based measures). Our results do help to clarify this issue and could be an important initial step towards bringing laboratory techniques into settings where intervention and prevention approaches are utilized.

Limitations and future directions

Despite the novel nature of the current study, several limitations were noted. Perhaps the most obvious of these pertains to the sample size. Although a number of ERP studies use samples similar to our own, additional power would help provide support for the legitimacy of our findings. Future studies should be conducted using larger samples of Abstainers and Relapsers to confirm the intriguing result that RT slowing in the Stroop task may represent a predictor of abstinence rather than a predictor of vulnerability to smoking recurrence.

Also, due to the non-clinical setting used to conduct this research project, we did not use biochemical measures for assessing abstinence in our smokers nor did we include such measures as part of our initial assessment. Although we used a widely accepted measure to determine our smokers’ eligibility (FTND), having such data may have allowed for other interpretations of our findings to be made and may have helped us define our groups more accurately. Although past research suggests that substance abusers can be fairly honest about their substance usage [34], objective measures would certainly not detract from a study of this nature. Finally, our sample used a relatively young group of males and females who were recruited from in and around the university community [35,36]. These participants may have higher cognitive functioning than participants who come from lower socioeconomic status neighborhoods, which could impact the generalizability of the results (especially given that cigarette smoking is more prevalent in areas such as these). This sampling issue warrants a replication of our study with participants who are older and perhaps lower in socioeconomic status. Furthermore, we did not screen for ethnicity and future studies may wish to assess this as it may be a variable that relates to relapse vulnerability.

Despite these limitations, our study provides important information about how the brains of recently abstinent smokers who later relapsed or achieved successful abstinence respond to smoking-related words, as well as how abstinent smokers process this form of visual information [37-39]. To our knowledge, this is the first study to investigate the neural correlates of smoking and neutral word exposure in groups of smokers who successfully abstained from smoking, those who failed to achieve longer terms of abstinence, and those who had never smoked using a high-density electrode array to record ERPs. Given that a younger sample was recruited, these results may also be especially informative for policy makers that wish to take a preventative approach to this global health problem. Young smokers are also frequently targeted by big tobacco companies, and understanding how reactivity to smoking cues manifests itself in this population may serve to inform those wishing to intervene in this harmful behavioural pattern. Nonetheless, it would be useful if future ERP studies could replicate the procedures used in the current study given that findings obtained using this paradigm remain sparse.

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