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Frontoparietal Attentional Network Activation Differs Between Smokers and Nonsmokers during Affective Cognition

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Abstract

Smoking withdrawal-induced disruption of affect and cognition is associated with dysregulated prefrontal brain function although little is known regarding the neural foci of smoker-nonsmoker differences during affective cognition. Thus, the current study utilized fMRI to identify smoker-nonsmoker differences in affective cognition. Thirty-four healthy volunteers (17 smokers, 17 nonsmokers) underwent fMRI during an affective Stroop task (aST). The aST includes emotional cue-reactivity trials, and response selection trials that contain either neutral or negative emotional distractors. Smokers had less activation during negative cue-reactivity trials in regions subserving emotional awareness (i.e. posterior cingulate), inhibitory control (i.e. inferior frontal gyrus) and conflict resolution (i.e. anterior cingulate); whereas during response selection trials with negative emotional distractors, smokers had greater activation in a frontoparietal attentional network (i.e. middle frontal and supramarginal gyri). Exploratory analyses revealed that task accuracy was positively correlated with ACC and IFG BOLD response. These findings suggests that chronic nicotine use may reduce inhibitory control and conflict resolution of emotional distraction, and result in recruiting additional attentional resources during emotional interference on cognition.

Keywords

nicotine; affect; emotion; fMRI; cue-reactivity

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1. Introduction

The ability to exercise cognitive control in the face of emotionally distracting information is important during response selection. However, research suggest that individuals with substance abuse disorders experience altered emotional information processes and impaired decision making (Verdejo-Garcia et al., 2006). In particular, evidence suggests that smokers exhibit aberrant cognitive and affective function compared to their nonsmoking counterparts. Large population-based studies have shown that compared to nonsmokers, smokers perform worse on cognitive tasks across the lifespan (Paul et al., 2006; Weiser et al., 2010). For example, adolescent smokers perform worse on cognitive tasks than nonsmokers and individuals that begin smoking after the age of 18 have been found to have a lower IQ than nonsmokers (Weiser et al., 2010). In a well-controlled study of healthy adult smokers and nonsmokers, smoking was associated with deficits in executive function, and age-related decline in memory processes was found in smokers but not in nonsmokers (Paul et al., 2006). Furthermore, when controlling for age, smokers exhibit worse performance than nonsmokers on a sustained attention task (Foulds et al., 1996). In addition to these differences in cognition, differences between nonsmokers and smokers are found in affective function. Smokers as compared to nonsmokers have higher trait negative affect (Gilbert, 1988), greater number of subclinical depression symptoms (Lerman et al., 1996) and greater sensitivity to negative emotional stimuli (Cane et al., 2009).

Although smoker-nonsmoker differences in cognitive and affective function are well documented, far less is known about the neural bases of these effects. Compared to nonsmokers, smokers have been shown to exhibit reduced gray matter volume and/or density in brain regions subserving cognitive control of attention and emotional information processing, including bilateral frontal and prefrontal cortical areas (Brody et al., 2004; Gallinat et al., 2006; Yu et al., 2011). Smoker-nonsmoker differences in GM volume/density have been hypothesized to result either from the brain damaging effects of cigarette smoke (Kühn et al., 2010; Swan and Lessov-Schlaggar, 2007b) and/or reflect the above noted predisposing neurocognitive factors such as impaired attention and dysregulated affect. However, very little work has reported on smoker-nonsmoker differences in neurocognition. In a recent study investigating the functional neuroanatomical correlates of attention, smokers relative to nonsmokers exhibited reduced attention-related neural activation in visual cortex and increased activation in parietal cortex that correlated with time on task (Vossel et al., 2011). Yet, smoker-nonsmoker differences in brain cue-reactivity to emotional stimuli and the effects of emotional cues on attention remain unclear. Identifying the neural correlates of smoker-nonsmoker differences in emotional processing and attention may help to provide further mechanistic insight into the effects of chronic nicotine use and dependence.

In the present study we sought to identify functional neuroanatomical correlates of smoker-nonsmoker differences in cognitive and affective brain function using a paradigm that allows for an assessment of the effects of negative emotional stimuli on cognitive task performance (i.e. affective cognition). Smokers exhibit greater disruption of attentional control on the Emotional Stroop task when presented with negative as compared to neutral words (Drobes et al., 2006), and prior research suggests that, compared to nonsmokers, nicotine dependent individuals are more susceptible to the distracting effects of negative emotional stimuli on executive control during Stroop tasks (Cane et al., 2009). Though these two studies provide behavioral evidence for associations between nicotine dependence and greater emotional interference on cognition, the neural correlates of this effect have not been thoroughly investigated.

Outside of the context of nicotine dependence, a prevailing brain model of cognitive control over emotional interference posits a dual-system neural network model with reciprocal interactions: a dorsal brain system (e.g. dlPFC, dACC) subserving executive function and top-down control, and a ventral brain system (e.g. amygdala) subserving emotional processing and bottom-up impulses (Drevets and Raichle, 1998; Gyurak et al., 2011; Kim and Hamann, 2007). Thus, effective top-down control reduces emotional interference on ongoing cognitive demands. Furthermore, a recent model posits that self-regulation failure occurs when the reciprocal balance between bottom-up and top-down neural circuits become tipped in favor of bottom-up processes (Heatherton and Wagner, 2011).

An imbalance between these dual brain systems may underlie the greater emotional interference on cognition observed among nicotine dependent individuals. Indeed, we recently reported that among nicotine dependent smokers, withdrawal disrupts frontal executive neural circuitry function, but not limbic response during the Affective Stroop Task (Froeliger et al., 2012) and the emotional Oddball task (Froeliger et al., in press), suggesting that dysregulated top-down control mechanisms may be primary targets in nicotine dependence and withdrawal. However, smoker-nonsmoker differences were not explored in the previous studies, thus secondary analyses of those data provide an opportunity to evaluate differences in neural function associated with chronic nicotine use and better characterize relations between chronic nicotine use, executive and limbic function.

Therefore, in the present study we examined differences in brain function between smokers and nonsmokers while performing a task probing affective cognition. Dependent smokers (n=17) and nonsmoker matched controls (n=17) were scanned while they performed an event-related Affective Stroop Task (aST)—a probe of emotion and cognitive function that has been validated in healthy controls (Blair et al., 2007), smokers in nicotine withdrawal (Froeliger et al., 2012), and psychiatric populations including post-traumatic stress disorder (PTSD) (Mueller-Pfeiffer et al., 2010; Vythilingam et al., 2007) and major depressive disorder (MDD) (Hasler et al., 2009) patient populations. In light of our previous finding of hyperactivation in frontal executive neural circuitry during the Affective Stroop task among smokers in withdrawal (Froeliger et al., 2012), and given evidence that effortful cognitive control over emotionally distracting information involves the recruitment of frontal executive neural circuitry, including the dorsolateral prefrontal cortex (dlPFC) (Ochsner et al., 2002), we hypothesized that smokers as compared to nonsmokers would exhibit greater task-related brain activation in dlPFC when presented with negative emotional distractors.

2. Experimental Procedures

2.1. Participants

Thirty-four participants [smokers (n=17); nonsmokers (N=17)] from the community signed a Duke IRB approved informed consent and were enrolled in the study. Smokers had to report smoking 10 cigarettes per day for at least two years, have an afternoon expired-air carbon monoxide (CO) level > 10 ppm, be right-handed, free of serious health problems, not having an active or a history of psychiatric illness including drug abuse (except nicotine dependence among smokers) as assessed through a screening questionnaire, free of medications altering CNS functioning, test negative for illicit drug use, not have any conditions making MRI research unsafe, and among females, have a negative urine pregnancy test. The same inclusion/exclusion criteria were applied to the group of age- and sex-match nonsmokers except they had to report 1) having smoked < 50 cigarettes in their lifetime, 2) not having smoked at all in the last 6 months, and 3) have an afternoon expired CO concentration of 5 ppm.

2.2. Procedures

Eligible participants completed one training session during which they practiced the experimental task and were placed in a mock scanner in order to habituate to the scanning environment. Following training, smokers and nonsmokers completed a scanning session; smokers were allowed to smoke as usual up until the time of scanning. Smokers were also involved in a separate scanning visit during which time they were nicotine deprived (satiated/abstinent sessions were counterbalanced). Data from the within-subjects analyses comparing smoking satiety vs abstinence is reported elsewhere (Froeliger et al., 2012) and is not included in the present manuscript.

Expired air CO concentrations were measured using a handheld CO monitor (Vitalograph Inc., Lenexa, KS) and were calculated by subtracting the background (ambient) CO from the peak CO reading.

2.3. Assessment of Affect and Nicotine Dependence

Baseline negative affect was assessed with the Center for Epidemiological Studies-Depression (CES-D) scale (Radloff, 1977). Nicotine dependence was assessed with the Fagerström Test of Nicotine Dependence (FTND) (Heatherton et al., 1991).

2.4. Affective Stroop Task

During the imaging session, participants performed two runs of the aST (Blair et al., 2007; Froeliger et al., 2012). Stimuli consisted of number grids and distractor images. The number grids consisted of numerals (1's through 6's) randomly presented within a 9-point grid-field. Distractor stimuli were negative and neutral valence images selected from the IAPS (Lang et al., 1997) on the basis of 9-point arousal (1-lowest, 9-highest) and valence (1-negative to 9-positive) scales. The task is comprised of two distinct trial types: *decision-making trials* and *cue-reactivity* (i.e. view-only) *trials*. Decision-making trials began with a fixation cross, followed by a number grid, a negative or neutral distractor image, a unique number grid, and concluded with the representation of the distractor image, each for 800ms. Participants were instructed to report by button press which number grid presented (1st or 2nd) contained greater numerosity (the quantity of numbers presented). Task trials were further broken down into two subcategories: congruent and incongruent trials. During congruent trials, the number grids presented numerals with a face value congruent with the numerosity (e.g., two 2's; five 5's). During the incongruent trials, the face value of the numerals did not match the numerosity (e.g., four 3's; three 4's). Response accuracy and reaction times (RT's) were recorded for each trial. During the *Cue-Reactivity trials* the numerical grids were replaced with fixations and no responses were recorded. During each 8 1/2 minute run, each event type (negative congruent, incongruent; neutral congruent, incongruent; negative view; neutral view) were randomly presented equally (n=15), resulting in 30 trials/event during each session.

2.5. Analysis of Behavioral Data

Behavioral analysis of smoker-nonsmoker differences in task performance (i.e. Task Accuracy; RT's) were analyzed with a 2 (Group: smoker, nonsmoker) $\times$ 2 (Task Condition: congruent, incongruent) $\times$ 2 (Valence: negative, neutral) ANOVA.

2.6. fMRI Methods

A 3T General Electric Signa EXCITE HD scanner (Milwaukee, WI) equipped with 40 mT/m gradients was used for image acquisition. Blood-oxygenation-level-dependent (BOLD) functional images were collected for 34 contiguous slices (3.8 mm thick) parallel to the horizontal plane connecting the anterior and posterior commissures using a gradient-recalled

inward spiral pulse imaging with K-space trajectory (TR = 1500 ms, TE = 30 ms, FOV = 25.6 cm, matrix = 64×64, flip angle = 60°, 4 × 4 mm in-plane resolution).

Preprocessing was conducted using statistical parametric mapping software (SPM8; Wellcome Department of Imaging Neuroscience, London) to remove noise and artifacts. The first four volumes of each run were discarded to allow for T1 stabilization. All functional images underwent correction for acquisition timing and for head motion using rigid-body rotation and translation (Friston et al., 1994). Each participant's data was then subsequently warped into a standard stereotaxic space (Montreal Neurological Institute) with an isotropic 2 mm voxel size and smoothed with an 8 mm FWHM Gaussian filter.

2.6.1. Imaging Data Analysis—Each participant's data was entered into a first-level, whole-brain analysis using the General Linear Model (Friston et al., 1994) to examine activation in response to each event type; negative congruent, neutral congruent, negative incongruent, neutral incongruent, negative view, neutral view. Each trial was modeled as a boxcar function equal to the duration of the trial and convolved with a canonical hemodynamic response function (HRF). Motion parameters were included as nuisance covariates, and a high-pass filter (128 seconds) was applied to remove slow signal drift. Contrast images were then created (see below) for use in random effects analyses. Statistical images were thresholded with a mask containing regions of interest (ROI) that have been previously found to play a role in emotion-cognition interactions (Blair et al., 2007; Dolcos and McCarthy, 2006; Ochsner et al., 2002). These included bilateral posterior, dorsal and paracingulate cortices; inferior, middle and superior frontal gyri; inferior parietal lobule (IPL); insula and amygdala. These ROI's were obtained from automated anatomical labeling (AAL) in Marina (Walter et al., 2003).

The goals of the analyses were to identify group differences (smoker, nonsmoker) in 1) negative emotional cue-reactivity and 2) the effects of emotional distraction on task-related cognitive brain function. 1) Negative emotional cue-reactivity consisted of the negative view and neutral view trials only. For these trials, a negative>neutral contrast image was generated for use in the random-effects analyses. Group differences in the effects of negative emotional cue-reactivity (e.g. negative-neutral view trial contrast) were evaluated by conducting a between-subjects (Group: smoker, nonsmoker) random effects ANOVA. 2) The effects of emotional distraction on task-related cognitive brain function consisted of negative congruent, neutral congruent, negative incongruent, neutral incongruent trials. Contrast images were generated for 1) Mean Negative distractor Response Selection Trials (negative incongruent, negative congruent] and 2) Mean Neutral distractor Response Selection trials [neutral incongruent, neutral congruent]; and then a Negative>Neutral distractor response selection trial contrast was generated for use in the random-effects analyses. Similarly, smoker-nonsmoker differences in the effects of emotional distractors on response selection-BOLD activation (e.g. negative-neutral response selection trial contrast) were evaluated by conducting a between-subjects (Group: smoker, nonsmoker) random effects ANOVA. In order to control for group differences in baseline sub-clinical depression symptom severity that could affect cue-reactivity or cognitive performance (Froeliger et al., in press), CESD score was included as a nuisance covariate in both the cue-reactivity and cognitive models.

In all analyses, voxels were considered significant if they passed a statistical threshold of $p < .005$, uncorrected, and were part of a 432- μL cluster of contiguous significant voxels, resulting in a cluster-corrected $p < .05$. Cluster size for the comparisons was determined by performing 1,000 Monte Carlo simulations (Ward, 2000).

3. Results

3.1. Sample characteristics

Data from one smoker participant was excluded from analyses due to scanner-related issues, and from one nonsmoker participant due to excessive motion during the task. The final sample of smokers ($n=17$) and nonsmokers ($n=17$) did not significantly differ on any demographic variables (Table 1).

3.2. Biochemical confirmation of smoking status

Significant differences in expired breath CO concentrations (ppm) at baseline confirmed smoker- nonsmoker status: 26 (SD=13.4) and 1.5 (SD=1) respectively; $t=17$, $p<.001$. Expired breath CO concentrations indicated compliance with study requirement for smokers to continue to smoke as usual on the experimental day (mean CO=26.2, SD = 13).

3.3. Task Performance

Reaction times—RT's were slower during trials with negative ($M= 852.8$ msec, $SD= 202.9$) as compared to neutral ($M= 828.6$ msec, $SD= 201.2$) distractors, ($F=11.1$, $df= 1,32$, $p=.002$). No other significant main effects or interactions were observed ($p's > .1$).

Task Accuracy performance—No significant main effects or interactions were found (all $p's > .1$).

3.4. Imaging Results

Main effect of Smoking Status on Negative Emotional Cue-Reactivity—During negative emotional cue-reactivity trials, nonsmokers as compared to smokers had greater BOLD-response in left anterior and posterior cingulate cortices (ACC; PCC), and bilateral inferior frontal gyri (IFG) (Table 2; Figure 1). No regions were found where smokers were more cue-reactive than non-smokers.

Main effect of Smoking Status on Emotional Distractor Response Selection trials—During response selection trials where negative emotional distractors were present, smokers had greater BOLD response than nonsmokers in right middle frontal gyrus (MFG) and right inferior parietal lobule (IPL) (Table 3; Figure 2).

Follow-up exploratory analyses of smokers scan order—Data from nearly half of smoker participants ($n=8$) were obtained during the first of two fMRI visits, whereas data from the remaining ($n=9$) was collected during a second fMRI visit. Therefore, to evaluate whether there were differences in task-related brain function between the smokers as a function of scan visit, we conducted a between-subjects ANOVA comparing 1st visit smokers ($n=8$) with 2nd visit smokers ($n=9$), and applied a more liberal significance threshold ($p<.005$, uncorrected). No significant clusters were identified. As a follow-up we also re-ran the between-subjects ANOVA with all nonsmoker controls ($n=18$) and only including smokers that were 1st scanned during the smoking satiated condition ($n=8$). The same clusters and direction of effects for the main findings were identified in this limited sample model as in the full model.

Exploratory analyses of relations between behavioral performance and brain findings—For each group, zero-order correlations were computed for behavioral performance difference [negative-neutral] scores (i.e. RT's and Accuracy) and parameter estimates from each significant cluster from the main effects models. With regard to smokers' brain responses during cue-reactivity trials, positive correlations were observed

between task accuracy and BOLD response in left ACC ($x=-6$, $y=30$, $z=26$), [$r=.53$] and right IFG ($x=44$, $y=30$, $z=4$), [$r=.51$]; whereas a negative correlation was observed between reaction time performance and BOLD response in left IFG cluster ($x=-48$, $y=14$, $z=12$) [$r=-.40$], all p 's<.05. No significant positive or negative correlations were found between behavioral and brain measures among nonsmokers.

4. Discussion

The present study explored smoker-nonsmoker differences in negative emotional cue-reactivity, and tested the hypothesis that smokers as compared to nonsmokers would exhibit greater task-related brain activation in the executive control system during task trials when presented with negative emotional distractors. Results from the present study indicated that smokers exhibited relative hypoactivity to negative emotional cues within the PCC, ACC, and IFG when compared with nonsmokers. Moreover, the magnitude of activation in the latter two brain regions was related to task-related performance in smokers. With regard to the effects of emotional distractors on response selection, the present study confirmed the study hypothesis by finding that smokers, as compared to nonsmokers, exhibited greater BOLD response in dlPFC (i.e. middle frontal gyrus) and inferior parietal lobule to task trials with negative emotional distractors. The current study builds upon the extant literature by demonstrating that brain function across executive control and attention areas during affective cognition is mediated by smoking status.

Effects of smoking status on negative emotional cue-reactivity

Relative to nonsmokers, smokers exhibited less cue-reactivity to negative emotional images in brain structures subserving emotional awareness (i.e. PCC), conflict resolution (i.e. ACC) and inhibitory control (i.e. IFG) processes. Outside of the context of nicotine dependence, a current neurobiological model of drug addiction posits that chronic drug abuse modulates brain processing of motivationally-salient environmental stimuli (Koob and Le Moal, 2008) and disrupts frontally mediated inhibitory control processes (Koob and Volkow, 2010). Within the context of nicotine dependence, an attentional bias model (Gilbert, 1995) posits that nicotine shifts or biases attention away from processing negative emotional stimuli via frontally mediated circuitry, subsequently reinforcing smoking by reducing negative affect. Current study findings support these models by demonstrating that chronic nicotine use is associated with attenuated executive control processing of negative emotional stimuli. Interestingly, exploratory analyses revealed that the magnitude of activation in the ACC and rIFG positively correlated with better task performance. Thus, the observed relations between behavioral performance, conflict resolution, and inhibitory control mechanisms may suggest that smoker's failure to attend to and resolve negative emotional conflict may have downstream adverse effects on cognitive performance.

Effects of emotional distraction and smoking group status on a frontoparietal attention network

Smokers exhibited greater brain activation across an extended attentional network (i.e. right MFG and IPL) during task trials (i.e. response selection) that contained negative emotional distractors. Attentional control is subserved via frontoparietal circuitry including inferior parietal lobule (Cabeza and Nyberg, 2000; Corbetta and Shulman, 2002) and dlPFC (Cabeza and Nyberg, 2000).

Prior research with smokers has demonstrated smoking withdrawal results in potentiated BOLD signal in dlPFC across a broad range of cognitive tasks (Froeliger et al., 2012; Froeliger et al., in press; Jacobsen et al., 2007; Kozink et al., 2010; Xu et al., 2005). The dlPFC subserves top down cognitive processes including attention (Cabeza and Nyberg,

2000) and goal-directed processes (Blair et al., 2007). In contrast, the IPL is involved in bottom up reorienting of attention to salient stimuli (Corbetta and Shulman, 2002). Previous fMRI studies with smokers and nonsmokers performing the intention/attention task (IAT) report that in the absence of any group differences in behavioral performance, smokers had greater activation in iPL (Rose et al., 2010).

Taken as a whole, the pattern of results from the current study are consistent with two complementary models: one where parallel frontal and parietal attentional control networks become engaged during effortful cognitive control (Egner et al., 2007), and the second which posits that resolving emotional distraction on cognition requires recruitment of more frontal executive resources in order to meet task demands (Blair et al., 2007; Dolcos and McCarthy, 2006; Ochsner et al., 2002). These findings suggest that nicotine dependence, outside of the context of withdrawal, may be associated with 1) attenuated executive control over processing negative emotional information and 2) greater emotional interference on frontal-executive brain function during cognitive demands, putatively to be further exacerbated following withdrawal-induced dysregulation of frontal brain function during affective cognition (Froeliger et al., 2012; Froeliger et al., in press). Though the alterations in neurotransmission underlying these neurocognitive differences cannot be pinpointed in the present study, prior research demonstrates that nicotine modulates multiple neurotransmitter systems that play a critical role in attention and affect including cholinergic (Everitt and Robbins, 1997; Robbins et al., 1997), dopaminergic (Damsma et al., 1989; Picciotto et al., 2001; Picciotto et al., 1998; Pierce and Kumaresan, 2006) and noradrenergic (Fu et al., 1998; Fu et al., 1997; Matta et al., 1990) systems. Though a number of studies suggest that nicotine may enhance cognition in both smokers (see (Levin et al., 2006) and nonsmokers (Ernst et al., 2001; Foulds et al., 1996; Froeliger et al., 2009; Heishman et al., 2010; Wesnes and Warburton, 1984); (but also see (Ernst et al., 2001; Foulds et al., 1996; Foulds et al., 1997)), long-term nicotine use may have deleterious effects on neurotransmission. For instance, nicotine's effects vary over time and with repeated use by both activating and desensitizing nicotinic acetylcholine receptors (nAChR's) differently (Picciotto et al., 2002), and by disrupting dopaminergic, noradrenergic and cholinergic activity in frontal cortex. Furthermore, repeated exposure to tobacco smoke is associated with atrophy in frontal brain volume and impaired executive function (Brody et al., 2004; Durazzo et al., 2010; Swan and Lessov-Schlaggar, 2007a).

The present study included a well-controlled matched sample of smokers and nonsmokers, an fMRI task that allows for modeling affective cognition and the investigation into the neurocognitive basis of baseline differences between smokers and nonsmokers during affective cognition -- areas of research currently under-represented in the literature. These findings suggest that nicotine dependence is associated with underlying differences in frontal executive brain function that may either be a risk factor for nicotine dependence or a result from chronic nicotine exposure. As noted above, smokers exhibit decreased grey matter in bilateral frontal and anterior cingulate cortices compared to non-smokers and the observed effects may be a correlate of this difference. Other limitations include a relatively small sample size, not characterizing individual differences (e.g. personality), the lack of structured assessment of psychiatric comorbidity, an absence of differences in behavioral performance, and the fact that smokers were scanned twice whereas nonsmokers were only scanned once. Furthermore, in the current study smokers had higher subclinical depressive symptoms than nonsmokers. Though we controlled for depressive symptom severity by entering CESD scores as a nuisance covariate in the statistical models, nicotine dependence and trait negative affect are tightly intertwined. For instance, subclinical depression symptom severity predict the likelihood of being a dependent smoker (Anda et al., 1990; Lerman et al., 1996) and worsen cessation outcomes (Anda et al., 1990; Cinciripini et al., 2003). Smokers report smoking in the face of NA or stress-inducing situations (Shiffman

and Waters, 2004) and often report that smoking reduces NA (Shiffman and Waters, 2004; Spielberger, 1986). Therefore, chronic nicotine use and depressive symptoms are likely not orthogonal, rather in conjunction they may reflect a neurobiological difference between smokers and nonsmokers by which smokers may be more ideally psychobiological modulated by nicotine—putatively to help reduce negative affect (Conklin and Perkins, 2005; Fucito and Juliano, 2009; Lerman et al., 1996; McClernon et al., 2006; Tizabi et al., 2010; Tizabi et al., 1999). Future large-scale studies that evaluate depressive symptoms severity and smoking status will help to better identify brain-behavior differences between smokers and nonsmokers and neural correlates of emotion-cognition interactions in nicotine dependence.

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Figure 1.

Brain regions where smokers had less BOLD response than nonsmokers during negative emotional cue-reactivity.

Statistical images were thresholded using a cluster corrected significance threshold of $p=.05$ ($p<.005$; $K=54$), corresponding to a height threshold of $F > 9.1$. ACC = Anterior Cingulate Cortex; IFG= Inferior Frontal Gyri; PCC= Posterior Cingulate Cortex

Figure 2.

Brain regions where smokers had greater BOLD response than nonsmokers due to negative emotional distraction on response selection.

Statistical images were thresholded using a cluster corrected significance threshold of $p=.05$ ($p<.005$; $K=54$), corresponding to a height threshold of $F > 9.1$. MFG= Middle Frontal Gyrus; IPL= Inferior Parietal Lobule

Table 1**Subject Demographics / Baseline Self-Report**

	Smokers (N=17)	Nonsmokers (N=17)	t / x2	Sig. (2- tailed)
% Female	55%	55%	0.0	ns
Mean Age (SD)	31.9 (8.0)	30.4 (8.2)	0.5	ns
Years of Education (SD)	14.5 (2.2)	15.7 (2.6)	1.5	ns
Race				
Asians	2	1		
Blacks	4	6		
Caucasians	11	10		
Baseline				
CESD score, mean (SD)	13.4 (10.8)	3.9 (3.2)	3.5	0.001
FTND score, mean (SD)	5.1 (2)			
Years Smoking (SD)	14 (7.9)			
Avg. Daily # Cig. (SD)	16.9 (4.9)			
CO (Screening)	26.0 (13.4)	1.5 (1)	7.5	<.000

Cue-Reactivity Trials; Brain regions where a main effect of Smoking Status on BOLD response to negative emotional images (negative-neutral contrast).^a

Table 2

Direction	Side	Lobe	Brain Area	Brodmann Area	Cluster Size (mm ³)	MNI x,y,z	F
NS>Smoker	Left	Limbic	Anterior Cingulate	32	31560	-6 30 26	27.9
	Left	Limbic	Posterior Cingulate	31	616	-2 -38 34	10.9
	Right	Frontal	Inferior Frontal Gyrus	13	1480	44 30 4	22.0
	Left	Frontal	Inferior Frontal Gyrus	47	2464	-46 20 -10	27.2
	Left	Frontal	Inferior Frontal Gyrus	44	1952	-48 14 12	18.9

Response Selection Trials: Brain regions where a main effect of Smoking Status on BOLD response to negative emotional distractor task trials (negative-neutral contrast).^{a,b}

Table 3

Direction	Side	Lobe	Brain Area	Brodmann Area	Cluster Size (mm ³)	MNI x,y,z	F
Smoker>NS	Right	Frontal	Middle Frontal Gyrus	10	1472	30 36 14	14.9
	Right	Parietal	Inferior Parietal Lobule	40	512	32 -44 42	14.4

^aNonsmokers (NS) as compared to Nicotine Dependent Smokers while smoking satiated (Smoker)
BOLD = Blood oxygenation level-dependent; MNI = Montreal Neurological Institute Coordinates.