

Supplemental materials

1. Methods

1.1. fMRI Stroop Task

A week to ten days prior to initiating the treatment program, all participants performed the fMRI Stroop color-word interference task as described in our previous publications (Brewer et al., 2008; Devito et al., 2012). Briefly, participants were shown a color-word (e.g., "BLUE") that was printed in either a congruent (e.g., blue) or an incongruent (e.g., green) color. Adolescents were allowed to smoke an hour prior to this fMRI session in order to reduce tobacco-abstinence effects. Although all subjects were invited to smoke prior to scanning, some may have declined due to recent smoking. Data on the time between completion of last cigarette and onset of fMRI were not systematically collected (but should be in future studies). Subjects completed two practice runs prior to scanning. During scanning, word stimuli were presented on the screen for 1300msec with a 350msec inter-trial interval with incongruent stimuli pseudo-randomly presented every 13th-16th congruent stimuli. There were seven incongruent events in each run, and participants completed a total of 6 runs with 105 stimuli (Brewer et al., 2008). Behavioral Stroop performance was assessed out-of-scanner during five runs presented immediately following scanning. A microphone recorded verbal responses as reaction times on each trial and errors on incongruent trials were manually assessed from recordings by research staff. One subject had missing behavioral data on two runs. In this version of the Stroop task, responses were not recorded while participants were in the MRI. Participants were asked to silently name the color to avoid motion associated with speech and reduce working memory load related to translating mental/verbal responses to motor responses (e.g. Brewer et al., 2008; Devito et al.,

2012; Leung, Skudlarski, Gatenby, Peterson, & Gore, 2000; Worhunsky et al., 2013).

This version of the Stroop has been found to show similar patterns of brain activations as have other cognitive control tasks that involve in-scanner responses (e.g. the Simon – Petersen et al., 2002).

1.2 fMRI Data acquisition and Analyses

Images were obtained with a Siemens TIM Trio 3T MRI system (Siemens AG, Erlangen, Germany) and analyzed using methods described in our previous publications [Brewer et al., 2008; Devito et al., 2012]. Localizers and functional images were collected using an echo-planar image gradient-echo pulse sequence (repetition time, TR = 1500 msec, echo time, TE = 27 msec, flip angle = 60°, field of view [FOV] = 22cm × 22cm, 64×64 matrix, 3.4mm in-plane resolution, 4mm slice thickness with 1 mm skip, 25 slices). Functional images were parallel to the plane transecting the anterior and posterior commissures, and were collected over six runs. Each run consisted of 124 volumes, including an initial rest period of 6 volumes that were removed from analyses.

Brain images were pre-processed using SPM5 (Wellcome Functional Imaging Laboratory, London, UK), normalized to the Montreal Neurological Institute template and smoothed with a 6mm kernel full-width half-maximum. First-level analysis used an event-related design modeling the onset and offset of each congruent and incongruent stimulus using robust regression (Kober et al., 2010). Trials with movement of greater than 4 mm in any direction were excluded from analyses. Motion parameters were included as additional regressors of no interest. A temporal high-pass filter of 128sec was also included to remove low-frequency signals. Changes in Stroop-related activity were assessed at a whole-brain level using t-tests comparing incongruent versus congruent trials. Both first- and second-level random effects analyses were conducted

with Neuroelf analysis package (www.neuroelf.net). A Monte-Carlo simulation was used to estimate threshold of voxel-height and cluster-size for correcting multiple comparisons with a family-wise- error (FWE) rate of 5%. Following our prior work, we used a simulations program modeled after AFNI's Alpha Sim and implemented in MATLAB, producing whole-brain family-wise- error correction (Kober et al., 2010; Landi et al., 2011; Montoya et al., 2012; Balodis et al., 2012). We used a connectivity radius of 1.5 voxels – whereby clusters are considered connected if they touch by 1 full voxel or edge, but not if they are merely connected by vertex. This is a common default, which is often considered conservative. We also used the FWHM of our own data smoothing, as is customary. In sum, we report a base map threshold of two-tailed $p < .05$ ($p < .025$ at each tail) and an added cluster of 280 to create a combined whole-brain family-wise-error correction at $p < .05$.

2. Results

Baseline cigarette use measures correlated with pre-treatment fMRI Stroop measures (Supplemental Table 1 and Supplemental Figure 3). Specifically, levels of smoking (mean cigarettes/day) correlated with activations in multiple regions including the insula (Supplemental Table 1 and Supplemental Figure 3). There were no significant correlations between baseline cotinine levels and Stroop activity.

Supplemental Table 1.

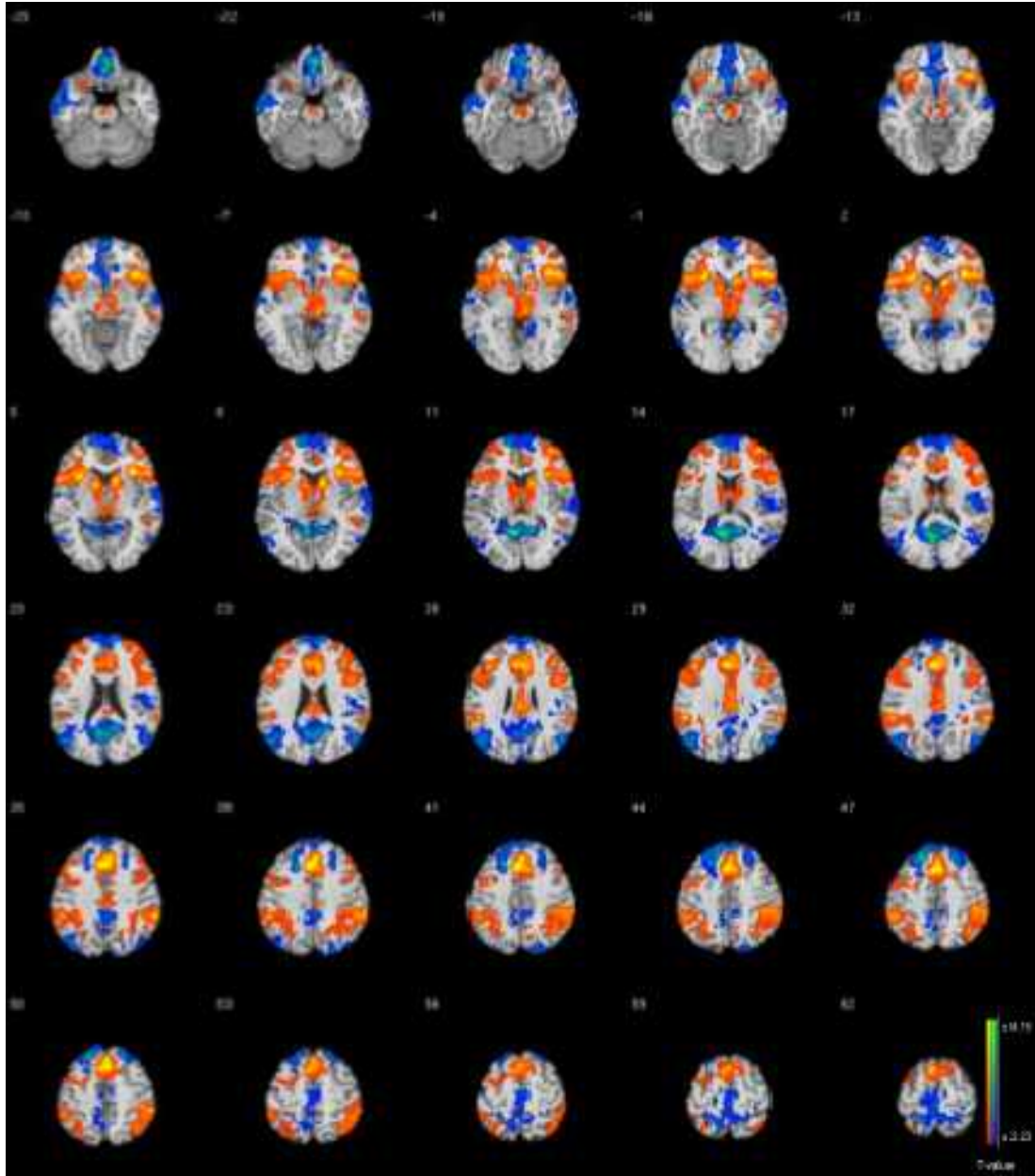
Stroop main effect correlations with reported mean cigarettes per day at baseline

Stroop Main Effect Contrast	Structure	BA	Left/Right	MNI Coordinates			k	Peak R-value
				x	y	z		
Incongruent > Congruent	Superior Temporal Gyrus	13	R	48	-42	15	406	-0.97

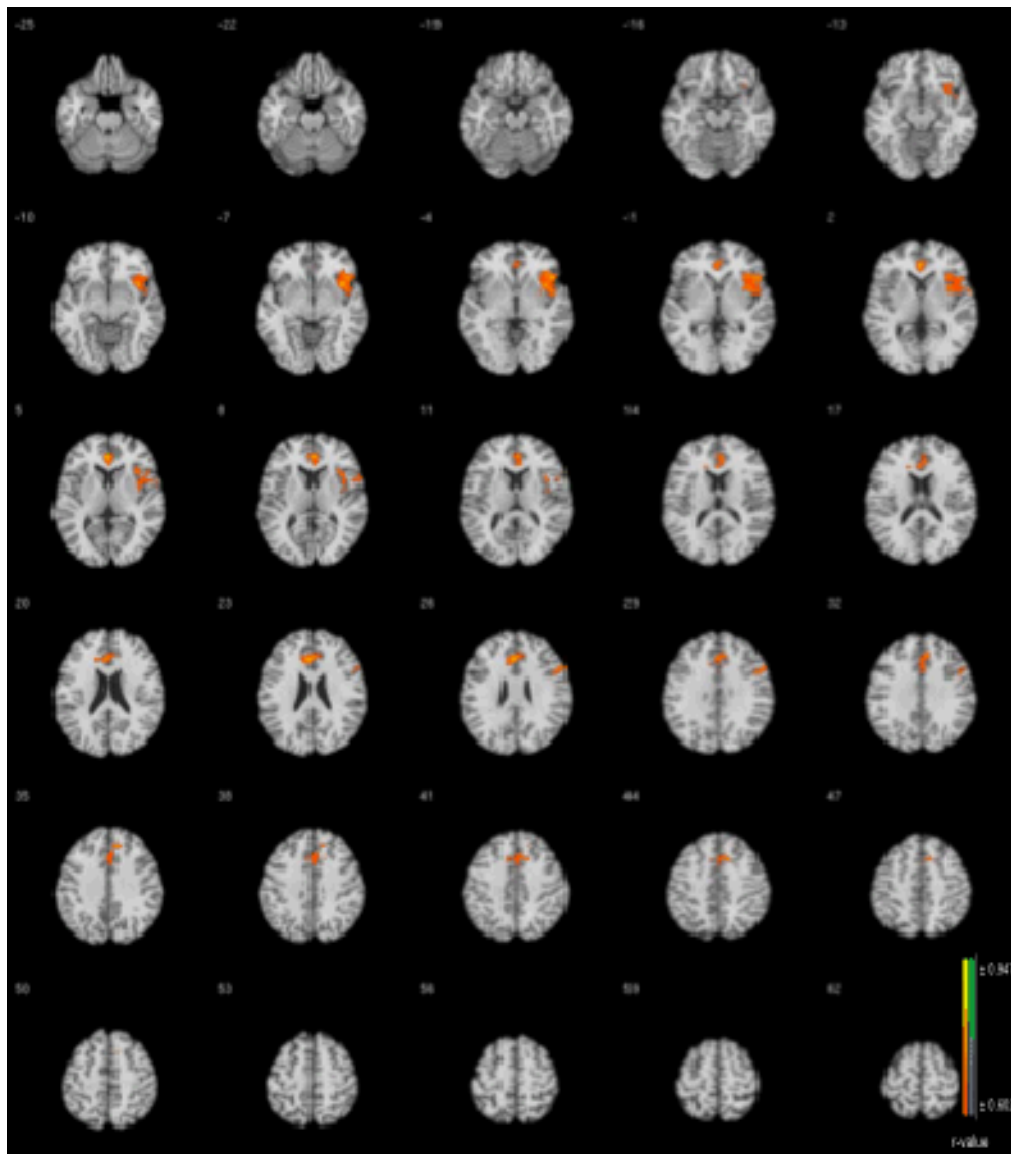
BA = Brodman's Area

ROI = Region of Interest

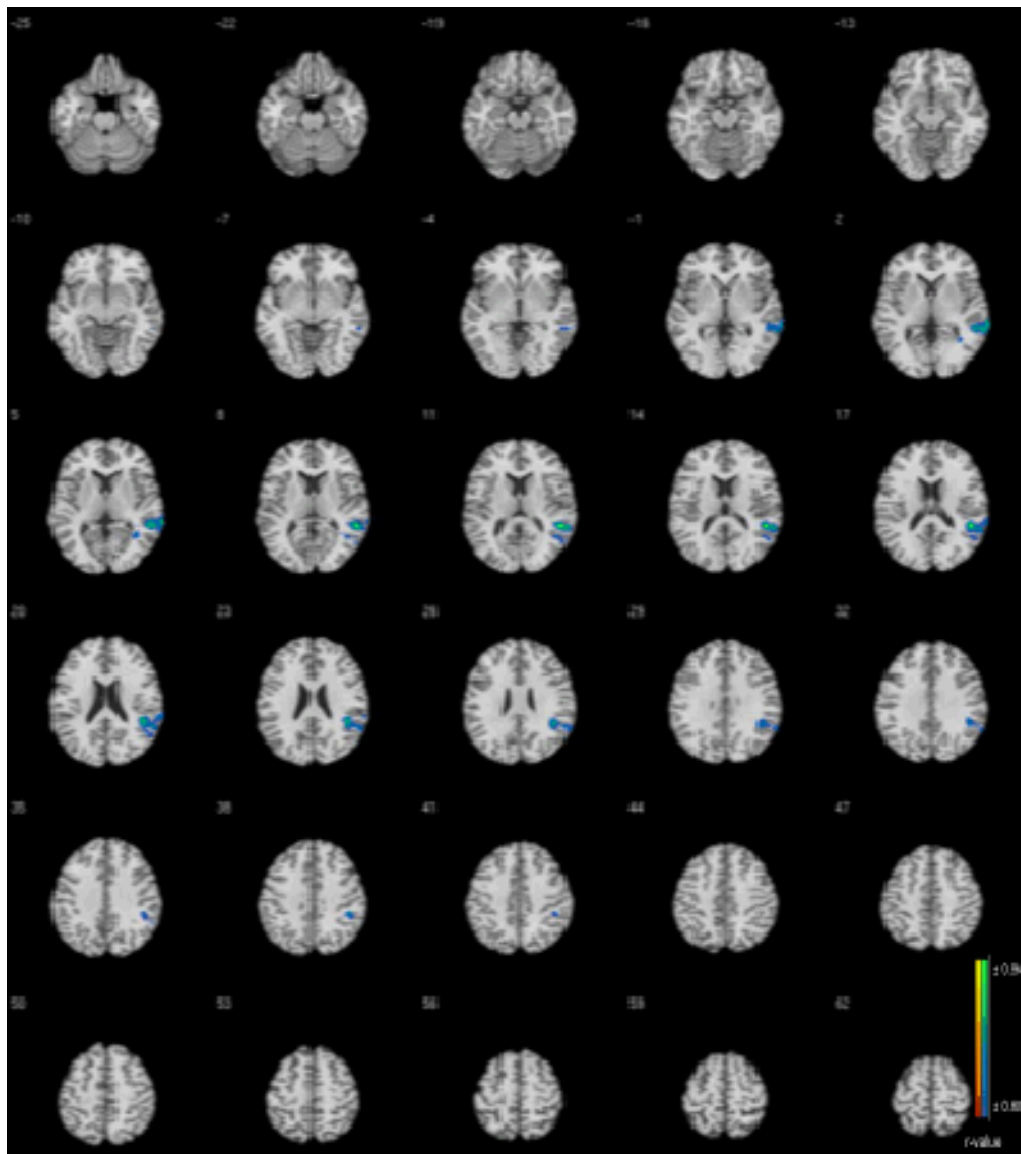
k = cluster size in voxels



Supplemental Figure 1. Main Effect of Stroop Task Performance. Change in fMRI BOLD signal on Stroop-effect, contrasting incongruent trials with congruent trials in $N=11$ adolescent participants. The contrast map is thresholded at an uncorrected level of $p < 0.05$ two-tailed and FWE-corrected at $p < 0.05$ with a cluster threshold of 280. Blue color demonstrates areas of significant differences between incongruent and congruent conditions where relatively less activity occurs in the incongruent condition. Red color indicates areas of relative greater activity during the incongruent condition. The right side of the brain is on the right. Maps begin at $z=-25$ and increase in steps of 3 to $z=62$.



Supplemental Figure 2. Regional Brain Activation During Stroop Task Performance and Correlations with Percent Change in Cotinine Levels. Change in fMRI BOLD signal on Stroop-effect, contrasting incongruent trials with congruent trials, correlated with percent change in cotinine levels in $N=11$ adolescent participants. The contrast map is thresholded at an uncorrected level of $p < 0.05$ two-tailed and FWE-corrected at $p < 0.05$ with a cluster threshold of 280. Orange/yellow indicates areas of positive correlations and blue indicates areas of negative correlations between % change in cotinine levels and % BOLD signal changes in the incongruent versus congruent contrast. The right side of the brain is on the right. Maps begin at $z=25$ and increase in steps of 3 to $z=62$. BOLD = blood-oxygenation-level-dependent; FWE = family-wise error.



Supplemental Figure 3. Correlations between reported baseline mean cigarettes/day and Stroop performance.

Correlational maps demonstrate relationship between mean number of daily cigarettes reported by participants ($n=11$) during incongruent trials contrasted with congruent trials on the Stroop task. All contrast maps are thresholded at an uncorrected level of $p < 0.05$ two-tailed and FWE-corrected at $p < 0.05$ with a cluster threshold of 280. Blue color demonstrates areas with negative correlations and red color indicates areas with positive correlations. The right side of the brain is on the right. Axial correlational maps on the left begin at $z=-25$ and increase in steps of 3 to $z=62$.

References for supplemental section

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