

Common Prefrontal Regions Activate During Self-Control of Craving, Emotion, and Motor Impulses in Smokers

Clinical Psychological Science
2014, Vol. 2(5) 611–619
© The Author(s) 2014
Reprints and permissions:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/2167702614522037
cpx.sagepub.com


**Golnaz Tabibnia^{1,2}, J. David Creswell¹, Thomas E. Kraynak³,
Cecilia Westbrook⁴, Erica Julson⁵, and Hilary A. Tindle³**

¹Department of Social and Decision Sciences, Carnegie Mellon University; ²Department of Psychology and Social Behavior, University of California, Irvine; ³University of Pittsburgh; ⁴Department of Psychology and School of Medicine and Public Health, University of Wisconsin, Madison; and ⁵School of Kinesiology and Nutritional Science, California State University, Los Angeles

Abstract

It has been posited that self-regulation of behaviors, emotions, and temptations may rely on a common resource. Recent reviews have suggested that this common resource may include the inferior frontal cortex. However, to our knowledge, no single functional neuroimaging study has investigated this hypothesis. We obtained functional MRI scans of 25 abstinent, treatment-seeking cigarette smokers as they completed motor, affective, and craving self-control tasks before smoking-cessation treatment. We identified two regions in the left inferior frontal cortex and a region in the presupplementary motor area that were commonly activated in all three tasks. Furthermore, psychophysiological-interaction analyses suggested that the inferior frontal cortex may involve dissociable pathways in each self-control domain. Specifically, the inferior frontal cortex showed negative functional connectivity with large portions of the thalamus and precentral gyrus during motor stopping, with the insula and other portions of the thalamus during craving regulation, and, potentially, with a small limbic region during emotion regulation. We discuss implications for understanding self-control mechanisms.

Keywords

smoking, self-control, inhibitory control, emotion regulation, craving, fMRI

Received 5/31/13; Revision accepted 12/23/13

Successful inhibitory control, or self-control, is key to recovery from addiction, including cigarette smoking. According to Shiffman and colleagues' situational model of relapse (Shiffman, 2005; Shiffman, Paty, Gnys, Kassel, & Hickcox, 1996), the potential for relapse is high across a number of everyday life situations (an argument; sensory cues, such as the smell of cigarette smoke; or the offer of a cigarette) that trigger cognitive, affective, and motor impulses that can lead people to smoke. Behavioral training designed to teach smokers to successfully navigate these high-risk situations has been the cornerstone of smoking-cessation programs for decades. Yet the vast majority of quit attempts end in relapse within 1 year (Hughes, Keely, & Naud, 2004), largely because of failure of self-control. Thus, an improved understanding of the mechanisms underlying self-control is urgently needed to improve the care of not only more than 40 million U.S.

adults who currently smoke cigarettes (Centers for Disease Control and Prevention, 2012) but also those individuals who suffer from other conditions, including substance use and overeating, that involve impairment of self-control.

It has been suggested that self-control of behaviors, emotions, and temptations relies on a common domain-general resource (Muraven & Baumeister, 2000). This resource is theorized to include regions of the prefrontal cortex, particularly the inferior frontal cortex (IFC), a region that has been implicated in different types of

Corresponding Author:

Golnaz Tabibnia, Department of Psychology and Social Behavior, University of California, Irvine, 5300 Social and Behavioral Sciences Gateway, Irvine, CA 92697-7050
E-mail: tabibnia@uci.edu

self-control (Berkman, Burklund, & Lieberman, 2009; Cohen & Lieberman, 2009; Tabibnia et al., 2011). For example, the IFC is activated during motor inhibitory control, such as in the stop-signal task (Aron & Poldrack, 2006; Leung & Cai, 2007); during cognitive inhibition, such as in the color-word Stroop task (Leung, Skudlarski, Gatenby, Peterson, & Gore, 2000) and in thought suppression (Mitchell et al., 2007); during emotion regulation (Kim & Hamann, 2007; Ochsner et al., 2004; Wager, Davidson, Hughes, Lindquist, & Ochsner, 2008); and during regulation of craving for food and cigarettes (Hartwell et al., 2011; Kober et al., 2010). Although these are distinct regulatory processes (Gross, 2002), they share a common feature, namely, that of inhibiting a dominant response. Despite the broad-ranging evidence that self-control in different psychological domains activates the IFC, to our knowledge, no single functional neuroimaging study has investigated whether the IFC may be a common regulatory region across motor, affective, and craving self-control tasks in the same group of individuals. This is an important gap, given that everyday situations call for successful regulation across multiple domains.

Although different self-control tasks may recruit the IFC, the downstream regions potentially regulated by the IFC could be distinct. The self-control pathway that has been most extensively studied is that of motor inhibitory control. With the help of the presupplementary motor area (preSMA) and the subthalamic nucleus, the IFC is thought to enable motor stopping by causing inhibition of the globus pallidus, the thalamus, and, ultimately, the primary motor cortex (Aron, 2011). In contrast, emotion regulation may involve IFC inhibition of amygdala and subcortical emotion-processing regions (Ochsner & Gross, 2005), and regulation of craving may involve an IFC-striatum inhibitory control circuit (Heatherington & Wagner, 2011; Kober et al., 2010). To investigate the extent of overlap in the mechanisms underlying different types of self-control, in the current study, we first tested for common activation of the IFC in different self-control tasks and then examined whether IFC inhibitory control functional connectivity might change depending on the nature of the task (motor, emotion, or craving self-control).

To examine self-regulation in a real-world domain, we tested these hypotheses in a sample of daily smokers who were motivated to quit. Specifically, abstinent smokers underwent functional (f)MRI as they completed the stop-signal task, a task involving cognitive reappraisal of distress, and a task involving cognitive reappraisal of cigarette craving. Neural response in the IFC, preSMA, and subthalamic nucleus were measured in each task, and a conjunction analysis was performed to identify overlapping regions. We hypothesized that the IFC would be commonly activated across these three self-control tasks and that the downstream pathways of the IFC would be at least partially distinct in each task.

Method and Materials

Participants

Twenty-five right-handed adult smokers were recruited as part of the Healthier Brains in Treating Smoking study (principal investigator H. A. Tindle), using flier, radio, and newspaper advertisements. Table 1 lists participant details. Exclusion criteria included pregnancy and concurrent substance use, as verified by urinalysis, as well as medication that could affect the nervous system, history of brain injury, cognitive impairment (such as dementia), and any untreated psychiatric illness.¹

Stop-signal task

Motor inhibitory control was assessed using the stop-signal task (Aron & Poldrack, 2006; Logan, Schachar, & Tannock, 1997). Before undergoing scanning, participants completed a practice block of 64 trials (16 stop trials). The scan-period task consisted of 128 trials (32 stop trials). Each trial began with a blank screen for a jittered duration (0–2,500 ms, distributed exponentially), followed by an empty circle (500 ms), and then followed by a left- or right-pointing arrow inside the circle (2,000 ms). Participants were instructed to respond as quickly as possible with a left or a right key press but to stop pressing if the arrow was followed by a “stop-signal” tone (25% of trials). This signal was presented at a variable delay (the stop-signal delay) once the arrow had appeared. After a successful stop trial, the stop-signal delay was increased by 50 ms; after an unsuccessful stop trial, it was decreased by 50 ms and eventually titrated to a stop-signal delay resulting in a 50% successful inhibition rate. All participants reached a 44% to 56% successful inhibition rate.

Reappraisal tasks

Craving and emotion regulation were assessed using a modified version of the emotion-reappraisal task (Ochsner, Bunge, Gross, & Gabrieli, 2002). The experimental conditions of interest were look and reappraise (reinterpret). A third condition, mindfully attend, was also included (see Westbrook et al., 2011, for a discussion). Each trial began with a 2-s instruction screen (“Look,” “Re-Interpret,” or “Mindfully Attend”), followed by a fixation cross of jittered duration (0–2,500 ms, distributed exponentially), and then followed by a picture for 8 s. Using a data glove (Psychology Software Tools, Pittsburgh, PA), participants then had 4 s to rate their craving and 4 s to rate their negative emotion, on scales from 1 (*weak craving or weakly negative*) to 5 (*strong craving or strongly negative*), before viewing a fixation cross for 2 s (rest).

There were three types of pictures (distressing, smoking, and neutral; see Westbrook et al., 2011, and the

Table 1. Participant Characteristics

Characteristic	Mean	Percentage
Age	42 (12.64)	
Sex		
Female		52
Male		48
Race		
African American		76
Caucasian		24
Annual income		
< \$20,000		52
\$20,000–\$50,000		20
\$50,000–\$75,000		24
> \$75,000		4
Beck Depression Inventory II		
Score	5.52 (4.47)	
Scored \leq 13		88
Smoking status		
Nicotine dependence (FTND)	4.80 (2.04)	
Cigarettes per day	17.83 (6.51)	
Years of smoking	24.96 (11.70)	
Baseline carbon monoxide level (parts per million)	14.56 (7.73)	

Note: Standard deviations are shown in parentheses. FTND = Fagerström Test for Nicotine Dependence.

Methods: Pictures in the Reappraisal Tasks section in the SOM-U in the Supplemental Material available online.) The neutral pictures were always preceded by the instruction “Look”; the smoking and distressing pictures were preceded by one of three instructions (“Look,” “Re-Interpret,” or “Mindfully Attend”). On look trials, participants were instructed to passively view the picture. On reinterpret trials, they were instructed to reappraise the picture in a neutral manner to make it less distressing or less craving inducing; for example, they could consider a distressing picture to be a scene from a movie or consider a cigarette to be fake or a toy cigarette. The task was presented via E-Prime 2.0 Professional (Psychology Software Tools, Pittsburgh, PA).

Imaging

Scans were performed at the Brain Imaging Research Center jointly established by Carnegie Mellon University and the University of Pittsburgh. Image acquisition and preprocessing procedures are described in the fMRI Methods section in the SOM-R in the Supplemental Material.

For each participant, each condition (e.g., reappraise smoking) was modeled as an event convolved with the canonical hemodynamic response function. The rest period after instruction was modeled as an explicit baseline, and rests between trials were left unmodeled.

Planned comparisons between conditions of interest were computed in SPM8 as linear contrasts. The single-participant results were then combined into a random-effects group analysis. To identify activations that overlap in the three self-control tasks, we conducted a three-way conjunction analysis with the following whole-brain contrasts: stop success > go success, reappraise distressing > look distressing, and reappraise smoking > look smoking. Active voxels were those exhibiting above-threshold activation in all three contrasts when tested against the conjunction null hypothesis (Nichols, Brett, Andersson, Wager, & Poline, 2005).

To test the neural pathways by which the IFC may exert self-control in different domains, we conducted analyses of psychophysiological interaction (PPI; Friston et al., 1997) using the SPM PPI toolbox. For each participant, volumes of interest were extracted from the two IFC clusters identified in the conjunction analysis and used as seeds in single-participant whole-brain PPI analyses. These single-participant results were combined into group-level *t* tests to identify regions exhibiting more negative connectivity with the seed region during the self-control condition (stop success, reappraise distressing, and reappraise smoking) compared with the control condition (go success, look distressing, and look smoking, respectively). The fMRI Methods section in the SOM-R in the Supplemental Material describes the regions of interest and thresholding procedures.

Results

Self-reported ratings

As expected, viewing smoking cues increased craving and viewing distressing cues increased distress relative to viewing neutral cues. Smoking cues marginally increased distress, but distressing cues did not increase craving relative to neutral cues. As expected, reappraisal of smoking cues and distressing cues reduced the craving and distress, respectively. Reappraisal of smoking cues did not affect distress, and reappraisal of distressing cues did not affect craving (see Fig. S1 in the SOM-R in the Supplemental Material).

Overlap of activation

Each self-control task activated areas previously reported in studies of the stop-signal task (Aron & Poldrack, 2006; Leung & Cai, 2007), emotion regulation (Kim & Hamann, 2007; Ochsner et al., 2004; Wager et al., 2008), and craving regulation (Kober et al., 2010), respectively. As depicted in Figure 1, the three tasks elicited similar patterns of activation.

To identify the overlap in activation among the three self-control tasks, we conducted an inclusive three-way conjunction analysis with the three main contrasts, namely, stop success > go success, reappraise smoking > look smoking, and reappraise distressing > look distressing.

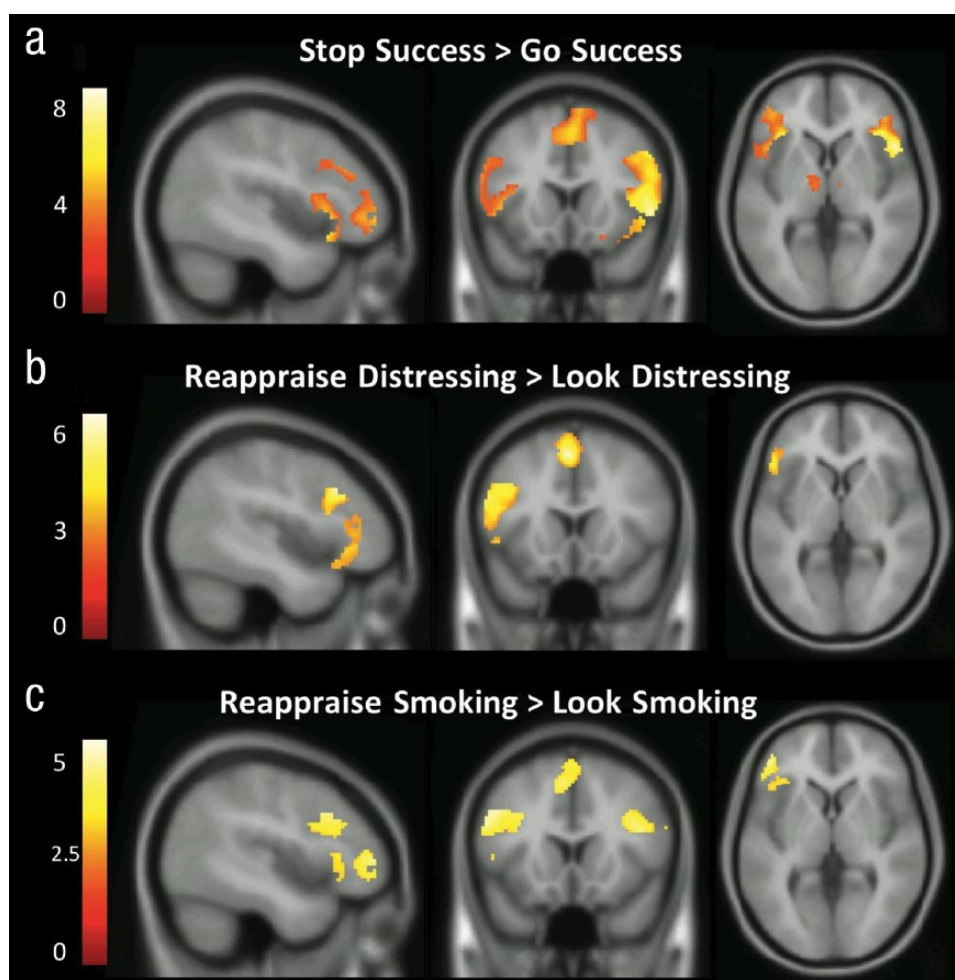


Fig. 1. Activation during each of the three tasks, after small-volume correction for anatomically defined regions of interest. During the stop success > go success task (a), activation is seen in the right and left inferior frontal cortex (IFC), the presupplementary motor area (preSMA), and the thalamus. During the reappraise distressing > look distressing task (b), activation is seen in the left IFC and the preSMA. During the reappraise smoking > look smoking task (c), activation is seen in the right and left IFC and the preSMA. Cluster coordinates and statistics are listed in Tables U1–U3 in the SOM-U in the Supplemental Material. Sagittal ($x = -44$), coronal ($y = 16$), and horizontal ($z = 2$) cross-sections are thresholded at $p < .001$, uncorrected.

The conjunction analysis identified three clusters: one centered at the left IFC pars triangularis (IFCtri) and middle frontal gyrus, one centered at the left IFC pars orbitalis (IFCorb), and one centered at the preSMA (see Fig. U1 in the SOM-U in the Supplemental Material). A whole-brain conjunction analysis also identified only these three clusters as overlapping among the three tasks.

PPI: Functional connectivity

To identify neural regions that were functionally connected with the two IFC regions identified in the conjunction analysis, we conducted two separate sets of PPI analyses: one using the IFCorb cluster as a seed and the other using the IFCtri cluster as a seed.

As listed in Table S1 in the SOM-R in the Supplemental Material, the IFCorb showed greater negative functional connectivity during stop success than during go success with a number of regions, including the left ventrolateral thalamus and bilateral precentral gyrus. In other words, when the IFCorb was more active, these regions were concomitantly less active, which is consistent with the possibility of inhibition by the IFC. During reappraise smoking relative to look smoking, there was greater negative functional connectivity of the IFCorb with the right anterior insula, left middle insula, and ventral anterior thalamus, among other regions. During reappraise distressing relative to look distressing, there was greater negative functional connectivity of the IFCorb with only two small clusters: the left amygdala and left ventral caudate/subcallosal gyrus. These connectivity results were specific to each regulatory task; a conjunction analysis of these three negative PPI analyses indicated no overlapping regions.

As listed in Table S2 in the SOM-R in the Supplemental Material, the IFCtri showed greater negative functional connectivity with a number of regions, including the bilateral precentral gyrus, bilateral thalamus, and left globus pallidus, during stop success compared with go success. No regions showed greater negative functional connectivity with the IFCtri during reappraise smoking compared with look smoking. During reappraise distressing relative to look distressing, only the posterior thalamus showed greater negative functional connectivity with the IFCtri. A conjunction analysis of these three negative PPI analyses indicated no overlapping regions (for positive PPI results, see Tables U4 and U5 in the SOM-U in the Supplemental Material).

Discussion

This study identifies two regions in the left IFC and a region in the preSMA that were activated in smokers during performance of self-control tasks across motor, affective, and craving domains. The three regions were the

only clusters that were commonly activated across all three tasks. These results are consistent with meta-analytic reports that have shown that regulation of motor, affective, and craving impulses involve a common neural network in addiction (Li & Sinha, 2008). Our findings extend prior work by demonstrating this commonality in the same people across multiple tasks, which suggests that the IFC may be a common domain-general region for the regulation of emotion, craving, and motor impulses. Our results also provide a functional neural basis for the previous finding that greater IFC gray-matter intensity is associated with better motor inhibitory control and emotion regulation (Tabibnia et al., 2011). The additional observations that methamphetamine-dependent individuals exhibit deficits in these self-control tasks and in IFC gray-matter intensity, and that lower IFC gray-matter is associated with increased drug craving (Tabibnia et al., 2011), further highlight the importance of this region in substance dependence.

We also found that the IFC involves nonoverlapping pathways of regulation during different forms of self-control. Specifically, the IFC showed negative functional connectivity with large portions of the thalamus and precentral gyrus during motor stopping, with the insula and other portions of the thalamus during craving regulation, and, potentially, with a small limbic region, including the amygdala and subcallosal gyrus, during regulation of distress.

Previous studies have demonstrated overlap of prefrontal activation during individual nonaffective self-control tasks. For example, several studies have reported common activation of the IFC between motor inhibitory control and suppression of distracting information in the flanker task (Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002; Wager et al., 2005) or set shifting in the Wisconsin Card Sorting Task (Konishi et al., 1999). Ochsner, Hughes, Robertson, Cooper, and Gabrieli (2009) found overlap of activation in the IFC and the preSMA during suppression of semantic versus affective information in modified flanker tasks. The affective flanker task did not involve emotion regulation but, rather, suppression of a response to one affective stimulus in favor of another affective stimulus.

Our finding that the two IFC clusters were activated during self-control is consistent with prior reports. Activation has been shown in the IFCorb and the IFCtri in both hemispheres during motor stopping (Aron & Poldrack, 2006; Chikazoe, Konishi, Asari, Jimura, & Miyashita, 2007; Leung & Cai, 2007; Rubia et al., 2001) and during regulation of negative emotional response (Kim & Hamann, 2007; Lieberman et al., 2007; Ochsner et al., 2002; Ochsner et al., 2004). The left IFCorb and the IFC pars opercularis were activated during a craving-regulation technique that involved thinking about the long-term consequences of smoking (Kober et al., 2010).

Similarly, in a test of behavioral self-control involving a smoking apparatus in the fMRI environment, abstinent smokers who refrained from inhaling the available smoke activated the IFCorb and the IFCTri (Monterosso et al., 2009).

In the current study, we explored the regulatory pathways from the IFC with PPI analyses. Results of these analyses suggest that the IFCorb, rather than the IFCTri, could be primarily driving the regulation of downstream cortical and subcortical regions during self-control across tasks. Our finding that IFCorb activity is more negatively correlated with activity in the thalamus and precentral gyrus during stop success than during go success is consistent with the proposed pathway of motor inhibition from the IFC to the primary motor cortex (Aron, 2011; Chambers, Garavan, & Bellgrove, 2009). Consistent with our PPI results in reappraise distressing > look distressing, results from previous studies have demonstrated an inverse relationship between the IFCorb and amygdala activity during regulation of negative emotions (Lieberman et al., 2007; Wager et al., 2008). Although, to our knowledge, no previous study has demonstrated an inverse relationship between the IFC and insula activity during craving regulation, the insula would be a plausible target for downregulation, given its critical role in craving, including cigarette craving (Craig, 2009; Naqvi, Rudrauf, Damasio, & Bechara, 2007).

Brain regions other than the IFC undoubtedly play an important role in self-control as well. For example, the preSMA and the dorsomedial prefrontal cortex in general have been implicated in self-control across myriad neuroimaging and lesion studies (Nachev, Kennard, & Husain, 2008). In the current study, the preSMA was identified, along with the IFC, as a common region for different types of self-control. Although the precise functional role of this region in self-control is still unclear, some researchers have suggested that the preSMA may generate the control signal, whereas the IFC implements it (Aron, 2011).

Although craving induction often increases negative affect and distressing cues often increase craving, that is not always the case (e.g., Shiffman et al., 2013). Given the generally low levels of cue-elicited craving and distress reported by our participants and other researchers (Shiffman et al., 2013), it is possible that more evocative or personalized cues would be more effective in eliciting affective and motivational states. Our findings that reappraising distressing cues does not reduce craving and reappraising craving cues does not reduce distress may seem to contradict the domain-general model of self-control, which predicts that any kind of reappraisal will activate the common self-control network and, therefore, have some “spillover” effect of incidentally reducing other affective/motivational states as well (Berkman et al., 2009; Verbruggen, Adams, & Chambers,

2012). However, it is plausible that reappraisal spills over only if there is at least a moderate level of craving or distress (i.e., if a strong need for reappraisal exists). Considering the low levels of craving and distress evoked by our stimuli, we may not have been able to detect this process if it occurred.

Limitations

One limitation of the current study is that it lacked a condition in which participants engaged in reappraisal after presentation of neutral stimuli. Without this control, it is difficult to determine whether the self-control processes attenuated general levels of craving/distress or cue-specific levels. Nonetheless, our current results are consistent with the notion that reappraisal of evocative cues does not reduce general levels of craving and distress. If reappraisal were reducing general levels of craving and distress, reappraisal of distressing cues should have reduced craving and reappraisal of smoking cues should have reduced distress. However, we did not observe these effects.

Reporting a relationship between brain activation and behavioral indices of self-control would bolster the claim that a neural substrate of self-control has been identified. However, with a sample size of 25, our study was underpowered to detect small or moderate brain-behavior correlations. In addition, the current results could be strengthened by using machine-learning techniques to assess patterns of activity rather than overlap in activity based on traditional univariate analyses.

Implications and conclusions

The finding that common regions of the IFC are involved in different kinds of self-control supports the popular (albeit understudied) common-resource account of self-control (Muraven & Baumeister, 2000). When this common resource breaks down, there may be consequences across multiple domains, thereby offering one possible reason for the observed comorbidity of substance use and disorders of mood and anxiety (Lasser et al., 2000). Tasks included in the current study are highly relevant to real-life domains in which treatment-seeking smokers desire more self-control, including regulation of craving and inhibition of motor behavior. One important question raised by this work is whether the observed effects indicate a common resource for smokers specifically or whether they generalize to other clinical populations (e.g., dieters) and healthy populations in self-regulatory contexts.

Psychotherapies that attempt to enhance patients' self-regulation skills, such as cognitive behavioral therapy and interpersonal psychotherapy, do alter function in prefrontal cortex regions that include the IFC (Frewen,

Dozois, & Lanius, 2008). In the current study, we assessed participants at baseline only; in future studies, researchers will need to investigate whether these laboratory measures of control (and the common IFC resource) predict future ability to resist temptations to smoke, successfully quit smoking, and achieve other clinical outcomes (Berkman & Falk, 2013). In fact, structural and functional integrity in the IFC could be neural markers or endophenotypes for disorders of self-control, which potentially would allow for more accurate methods of diagnosis (Bearden & Freimer, 2006) and better predictors of treatment outcome (Berkman, Falk, & Lieberman, 2011).

Another question raised by the current findings is whether engaging in self-control training in one domain (e.g., regulation of craving) can facilitate successful self-control in another domain (e.g., regulation of negative affect) in smokers. For example, the improvement of motor inhibitory control with practice can reduce risky financial decisions (Verbruggen et al., 2012) and reduce emotion-related brain activation (Berkman et al., 2009). Whether such training and “cross”-domain application can be achieved with smokers is a topic for future study.

Tobacco use is the leading cause of preventable disease and death in the United States (Centers for Disease Control and Prevention, 2012), accounting for approximately one fourth of the deaths among U.S. adults. Given that failure to regulate negative affect and cigarette craving are major barriers to long-term abstinence (Shiffman & Waters, 2004), understanding the neural underpinnings of self-control may offer insights to identifying individuals who are likely to experience more difficulty quitting and may help inform future cessation interventions.

Author Contributions

HAT designed the original study and supervised the overall program, with GT, JDC, and CW contributing to study design. GT, JDC, CW, EJ, and HAT created the experimental materials and contributed to data collection. All authors contributed to data analysis and data review. GT drafted the manuscript with the help of JDC, TEK, CW, and HAT.

Acknowledgments

The authors would like to acknowledge Judd Brewer, Edythe London, James Bursley, Fadel Zeidan, the Pittsburgh Brain Imaging Research Center and the Pittsburgh Mind Body Center, Jill Delaney, and Courtney Watson for support, assistance, and advice at various stages of this project.

Declaration of Conflicting Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

Funding

Support for this work was provided by the Pittsburgh Foundation Charles and Nancy Emmerling Fund, the National Center for

Research Resources (NCRR), National Institutes of Health (NIH) Training Grant KL2 000146, NIH Roadmap for Medical Research Grant KL2 RR024154-05, a grant from the Pittsburgh Mind Body Center, and the Pennsylvania Department of Health's Commonwealth Universal Research Enhancement Program to H. A. Tindle; Mind and Life Institute Varela Awards to H. A. Tindle and C. Westbrook; the Pittsburgh Life Sciences Greenhouse Opportunity Fund to G. Tabibnia and J. D. Creswell; and a National Institute of Mental Health award (part of Grant T32 MH17140) to G. Tabibnia. The content of this article does not necessarily represent the views of the NCRR or NIH.

Supplemental Material

Additional supporting information may be found at <http://cpx.sagepub.com/content/by/supplemental-data>

Note

1. This study was approved by the internal review boards at the University of Pittsburgh and Carnegie Mellon University and was conducted in accordance with the World Medical Association Declaration of Helsinki. All participants smoked at least 10 cigarettes a day and reported a strong desire to quit and a willingness to participate in smoking-cessation classes. Scanning was conducted prior to treatment and after participants abstained from smoking for 12 hr. Abstinence was validated using a carbon monoxide monitor (Bedfont, Rochester, England). Participants also performed a urine screen for cocaine, THC, methamphetamine, and opioids. Those who tested positive for any substance were rescheduled; three failures resulted in removal from the study.

References

- Aron, A. R. (2011). From reactive to proactive and selective control: Developing a richer model for stopping inappropriate responses. *Biological Psychiatry*, *69*(12), e55–e68.
- Aron, A. R., & Poldrack, R. A. (2006). Cortical and subcortical contributions to stop signal response inhibition: Role of the subthalamic nucleus. *Journal of Neuroscience*, *26*, 2424–2433.
- Bearden, C. E., & Freimer, N. B. (2006). Endophenotypes for psychiatric disorders: Ready for primetime? *Trends in Genetics*, *22*, 306–313.
- Berkman, E. T., Burklund, L., & Lieberman, M. D. (2009). Inhibitory spillover: Intentional motor inhibition produces incidental limbic inhibition via right inferior frontal cortex. *NeuroImage*, *47*, 705–712.
- Berkman, E. T., & Falk, E. B. (2013). Beyond brain mapping: Using neural measures to predict real-world outcomes. *Current Directions in Psychological Science*, *22*, 45–50.
- Berkman, E. T., Falk, E. B., & Lieberman, M. D. (2011). In the trenches of real-world self-control: Neural correlates of breaking the link between craving and smoking. *Psychological Science*, *22*, 498–506.
- Bunge, S. A., Dudukovic, N. M., Thomason, M. E., Vaidya, C. J., & Gabrieli, J. D. (2002). Immature frontal lobe contributions to cognitive control in children: Evidence from fMRI. *Neuron*, *33*, 301–311.
- Centers for Disease Control and Prevention. (2012). *Tobacco use: Targeting the nation's leading killer, at a glance*

2011. Retrieved from <http://www.cdc.gov/chronicdisease/resources/publications/aag/osh.htm>
- Chambers, C. D., Garavan, H., & Bellgrove, M. A. (2009). Insights into the neural basis of response inhibition from cognitive and clinical neuroscience. *Neuroscience & Biobehavioral Reviews*, *33*, 631–646.
- Chikazoe, J., Konishi, S., Asari, T., Jimura, K., & Miyashita, Y. (2007). Activation of right inferior frontal gyrus during response inhibition across response modalities. *Journal of Cognitive Neuroscience*, *19*, 69–80.
- Cohen, J. R., & Lieberman, M. D. (2009). The common neural basis of exerting self-control in multiple domains. In R. Hassin, K. Ochsner, & Y. Trope (Eds.), *Self control in society, mind, and brain* (pp. 141–162). Oxford, England: Oxford University Press.
- Craig, A. D. (2009). How do you feel now? The anterior insula and human awareness. *Nature Reviews Neuroscience*, *10*, 59–70.
- Frewen, P. A., Dozois, D. J. A., & Lanius, R. A. (2008). Neuroimaging studies of psychological interventions for mood and anxiety disorders: Empirical and methodological review. *Clinical Psychology Review*, *28*, 228–246.
- Friston, K. J., Buechel, C., Fink, G. R., Morris, J., Rolls, E., & Dolan, R. J. (1997). Psychophysiological and modulatory interactions in neuroimaging. *NeuroImage*, *6*, 218–229.
- Gross, J. J. (2002). Emotion regulation: Affective, cognitive, and social consequences. *Psychophysiology*, *39*, 281–291.
- Hartwell, K. J., Johnson, K. A., Li, X., Myrick, H., LeMatty, T., George, M. S., & Brady, K. T. (2011). Neural correlates of craving and resisting craving for tobacco in nicotine dependent smokers. *Addiction Biology*, *16*, 654–666.
- Heatheron, T. F., & Wagner, D. D. (2011). Cognitive neuroscience of self-regulation failure. *Trends in Cognitive Sciences*, *15*, 132–139.
- Hughes, J. R., Keely, J., & Naud, S. (2004). Shape of the relapse curve and long-term abstinence among untreated smokers. *Addiction*, *99*, 29–38.
- Kim, S. H., & Hamann, S. (2007). Neural correlates of positive and negative emotion regulation. *Journal of Cognitive Neuroscience*, *19*, 776–798.
- Kober, H., Mende-Siedlecki, P., Kross, E. F., Weber, J., Mischel, W., Hart, C. L., & Ochsner, K. N. (2010). Prefrontal-striatal pathway underlies cognitive regulation of craving. *Proceedings of the National Academy of Sciences, USA*, *107*, 14811–14816.
- Konishi, S., Nakajima, K., Uchida, I., Kikyo, H., Kameyama, M., & Miyashita, Y. (1999). Common inhibitory mechanism in human inferior prefrontal cortex revealed by event-related functional MRI. *Brain*, *122*, 981–991.
- Lasser, K., Boyd, J., Woolhandler, S., Himmelstein, D. U., McCormick, D., & Bor, D. H. (2000). Smoking and mental illness: A population-based prevalence study. *JAMA: The Journal of the American Medical Association*, *284*, 2606–2610.
- Leung, H. C., & Cai, W. (2007). Common and differential ventrolateral prefrontal activity during inhibition of hand and eye movements. *Journal of Neuroscience*, *27*, 9893–9900.
- Leung, H. C., Skudlarski, P., Gatenby, J. C., Peterson, B. S., & Gore, J. C. (2000). An event-related functional MRI study of the Stroop color word interference task. *Cerebral Cortex*, *10*, 552–560.
- Li, C. S., & Sinha, R. (2008). Inhibitory control and emotional stress regulation: Neuroimaging evidence for frontal-limbic dysfunction in psycho-stimulant addiction. *Neuroscience & Biobehavioral Reviews*, *32*, 581–597.
- Lieberman, M. D., Eisenberger, N. I., Crockett, M. J., Tom, S. M., Pfeifer, J. H., & Way, B. M. (2007). Putting feelings into words: Affect labeling disrupts amygdala activity in response to affective stimuli. *Psychological Science*, *18*, 421–428.
- Logan, G. D., Schachar, R. J., & Tannock, R. (1997). Impulsivity and inhibitory control. *Psychological Science*, *8*, 60–64.
- Mitchell, J. P., Heatheron, T. F., Kelley, W. M., Wyland, C. L., Wegner, D. M., & Neil Macrae, C. (2007). Separating sustained from transient aspects of cognitive control during thought suppression. *Psychological Science*, *18*, 292–297.
- Monterosso, J. R., Mann, T., Ward, A., Ainslie, G., Bramen, J., Brody, A. L., & London, E. D. (2009). Neural recruitment during self-control of smoking: A pilot fMRI study. In D. Ross, H. Kincaid, D. Spurrett, & P. Collins (Eds.), *What is addiction?* (pp. 269–290). Cambridge, MA: MIT Press.
- Muraven, M., & Baumeister, R. F. (2000). Self-regulation and depletion of limited resources: Does self-control resemble a muscle? *Psychological Bulletin*, *126*, 247–259.
- Nachev, P., Kennard, C., & Husain, M. (2008). Functional role of the supplementary and pre-supplementary motor areas. *Nature Reviews Neuroscience*, *9*, 856–869.
- Naqvi, N. H., Rudrauf, D., Damasio, H., & Bechara, A. (2007). Damage to the insula disrupts addiction to cigarette smoking. *Science*, *315*, 531–534.
- Nichols, T., Brett, M., Andersson, J., Wager, T., & Poline, J. B. (2005). Valid conjunction inference with the minimum statistic. *NeuroImage*, *25*, 653–660.
- Ochsner, K. N., Bunge, S. A., Gross, J. J., & Gabrieli, J. D. (2002). Rethinking feelings: An fMRI study of the cognitive regulation of emotion. *Journal of Cognitive Neuroscience*, *14*, 1215–1229.
- Ochsner, K. N., & Gross, J. J. (2005). The cognitive control of emotion. *Trends in Cognitive Sciences*, *9*, 242–249.
- Ochsner, K. N., Hughes, B., Robertson, E. R., Cooper, J. C., & Gabrieli, J. D. (2009). Neural systems supporting the control of affective and cognitive conflicts. *Journal of Cognitive Neuroscience*, *21*, 1842–1855.
- Ochsner, K. N., Ray, R. D., Cooper, J. C., Robertson, E. R., Chopra, S., Gabrieli, J. D., & Gross, J. J. (2004). For better or for worse: Neural systems supporting the cognitive down- and up-regulation of negative emotion. *NeuroImage*, *23*, 483–499.
- Rubia, K., Russell, T., Overmeyer, S., Brammer, M. J., Bullmore, E. T., Sharma, T., . . . Taylor, E. (2001). Mapping motor inhibition: Conjunctive brain activations across different versions of go/no-go and stop tasks. *NeuroImage*, *13*, 250–261.
- Shiffman, S. (2005). Dynamic influences on smoking relapse process. *Journal of Personality*, *73*, 1715–1748.

- Shiffman, S., Dunbar, M., Kirchner, T., Li, X., Tindle, H., Anderson, S., & Scholl, S. (2013). Smoker reactivity to cues: Effects on craving and on smoking behavior. *J Abnorm Psychol*, *122*(1), 264–280.
- Shiffman, S., Paty, J. A., Gnys, M., Kassel, J. A., & Hickcox, M. (1996). First lapses to smoking: Within-subjects analysis of real-time reports. *Journal of Consulting and Clinical Psychology*, *64*, 366–379.
- Shiffman, S., & Waters, A. J. (2004). Negative affect and smoking lapses: A prospective analysis. *Journal of Consulting and Clinical Psychology*, *72*, 192–201.
- Tabibnia, G., Monterosso, J. R., Baicy, K., Aron, A. R., Poldrack, R. A., Chakrapani, S., . . . London, E. D. (2011). Different forms of self-control share a neurocognitive substrate. *Journal of Neuroscience*, *31*, 4805–4810.
- Verbruggen, F., Adams, R., & Chambers, C. D. (2012). Proactive motor control reduces monetary risk taking in gambling. *Psychological Science*, *23*, 805–815.
- Wager, T. D., Davidson, M. L., Hughes, B. L., Lindquist, M. A., & Ochsner, K. N. (2008). Prefrontal-subcortical pathways mediating successful emotion regulation. *Neuron*, *59*, 1037–1050.
- Wager, T. D., Sylvester, C. Y., Lacey, S. C., Nee, D. E., Franklin, M., & Jonides, J. (2005). Common and unique components of response inhibition revealed by fMRI. *NeuroImage*, *27*, 323–340.
- Westbrook, C., Creswell, J. D., Tabibnia, G., Julson, E., Kober, H., & Tindle, H. A. (2011). Mindful attention reduces neural and self-reported cue-induced craving in smokers. *Social Cognitive and Affective Neuroscience*, *8*, 73–84.