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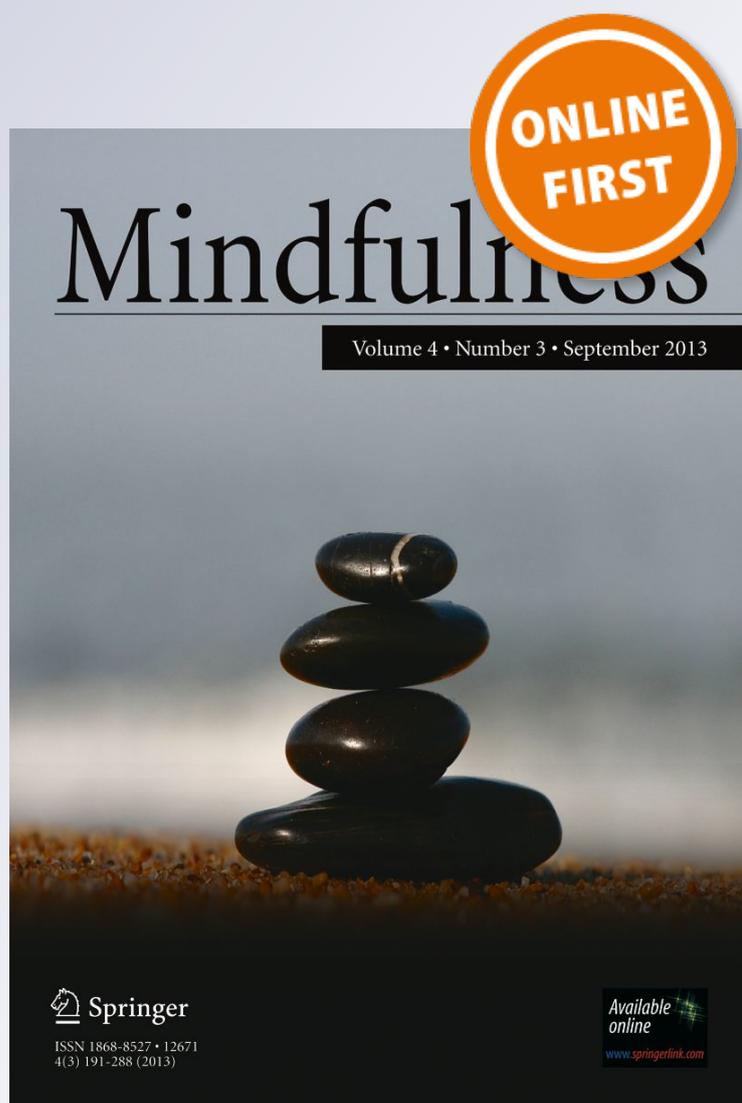
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The Effect of Brief Mindfulness Training on Brain Reactivity to Food Cues During Nicotine Withdrawal: A Pilot Functional Imaging Study

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Abstract

Objectives Many individuals who smoke relapse due to weight gain. Mindfulness training has been shown to help smokers quit smoking and, in other populations, has been used to help people lose weight. This study was designed to assess the effect of 1 week of mindfulness practice on food cravings in smokers during 12-hour smoking abstinence.

Methods We assessed daily smokers with a history of smoking lapse after weight gain. Participants were provided with brief training in mindfulness meditation and mindful eating and were asked to practice each skill daily for 1 week. Before and after this week of mindfulness practice, participants completed surveys to rate their nicotine dependence and food cravings and underwent testing via functional magnetic resonance imaging.

Results Study results included pre–post intervention reduction in brain activity in dorsomedial prefrontal cortex, visual areas, and premotor areas, regions potentially associated with response to food images.

Conclusions The study was small; however, it suggests the possibility that mindfulness training might be used to decrease food cravings after smoking cessation.

Keywords Mindfulness · Functional magnetic resonance imaging · Weight · Food cravings · Smoking cessation

An estimated 15% of Americans smoke cigarettes (Jamal 2016). Although tobacco use is the leading cause of preventable morbidity and mortality in the USA, smoking is notoriously difficult to treat (Fiore 2008). For those who are able to quit, weight gain is common and predicts relapse (Aubin et al. 2012; Borrelli et al. 2001; Mukhopadhyay and Wendel 2011). People who quit smoking gain an average of 5–10 pounds; however, one-third of all smokers gain over 20

pounds (Aubin et al. 2012; Eisenberg and Quinn 2006; O'Hara et al. 1998; Pistelli et al. 2016; Williamson et al. 1991). Some studies suggest that a key mechanism of post-quit weight gain is increased caloric consumption due to hedonic eating, or eating for pleasure (Epel et al. 2011; Filozof et al. 2004). Nicotine has been shown to suppress appetite via activation of pro-opiomelanocortin neurons in the hypothalamus (Mineur et al. 2011). Thus far, studies have not yet identified pharmacologic or cognitive behavioral smoking cessation treatments that are effective at attenuating post-quit weight gain (Farley et al. 2012; Filozof et al. 2004; Spring et al. 2009).

A new approach worth investigating is the use of mindfulness training, which has been found to be an effective therapy for smoking cessation (Davis et al. 2013; 2014a, b) and also for treating binge eating disorders (Kristeller and Hallett 1999; Spring et al. 2009). Mindfulness training has demonstrated effects in the medial cortex, insula, amygdala, lateral frontal regions, and basal ganglia with postulated impacts on automatic thinking and emotion regulation (Marchand 2014). One study of 19 subjects assessed a 7-week manualized program on mindful acceptance of eating

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and found significant reduction in food cravings and numeric but non-significant difference in weight change compared with controls (Alberts et al. 2010). Thus, it seems possible that mindfulness training could be an effective therapy for post-quit weight gain by reducing food cravings. This pilot study was designed to assess the effect of a brief mindfulness training on food craving in daily smokers during 12-hour abstinence, as measured by functional magnetic resonance imaging (fMRI) of neural activity during exposure to visual food cues. To our knowledge, mindfulness training has never been studied for its effect on food craving during the post-quit period.

Method

Participants

Participants ($N = 5$) were recruited from a metropolitan area. Inclusion criteria included age of at least 18 years, smoking at least 10 cigarettes per day, a history of prior smoking lapse caused by weight gain, and a body mass index between 19 and 35. Exclusion criteria included use of other tobacco products, use of smoking cessation medication, chance of pregnancy, and medical contraindications to fMRI.

Procedures

The study was designed to assess the impact in smokers of 1 week of mindfulness practice on food craving and brain reactivity to images of food during 12-hour smoking abstinence. Primary outcome was a change in blood oxygen level-dependent activation assessed through functional magnetic resonance imaging in response to food images relative to scrambled images, before and after the week of mindfulness practice.

All participants received 1 hour of training in mindfulness meditation and mindful eating provided by a senior mindfulness instructor. Participants were then asked to practice meditation for 30 min per day and mindful eating once per day for 1 week. Aside from mindfulness practice, participants were instructed to eat and smoke as usual for the week. Practice compliance was recorded daily through phone-based assessments.

Measures

Nicotine dependence and food cravings were assessed as traits at baseline through the following commonly used standardized scales: six-item Fagerstrom Test for Nicotine Dependence (FTND) (Pomerleau et al. 1994) and 15-item Food Cravings Questionnaire-Trait Reduced (FCQ-TR) to assess for correlation between nicotine dependence and food

craving (Meule et al. 2014). Stress and mindfulness were measured using the 10-item Perceived Stress Scale (PSS) (Cohen et al. 1994) and 39-item Five Facet Mindfulness Questionnaire (FFMQ) (Baer et al. 2008) before and after the intervention to assess impact of mindfulness training on stress and mindfulness. All measures used in this study were self-report measures. Likert-type scales were used in FCQ-TR, PSS, and FFMQ.

Imaging Procedures

Participants were scanned using a GE MR 75- 3.0 Tesla scanner using sense-spiral sequence with a 24 cm field of view, 34 4 mm slices, TR = 1.5 s. An anatomic scan preceded functional imaging. Participants were asked to refrain from smoking and eating for 12 hours prior to fMRI on each of the two testing days; this was confirmed by carbon monoxide (CO) breath test with CO < 7 ppm considered smoking abstinence (Deveci et al. 2004). Pre- and post-intervention fMRIs recorded an anatomical scan for pre-processing and neural reactivity during visual presentation of food images categorized by nutritional content (high or low fat; high or low protein, carbohydrate, sugar) and control images, with all images scrambled and matched (Fig. 1). The imaging protocol utilized a block design with four runs and eight blocks per run. Each block contained images randomized from one category of nutritional content or control images. Each run included six blocks of food images (six images per set for 3.5 to 7 seconds each with variable inter-stimulus interval) and two blocks of control images comprised of non-food images matched for light. Blocks were followed by a 20-second pause for craving rating. During the post-intervention fMRI, participants were asked to practice mindfulness during the image exposure tasks.

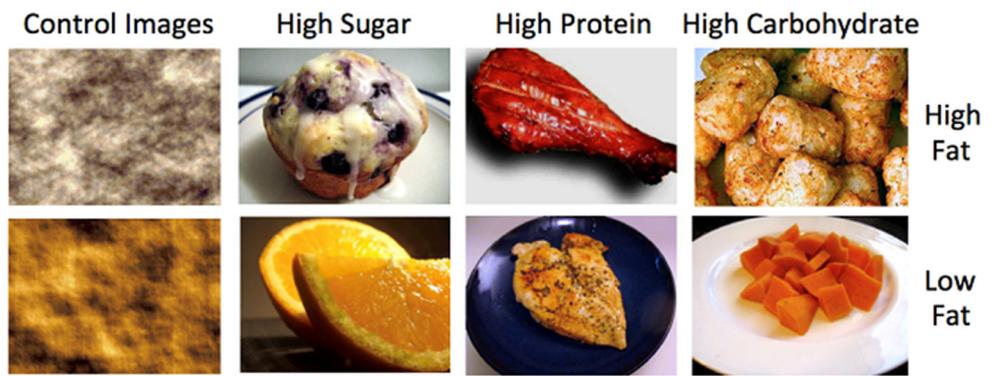
Data Analyses

Standard preprocessing was performed in FMRIB Software Library (FSL), a comprehensive library of imaging analysis tools. First-level models created contrasts for all food images vs. control images within each subject; second-level models combined data across runs. Group models comparing pre- with post-intervention changes in reactivity for food vs. control images were evaluated across the whole brain using paired sample t tests within an FSL fixed effects model. Cluster-correction across the whole brain search volume was used to control for multiple comparisons. Thresholding for significant voxels was defined as $Z = 3.1$, with cluster correction of $P < 0.05$.

Results

The study sample was daily smokers, 40% women, 60% African American, mean pack years = 17.1. All participants reported

Fig. 1 Control images and food images as categorized by nutrient content



practicing mindfulness for at least 30 min per day for 1 week. There were no significant pre- to post-intervention changes on the Perceived Stress Scale and Five Facet Mindfulness

Questionnaire. FTND scores were correlated with FCQ-TR at baseline ($R = 0.8, P < 0.05$). Functional imaging data showed significant pre-post intervention reduction on brain activity in the

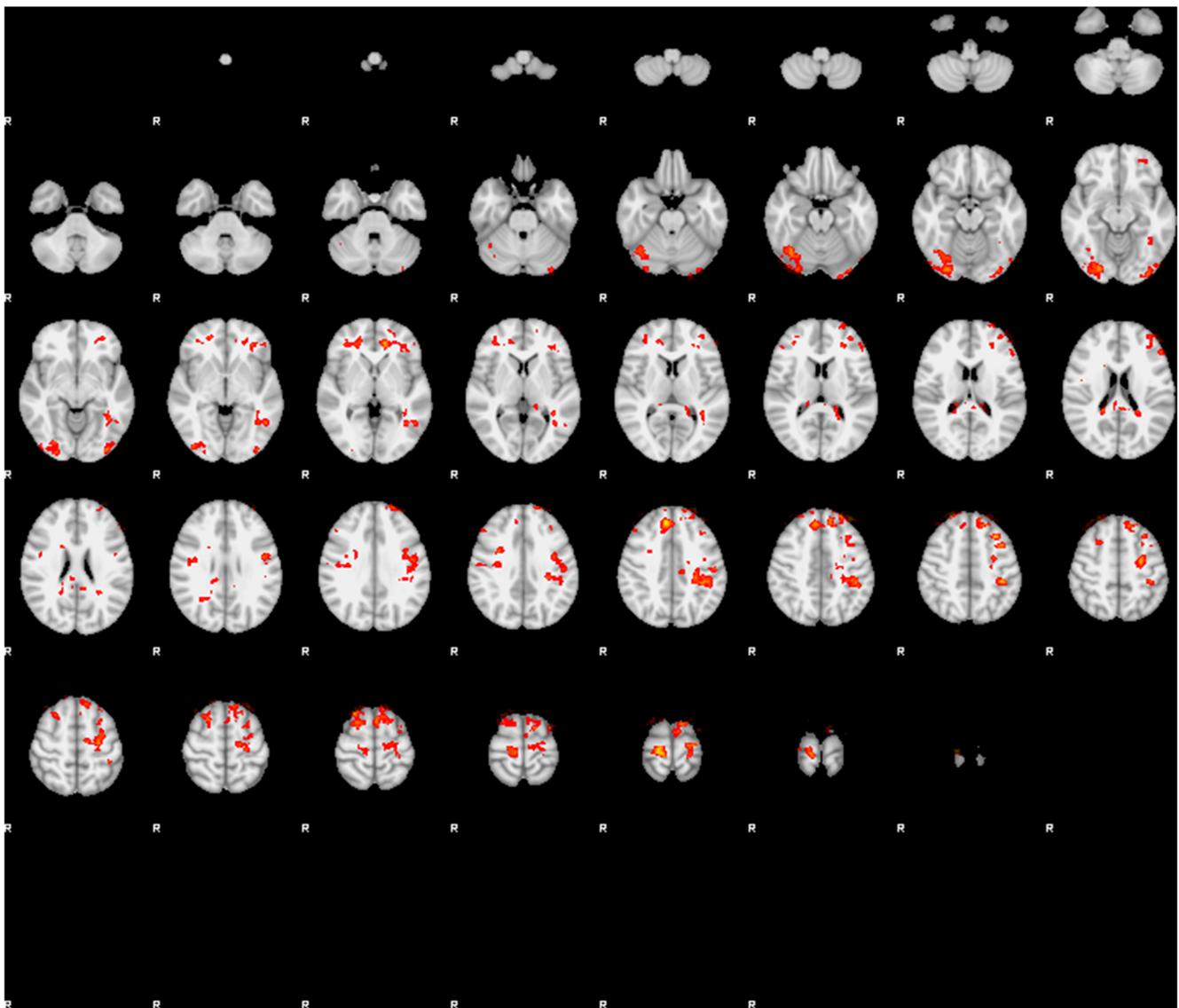


Fig. 2 Pre-post mindfulness training comparison of all food images vs. control images across the whole-brain, thresholded at $Z-3.1$, cluster correction of $P < .05$.

Table 1 Anatomical structures corresponding with coordinates of significantly decreased activity

Region	Coordinates			Voxels	Z-Max
	x	y	z		
Right occipital fusiform gyrus	24	− 84	− 14	288	4.58
Left post-central gyrus/superior parietal lobule	− 38	− 34	48	205	5.06
Right precentral gyrus	18	− 26	80	162	5.93
Right dorsomedial prefrontal cortex	26	22	66	126	4.72
Left dorsomedial prefrontal cortex	− 12	34	52	111	4.09
Left premotor cortex	− 26	− 10	52	101	4.75
Right superior frontal gyrus/paracingulate gyrus	8	38	40	99	5.57

dorsomedial prefrontal cortex, visual areas, and premotor cortex for food greater than control (Fig. 2 and Table 1). In all regions, there was a large estimated effect size with *Z* scores greater than 4 (Table 1).

Discussion

Major findings in this study included an association between nicotine dependence and food craving during 12-hour smoking abstinence and significant pre–post intervention reduction on brain activity in specific areas of the brain in response to food cues, including left and right dorsomedial prefrontal cortex (dMPFC), visual areas, and premotor cortex. These changes could be attributed to downregulation of sensory processing of food images due to mindfulness practice. For example, the reduction in dMPFC activity could be a result of mindfulness decreasing internal negotiation or implementation of willpower to manage cravings, and the reduction in visual areas could be attributed to reduced cue salience as a result of mindfulness training. Our findings suggest that mindfulness training may impact brain activity related to food cues during the post-quit smoking period.

Limitations and Future Research

This study is small and did not provide a control group. The small sample size reduces power to demonstrate significant results, and the fixed effects analysis limits generalizability beyond the current sample. The lack of a control group means that changes observed could be the result of repetition of fMRI tasks rather than self-regulation. In order to determine the actual effect of mindfulness training on post-quit weight gain, further research is required, including a larger comparative trial with outcomes that include weight changes and longer smoking abstinence.

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Author Contributions EK designed the study, conducted recruitment, ran participants through all components of the study, collected data, and drafted the manuscript. MS oversaw imaging design, analyzed imaging data, wrote results, and compiled tables and figures. JD obtained funding for the study, supervised all components of the study, provided mindfulness training to participants, and co-wrote and edited the manuscript. All authors approved the final version of the manuscript for submission.

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Compliance with Ethical Standards

Ethical approval This study was approved by the Duke University Institutional Review Board (PRO00079233).

Informed Consent Informed consent was obtained from all individual participants in the study.

Conflict of Interest EK has received no research grant funding, no significant honorarium funding, and declares no conflict of interest. MS has received research grant funding from NIH and Brain and Behavior Research. MS received no significant honorarium funding and declares no conflict of interest. JD has received research grant funding from Pfizer Inc. and Axsome Therapeutics Inc. JD has received no significant honorarium funding and declares no conflict of interest.

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