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Short communication

Young adult smokers' neural response to graphic cigarette warning labels

Adam E. Green [a,1], Darren Mays [b,*,1], Emily B. Falk [c], Donna Vallone [d,e,f], Natalie Gallagher [a], Amanda Richardson [g], Kenneth P. Tercyak [b], David B. Abrams [b,d,e], Raymond S. Niaura [b,d,e]

[a] Department of Psychology, Georgetown University, Washington, DC, USA
[b] Georgetown University Medical Center, Lombardi Comprehensive Cancer Center, Washington, DC, USA
[c] Annenberg School for Communication, University of Pennsylvania, Philadelphia, PA, USA
[d] Truth Initiative, Washington, DC, USA
[e] Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA
[f] Global Institute of Public Health, New York University, New York, NY
[g] University of North Carolina Gillings School of Public Health, Chapel Hill, NC, USA

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A B S T R A C T

Introduction: The study examined young adult smokers' neural response to graphic warning labels (GWLs) on cigarette packs using functional magnetic resonance imaging (fMRI).
Methods: Nineteen young adult smokers (*M* age 22.9, 52.6% male, 68.4% non-white, *M* 4.3 cigarettes/day) completed pre-scan, self-report measures of demographics, cigarette smoking behavior, and nicotine dependence, and an fMRI scanning session. During the scanning session participants viewed cigarette pack images (total 64 stimuli, viewed 4 s each) that varied based on the warning label (graphic or visually occluded control) and pack branding (branded or plain packaging) in an event-related experimental design. Participants reported motivation to quit (MTQ) in response to each image using a push-button control. Whole-brain blood oxygenation level-dependent (BOLD) functional images were acquired during the task.
Results: GWLs produced significantly greater self-reported MTQ than control warnings ($p < .001$). Imaging data indicate stronger neural activation in response to GWLs than the control warnings at a cluster-corrected threshold $p < .001$ in medial prefrontal cortex, amygdala, medial temporal lobe, and occipital cortex. There were no significant differences in response to warnings on branded versus plain cigarette packages.
Conclusions: In this sample of young adult smokers, GWLs promoted neural activation in brain regions involved in cognitive and affective decision-making and memory formation and the effects of GWLs did not differ on branded or plain cigarette packaging. These findings complement other recent neuroimaging GWL studies conducted with older adult smokers and with adolescents by demonstrating similar patterns of neural activation in response to GWLs among young adult smokers.

1. Introduction

Graphic warning labels (GWLs) for cigarette packs have been implemented in more than 65 countries (Sanders-Jackson, Song, Hiilamo, & Glantz, 2013) based on evidence that they are more effective than text-only warnings for reducing smoking (Noar et al., 2015). Research can continue to inform GWL implementation in at least two important ways. Studies investigating optimal approaches to designing GWL messages can inform changes to GWLs to ensure sustained effectiveness. In contexts such as the U.S. where law requires GWLs (U.S. Congress, 2009) but lawsuits have delayed their implementation, research addressing concerns raised by the courts can support implementation (Kraemer & Baig, 2013).

Studies investigating GWLs have relied largely on self-report methods, demonstrating that GWLs generate stronger cognitive and emotional responses, are better recalled, and produce stronger motivation to quit smoking than text-only warnings (Azagba & Sharaf, 2013; Borland, Wilson, Fong, et al., 2009; Emery, Romer, Sheerin, Jamieson, & Peters, 2014; Hammond, Fong, McNeill, Borland, & Cummings, 2006; Nonnemaker, Choiniere, Farrelly, Kamyab, & Davis, 2015; Peters, Romer, Slovic, et al., 2007). However, self-report measures of such constructs do not fully predict future behavior, and biobehavioral methods may help better understand GWL impact (Armitage, Norman, Alganem, & Conner, 2015; Falk, Berkman, Whalen, & Lieberman, 2011; Webb & Sheeran, 2006).

Functional magnetic resonance imaging (fMRI) can ascertain information on smokers' responses to GWLs that is not readily captured by self-report (Falk, 2010). fMRI-measured neural activity in brain regions

* Corresponding author at: Department of Oncology, Georgetown University Medical Center, Lombardi Comprehensive Cancer Center, 3300 Whitehaven Street, NW, Suite 4100, Washington, DC 20007, USA.
E-mail address: Darren.Mays@georgetown.edu (D. Mays).
[1] A.E. Green and D. Mays contributed equally to this work.

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involved in emotional (i.e., amygdala) and cognitive (i.e., medial prefrontal cortex) processing of antismoking messages predicts cessation outcomes, explaining ≥20% additional variance in cessation behavior than self-report responses to messages (Chua, Ho, Jasinska, et al., 2011; Falk, Berkman, Mann, Harrison, & Lieberman, 2010; Falk et al., 2011; Jasinska et al., 2012; Wang, Ruparel, Loughead, et al., 2013). Two studies also showed that GWLs produce activation in brain regions involved with emotion, cognition, and memory formation among current smokers (Newman-Norlund, Thrasher, Fridriksson, et al., 2014; Wang, Lowen, Romer, Giorno, & Langleben, 2015). Other research links frontoinsular neural activity to craving reduction in response to GWLs (Do & Galvan, 2015) and demonstrates that neural responses in similar brain systems implicated in motivation, cognition, and memory are associated with population-level success of GWL-type messages for promoting cessation (Falk, O'Donnell, Tompson, et al., 2016).

This study extends this research by investigating young adult smokers' neural responses to GWLs and assessing whether effects differ by branded or plain cigarette packaging. Studies of neural responses to GWLs have been conducted with older adult smokers (Newman-Norlund et al., 2014; Wang et al., 2015) and adolescents (Do & Galvan, 2015). However, young adults are a priority for tobacco control due to high rates of smoking experimentation, frequent transitions to regular smoking, and the high prevalence of smoking in this group (Do & Galvan, 2015; Falk et al., 2016). Plain packaging is hypothesized to draw greater attention to and increase the effects of GWLs by eliminating tobacco industry branding, but this has not yet been tested using a neuroimaging paradigm. Examining young adult smokers' neural response to GWLs on branded and plain packaging can extend the evidence surrounding potential mechanisms of GWL action and inform future research and policy.

2. Methods

2.1. Participants and procedures

Participants were recruited through online and community-based advertisements and screened for eligibility. Eligible participants were ages 18 to 30 years, current smokers defined using validated epidemiologic measures and criteria as smoking ≥100 lifetime cigarettes and now smoking cigarettes all or some days (Agaku, King, Husten, et al., 2014). Participants also reported Camel, Marlboro, or Newport as their preferred cigarette brand. The latter criterion was imposed to tailor experimental stimuli to smokers' preferred brand, described below. All participants also met fMRI safety requirements (Kanal, Borgstede, Barkovich, et al., 2002). Eligible participants were scheduled for an in-person appointment to provide informed consent and complete a pre-scan, self-report assessment and fMRI scanning session. Prior to the appointment, participants were instructed to smoke as they normally would that day. All participants provided written informed consent, and all procedures were approved by an institutional review board.

2.2. Pre-scan measures

Pre-scan measures included demographics, cigarette smoking behaviors (Agaku et al., 2014), nicotine dependence (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991), and motivation to quit smoking (Mays, Niaura, et al., 2015; Mays, Turner, et al., 2015).

2.3. Experimental design

The study employed a two (graphic warning or control) by two (branded or plain cigarette pack) within-subjects design. Stimuli were adapted from a prior experiment (Mays, Niaura, et al., 2015; Mays, Turner, et al., 2015). GWLs tested were four of the warnings proposed for use in the U.S. by the Food and Drug Administration (FDA) communicating the smoking-associated risks of lung disease, cancer, stroke/heart attack, and mortality. These four warnings have been effective at eliciting cognitive and emotional responses in prior studies with young adults (Cameron, Pepper, & Brewer, 2015; Hammond, Reid, Driezen, & Boudreau, 2013). Similar to another recent study (Wang et al., 2015), control warnings included the same warning text as GWLs but were composed of geometric shapes overlayed on the GWLs to produce a similar appearance while visually occluding graphic content.

GWLs and control warnings were displayed on cigarette pack images sized to the dimensions of a standard cigarette pack. The pack brand (Camel, Marlboro, or Newport) was tailored to smokers' preferred brand to account for brand preferences within the design (Bansal-Travers, Hammond, Smith, & Cummings, 2011). Branded packs were created using pack images available from an online database at the time of the study (Tobacco Labelling Resource Centre, n.d.). Plain packs displayed the brand name in standard font and were brown in color and stripped of all branding (Mays, Niaura, et al., 2015; Mays, Turner, et al., 2015). Stimuli were presented in randomized order such that the same warning did not appear consecutively and there were no more than two consecutive repeats from the same condition. Example GWL and control warnings are shown in Fig. 1; complete stimuli including pack images are available from the corresponding author.

Participants viewed each pack image in the scanner for 4 s. During the scan participants used a push-button control to report how much each image motivated them to quit smoking, with response options from (1) Not At All to (4) A Lot (Mays, Niaura, et al., 2015; Mays, Turner, et al., 2015).

2.4. Imaging data acquisition

Functional data were acquired in an event-related paradigm performed using a 3-T Allegra System (Siemens, Erlangen, Germany) to collect whole-brain T2*-weighted blood oxygenation level dependent (BOLD) functional images (asymmetric spin-echo echo-planar sequence; whole-brain repetition time, TR = 2000 ms; echo time = 25 ms; field of view = 256 mm; flip angle = 80°; matrix = 64×64; axial slices 4 mm thick). Sequential whole-brain volumes (32 contiguous slices) were collected during one event-related functional run. Sixty-four task trials were presented in total, lasting 4 s each with “jitter” interleaved between trials across a range from 250 to 4250 ms. The scanning run began with an unanalyzed fixation period equal to 3 TRs, which allowed the scanner to reach steady state.

2.5. Statistical analyses

fMRI data processing was carried out using FEAT (fMRI Expert Analysis Tool) Version 5.98, part of FSL (FMRIB's Software Library) (FSL, n.d.). General Linear Model-based analysis in FEAT uses FSL tools including Brain Extraction Tool (BET) (Smith, 2002), an affine registration tool, FMRIB's Linear Image Registration Tool (FLIRT) (Jenkinson, Bannister, Brady, & Smith, 2002; Jenkinson & Smith, 2001), and a motion-correction tool based on FLIRT (MCFLIRT) (Jenkinson et al., 2002). FEAT carries out standard-space registration after time-series statistics. FSL time-series statistics correct for temporal smoothness by applying pre-whitening (Woolrich, Ripley, Brady, & Smith, 2001). The following pre-statistics processing was applied: spatial smoothing using a Gaussian kernel of FWHM 5 mm; grand-mean intensity normalization of the entire 4D dataset by a single multiplicative factor; highpass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 50.0 s). Registration to high resolution structural and, subsequently, standard space images was performed using FLIRT. At the individual subjects level, a design matrix was fitted to each subject's data as part of a general linear model with each condition modeled as events with a specified duration (i.e., the time from stimulus onset to onset of the response) convolved with a canonical hemodynamic response function. Higher-level analysis was performed using FMRIB's Local Analysis