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ORIGINAL INVESTIGATION

Alpha Oscillations in Response to Affective and Cigarette-Related Stimuli in Smokers

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ABSTRACT

Introduction: The presence of cigarette-related cues has been associated with smoking relapse. These cues are believed to activate brain mechanisms underlying emotion, attention, and memory. Electroencephalography (EEG) alpha desynchronization (i.e., reduction in alpha power) has been suggested to index the engagement of these mechanisms. Analyzing EEG alpha desynchronization in response to affective and smoking cues might improve our understanding of how smokers process these cues, and the potential impact of this processing on relapse.

Methods: Before the start of a medication-assisted cessation attempt, we recorded EEG from 179 smokers during the presentation of neutral, pleasant, unpleasant, and cigarette-related pictures. Wavelet analysis was used to extract EEG alpha oscillations (8–12 Hz) in response to these pictures. Alpha oscillations were analyzed as a function of picture valence and arousal dimensions.

Results: Emotional and cigarette-related stimuli induced a higher level of alpha desynchronization (i.e., less power in the alpha frequency band) than neutral stimuli. In addition, the level of alpha desynchronization induced by cigarette-related stimuli was similar to that induced by highly arousing stimuli (i.e., erotica and mutilations).

Conclusions: These results suggest that, for smokers, cigarette-related cues are motivationally significant stimuli that may engage emotional, attentional, and memory-related neural mechanisms at a level comparable to that seen in response to highly arousing stimuli. This finding suggests that activation of emotional, attentional, and memory-related brain mechanisms may be an important contributor to cue-induced smoking relapse.

INTRODUCTION

Notwithstanding decades of smoking-cessation campaigns, smoking remains the leading cause of preventable death in the United States (Mokdad, Marks, Stroup, & Gerberding, 2004; Schroeder & Warner, 2010). Smokers attempting to quit face very slim odds of success: more than 85% of all smoking-cessation attempts end with relapse (National Institute on Drug Abuse, 2009). Nicotine, the major addictive ingredient in tobacco (Di Chiara, 2000), exerts its addictive power by altering emotion, attention, learning, and memory mechanisms (Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Dani & De Biasi, 2001; Hyman, Malenka, & Nestler, 2006; Volkow et al., 2010). Previous research has shown that, through a conditioning process, drug-related cues become motivationally significant and can reinstate drug use even after prolonged periods of abstinence (Hyman et al., 2006; Robbins, Ersche, & Everitt, 2008; Robinson & Berridge, 2003). In addition, smokers often report the presence of cigarette-related cues as a precipitating cause of relapse (Shiffman, Paty, Gnys, Kassel, & Hickcox, 1996). Meta-analyses of human neuroimaging studies have also shown that drug-related cues reliably activate brain circuits involved in reward processing, emotion, attention, and memory to a greater extent than neutral cues (Chase, Eickhoff, Laird, & Hogarth, 2011; Engelmann et al., 2012; Kühn & Gallinat, 2011).

Although these data seem to support the idea that drug-related cues hold abnormally high motivational significance for addicts, this may not always be the case. On self-report measures, smokers consistently rate cigarette-related cues as less arousing

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than intrinsically emotional cues (Cinciripini et al., 2006; Engelmann, Gewirtz, & Cuthbert, 2011; Geier, Mucha, & Pauli, 2000). Additionally, a recent study in our laboratory found a similar effect using event-related potentials to measure brain electrical activity evoked by cigarette-related and emotional stimuli in smokers. We found that smokers had smaller late positive potentials (LPPs) to cigarette-related pictures than to highly arousing, intrinsically emotional pictures (Versace et al., in press). The LPP is usually interpreted as a measure of motivated attention (Hajcak, MacNamara, & Olvet, 2010; Lang & Bradley, 2010; Schupp, Flaisch, Stockburger, & Junghöfer, 2006), which suggests that the smokers in our study did not appear to respond to cigarette-related cues as though the cues were highly motivationally significant. This result seems to contradict the hypothesis that, as conditioned drug cues, cigarette-related cues hold excessive motivational salience for smokers to such an extent as to precipitate relapse (Robinson & Berridge, 2003; Volkow, Fowler, & Wang, 2004; Volkow et al., 2010).

One reason that the LPP may be smaller in response to cigarette-related stimuli than to intrinsically emotional stimuli is that it might not fully index the activation of all the brain mechanisms involved in generating the conditioned responses to drug-related cues. Several theoretical models emphasize that reward, motivation, attention, memory, and executive functions play a critical role in drug addiction (Hyman, 2005; Hyman et al., 2006; Robbins & Everitt, 1999; Volkow et al., 2010). Thus, to better understand how the brain mechanistically responds to drug-related cues, the information about motivational significance provided by LPP analysis should be integrated with additional information obtained using other measures of brain activity.

One useful measure is the alpha event-related desynchronization (ERD), a reduction of power in the electroencephalography (EEG) alpha frequency band following the onset of a stimulus. Alpha ERD has been proposed to reflect the activation of the "Knowledge System" (KS; Klimesch, Fellinger, & Freunberger, 2011). According to their model, accessing and retrieving information from the KS is necessary for proper perception and recognition of external stimuli. Both top-down (e.g., expectancies) and bottom-up (e.g., stimulus properties) components can influence access to the KS (Klimesch, 2011). Notably, emotional stimuli, which capture attentional resources and activate action dispositions (Lang & Bradley, 2010), induce higher levels of alpha desynchronization than neutral stimuli (De Cesarei & Codispoti, 2011; Simons, Detenber, Cuthbert, Schwartz, & Reiss, 2003). The higher level of alpha desynchronization induced by emotional stimuli may represent a neural correlate of the retrieval of motivationally significant information from the KS (Klimesch et al., 2011).

Although several studies have used EEG frequency analysis to characterize spontaneous brain oscillations following nicotine satiation or withdrawal (Domino et al., 2009; Gilbert et al., 1999; Gilbert, Meliska, Welser, & Estes, 1994; Hasenfratz & Bättig, 1993; Knott, 1988; Pickworth, Herning, & Henningfield, 1989), event-related changes in alpha oscillations induced by the presentation of cigarette-related cues have rarely been examined (Littel, Franken, & Van Strien, 2009). Therefore, the effect of cigarette-related cues on alpha ERD is unclear. To address this gap in the literature, we conducted a secondary analysis of EEG data on which we previously examined the LPP in response to cigarette-related and emotional stimuli. We quantified alpha (8–12 Hz) ERD using wavelet analysis, and proposed the following three hypotheses: (a) Similar to emotional stimuli, cigarette-related cues will induce a higher level of alpha ERD than neutral stimuli; (b) Because normative arousal levels of emotional stimuli have been shown to modulate alpha desynchronization in previous studies that did not target smokers (De Cesarei & Codispoti, 2011; Simons et al., 2003), the magnitude of alpha ERD induced by emotional stimuli will increase linearly as a function of the normative arousal levels of the stimuli used in our study of smokers; (c) Considering the role of cigarette-related cues in precipitating smoking relapse (Shiffman et al., 1996), these cues might be of significant motivational salience to smokers (Robinson & Berridge, 2003; Volkow et al., 2004, 2010), and thus be able to induce alpha ERD at a level comparable to that of other highly arousing stimuli.

METHODS

Participants

Participants from the Houston metropolitan area were recruited into the smoking-cessation study that was approved by The University of Texas MD Anderson Cancer Center's Institutional Review Board. All participants (n = 179) provided written informed consent. Eligible smokers wanted to quit smoking, were 18–65 years old, were fluent in English, smoked five or more cigarettes per day, had an expired carbon monoxide (CO) level of at least 6 ppm, and reported no uncontrolled medical illnesses. Individuals were excluded from the study if they were taking psychotropic medications, had psychiatric disorders, were abusing substances other than nicotine, were involved in any other smoking-cessation treatment, or had contraindications for bupropion or varenicline, which were used in the smoking-cessation phase of the study.

Experimental Design

The purpose of the smoking-cessation study was to evaluate the efficacy of bupropion and varenicline for smoking cessation and to identify psychophysiological differences associated with the treatment response. As part of the clinical trial, smokers participated in three laboratory psychophysiological assessment sessions: one at baseline (before any treatment) and two after the start of their quit attempt. This article deals exclusively with data obtained during the baseline session. Some of the data collected from these participants during the baseline session have been published previously (Cui et al., 2012; Versace et al., in press, 2011).

The experimental procedure has been described in detail elsewhere (Versace et al., 2011). Briefly, we first collected smokers' demographic information (e.g., age, sex, and race) and smoking characteristics (e.g., smoking history, daily consumption, expired CO, and Fagerström Test for Nicotine Dependence (FTND) score; Heatherton, Kozlowski, Frecker, & Fagerström, 1991). Next, we obtained several psychophysiological measures that included dense-sensor array EEG recording during the presentation of pictures from four valence categories: pleasant, unpleasant, neutral, and cigarette related. Three equivalent picture sets containing 96 pictures (24 per category) were created by selecting images from the International Affective Picture System (Lang, Bradley, & Cuthbert, 2005) and other smoking-related picture sets used in previous studies (Carter et al., 2006; Gilbert et al., 2005). Subjects were randomly assigned to view one of these three sets during the baseline session. During the session, each picture was presented for 4 s, separated by an inter-trial interval of 3–5 s, and delivered in a random order with respect to category with the restriction that no more than two pictures from the same valence category were presented consecutively. Each picture was presented twice during the session (once during each half of the session), resulting in a total of 192 picture-viewing trials.

In addition to classifying the pictures with respect to valence, we classified them with respect to emotional arousal, which allowed us to conduct analyses of alpha ERD as a function of both valence and arousal. Three arousal categories (low, medium, and high) were formed on the basis of normative ratings (on a Likert scale of 1–9) of the pictures as follows. The neutral pictures, by definition, were considered low arousal. They consisted of two subcategories: people and objects (e.g., household items), the average normative arousal ratings for which were 3.55 and 2.76, respectively. The medium- and high-arousal pictures consisted of subcategories of pictures from the pleasant and unpleasant valence categories. For medium-arousal pictures, the subcategories were pleasant objects (e.g., food and landscapes), romantic scenes, unpleasant objects (e.g., accidents and pollution), and sad scenes, the normative arousal ratings for which were 4.67, 4.90, 5.45, and 4.82, respectively. For high-arousal pictures, the subcategories were erotica and mutilations, the normative arousal ratings for which were 6.29 and 6.36, respectively. Cigarette-related pictures, which have not been normed with respect to valence and arousal ratings but have been rated as more arousing than neutral and less arousing than emotional pictures in previous studies (Cinciripini et al., 2006; Engelmann et al., 2011; Geier et al., 2000), were considered a separate category, so that they could be compared with the low-, medium-, and high-arousal pictures. Finally, it should be noted that the normative ratings of valence and arousal for the emotional pictures did not differ across the three picture sets, and the specific pictures selected from the International Affective Picture System are listed in one of our previous reports (Versace et al., in press).

Data Acquisition and Reduction

The EEG signals were recorded using a 129-channel geodesic sensor net, filtered (0.1–100 Hz), amplified, and digitized at a sampling rate of 250 Hz using an AC-coupled, high-input impedance (200 MΩ) amplifier (Geodesic EEG System 200; Electrical Geodesics Inc.). The EEG data were visually inspected offline to examine the overall data quality. On average, about 2% of the channels were contaminated by artifacts for more than 50% of the recording and were interpolated using spherical splines. Then, a spatial filtering method implemented in BESA (v 5.1.8.10, MEGIS Software GmbH) was used to remove eyeblink artifacts. Next, EEG data were transformed to average reference and segmented into 1850-ms epochs (800 ms before through 1050 ms after picture onset). Within each epoch, channels contaminated by artifacts (e.g., absolute EEG difference larger than 100 μV and difference between two contiguous data points larger than 25 μV) were identified. If fewer than 90% of the channels in an epoch were artifact free, the epoch was excluded from further analyses. This criterion resulted in the loss of approximately 17% of all epochs.

A continuous wavelet transformation was conducted using BrainVision Analyzer software (v 1.05.0005, Brain Products GmbH). A complex Morlet wavelet (Herrmann, Grigutsch, & Busch, 2005) was used to decompose the EEG signals for each channel in the range of 6–30 Hz. The step between successive frequencies was set at 1 Hz, and the Morlet parameter c was set to 7.0. For each picture-viewing trial, we extracted the time course of power information for signals falling in the range of alpha oscillations (8–12 Hz). The data were baseline-corrected by converting power to a decibel (dB) scale (Delorme & Makeig, 2004), using the average power in the window lasting from 500 to 200 ms before picture onset as the baseline. To examine whether baseline levels of alpha power changed over the course of the picture-viewing session, we tested for significant effects of block (first half or second half of the experiment) and valence category (neutral, pleasant, unpleasant, and cigarette related) on alpha power measured during the baseline window using a mixed model in which subject was modeled as a random effect (PROC MIXED; SAS v9.2, SAS Institute).

Data Analysis

Following previously published procedures (De Cesarei & Codispoti, 2011), we computed picture-related alpha ERD by averaging across parieto-occipital sensors (P7, P5, P3, P1, P2, P4, P6, P8, PO7, PO5, PO3, PO2, PO4, PO6, O3, O1, O2, and O4). Then, we obtained a single estimate of alpha ERD per picture-category per-subject by averaging alpha ERD between 400 and 800 ms after picture onset (Figure 1). These estimates were analyzed using mixed models (PROC MIXED) with subject modeled as a random effect.

To test our first hypothesis (i.e., that cigarette-related cues will induce a higher level of alpha ERD than neutral stimuli and similar levels of alpha ERD to emotional stimuli), we examined the effects of valence category (neutral, pleasant, unpleasant, and cigarette related) on alpha ERD magnitude. The primary model included valence category as the only fixed effects predictor. We also ran some secondary analyses by including additional predictors. We assessed changes in alpha ERD over the course of the experiment by including block (first vs. second half of the experiment) as an additional fixed effect. We examined the relationship between alpha ERD and measures of nicotine dependence by running models with the number of cigarettes smoked per day, FTND score, or baseline CO level as an additional fixed effect.

To test our second hypothesis (i.e., that the magnitude of alpha ERD induced by emotional stimuli will increase linearly as a function of the normative arousal levels of the stimuli), we computed the correlation between alpha ERD magnitude and the normative arousal levels of the picture subcategory (neutral objects and people, pleasant and unpleasant objects, romance, erotica, sadness, and mutilations) using Pearson's r (PROC CORR).

To test our third hypothesis (i.e., that cigarette-related stimuli induce alpha ERD at a level comparable to that of other highly arousing stimuli), we used the mixed models procedure (PROC MIXED) to compare the level of alpha-ERD induced by cigarette-related stimuli in comparison to the low-, medium-, and high-arousal stimuli.

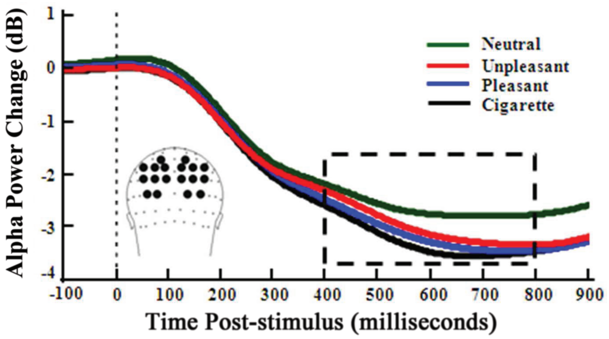

Figure 1. Picture-induced alpha ERD in the parieto-occipital area. Alpha ERD is defined as a decrease in alpha power in response to a stimulus and is quantified using a dB scale. Hence, larger decreases in alpha power are indicative of greater levels of alpha ERD. The box indicates the time window used to compute the alpha ERD for each category that was used in the statistical analyses. The head inset indicates the electrodes in the parieto-occipital area that were used to compute the alpha ERD. The vertical dashed line at 0 ms indicates the onset of the picture stimulus.

Table 1. Sample Characteristics (Total n = 179)

Variable	Measure
	N (%)
Race/Ethnicity	
African American, non-Hispanic	49 (27.4)
White, non-Hispanic	103 (57.5)
Hispanic	18 (10.1)
Other	9 (5.0)
Sex	
Male	117 (65.4)
Female	62 (34.6)
	Mean (SD)
Age (years)	45.2 (10.5)
Daily cigarette consumption	19.0 (8.3)
Years smoked	24.6 (11.6)
Expired carbon monoxide (ppm)	25.7 (13.9)
FTND score	4.6 (2.1)

Note. ppm = parts per million; FTND = Fagerström Test for Nicotine Dependence.

For all tests, the significance level was set at $p < .05$, and the p values from pairwise comparisons were adjusted using Tukey's Honestly Significance Difference test.

RESULTS

Demographics and Smoking Characteristics of the Sample

Table 1 summarizes the basic demographics and smoking characteristics of the sample. Most of the participants were White or African American men in their mid-forties. On average, they had smoked for more than 24 years, consumed about 20 cigarettes per day, had an expired CO level of 25.7 ppm, and scored 4.6 on the FTND.

Baseline Levels of Alpha Power

Alpha power measured during the prestimulus baseline decreased from the first to the second half of the experiment (first half: 356.47±29.35 vs. second half 318.74±29.35; $F_{(1,178)} = 29.30$, $p < .0001$), probably reflecting the increased tiredness and reduced alertness of the participants. Importantly, this effect did not interact with picture categories ($F_{(3,354)} = 0.19$, $p = .9$), which was likely due to our counter-balanced picture presentation across the two blocks.

Alpha ERD as a Function of Picture Valence Category

Alpha ERD evoked by all pictures appeared to decrease slightly from the first half block (−3.64 ±.17 dB) of the experiment to the second half (−3.54 ± .17 dB). This difference approached statistical significance ($F_{(1,178)} = 3.58$, $p = .06$), suggesting that pictures presented in the first block may have been more evocative than those presented in the second block. However, the interaction between block and picture valence was not significant ($F_{(3,534)} = 0.40$, $p = .75$), indicating similar decreases in alpha ERD between the picture categories. Therefore, in the following analyses, alpha ERD was an average across the two blocks of the entire experiment.

We found that alpha ERD magnitude varied as a function of the picture valence category ($F_{(3,534)} = 19.08$, $p < .0001$; Figure 2). Subsequent pairwise comparisons confirmed our first hypothesis that pleasant, unpleasant, and cigarette-related pictures induced alpha ERD at a greater level than neutral stimuli (all $ps < .001$). The contrasts of alpha ERD between pleasant and unpleasant and between pleasant and cigarette-related conditions were not statistically significant ($p > .3$), while cigarette-related stimuli induced alpha ERD at a higher level than unpleasant stimuli ($p < .05$).

We also examined whether there was a relationship between the alpha ERD to cigarette-related stimuli and nicotine addiction measures. We found that the FTND scores, cigarettes per day, and CO levels did not modulate smokers' alpha ERD levels induced by cigarette-related stimuli as indicated by the null interactions between picture valence and FTND scores ($F_{(3,531)} = 1.61$, $p = .19$), cigarettes per day ($F_{(3,531)} = 1.38$, $p = .25$), or CO levels ($F_{(3,525)} = 0.76$, $p = .52$).

Alpha ERD and Emotional Arousal

Our second hypothesis was that alpha ERD would be correlated with normative arousal ratings of the pictures. To test this hypothesis, we conducted a regression analysis with the mean level of alpha ERD to each picture subcategory (neutral people, neutral objects, pleasant objects, unpleasant objects, sadness, romance, erotica, and mutilations) as a response and the normative arousal level of these categories as a predictor. This analysis revealed a significant correlation between alpha ERD magnitude and normative arousal levels (Pearson's $r = -.71$, $p < .05$). Low-arousal pictures (neutral people and objects) induced the lowest levels of alpha-ERD, followed by increasing levels of alpha-ERD for medium-arousal (pleasant and unpleasant objects, sadness, and romance) and high-arousal (erotica and mutilations) pictures (Figure 3).

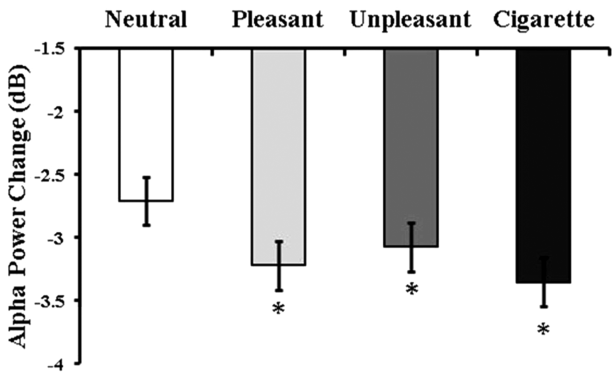

Figure 2. Emotional and cigarette-related stimuli induced greater alpha ERD than neutral stimuli. Values plotted depict the mean changes in alpha power between a prestimulus baseline and a window lasting 400–800 ms after stimulus onset, where larger decreases in alpha power are indicative of greater levels of alpha ERD. Error bars are the standard errors of means. *Indicates a significant difference from neutral pictures ($p < .001$ after adjusting for multiple comparisons).

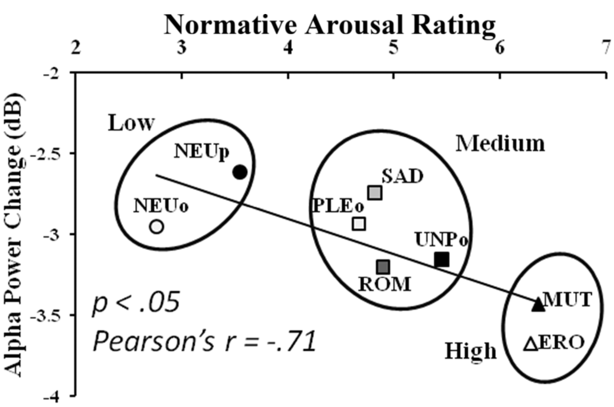

Figure 3. Significant correlation between alpha ERD magnitude and the normative arousal levels of the stimulus subcategories. Mean normative arousal levels for each stimulus category are plotted on the x-axis. Mean changes in alpha power from a prestimulus baseline and a window lasting 400–800 ms after stimulus onset are plotted on the y-axis, where larger decreases in alpha power are indicative of greater levels of alpha ERD. The diagonal line indicates the least-squares regression line from a model using the normative arousal ratings to predict the picture-induced changes in alpha power. Circles indicate groupings of Stimulus subcategories into overall categories of low, medium, and high arousal. Picture subcategories are indicated by the following abbreviations: NEUo = neutral objects; NEUp = neutral people; PLEo = pleasant objects; SAD = sad scenes; ROM = romantic scenes; UNPo = unpleasant objects; ERO = erotica; MUT = mutilations.

Motivational Significance of Cigarette-Related Stimuli

To test our third hypothesis that alpha ERD to cigarette-related pictures would be similar to the level induced by highly arousing stimuli, we compared the extent to which alpha ERD was induced by cigarette-related stimuli in comparison to the picture groups with various normative arousal levels (low, medium, and high). Consistent with our hypothesis, cigarette-related stimuli induced a level of alpha ERD that was similar to levels observed in response to highly arousing stimuli. Our test of this model found a significant effect of picture category on alpha ERD ($F_{(3,534)} = 27.88$, $p < .0001$; Figure 4). Pairwise comparisons revealed that, the differences in alpha ERD between cigarette-related stimuli and the low- and medium-arousal pictures were statistically significant (*ps* < .001), but the difference in alpha ERD between cigarette-related and high-arousal pictures was not significant ($p = .2$).

DISCUSSION

In this study, we analyzed smokers' EEG alpha oscillations in response to neutral, pleasant, unpleasant, and cigarette-related stimuli, and found that the magnitude of alpha ERD induced by cigarette-related stimuli was comparable to that induced by highly arousing stimuli (i.e., erotica and mutilations). This finding is important because it helps to clarify the brain mechanisms activated in addicted individuals by the presence of drug-related cues.

Exposure to cigarette-related cues is thought to precipitate smoking relapse (Shiffman et al., 1996). However, smokers tend to rate these stimuli as low or moderately arousing (Cinciripini et al., 2006; Engelmann et al., 2011; Geier et al., 2000), which is somewhat at odds with the notion that cigarette-related cues precipitate relapse because they are attributed a high level of incentive salience (Robinson & Berridge, 2003). Self-report measures cannot provide reliable information about the brain mechanisms activated by drug cues. Therefore, in a previous report, we analyzed smokers' LPPs in response to emotional and cigarette-related cues among the same sample of smokers studied here. We found that, although LPPs evoked by cigarette-related cues were significantly larger than those evoked by neutral stimuli, their magnitude did not rise to the levels observed in response to highly arousing stimuli (Versace et al., in press). The LPP is generally considered a measure of motivational significance, reflecting allocation of attentional resources for the processing of emotional stimuli (Hajcak et al., 2010; Lang & Bradley, 2010; Schupp et al., 2006). Thus, our previous LPP results suggest that smokers attend to cigarette-related cues, but perhaps to a lesser degree than other highly arousing emotional stimuli. This finding is somewhat inconsistent with current models of addiction which suggest that drug cues acquire high levels of motivational significance (Robinson & Berridge, 2003; Volkow et al., 2004). However, in this secondary analysis of the same data from which we originally derived our LPP results, we found that the level of alpha ERD induced by cigarette-related stimuli was comparable to that induced by highly arousing stimuli (i.e., erotica and mutilations). Given that levels of alpha ERD are elevated by emotional stimuli (De Cesarei & Codispoti, 2011; Simons et al., 2003), our finding of comparable alpha ERD level between cigarette-related and highly arousing stimuli highlights the high level of motivational significance of cigarette-related stimuli, which may contribute to the cue-related smoking relapse.

The alpha ERD responses to affective and cigarette-related stimuli reported here show considerable temporal similarity with our primary analysis of the LPP responses (Versace et al., in press, 2011). In both analyses, emotional stimuli (including cigarettes) differed from the neutral stimuli beginning approximately 300–400 ms after stimulus onset. This temporal overlap

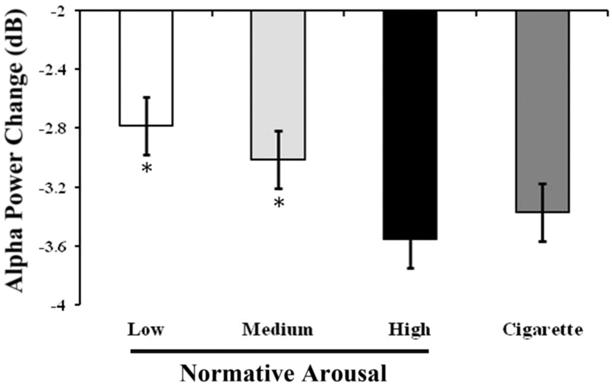

Figure 4. Cigarette-related stimuli induced comparable alpha ERD to highly arousing emotional stimuli. Mean changes in alpha power from a prestimulus baseline and a window lasting 400–800 ms after stimulus onset are plotted as a function of stimulus category, where Low, Medium, and High refer to pictures categorized on the basis of normative arousal ratings and Cigarette indicates cigarette-related pictures. Larger decreases in alpha power are indicative of greater levels of alpha ERD. Cigarette-related stimuli induced greater alpha ERD than low- and medium-arousing stimuli, but a similar level of alpha ERD to highly arousing stimuli. *Indicates a significant difference from cigarette-related stimuli ($p < .001$, adjusted for multiple comparisons).

is consistent with the idea that both LPP and alpha ERD reflect neural mechanisms related to emotional and attentional processes (De Cesarei & Codispoti, 2011).

It has been hypothesized that the LPP is a measure of emotional and attentional processes (Hajcak et al., 2010; Lang & Bradley, 2010; Schupp et al., 2006). Unlike what we previously observed by analyzing the LPP (Versace et al., in press, 2011), the alpha ERD induced by cigarette-related and highly arousing stimuli was similar. One possible cause for this discrepancy may be that in addition to emotional and attentional processes, alpha ERD may also index neural processes related to activation of the KS, as suggested by Klimesch et al. (2011). The involvement of memory processes in addiction has been supported by many studies (Hyman, 2005; Hyman et al., 2006; Robbins & Everitt, 1999; Volkow et al., 2010). However, this interpretation is speculative, and should be treated with caution, as we did not directly assess the relationships between the alpha ERD levels and memory processes or the KS. Therefore, future studies should be carried out to examine how the alpha desynchronization levels will be altered as a function of memory performance and the presence of drug-related cues among addicts.

Our finding of alpha ERD in response to cigarette-related cues should be interpreted with some caveats. First, we do not know whether our finding was specific to smokers, or whether nonsmokers show similar responses to cigarette-related cues. This needs to be directly tested, but significant alpha ERD to cigarette-related cues among nonsmokers is not expected in light of previous studies in which self-report, psychophysiological, or blood oxygenation level–dependent responses were directly compared between smokers and nonsmokers (David et al., 2005; Due, Huettel, Hall, & Rubin, 2002; Engelmann et al., 2011; Geier et al., 2000; Littel & Franken, 2007; Rubinstein, Luks, Dryden, Rait, & Simpson, 2011; Warren & McDonough, 1999). In all of these studies, nonsmokers showed no evidence of significant reactivity to cigarette-related cues. Second, our sample consisted of smokers that were seeking smoking-cessation treatment. Although the laboratory session was conducted prior to the start of any treatment, the generalizability of our findings to smokers who are not interested in quitting cannot be assumed. Thus, future research examining the alpha ERD levels among smokers not interested in quitting smoking is needed. Third, the smokers in this study were not deprived of cigarettes; so, the effects of cigarette deprivation on alpha ERD to cigarette-related cues are unknown. Future studies should evaluate whether there is an increase in the salience of cigarette-related stimuli as indicated by an increased alpha desynchronization levels.

In conclusion, we found that cigarette-related stimuli induced alpha ERD at a level similar to that induced by highly arousing emotional stimuli (i.e., erotica and mutilations). This suggests that cigarette-related cues are motivationally significant for smokers, capable of capturing significant attentional resources and presumably activating memories of previous drug-use experiences. This may be one mechanism by which cue-induced relapse occurs.

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DECLARATION OF INTERESTS

PMC served on the scientific advisory board of Pfizer Pharmaceuticals, conducted educational talks sponsored by Pfizer on smoking cessation (2006–2008), and has received grant support from Pfizer. MK-H has conducted educational talks sponsored by Pfizer Pharmaceuticals, and has participated as study physician and co-investigator in two studies funded by Pfizer Pharmaceuticals. The other authors declare no conflict of interest. In 2011, FV received an independently reviewed competitive grant supported by Pfizer (Global Research Award for Nicotine Dependence).

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