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Cognitive avoidance and aversive cues related to tobacco in male smokers

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ABSTRACT

Background: Treatment using aversive conditioning has been suggested for smoking cessation. The efficacy of this method is thought to be associated with cognitive avoidance. We compare differences in avoidance traits and patterns of associated brain activation in response to cues that induce cravings versus aversion between smokers and non-smokers.

Methods: Fifteen smokers and fifteen non-smokers completed cue reactivity tasks while undergoing functional magnetic resonance imaging (fMRI) to examine brain responses to craving-inducing cues (Cr) and aversion-inducing cues (Av). Participant avoidant traits were also assessed.

Results: Activation of the left frontal subcallosal gyrus in response to Cr was greater in smokers than in non-smokers. Smokers showed less activation in the right temporal lobe in response to Av than did non-smokers. Brain activation in response to Cr in the left frontal subcallosal gyrus was positively correlated with Fagerstrom Test for Nicotine Dependence (FTND) scores in smokers. Brain activation in response to Av in the right temporal lobe was negatively correlated with the Korean Version of the Cognitive Avoidance Questionnaire (KCAQ) scores in non-smokers.

Conclusions: Cognitive avoidance in smokers during aversive stimulation might result in sustaining addictive behaviors. On the other hand, non-smokers may be able to emotionally confront the adverse effects of smoking.

1. Introduction

1.1. The population of smokers and policies to stop smoking

Tobacco use disorder is the most common substance use disorder worldwide and smoking is a leading cause of death (Jaffe, 1990; World Health Organization, 2008). Among the > 2000 compounds contained in cigarettes, nicotine is regarded as the only component associated with dependence, tolerance and reinforcement, which lead to addiction (Henningfield, Miyasato, & Jasinski, 1983; Stolerman & Jarvis, 1995). In 2013, almost 55.8 million Americans (21.3% of the population) were current cigarette smokers (National Institute on Drug Abuse, 2015) and, similarly, about 10 million Koreans (24.2% of the population) were current smokers in 2014 (Ministry of Health and Welfare and Korea Centers for Disease Control and Prevention, 2014). The Centers for Disease Control and Prevention (CDC) reported that cigarette smoking leads to over 480,000 premature deaths in the United States each year—about 1 in every 5 deaths—and an extra 16 million people suffer from severe diseases caused by smoking (National Institute on Drug Abuse, 2015). For these reasons, refined pharmacological and psychotherapeutic treatments have been used to increase abstinence rates; however, even the most helpful methods have long-term success rates of only ~30% (Piasecki, 2006). Because the abstinence rate is intensely influenced by tobacco cue reactivity (Ferguson & Shiffman, 2009), a better understanding of the neurobiological mechanisms of cue reactivity and the relationship between neurobiological mechanisms and individual behavioral traits may facilitate the development of new treatments.

1.2. Aversive conditioning for smoking cessation

To stop habitual substance use, a strategy or treatment using aversive conditioning has been suggested (Cannon & Baker, 1981; Kim, Han, Min, Kim, & Cheong, 2014). Bad experiences in response to aversive conditioning have been paired with the pleasurable stimulus of smoking to extinguish cravings for the substance and eliminate substance use behaviors (McLellan, Lewis, O'Brien, & Kleber, 2000). In a virtual reality program treatment for patients with alcohol depen-

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dence, Lee et al. (2009) paired alcohol cues with the aversive consequences of drinking, resulting in successful alcohol consumption reduction. In several campaigns and studies to stop smoking, strategies using aversive conditioning have reported good efficacy for ending smoking. Johnson and Karkut (1994) reported that 86% of elderly men and 87% of elderly women continued in abstinence after intervention with a combination of hypnosis and aversion. In a survey of 707 German non-smoking adolescents aged 12 to 15 years, the most important motive for not smoking was esthetic aversion (38.6%) except for health-related arguments (Schneider, Loeber, Janssen, Roehrig, & Solle, 2010). In a review of 25 studies using aversive techniques, the efficacy of aversive methods was controversial with an odds ratio (OR) of 1.15 (95% confidence interval [CI] 0.73 to 1.82) with a dose-response to the level of aversive stimulation (OR 1.66, 95% CI: 1.00 to 2.78) (Hajek & Stead, 2004). Because of the controversial efficacy of aversive stimuli, a better understanding of the treatment mechanism of aversive stimuli on brain responses is needed.

1.3. Brain response study on smoking cessation

Previous functional magnetic resonance imaging (fMRI) studies have found that the anterior cingulate, anterior insula and amygdala are associated with aversive conditioning, emotional learning and the fear response in smokers (Büchel, Morris, Dolan, & Friston, 1998; Cheng, Knight, Smith, Stein, & Helmstetter, 2003; Phelps & LeDoux, 2005; Selden, Everitt, Jarrard, & Robbins, 1991). Additionally, smoking behavior and dependence are negatively correlated with neural activation during inhibition tasks (Galvan, Poldrack, Baker, McGlennen, & London, 2011).

Several researchers have identified the brain regions activated by smoking-related cues and have investigated the correlations between craving and functional brain reactivity using fMRI. According to fMRI studies investigating nicotine dependence, the medial lateral frontal cortex, anterior cingulate cortex (ACC), cuneus, precuneus, occipital cortex, and lateral prefrontal cortex (PFC) are activated in response to smoking-related cues (Brody et al., 2002; Due, Huettel, Hall, & Rubin, 2014; Lee, Lim, Wiederhold, & Graham, 2005; McClernon, Kozink, & Rose, 2008; Smolka et al., 2006; Wilson, Sayette, Delgado, & Fiez, 2005; Zubieta et al., 2014).

1.4. Cognitive avoidance and addictive behaviors

Cognitive avoidance, or avoidance coping, leads to interference in the reconstruction of negative thoughts and schemas, in that way preserving false trust (Clark, 1986). Although cognitive avoidance refers to the efforts that an individual uses to defend him or herself from danger or aversive situations, it is not an adaptive strategy because it is characterized by trying to avoid dealing with a stressor and does not result in the modification or elimination of undesirable conditions (Friedman & Silver, 2007; Pearlin & Schooler, 1978; Zeidner & Endler, 1996).

In a study of the correlation between smoker personality traits assessed with the Tridimensional Personality Questionnaire (TPQ) and Fagerstrom Tolerance Questionnaire, harm avoidance scores were positively correlated with addictive smoking scores (Pomerleau, Pomerleau, Flessland, & Basson, 1992). In contrast, Paulus, Rogalsky, Simmons, Feinstein, and Stein (2003) have suggested that harm avoidance and risk-taking behaviors are positively associated with activation of the insula. Considering these contradictory findings about personal avoidance traits and addictive behaviors, more research is needed. To the best of our knowledge, no previous studies have investigated functional brain activation in response to smoking-related aversive cues in addition to examining the correlations among functional brain changes, avoidant traits, and degree of nicotine dependence.

1.5. Hypothesis

In this study, using fMRI, we aimed to investigate differential brain activation in response to craving cues or aversive cues between smokers and non-smokers. In addition, we aimed to evaluate the correlations among cue-elicited brain activation and measures of the level of nicotine dependence and cognitive avoidance. Based on previous studies, we hypothesized that smokers would show increased activation in the mesolimbic circuit and frontal regions associated with reward in response to cigarette craving cues compared to non-smokers. We also hypothesized that smokers would show decreased activation in the regions associated with aversive conditioning, such as anterior cingulate, insula and amygdala, in response to aversion cues compared to non-smokers. In addition, we hypothesized that the decreased functional reactivity in those regions would be correlated with the level of cognitive avoidance.

2. Material and methods

2.1. Participants

A total of 17 male patients with nicotine dependence (smokers) agreed to participate in this study. Sixteen age-matched male healthy control subjects with no history of smoking were also recruited. The inclusion criteria for nicotine dependence were as follows: (1) nicotine dependence based on the Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Patient Edition (SCID-I/P) (Brody et al., 2002) and (2) a score of ≥ 4 on the Fagerstrom Test for Nicotine Dependence (FTND) (Heatherton, Kozlowski, Frecker, & FAGERSTROM, 1991; Huang, Lin, & Wang, 2008), which includes self-assessment questions for the severity of nicotine dependence. The inclusion criteria for the healthy control group were male gender and no past or current tobacco use. The exclusion criteria for both groups were: (1) past or current episodes of any other axis I psychiatric diagnosis based on the SCID-I or severe medical illness, (2) past or current substance abuse or dependence other than nicotine, as verified by the SCID-I, (3) current psychotropic medication use, (4) history of head trauma, and (5) claustrophobia. The Chung-Ang University Hospital Institutional Review Board approved the research protocol for this study, and all participants provided written informed consent.

Among the 17 enrolled patients with nicotine dependence, two smokers were excluded because they had a history of heavy alcohol use and one healthy subject was excluded due to depression risk and a high BDI score. A final total of 15 smokers and 15 healthy control participants underwent fMRI scanning and completed the study.

2.2. Study procedure

The use of tobacco and avoidant traits were evaluated with the FTND (Heatherton et al., 1991) and the Korean Version of the Cognitive Avoidance Questionnaire (KCAQ), which assesses five worry-related cognitive avoidance strategies, namely, thought suppression, thought substitution, distraction, avoidance of threatening stimuli, and transformation of images into thoughts. The KCAQ was translated into Korean, and a Cronbach's alpha coefficient of 0.94 and a test–retest reliability of 0.71 were reported in a sample of 277 Korean adults (Song & Kim, 2009). Additionally, the level of depressive mood and anxiety in all participants were assessed using the Beck Depression Inventory (BDI) (Beck, Steer, & Carbin, 1988) and Beck Anxiety Inventory (BAI) (Beck & Steer, 1990), respectively.

2.3. Assessment of brain activity and craving for nicotine

Brain activation in response to tobacco-related cues (craving and aversive scenes) was assessed using a 1.5 Tesla Espree MRI scanner (Siemens, Munich, Germany). All participants were asked to view two