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The brain activations for both cue-induced gaming urge and smoking craving among subjects comorbid with Internet gaming addiction and nicotine dependence

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ABSTRACT

Internet gaming addiction (IGA) has been classified as an addictive disorder in the proposed DSM 5 draft. However, whether its underlying addiction mechanism is similar to other substance use disorders has not been confirmed. The present functional magnetic resonance images study is aimed at evaluating the brain correlates of cue-induced gaming urge or smoking craving in subjects with both IGA and nicotine dependence to make a simultaneous comparison of cue induced brain reactivity for gaming and smoking. For this purpose, 16 subjects with both IGA and nicotine dependence (comorbid group) and 16 controls were recruited from the community. All subjects were made to undergo 3-T fMRIs scans while viewing images associated with online games, smoking, and neutral images, which were arranged according to an event-related design. The resultant image data was analyzed with full factorial and conjunction analysis of SPM5. The results demonstrate that anterior cingulate, and parahippocampus activates higher for both cue-induced gaming urge and smoking craving among the comorbid group in comparison to the control group. The conjunction analysis demonstrates that bilateral parahippocampal gyrus activates to a greater degree for both gaming urge and smoking craving among the comorbid group in comparison to the control group. Accordingly, the study demonstrates that both IGA and nicotine dependence share similar mechanisms of cue-induced reactivity over the fronto-limbic network, particularly for the parahippocampus. The results support that the context representation provided by the parahippocampus is a key mechanism for not only cue-induced smoking craving, but also for cue-induced gaming urge.

1. Introduction

The Internet is one of the most important communication and social interaction media in modern life. However, a loss of control over Internet use results in disturbing negative consequences (Ko et al., 2009c). This behavior phenomena has been named as Internet addiction (Ko et al., 2009c) or problematic Internet use (Shapira et al., 2000). Although the DSM 5 draft has defined it as “Internet use disorder” in Section III of Substance Use and Addictive Disorders, the term was required to be validated by further study (American Psychiatric Association (APA), 2012). Internet addiction has been reported in varying geographic populations, including both the eastern and western populations, as well as in varying age groups, including adolescents, college students, and adults (Ko et al., 2012). Although it is classified as an addictive disorder now, whether it has the same neurobiological mechanism as substance use disorder has not been confirmed.

Previous epidemiological studies have demonstrated that Internet gaming addiction (IGA) is often comorbid with depressive disorder and attention deficit/hyperactivity, which are also common comorbidities in substance use disorder (Ko et al., 2008a, 2009b; Erfan et al., 2010; Frodl, 2010). The personalities and psychosocial tendencies, such as novelty seeking and high behavioral activation, which have been reported to predict substance use

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disorder, were also found to be associated with Internet addiction (Ko et al., 2006; Yen et al., 2009). In addition, Internet addiction is significantly associated with substance exposure, problematic alcohol use, and harmful alcohol use (Ko et al., 2006, 2008b; Yen et al., 2009). Although these epidemiological results suggest that Internet addiction shares clinical features with substance use disorder, the similarity of the neurobiological mechanism between IGA and substance use disorder has not been confirmed.

"Craving" has been defined as the strong desire to pursue a substance, and is explained by multiple models (Skinner and Aubin, 2010). The Conditioned Model suggests that the uncontrolled desire is a conditioned withdrawal response to addiction-related cues. The Cognitive Model suggests that substance-related cues trigger positive expectations and determine the craving for the substance. The Incentive Sensitization Theory suggests that long-term substance use results in neurobiological changes. When consumption stops, imbalances in the brain induce cravings for the substance in order to reestablish homeostasis (Skinner and Aubin, 2010). All these models suggest that cues have a key role in provoking positive expectations, imbalanced motivational states, and withdrawal syndromes, which contribute to craving responses (Skinner and Aubin, 2010; Sinha and Li, 2007; Heinz et al., 2009).

In recent years, functional magnetic resonance images (fMRIs) have become a major tool for evaluating the brain mechanism of the cue-induced craving response in addiction research (Heinz et al., 2009). Thus far, it has been suggested that a variety of brain regions are associated with cue-induced craving responses. The anterior cingulate is involved in attention and memory processes, which encode the motivational value of substance cue; the orbitofrontal cortex (OFC) is involved in the evaluation of reward of stimuli and the explicit representation of reward expectancy for the substance; the Dorsolateral prefrontal cortex (DLPFC) generates and maintains goal-directed behavior aimed at obtaining the drug reward; the amygdala specifies the emotional salience of the cue and initiates conditioned and unconditioned approach behavior for the substance; the nucleus accumbens connects the motivational aspects of the salient stimuli with motor reactions; the dorsal striatum consolidates stimulus–reaction patterns and is involved in the habit formation of addictive behavior; the parahippocampus connects the environmental cues to the internal states associated with substance use; and the visual memories associated with substance use are reprocessed in the precuneus and serve as conditioned stimuli that provoke conditioned responses (Wilson et al., 2004; Park et al., 2007; Ferguson and Shiffman, 2009; McClernon et al., 2009). These brain areas are hypothesized to contribute to cue-induced craving response, and therefore would be activated under gaming or smoking cue exposure.

In a study conducted on subjects with IGA by Ko et al. (2009a), the gaming cues activated the anterior cingulate, orbital frontal lobe, nucleus accumbens, dorsal striatum, and the DLPFC. Subsequent studies also demonstrated that, in addition to the DLPFC, the parahippocampus is also activated by exposure to gaming cues (Han et al., 2010, 2011). However, these previous fMRIs studies of IGA were all block designed and most researches for substance use disorder followed event-related design. A recent event-related design fMRIs study demonstrated that the DLPFC, precuneus, parahippocampus, and posterior and anterior cingulates were activated in response to gaming cues among IGA subjects (Ko et al., in press). However, owing to the widely varying study designs, sample sizes, and analytical methods between the studies of substance use disorder and studies of IGA, it has not been confirmed whether these disorders share similar neurobiological mechanisms. It is thus necessary to compare the brain responses to gaming urge and the responses to substance craving in the same design to test for shared mechanisms between IGA and substance use disorder.

Thus, the present fMRI study is aimed at comparing the brain activity observed in the response to gaming cues and smoking cues, and determining whether the brain activity elicited by gaming cues is similar to that elicited by smoking cues in subjects with concurrent IGA and nicotine dependence. It was observed that evaluating subjects with comorbid addiction enables the simultaneous comparison of cue-induced reactivity for both gaming and smoking in the same subject. Further, the neuronal network, which is common to the cue-induced brain reactivity response in both IGA and nicotine dependence, is also identified by conjunction analysis.

2. Methods

2.1. Participants

Sixteen subjects with IGA and nicotine dependence (comorbid group) were recruited by an advertisement. The advertisement requested volunteers who smoked 10 or more cigarettes a day and played online games for 4 or more hours on weekdays and 8 or more hours on weekends over the past one year. Further, a control group of 16 subjects with no history of either gaming addiction or nicotine dependence was also recruited. The recruitment criteria were—age 20 years or older, male gender, and right-handed. A detailed explanation of the study was given, and subsequently, informed consent was obtained from all participants. All subjects were interviewed by a psychiatrist to confirm the diagnoses of IGA and nicotine dependence, in accordance with the Diagnostic Criteria for Internet Addiction (DCIA) developed by Ko et al. (2009c) and the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) (American Psychiatric Association, 2000), respectively. It was observed that all enrolled comorbid subjects were currently addicted to the same popular online game. In the control group, no subjects had ever met the DCIA criteria for Internet addiction or the DSM criteria for nicotine dependence. The exclusion criteria included a history of any of the following—substance use disorders other than nicotine addiction, major depressive episode, bipolar I disorder, psychotic disorder, neurological illness or injury, mental retardation, and intolerance of magnetic resonance imaging. Further, subjects who were currently using any psychotropic medication were also excluded. The study was approved by the Kaohsiung Medical University Institutional Review Board.

2.2. Image acquisition

The fMRIs experiments were performed with a 3 T General Electric MR scanner (Sigma VH/I, software: version 4.0). After placing the head of the participant inside a head coil with foam padding, liquid crystal display goggles were placed over the participant's eyes. The magnetic resonance (MR) sequence for functional imaging was a gradient-recalled echo planar imaging (EPI) sequence (64×64 matrix; 24 cm field of view; 35 ms echo time [TE]; 2.5 s repetition time [TR]; 3 mm slice thickness with 0 mm gap). Thirty five image planes were collected parallel to the anterior commissure and posterior commissure (AC–PC) line with the aid of sagittal localizer images. The head motion was corrected by postprocessing using SPM5.

2.3. Process

Prior to scanning, all the subjects were asked to complete the Chen Internet Addiction Scale (CIAS), Fagerström Nicotine