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Differences in functional connectivity between alcohol dependence and internet gaming disorder

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ABSTRACT

Introduction: Internet gaming disorder (IGD) and alcohol dependence (AD) have been reported to share clinical characteristics including craving and over-engagement despite negative consequences. However, there are also clinical factors that differ between individuals with IGD and those with AD in terms of chemical intoxication, prevalence age, and visual and auditory stimulation.
Methods: We assessed brain functional connectivity within the prefrontal, striatum, and temporal lobe in 15 patients with IGD and in 16 patients with AD. Symptoms of depression, anxiety, and the attention deficit hyperactivity disorder were assessed in patients with IGD and in patients with AD.
Results: Both AD and IGD subjects have positive functional connectivity between the dorsolateral prefrontal cortex (DLPFC), cingulate, and cerebellum. In addition, both groups have negative functional connectivity between the DLPFC and the orbitofrontal cortex. However, the AD subjects have positive functional connectivity between the DLPFC, temporal lobe and striatal areas while IGD subjects have negative functional connectivity between the DLPFC, temporal lobe and striatal areas.
Conclusions: AD and IGD subjects may share deficits in executive function, including problems with self-control and adaptive responding. However, the negative connectivity between the DLPFC and the striatal areas in IGD subjects, different from the connectivity observed in AD subjects, may be due to the earlier prevalence age, different comorbid diseases as well as visual and auditory stimulation.

1. Introduction

1.1. Clinical characteristics of internet gaming disorder and alcohol dependence

Clinical studies of internet addiction have suggested the following diagnostic criteria: time spent longer than initially intended and planned, time distortion, compulsive behaviors, failure of stopping or controlling use, deception about extent of use, utilization of the internet activity to cope with or escape problems, and preoccupation with internet use when offline (Atmaca, 2007; Shapira et al., 2003; Young, 1996). More specifically, DSM-V also suggested internet gaming disorder in the section for future study (American Psychiatric Association, 2013). The clinical characteristics of internet gaming disorder (IGD) include craving and over-engagement despite negative consequences. Many of these behavioral symptoms are shared with those observed in patients with alcohol dependence (AD) (Karim & Chaudhri, 2012). The craving induced by alcohol or other substances has been closely associated with activity of the dorsolateral prefrontal cortex (DLPFC) (George et al., 2001). The DLPFC is also thought to play important roles in mediating the clinical symptoms of alcohol dependence, including impulsivity, aggravation of abuse potential, and executive dysfunction (Jasinska, Stein, Kaiser, Naumer, & Yalachkov, 2014). Deficits of DLPFC function have been reported in subjects with IGD (Han, Kim, Lee, Min, & Renshaw, 2010; Ko et al., 2009). For example, brain activity within the DLPFC has also been positively correlated with craving in response to online game cues in subjects with IGD (Ko et al., 2009).

However, there are also clinical characteristics that differ between individuals with IGD and those with AD. First, IGD does not involve chemical intoxication or physical withdrawal as is the case with alcohol, nicotine, and drug use disorders (Grant, Potenza, Weinstein, & Gorelick, 2011). Second, the main sensory system inputs in response to internet game play are the result of visual and auditory attention (Dong, Huang, & Du, 2012). Extreme internet game play may cause visual acuity loss or hearing problems (Bovo, Ciorba, & Martini, 2011; DellaCroce & Vitale, 2008). Long term game play in pro-gamers has been correlated with the increased cortical volume within the parietal cortex which

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might be related to increased visuo-spatial attention (Hyun et al., 2013; Song, Han, & Shim, 2013). For these reasons, we believe that internet game play may change activity within brain regions which are related to visual and auditory stimulation. Third, demographic cohort studies of alcohol dependence report a wide range of ages from childhood to old adults (Peltzer & Phaswana-Mafuya, 2013). In a USA national longitudinal study of adolescent health, life time alcohol dependence reaches a peak age of onset at 23 years (Haberstick et al., 2014). However, few studies report cases of internet gaming disorder in patients over 40 years of age (Choi et al., 2009; Lee, Han, Kim, & Renshaw, 2013; Whang, Lee, & Chang, 2003). In a survey of 908 Dutch adolescents and adults, with ages ranging from 14 to 80, the most vulnerable period for online game addiction was adolescence (Haagsma, Pieterse, & Peters, 2012). For these reasons, some investigators regard IGD as an impulse control disorder (Beard & Wolf, 2001). Other investigators regard it as a behavioral addiction (Grant et al., 2011).

1.2. Brain connectivity in internet gaming disorder vs alcohol dependence

Several cue-induced functional magnetic resonance imaging studies of internet gaming disorder have noted that brain regions which activate in response to online game cues in patients with online game addiction are similar to those observed following alcohol cue presentation in patients with alcohol dependence (Han et al., 2010; Ko et al., 2009; Leeman & Potenza, 2013). Corticostriatal tracts, including the dorsolateral prefrontal cortex, limbic lobe, and striatal areas are thought to be candidate regions that facilitate craving for maintaining alcohol in patients with alcohol dependence (Filbey et al., 2008; Lopez, Akil, & Watson, 1999). Interestingly, the same tract has been reported to activate in patients with online game addiction (Han et al., 2010; Ko et al., 2009).

However, recent studies using resting state fMRI have also noted differences in brain connectivity between individuals with AD and those with IGD. Resting state functional MRI has been used to assess the integration and connectivity of neural activities during the resting state (Jiang et al., 2008). Functional connectivity refers to the temporal correlation of a neurophysiological index (signal synchronicity of low frequency fluctuation activity) measured among different brain areas which are consistent with intrinsic brain network organization or network dysfunction (Biswal, Yetkin, Haughton, & Hyde, 1995; Friston, Frith, Liddle, & Frackowiak, 1993). Positive connection refers to positive correlations between functionally related brain regions and negative connections indicate negative correlations between brain regions with opposing functional roles (Greicius, Krasnow, Reiss, & Menon, 2003). Strong (more) connectivity between regions A and B indicates that both regions A and B are activated simultaneously (Biswal et al., 1995; Friston et al., 1993). Seed base analysis requires an a priori a region which is selected to serve as a seed, from which to evaluate connectivity with other brain regions (Biswal et al., 2010). Recently, this technique has been used to detect abnormal functional integration in individuals with a range of psychiatric disorders (Deco, Jirsa, & McIntosh, 2011). Khalili-Mahani et al. (2012) have reported that activity within the medial frontal cortex, dorsolateral prefrontal cortex, parietal lobe, temporal lobe, and cerebellum was more connected as a result of alcohol intake. In patients addicted to different drugs (heroin), increased functional connectivity between nucleus accumbens, ventral/rostal anterior cingulate gyrus, amygdala, and orbitofrontal cortex has been as observed (Ma et al., 2010). In the case of internet gaming disorder, patients with IGD showed enhanced functional connectivity in the brainstem, inferior parietal lobule, left posterior cerebellum, and left middle frontal gyrus, relative to healthy control subjects (Dong et al., 2012). In addition, IGD subjects showed decreased functional connectivity in the temporal, occipital and parietal brain regions (Dong et al., 2012). Because the DLPFC is thought to mediate clinical symptoms of AD and IGD (Han et al., 2010; Jasinska et al., 2014; Ko et al., 2009), we selected the DLPFC as a seed region to assess functional connectivity within corticostriatal–limbic tracts in AD and IGD.

1.3. Hypothesis

Based on previous studies of alcohol dependence and internet gaming disorder, deficits of DLPFC function have been commonly observed in individuals with either disorder. However, no study has directly compared AD subjects and IGD subjects, in part due to differences in the prevalence age. In this direct comparison of AD subjects and IGD subjects, we hypothesized that there would be differential brain functional connectivity from the DLPFC to the striatum and temporal lobe between AD subjects and IGD subjects.

2. Methods

2.1. Subjects

Among 303 patients who visited the online game clinic and research center and agreed to participate in a fMRI research study, 20 internet gaming disorder (IGD) inpatients in their thirties were recruited. Twenty male patients approximately of the same age with alcohol dependence (AD) also agreed to participate in our research. The inclusion criteria for IGD were as follows: (1) The criteria for internet gaming disorder in the current study as suggested by the research criteria in DSM-V (American Psychiatric Association, 2013). In addition, more conditions were added: (2) individuals in their thirties; (3) online game play time ≥ 4 h per day/30 h per week; and (4) Young Internet Addiction Scale scores > 50. The inclusion criteria for alcohol dependence include (1) individuals who met the criteria for alcohol dependence (American Psychiatric Association, 2013); (2) individuals in their thirties; (3) individuals with a Michigan alcohol screening test (MAST) score of >19 for alcohol problems; and (4) individuals with impaired behaviors or distress due to maladaptive patterns. The exclusion criteria for internet gaming disorder and alcohol dependence include (1) patients with history or current episode of other Axis I psychiatric diseases; (2) patients with other substance abuse history (except for tobacco); (3) patients with medical illness; and (4) patients with claustrophobia. Three AD subjects and three IGD subjects were excluded due to comorbidity with major depressive disorder. One AD subject and one IGD subject were excluded due to comorbidity with ADHD. One IGD subject failed to complete the fMRI scan due to claustrophobia. Finally, 15 IGD inpatients and 16 AD inpatients completed the research protocol. The Chung Ang University Hospital Institutional Review Board approved the research protocol for this study. Written informed consent was provided by all participants.

2.2. Study procedure

During the detox period, both AD subjects and IGD subjects were hospitalized to ensure alcohol or internet game playing abstinence. On hospital days 10–12, fMRI scanning was performed in both AD subjects and IGD subjects. Over a period of 5–10 days, patients with alcohol dependence were detoxified with lorazepam, thiamine, and multivitamins in accordance with published protocols (Asplund, Aaronson, & Aaronson, 2004). After detoxification, craving for alcohol, the severity of internet addiction, symptoms of depression, anxiety, and attention deficit hyperactivity disorder (ADHD) and severity of clinical global status (CGI-s) were assessed with the Young Internet Addiction Scale (YIAS) (Young, 1996), the Korean Alcohol Urge Questionnaire (AUQ-K) (Kim et al., 2008), the Beck Depression Inventory (BDI) (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), Beck Anxiety Inventory (BAI) (Beck, Epstein, Brown, & Steer, 1988), and the adult ADHD rating scale (K-AADHD) (Kim, 2003), respectively. A BDI score >21 is "suggestive of clinical depression" and BAI scores >22 reflect an anxiety state of sufficient severity to merit clinical assessment. Both IGD and AD subjects