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Altered gray matter density and disrupted functional connectivity of the amygdala in adults with Internet gaming disorder

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ABSTRACT

Objectives: The aim of this study was to evaluate the altered brain structure and functional connectivity (FC) among subjects with Internet gaming disorder (IGD).
Methods: We recruited 30 males with IGD and 30 controls and evaluated their gray matter density (GMD) and FC using resting fMRI. The severities of IGD, gaming urge, and impulsivity were also assessed.
Results: The results demonstrated that the subjects with IGD had a higher impulsivity and a greater severity of IGD. The subjects with IGD had a lower GMD over the bilateral amygdala than the controls. Further, the subjects with IGD had lower FC with the left amygdala over the left dorsolateral prefrontal lobe (DLPFC) and with the right amygdala over the left DLPFC and orbital frontal lobe (OFL). They also had higher FC with the bilateral amygdala over the contralateral insula than the controls. The FC between the left amygdala and DLPFC was negatively correlated with impulsivity. The FC of the right amygdala to the left DLPFC and orbital frontal lobe was also negatively correlated with impulsivity. Our results indicated that the altered GMD over the amygdala might represent vulnerability to IGD, such as impulsivity. Further analysis of the amygdala demonstrated impaired FC to the frontal lobe, which represents impulsivity.
Conclusion: The results of this study suggested that the amygdala plays a very influential role in the mechanism of IGD. Its detailed role should be further evaluated in future study and should be considered in the treatment of IGD.

1. Introduction

The Internet is a popular communication medium in modern life. Although it is convenient and available 24 h a day, loss of control of Internet use may result in negative psychosocial consequences (Young and Case, 2004). In recent years, Internet addiction has become prevalent not only in Western but also in Eastern societies (Yen et al., 2010). Internet gaming is a popular online activity predicting the risk of Internet addiction (Ko et al., 2007). Internet gaming disorder (IGD) is one of the more popular subtypes (57.5%) of Internet addiction (Kishi et al., 2009). As Internet gaming is of significant public importance, the DSM-5 includes IGD in the conditions for future study (APA, 2013). It is necessary to clarify the mechanisms of IGD to provide adequate evidence to support that Internet gaming disorder has merit as an independent disorder and to develop effective treatment.

The proposed DSM-5 suggested 9 criteria for IGD as follows: preoccupation, withdrawal symptoms, tolerance, unsuccessful control, impaired decision-making, loss of interests in previous hobbies, escape, deceit about Internet gaming, and impaired essential function (APA, 2013). The point prevalence in adolescents was estimated to be 8.4% for males and 4.5% for females in the DSM-5. The target of the uncontrolled behavior is specific in Internet gaming, such as massive multiplayer online role-playing games (MMORPGs) (Billieux et al., 2011), but is not specific in gambling behavior online. IGD has been reported

Abbreviations: IGD, Internet gaming disorder; FC, functional connectivity; GMD, gray matter density; DLPFC, dorsolateral prefrontal lobe; OFL, orbital frontal lobe; VBM, Voxel-based morphometry; ReHo, Regional Homogeneity; MR, magnetic resonance; EPI, echo planar imaging; FSPGR, Spoiled Gradient Echo; QGU-B, Questionnaire on Gaming Urge, Brief Version; BIS-11, Barratt Impulsivity Scale 11; ReHo, Regional Homogeneity; SPM, Statistical Parametric Mapping; WM, white matter; CSF, cerebrospinal fluid; MNI, Montreal Neurological Institute; ROIs, Region of Interests; SMA, supplement motor area.

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to result in social, financial, marital, family and/or professional difficulties (Achab et al., 2011) and is associated with depression, anxiety, and social phobias (Gentile et al., 2011). The general characteristics of the Internet, such as anonymity, high availability, or information and efficiency (Chiang & Su, 2012), might contribute to addiction to online gaming, but not to other addictive behaviors or off-line gaming. Further, there are factors, such as motivation factors or structure characteristics of individual Internet activities (Billieux, 2012), associated with addiction to specific Internet activities. Thus, this suggests that IGD should be diagnosed as an independent disorder to be further researched (Petry and O'Brien, 2013).

Subjects with IGD participate for an extensive time in online gaming that includes cognitive exercises and a designed rewarding experience. Long-term and repeated gaming might make a difference to the structure or function of the brain. On the other hand, alterations in brain structure or function might also represent characteristics such as impulsivity, which precedes IGD. Evaluation of the brain structure and functioning in IGD could provide insight into how IGD changes the brain or how differences in the brain predispose individuals to IGD.

Voxel-based morphometry (VBM) is widely used as an imaging tool to evaluate patterns of brain anatomy change, particularly gray matter, in behavioral or cognitive disorders (Amico et al., 2011; Ridgway et al., 2008). The VBM technique allows voxel-wise comparisons of the local density or volume of gray matter between groups (Ashburner and Friston, 2000). It is a powerful tool to detect structural changes that may vary progressively during the course of a mental disorder. Previous reports have demonstrated that video gaming may affect the gray matter volume over the bilateral entorhinal cortex, hippocampus, and occipital lobe, which reflects adaptive neural plasticity related to gaming experience (Kuhn and Gallinat, 2014). Zhou and colleagues found that adolescents with Internet addiction had a lower gray matter density (GMD) over the left anterior, posterior cingulate and insula (Zhou et al., 2011). Yuan and colleagues found a lower GMD over the bilateral dorsolateral prefrontal cortex, supplementary motor area, and orbital frontal lobe among adolescents with Internet addiction (Yuan et al., 2011). Weng and colleagues found that subjects with IGD had a lower GMD over the right orbital frontal lobe, bilateral insula, and right supplement motor area (Weng et al., 2013). However, the diagnosis of Internet addiction or IGD in these studies was based on self-reported questionnaires, not diagnostic interviewing. Besides, the numbers of subjects in these studies were limited, at lower than 20. Sample size is one factor amenable to manipulation and contributes to the statistical power (Desmond and Glover, 2002). Murphy & Garavan suggested that a subject number of $N = 20$ is required in order to reach an effective power in analyses using fMRI study (Murphy and Garavan, 2004). Desmond & Glover suggested that 24 or more subjects are required to reach the significant threshold after correcting for multiple comparisons in fMRI studies (Desmond and Glover, 2002). Further, all these studies evaluated the GMD in adolescents, a stage at which the brain is still developing (Dayan et al., 2010). Evaluation of the GMD in young adults could represent the brain structure at near maturity. Thus, evaluation of the GMD in subjects with IGD as defined by diagnostic interviewing including an adequate number of subjects is necessary in order to gain insight into the structural changes in IGD.

A growing body of evidence shows that distributed neural circuits exhibit spontaneous activity at rest. These slow-frequency fluctuations are temporally correlated within spatially-distinct but functionally-related networks. This resting-state functional connectivity (FC) has revealed a number of networks that are consistently found in healthy subjects and represent specific patterns of synchronous activity (Rosazza and Minati, 2011). Evaluation of the resting-state FC provides an opportunity to characterize distributed circuit abnormalities in neuropsychiatric illnesses. For example, the FCs of the amygdala, insula, and nucleus accumbens as evaluated by seed analysis have been found to be decreased among subjects with opioid dependence (Upadhyay et al., 2010). The specific neurobiological network underlying reward, affective and cognitive processes has been represented by the FC to reveal the possible mechanism of addictive disorder (Sutherland et al., 2012).

There are behavioral similarities of IGD to gambling disorder or substance use disorder (APA, 2013; Ko et al., 2005). Subjects with IGD show a lack of control on online gaming use (Ko et al., 2009). They had higher score in impulsivity (Lee et al., 2012) and demonstrated a deficit in inhibitory control in cognitive task (Choi et al., 2014). The altered response inhibition function was also demonstrated in electrophysiological or functional MRI study (Dong et al., 2010; Ko et al., in press). Further, the impulsivity was found to be a risk factor to develop IGD among adolescents (Gentile et al., 2011). Thus, impulsivity is an essential characteristic of IGD. To evaluate the brain structure or FC characteristic of IGD might provide insight about the neurobiological presentation of impulsivity among subjects with IGD.

The default network resting-state connection of subjects with IGD has been evaluated by regional homogeneity (Dong et al., 2012). IGA subjects, 15 men, showed enhanced Regional Homogeneity (ReHo) in the brainstem, inferior parietal lobule, left posterior cerebellum, and left middle frontal gyrus as compared with 14 controls. Another resting functional analysis demonstrated altered default network resting-state FC to the posterior cingulate in 17 adolescents with Internet gaming addiction (Ding et al., 2013). Compared with the control group, subjects with IGD exhibited increased FCs in the bilateral cerebellum posterior lobe and middle temporal gyrus. The bilateral inferior parietal lobule and right inferior temporal gyrus exhibited decreased connectivity. Two studies of different age groups demonstrated different results for the default model network in IGD. This suggests that further study with a greater sample size is necessary to resolve the controversial results. Further, the FC to specific brain regions that contribute reward, emotion, or cognitive control should be evaluated to shed light on the mechanisms of IGD.

Both GMD and FC were evaluated in a wide variety of psychiatric conditions (Yang et al., 2013; Yi et al., 2012), including addictions (Ide et al., 2014; Liao et al., 2011; Zhang et al., 2014a). Combined evaluation could assess the compatibility difference in both brain structure and FC (Qin et al., 2014; Wang et al., 2014). For example, an abnormal structure or function of the amygdala is a common component of neurodevelopmental disorders (Schumann et al., 2011). Qiu and colleagues evaluated the GMD enlargement in the amygdala using VMB and then assessed the connectivity of the amygdala (Qin et al., 2014) in order to demonstrate structural and functional changes. Thus, it is reasonable to evaluate the structure alteration first and then analyze the FCs to these altered regions in order to reflect the mechanisms of psychiatric disorders, such as social anxiety (Liao et al., 2011) and heroin dependence (Yuan et al., 2010). However, no study has combined VBM analysis with resting state FC analysis in subjects with IGD.

Thus, we hypothesized that subjects with IGD had alterations in the GMD and FC of brain regions that represent the essential mechanism, such as impulsivity (Choi et al., 2014; Lee et al., 2012), of IGD. Then, this study aimed to: 1) explore the brain regions with altered GMD among subjects with IGD; 2) evaluate the altered FC of these brain regions; and 3) test the correlations between FC and the severity of impulsivity.

2. Methods

2.1. Participants

Male right-handed participants were recruited through an advertisement posted on a University campus. All subjects in the IGD group were interviewed by a psychiatrist to confirm the diagnosis of IGD for more than two years according to the diagnostic criteria for Internet addiction (DCIA) (Ko et al., 2009). The subjects were currently addicted to online gaming and spent an average of 4 or more hours/day on