Progress in Neuro-Psychopharmacology & Biological Psychiatry 60 (2015) 104–111

Contents lists available at ScienceDirect

Progress in Neuro-Psychopharmacology & Biological Psychiatry

journal homepage: www.elsevier.com/locate/pnp

Resting-state regional homogeneity as a biological marker for patients with Internet gaming disorder: A comparison with patients with alcohol use disorder and healthy controls

Heejung Kim [a,b], Yu Kyeong Kim [a,b], Ah Reum Gwak [c], Jae-A Lim [c], Jun-Young Lee [c,d], Hee Yeon Jung [c,d], Bo Kyung Sohn [c,d], Sam-Wook Choi [e], Dai Jin Kim [f], Jung-Seok Choi [c,d,*]

[a] Department of Nuclear Medicine, SMG-SNU Boramae Medical center, Seoul, Republic of Korea
[b] Institute of Radiation Medicine, Medical Research Center, Seoul National University, Seoul, Republic of Korea
[c] Department of Psychiatry, SMG-SNU Boramae Medical Center, Seoul, Republic of Korea
[d] Department of Psychiatry and Behavioral Science, Seoul National University College of Medicine, Seoul, Republic of Korea
[e] Department of Psychiatry, GangnamEulji Hospital, Eulji University, Seoul, Republic of Korea
[f] Department of Psychiatry, Seoul St. Mary's Hospital, The Catholic University of Korea College of Medicine, Seoul, Republic of Korea

ARTICLE INFO

Article history:
Received 5 November 2014
Received in revised form 28 January 2015
Accepted 8 February 2015
Available online 14 February 2015

Keywords:
Alcohol use disorder
fMRI
Internet gaming disorder
Regional homogeneity
Resting-state

ABSTRACT

Objective: Internet gaming disorder (IGD) shares core clinical features with other addictive disorders, such as gambling disorder and substance use disorder. Designation of IGD as a formal disorder requires elucidation of its neurobiological features and comparison of these with those of other addictive disorders. The aims of the present study were to identify the neurobiological features of the resting-state brain of patients with IGD, alcohol use disorder (AUD), and healthy controls, and to examine brain regions related to the clinical characteristics of IGD.
Method: Functional magnetic resonance imaging was performed on 16 subjects with IGD, 14 subjects with AUD, and 15 healthy controls during the resting-state. We computed regional homogeneity (ReHo) measures to identify intrinsic local connectivity and to explore associations with clinical status and impulsivity.
Results: We found significantly increased ReHo in the posterior cingulate cortex (PCC) of the IGD and AUD groups, and decreased ReHo in the right superior temporal gyrus (STG) of those with IGD, compared with the AUD and HC groups. We also found decreased ReHo in the anterior cingulate cortex of patients with AUD. Scores on Internet addiction severity were positively correlated with ReHo in the medial frontal cortex, precuneus/PCC, and left inferior temporal cortex (ITC) among those with IGD. Furthermore, impulsivity scores were negatively correlated with that in the left ITC in individuals with IGD.
Conclusion: Our results provide evidence of distinctive functional changes in the resting-state of patients with IGD and demonstrate that increased ReHo in the PCC may be a common neurobiological feature of IGD and AUD and that reduced ReHo in the STG may be a candidate neurobiological marker for IGD, differentiating individuals with this disorder from those with AUD and healthy controls.

1. Introduction

Internet addiction, defined as an inability to control Internet use, may lead to serious impairments in psychological and social functioning (Griffiths, 1997; Young, 1996). Internet addiction also can be defined as a behavioral addiction (Cho et al., 2014). This disorder shares core clinical features with gambling disorder, which is considered a behavioral addiction, and these shared features include continued engagement in the addictive behavior despite adverse consequences, loss of control over such behavior, and craving that is experienced prior to engagement in the behavior (Muller et al., 2014). Additionally, a previous study reported that Internet addiction shared characteristics with alcohol use disorder (AUD) in terms of emotion, temperament, and personality (Hwang et al., 2014). Internet addiction can involve participation in various activities, such as Internet gaming, social networking services,

Abbreviations: ACC, anterior cingulate cortex; ANOVA, analysis of variance; AUD, alcohol use disorder; AUDIT-K, Korean version of alcohol use disorder identification test; BAI, Beck anxiety inventory; BDI, Beck depression inventory; BIS-11, Barratt impulsiveness scale-version 11; BOLD, blood oxygenation level-dependent; DMN, default mode network; DPARSF, data processing assistant for resting-state fMRI; DSM-5, Diagnostic and Statistical Manual of Mental Disorders, fifth-edition; EPI, echo-planar image; fMRI, functional magnetic resonance imaging; IAT, Internet addiction test; IGD, Internet gaming disorder; IQ, intelligence quotient; ITC, inferior temporal cortex; KCC, Kendall's coefficient of concordance; MedFC, medial frontal cortex; MFC, middle frontal cortex; MNI, Montreal Neurological Institute; MOC, middle occipital cortex; MTG, middle temporal gyrus; PCC, posterior cingulate cortex; PrecC, precentral cortex; ReHo, regional homogeneity; SCID, Structured Clinical Interview for DSM-IV; STG, superior temporal gyrus; WAIS-III, Wechsler adult intelligence scale-III

* Corresponding author at: Department of Psychiatry, SMG-SNU Boramae Medical Center, 20 Boramae-Ro 5-Gil, Dongjak-Gu, Seoul 156-707, Republic of Korea. Tel.: +82 2 870 3461; fax: +82 2 831 2826.
E-mail address: choijs73@gmail.com (J.-S. Choi).

http://dx.doi.org/10.1016/j.pnpbp.2015.02.004
0278-5846/

viewing pornography, and shopping. Recently, the Diagnostic and Statistical Manual of Mental Disorders, fifth-edition (DSM-5) included Internet gaming disorder (IGD) as a condition for further study. Designation of IGD as a formal disorder requires elucidation of its neurobiological features and a comparison of these with those of other addictive disorders, such as substance use disorders.

Recent neuroimaging studies have reported that significant changes in brain functioning are associated with IGD. The majority of these studies utilized functional magnetic resonance imaging (fMRI) performed during tasks assessing reward sensitivity (Dong et al., 2011) or response inhibition (Ko et al., 2014). On the other hand, the brain consumes 20% of the body's total energy when at rest (Raichle and Mintun, 2006; Shulman et al., 2004). A network of brain regions exhibits increased activity during the resting-state (default-mode network, DMN), and this activity appears to reflect ongoing cognitive processes (Andrews-Hanna et al., 2010). In other words, the brain's intrinsic activity during the resting-state affects subsequent stimulus- or task-induced activity (Greicius and Menon, 2004). Previous research has shown that patients with IGD demonstrated dysfunctional brain electrical activities during the resting-state. Specifically decreased beta power and increased gamma power during the resting-state were found in patients with IGD compared with healthy controls, and these brain changes were related to impulsivity (Choi et al., 2013). Thus, investigation of the brains of patients with IGD during the resting-state may increase our understanding of the intrinsic brain changes underlying the cognitive dysfunction observed in IGD.

Resting-state fMRI is a good method for investigating spontaneous blood oxygenation level-dependent (BOLD) fluctuations, which provides data that complement those obtained via task-associated fMRI, and for examining brain dysfunction, such as disease characteristics during the resting-state (Cole et al., 2010). Regional homogeneity (ReHo) analysis is used to measure regional coherence of BOLD signals, that is, the degree of regional synchronization that occurs over the course of the resting-state fMRI (Zang et al., 2004). Thus, the ReHo value indicates the local connectivity of the temporal correlations between a given voxel and adjacent voxels (Zang et al., 2004; Zuo et al., 2013). Abnormal ReHo may be related to pathological changes in or unbalanced temporal aspects of the brain that are associated with specific disease (Fang et al., 2013). Recently, ReHo measurement has been considered a kind of marker for changes in spontaneous neural activity in the resting-brain (Fang et al., 2013).

In this study, we used ReHo analysis of resting-state fMRI data to investigate local neuronal abnormalities in subjects with IGD. The aims of the present study were 1) to identify the neurobiological features of the resting-state brain of patients with IGD, AUD, and healthy controls, and 2) to examine brain regions related to the clinical characteristics of IGD. AUD is a worldwide substance abuse problem and there have been reports about disruption on brain functional network, DMN, and reward network (Park et al., 2010). So, we selected the AUD group as a comparison group. We hypothesized that both the IGD and AUD groups would show local neural abnormalities in the regions involved in the reward pathway, response inhibition, or impulsivity, which are core features of addictive disorder, that is, IGD as a behavioral addiction may share similar neurobiological abnormalities with other substance addictive disorders, although IGD does not involve a chemical intoxicant or substance. We also hypothesized that the IGD group would show abnormal neural activities in the brain regions associated with the processing of audiovisual information due to long-time Internet gaming exposure. To our knowledge, this is the first study to investigate the resting-state fMRI of patients with IGD, and to compare it with that of patients with AUD and healthy controls.

2. Materials and methods

2.1. Participants

We recruited a total of 45 young males to participate in this study during 2013 to 2014: 16 were diagnosed with IGD (age: 21.63 ± 5.92 years), 14 were diagnosed with AUD (age: 28.64 ± 5.92 years), and 15 were healthy controls (age: 25.40 ± 5.92). All patients were seeking treatment at the outpatient clinics of SMG-SNU Boramae Medical Center in Seoul, South Korea due to excessive participation in Internet gaming or alcohol consumption.

Patients with IGD were diagnosed according to the DSM-5 criteria and were also assessed using the Young's Internet addiction test (IAT) (Young, 1996). Previous studies have defined excessive Internet users as those with IAT total scores of at least 50 (Hardie and Ming, 2007; Young, 1996). We included those subjects with scores of at least 70 on the IAT who spent more than 4 h per day and 30 h per week using the Internet so that we could study only those with a severe Internet addiction rather than those who were merely at high risk due to excessive Internet use. The mean IAT score of patients in the IGD group was 75.81 ± 4.72, and their mean times spent using the Internet game per day and per week were 5.95 ± 2.27 and 45.95 ± 15.87 h, respectively. Additionally, the Structured Clinical Interview for DSM-IV (SCID) was used to identify past and current psychiatric illnesses.

Diagnoses of AUD were based on the SCID, which was administered by a clinically experienced psychiatrist. The severity of AUD was assessed by the Korean version of Alcohol Use Disorder Identification Test (AUDIT-K) (Kim et al., 1991). The mean AUDIT-K score for the AUD group was 27.00 ± 4.04. The mean amount of alcohol consumed per day by the AUD group was 12.60 ± 4.65 standard drinks. Patients with AUD used the Internet game less than 2 h per day and had abstained from alcohol use for at least 2 weeks prior to their participation in the study. Abstinence from alcohol was verified by self-reports and reports from caregivers. We regarded these as reliable because the participants attended regular follow-up visits to our outpatient clinic and showed good adherence to treatment.

Healthy controls were recruited from the local community and had no history of any psychiatric disorder. Healthy controls used the Internet game less than 2 h per day and drank fewer than 14 standard drinks per week and fewer than four standard drinks per occasion. They also had no lifetime history of AUD.

Participants also completed the Beck Depression Inventory (BDI) (Beck et al., 1961), the Beck Anxiety Inventory (BAI) (Beck et al., 1988), and the Barratt Impulsiveness Scale—version 11 (BIS-11) (Barratt, 1985). The BDI and the BAI were administered to all subjects to measure depressive and anxiety symptoms, respectively. The BIS-11 (Barratt, 1985) was used to measure trait impulsivity. All scales were validated in Korea. The Institutional Review Board of the SMG-SNU Boramae Medical Center approved the study protocol, and all subjects provided written informed consent prior to participation. Exclusion criteria were a history of significant head injury, seizure disorder, mental retardation, and psychotic disorder. All participants were medication-naïve at the time of assessment. The Korean version of the Wechsler Adult Intelligence Scale (WAIS-III) was administered to all subjects to estimate intelligence quotient (IQ), and we included only subjects with WAIS-III scores of at least 80.

2.2. Image acquisition

FMRI resting data were acquired using a Philips Achieva 3-T MRI scanner (Philips Medical Systems, Netherlands) using a standard whole-head coil. We obtained 180 T2* weighted echo-planar image (EPI) volumes in each of the 35 axial planes parallel to the anterior and posterior commissure lines (slice thickness = 4 mm, field of view; in-plane resolution = 64 × 64; FOV = 220 × 220 mm; voxel size = 1.53 × 1.53 × 4 mm; repetition time, TR = 2700 ms; echo time, TE = 35 ms; and flip angle = 90°). The total time of resting acquisition was 8 min 6 s. A high-resolution T1-weighted spoiled gradient recalled 3D MRI sequence was obtained covering the whole brain for anatomical reference (224 slices, TR = 9.9 ms, TE = 4.6 ms, slice thickness = 1.0 mm, flip angle = 8°, FOV = 220 × 220 mm, voxel size = 1 × 1 × 1 mm). During fMRI scanning, participants were