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Altered brain functional networks in people with Internet gaming disorder: Evidence from resting-state fMRI

Lingxiao Wang [a], Lingdan Wu [b], Xiao Lin [c], Yifen Zhang [a], Hongli Zhou [a], Xiaoxia Du [d], Guangheng Dong [a,*]

[a] *Department of Psychology, Zhejiang Normal University, Jinhua, China*
[b] *Department of Psychology, University of Konstanz, Konstanz, Germany*
[c] *Center for Life Science, Peking University, Beijing, China*
[d] *Department of Physics, Shanghai Key Laboratory of Magnetic Resonance, East China Normal University, Shanghai, China*

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ABSTRACT

Although numerous neuroimaging studies have detected structural and functional abnormality in specific brain regions and connections in subjects with Internet gaming disorder (IGD), the topological organization of the whole-brain network in IGD remain unclear. In this study, we applied graph theoretical analysis to explore the intrinsic topological properties of brain networks in Internet gaming disorder (IGD). 37 IGD subjects and 35 matched healthy control (HC) subjects underwent a resting-state functional magnetic resonance imaging scan. The functional networks were constructed by thresholding partial correlation matrices of 90 brain regions. Then we applied graph-based approaches to analysis their topological attributes, including small-worldness, nodal metrics, and efficiency. Both IGD and HC subjects show efficient and economic brain network, and small-world topology. Although there was no significant group difference in global topology metrics, the IGD subjects showed reduced regional centralities in the prefrontal cortex, left posterior cingulate cortex, right amygdala, and bilateral lingual gyrus, and increased functional connectivity in sensory-motor-related brain networks compared to the HC subjects. These results imply that people with IGD may be associated with functional network dysfunction, including impaired executive control and emotional management, but enhanced coordination among visual, sensorimotor, auditory and visuospatial systems.

1. Introduction

Internet gaming disorder (IGD) has been considered as a serious public health issue all over the world with an increasing number of internet users over the past decades (Block, 2007; Cao et al., 2007; Fitzpatrick, 2008; Ko et al., 2012; Yuan et al., 2011). IGD is defined as a failure to control one's desire to excessively play online games with serious negative consequences (Ko et al., 2014b; Petry et al., 2014; Young, 1999). It has been reported as a cause of domestic, professional, financial and social difficulties (Achab et al., 2011) and is linked to anxiety, depression, and social phobias (Gentile et al., 2011). Although there is no intake of chemical intoxicant or substance, IGD shares many characteristics with chemical or substance addictions (American Psychiatric Association, 2013; Lesieur and Blume, 1993). Similar to substance addicts (Ko, 2014a; Ko et al., 2009), people with IGD show high levels of impulsivity (Ko et al., 2014a; Liu et al., 2014), unsuccessful cognitive control (American Psychiatric Association, 2013; Dong et al., 2012a), and impaired decision-making (Lin et al., 2015a). Given the similarities, the DSM-5 generated the diagnostic criteria of IGD and included it as a condition for further study in section III (American Psychiatric Association, 2013).

Persistent and recurrent online gaming provide players with repetitive rewarding experience and cognitive exercises, which might change the function and structure of the brain (Ko et al., 2015). Previous neuroimaging studies have reported that IGD is associated with widespread local alterations in many brain regions, including bilateral dorsolateral prefrontal cortex, orbitofrontal cortex, amygdala, caudate, insula, and partial temporal, occipital, and parietal regions (Ding et al., 2014; Dong et al., 2013a, 2012b; Han et al., 2010; Hoeft et al., 2008). Moreover, disrupted functional connectivity in specific regions or brain networks have been evident in IGD, such as decreased executive control network connectivity (Dong et al., 2015), decreased inter-hemispheric prefrontal lobe (Wang et al., 2015) and bilateral inferior parietal

* Corresponding author.
E-mail address: dongguangheng@zjnu.edu.cn (G. Dong).

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connectivity, and increased middle temporal gyrus and bilateral cerebellum posterior lobe connectivity (Ding et al., 2013). However, most neuroimaging researches were based on local regions of interest. Little is known about whether IGD alters the global topological properties of whole-brain networks.

Recently, graph theoretical analysis (GTA) provides a powerful framework to quantitatively characterize the topological organization of brain networks (Bassett and Bullmore, 2006; He and Evans, 2010; Wang et al., 2010a). GTA models the whole brain as a complex network, which is represented graphically by a set of nodes and edges (He and Evans, 2010). The nodes represent regions or voxels and the edges represent functional or structural connectivity among the nodes. Previous studies showed that the normal-brain intrinsic activity is functionally organized as a small-world, high efficient network, characterized by a high global integration and a high local specialization between brain regions (Achard et al., 2006; Hagmann et al., 2007; He et al., 2007; Salvador et al., 2005; Stam, 2004). Disrupted small-world brain network pattern has been observed in various diseases, such as schizophrenia (Liu et al., 2008; Lynall et al., 2010), Alzheimer's disease (He et al., 2008; Stam et al., 2009), attention-deficit hyperactivity disorder (Wang et al., 2009) and drug addictions (Liu et al., 2009). Recent researches have demonstrated that IGD shares similar neurobiological abnormalities with drug addictions (Ding et al., 2013; Zhang et al., 2015). Thus, the present study aimed to assess whether the global topological organization of the brain is disrupted in subjects with IGD, which may provide a further understanding of IGD and pave a way for the treatment of IGD.

Resting-state functional magnetic resonance imaging (R-fMRI), a relatively non-invasive imaging technique, has been extensively employed to reveal the intrinsic functional characteristics of the brain (Fox and Raichle, 2007; Schölvinck et al., 2010; Wang et al., 2010a). R-fMRI measures spontaneous low-frequency blood oxygen level-dependent (BOLD) signal fluctuations, when subjects are lying quietly in the scanner without doing a task (Guerra-Carrillo et al., 2014). In the current study, we combined GTA with R-fMRI to investigate the large-scale properties of brain functional organization and its disruption in subjects with IGD. Based on the findings mentioned above, we expected to detect different functional organization of whole-brain network between subjects with IGD and healthy controls.

Numerous previous studies have demonstrated that subjects with IGD are associated with impaired executive control ability (Dong et al., 2013b, 2015, 2010, 2011; Zhou et al., 2012). We hypothesized that the IGD subjects would show alteration in executive-control-related brain regions. IGD has been reported to be commonly comorbid with anxiety and depression (Gentile et al., 2011). Therefore, we expected to detect an alteration in emotion-related brain regions among subjects with IGD. Additionally, given the characteristics of online-gaming, a good coordination among hand movements, auditory sensory and visual sensory is required in game playing. Previous studies have demonstrated that people with IGD have enhanced coordination between sensory and motor systems (Dong et al., 2012b). Accordingly, we expected that the IGD subjects would show enhanced functional connectivity between multi-sensory and motor related brain regions.

2. Methods

2.1. Participants

This research was approved by the Human Investigations Committee of Zhejiang Normal University. 72 right-handed male university students were recruited in this study. Only males were included because of the high IGD prevalence in males (Király et al., 2014; Li et al., 2014). All participants signed an informed consent and underwent structured psychiatric interviews (MINI) proposed by an experienced psychiatrist (Lecrubier et al., 1997). The MINI results showed that all participants were free from psychiatric/neurological disorders, such as schizophrenia, anxiety, depression, and substance dependence. All participants reported no previous experience with gambling or illicit drugs (e.g., marijuana, heroin). Additionally, although all participants reported consumption of alcohol, none of them met DSM-5 criteria for dependence of any substances. All participants were asked not to take any medicine or substances including coffee, tea, and alcohol, on the day of scanning.

The subjects of IGD were diagnosed by Young's online Internet addiction test (IAT) (Young, 2009) and the nine DSM-5 criteria of IGD (Petry et al., 2014). Young's IAT contains 20 items, with each item assessing the degree of problems associated with Internet use on a 5-point-scale. Specifically, it measures compulsive use, withdrawal symptoms, psychological dependence, and related problems in family, work, school, sleep, and time management. Researches have proved the reliability and validity of Young's IAT in classifying IAD (Widyanto et al., 2011; Widyanto and McMurran, 2004). People who scored between 31 and 49 points are considered as average online users. They may surf the Internet a bit too long at times, but still have control over their usage. Scores between 50 and 80 represent occasional or frequent Internet-related problems due to uncontrolled Internet usage (http://netaddiction.com/internet-addiction-test/). We used the cut-off scores of 50 to differentiate IAD subjects from healthy controls. Then, to identify IGD, subjects with IAD were asked with the following question – 'do you spend most of your online time ($>80\%$) playing online games (Yes, No)'. Only those who answered 'Yes' were included in the IGD group. Further, subjects were screened with the DSM-5 criteria. The DSM-5 criteria for IGD includes nine items, with each item reflecting a DSM-5 criterion. Subjects who met five or more criteria were considered as IGD. In the present study, the IGD group (37 subjects) had much higher IAT score than the healthy controls (HC: 35 subjects), IGD: 73 ± 11.27, HC: 29 ± 10.80, $t\ (70) = -17.2$, $p < 0.001$. And the two groups showed no significant difference in age (IGD: 21.6 $\pm$ 1.64 years; HC: 21.6 $\pm$ 1.54 years; $t\ (70) = -0.054$, $p > 0.05$).

2.2. Image acquisition and pre-processing

All participants underwent an R-fMRI scan in a 3 T system (Siemens, Magnetom Trio Tim). The sequence parameters were as follows: repetition time (TR)=2000 ms; echo time (TE)=30 ms; flip angle=90°; interleaved sequence; 33 slice per volume; 3 mm thickness; field of view= $220 \times 220\ mm^2$; and matrix=64×64. Each functional run included 210 imaging volumes for each participant. All participants were instructed to lie quietly in the scanner and keep eyes closed during the acquisition.

Resting-state imaging data were analyzed using DPARSF (Chao-Gan and Yu-Feng, 2010) and REST (Song et al., 2011). Prior to the data preprocessing, the first 10 time points of each participant were discarded to avoid the impact of magnetization stabilization. Then, the remaining data were slice-timed, reoriented, and realigned to the first volume. None of the subjects were excluded based on the criteria of translational movement < 3.0 mm and $< 3.0°$ rotation. Next, the images were normalized to the Montreal Neurological Institute (MNI) space with $3 \times 3 \times 3\ mm^3$ resolution. Then, a regression of nuisance signals including cerebral spinal fluid, white matter, six motion vectors, and global signal was performed. Finally, the data were filtered with a temporal band pass between 0.01 and 0.08 Hz.