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Decreased functional connectivity in an executive control network is related to impaired executive function in Internet gaming disorder

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ABSTRACT

Background: Resting brain spontaneous neural activities across cortical regions have been correlated with specific functional properties in psychiatric groups. Individuals with Internet gaming disorder (IGD) demonstrate impaired executive control. Thus, it is important to examine executive control networks (ECNs) during resting states and their relationships to executive control during task performance.
Methods: Thirty-five IGD and 36 healthy control participants underwent a resting-state fMRI scan and performed a Stroop task inside and outside of the MRI scanner. Correlations between Stroop effect and functional connectivity among ECN regions of interest (ROIs) were calculated within and between groups.
Results: IGD subjects show lower functional connectivity in ECNs than do HC participants during resting state; functional-connectivity measures in ECNs were negatively correlated with Stroop effect and positively correlated with brain activations in executive-control regions across groups. Within groups, negative trends were found between Stroop effect and functional connectivity in ECNs in IGD and HC groups, separately; positive trends were found between functional connectivity in ECNs and brain activations in Stroop task in IGD and HC groups, separately.
Conclusions: Higher functional connectivity in ECNs may underlie better executive control and may provide resilience with respect to IGD. Lower functional connectivity in ECNs may represent an important feature in understanding and treating IGD.

1. Introduction

Internet addiction disorder (IAD) or problematic Internet use is defined as the excessive or uncontrolled use of the Internet with negative consequences to psychological, social, and/or work functioning aspects (Dong and Potenza, 2014; Young, 1998). It has been proposed as a diagnostic entity and studied for more than a decade; however, a standardized definition is only recently emerging, and this disorder was not included in the fourth edition of the Diagnostic and Statistical Manual (DSM) (Block, 2008; Liu et al., 2011; Shaw and Black, 2008). The DSM-5 committee considering substance-use disorders and addictions generated criteria for Internet gaming disorder (IGD, a subtype of IAD, refers to those who addicted to Internet online games), and this condition is included in the DSM's section 3, for disorders warranting additional study (American Psychiatric Association, 2013; Petry and O'Brien, 2013). People's online experience may change their cognitive function in a manner that may perpetuate Internet use, which may occur in the absence of drug-taking (Dong et al., 2011b; Holden, 2001; Weinstein and Lejoyeux, 2010), and individuals with certain brain and behavioral characteristics may have increased dispositions for developing IAD. However, the precise mechanisms underlying IAD are not well understood (Yau et al., 2012).

Internet addiction may consist of multiple subtypes; for example, subtypes relating to gaming, sexual preoccupations, and email/text messaging have been proposed (Block, 2008). In China, arguably the most important subtype of IAD may be IGD (Dong et al., 2011a, 2012, 2013c). One key feature of IGD is lost or diminished self-control over participation in Internet game-playing. Executive function enables individuals to inhibit their desires and limit engagement in hedonic behaviors under unfavorable circumstances (Dong et al., 2013a; Everitt et al., 2007; Goldstein and Volkow, 2011; Lin et al., 2014; Sofuoglu et al., 2013). Behavioral and/or brain differences between IGD and healthy controls have been observed during task performance on go/no-go (Dong et al., 2010), attention bias (Ko et al., 2013), set-shifting (Dong et al., 2014; Zhou et al., 2012), Stroop (Dong et al., 2011c), and error-processing (Dong et al., 2013c) tasks. Together, these data provide a neurobiological explanation for behavioral control difficulties that individuals with IGD often exhibit.

Abbreviations: IAD, Internet addiction disorder; IAT, Internet addiction test; IGD, Internet gaming disorder; ECN, Executive control network; DSM, Diagnostic and Statistical Manual; FC, Functional connectivity; fMRI, functional magnetic resonance imaging; HC, Healthy control; ROI, Region of interest.

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Although executive control tasks performed during imaging are important for observing effects of IGD within circumscribed brain areas (Dong et al., 2010, 2011c, 2014; Lin et al., 2015; Zhou et al., 2012), additional insight may be obtained by measuring alterations in interactions among brain regions (Chambers et al., 2003; Koob and Volkow, 2010; Soderpalm and Ericson, 2013). Neural activities in the human brain during rest, termed resting-state functional magnetic resonance imaging, have found that spontaneous neural activities are correlated across cortical regions in a non-random fashion (Fox and Raichle, 2007; Greicius et al., 2009; Zhu et al., 2011). These correlations may reflect functional connectivity (FC) among specific brain regions (Honey et al., 2009; Vincent et al., 2007). Studies on the functional connectivity in IAD subjects have already revealed some abnormal features. Hong et al., found a widespread and decrease of functional connectivity in the cortico-subcortical circuit (~24% with prefrontal and ~27% with parietal cortex) in 12 adolescents who were diagnosed with IAD (Hong et al., 2013); Li et al., found ineffective connectivity in the frontal–basal ganglia pathway in IAD adolescents, which was thought engaged in response inhibition (Li et al., 2014); Wee et al., found significant disruption in the functional connectome between regions located in the frontal, occipital, and parietal lobes in IAD subjects (Wee et al., 2014). Despite findings indicating FC across cortical regions, little is known about the psychological significance of these relationships, especially in clinical diagnoses like IGD.

In this study, we examine FC relationships in executive control networks (ECNs) during resting state and behavioral and neural measures of executive control (during Stroop performance) in 35 subjects with IGD and 36 healthy control (HC) subjects. The temporal binding model suggests that the synchronization of brain signals between neural systems is facilitates neural communications (Engel et al., 2001). Consistent with this model, resting brain activity can relate importantly to behavioral performance. For example, resting-state activity across face-selective cortical regions has been correlated with behavioral performance in a face performance task (Zhu et al., 2011). Individual differences in attitudes toward risk-taking have been related to the brain FC and may have implications for engaging in real-world risky behaviors (Cox et al., 2010). Thus, we hypothesized that executive control function might be indexed by resting-state brain activities in ECNs. To test this hypothesis, we examined correlations in spontaneous blood oxygen level dependence (BOLD) fluctuations among ECN brain regions during resting state and Stroop-related behavioral performance and brain activities.

Resting-state FC has been shown to differ between groups or as a function of clinically relevant measures. Performance deficits in cognitive control in drug-addicted individuals have been associated with reduced FC (Franken et al., 2010; Honey et al., 2009). Amygdala/medial–prefrontal–cortical connectivity at rest has been related to individual differences in anxiety (Kim et al., 2011). The aftermath of acute stress has been related to prolonged activation in an amygdala-related connectivity network (van Marle et al., 2010). Trauma victims (individuals exposed to earthquakes) show reduced temporal synchronization within the 'default mode' of resting-state brain function (Lui et al., 2009). Reduced FC between seeds within ECNs is consistent with behavioral and task-based imaging findings and self-reported cognitive deficits in drug-addicted populations (Ersche et al., 2006; Kelly et al., 2011). IGD subjects show impaired executive control ability relative to HC subjects (Dong et al., 2010, 2011c, 2013b; Ko et al., 2013; Zhou et al., 2012). Thus, we hypothesized that the impaired executive control in IGD would relate to decreased resting-state FC. To test this hypothesis, we examined between-group differences in FC in ECNs and examined whether FC related to brain activations and behavioral performance on the Stroop task.

2. Methods

2.1. Participant selection

The experiment conforms to The Code of Ethics of the World Medical Association (Declaration of Helsinki). The Human Investigations Committee of Zhejiang Normal University approved this research. Participants were university students and were recruited through advertisements. Participants were right-handed males (35 IGD and 36 HC subjects). IGD and HC groups did not significantly differ in age (IGD mean (SD) = 22.21 (3.08) years; HC mean (SD) = 22.81 (2.36) years; $t = 0.69$, $p = 0.49$). All subjects participated in a resting-state fMRI scan. 31 (16 IGD, 15 HC) performed a Stroop task in the scanner. The other 40 subjects (19 IGD, 21 HC) performed the same Stroop task outside of the scanner. Only males were included due to higher IGD prevalence in men than in women.

All participants provided written informed consent and underwent structured psychiatric interviews (MINI) (Lecrubier et al., 1997) performed by an experienced psychiatrist. The MINI was designed to meet the need for a short but accurate structured psychiatric interview for multicenter clinical trials and epidemiology studies. All participants were free of Axis-I psychiatric disorders assessed by the MINI (depression, anxiety disorder, schizophrenia, and substance dependence). Depression was further assessed with the Beck depression inventory (Beck et al., 1961) and only participants scoring less than 5 were included (IGD, 3.1 ± 0.53; HC, 2.4 ± 0.42). IGD and HC subjects did not fulfill DSM-IV criteria for abuse or dependence of any substances, although all IGD and HC participants reported some lifetime alcohol consumption. All participants were medication-free and were instructed not to use any substances, including coffee, on the day of scanning.

IAD was determined based on Young's online Internet Addiction Test (IAT) (Young, 2009) scores of 50 or higher (In this study, IAT score in IGD group: 64.4 ± 6.5; IAT score in HC: 22.8 ± 4.7). Young's IAT consists of 20 items associated with online Internet use including psychological dependence, compulsive use, withdrawal, related problems in school or work, sleep, family or time management. The IAT has demonstrated validity and reliability and may be used in classifying IAD (Widyanto and McMurran, 2004; Widyanto et al., 2011). For each item, a graded response is selected from 1 = "Rarely" to 5 = "Always", or "Does not Apply". Scores over 50 indicate occasional or frequent Internet-related problems and scores over 80 indicate significant problems (www.netaddiction.com). To classify IGD, individuals with IAD also needed to respond positively to the following question: 'you spend most of your online time playing games (>80%) (Yes, No)'.

2.2. Task and scanning

Magnetic resonance imaging data were acquired using a Siemens Trio 3 T scanner (Siemens, Erlangen, Germany) in East-China Normal University (Shanghai, China). The whole scanning process consisted of two parts: a resting state scan lasts for 7 min and a Stroop task lasts for 15 min.

2.3. Imaging parameters

Structural images were collected using a T1-weighted three-dimensional spoiled gradient-recalled sequence covering the whole brain (176 slices, repetition time = 1700 ms, echo time TE = 3.93 ms, slice thickness = 1.0 mm, skip = 0 mm, flip angle = 15, inversion time 1100 ms, field of view = 240 * 240 mm, in-plane resolution = 256 * 256). Functional MRI was performed on a 3 T scanner (Siemens Trio) with a gradient-echo EPI T2 sensitive pulse sequence in 33 slices (interleaved sequence, 3 mm thickness, TR = 2000 ms, flip angle 90°, field of view 220×220 mm^2, matrix 64×64). Stimuli were presented using Invivo synchronous system (Invivo Company, www.invivocorp.com/) through a screen in the head coil, enabling participants to view the stimuli.

2.4. Resting-state

The 'resting-state' was defined as no specific cognitive task during the fMRI scan. Participants were instructed to remain still, close their