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Altered functional connectivity in default mode network in Internet gaming disorder: Influence of childhood ADHD

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ABSTRACT

Objective: Internet gaming disorder (IGD) is a type of behavioral addiction characterized by abnormal executive control, leading to loss of control over excessive gaming. Attention deficit and hyperactivity disorder (ADHD) is one of the most common comorbid disorders in IGD, involving delayed development of the executive control system, which could predispose individuals to gaming addiction. We investigated the influence of childhood ADHD on neural network features of IGD.
Methods: Resting-state functional magnetic resonance imaging analysis was performed on 44 young, male IGD subjects with and without childhood ADHD and 19 age-matched, healthy male controls. Posterior cingulate cortex (PCC)-seeded connectivity was evaluated to assess abnormalities in default mode network (DMN) connectivity, which is associated with deficits in executive control.
Results: IGD subjects without childhood ADHD showed expanded functional connectivity (FC) between DMN-related regions (PCC, medial prefrontal cortex, thalamus) compared with controls. These subjects also exhibited expanded FC between the PCC and brain regions implicated in salience processing (anterior insula, orbitofrontal cortex) compared with IGD subjects with childhood ADHD. IGD subjects with childhood ADHD showed expanded FC between the PCC and cerebellum (crus II), a region involved in executive control. The strength of connectivity between the PCC and cerebellum (crus II) was positively correlated with self-reporting scales reflecting impulsiveness.
Conclusion: Individuals with IGD showed altered PCC-based FC, the characteristics of which might be dependent upon history of childhood ADHD. Our findings suggest that altered neural networks for executive control in ADHD would be a predisposition for developing IGD.

1. Introduction

Internet gaming disorder (IGD) is defined as excessive, compulsive internet gaming despite negative psychosocial consequences. IGD is a type of behavioral addiction characterized by multiple cognitive and behavioral symptoms similar to those of other addictive disorders (Kim et al., 2016; Kuss, 2013). It has been suggested that behavioral addictions involve dopaminergic dysfunction during reward processing and dysfunction in executive control (Fauth-Buhler et al., 2016). Executive control dysfunction is commonly associated with impulsivity, disinhibition, and compulsive behaviors. Indeed, various studies on IGD report impulsivity (Lee et al., 2015), impaired inhibition (Ding et al., 2014), and compulsivity (Dong et al., 2014), characteristics that can lead to loss of control during internet gaming.

Over the last several years, researchers have increased efforts to investigate distinguishable clinical features and the precise etiologies of IGD. Careful consideration, however, must be taken in understanding IGD as a distinct psychiatric disorder. Importantly, IGD subjects display diverse clinical presentations, which are significantly influenced by psychosocial factors (Lee and McKenzie, 2015; Park et al., 2016) and comorbid conditions (Han et al., 2015). Especially, there have been numerous evidences that imply strong association between IGD and ADHD (Cao et al., 2007; Ko et al., 2009; Yoo et al., 2004). ADHD frequently involves impaired processing in executive control, including performance monitoring (Weigard et al., 2016), reward processing (Fosco et al., 2015), and salience processing (Tegelbeckers et al., 2015). ADHD is one of the aberrant neurodevelopmental conditions. Neuroanatomic studies have

Abbreviations: ADHD, attention deficit and hyperactivity disorder; ANOVA, analysis of variance; AUDIT, alcohol use disorder identification test; BAI, Beck anxiety inventory; BDI, Beck depression inventory; BIS-11, Barratt impulsiveness scale-version 11; CAARS, Conners' adult ADHD rating scales; DMN, default mode network; FC, functional connectivity; fMRI, functional magnetic resonance imaging; IAT, internet addiction test; IGD, internet gaming disorder; IQ, intelligence quotient; MNI, Montreal Neurological Institute; mPFC, medial prefrontal cortex; PCC, posterior cingulate cortex; ROI, region of interest; SCID, structured clinical interview for DSM-IV; WAIS-III, Wechsler adult intelligence scale-III; WURS, Wender Utah rating scale.

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found that cortical maturation is delayed in ADHD (Shaw et al., 2007; Shaw et al., 2012b). This delay is most prominent in regions implicated in cognitive processing, such as executive control of attention and evaluation of reward. The executive dysfunction in subjects with ADHD might lead to loss of control over addictive drug use or behavior, and long-term outcomes of them are known to often involve addictive disorders (Shaw et al., 2012a). Taken together, we speculated that adolescents with a history of childhood ADHD could be more vulnerable to pathologic internet gaming as a result of delayed development of the executive control system.

Recently, neuroimaging studies have focused on functional brain networks to further understand cognitive processing. Dynamic interplay between networks of co-active brain regions may underlie cognitive processes (Bressler and Menon, 2010). Resting-state functional magnetic resonance imaging (fMRI) is a powerful method for exploring functional brain networks, which exhibit spontaneous synchronous fluctuations during non-goal-directed tasks. The most well-studied resting-state functional connectivity (FC) system is known as the default mode network (DMN), because high-amplitude fluctuations in this system reflect the brain's physiological baseline (Buckner et al., 2008). Key nodes in the DMN include the precuneus, posterior cingulate cortex (PCC), and medial prefrontal cortex (mPFC). Effective interconnection between the DMN and other large scale brain networks are thought to be important for cognitive function (Menon, 2011). Especially, several studies investigating large-scale brain networks have reported anti-correlated interaction between the DMN and the executive control network (Greicius et al., 2003; Raichle et al., 2001). Researchers have revealed that the DMN activity and functional connection between the DMN and other brain networks would influence on executive functions (Hampson et al., 2010; Spreng et al., 2010).

We investigated neural networks involved in deficits in executive control in IGD. We hypothesize that IGD can develop via two distinct pathways according to subject history of childhood ADHD. First, we postulate that in IGD subjects with childhood ADHD, delayed development of the executive control system predisposes subjects to lack of control during internet gaming. This excessive internet gaming stems from abnormalities in executive control from early childhood, rather than from distinguishable mechanisms of addiction. Secondly, we postulate that in IGD subjects without childhood ADHD, excessive internet gaming during adolescence induces detrimental changes in the maturation of the prefrontal cortex. Mechanisms of addiction (such as altered reward processing and enhanced strength of conditioned responses), in combination with prefrontal dysfunction, may lead to excessive and compulsive internet gaming behavior in these subjects. To test these hypotheses, we compared resting FC in the DMN in IGD subjects with and without a history of childhood ADHD. Because previous studies have identified PCC as the core hub of the DMN (Fransson and Marrelec, 2008), we designated the PCC as the seed region in our study. We assessed the relationship between altered FC and executive control deficits using scales for impulsiveness and adult ADHD rating scales.

2. Materials and methods

2.1. Participants

Participants were recruited from the local community through online advertisements, flyers, and word of mouth. The Institutional Review Board at Severance Mental Health Hospital, Yonsei University approved all protocols for this study. Written informed consent was obtained from all subjects prior to participation.

Study participants consisted of 44 young, male adult subjects with IGD (IGD group; 24.0 ± 2.6 years old) and 19 age-matched, healthy male controls (Table 1). All participants were evaluated for internet use patterns and undertook the internet addiction test (IAT) (Young, 1998) for screening of IGD. Participants who reported that gaming was the main purpose of their internet use and scored above 50 points in the IAT were classified as having IGD. Healthy controls (including non-gamers, n = 19) spent <2 h per day on internet gaming and scored below 50 points in the IAT.

IGD participants were divided into two groups according to the Wender Utah rating scale (WURS) (Ward et al., 1993): subjects with a childhood history of ADHD (IGD_{ADHD+} group, n = 20; 23.6 ± 2.5 years old) and subjects without a history of childhood ADHD (IGD_{ADHD-} group, n = 24; 24.3 ± 2.7 years old). Adult ADHD symptoms were assessed using the Conners' adult ADHD rating scales (CAARS) (Cleland et al., 2006). All participants were evaluated using the structured clinical interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (SCID), to determine the presence of other mental disorders. All participants undertook the Korean version of the Wechsler adult intelligence scale III (WAIS-III) to estimate intelligence quotient (IQ). All participants were right-handed and completed self-report questionnaires, including the alcohol use disorders identification test (AUDIT) (Saunders et al., 1993), the Beck depression inventory (BDI) (Beck et al., 1961), and the Beck anxiety inventory (BAI) (Yook, 1997). Impulsivity was assessed using the Barratt impulsiveness scale-version 11 (BIS-11) (Patton et al., 1995). The BIS-11 consists of

Table 1
Demographic and clinical variables of participants.

	Controls (n = 19)	IGD_{ADHD-} (n = 24)	IGD_{ADHD+} (n = 20)	Test	P-value	Post Hoc Bonferroni
Age	23.6 ± 2.0	24.3 ± 2.7	23.6 ± 2.5	F(2,60) = 0.559	0.575	
Verbal IQ	103.4 ± 12.5	101.9 ± 13.1	98.0 ± 11.3	F(2,60) = 1.012	0.370	
Performance IQ	104.2 ± 18.8	100.6 ± 17.7	104.8 ± 14.3	F(2,60) = 0.386	0.682	
IAT	27.7 ± 12.1	60.2 ± 9.0	67.4 ± 10.6	F(2,60) = 80.570	<0.001	IGD_{ADHD-}, IGD_{ADHD+} > HC
WURS	24.0 ± 13.7	26.8 ± 13.1	60.8 ± 12.6	F(2,60) = 50.322	<0.001	IGD_{ADHD+} > HC, IGD_{ADHD-}
CAARS						
Inattention/Memory	48.0 ± 5.7	53.3 ± 7.8	55.4 ± 4.2	F(2,60) = 7.344	0.001	IGD_{ADHD-}, IGD_{ADHD+} > HC
Hyperactivity/Restlessness	46.7 ± 6.6	51.8 ± 5.6	52.4 ± 5.5	F(2,60) = 5.416	0.007	IGD_{ADHD-}, IGD_{ADHD+} > HC
Impulsivity/Emotional lability	48.6 ± 6.2	52.8 ± 5.8	54.8 ± 5.5	F(2,60) = 5.594	0.006	IGD_{ADHD+} > HC
Problems with self-concept	61.0 ± 9.4	69.8 ± 9.5	71.7 ± 9.4	F(2,60) = 7.165	0.002	IGD_{ADHD-}, IGD_{ADHD+} > HC
AUDIT	8.8 ± 5.6	10.7 ± 8.5	12.2 ± 8.7	F(2,60) = 0.888	0.418	
BDI	6.0 ± 4.8	12.1 ± 6.1	14.6 ± 6.9	F(2,60) = 10.486	<0.001	IGD_{ADHD-}, IGD_{ADHD+} > HC
BAI	4.5 ± 4.8	8.5 ± 5.6	13.1 ± 5.4	F(2,60) = 12.903	<0.001	IGD_{ADHD+} > HC, IGD_{ADHD-}
BIS	51.4 ± 8.1	58.5 ± 9.2	60.8 ± 11.3	F(2,60) = 5.069	0.009	IGD_{ADHD+} > HC
Cognitive	15.8 ± 2.9	17.1 ± 3.1	16.4 ± 2.8	F(2,60) = 1.126	0.331	
Motor	14.9 ± 3.2	17.7 ± 3.7	19.8 ± 5.0	F(2,60) = 7.307	0.001	IGD_{ADHD+} > HC
Non-Planning	20.7 ± 3.8	23.7 ± 3.8	24.5 ± 5.4	F(2,60) = 4.014	0.023	IGD_{ADHD+} > HC

ADHD: attention deficit hyperactivity disorder, AUDIT: alcohol use disorders identification test, BAI: Beck anxiety inventory, BDI: Beck depression inventory, BIS: Barratt impulsiveness scale, CAARS: Conners' adult ADHD rating scales, HC: healthy controls, IAT: internet addiction test, IGD: internet gaming disorder, IQ: intelligence quotient, WURS: Wender Utah rating scale.