Brain connectivity and psychiatric comorbidity in adolescents with Internet gaming disorder

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ABSTRACT

Prolonged Internet video game play may have multiple and complex effects on human cognition and brain development in both negative and positive ways. There is not currently a consensus on the principle effects of video game play neither on brain development nor on the relationship to psychiatric comorbidity. In this study, 78 adolescents with Internet gaming disorder (IGD) and 73 comparison subjects without IGD, including subgroups with no other psychiatric comorbid disease, with major depressive disorder and with attention deficit hyperactivity disorder (ADHD), were included in a 3 T resting state functional magnetic resonance imaging analysis. The severity of Internet gaming disorder, depression, anxiety and ADHD symptoms were assessed with the Young Internet Addiction Scale, the Beck Depression Inventory, the Beck Anxiety Inventory and the Korean ADHD rating scales, respectively. Patients with IGD showed an increased functional correlation between seven pairs of regions, all satisfying q < 0.05 False discovery rates in light of multiple statistical tests: left frontal eye field to dorsal anterior cingulate, left frontal eye field to right anterior insula, left dorsolateral prefrontal cortex (DLPFC) to left temporoparietal junction (TPJ), right DLPFC to right TPJ, right auditory cortex to right motor cortex, right auditory cortex to supplementary motor area and right auditory cortex to dorsal anterior cingulate. These findings may represent a training effect of extended game play and suggest a risk or predisposition in game players for over-connectivity of the default mode and executive control networks that may relate to psychiatric comorbidity.

Keywords Brain connectivity, fMRI, functional magnetic resonance imaging, Internet gaming disorder.

INTRODUCTION

Internet gaming disorder in adolescents

Internet and computer gaming now rank among the most popular leisure activities and represent a large and growing segment of the entertainment industry. More than one billion people worldwide are thought to participate in Internet games, and the growth rate of the Internet gaming industry has been estimated at 8 percent per year in 2012 (PC Gaming Alliance 2013). As Internet gaming has become more prevalent, several studies of Internet gaming-related pathology have been published, outlining the negative consequences of excessive Internet game play, the prevalence and the related risk factors (Griffiths, Kuss & King 2012). However, it has been difficult to define compulsive video game play as a disorder because of the following: (1) there are no gold standard criteria for Internet addiction; (2) the prevalence rates differ with respect to cultural environment and are further complicated by the use of different assessment tools and diagnostic standards; and (3) Internet addiction is significantly affected by social and family environment, psychosocial factors and comorbid symptoms (Kuss et al. 2014).

While considerable media and scholarly attention have focused on the potential detrimental consequences of compulsive Internet video game play (Sharif & Sargent 2006; Gentile et al. 2011), more constructive and positive consequences of video game play have also been suggested. For example, there is reported to be an association with learning in the context of a video game (Blumberg, Rosenthal & Randall 2008), enhancement of selective attention in response to unexpected events (Hubert-Wallander et al. 2011) and improved understanding of
social and contextual cues (De Kort, Ijsselsein & Gajadhar 2008). In addition, few studies have been able to disentangle the effects of comorbid conditions, such as attention deficit hyperactivity disorder (ADHD), major depression (MDD), anxiety disorder and personality disorders (Xiuqin et al. 2010), despite consistent studies noting that a large numbers of ‘Internet gaming disorder’ (IGD) patients have comorbidity with ADHD and MDD (Ha et al. 2006). Internet video gaming may therefore have multiple effects on human cognition and brain development (Bavelier et al. 2011). Nevertheless, such consequences are poorly understood, and there is no consensus with respect to the principle effects of video game play on brain development. Because of this lack of consensus, IGD is not recognized as a formal diagnosis in the Diagnostic and Statistical Manual for Psychiatric Disorders (American Psychiatry Association 2013).

**Functional brain activity during Internet game play**

In response to pictures or videos depicting Internet game play, IGD subjects have been reported to show increased activation in brain regions within the frontal cortex [inferior frontal, orbitofrontal, anterior cingulate and dorsolateral prefrontal cortex (DLPFC)], temporal cortex (hippocampus and parahippocampal gyrus), parietal cortex, occipital cortex and basal ganglia (thalamus nucleus accumbens and caudate nucleus) (Ko et al. 2009; Han et al. 2010a; Sun et al. 2012). In resting state functional magnetic resonance imaging (fMRI) studies, the results have been more heterogeneous (Ding et al. 2013; Wee et al. 2014). Hong et al. (2014) reported that IGD adolescents had reduced functional connectivity from dorsal putamen to the posterior insula-parietal operculum. More time spent playing Internet games was associated with greater functional connectivity between the dorsal putamen and bilateral primary somatosensory cortices (Hong et al. 2014). Wee et al. (2014) found evidence for disruption of long-range connections between frontal, parietal and occipital cortices in IGD patients. Ding et al. (2013) reported that Internet addiction scores were positively associated with functional connectivity between posterior cingulate gyrus and right preconus, posterior cingulate gyrus, thalamus, caudate, nucleus accumbens, supplementary motor area (SMA) and lingual gyrus (Table 1).

Regions found in fMRI studies of IGD have previously been associated with mood, craving, addiction, attention, impulsive behaviors and personality in complex human behaviors (Farb, Anderson & Segal 2012). In addition, coordinated attention to salient events during Internet game play requires integration of information from multiple senses (Seeley et al. 2007). Moreover, inconsistent neuroimaging findings in resting state studies with cross-sectional, small samples and simple fMRI paradigm designs have limited determination of whether those brain regions represent causal factors for IGD as opposed to training effects of excessive Internet game play. Brain function governing complex human behavior is thought to involve distributed brain networks, including the salience network (anterior insular and cingulate cortices) and dorsal (frontal eyefield, intraparietal sulcus and visual cortex) and ventral attention system (ventral frontal cortex, temporal parietal junction and auditory–visual cortices) (Greicius et al. 2003; Fox et al. 2006).

**Hypothesis**

Based on previous studies, but with a larger sample size and new analytic methods, we hypothesized that Internet video game play would increase brain connectivity within brain attentional networks in patients with IGD as well as in IGD patients with comorbid ADHD or MDD.

**METHODS**

**Subjects**

One hundred eighty male adolescents (10–19 years old) who visited the Department of Psychiatry at Chung-Ang University Hospital, including 106 patients seeking treatment for IGD and 80 comparison subjects without IGD, were studied. Both IGD adolescents and control adolescents were diagnosed using the Korean Kiddie Schedule for Affective Disorders and Schizophrenia—Present and Lifetime version (Kim et al. 2004). A child psychiatrist (D. H. H.) interviewed all adolescents to confirm the diagnosis of comorbidities (Table 2).

All subjects were also asked to complete questionnaires regarding the pattern of on-line game play (Han et al. 2014), the Young Internet Addiction Scale (YIAS) (Young 1996), the Beck Depression Inventory (Beck et al. 1961) and the Beck Anxiety Inventory (Beck et al. 1988). Parents and main caretakers completed the Korean ADHD rating scale (K-ARS) for patients (So et al. 2002). Internal consistency of the K-ARS has been reported to range from 0.77 to 0.89 (So et al. 2002). The criteria for the IGD group have been employed in previous studies (Han, Hwang & Renshaw 2010b; Kim et al. 2012): (1) male adolescents less than 19 years of age; (2) right handed; (3) excessive on-line game play time (more than 4 hours per day/30 hours per week); (4) YIAS scores >50; (5) irritable, anxious and aggressive behavior when forced to stop on-line game play; and (6) impaired behaviors or distress, economic crisis and maladaptive regular life patterns including disrupted diurnal rhythms (sleeping during the day due to gaming at night), irregular meals, failure to maintain personal hygiene and school refusal. Exclusion criteria for the IGD
<table>
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<th>Authors</th>
<th>Subjects</th>
<th>Controlled comorbidity</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhang et al. (2015)</td>
<td>74 IGD young adults versus 41 healthy controls</td>
<td>History of SUD use and gambling, Psychiatric conditions including depression and anxiety disorder</td>
<td>↑FC between anterior insular, ACC, putamen, angular gyrus and precuneus</td>
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<td>Hong et al. (2015)</td>
<td>12 IGD adolescents versus 11 healthy controls</td>
<td>Psychiatric disorders</td>
<td>↑FC between posterior insular, postcentral gyrus, precenral gyrus, supplemental motor area and superior temporal gyrus</td>
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<td>Wee et al. (2014)</td>
<td>17 IGD adolescents versus 16 healthy controls</td>
<td>History of SUD, Psychiatric conditions including affective disorder, anxiety, compulsivity, schizophrenia and autism, Physical disorder related to motion, digestive, nervous, respiratory, circulation, endocrine and reproduction</td>
<td>↑FC between dorsal putamen to the posterior insula-parietal operculum</td>
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<td>Ding et al. (2013)</td>
<td>17 IGD adolescents versus 24 healthy controls</td>
<td>History of SUD, Hx of schizophrenia, depression, anxiety disorder and psychotic episodes, Hx of psychotherapy or any medications, Physical disorder related to motion, digestive, nervous, respiratory, circulation, endocrine and reproductive</td>
<td>↑FC between bilateral cerebellum posterior lobe and middle temporal gyrus</td>
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<td>Liu et al. (2010)</td>
<td>19 IGD college students versus 19 healthy controls</td>
<td>History of psychiatric diseases</td>
<td>↑Regional homogeneity within cerebellum, brainstem, right cingulate gyrus, bilateral parahippocampus, right frontal lobe, left superior frontal gyrus, right inferior temporal gyrus, left superior temporal gyrus and middle temporal gyrus</td>
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<tr>
<td>Wang et al. (2015)</td>
<td>17 IGD adolescents versus 24 healthy controls</td>
<td>History of SUD, Hx of schizophrenia, depression, anxiety disorder and psychotic episodes, Hx of psychotherapy or any medications, Physical disorder related to motion, digestive, nervous, respiratory, circulation, endocrine and reproductive</td>
<td>↑FC between the left and right superior frontal gyrus (orbital part), inferior frontal gyrus (orbital part), middle frontal gyrus and superior frontal gyrus</td>
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<td>Kim et al. (2015)</td>
<td>16 IGD adolescents versus 15 healthy controls</td>
<td>Depression, anxiety disorder and impulsivity, Hx of head injury, seizure, mental retardation and psychotic disorder</td>
<td>↑FC within the PCC of the IGD</td>
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<td>Dong, Huang and Du (2012)</td>
<td>15 IGD adolescents versus 14 healthy controls</td>
<td>History of SUD, Psychiatric conditions including affective disorder, anxiety, compulsivity, schizophrenia and autism, Drug naïve</td>
<td>↑Regional homogeneity within brainstem, inferior parietal lobule, left posterior cerebellum and left middle frontal gyrus</td>
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</table>

fMRI = functional magnetic resonance imaging; IGD = Internet gaming disorder; Hx of SUD = history of substance abuse; FC = functional connectivity; ACC = anterior cingulate cortex; STG = superior temporal gyrus; ↑ = increase; ↓ = decrease; PCC = posterior cingulate cortex.
group included the following: (1) adolescents with a history of psychotic disorders and psychotropic medication usage; (2) IQ < 80; (3) substance abuse history; (4) adolescents with neurological or medical disorders; and (5) participants with claustrophobia. The criteria for the control group included the following: (1) male adolescents with age less than 19 years and (2) right handed. Exclusion criteria for control group included the following: (1) male adolescents with psychiatric disorders except for ADHD or MDD; (2) adolescents taking psychiatric medications; (3) IQ < 80; (4) substance abuse history; (5) adolescents with neurological or medical disorders; and (6) participants with claustrophobia.

Of 104 IGD adolescent participants referred for brain imaging, 24 adolescents had no other psychiatric comorbid disease, 41 adolescents had comorbid MDD and 35 adolescents had ADHD. In addition, four adolescents had comorbid psychotic disorders including schizophrenia and psychotic disorder NOS. Of the 76 control subjects without IGD, 23 adolescents had no psychiatric disorder, 20 adolescents had MDD and 33 adolescents had ADHD. Twelve-four adolescents had contraindications to or did not complete resting state MRI scanning.

Twenty-one IGD adolescents with ADHD had taken stimulants. MDD adolescents had no history of taking antidepressant medication. One data set from the IGD group (in the MDD cohort) and three data sets from the control group (two in the ADHD and one within the MDD cohort) did not have images that were acceptable for analysis. Ultimately, 78 IGD adolescents (24 adolescents with no other psychiatric comorbid disease, 40 adolescents with comorbid MDD and 14 adolescents had ADHD) as well as 73 control subjects without IGD (23 adolescents with no psychiatric disorder, 19 adolescents with MDD and 31 adolescents with ADHD) were included in the imaging analysis. The Chung-Ang University Hospital Institutional Review Board approved the research protocol for this study. Written informed consent was provided by parents, and assent was obtained for adolescent participants.

### Table 2 Demographic characteristics.

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<tr>
<th>IGD groups (78)</th>
<th>Control groups (73)</th>
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<tr>
<td></td>
<td>+ADHD (14)</td>
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<tr>
<td>Agea</td>
<td>14.7 ± 2.0</td>
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<td></td>
<td>14.6 ± 2.0</td>
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<tr>
<td>Educationb</td>
<td>7.5 ± 1.6</td>
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<tr>
<td></td>
<td>7.3 ± 1.6</td>
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<tr>
<td>Genre</td>
<td>RPG</td>
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<td></td>
<td>Others</td>
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<tr>
<td>None</td>
<td>—</td>
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<tr>
<td>YIASc</td>
<td>69.9 ± 10.0</td>
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<td></td>
<td>73.7 ± 11.3</td>
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<td></td>
<td>11.7 ± 9.1</td>
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<td>26.8 ± 7.9</td>
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<td>BDIe</td>
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<td>10.3 ± 4.1</td>
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<td>6.9 ± 1.4</td>
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</table>

ANOVA between IGD + ADHD, IGD + MDD and pure IGD in IGD group. ANOVA between control ADHD, MDD and HC in healthy control group. aIGD: F = 7.9, MS = 26.8, P < 0.01, +MDD < +ADHD + Pure; Control: F = 0.6, MS = 1.98, P = 0.6. bIGD: F = 9.7, MS = 20.9, P < 0.01. cIGD: F = 422.1, P < 0.01, Pure = +ADHD; Control: F = 24.5, MS = 151.4, P < 0.01. dIGD: F = 24.5, MS = 151.4, P < 0.01, +MDD c + ADHD; Control: F = 210.9, MS = 5303.0, P < 0.01, +ADHD c + ADHD + Pure; Control: F = 351.4, MS = 4878.2, P < 0.01. eIGD: F = 7.9, MS = 26.8, P < 0.01, +ADHD < + ADHD + Pure; Control: F = 0.6, MS = 1.98, P = 0.6. fIGD: F = 468.8, MS = 151.4, P < 0.01, +ADHD c + ADHD; Control: F = 210.9, MS = 5303.0, P < 0.01, +ADHD c + ADHD + Pure; Control: F = 351.4, MS = 4878.2, P < 0.01, +ADHD c + ADH.

**Imaging processing and analysis**

Resting state brain activity was assessed using 3 T blood oxygen level dependent functional magnetic resonance imaging (Philips Achieva 3.0 Tesla TX MRI scanner...
TR = 3 seconds, 12 minute scan, 240 volumes, 128 × 128 matrix, 40 slices at 4.0 mm slice thickness. Pre-processing included despiking (AFNI, National Institute of Mental Health, Bethesda Maryland: 3dDespike), motion correction (SPM 12b), coregistration to MPRAGE image (SPM 12b), normalization to MNI space (SPM 12b), temporal detrend (Matlab: detrend.m), bandpass filtering (Matlab (Mathworks, Natick, MA): idealfilter.m) and voxelwise regression of identically bandpass filtered time series of six head motion parameters, degraded CSF, degraded white matter and facial soft tissues (Matlab) as previously described (Anderson et al., 2011; Anderson et al., 2013). To address the possibility of micro-head movements affecting connectivity results (Power et al., 2012; Van Dijk, Sabuncu & Buckner, 2012), censoring of time points with head motion > 0.2 mm was performed (Power et al., 2012). No regression of the global signal was performed (Murphy et al., 2009; Anderson et al., 2011; Saad et al., 2012). We extracted 25 regions from the Yeo et al. functional parcellation of the brain (Yeo et al., 2011) to identify whether patients seeking treatment for IGD show differential functional connectivity between hubs of major functional brain networks. The 25 subregions selected (Fig. 1) represented hubs of all seven canonical brain networks of Yeo et al. (2011). Fisher-transformed correlation coefficients were measured for each pair of regions of interest in each subject.

Statistical analysis

A two-tailed t-test was used to evaluate adolescents with IGD compared with adolescents without IGD, and multiple comparison correction over 300 pairs of 25 regions was performed using an acceptable false discovery rate \( q < 0.05 \). Similar t-tests were performed on subsamples not only of adolescents with and without IGD but who also exhibited no psychiatric comorbidity, ADHD or MDD. A linear model was constructed for each connection including functional connectivity, age in months, root-mean-square mean head motion, YIAS score, ADHD score, BDI score and BAI score. Partial correlation of each covariate was calculated to assess the specific impact of each covariate on connectivity.

RESULTS

Patients with IGD showed increased functional correlations between seven pairs of regions (Fig. 2), all satisfying \( q < 0.05 \) False discovery rate over all statistical tests: left frontal eye field to dorsal anterior cingulate (\( P = 0.00018 \)), left frontal eye field to right anterior insula (\( P = 0.00023 \)), left DLPFC to left temporoparietal junction (TPJ, \( P = 0.00046 \)), right DLPFC to right TPJ (\( P = 0.00012 \)), right auditory cortex to right motor cortex (\( P = 0.00074 \)), right auditory cortex to SMA (\( P = 0.00098 \)) and right auditory cortex to dorsal anterior cingulate (\( P = 0.00080 \)).

In analyses using a threshold of \( P < 0.05 \), uncorrected for multiple comparisons, results demonstrate that primarily hyperconnectivity was observed with greatest involvement of the bilateral anterior insula and anterior cingulate cortex, frontal eye fields, SMA, and auditory and motor cortices (Fig. 3). Data are also shown in Fig. 3 comparing subsets of the patient sample grouped by comorbidity. In patient subsamples with no other comorbidities, with ADHD and with MDD, higher connectivity was
observed in all three samples between the left frontal eye field and salience network (anterior insula and dorsal anterior cingulate), as well as between ipsilateral DLPFC and TPJ. Three factor ANOVA with IGD, ADHD and MDD as variables did not show FDR multiple comparison corrected results that were significant for ADHD or MDD.

To further test this hypothesis, we used a general linear model including age, mean head motion, depression, anxiety, ADHD score and YIAS. YIAS measurements showed partial correlations with connectivity between very similar regions of interest as seen in Fig. 2 (top left) with all seven of the connections from Fig. 2 showing positive correlations with YIAS score ($P < 0.05$), when psychiatric comorbidities of ADHD, anxiety and MDD were included in the model.

Relationships are also shown ($P < 0.05$, uncorrected) between connectivity and age, head motion, ADHD Score, Beck Anxiety Inventory and Beck Depression Inventory. Residual partial correlation to mean head motion showed greatest effects of a negative correlation between medial orbitofrontal cortex and other regions, consistent with known susceptibility in the frontal poles from nodding motions but different from the effects associated with Internet game play. No differences were observed in root-mean-square head motion between the IGD and the non-IGD groups ($P = 0.84$, two-tailed $t$-test), discounting head motion as a plausible explanation for connectivity differences associated with video game play.

**DISCUSSION**

The current results showed an association between chronic exposure to Internet game play and increased connectivity between the salience network (anterior insula and dorsal anterior cingulate) and frontal eye fields, between ipsilateral DLPFC and TPJ and between auditory cortex and motor cortex and SMA. These findings of increased connectivity are not explained by other psychiatric comorbidities in the patient sample, are positively and significantly associated with quantitative metrics of Internet addiction and are not explained by age or head motion. These results demonstrate a correlative relationship between functional connectivity and Internet game exposure, and the specific connections involved are all expected to be engaged during video game play.

**Frontal eye field, anterior cingulate, anterior insular, auditory cortex, motor cortex and supplementary motor cortices**

Coordinated attention to salient events during Internet game play requires integration of information from multiple senses including visual–auditory integration, object and movement detection, decision-making and tremendous amount of semantic information (Williams & Kirschner 2012; Levac et al. 2014). For data processing using multisensory auditory–visual attention, the right frontal–cingulate–parietal network has been implicated (Supekar & Menon 2012). More specifically, that network includes anterior insular, ventrolateral prefrontal cortex, dorsolateral prefrontal cortex and posterior parietal cortex (Menon & Uddin 2010).

The frontal eye fields in superior frontal cortex are activated in response to finger pointing and saccade tasks (Hagler, Riecke & Sereno 2007). Saccadic movement of the eyes is associated with detection of an object as well as control of attention and decision-making (Gold & Shadlen 2007). As a component of the dorsal attention
network (frontal eye field, intraparietal sulcus and visual cortex), the frontal eye field is thought to be associated with direction-specific responses (Bressler et al. 2008). In a dual N-back task including auditory and visual stimuli, Medeiros-Ward, Watson and Strayer (2015) reported that supertaskers (who were extraordinary at multi-tasking) used anterior cingulate and posterior frontopolar prefrontal cortices more efficiently compared with controls. Frontal eye fields are likely to represent a critical substrate for effective video game play, given the constant need for redirecting one’s eyes and attention to targets of interest. Anterior insula is thought to facilitate multisensory attention including auditory–visual attention (Chen et al. 2015). In addition, the insula serves as a major control hub linking frontal, cingulate and parietal cortices and signals from anterior insula, which project to dorsal anterior cingulate during auditory–visual attention (Chen et al. 2015).

The anterior insula, together with the dorsal anterior cingulate cortex, comprise the brain’s novelty detection or salience network (Seeley et al. 2007), active during unexpected, novel or salient stimulus perception regardless of the underlying sensory modality. Greatest involvement of the salience network (bilateral anterior insula and anterior cingulate cortex) and the regions that are associated with rapid motor responses to audiovisual stimuli (motor cortex, SMA, and auditory and motor cortices) was observed. This network is also likely to play a critical role in game play, given the recurrent need to quickly identify salient changes in the gaming environment and translate those to rapid action.

Figure 3 Differences in functional connectivity in subsamples of Internet game players with varying comorbidities. Color bars show t-statistics between groups in each case. Top left: all subjects with and without chronic compulsive game play. Results are thresholded for display at $P < 0.05$, uncorrected. Top right: connectivity differences for subjects with and without chronic compulsive game play, but without other comorbidity. Bottom left: connectivity differences for participants with ADHD and compulsive game play compared with participants with ADHD without compulsive game play. Bottom right: connectivity differences for participants with major depressive disorder and compulsive game play compared with participants with major depressive disorder without compulsive game play. DLPFC = dorsolateral prefrontal cortex; FEF = frontal eye field; IPS = intraparietal sulcus; SMA = supplementary motor area; MT = middle temporal; TPJ = temporoparietal junction; PCC = posterior cingulate cortex; MPF = medial prefrontal cortex.
Our results dovetail with the study of Zhang et al. (2015) on functional connectivity with a large sample of IGD (N = 74). Zhang et al. (2015) suggested that the insula is particularly important in brain responses to Internet game play resulting in the manifestation of IGD symptoms. However, there were differences between our study and the study of Zhang et al. (2015). First, our study analyzed 25 subregions representing hubs of all seven canonical brain networks, while Zhang et al. (2015) used four spherical seed regions in the insula for resting state fMRI analysis. Second, Zhang et al. (2015) excluded subjects with depression, anxiety and substance dependence. However, our study investigated subjects with MDD and ADHD and included those subjects in analysis. Our findings independently confirm hyperconnectivity from the anterior insula to anterior cingulate, SMA and motor cortex in agreement with the results reported by Zhang et al. (2015).

Taken together, our results suggest that chronic Internet game play may increase functional connectivity, specifically between regions that are associated with motion detection, visual–auditory multi-tasking and efficient processing of dynamical audiovisual stimuli. Such effects are consistent with the possibility of a constructive, adaptive effect of prolonged Internet game play (Blumberg et al. 2008; De Kort et al. 2008; Hubert-Wallander et al. 2011) facilitating more rapid responses of attention to sensory perception.

**Dorsolateral prefrontal cortex and temporoparietal junction**

Coactivation of the dorsal attention network (frontal eye field, intraparietal sulcus and visual cortex) and ventral attention network (ventral frontal cortex, temporal parietal junction and visual cortex) can be frequently seen in the context of stimulus-driven attention to salient behaviorally relevant events with the components of orienting to exogenous cues, reorienting to unexpected events and response to contextual cues (Corbetta & Shulman 2002). The story, one of Internet gaming’s core structures, is associated with contextual cues and social cognition (Prensky 2001). In addition, action video games are thought to facilitate selective attention in response to unexpected events and perceptual templates (Prensky 2001; Bejjanki et al. 2014). The TPJ is a component of the default mode network, associated with storage of semantic memories and information (Andrews-Hanna et al. 2010) and has different cognitive domains such as attention, social cognition and episodic memory (Kamourieh et al. 2015). Multitasking, compared with both visual and auditory single trials, activated a predominantly right-sided fronto-parietal network (Deprez et al. 2013). When adding the additional short-term memory task, a larger and more bilateral frontoparietal network was activated (Deprez et al. 2013), and the activation of TPJ was suppressed (Todd, Fougnie & Marois 2005). However, the TPJ activated in response to salient non-targets including information of target stimulus (contextual cueing) in a visual search array (Geng & Mangun 2011).

Increased connectivity between DLPFC and TPJ may have multifactorial effects, potentially positive and negative. Communication between brain regions thought to process attention and working memory (DLPFC), and semantic knowledge (TPJ) may facilitate more rapid decision-making and integration of attention and internally directed cognitive networks. Yet there is a growing literature that such overconnectivity of the default mode and brain attentional networks may also be maladaptive. Overconnectivity of these networks, which are competitive or anticorrelated in typical development (Fox et al. 2005), has been observed in several neurodevelopmental and neuropsychiatric conditions including autism (Anderson et al. 2011), Down syndrome (Anderson et al. 2013) and schizophrenia (Whitfield-Gabrieli et al. 2009), and segregation of the default mode and attention control networks has been associated with improved performance on executive tasks requiring response inhibition (Thomason et al. 2008).

**Comparing subsets of the patient sample grouped by comorbidities**

Several studies have suggested that psychiatric comorbidities including MDD, bipolar disorder and suicidal ideation may be associated with clinical symptom aggravation and cognitive dysfunction in IGD patients (Park et al. 2011; Park et al. 2013). In 538 female adolescents, MDD, bipolar disorder and suicidal ideation were noted to worsen the symptoms associated with IGD (Park et al. 2013). Park et al. (2011) suggested that the IGD group showed reduced comprehension compared with healthy adolescents.

However, the present results indicate that YIAS scores in the IGD + MDD group were lower than those in the pure IGD group. Moreover, all patient subsamples including those with no other comorbidities, those with ADHD and those with MDD showed higher connectivity in similar brain regions between the salience network and the regions linked with rapid motor responses to visual and audiovisual stimuli and semantic memory (frontal eye field, motor cortex, DLPFC and TPJ). These changes were not significantly associated with the usual metrics of ADHD or depression in adolescents. MDD adolescents were observed to have decreased connectivity within the visual and auditory attention networks (Baune et al. 2014), and ADHD adolescents have been reported to have decreased connectivity within the salience network.
Resting state fMRI results demonstrate increased functional connectivity between the frontal eye fields and the salience network as well as between auditory and motor cortices in patients seeking treatment for IGD, many of the patients in the sample exhibited psychiatric comorbidity. In addition, evaluating ‘connections’ between 300 pairs of 25 regions with multiple comparison correction raises the risk of type II statistical error. Readers should therefore be cautious in interpreting the study results. Second, the cross-sectional design of the study cannot fully differentiate the causes and effects of Internet game play in adolescents. Future studies may benefit from longitudinal assessments of these effects. Finally, the present study recruited only male patients. Females with excessive Internet use typically experience a higher comorbidity of mood disorders compared with male patients (Park et al. 2013). In addition, differences in brain connectivity between non-compulsive, habitual gamers and IGD patients merit further study.

CONCLUSIONS

Resting state fMRI results demonstrate increased functional connectivity between the frontal eye fields and the salience network as well as between auditory and motor cortices in patients seeking treatment for IGD relative to comparison subjects without IGD. This may represent a training effect of extended game play and could reflect adaptive functional gain in individuals with prolonged Internet game experience, rather than a cause of ADHD or MDD. Increased connectivity between executive and default mode regions may also represent a training effect, which could potentially increase the risk of maladaptive executive function or psychiatric comorbidity, given the literature associating greater segregation of default mode and executive function networks with improved performance on tasks requiring focused attention.

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Conflicts of Interest

None declared.

References


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