



Research paper

A failure of suppression within the default mode network in depressed adolescents with compulsive internet game play



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ABSTRACT

Background: Individuals who are chronic, compulsive video game players experience an elevated incidence of major depression. Excessive or problematic game play can interact with depression clinically, and may magnify impulsive behavior associated with video gaming.

Methods: Functional brain imaging was performed during a Wisconsin Card Sorting Test (WCST) task in 42 healthy control and 95 volunteers seeking treatment for compulsive video game playing, including 60 participants without major depression (pure internet gaming disorder, pure IGD) and 35 participants comorbid with major depression (IGD+MDD).

Results: In response to the WCST in contrast to fixation, activation was observed in canonical brain attentional networks including bilateral intraparietal sulcus, frontal eye fields, and middle temporal cortical regions as well as dorsolateral prefrontal, inferior parietal and anterior insula, anterior cingulate cortex in all participants. For WCST > Fixation contrasts, the IGD+MDD group exhibited greater relative activation within the left hippocampus, compared to healthy control participants. For WCST > Fixation contrasts, the IGD+MDD group exhibited greater relative activation within the left hippocampus and the right parahippocampal gyrus immediately posterior to the hippocampus, compared to the pure IGD group.

Conclusions: In cohorts of individuals with a history of compulsive internet game play, individuals with depression showed failure to suppress default mode network activity during an attentionally demanding task, compared to individuals without depression, including comparison groups with and without a history of compulsive video gaming. This reduced suppression of the brain regions within the default mode network may be a consequence of depressive neurophysiology or represent a predisposition for depression within compulsive game players.

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1. Introduction

1.1. Impulse control, perseverative errors and major depressive disorder

Repetitive behavioral errors due to impaired performance monitoring have been associated with a number of clinical conditions, including major depressive disorder (MDD) (Steele et al., 2007), schizophrenia (Carter et al., 2001) and drug addiction (Kaufman et al., 2003). Moreover, negative affect in patients with MDD has been suggested to magnify impulsive behaviors (Selby et al., 2014). Impairments in performance monitoring in MDD have

been associated with deficits within a feedback system (Steffens et al., 2001). From this perspective, the increased risk of committing a subsequent error (perseverative error) in MDD patients might be due to a ‘catastrophic response to failure’ as well as a failure to receive feedback (Beats et al., 1996; Elliott et al., 1997).

Internet gaming disorder (IGD) is a relatively new condition characterized by compulsive online game play that leads to grave impairment or distress, warranting more clinical research (Section 3), DSM-V (APA, 2014). Actually, Lee et al (2015) suggested that IGD adolescents showed higher cognitive impulsivity, compared to healthy adolescents. Choi et al (2014) also reported that both adults with IGD and alcohol dependence had increased impulsivity and compulsivity, compared to healthy adults. Although IGD has not been categorized as a formal disorder (APA, 2014), excessive and problematic online game play has been primarily discussed in the psychiatric literature in relation to impulse control disorders (Dell’Osso et al., 2008).

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Several studies of IGD have reported an association between the prevalence of IGD and MDD (Ha et al., 2007; Shapira et al., 2000). Moreover, Hyun et al. (2015) reported that MDD and ADHD were the two most common comorbid disorders in IGD. Han and Renshaw (2012) have reported that bupropion treatment of depression improved the severity of excessive online game play in MDD patients with IGD. These features suggest that IGD may also be associated with disruption of impulse control behavior. With evidence of high comorbidity, sharing of impulsivity, and treatment response between MDD and IGD, we sought to study whether depression and IGD interact in brain network physiology and whether such interactions may constrain hypotheses about treatment strategies in IGD patients with depression.

1.2. Wisconsin card sorting test and impulsivity

The Wisconsin Card Sorting Test (WCST) is a neuropsychological test requiring the ability to display attentional flexibility and executive function in response to changing schedules of reinforcement (Monchi et al., 2001). Several early studies reported the sensitivity of the WCST to frontal lobe pathology (Nelson, 1976). In addition, other brain areas including temporal, parieto-temporal, and parieto-occipital cortices have also been reported to influence WCST performance (Nyhus and Barcelo, 2009). In clinical studies, the WCST has been used to assess set shifting and impulsivity in patients with schizophrenia, MDD, alcohol dependence, pathologic gambling, and internet gaming disorder (Hori et al., 2012; Salgado et al., 2009; Zhou et al., 2014). Han et al. (2015) reported that total errors including perseverative and non-perseverative errors were associated with depressive symptoms in adolescents with MDD. The WCST consists of four key cards and 128 response cards with three perceptual dimensions (color, form, or number of geometric figures). WCST results are typically reported in terms of the number of categories completed, the number of perseverative errors, and the number of non-perseverative errors for assessing a subject's attentional and executive function (Barcelo and Knight, 2002).

1.3. Impulse control and brain activity

Recent fMRI studies have revealed that the brain's default mode network (DMN) is more active during the resting state (not engaging in a specific attention demanding or stimulus condition) than that during an attention demanding task (Raichle et al., 2001). The core regions of the DMN are the medial frontal cortex, posterior cingulate and retrosplenial cortex, inferior parietal lobule, and inferior and medial temporal cortex including hippocampus and parahippocampal gyrus. The core regions of the DMN are activated during rest and are dampened in response to task performance (task suppression) (Fox et al., 2005). Hyperactivity of the DMN has been reported in patients with MDD (Buckner et al., 2008; Grimm et al., 2009; Hamilton et al., 2011). In MDD patients, reduced DMN suppression during attentional tasks was thought to be associated with reappraisal of negative pictures, self-referential thinking, remembering past, and deficit in planning for the future and evaluating survival cues (Buckner et al., 2008). In addition, failure of suppression is also associated with maladaptive behaviors including compulsive and addictive behaviors, rumination, and hopelessness (Grimm et al., 2009; Hamilton et al., 2011). In a resting state fMRI study, increased functional connectivity within the default mode network was also reported in IGD adolescents (Ding et al., 2013). Additionally, a cross-sectional study including resting state analyses of many of the same patients included in this report found that IGD patients exhibited significantly higher connectivity between dorsolateral prefrontal cortex and temporoparietal junction bilaterally, suggesting decreased segregation of attentional and default mode networks (Han et al., 2015).

1.4. Hypothesis

To assess how major depressive disorder can affect IGD, we compared IGD+MDD patients and pure IGD patients. Considering the clinical characteristics of MDD including rumination and compulsive behavior, we hypothesized that IGD patients with MDD would have more severe symptoms of compulsive internet game play, compared to IGD patients without MDD. In addition, we anticipated that a failure of suppression within the default mode network would be observed in IGD patients with MDD.

2. Methods

2.1. Participants

One hundred eighty seven male subjects who visited the On-line game Clinical and Research Center at Chung Ang University Hospital included 145 patients seeking treatment for internet gaming disorder (IGD) and 42 healthy comparison subjects. Of 145 IGD subjects referred for brain imaging, 60 subjects had no other psychiatric comorbid disease (pure IGD), 35 subjects had comorbid MDD (IGD+MDD), 41 subjects had comorbid ADHD, 7 subjects had comorbid neurodevelopmental or psychiatric conditions including autism spectrum disorder, schizophrenia, and psychotic disorder NOS. Two subjects did not complete fMRI scanning. Finally, 60 pure IGD subjects, 35 IGD+MDD subjects, and 42 healthy control subjects 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 subjects. In case of participants under age 18, written informed consent was provided by parents and assent was obtained from adolescents. Both all IGD subjects and healthy control subjects were screened with the Structured Clinical Interview of DSM-IV-TR (Ha et al., 2006) and interviewed by a board certified child psychiatrist (D.H.H.). All subjects were also asked to complete questionnaires including the Young Internet Addiction Scale (YIAS) (Young, 1996), the Korean ADHD rating scale (So et al., 2002), the Beck Depression Inventory (BDI) (Beck et al., 1961), and the Beck Anxiety Inventory (Beck et al., 1988). BDI is a 21-question self-report questionnaire, one of most widely used scales for measuring the severity of depressive symptoms in adult and adolescent (Ambrosini et al., 1991). The inclusion criteria for IGD have been reported in previous studies (Han et al., 2010; Kim et al., 2012): (1) male adolescent or young adult (age from 13 to 23), (2) right-handed, (3) excessive and problematic on-line game play time (more than 4 hours per day/30 hours per week), (4) YIAS score above 50, (5) irritable and aggressive behavior when asked to stop internet game play, and (6) disrupted behaviors or distress, and economic problems, as well as irregular meals, failure to maintain personal hygiene, and school refusal. Exclusion criteria for the IGD group included: (1) subjects with psychotic disorders, (2) IQ < 80, (3) substance abuse history, (4) subjects with neurological or medical disorders, and (5) participants with claustrophobia. Among 95 IGD subjects, IGD subjects with BDI scores ≥ 10 were interviewed by a child psychiatrist (D.H.H.). Previous studies have suggested that BDI scores ≥ 10 indicated the presence of depressive symptoms (Lesperance et al., 1996). IGD+MDD group was defined with BDI scores ≥ 10 and diagnosis by child psychiatrist. MDD subjects had BDI scores ≥ 10 and were interviewed by a child psychiatrist (D.H.H.). All subjects had no history of treatment medication. The inclusion criteria for the control group included: (1) male adolescent or young adult (age from 13 to 23), and (2) right handed. Exclusion criteria for the control group included: (1) subjects with psychiatric and medical disorders, (2) subjects taking psychiatric medications, (3) IQ < 80,

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