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Diffusion tensor imaging reveals thalamus and posterior cingulate cortex abnormalities in internet gaming addicts

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ABSTRACT

Internet gaming addiction (IGA) is increasingly recognized as a widespread disorder with serious psychological and health consequences. Diminished white matter integrity has been demonstrated in a wide range of other addictive disorders which share clinical characteristics with IGA. Abnormal white matter integrity in addictive populations has been associated with addiction severity, treatment response and cognitive impairments. This study assessed white matter integrity in individuals with internet gaming addiction (IGA) using diffusion tensor imaging (DTI). IGA subjects ($N = 16$) showed higher fractional anisotropy (FA), indicating greater white matter integrity, in the thalamus and left posterior cingulate cortex (PCC) relative to healthy controls ($N = 15$). Higher FA in the thalamus was associated with greater severity of internet addiction. Increased regional FA in individuals with internet gaming addiction may be a pre-existing vulnerability factor for IGA, or may arise secondary to IGA, perhaps as a direct result of excessive internet game playing.

1. Introduction

Internet Gaming Addiction (IGA), a subtype of internet addiction disorder (IAD), is characterized by excessive or uncontrolled internet game use with negative consequences for aspects of psychological, social and/or work functioning (Young, 1998). Although internet addiction disorder is increasingly recognized as a widespread public health concern (Dong et al., 2011b; Kim et al., 2010; Niemz et al., 2005; Young, 1998), the neurobiological underpinnings of this disorder have received relatively little study (Block, 2006; Dong et al., in press, 2010; Liu and Potenza, 2007; Yuan et al., 2011).

Internet addiction disorder is often conceptualized as a 'behavioral addiction' since its proposed diagnostic criteria closely parallel those for substance use disorders and pathological gambling, although IAD is not formally included in the current edition of the Diagnostic and Statistical Manual of Psychiatric Disorders (DSM-IV) (Block, 2008). At least three subtypes of internet addiction have been identified, namely, excessive gaming, sexual pre-occupations, and e-mail/text messaging (Block, 2008). Although these variants share four defining characteristics (i.e. excessive use, withdrawal, tolerance, and negative repercussions) (Beard and Wolf, 2001; Block, 2008), significant difference may exist among these IAD subtypes. In some countries, such as in China, internet gaming addiction (IGA) is the most prevalent form of IAD. Despite this, consensus is still lacking on the operational definition and diagnostic standards for IGA (Blaszczynski, 2008; Griffiths, 2008; Wood, 2008), leaving most researchers to define this specific IGA subgroup through more established general measures of internet addiction (Ko et al., 2009; van den Eijnden et al., 2010). In the present study, the IGA group is comprised of individuals who met general IAD criteria and report spending "most of their online time playing online games (>80%)".

Since IAD appears to share clinical phenomena with substance use disorders and behavioral addictions (e.g., experience of euphoria, craving and/or withdrawal; development of tolerance) (Beard and Wolf, 2001; Block, 2008; Grant et al., 2010), the neurobiological underpinnings of IAD are hypothesized to overlap with those of other addictive disorders. Disruptions to neural systems underlying reward processing and impulse control are thought to play crucial roles in the development and maintenance of drug addiction (Robbins and Everitt, 1999; Volkow et al., 2002). Several lines of evidence converge toward the hypothesis that drug addicts have a disrupted reward system and that addictive

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behaviors (e.g., drug taking, gambling) may serve as maladaptive means for compensating for this deficit (Robbins and Everitt, 1999). Blunted neural response to monetary reward have been demonstrated in internet addiction and pathological gambling (de Ruiter et al., 2009; Reuter et al., 2005; Dong et al., 2011a), suggesting behavioral addictions and substance dependence may be characterized by similar disruptions to reward circuitry. Despite serious mental health and social consequences of IGA in young adults, very few studies have directly assessed the whether the integrity of neural circuitry is disrupted in individuals who display problematic, under-controlled online game playing.

Diffusion tensor imaging (DTI) assesses integrity of white matter microstructures by indexing the degree to which water diffusion deviates from isotropic diffusion in the white matter, with greater deviations from isotropic diffusion indicating more uniform directionality of water diffusion along the axon, implying greater white matter integrity. A fractional anisotropy (FA) value is calculating from the normalized standard deviation of axial eigenvalue (λ_1) (i.e. a marker of diffusion along the axon) and radial eigenvalue ($\lambda_{\Re}$) (i.e. a marker of diffusion perpendicular to the axon) (Alexander et al., 2007; Xu et al., in press). White matter integrity has been shown to be disrupted in individuals with substance use disorders (Bora et al., 2012; Jacobus et al., 2009) and to relate to cognitive function (Piras et al., 2010; Tuch et al., 2005; Takeuchi et al., 2011), substance-related symptoms (Clark et al., 2012) and addiction treatment outcome (Xu et al., 2010). Such relationships may reflect pre-existing individual differences that influence vulnerability to addiction or damage, which arises secondary to addictive disorders (de Laat et al., 2011; Stanek et al., 2011; Tang et al., 2010; Xu et al., 2010). The possibility of neuroplasticity improvements in white matter integrity is indicated by associations between greater white matter integrity with substance use abstinence (relative to active use) (Bell et al., 2011) and with prolonged cognitive or motor training (e.g., musical instrument training; abacus use; Boduk playing) (Hu et al., 2011; Imfeld et al., 2009). The thalamus is generally believed to act as a relay between a variety of subcortical areas and the cerebral cortex, including the mesolimbic pathway (such as the hippocampus and medial prefrontal cortex). Integrity of these connections is essential for reward sensitivity, and IAD subjects show enhanced reward sensation (Dong et al., 2011a). Thus, investigate the pattern of thalamus is its connection to hippocampus and is important. Long-term internet game can be conceived of as a form of cognitive-motor 'training' and, as such, may be expected to result in white matter integrity improvements in thalamo-cortical circuitry important for reward processing, motor control and impulse control.

2. Methods and materials

2.1. Subjects

This research, conducted in September 2010, was approved by the Human Investigations Committee of Zhejiang Normal University. All participants provided written informed consent. Participants were right-handed males (16 IGA, 15 healthy controls (HC)). IGA and HC groups did not significantly differ in age (IGA mean = 22.2, SD = 3.3 years; HC mean = 21.6, SD = 2.6 years; $t(29) = 0.83$, $p > 0.05$). Only males were included due to higher IAD prevalence in men than women. Participants were university students and were recruited through advertisements. All participants underwent structured psychiatric interviews (M.I.N.I.) (Lecrubier et al., 1997) performed by an experienced psychiatrist with an administration time of approximately 15 min, 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 listed in M.I.N.I. Depression was further assessed with the Beck Depression Inventory (Beck et al., 1961) and no participants scoring higher than 5 were included. IGA and HC did not fulfill DSM-IV criteria for abuse or dependence of substances, including alcohol, although all IGA and HC participants reported having consumed alcohol in their lifetime. All participants were medication free and were instructed not to use any substances of abuse, including coffee, on the day of scanning. No participants reported previous experience with illicit drugs (e.g., cocaine, marijuana).

Internet addiction disorder, of which internet gaming addiction is one sub-type, was determined based on Young's online internet addiction test (IAT) (Young, 2009) scores of 80 or higher (This cut-off is much stringent than the proposed 50 in Young's criteria. Scored more than 80 in IAT mean 'Your Internet usage is causing significant problems in your life'). The IAT was proved to be a valid and reliable instrument that can be used in classifying IAD. Factor analysis of the IAT revealed six factors-salience, excessive use, neglecting work, anticipation, lack of control and neglecting social life (Widyanto et al., 2011; Widyanto and McMurran, 2004). All participants meeting criteria for internet addiction disorder fulfilled the sub-group classification of internet gaming addiction (IGA) by reporting spending most of their time online (>80%) playing online games. 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. 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 internet addiction disorder-related life problems (www.netaddiction.com). HCs all scored lower than 30 on Young's IAT (mean = 16.3, SD = 4.3).

Furthermore, all individuals were assessed using a Chinese "Internet addiction test" developed by the Beijing Military Region Central Hospital (Tao et al., 2008; Wang et al., 2009). Internet addicts should satisfy several requirements. First, participants should spend more than 6 h online everyday aside from work. Second, participants should show symptoms such as psychological dependence, abstinent reaction, compulsive use, social withdrawal, and negative effect on body and mental health for more than three months. The scale was tested in more than 1300 clinical trials, which proved to be valid in distinguishing IAD subjects (Wang et al., 2009). In the subtypes of the participants, all participants were internet gaming addicts (they spent most of their time playing online internet games).

2.2. Scanning procedures

DTI data were acquired with a 3.0T Siemens Trio scanner. Diffusion sensitizing gradients were applied along 64 non-collinear directions using b-value image 0 and 1000 s/mm^2 (TR = 6800 ms, TE = 93 ms, matrix = 128*128, FOV = 256 mm*256 mm), 50 contiguous slices were acquired interleaved, and each slice was 2.5 mm thick. The entire scan lasted 12 min.

2.3. Image preprocessing

Eddy current distortions and head motion artifacts in the DTI dataset were corrected by applying affine alignment of each diffusion-weighted image to the non-diffusion image, using FMRIB's diffusion toolbox (FSL, www.fmrib.ox.ac.uk/fsl) (Smith et al., 2006, 2004). Diffusion tensor elements were then estimated using the Stejskal and Tanner equation (Basser et al., 1994). All eigenvalues and FA maps were calculated using DTIFit within