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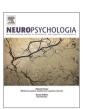
Neuropsychologia ■ (■■■) ■■■-■■■



Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia



Brain structures and functional connectivity associated with individual differences in Internet tendency in healthy young adults

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ARTICLE INFO

Article history: Received 9 October 2014 Received in revised form 2 February 2015 Accepted 14 February 2015

Keywords:
Internet addiction
Voxel-based morphometry
Resting-state functional connectivity
Cognitive control network
Default mode network

ABSTRACT

Internet addiction (IA) incurs significant social and financial costs in the form of physical side-effects, academic and occupational impairment, and serious relationship problems. The majority of previous studies on Internet addiction disorders (IAD) have focused on structural and functional abnormalities, while few studies have simultaneously investigated the structural and functional brain alterations underlying individual differences in IA tendencies measured by questionnaires in a healthy sample. Here we combined structural (regional gray matter volume, rGMV) and functional (resting-state functional connectivity, rsFC) information to explore the neural mechanisms underlying IAT in a large sample of 260 healthy young adults. The results showed that IAT scores were significantly and positively correlated with rGMV in the right dorsolateral prefrontal cortex (DLPFC, one key node of the cognitive control network, CCN), which might reflect reduced functioning of inhibitory control. More interestingly, decreased anticorrelations between the right DLPFC and the medial prefrontal cortex/rostral anterior cingulate cortex (mPFC/rACC, one key node of the default mode network, DMN) were associated with higher IAT scores, which might be associated with reduced efficiency of the CCN and DMN (e.g., diminished cognitive control and self-monitoring). Furthermore, the Stroop interference effect was positively associated with the volume of the DLPFC and with the IA scores, as well as with the connectivity between DLPFC and mPFC, which further indicated that rGMV variations in the DLPFC and decreased anticonnections between the DLPFC and mPFC may reflect addiction-related reduced inhibitory control and cognitive efficiency. These findings suggest the combination of structural and functional information can provide a valuable basis for further understanding of the mechanisms and pathogenesis of IA.

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1. Introduction

Once individuals spend too much time on Internet-related activities, they may have a problem of Internet tendency, which could lead to Internet addiction (IA). IA is considered as the inability to control one's use of the Internet, which could be considered as an impulse-control spectrum disorder and one type of behavioral addiction, and always results in social, psychological and/or work difficulties (Holden, 2001; Young, 1997; Young and Rogers, 1998). One study found that 11% of adolescents in Greece exhibited behaviors that corresponded to the criteria for IA

http://dx.doi.org/10.1016/j.neuropsychologia.2015.02.019 0028-3932/© 2015 Published by Elsevier Ltd.

(Siomos et al., 2008), and about 18% of teenagers in Korea who play computer games were diagnosed as patients suffering from IA (Whang et al., 2003). IA also has become a serious threat to the mental health of teenagers in China in recent decades. Current data suggests that 2.4% of adolescents show Internet addiction (Cao and Su, 2007), and 19.1% of Chinese adolescents in Hong Kong are classified as having IA (Shek et al., 2008). These findings might indicate that IA is prevalent worldwide, especially amongst adolescents, suggesting that it is a serious mental health problem which has expanded incredibly and gathered widespread attention. Moreover, a variety of psychiatric disorders, such as depression (Kim et al., 2006; Young and Rogers, 1998), anxiety (Greenfield, 1999) and maladaptive cognitions (Bidi et al., 2012; Spada et al., 2008) have been found to be related to Internet addiction. It is important to recognize that psychological interventions and behavioral treatments for IA are not very efficacious

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(Block, 2007), which might be at least partly due to the fact that the cognitive and neural mechanisms underlying individual differences in IA are unclear.

Numerous studies have explored the brain structural and functional correlates of Internet addiction disorder (IAD) in recent years, by utilizing structural and functional magnetic resonance imaging (MRI). These neuroimaging studies of IAD usually have identified abnormalities in frontal brain regions (especially the dorsolateral prefrontal cortex, DLPFC) that are believed to be responsible for cognitive control and control of inhibition (Bechara, 2005; Feil et al., 2010; Havashi et al., 2013; Kuss and Griffiths, 2012; Widvanto and Griffiths, 2006), For example, a voxelbased morphometry (VBM) study showed that decreased gray matter volumes (GMVs) in the bilateral DLPFC, the supplementary motor area (SMA), the orbitofrontal cortex (OFC), the cerebellum, and the left rostral anterior cingulate cortex (rACC) were associated with IA, suggesting that the brain structural abnormalities involved in IAD might be related to a dysfunction of cognitive control (Yuan et al., 2011). Another study found that the right DLPFC, right OFC, right nucleus accumbens, bilateral ACC and medial frontal cortex were activated stronger in response to gaming cues in a group addicted to Internet gaming compared to a control group (Ko et al., 2009). Moreover, patients suffering from IA had more brain activation in the left DLPFC, left occipital lobe cuneus, and left parahippocampal gyrus relative to healthy subjects when exposed to game cues (Han et al., 2010). Overall, these findings revealed that abnormal brain structure and function of frontal brain regions (especially the DLPFC) were closely related to IA, the aggravation of which might be associated with weakened cognitive control and stronger craving responses (Caplan, 2002; Davis, 2001; Dong et al., 2012; Kuss and Griffiths, 2012; Şenormancı et al., 2010; Widyanto and Griffiths, 2006).

Other studies have revealed that a number of regions in the cognitive control network (CCN), such as the DLPFC, play an important role in substance addiction, suggesting that structural deficits and functional abnormalities in individuals with substance addiction might be similar to those in IAD (e.g., similar behavior symptoms, such as tolerance, withdrawal, preoccupation, and negative repercussions; Feng et al., 2013; Hong et al., 2013; Ko et al., 2009; Ng and Wiemer-Hastings, 2005; Young, 1997). Studies of alcohol-dependent patients found DLPFC volume abnormalities and abnormal functional connectivity between the DLPFC and the striatum, which may reflect impairments in reward-related learning and the magnitude of alcohol craving (Makris et al., 2008). A recent study have reported the alterations in the frontostriatal circuitry associated with higher IAT scores, which could reflect the striatal over-activation and the diminished top-down modulation of prefrontal areas (Kühn and Gallinat, 2014). Similarly, cocaine-dependent abusers also show reduced cortical thickness in the DLPFC, which has been found to be associated with abnormal decision making (Makris et al., 2008). In conclusion, all the above studies suggest that the DLPFC (a core region of the CCN) plays an important role in addiction, which includes increased addiction-related weakened cognitive control and impulsive decision making (Hooker et al., 2010; Kühn et al., 2012).

Moreover, in addition to the core regions of the CCN (especially the DLPFC), a close correlation between the core regions of the default mode network [DMN; such as the posterior cingulate cortex (PCC) and medial prefrontal cortex (mPFC)] and addiction has attracted more attention. For instance, Ding et al. (2013) reported the DMN in adolescents with Internet gaming addiction was altered. They found connectivity with the PCC (the key node of the DMN) was positively correlated with IA scores in the right precuneus, SMA, thalamus, PCC, caudate, nucleus accumbens and lingual gyrus, while it was negatively correlated with the right cerebellar anterior lobe and the left superior parietal lobule

(Fransson and Marrelec, 2008). Furthermore, Dong et al. (2012) reported diminished efficiency of response-inhibition processes in patients suffering from IA, which has been associated with increased neural activity in the ACC (a region within the CCN; Cole and Schneider, 2007). Another study found that patients suffering from IA engaged more cognitive processes in a decision-making task because of insufficient executive functioning during this task (Dong et al., 2013a). Subsequently, it has been shown that compared with controls, IAD subjects exhibit higher superior frontal gyrus activity after continuous wins and decreased PCC activity after continuous losses (Dong et al., 2013b). In addition, previous studies also found the DMN and rACC network of heroin-dependent individuals were different compared with healthy subjects. which might suggest that the aberrance of the DMN and rACC might be linked to addiction (Yuan et al., 2010). Moreover, Ma et al. (2011, 2010) also found enhanced resting-state functional connectivity (rsFC) in the hippocampus (a prominent node within the DMN) and reduced connectivity in the ACC (within the DMN) in drug addicts, which might reflect addiction-related abnormally increased memory processing, or diminished cognitive control related to attentional orientation and self-monitoring. It should be noted that in previous neuroscientific studies, the regions associated with addiction were mostly the core regions of the DMN (such as the PCC and mPFC) and the CCN (such as the DLPFC and dACC), and these two networks were considered to be anti-correlated (Cole and Schneider, 2007; Fox et al., 2005; Jović and Dinđić, 2011; Ma et al., 2010; Volkow et al., 2004).

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However, up until now, the majority of previous research has studied individuals whose behaviors corresponded to the diagnostic criteria for IA (i.e., the Internet usage was causing significant problems in their life), and compared these IA subjects with healthy controls. These studies focused on the consequences of enhanced behavioral addiction and considered the control sample to be a heterogeneous group. In addition, strictly speaking, video gaming or Internet gaming addiction (IGA) is only a subtype of IAD and significant difference may exist among the different IAD subtypes (Block, 2008). We can therefore only generalize the observed volumetric and activity differences in Kühn et al. (2011) and Dong et al. (2012) to the specific IGA subgroup but not to general IAD subjects. More importantly, although the relevant clinical studies already existed, there were some discrepancies in healthy sample. Evidently, non-addicted, healthy individuals who score high on IA tests (i.e., potential problematic Internet users) might be more susceptible to IAD, so investigation of the neural basis underlying individual differences in IA tendencies in young healthy subjects is important. Although a recent study has linked IA tendency (excessive but non-pathological Internet use) to GMV and functional connectivity (Kühn and Gallinat, 2014), it investigated relatively small sample consisting of only male participants. To increase the power of the statistical analyses and enhance generalization of the findings, structural and functional investigations with larger sample sizes for both genders are

Therefore, in light of the above findings, we wanted to test the relationship between individual differences in IA and GMV at a whole-brain level in the healthy population, using voxel-based morphometry (VBM) on structural magnetic resonance images. The VBM is regarded as non-invasive structural MRI to identify brain anatomy associated with differences in behavior (Kanai and Rees, 2011; Takeuchi et al., 2012). Since neuroimaging measures of brain structure could be used to provide better insights into brain mechanisms about stable individual personality traits, the examination of anatomical features using structural imaging (e.g. VBM) might be more efficacious than using fMRI for investigating the tendency toward IA (Ashburner and Friston, 2000; Hayakawa et al., 2013; Hong et al., 2013; Takeuchi et al., 2012). Furthermore,

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