Impaired Error-Monitoring Function in People with Internet Addiction Disorder: An Event-Related fMRI Study

Guangheng Dong^a Yue Shen^b Jie Huang^a Xiaoxia Du^c

^aDepartment of Psychology, Zhejiang Normal University, Jinhua, ^bDepartment of Psychology, Liaoning Normal University, Dalian, and ^cDepartment of Physics, Shanghai Key Laboratory of Magnetic Resonance, East China Normal University, Shanghai, PR China

Key Words

Internet addiction · Error monitoring · Reward sensitivity

Abstract

Background: Internet addiction disorder (IAD) is rapidly becoming a prevalent mental health concern around the world. The neurobiological underpinnings of IAD should be studied to unravel the potential heterogeneity. This study was set to investigate the error-monitoring ability in IAD subjects. **Methods:** Fifteen IAD subjects and 15 healthy controls (HC) participated in this study. Participants were asked to perform a fast Stroop task that may show error responses. Behavioral and neurobiological results in relation to error responses were compared between IAD subjects and HC. **Results:** Compared to HC, IAD subjects showed increased activation in the anterior cingulate cortex (ACC) and decreased activation in the orbitofrontal cortex following error responses. Significant correlation was found between ACC activation and the Internet addiction test scores. **Conclusions:** IAD subjects show an impaired error-monitoring ability compared to HC, which can be detected by the hyperactivation in ACC in error responses.

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Introduction

Internet addiction disorder (IAD), also described as pathological Internet use, is marked by an inability to control one's Internet use, which eventually leads to psychological, social or work difficulties [1–3]. Whether IAD is an addiction and whether it merits inclusion in DSM (Diagnostic and Statistical Manual of Mental Disorders)-V is still in controversy [4]. In addition to this, the nosology and optimal diagnostic criteria for IAD remain controversial [4]. IAD is often considered a behavioral addiction and may share similar neuropsychological (i.e. development of euphoria, craving, and tolerance) and personality characteristics with other addictions [5], especially behavioral addiction [6]. Although significant prevalence estimates and associations with adverse consequences have been addressed [3, 7–11], IAD has received relatively little study, particularly in its neurobiological underpinnings [12, 13].

What makes IAD subjects continue playing online even when faced to the severe negative consequences of their behaviors? One possible explanation, by analogizing with other addictions, is that their error-monitoring ability is impaired. Studies in gambling addiction, another type of

behavioral addiction, showed that problem gambling was characterized by decreased sensitivity to loss and punishment [14–18]. Our previous functional magnetic resonance imaging (fMRI) study using a guessing task found that IAD subjects show decreased sensitivity to punishment [19]. Littel et al. [20] found impaired error-processing ability in excessive computer game players. In addition to this, impaired error processing was found in other types of addictions, such as cocaine dependence [21], nicotine dependence [22], cannabis users [23], and alcohol dependence [24]. As we mentioned above, IAD may share similar neuropsychological and personality characteristics with other addictions [5]. Thus, we speculate that the same condition might manifest in IAD subjects.

The role of the anterior cingulate cortex (ACC) in error processing was revealed by plenty of fMRI studies [25–27]. Researches in obsessive-compulsive disorder (OCD) [28, 29] and severe traumatic brain injury patients [30] showed hyperactivity in ACC in error responses, which suggested an impaired error-monitoring ability. IAD was speculated to be related to impaired inhibitory control or impulse control failure [3, 31]. The preexisting impulsivity may increase one's vulnerability to develop addictive disorders and, conversely, engagement in addictive behaviors may exacerbate aspects of impulsivity [for review, see 32, 33]. IAD individuals demonstrate high impulsivity as measured by event-related potential (ERP) [34, 35] and self-report impulsivity results [36]. Thus, we may conclude that impaired error-monitoring ability might play an important role in the pathogenesis of IAD.

Error-monitoring ability is usually measured by error-related negativity (ERN) in ERP studies. When participants make errors in the fast response tasks, the ERN, presents as a negative deflection approximately 50–100 ms following the erroneous response [37, 38]. The ERN reflects a response-conflict monitoring process and is thought to reflect error-processing activity of the ACC [39]. The literature is mixed in terms of whether higher error-monitoring performance is associated with enhanced or diminished regional blood oxygen level dependence (BOLD) signal, perhaps arising from methodological differences. First, studies in addiction subjects showed neural deficits associated with error processing [18, 23, 24]. Second, studies using fMRI also showed activity increases in this region on negative feedback [40, 41]. Studies also proved that certain disturbances in cognition and behavior in common mental disorders such as schizophrenia and OCD can be understood as resulting from alternation in performance-monitoring functions associated with this region [42].

In view of the previous findings on error detection and the features of IAD, we hypothesized that IAD subjects show an impaired error-monitoring ability compared to healthy controls (HC), which can be detected by the changed activation in the ACC brain region in incorrect responses. To test this hypothesis, we used fMRI to compare the brain activities in a group of IAD subjects with that of a group of comparison subjects, using a fast color-word Stroop task that can produce response errors. We will test the following predictions: (1) the ACC will show increased/decreased activity in IAD subjects during incorrect response trials and (2) the degree of activation in incorrect response trials will show correlation with the severity of IAD symptoms.

Methods

Participant Selection

All participants were students recruited through advertisement in our university. They were all IAD participants suffering from the same Internet behavior, namely online gaming. IAD was determined based on Young's online Internet addiction test (IAT) (<http://www.netaddiction.com>) scores of 80 or higher (mean = 84.4, SD = 4.36). The IAT has been proven a valid and reliable instrument for classifying IAD [43, 44]. The 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 IAD-related life problems (<http://www.netaddiction.com>). In the present study, HC scored lower than 30 on Young's IAT (mean = 14.3, SD = 2.17). In addition to this, all participants meeting criteria for IAD fulfilled the subgroup classification of Internet gaming addiction by reporting spending most of their time online (>80%) playing games.

Sixteen IAD subjects and 16 HC were recruited in this study. Two of them were excluded from further analysis because of their responses [their accuracy rates are too low (<80%) or too high (100%)]. The remaining 30 participants were right handed, non-smoking males (15 IAD and 15 HC). The IAD and HC groups did not significantly differ in age (mean IAD = 23.8 years, SD = 3.7; mean HC = 24.1 years, SD = 3.3). Only males were included due to a higher IAD prevalence in men than women. Participants were recruited through advertisements and all were free of active substance abuse, axis I psychiatric disorders, neurological, or medical disorders. They underwent structured psychiatric interviews (MINI) 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 [45]. All participants were free of axis I psychiatric disorders listed in the MINI. IAD and HC reported alcohol use, but did not fulfill the DSM-IV abuse or dependence criteria. They were medication free and were instructed not to use any substances of

abuse, including coffee, on the day of scanning. The Human Investigations Committee of Zhejiang Normal University (2011.2) approved this research. All participants provided written informed consent.

Task and Procedure

An event-related color-word fMRI Stroop task was used in our study. Three target color words (e.g. red, green, yellow) were presented randomly in congruent (e.g. the word 'RED' in red ink) or incongruent (e.g. the word 'RED' in green ink) trials. The task consisted of 2 sessions of 123 trials each. Each trial was presented for 2,000 ms, and participants were asked to press a button to indicate the ink color of the word as soon as possible using 3 buttons (i.e. green = thumb, red = index finger, yellow = middle finger) of a 5-button response box (Invivo Corp., <http://www.invivocorp.com/>). A black screen appeared for a random interval of 600–1,400 ms (average 1,000 ms) between the trials. Stimuli were presented and behavioral data were collected using E-prime software (Psychology Software Tools, Inc.). Each condition (incongruent, congruent) accounted for 50% and all trials were presented randomly.

Participants were guaranteed USD 50 for participation, and to encourage a quick and accurate task performance, they were told that they would be rewarded with an additional USD 0–50 based on their task performance [$1/(\text{reaction time} \times \text{error rate})$]. Participants completed an out-of-scanner practice session which continued until they reached an accuracy rate of 90% or higher.

Image Acquisition and Preprocessing

fMRI was performed on a 3T system (Siemens Trio) with a gradient-echo EPI T2-sensitive pulse sequence in 33 slices (interleaved sequence, 3 mm thickness, TR = 2,000 ms, TE = 30, flip angle 90°, field of view 220 × 220 mm², matrix 64 × 64). Stimuli were presented using the Invivo synchronous system (Invivo Company, <http://www.invivocorp.com/>) through a monitor in the head coil, enabling participants to view the stimuli presented on the screen.

Imaging analysis was conducted using SPM8 (<http://www.fil.ion.ucl.ac.uk/spm>). Images were slice-timed, reoriented, and realigned to the first volume. T1-co-registered volumes were then normalized to an SPM T1 template resulting in an isometric voxel size of 3 × 3 × 3 mm³ and spatially smoothed using an 8-mm full-width-at-half-maximum Gaussian kernel.

First-Level fMRI Analysis

A general linear model (GLM) was applied to identify the blood oxygen level dependence (BOLD) signal in relation to two event types of interest: error and right response trials. The numbers of error responses in the participants ranged from 3–20 (mean 8.4). Since there were error responses not only in incongruent trials, but also in congruent trials, we did not exclude the right responses trials in congruent condition (for detailed behavioral data see the 'Behavioral Performance' chapter). Six head movement predictors derived from the realignment stage were included in the GLM design matrix as covariates of no interest. The GLM was independently applied to each voxel to identify voxels that were significantly activated for the event types of interest. A high-pass filter (cutoff period = 128 s) was applied to improve the signal-to-noise ratio by filtering out low-frequency noise.

Second Level Group fMRI Analysis

Second level analyses, performed at the group level, treated intersubject variability as a random effect. Firstly, we determined which voxels showed a main effect of incorrect response versus correct response trials within each group (IAD and HC). Secondly, we tested which voxels significantly differed in BOLD signal between the IAD and HC groups [$(\text{IAD}_{\text{incorrect}} - \text{IAD}_{\text{correct}}) - (\text{HC}_{\text{incorrect}} - \text{HC}_{\text{correct}})$], after correcting for multiple testing at the whole brain level with false discovery rate (FDR) to a threshold of $p < 0.05$. Finally, we extracted the BOLD signal from the peak voxel within each cluster that demonstrated between-group differences and entered these data for all participants into correlation analyses with correct incongruent trial reaction time, accuracy rate and Young's IAT score.

Correlation Analysis

Correlation analysis was performed between brain activities and the behavioral performances to support our hypothesis. We calculated two correlations. First, correlation between the brain activity (beta value) in ACC and the IAT score in the IAD group. Second, we calculated the correlation between the peak activity (beta value) in ACC and the accuracy rate during this task.

Results

Behavioral Performances

Behavioral performances were calculated between different groups using the nonparametric independent t test. IAD subjects showed lower accuracy rates and longer response times. However, no significant difference was found in accuracy rates and reaction times between the IAD and HC groups (table 1).

Imaging Results

A group (IAD, HC) condition (correct, incorrect) ANOVA revealed that IAD subjects displayed a higher activation in ACC (Brodmann's area 24) and a decreased activation in the orbitofrontal cortex (OFC) (Brodmann's area 11) in frontal brain areas when compared to HC (fig. 1, table 2). The beta figure of ACC shows that this difference was caused mostly by the enhanced brain activity in incorrect responses and the decreased brain activity in correct responses in IAD subjects.

Correlation Analysis

We analyzed the correlation between error-related ACC activity (beta value) and the IAT scores and accuracy rate. Marginally significant correlation was found between ACC activity and the IAT score ($r = 0.381$, $p = 0.056$). No significant correlation was found between ACC activation and accuracy rates in all subjects ($r = 0.101$, $p = 0.263$; fig. 2).

Fig. 1. Left panel: activation differences in IAD subjects and HC following incorrect responses ($p < 0.05$, FDR corrected and with extent threshold: $k > 10$ voxels; voxel size = $3 \times 3 \times 3$). The figures are shown in different coordinates to give the best view of the results. Right panel: beta figure of ACC in correct and incorrect responses.

Table 1. Behavioral results of the Stroop task in different groups (mean $\pm$ SD)

	Internet addicts	HC	t value	Sig (2-tailed)
Accuracy rate				
Congruent trials	0.959 $\pm$ 0.056	0.978 $\pm$ 0.013	-1.267	0.224
Incongruent trials	0.939 $\pm$ 0.051	0.947 $\pm$ 0.046	-0.436	0.667
All trials	0.956 $\pm$ 0.032	0.962 $\pm$ 0.027	-0.592	0.558
Reaction time, ms				
Congruent trials	686 $\pm$ 140	595 $\pm$ 90	2.104	0.046
Incongruent trials	786 $\pm$ 165	699 $\pm$ 137	1.577	0.126
Right responses	733 $\pm$ 148	643 $\pm$ 110	1.892	0.070
Error responses	778 $\pm$ 208	765 $\pm$ 213	0.164	0.871
All trials	736 $\pm$ 151	657 $\pm$ 114	1.609	0.120

Discussion

This study investigated the error-monitoring ability in IAD subjects compared to HC with a Stroop task. The results of this study support to the hypothesis that ACC hyperactivity in IAD plays an important role in the pathogenesis of this disorder.

Hyperactivation in ACC and Impaired Error-Monitoring Ability

Consistent with our hypothesis, IAD subjects showed a more enhanced ACC activation than HC after incorrect responses. This result is in agreement with the error-monitoring features found in OCD [28, 29] and severe traumatic brain injury [30] patients that were supposed to have a more impaired error-monitoring ability than HC. However, it contradicts the results from several ERP [20, 22] and fMRI [23, 24] studies that found lower activations in addiction groups.

The discrepancy between the present and previous results might have several reasons. First, it might be caused by different tasks used in the studies. For example, Luijten et al. [22] employed a flanker task and Hester et al. [23] a go/no-go task, and Li et al. [24] used a stop signal task in their studies. Different tasks might bring different features of the error responses. Second, the difference might be caused by the characteristics of the Stroop task employed in this study. Most Stroop tasks focus on either reaction speed or accuracy during responses. However, in our study, we asked them to respond 'quickly and accurate'.

Besides to the imaging results, the outcomes also show that ACC activation is positively related with IAT scores, which means that people who have a higher IAT score show a higher ACC activation. The beta figure of ACC shows that this difference is caused by the enhanced brain activity in incorrect responses and decreased brain activity in correct responses in IAD subjects. This suggests that IAD subjects reacted much fiercer than HC to their selec-

Fig. 2. Correlation between ACC activation and IAT score in IAD subjects (left panel). Correlation between ACC activation and accuracy rate in all subjects (right panel).

Table 2. Regional brain activity changes in Internet addicts and HC

x/y/z ^a	Peak t value	Number of voxels ^b	FDR corrected p value	Brain region ^c	Brodmann's area
Increased -15/-9/52	4.3006	13	0.031	Left ACC	24
Decreased -21/42/-9	-4.4102	33	0.024	Left OFC	11

^a Peak MNI coordinates. ^b $p < 0.05$, FDR corrected and at least 10 voxels; voxel size = $3 \times 3 \times 3$. ^c The brain regions were referenced to the software Xjview (<http://www.alivelearn.net/xjview8>) and double-checked with an atlas.

tion results. From the results we discussed, we may speculate that hyperactivation in ACC in incorrect trials means that the error-monitoring ability was impaired in IAD subjects.

There are three theories explaining why a higher ACC activation indicates an impaired error-monitoring ability in IAD subjects. First, higher activation in incorrect responses reflected subjects' experience to correct their actions repeatedly [46]. Previous studies showed that following conflict detection, regions associated with attentional control were engaged to resolve the conflict [42], and the increased activity in ACC reflected the detection that an error was made based on a comparison between actual movement and the intended movement [47, 48]. From this point of view, IAD subjects need more attentional endeavor to check their error behaviors (conflicts) and correct their actions during the error-monitoring process compared to HC. Second, in ERP studies, re-

searchers believe that higher error-related activation means that subjects cannot disengage from the processing of distressing thoughts, and therefore have an increased ERN [49–51]. The higher activation seen in the fMRI results may also reflect this mental process. Based on this theory, IAD subjects are supposed to recover much harder from the distressing thoughts caused by their error responses. Third, the disruption of ACC functioning contributes to impaired cognitive control in IAD through impairment in its performance-monitoring function [52]. In the presence of response conflict, people are known to sometimes make impulsive errors based on partial, incomplete analysis of the stimulus. Executive control ability is responsible for all these controlling and regulating actions. Error-monitoring ability is one of the subtype functions of executive control ability. Previous studies have proven that IAD subjects show impaired executive control ability compared to HC [53, 54]. Thus, an

impaired executive control ability may contribute to an impaired error-monitoring ability in IAD subjects. All these theories sound reasonable and may provide some explanations for the higher activation in ACC and impaired error-monitoring ability in IAD subjects.

Decreased OFC Activation and Sensitivity to Punishment

It is widely agreed that the OFC is important for value-guided behaviors [55, 56]. Neuroimaging studies found that OFC was activated by pleasant touch and rewarding [57, 58]. A hallmark personality characteristic in IAD is impulsivity, which is often characterized by enhanced sensitivity to reward and reduced sensitivity to punishment [10, 19]. This is similar to other types of addictions [59–61]. The decreased activation of the OFC might be explained by a lower sensitivity to reward or punishment. In this study, we focused on subjects' error-monitoring ability; however, a quick and accurate task performance was incentivized by informing the participants that they would be rewarded with additional payments based on their performance, which may have led to recruitment of reward-related circuitry during task performance. More error responses denote less additional reward for the participant. The reward sensitivity to the incentives may lead to OFC activation differences in the different groups.

This means that IAD subjects show less sensitivity to the potential loss concerning their behaviors. In summary, the decreased sensitivity to punishment may provide some explanation why IAD subjects show decreased OFC activation compared to HC in this study.

The results from this study revealed several important findings that can deepen our understanding about the biological reactions of Internet addiction. However, several limitations should be considered. First, the present study only revealed the current mental states of the IAD subjects, we cannot conclude whether they are reasons of IAD or results from IAD. Future studies should pay attention to this issue. Second, the behavioral results do not provide strong support to the imaging results, which limits the whole discussion on why there was a higher ACC activation.

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Disclosure Statement

The authors have no conflicts of interest to disclose.

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