



Neural substrates of deficient cognitive control in individuals with severe internet gaming disorder

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ABSTRACT

Background and aims: Internet gaming disorder (IGD) is rapidly becoming a worldwide health concern. The prefrontal-subcortical model of self-regulation emphasizes that an impaired prefrontal cognitive control system and an overwhelming subcortical reward-seeking system are both crucial factors in health problems, including addiction. This study focused on the cognitive control system of IGD, aiming to investigate whether cognitive control is altered and the underlying neural correlates in college students with IGD. **Methods:** Thirty college students with IGD and twenty-five matched healthy controls were asked to complete a stop-signal task that measures cognitive control while being monitored by functional magnetic resonance imaging (fMRI). **Results:** Compared to the controls, only the college students with severe IGD, rather than those with mild IGD, had deficient brain activity involved in inhibitory control and response execution (specifically, the inferior frontal gyrus, anterior cingulate cortex and primary motor cortex); this result implies that cognitive control deficits are closely linked to addiction severity in individuals with IGD. Regarding performance monitoring function, college students with IGD exhibited unabated behavioral and brain activity, as did the control group. **Conclusions:** Combined with our previous finding that the subcortical reward system was enhanced in individuals with IGD, the present findings extend the prefrontal-subcortical model of self-regulation from the perspective of IGD in a college student population and thus provide useful insight for the effective prevention and treatment of IGD.

1. Introduction

Appropriate game playing can relax and relieve pressure; however, excessive and uncontrollable game playing can lead to multiple functional impairments, which is defined as internet gaming disorder (IGD) (APA, 2013; Petry et al., 2014). Studies have reported that individuals with IGD have heightened depression/anxiety levels, insomnia, worse work/school performance, and poor family and social relationships (Kuss and Griffiths, 2012; Petry et al., 2014). Considering the severe consequences and high prevalence of IGD worldwide, it was included in the fifth edition of the Diagnostic and Statistical Manual of Mental

Disorders (DSM-5) as a tentative disorder (APA, 2013). After that, IGD was formally included in the eleventh edition of the International Classification of Diseases (ICD-11) as one of the disorders due to addiction. A profound understanding of the pathogenesis of IGD and improvements that lead to effective treatment are urgently needed.

Based on a large number of neuroimaging studies, researchers proposed a prefrontal-subcortical model of self-regulation, which emphasizes that an impaired prefrontal cognitive control system and an overwhelming subcortical reward-seeking system are both crucial factors in health problems, including addictive disorders (Heatherton and Wagner, 2011). In our prior work, we revealed an enhanced subcortical

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reward-seeking system (i.e., the nucleus accumbens and caudate) in college students with IGD (Wang et al., 2021). In the present study, we focused on the cognitive control system of IGD, aiming to investigate whether cognitive control is altered and the underlying neural correlates in college students with IGD.

Research on cognitive control dysfunction in individuals with IGD has not reached a consensus. Cognitive control refers to individuals' capacity to facilitate the attainment of current goals by selecting and successfully monitoring behaviors and even thoughts (Hughes et al., 2005). Cognitive control encompasses a series of cognitive processes, such as response execution, inhibitory control, and performance monitoring (Cools and D'Esposito, 2011). The go/no-go, Stroop and stop-signal paradigms have been widely used to examine cognitive control (especially inhibitory control) in IGD and other addictions. Using a go/no-go task, one event-related potential (ERP) study found that individuals with IGD made significantly more errors than healthy controls (HCs) under the no-go condition in which individuals needed to inhibit the prepotent response; meanwhile, they exhibited decreased amplitude in the P3 component associated with inhibition of prepotent actions, which demonstrated insufficient inhibitory control ability in individuals with IGD (Li et al., 2019). By employing a go/no-go task, three task-state functional magnetic resonance imaging (fMRI) studies also found insufficient inhibitory control in individuals with IGD relative to HCs, as indicated by their increased error counts and reduced brain activity in areas commonly activated by inhibition (e.g., the dorsal lateral prefrontal cortex (DLPFC), inferior frontal gyrus (IFG) and inferior parietal lobe (IPL)) under the no-go condition (Chen et al., 2015; Liu et al., 2014). Nevertheless, other task-state fMRI studies using a go/no-go task found only a difference in neural activation between individuals with IGD and HCs, i.e., individuals with IGD exhibited higher activation in the IFG, IPL, and anterior cingulate cortex (ACC) under the no-go condition than HCs, while the two groups had similar inhibitory control ability at the behavioral level (Ding et al., 2014; Ko et al., 2014).

Using the Stroop task, one study found increased error rates under the inconsistent condition in which individuals needed to inhibit prepotent responses and a decreased cortical thickness of frontoparietal regions in IGD participants compared to HCs, indicating their insufficient inhibitory control (Yuan et al., 2013). On the other hand, another two fMRI studies using the Stroop task found that the IGD participants had lower activation in the DLPFC, ACC and orbital frontal cortex (OFC) than HCs under the inconsistent condition, while they showed unabated inhibition abilities behaviorally similar to those of HCs (Dong et al., 2015; Luijten et al., 2015). Additionally, using a stop-signal task, two studies that recruited IGD patients from medical centers or hospitals reported worse inhibitory control (more errors under the stop condition) (Choi et al., 2014) and impaired frontal-basal ganglia connectivity in internet addiction/IGD patients than in HCs (Li et al., 2014), whereas another two studies with IGD participants from colleges and the general public reported no significant behavioral difference between those with IGD and HCs in the stop-signal task (Irvine et al., 2013; Ma et al., 2021).

Studies on response execution of IGD are scant. Two behavioral studies found that IGD participants made more response errors under the go condition than HCs using the go/no-go (Zhou et al., 2014) and stop-signal tasks (Li et al., 2016; Wang et al., 2020), suggesting impaired response execution in individuals with IGD. Regarding performance monitoring, two studies using the go/no-go task and Stroop task revealed weaker error monitoring in individuals with IGD than HCs, as indicated by their lower N2 amplitude associated with error monitoring (Dong et al., 2010) and decreased activation of OFC associated with insensitivity to task performance (Dong et al., 2013). However, using the go/no-go task, two ERP studies found no difference in error monitoring-related N2 amplitude between the IGD group and HCs (Li et al., 2019; Littel et al., 2012), and another fMRI study using the go/no-go task also suggested unabated error monitoring ability in individuals with IGD (Luijten et al., 2015). In summary, previous studies have provided inconsistent findings regarding cognitive control in individuals with

IGD. More work is needed to examine behavioral performance in individuals with IGD and the neural correlates of cognitive control that underlie this disorder.

Considering that the stop-signal task was found to be more sensitive in detecting the inhibition deficits of substance abusers than the go/no-go task (Smith et al., 2014), we used the stop-signal task to simultaneously examine the three processes of cognitive control (response execution, inhibitory control, and performance monitoring) and their neural substrates of individuals with IGD in the present study. The stop-signal task measures one's ability to inhibit responses that have already begun (Barkley, 1997; Wright et al., 2014), which is critical for gamers to stop game-playing activities that are already underway. Given that compared to behavioral tasks, fMRI can detect subtle differences in neural responses and cognitive control deficits in substance abusers (Heitzeg et al., 2015), we hypothesized that IGD participants would at least show abnormal brain activity in control-related areas (e.g., IFG and ACC) on the stop-signal task, indicating their reduced cognitive control ability compared to HC participants. In addition, according to previous studies, we found that the IGD participants with severe clinical symptoms recruited from medical centers/hospitals showed worse behavioral cognitive control ability (Choi et al., 2014; Li et al., 2019; Wang et al., 2020), while the IGD participants recruited from colleges performed cognitive control tasks with abilities commensurate to those of HCs (Dong et al., 2015; Irvine et al., 2013; Ko et al., 2014). Different addiction severities of IGD participants might be the reason for previous inconsistent findings on cognitive control in IGD. Therefore, we hypothesized that compared with HCs, college students with severe IGD rather than college students with mild IGD would be more likely to show reduced cognitive control ability.

2. Materials and methods

2.1. Participants

The present study was approved by The Institutional Review Board of the Institute of Psychology, Chinese Academy of Sciences. Thirty right-handed college students with IGD and twenty-five matched HCs participated in this study. None of the participants reported historical or current neurological/psychiatric disorders or illegal drug use. Their smoking and alcohol status were assessed using the Alcohol Use Disorders Identification Test (AUDIT) (Liu et al., 2011) and the Fagerstrom Test for Nicotine Dependence (FTND) (Huang et al., 2006). No participant had smoking or alcohol addictions (FTND scores: $M \pm SD = 0.22 \pm 0.90$; AUDIT scores: $M \pm SD = 1.82 \pm 2.29$). In addition, all the participants were free of depression and anxiety disorders assessed by the Beck Depression Inventory (BDI) ($M \pm SD = 6.47 \pm 7.05$) (Wang et al., 2011) and State-Trait Anxiety Inventory (STAI) (STAI-S: $M \pm SD = 37.09 \pm 10.88$; STAI-T: $M \pm SD = 38.95 \pm 8.64$) (Zheng et al., 1993).

Classification of the IGD and HC groups was primarily based on Young's Internet Addiction Test (IAT) (Young, 1998) and the diagnostic criteria proposed by the DSM-5 (Petry et al., 2014). The IAT measures the degree of internet use-related problems, e.g., excessive internet use and abstinence syndrome. IAT has been demonstrated to be effective in screening internet addiction and IGD (Dong and Potenza, 2016; Dong et al., 2019; Lai et al., 2013). A score of 50 was used as the cutoff score to screen IGD. The DSM-5 diagnostic criteria for IGD contain nine criteria. Referring to Petry et al. (Petry et al., 2014), individuals who met five of the nine DSM-5 criteria were diagnosed with IGD. In summary, the screening criteria for the IGD participants included the following: 1) IAT score > 50 , 2) five or more DSM-5 criteria were met, 3) the main online internet activity was game playing, and 4) played games for > 21 h/week for at least 2 years. The screening criteria for the HC participants were as follows: 1) IAT score ≤ 30 , and 2) at most one DSM-5 criterion was met. As shown in Table 1, the IAT and DSM-5 scores and gaming time were significantly higher in the IGD group than in the HC group. All the participants completed the safety screening scale for MRI scanning and

Table 1
Demographic and behavioral characteristics of the two groups (IGD and HC).

	IGD(N = 30)	HC(N = 25)	<i>t</i>	<i>p</i>
Age (years)	22.60 ± 2.25	23.00 ± 2.50	-0.62	0.535
Education (years)	15.80 ± 1.86	16.36 ± 2.45	-0.96	0.340
Years playing online games	6.68 ± 4.05	0.40 ± 0.63	8.38	<0.001
Game playing per week (hours)	25.83 ± 7.78	0.24 ± 0.66	17.93	<0.001
IAT scores	69.53 ± 8.82	21.92 ± 3.16	27.54	<0.001
DSM-V criteria scores for IGD	6.70 ± 1.39	0.16 ± 0.37	24.66	<0.001
Self-control scale scores	108.87 ± 12.34	129.80 ± 13.42	-6.02	<0.001

Table values: mean ± standard deviation.

Abbreviations: IGD = Internet gaming disorder; HC = healthy controls; IAT = Internet addiction test; DSM-V = The fifth version of Diagnostic and Statistical Manual of Mental Disorders.

signed written informed content before the experiment in line with the Declaration of Helsinki.

In addition, the participants were instructed to complete a questionnaire measuring self-control ability, namely, a self-control scale (SCS). Prior research has reported that individuals who have high self-control scores are closely related to a wide range of positive performances in schoolwork, social life and emotional patterns (Tangney et al., 2004). Compared to the HC group, the IGD group reported significantly reduced SCS scores, indicating weaker self-control in the IGD group

(Table 1).

2.2. Experimental paradigm

Prior to entering the fMRI scanner, the participants first needed to complete a choice reaction task for 50 trials (Fig. 1A) and a training version of the stop-signal task for 20 trials (Fig. 1B). For the choice reaction task, the participants were asked to press keys (F for left arrow, J for right arrow) with the index finger of their left or right hand as rapidly and accurately as possible. This task measures participants' reaction time (RT) of response to arrows, thus determining each participant's deadline value, i.e., the 90th percentile of each participant's RTs to arrows in the choice reaction task. The deadline value is used in the feedback stage of the stop-signal task to ensure that participants would not delay their response to arrows to improve the accuracy of stop and go trials.

The stop-signal task consists of go trials and stop trials. The go trial was similar to the choice reaction task, and the participants responded to the direction of arrows as rapidly and accurately as possible. In the stop trials, the participants had to try their best to withhold their response to arrows when the green box turned red (stop signal) unpredictably. The stop signal appeared at a stop-signal delay (SSD), which was 250 ms and varied among 100–400 ms according to a staircase algorithm, i.e., it was increased by 50 ms after successful inhibition and was decreased by 50 ms after failed inhibition. This algorithm aimed to converge on a critical SSD where the participants had approximately 50% successful inhibition in stop trials, thereby allowing the calculation of the stop-signal reaction

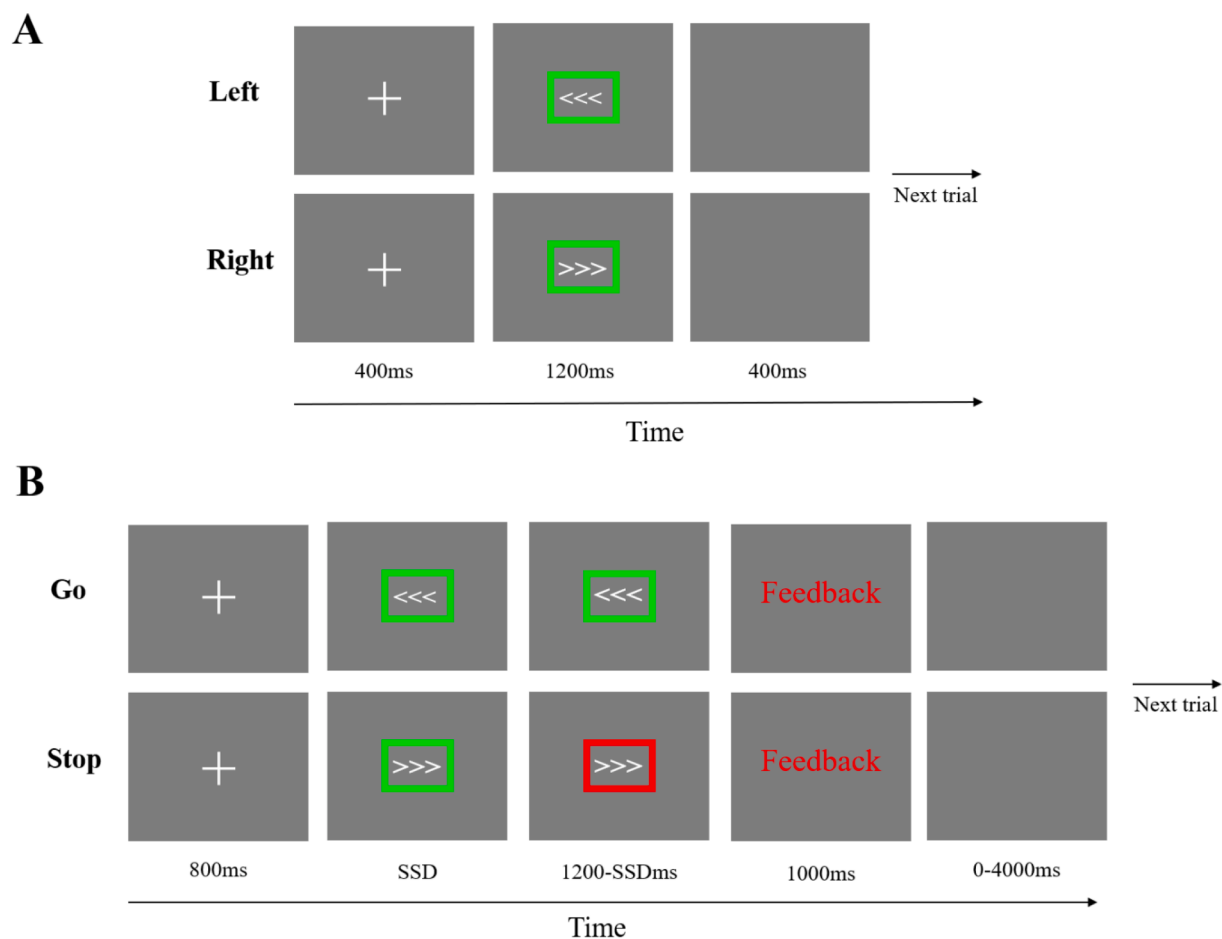


Fig. 1. The Experimental Paradigm. A: The timeline of the choice reaction task. The participants were instructed to press keys (F for left arrow, J for right arrow) with the index finger of their left or right hand as rapidly and accurately as possible. B: The timeline of the stop-signal task. The participants were instructed to respond to the direction of arrows as rapidly and accurately as possible in one go trial and to try their best to withhold their response to arrows when the green box turned red (stop signal) in one stop trial. After that, feedback according to the participants' performance was shown for 1000 ms.

time (SSRT) by subtracting the critical SSD from the mean reaction time (RT) in all correct-response go trials (Logan et al., 1984). According to the horse race model (Logan et al., 1994), the go and stop processes compete with each other in the race to the finish line, which demands participants not to delay their speed. To achieve this purpose, the participants were told that feedback according to their performance would be shown for 1000 ms after arrows disappeared. A “√” was shown when the participants successfully inhibited their responses in stop trials and responded accurately and quickly (RT < deadline value) to arrows in go trials. An “×” was shown in three cases: 1) failed inhibition in stop trials; 2) incorrect responses to arrows or no response in go trials; and 3) correct responses, but the RTs to arrows were longer than their deadline values. These rules ensured that the participants would not delay their response speed to improve the accuracy of stop and go trials, thus achieving the purpose of assessing their inhibitory control ability. The participants were told to try to inhibit their response while they respond to arrows as fast as possible and not to delay their response in anticipation of stop signals. After familiarizing themselves with the stop-signal task, the participants completed four runs of the task, each run lasting 5 min, under fMRI scanning. Each run comprised 60 trials with 36 go trials and 24 stop trials.

2.3. Imaging data acquisition

Imaging data were collected using a GE 3 T (Discovery MR750) scanner equipped for echo-planar imaging (EPI). The acquisition parameters of functional imaging were as follows: slice number = 37, interleaved sequence, slice thickness = 3.5 mm, echo time (TE) = 30 ms, repetition time (TR) = 2000 ms, voxel size = $3.5 \times 3.5 \times 3.5 \text{ mm}^3$, flip angle = 90° and field of view (FOV) = $224 \times 224 \text{ mm}^2$. Then, a high-resolution 3D BRAVO T1-weighted anatomical set was acquired with 196 slices, TE = 2.928 ms, TR = 6.652 ms, inversion time (TI) = 450 ms, voxel size = $1 \times 1 \times 1 \text{ mm}^3$, flip angle = 12° and FOV = $256 \times 256 \text{ mm}^2$.

2.4. Behavioral data analysis

First, go trials with no response, incorrect response and trials where the participants' RT exceeded the criteria ($\text{mean} - 3 \times \text{SD} < \text{RT} < \text{mean} + 3 \times \text{SD}$) were omitted from the behavioral and fMRI analysis. Then, the mean RT and accuracy rates for go trials were calculated to examine the participants' response execution ability. Second, the mean RT and accuracy rates for the stop trials were calculated to examine the participants' inhibitory control ability. According to the horse race model claiming that the go and stop processes compete with each other in the race to the finish line, the SSRT was calculated by subtracting the critical SSD from the mean go RT (Logan et al., 1994; Logan et al., 1984). As stated in the Experimental Paradigm section, the critical SSD was calculated based on a staircase algorithm.

Third, post-error slowing and signal altering were calculated to examine the participants' performance monitoring ability. Post-error slowing refers to instances in which the participants take longer to respond to the go stimulus in the current trial after they failed to inhibit their response in the previous stop trial than after they inhibited their response successfully in the previous stop trial (Rabbitt, 1966). Thus, post-error slowing was calculated by subtracting the mean RT in current go trials after successful inhibition in stop trials from the mean RT in current go trials after failed inhibition in stop trials. Pertinently, signal altering means that when the participants inhibited their response successfully in the previous stop trial, the participants' RT to the go stimulus in the current go trial was significantly prolonged compared to that when they responded correctly in the previous go trial (Li et al., 2006). Thus, signal altering was calculated by subtracting the mean RT in current go trials after successful inhibition in stop trials from the mean RT in current go trials after providing correct responses in go trials. Finally, all the indexes were compared between the IGD group and the HC group using an independent-sample *t*-test.

2.5. fMRI data analysis

fMRI data of all the participants were analyzed using the FMRIB Expert Analysis Tool (FEAT) module of FMRIB's Software Library (FSL v6.0.1, www.fmrib.ox.ac.uk/fsl). First, all images were preprocessed, i. e., realignment, removal of nonbrain sections, smoothing (FWHM = 5 mm), and high-pass filtering (100 s). Second, customized square waveforms for explanatory variables (EVs) of interest were created for images of each participant and convolved with a double-gamma hemodynamic response function (HRF). In the present task, brain activity during the go condition was modeled based on whether the participants responded to the go stimulus quickly (RT < deadline) or slowly (RT > deadline). Activity during the stop condition was modeled based on whether the participants inhibited their response successfully or unsuccessfully. Accordingly, four EVs of interest were included: fast and slow responses in go trials, as well as correct and incorrect responses in stop trials. Four EVs of interest were built and analyzed in the time window from the start of arrow presentation to the end of feedback presentation.

Third, for further group comparison analysis, statistical contrast maps of interest were built and analyzed. There were four contrasts of interest: (1) correct responses in stop trials > fast responses in go trials to dissociate brain regions responsible for response inhibition, (2) fast responses in go trials > correct responses in stop trials to dissociate regions responsible for response execution, (3) correct responses in stop trials > incorrect responses in stop trials to dissociate regions responsible for monitoring successful inhibition, and (4) incorrect responses in stop trials > correct responses in stop trials to dissociate regions responsible for monitoring failed inhibition. Fourth, the generated contrast maps of each participant were registered to Montreal Neurological Institute (MNI) standard space by their high-resolution T1-weighted anatomical image, generating images with $2 \times 2 \times 2 \text{ mm}^3$ spatial resolution.

Fifth, mixed-effect group comparison analysis was performed to examine task-related brain activation in each group and group differences (IGD vs. HC) during the four processes described above. Finally, cluster thresholding in the FEAT module, which is based on Gaussian random field theory (GRFT), was used for multiple comparison correction. This method first thresholds a Z-statistical image at a specific Z-threshold to define contiguous clusters, and then each cluster's *p* value estimated by GRFT is compared with a cluster probability threshold to show significant clusters. In the present study, images were corrected with a height threshold of $Z > 3.1$ and a cluster probability of $p < 0.05$ (Liu et al., 2021; Vaidya et al., 2018); (Wang et al., 2021), and the group comparison images were corrected within task-related brain regions in both groups. In addition, for each participant, we extracted the averaged parameter estimates of each region showing significant group differences to represent brain activation. To identify the relationship among brain activation, behavioral performance, control-related traits and severity of IGD, we performed Pearson correlation analysis of brain activation of each region and RT in go trials (GoRT) and SSRT among the whole IGD and HC groups, respectively, and performed Pearson correlation analysis of brain activation and IAT scores for the whole IGD group.

3. Results

3.1. Behavioral results

As stated above, the staircase algorithm used in the stop-signal task guaranteed that the participants had an approximately 50% success rate in stop trials. As shown in Table 2, both the IGD and HC groups had an accuracy rate of approximately 50% in stop trials despite the group difference, indicating that the present task was conducted successfully. For the other indexes of the stop-signal task, no significant group difference between the IGD group and the HC group was found. These results suggested that the two groups displayed similar inhibitory control and response execution and performance monitoring abilities.

Table 2
The behavioral results of the two groups (IGD and HC) in the stop-signal task.

	IGD(N = 30)	HC(N = 25)	<i>t</i>	<i>p</i>
GoRT (ms)	469 ± 43	493 ± 64	-1.60	0.118
Go_ACC (%)	95.26 ± 5.53	95.03 ± 3.94	0.17	0.864
SSRT (ms)	262 ± 36	260 ± 31	0.24	0.808
Stop_ACC (%)	48.23 ± 2.74	50.58 ± 4.39	-2.43	0.019
Critical SSD	207 ± 38	233 ± 56	-1.99	0.054
Post-error slowing (ms)	16 ± 24	19 ± 37	-0.37	0.710
Signal alerting (ms)	4 ± 28	17 ± 41	-1.33	0.190

Table values: mean ± standard deviation.

Abbreviations: IGD = Internet gaming disorder; HC = healthy controls; GoRT = reaction time in correct go trials; ACC = accuracy; SSRT = stop-signal reaction time; SSD = stop-signal delay.

Furthermore, to examine the hypothesis that inhibitory control might be impaired in individuals with more severe gaming addiction rather than in individuals with relatively mild gaming addiction, we attempted to classify individuals in the IGD group into two subgroups based on the participants' addiction severity (represented by the participants' IAT scores). The high-score IGD subgroup included IGD participants with higher IAT scores (76.93 ± 4.08), and the low-score IGD subgroup included IGD participants with lower IAT scores (62.13 ± 5.19 , $t(28) = 8.68$, $p < 0.001$). Then, we compared the behavioral performance of the HC group and the two subgroups of IGD using one-way ANOVA. Inconsistent with the hypothesis, the results revealed no group difference in any index between the three groups (Table 3). Overall, at the behavioral level, the IGD group exhibited cognitive control during the stop-signal task similar to that of the HC group.

3.2. FMRI results

As displayed in Fig. 2, the IGD and HC groups exhibited similar brain activation patterns during response inhibition, response execution, and successful and failed inhibition. Response inhibition involves the classic frontoparietal network, which contains regions such as the IFG and parietal lobe. Response execution involved regions responsible for motor preparation and execution, including the primary motor cortex, supplementary motor area (SMA) and cerebellum, as well as regions responsible for conflict detection (i.e., the ACC). Successful inhibition activated brain regions implicated in positive reward processing, e.g., the putamen and caudate. Failed inhibition activated regions implicated in negative emotional processing, e.g., the insula. However, we did not find any regions showing significant group differences between the IGD and HC groups.

Table 3
The behavioral results of the three groups in the stop-signal task.

	High IGD(N = 15)	Low IGD(N = 15)	HC(N = 25)	<i>F</i>	<i>p</i>
GoRT (ms)	481 ± 40	457 ± 44	493 ± 64	2.15	0.127
Go_ACC (%)	94.77 ± 5.42	95.74 ± 5.79	95.03 ± 3.94	0.16	0.851
SSRT (ms)	268 ± 41	256 ± 31	260 ± 31	0.48	0.620
Stop_ACC (%)	48.54 ± 2.89	47.92 ± 2.64	50.58 ± 4.39	3.02	0.058
Critical SSD	213 ± 39	201 ± 36	233 ± 56	2.34	0.106
Post-error slowing (ms)	20 ± 22	13 ± 25	19 ± 37	0.25	0.777
Signal alerting (ms)	10 ± 34	2 ± 19	17 ± 41	1.36	0.265

Table values: mean ± standard deviation

Abbreviations: IGD = Internet gaming disorder; High IGD = IGD with higher Internet Addiction Test (IAT) scores; Low IGD = IGD with lower Internet Addiction Test (IAT) scores; HC = healthy controls; GoRT = reaction time in correct go trials; ACC = accuracy; SSRT = stop-signal reaction time; SSD = stop-signal delay.

Furthermore, in line with the behavioral analysis, to examine the hypothesis about addiction severity of IGD, we compared the statistical contrast maps of interest of the high-score IGD subgroup and low-score IGD subgroup to those of the HC group. As a result, we found that there was no group difference between the low-score IGD subgroup and the HC group, whereas the high-score IGD subgroup showed decreased activation during response inhibition and response execution compared with the HC group (Fig. 3 and Table 4). Specifically, compared to the HC group, the high-score IGD subgroup exhibited significantly decreased activation in the right IFG during response inhibition and significantly decreased activation in the left ACC, right insula and left primary motor cortex during response execution. Moreover, significant correlations between the activation of these regions and behavioral indexes were found among the whole IGD group. No significant correlations were found among the whole HC group. Please see Fig. 3 for details.

Abbreviations

IGD = Internet gaming disorder

HC = healthy control

L = left

R = right

IFG = inferior frontal gyrus

ACC = anterior cingulate cortex

PMC = primary motor cortex

IAT = Internet addiction test

GoRT = reaction time in correct go trials

SSRT = stop-signal reaction time

SCS = self-control scale

4. Discussion

In the present study, we simultaneously examined the neural substrates of inhibitory control, response execution and performance monitoring in individuals with IGD using a stop-signal task. Our findings suggested specific deficits of cognitive control in individuals with severe IGD but not in those with mild IGD. Detailed results and implications are discussed below.

4.1. Deficient neural activity of inhibitory control and response execution in college students with severe IGD

At both the behavioral and neural levels, we found that the IGD group recruited from colleges showed unabated inhibition, response execution and performance monitoring, as did the HC group. This finding is in accordance with previous studies, which reported no difference in behavioral inhibition between HCs and individuals with IGD from colleges or the general public in the stop-signal task (Irvine et al., 2013) and go/no-go task (Dong et al., 2010; Ko et al., 2014). Importantly, in partial agreement with our hypothesis, the contrast results of the three groups showed that although there was no difference in behavioral performance at the behavioral level among these three groups, dysfunctional neural activity during inhibitory control and response execution was observed in the severe IGD subgroup but not in the mild IGD subgroup compared with the HC group.

The severe IGD subgroup exhibited lower right IFG activation than the HC group under response inhibition. Many studies have demonstrated that the IFG is critical for inhibitory control (Aron and Poldrack, 2006; Aron et al., 2004); (Chambers et al., 2006); (Swick et al., 2008). Patients with IFG lesions showed worse behavioral inhibition than HCs (Aron et al., 2004; Swick et al., 2008). Using the go/no-go task, previous studies reported deactivation of the IFG during response inhibition in nicotine-dependent people (Luijten et al., 2013), abstinent heroin-dependent people (Fu et al., 2008), and problem gamers (Luijten et al., 2015); providing neural evidence for deficient inhibitory control in individuals afflicted by substance addiction and problem gaming. Moreover, previous study revealed diminished frontal-basal ganglia connectivity in internet addicts relative to HCs during a go-stop

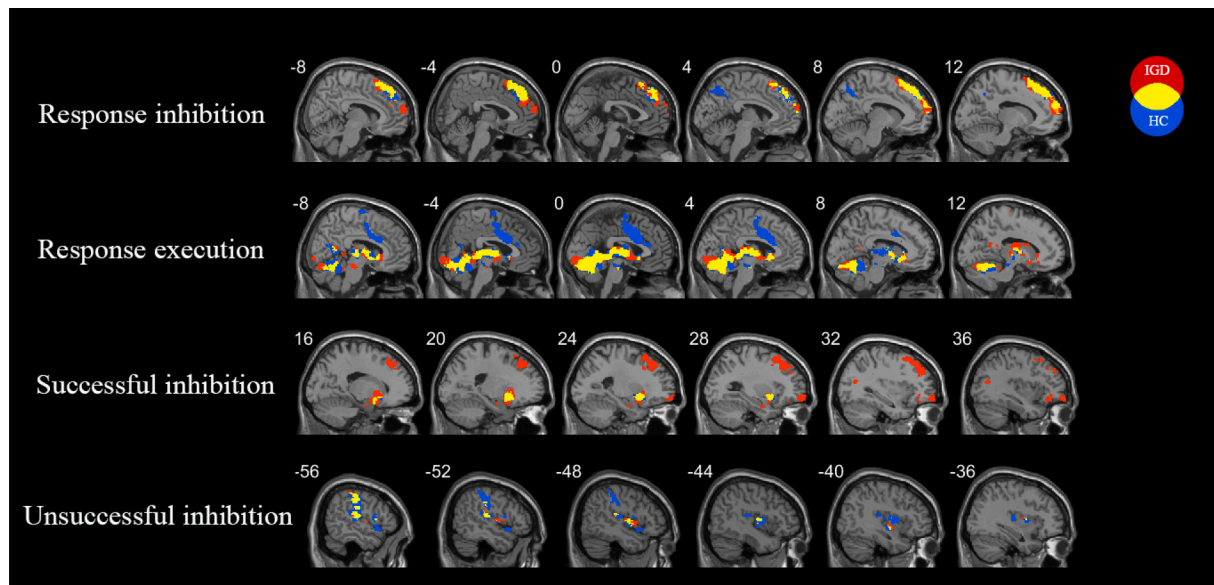


Fig. 2. Brain regions showing significant activation of the two groups (IGD and HC) in the stop-signal task. The images were corrected with a height threshold of $Z > 3.1$ and a cluster probability of $p < 0.05$. Clusters in red indicate the regions activated in the IGD group. Clusters in blue indicate the regions activated in the HC group. Clusters in yellow indicate the regions activated in both groups. Abbreviations: IGD = Internet gaming disorder; HC = healthy control. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

paradigm, demonstrating their deficient inhibitory control (Li et al., 2014). Combined with the correlational result that lower activation in the right IFG was associated with higher IGD severity, the present finding of right IFG hypoactivation in the severe IGD subgroup suggests insufficient inhibitory control in college students with severe IGD but not in those with relatively mild IGD.

Under response execution, hypoactivation of the left ACC and left primary motor cortex was observed in the severe IGD subgroup. Other studies using go/no-go and stop-signal tasks also identified the activation of these regions during response execution (Galván et al., 2011; Swick et al., 2011; Tapert et al., 2007). Pertinently, the primary motor cortex is well known to be involved in motor execution. We found that lower activation in the left primary motor cortex was associated with worse behavior execution (longer GoRT), which may corroborate the important role of the primary motor cortex in good individual performance in control-related tasks. The ACC is implicated in conflict monitoring and cognitive control (Botvinick et al., 2001; Stahl and Gibbons, 2007). The ACC selects the “best-suited” action by receiving information from systems with conflicting “interests” and forwards this action to the motor system (Holroyd et al., 2004). Studies have shown that greater activation of the ACC reflects superior task performance (Bush et al., 1999; Kerns et al., 2005; Zang et al., 2005), which is corroborated by the correlational finding that lower activation in the ACC was associated with worse behavior inhibition and execution (longer GoRT and SSRT). In summary, the deactivation of the left ACC and left primary motor cortex may suggest deficient action selection and conflict monitoring in college students with severe IGD, which further influences their task performance.

Additionally, inconsistent with the current results, two studies using the go/no-go task showed higher neural activation of control-related regions (e.g., IFG, IPL) in IGD participants than HCs (Ding et al., 2014; Ko et al., 2014). We speculated that there might be three reasons for the inconsistencies. First, previous researchers suggested that neural activation under experimental tasks of addicts was closely linked to the phase they were in, e.g., addiction severity, time of addiction or abstinence (Luijten et al., 2017). The addiction severity in the current study is lower than that of the two studies (Ko et al., 2014; Ding et al., 2014). In particular, the IGD participants in Ding et al.’s experiment were adolescents who had been cured in the hospital, and their severity was far

greater than that of the IGD college students in our study. Therefore, IGD participants in different phases might show different neural activation under control-related tasks. Second, in the present study, we recruited males who barely played games as HCs. However, in the two studies (Ding et al., 2014; Ko et al., 2014), the HCs were recreational game players. The gaming experience of the HCs might influence the direction of neural activation between IGD participants and HCs (Dong et al., 2017). Third, these two studies used the go/no-go task with event-related design, whereas another two studies showing lower activation in IGD participants used the go/no-go task with block design (Chen et al., 2015; Liu et al., 2014), and the present study used the stop-signal task with event-related design. Different experimental tasks and designs might generate different effects on the neural activation of IGD participants and HCs. Despite these inconsistencies, the current results are supported by most studies on cognitive control in addicts. One meta-analysis of 16 fMRI studies on neural activation of substance addicts under control-related tasks revealed hypoactivation in the ACC, IFG and DLPFC in addicts compared with HCs (Luijten et al., 2014). We expect future studies to corroborate the inconsistencies by controlling the factors described above, including the phase of IGD participants, the gaming experience of HCs and the experimental task.

4.2. Unabated neural activity of performance monitoring and behavioral performance in college students with severe IGD

No difference in brain activation during the successful inhibition and failed inhibition conditions was found between the severe IGD subgroup and the HC group. Successful inhibition activated regions responsible for positive reward processing, e.g., the striatum (Chevrier et al., 2007). Importantly, failed inhibition activated regions associated with negative emotional processing and conflict monitoring, e.g., the insula and ACC (Chevrier et al., 2007; Li et al., 2010). Failed inhibition reflects individual error processing, which is involved in monitoring performance errors and ongoing behavior to prevent future mistakes (Luijten et al., 2014). Combined with the behavioral results that the severe IGD subgroup had post-error slowing similar to the HC group, the similar activation in the two groups suggests unabated error monitoring function in the severe IGD subgroup. Actually, it is not surprising that the performance monitoring of the IGD group is as good as that of the HC group

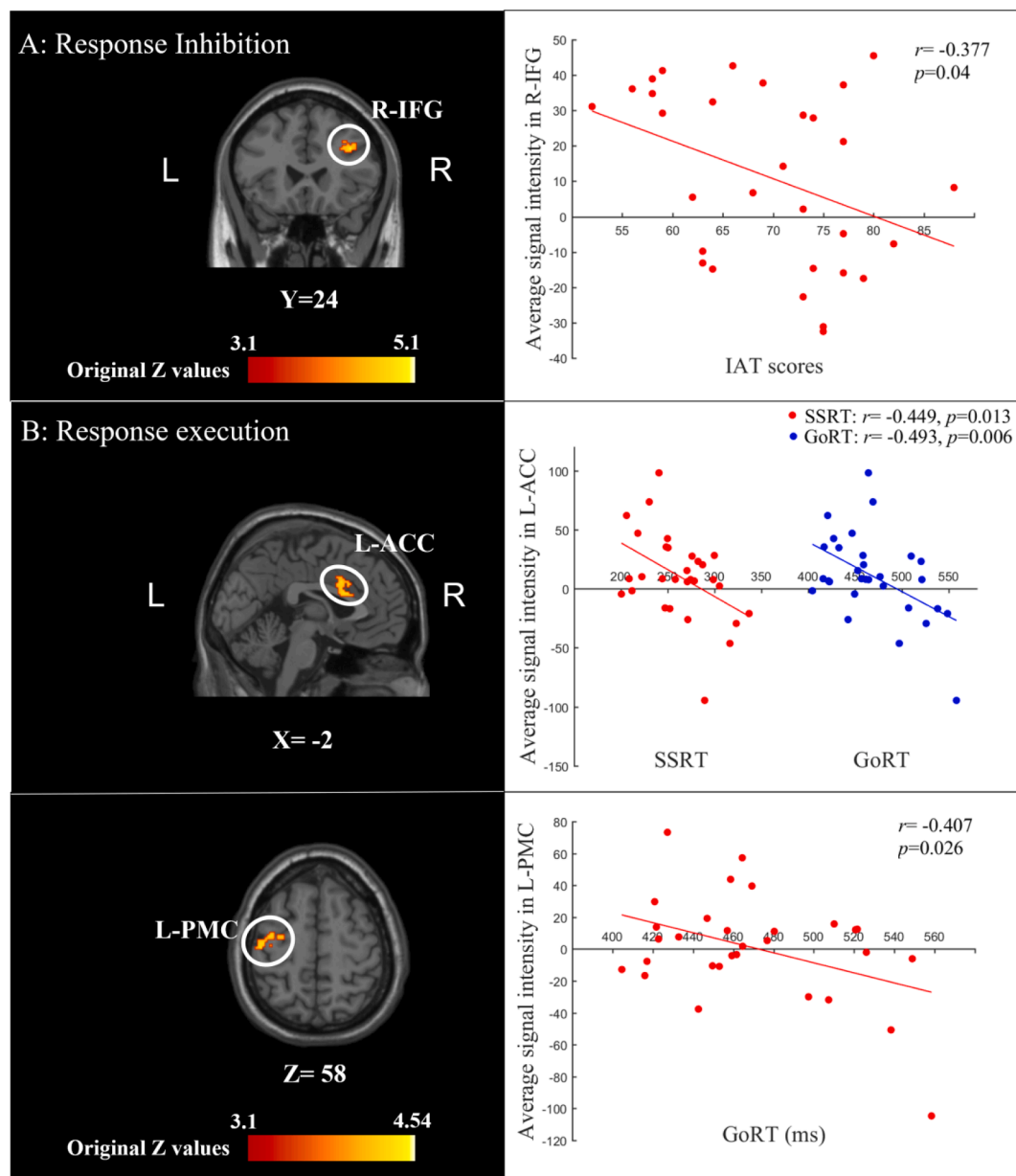


Fig. 3. Brain regions showing significant group differences (high-score IGD subgroup < HC) in the stop-signal task. A: The activation of the R-IFG during response inhibition correlated negatively with the participants' IAT scores among the whole IGD group. B: The activation of the L-ACC during response execution correlated negatively with the participants' GoRT and SSRT among the whole IGD group (false discovery rate (FDR)-corrected). The activation of the L-PMC correlated positively with the participants' GoRT among the whole IGD group.

when taking the gaming experience into account. When playing internet games, players need to achieve various tasks to rise in rank and build perfect avatars in the virtual network world. Players need to concentrate on their own performance in gaming and adjust their game strategies according to failed or successful experiences. These gaming experiences might compensate for the negative effect of excessive game playing on the IGD group. In addition, considering that the addiction severity of the IGD participants in the present study is not extremely high, i.e., lower than that of the IGD participants of two previous studies that found altered error monitoring in IGD (Dong et al., 2010; Dong et al., 2013), the addiction severity associated with IGD might account for the nonsignificant results. Despite this, consistent with the present findings, one study also found that problem gamers had intact error processing but exhibited deficient inhibitory control in a go/no-go task (Luijten et al., 2015). Overall, the present findings on neural activation during the stop-signal task demonstrate intact error processing in college

students with severe IGD.

The present study failed to identify deficits of cognitive control at the behavioral level in the severe IGD subgroup relative to HCs, despite the neural dysfunction of inhibition-execution-related regions in the severe IGD subgroup. Considering the previous findings stated in the introduction section, we speculated the possible reason for the lack of an intergroup difference might be that although the severity of the severe IGD subgroup was higher than that of the mild IGD subgroup in the present study, addiction severity in the severe IGD subgroup was still not high enough to impact their behavioral performance in contrast to IGD patients from hospitals, such that their cognitive control deficits could not be detected by behavioral tasks. Previous studies on cognitive control in substance abuse and IGD also identified dysfunctional brain activation in people with addiction relative to people without addiction, despite a lack of group differences at the behavioral level (Chen et al., 2015; de Ruiter et al., 2012; Tapert et al., 2007). To some degree, these

Table 4

Brain regions showing significant group differences in the stop-signal task (high-score IGD subgroup vs. HC).

Region	x	y	z	Cluster Size	BA	Max Z	Cluster p
<i>Response inhibition: high-score IGD subgroup < HC</i>							
Inferior frontal gyrus (R)	38	26	30	98	9	5.10	0.031
<i>Response execution: high-score IGD subgroup < HC</i>							
Primary motor cortex (L)	-46	-18	58	278	4	4.54	<0.001
Anterior cingulate cortex (L)	0	14	32	187	24	4.42	0.003

We list significant clusters of decreased (high-score IGD subgroup < HC) activation to different contrasts. Statistical images were corrected with a height threshold of $Z > 3.1$ and a cluster probability of $p < 0.05$. Shown are the coordinates of the local maxima in MNI space, the size of the clusters, the Brodmann area, the maximal Z value and p values of each cluster. Coordinates represent the local maxima in the corresponding contrast.

Abbreviations: IGD = Internet gaming disorder; HC = healthy controls; IAT = Internet addiction test; L = left; R = right.

observations might reflect the superior sensitivity of fMRI compared to behavioral measurements for detecting deficits among clinical populations Rose and Donohoe (Rose and Donohoe, 2013). Another explanation for the nonsignificant results might be that generalized cognitive control ability is unabated in individuals with IGD, whereas their cognitive control related to internet games might be altered. Several studies have found that IGD participants exhibit worse inhibition at both the behavioral and neural levels than HCs under the go/no-go task with game cues, while they exhibited unabated behavioral performance under the go/no-go task without game cues van Holst et al. (van Holst et al., 2012; Liu et al., 2014). Future studies employing the same addiction severity of IGD participants and the stop-signal task with game cues are needed to corroborate these previous findings and the current results. In summary, the present findings provide neural evidence for specific deficits of cognitive control in individuals with relatively severe IGD within the college student population and thus contribute to the early diagnosis and treatment of IGD. Moreover, the present findings imply that prefrontal cognitive control deficits are closely linked to the severity of addiction in IGD. Different addiction severities of IGD participants recruited in previous studies might be the reason for inconsistent findings.

5. Limitations

Two limitations should be noted. First, it is difficult to conclude whether the dysfunctions in the prefrontal control system are consequences or causes of IGD based on the present cross-sectional study (Wang et al., 2017). We expect future longitudinal studies to investigate the causal relationship between IGD and these dysfunctions. Second, the sample size of the severe IGD subgroup was small, which may limit the power of the results of brain activation differences between the IGD subgroup and the HC group. The conclusion of insufficient inhibitory control in college students with severe IGD should be taken cautiously. Future studies with larger sample sizes are needed to corroborate the conclusion of this study and explore the relationship between the severity of IGD and patients' cognitive control ability.

6. Conclusions

This study simultaneously examined the neural substrates of inhibitory control, response execution and performance monitoring in college students with IGD using a stop-signal task. The present results revealed deficient inhibition and response execution in college students with

severe IGD rather than in those with mild IGD. This finding implies that prefrontal cognitive control deficits are closely linked to the severity of addiction in IGD, which might account for the inconsistent results of previous studies on cognitive control. This finding also suggests that searching for treatments to improve inhibitory control and response execution will be crucial for alleviating severe IGD. On the other hand, both college students with severe and mild IGD showed unabated performance monitoring. In summary, taking the present findings together with our prior finding that the subcortical reward system is enhanced in college students with IGD, our work extends the prefrontal-subcortical model of self-regulation from the perspective of IGD in a college student population, thus providing useful insight for the effective prevention and treatment of IGD.

CRediT authorship contribution statement

Lingxiao Wang: Methodology, Software, Formal analysis, Investigation, Writing - original draft, Writing - review & editing, Visualization. **Guochun Yang:** Methodology, Software, Formal analysis. **Ya Zheng:** Methodology, Writing - review & editing. **Zhenghan Li:** Investigation, Writing - review & editing. **Ping Wei:** Writing - review & editing, Funding acquisition. **Qi Li:** Conceptualization, Methodology, Investigation, Writing - original draft, Writing - review & editing, Supervision, Funding acquisition. **Kesong Hu:** Writing - review & editing. **Xun Liu:** Conceptualization, Writing - review & editing, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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