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Brain responses to positive and negative events in individuals with internet gaming disorder during real gaming

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FULL-LENGTH REPORT

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ABSTRACT

Objective: This study sought to investigate brain responses to positive and negative events in individuals with internet gaming disorder (IGD) during real gaming as a direct assessment of the neural features of IGD. This investigation reflects the neural deficits in individuals with IGD while playing games, providing direct and effective targets for prevention and treatment of IGD. *Methods:* Thirty subjects with IGD and fifty-two matched recreational game use (RGU) subjects were scanned while playing an online game. Abnormal brain activities during positive and negative events were detected using a general linear model. Functional connectivity (FC) and correlation analyses between neural features and addiction severity were conducted to provide additional support for the underlying neural features. *Results:* Compared to the RGU subjects, the IGD subjects exhibited decreased activation in the dorsolateral prefrontal cortex (DLPFC) during positive events and decreased activation in the middle frontal gyrus (MFG), precentral gyrus and postcentral gyrus during negative events. Decreased FC between the DLPFC and putamen during positive events and between the MFG and amygdala during negative events were observed among the IGD subjects. Neural features and addiction severity were significantly correlated. *Conclusions:* Individuals with IGD exhibited deficits in regulating game craving, maladaptive habitual gaming behaviors and negative emotions when experiencing positive and negative events during real game-playing compared to RGU gamers. These abnormalities in neural substrates during real gaming provide direct evidence for explaining why individuals with IGD uncontrollably and continuously engage in game playing, despite negative consequences.

KEYWORDS

internet gaming disorder, real gaming, recreational game use, fMRI, regulation of craving, regulation of negative emotions

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INTRODUCTION

Internet gaming disorder (IGD) refers to the phenomenon in which individuals repeatedly and excessively immerse themselves in online games and the behavior is not controlled by the individual, causing multiple functional impairments (Brand, Rumpf, King, Potenza, &

Wegmann, 2020; G. Dong & Potenza, 2014; Weinstein, Livny, & Weizman, 2017). The American Psychiatric Association (APA) released an appendix to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) that mentioned IGD as a disease symptom and hoped to obtain more data from empirical and clinical research (APA, 2013). In addition, the World Health Organization (WHO) has included gaming disorder as a disorder due to addictive behaviors in the eleventh edition of the International Classification of Diseases (ICD-11) (https://icd.who.int/browse11/l-m/en). Therefore, a better understanding of IGD is needed to provide information that will facilitate the development of IGD therapy.

In theoretical models of addictive behaviors, researchers have proposed that impaired cognitive regulation and control over strong motivational drives may make it difficult for individuals with IGD to cease gaming, despite adverse consequences (Brand, 2022; Brand et al., 2019; Brand, Young, Laier, Wölfling, & Potenza, 2016). Numerous studies have emphasized the crucial roles of cognitive control and reward/emotional systems in understanding addictive behaviors (Cooper, Robison, & Mazei-Robison, 2017; G. Dong, Li, Wang, & Potenza, 2017; Gardner, 2011; Nora D. Volkow, Wang, Fowler, Tomasi, & Telang, 2011; L. Wang, Yang, Zheng, Li, Wei, et al., 2021). A growing number of studies have examined cognitive control and reward/emotional processing in individuals with IGD and the underlying neural mechanism using functional magnetic resonance imaging (fMRI). For example, using the stop-signal task, studies detected worse inhibitory control (more errors under the stop condition) in subjects with IGD than in controls, while they showed decreased activation in regions responsible for cognitive control (e.g., inferior frontal gyrus (IFG), anterior cingulate cortex (ACC), dorsolateral prefrontal cortex (DLPFC) and middle frontal gyrus (MFG)), indicating a deficient cognitive control ability in individuals with IGD (Choi et al., 2014; B. Li et al., 2014; Liu, Xue, et al., 2017; Ma et al., 2021; L. Wang, Yang, Zheng, Li, Wei, et al., 2021). Using the cue-reactivity task and emotional regulation task, studies reported impairments in cognitive control and reward/emotional processing in subjects with IGD compared to controls, as indicated by their higher desire for game-playing and disturbed response regulation to emotional stimuli, reduced brain activity in regions commonly activated by inhibition and regulation (e.g., DLPFC and MFG), and increased brain activity in regions activated by reward/emotional processing (e.g., the putamen, caudate and amygdala) (Brand, Young, & Laier, 2014; G. Dong et al., 2020; Liu, Yip, et al., 2017; L. Wang, Hu, et al., 2017; Zhang, Dong, et al., 2020). In summary, compared with the control group, the IGD group showed worse inhibitory control and an increased desire to play games, as well as blunted activation of brain regions crucial for cognitive control (e.g., DLPFC, IFG and MFG) and abnormal activation of brain regions associated with reward/emotional processing (e.g., the striatum).

Studies on IGD have mainly investigated cognitive control and reward/emotional processing functions through well-established experimental paradigms or experimenter-created conditions. However, limitations exist among these studies. First, most of these studies tested the brain features when subjects were not gaming, preventing the direct detection of the brain responses during game playing. Thus, these conclusions are reflective of out-of-gaming states instead of gaming states. Second, the brain responses in the gaming state are more situational and more reflective of the true state of gamers' brain responses. The brain responses during real gaming are able to provide direct evidence for the neural deficits related to addictive behavior and thus provide specific targets for prevention and treatment. Third, the brain responses during real gaming are not evoked by experimental tasks other than real gaming. For example, one study compared playing and watching games and found that winning and losing game events evoked greater changes in the striatum when subjects were playing games (Kätsyri, Hari, Ravaja, & Nummenmaa, 2013).

Therefore, this study was designed to investigate the brain responses in individuals with IGD when playing games (i.e., League of Legends (LOL), one of the popular games worldwide) and thus overcame the limitations of previous studies on IGD. Specifically, individuals with recreational game use (RGU) were recruited as the control group in the current study (Y. Wang et al., 2016). RGU individuals are gamers who play games recreationally without developing IGD. The inclusion of RGU individuals as the control group may avoid the effect of gaming experiences of different groups on the results. In addition, as different behaviors in gaming may involve different cognitive processes, emotional responses, and different brain responses (Bopp, Mekler, & Opwis, 2016; Brühlmann, Baumgartner, Wallner, Kriglstein, & Mekler, 2020), we aimed to examine the brain responses of subjects with IGD and RGU to different behaviors, i.e., positive and negative events. While playing the LOL game, the combat phase is the most attractive part for players, which is basically divided into attacking the enemy (positive event) and being attacked (negative event). Please see the Methods: Game and procedure section for detailed descriptions of these events.

Previous studies have revealed that playing games involves individual reward/emotional processing and corresponding cognitive regulation processing, as reflected by the significant activation of regions in the corticolimbic neural circuit, including the caudate, putamen, ACC, DLPFC, IFG and MFG (Hoeft, Watson, Kesler, Bettinger, & Reiss, 2008; Klasen et al., 2019). Together with the findings mentioned above, we hypothesized that (1) during positive events, subjects with IGD would show different responses in subcortical regions associated with positive reward/emotions and decreased brain activity in positive reward/emotions-regulation-related prefrontal regions compared to RGU subjects; (2) during negative events, subjects with IGD would show different responses in subcortical regions associated with negative reward/emotions and decreased activity in negative reward/emotions-regulation-related prefrontal regions compared to RGU subjects. In addition, previous studies revealed that individuals with IGD had deficient cognitive regulation and control over reward/emotions compared to controls, as indicated by their decreased functional connectivity (FC) between the regulation-related regions (e.g., DLPFC, IFG and MFG) and reward/emotion-related regions (e.g., putamen and amygdala) during rest (H. Dong et al., 2021; Jin et al., 2016; Ko et al., 2015; M. Wang, Zeng, et al., 2020). FC between regions of interest (ROIs) involving reward/emotions and regulation-related functions was examined to further investigate the relationship between cognitive regulation and reward/emotional processing during game playing in individuals with IGD. We hypothesized that subjects with IGD would show decreased FC between reward/emotion-related ROIs and corresponding regulation-related ROIs compared to RGU subjects during game playing.

METHODS

Participants

Thirty subjects with IGD (6 females, 24 males) and fifty-two RGU subjects (19 females and 33 males) were recruited for this study through advertisement. The number of females and males were matched between the IGD and RGU groups ($\chi^2 = 2.455$, $p = 0.117$). All the subjects included in this study were diagnosed using the Internet Addiction Test (IAT) (K. S. Young, 1998) and nine criteria for IGD proposed by DSM-5 (Petry et al., 2014). The validity and reliability of IAT in diagnosing individuals with internet addiction have been verified in previous studies (Lai et al., 2013; Pawlikowski, Altstötter-Gleich, & Brand, 2013; Widyanto & McMurran, 2004), and it has been widely used in previous studies on IGD (Cai et al., 2016; G. Dong & Potenza, 2016; L. Wang et al., 2023; L. Wang et al., 2022). The IAT contains 20 items with each scoring on a scale of 5 points (1-rarely, 5-always), which measures the degree of issues related to internet use, e.g., withdrawal symptoms, poor family/social relationships, bad academic performance and time management. Self-report scores over 50 indicate frequent issues due to uncontrollable internet use. Thus, consistent with previous studies, the cut-point of 50 was used in the present study to classify IGD and RGU subjects. The DSM-5 criteria for IGD contains nine items with each item depicting one of internet gaming use-related symptoms, such as unsuccessful attempts to stop gaming, preoccupation and abstinence syndrome. The cut-point of meeting five criteria in diagnosing IGD was conservatively chosen by the DSM-5 and Petry et al. (2014), which has also been widely used to diagnose IGD in previous studies (Ko et al., 2014; L. Wang, Wu, et al., 2017; L. Wang, Yang, Zheng, Li, Qi, et al., 2021; Yuan et al., 2016). In the present study, whether the subjects meet the nine DSM-5 criteria for IGD was determined by the clinical interview by an experienced psychiatrist.

Accordingly, the screening criteria for the IGD group were as follows: (1) IAT score greater than 50, (2) met at least five of the nine diagnostic criteria proposed by DSM-5, and (3) most of the time spent on the internet was occupied by playing online games (more than 80%). The screening criteria for the RGU group were as follows: (1) IAT score less than 50, (2) met fewer than five of the nine diagnostic criteria proposed by the DSM-5, (3) had similar gaming time and gaming history with the IGD group, which ensured that they had similar online game experiences, and (4) game behavior did not have a negative effect on their academic performance, work efficiency, daily life, family, or social relations. In addition, all the subjects were asked verbally if they had ever taken drugs, smoked or drunk alcohol and were required to complete some questionnaires if they had, but not if they had not. All the subjects reported having no experience with drugs intake and 57 subjects reported having no experience with either smoking or drinking. The remaining 25 subjects who had experiences with smoking and drinking were asked to complete the Fagerstrom Test for Nicotine Dependence (FTND) questionnaire to assess smoker's nicotine dependence (Huang, Lin, & Wang, 2006) and the Alcohol Use Disorders Identification Test (AUDIT) to assess drinkers' alcohol dependence (Q. Li, Babor, Hao, & Chen, 2011). None of the subjects had addictions to both nicotine and alcohol (FTND scores: $M \pm SD = 0.52 \pm 1.39$; AUDIT scores: $M \pm SD = 2.20 \pm 2.59$) and there was no difference in the FTND and AUDIT scores between the two groups (FTND score: t (23) = 0.626, $p = 0.537$; AUDIT scores: t (23) = −0.035, $p = 0.972$). And all the subjects were also assessed using a structured psychiatric interview (MINI) (Sheehan et al., 1998) to ensure they were free of previous or current psychiatric/neurological disorders (e.g., anxiety, depression, schizophrenia, and substance dependence).

The demographic information of the subjects is shown in Table 1. Age, education, gaming time, gaming history were matched between the two groups. The IAT score, DSM-5 score and craving of the IGD group were significantly higher than those of the RGU group, according to the inclusion criteria.

Game and procedure

The purpose of this study was to investigate the neural activities of individuals with IGD in real gaming situations. All the subjects were loyal players of LOL, a popular online game that has been shown to be addictive (Zastrow, 2017). Before the fMRI scanning, All the subjects were asked to rate their familiarity with the game (LOL) on a scale of 1–5 points (1-not familiar, 5-very familiar). They were all familiar with the game, and there was no difference between the IGD and RGU group (Table 1). Each subject underwent an about 18-min fMRI scan to play the LOL game. During the scanning, the subjects lay supine with their heads snugly fixed by earphone and foam pads to minimize their head movements. All the subjects in the present study met the criteria for head movement (≤3 mm and ≤3°). Before gaming, the subjects were asked to choose the man vs. machine mode to start the game, which is an easy mode in LOL game. Subjects who were not focused on the game, such as keep still for a long time and click the mouse randomly,

Table 1. Demographic information and group differences

Items	IGD ($M = 24$, $F = 6$)	RGU ($M = 33$, $F = 19$)	t	p
Age (years)	21.13 ± 2.33	21.44 ± 2.07	−0.62	0.54
IAT score	66.03 ± 10.75	40.17 ± 10.16	10.87	<0.001
DSM-5 score	5.87 ± 1.04	2.40 ± 1.32	12.33	<0.001
Craving	50.69 ± 15.55	36.25 ± 16.07	3.92	<0.001
Education (years)	14.93 ± 2.36	15.35 ± 2.02	−0.838	0.41
Gaming time (hours/week)	18.13 ± 10.37	15.69 ± 10.03	1.049	0.30
Gaming history (years)	3.8 ± 0.48	3.87 ± 0.40	−0.662	0.51
Game familiarity	4.41 ± 0.68	4.42 ± 0.69	−0.058	0.95

Table values: mean ± standard deviation
Abbreviations: IGD, internet gaming disorder; RGU, recreational game use; M, Male; F, Female; IAT, internet addiction test; DSM-5, the fifth edition of Diagnostic and Statistical Manual of Mental Disorders; Craving, self-reported craving before scan.

were removed from the study. These settings ensured that all the subjects performed equally during playing the game. An event-related approach was used to analyze the blood oxygen level-dependent (BOLD) signals accompanying specific game events. We observed the video of subjects playing LOL during fMRI scanning and coded in-game behaviors by recording the time points of behaviors. We divided the game behaviors into three types: positive behavior, negative behavior, and baseline behavior (to exclude individual differences). The operational definitions of the three types of behaviors are provided below.

1. The positive behavior is when the subject successfully attacks the enemy and escapes the enemy's attack. During this period, we chose a certain attack of the subjects on the enemy as the onset time of one trial and ensured that the number of events of this type was greater than 5.
2. Negative behavior occurs when the subject suffers passively from the enemy's attack and is unable to effectively return the attack. During this period, we chose a certain attack of the enemy as the onset time of one trial and ensured that the number of events of this type was greater than 5.
3. The baseline behavior is that the subjects do not attack or are not attacked in the game for a period of time. In this process, we chose an interval time point as the onset time of one trial and ensured that the number of events of this type was greater than 10.

Figure 1B shows examples of the three types of behavior and Table 2 shows the number of events in each type. Regarding the accuracy of behavior coding in game videos, the following precautions were implemented: (1) The coding operation is coded by two operators and one supervisor who are all experienced LOL players, and (2) before the coding operation, coding training was conducted for the operator for 1 h

Imaging acquisition

Functional MRI was performed on a 3 T scanner (Siemens Trio) with a gradient-echo EPI T2* weighted-sensitive pulse sequence in 33 slices (interleaved sequence, 3 mm thickness, TR = 2,000 ms, TE = 30 ms, flip angle = 90°, field of view = 220 × 220 mm^2, and matrix = 64 × 64). A real-time game screen was presented using an Invivo synchronous system (www.invivocorp.com) through a screen in the head coil, enabling subjects to view the game screen.

Data preprocessing

Figure 1 shows the whole analytical pipeline of this study. FMRI data were preprocessed using the DPABI version 5.0 toolbox (Yan, Wang, Zuo, & Zang, 2016). First, images were preprocessed through time and head movement corrections. Then, corrected images were registered to the corresponding EPI templates and spatially transformed to the standard MNI space with 3 × 3 × 3 mm^3 voxels. Finally, the normalized images were smoothed by a Gaussian kernel of 6 mm FWHM.

First-level regression analysis

After preprocessing, statistical parametric mapping (SPM) 12 (http://www.fil.ion.ucl.ac.uk/spm) was used to perform the general linear model (GLM) analysis of the BOLD signals related to the events of interest. In this study, our events of interest were the three types of behaviors (positive/negative/baseline). All types of trials (positive/negative/baseline trials) were included as conditions in the model to account for potential effects on the results. The six head movement parameters derived from the realignment stage were included in the model as covariates of no interest to remove the potential effects of head movement to the results. The GLM analysis was independently applied to each voxel to identify voxels that were significantly activated by the different types of trials.

Second-level group analysis

First, we determined voxels that showed a main effect in the positive and negative trials relative to the baseline among each subject. Therefore, we set two events: positive events (positive minus baseline) and negative events (negative minus baseline). Second, we examined clusters with significantly different BOLD signals between the two groups during each event within whole brain (e.g., [IGD $_{positive}$ − IGD $_{baseline}$] − [RGU $_{positive}$ − RGU $_{baseline}$] for the positive event) using the FWE multiple comparison correction with a voxel-level threshold $p < 0.005$ and a cluster-level threshold $p < 0.05$.

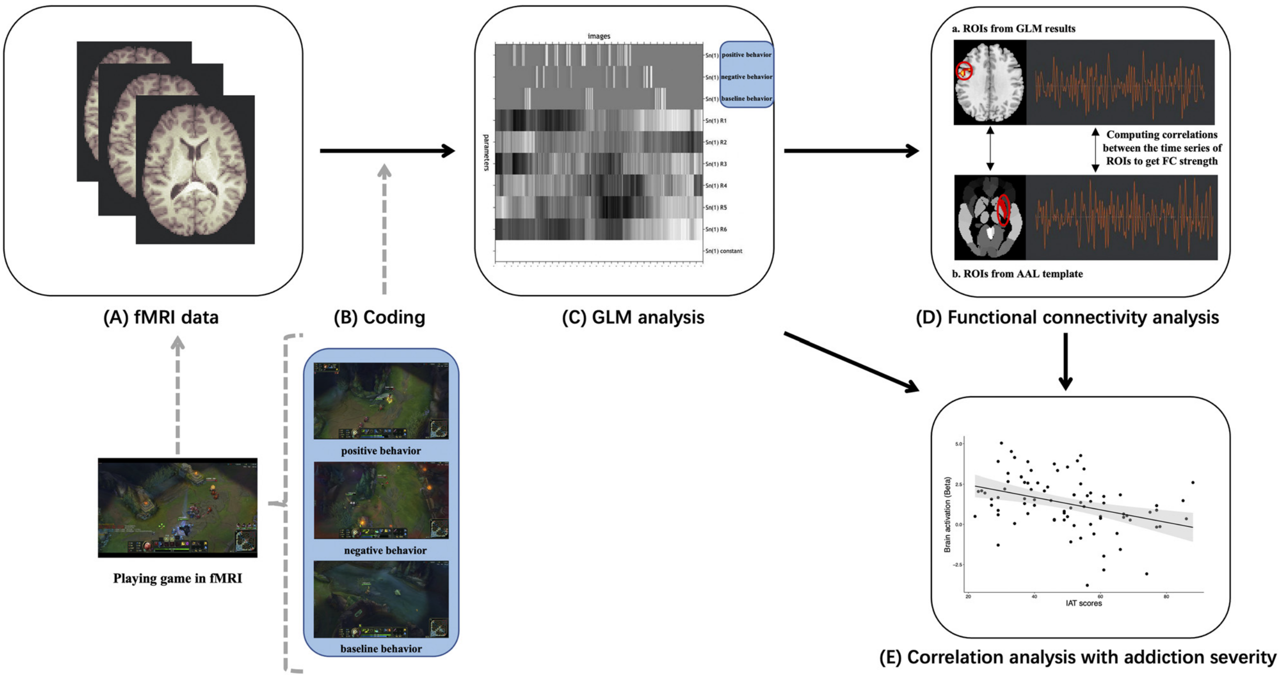

Fig. 1. **The analytical pipeline of this study**

(A) FMRI data were obtained when subjects played the game during the scan. (B) Subjects' gaming behaviors were coded into three types (blue) for further analysis. (C) A GLM containing positive, negative, baseline behaviors and six head movement parameters was conducted for every subject to generate brain activation in response to events of interest. Then, brain activation was compared between the IGD group and the RGU group. (D) An FC analysis was conducted between cognitive regulation-related ROIs obtained from GLM results and reward/emotion-related ROIs obtained from the AAL template. (E) The correlation between the GLM/FC results and the addiction severity of IGD (IAT/DSM-5 scores) was determined.

Abbreviations: fMRI, functional magnetic resonance imaging; GLM, general linear model; IGD, internet gaming disorder; RGU, recreational game use; FC, functional connectivity; ROIs, regions of interest; AAL, anatomical automatic labeling; IAT, internet addiction test; DSM-5, the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders.

Table 2. Number of events of the three behavior types

Behavior types	IGD	RGU	t	p
Positive	14.60 ± 6.36	13.73 ± 5.42	0.656	0.514
Negative	10.40 ± 3.40	9.46 ± 3.35	1.215	0.228
baseline	14.73 ± 1.48	14.79 ± 1.39	−0.169	0.866

Table values: mean ± standard deviation
Abbreviations: IGD, internet gaming disorder; RGU, recreational game use.

Additionally, to clarify the correlation between brain activity and addiction severity, we extracted the averaged BOLD signal from the survived clusters that showed between-group differences and analyzed the correlations between the BOLD signal and the clinical measures (IAT and DSM-5 scores) among all the subjects using the Pearson correlation analysis in SPSS v25.

Ethics

The study procedures were carried out in conformity to the Declaration of Helsinki. The Institutional Review Board of Hangzhou Normal University approved the current study. All participants provided written informed content and the safety screening scale for MRI scan before the study.

RESULTS

Brain responses during positive events

As shown in Fig. 2, a large part of subcortical and prefrontal cortex was activated by positive events, such as caudate, putamen, DLPFC and IFG, as well as some part of temporal lobe. For group differences, as shown in Fig. 3A and Table 3, compared with the RGU group, brain responses of subjects with IGD were significantly lower in the left DLPFC and left middle and inferior temporal gyrus. We verified the relationship between brain activation during positive events and addiction severity and found that the brain activation of the left DLPFC negatively correlated with the IAT (Fig. 3B) and DSM-5 scores (Fig. 3C) among all the subjects.

Brain responses during negative events

As shown in Fig. 4, in contrast with regions in positive events, negative events activated a smaller part of prefrontal and subcortical cortex and distinct activation in ACC. For group differences, as shown in Fig. 5A and Table 3, compared with the RGU group, brain responses of subjects with IGD were significantly lower in the left MFG. We verified the relationship between brain activation and addiction severity during negative events and found that the

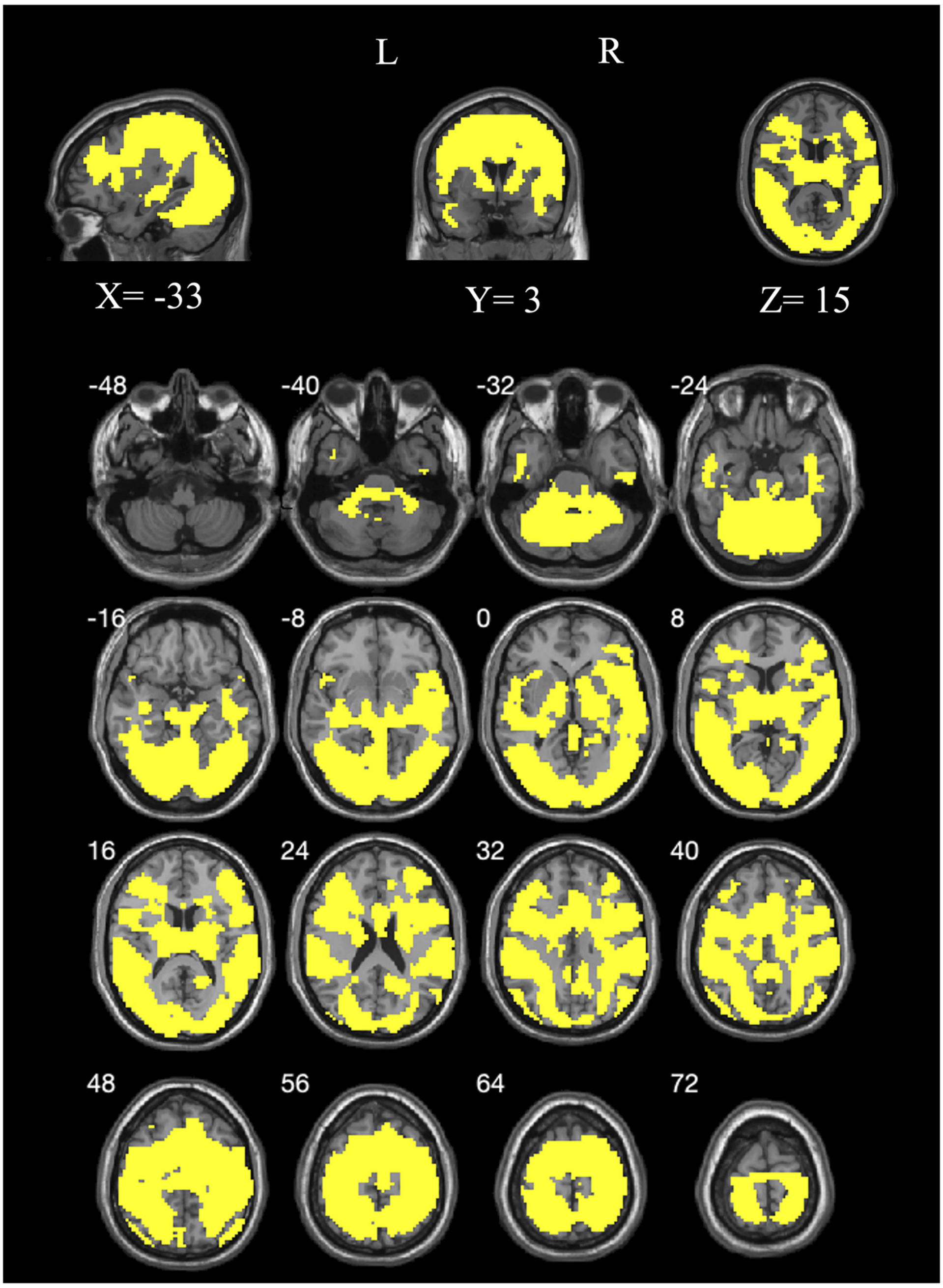

Fig. 2. **Regions showing significant activation during positive events among the IGD or RGU subjects**
The images were obtained after the FWE correction with a voxel-level threshold $p < 0.005$ and a cluster-level threshold $p < 0.05$.
Abbreviations: IGD, internet gaming disorder; RGU, recreational game use; L, left; R, right; BA, Brodmann's area; DLPFC, dorsolateral prefrontal cortex.

brain activation of the left MFG negatively correlated with the IAT (Fig. 5B) and DSM-5 scores (Fig. 5C) among all the subjects.

Analysis of functional connectivity and results

To further examine our hypotheses about the FC between reward/emotion regions and corresponding regulation-related regions in individuals with IGD, we analyzed the group differences (IGD vs. RGU) in FC between reward/emotion regions and regulation-related regions during the positive and negative events separately using the CONN toolbox v15 (Whitfield-Gabrieli & Nieto-Castanon, 2012). The putamen was found to be commonly activated by positive rewards and stimuli, including monetary reward-cues (Knutson & Cooper, 2005; Seo et al., 2014; Subramaniam et al., 2016; C. B. Young & Nusslock, 2016) and addiction-cues (Engelmann et al., 2012; Liu, Yip, et al., 2017; Timmeren, Holst, & Goudriaan, 2023), thus, it was suggested to be closely associated with craving for addictive behaviors. Also, a growing number of studies have found abnormal resting-state FC in the putamen-prefrontal circuit

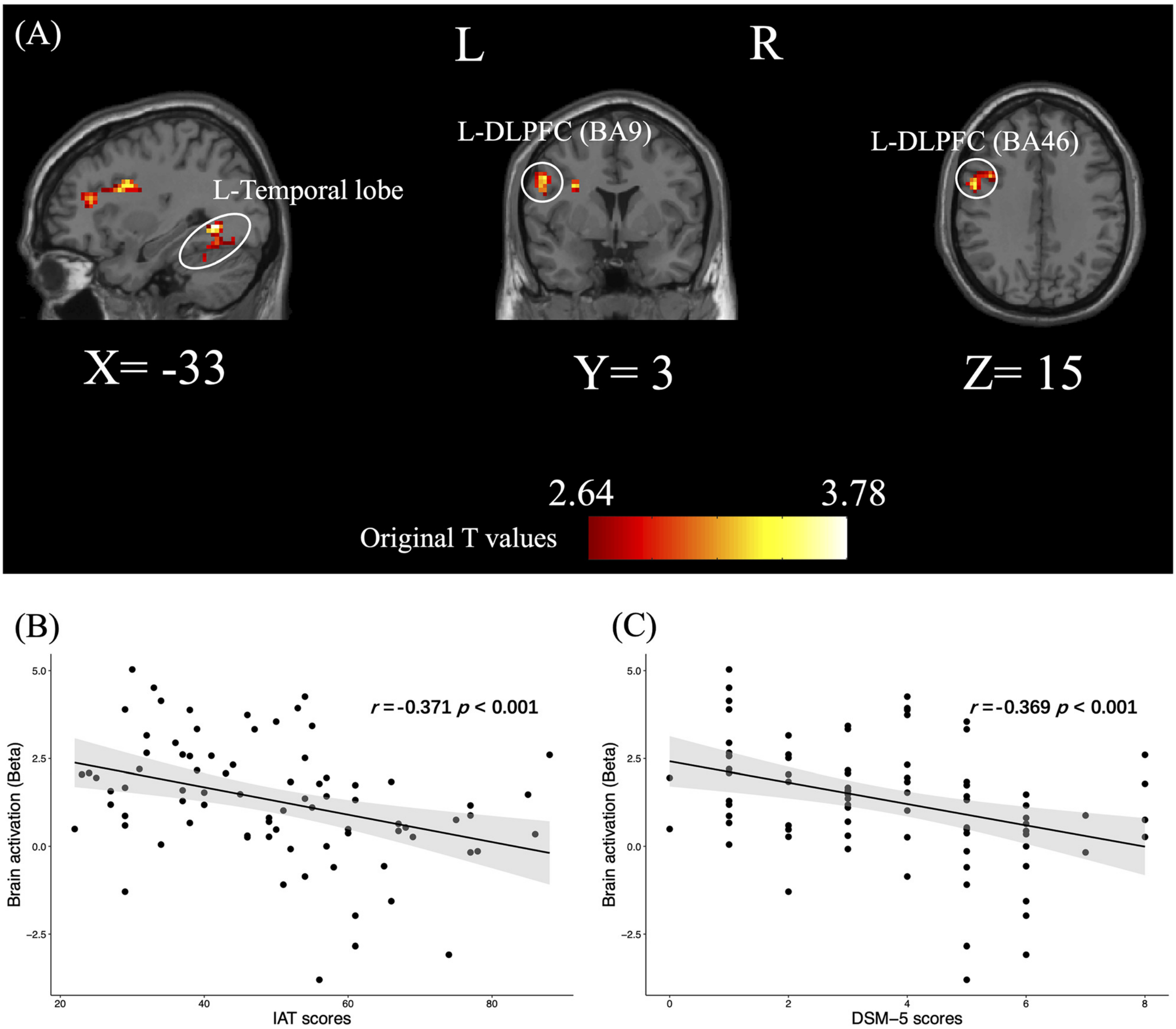

Fig. 3. **Regions showing group differences (IGD vs. RGU) in activation during positive events and correlations between brain activation and severity scores**

Subplot (A) illustrating the regions showing decreased activation in the IGD group compared to the RGU group during positive events (positive minus baseline). Subplot (B) illustrating the negative correlation between the brain activation of the left DLPFC and the IAT scores. Subplot (C) illustrating the negative correlation between the brain activation of the left DLPFC and the DSM-5 scores.

Abbreviations: IGD, internet gaming disorder; RGU, recreational game use; L, left; R, right; BA, Brodmann's area; DLPFC, dorsolateral prefrontal cortex; IAT, internet addiction test; DSM-5, the fifth edition of Diagnostic and Statistical Manual of Mental Disorders.

in IGD, such as decreased FC between the putamen and IFG (H. Dong et al., 2021), decreased FC between the ACC and putamen (Jin et al., 2016), and decreased FC between the mPFC and putamen (D. Lee, Namkoong, Lee, & Jung, 2021) in IGD subjects relative to HCs, which revealed typical neural features in IGD. Accordingly, the bilateral putamen from the anatomical automatic labeling (AAL) template was selected as reward-related ROIs for positive events (Fig. 6A). As for negative events, considering that the amygdala was known to be the important role in negative emotions (Koob & Volkow, 2016; Schaefer et al., 2002; Sharp, 2017) and abnormal FC between the amygdala and prefrontal cortex (e.g., DLPFC and orbital front lobe) in IGD have been found in previous studies (Everitt & Robbins, 2016; Kim et al., 2021). Accordingly, the bilateral amygdala from the AAL template was selected as emotion-related ROIs for negative events (Fig. 6C). For the regulation-related regions, the regions obtained from the GLM results were selected as ROIs (positive event: DLPFC (−54,3,33), negative event: MFG (−42, −3,60); radius: 6 mm, Fig. 6A and 6C) given their involvement in cognitive regulation of reward/emotions. After generating the FC values among these ROIs, an independent t-test was performed to examine the group differences in FC between these ROIs for each event. FDR correction was applied for each event to control false positive due to multiple comparison.

Table 3. Regions showing group differences (IGD vs. RGU) in activation during events of interest

Events	Regions[a]	BA[b]	Cluster size[c]	x, y, z[d]
IGD < RGU				
Positive				
	DLPFC (L)	9	189	−54, 3, 33
	DLPFC (L)	46		−39, 36, 15
	Inferior Temporal Gyrus (L)		203	−48, −60, −12
	Middle Temporal Gyrus(L)			−51, −48, −12
Negative				
	MFG (L)		473	−42, −3, 60
	Postcentral Gyrus (L)			−52, −21, 48
	Precentral Gyrus (L)			−48, −6, 51

[a] The brain regions were consulted from the xjView toolbox (https://www.alivelearn.net/xjview).
[b] Brodmann's area.
[c] Number of voxels.
[d] Peak MNI coordinates.
Abbreviations: IGD, internet gaming disorder; RGU, recreational game use; L, left; DLPFC, dorsolateral prefrontal cortex; MFG, middle frontal gyrus.

Table 4 shows the difference in functional connectivity between the two groups during the positive and negative events. During positive events, the IGD group showed weaker FC between the left DLPFC and right putamen than the RGU group, and this FC was associated with the IAT scores (Fig. 6B). During negative events, the IGD group showed weaker FC between the left MFG and right amygdala than the RGU group; however, the correlation between this FC and the IAT scores did not reach significance (Fig. 6D).

DISCUSSION

This study investigated the brain activity of subjects with IGD and RGU subjects during positive and negative in-game behaviors in a real gaming situation, which overcame the limitations of previous studies using experimental tasks, e.g., reflective of out-of-gaming states instead of gaming states. The current results revealed deficits in regulating game craving, maladaptive habitual gaming behaviors and negative emotions, as well as audiovisual and sensorimotor function in individuals with IGD during gaming. These findings may be critical for the development and maintenance of IGD and provide specific targets for future research into effective treatments for IGD, such as transcranial magnetic stimulation.

IGD subjects show deficient regulation of craving and habitual behaviors compared to RGU subjects during gaming

During positive events (i.e., the subjects successfully attack the enemy and escape the enemy's attack), the IGD subjects displayed significantly lower brain activity in the left DLPFC than the RGU subjects. This is consistent with previous findings on cue-reactivity and reward-based decision-making tasks that individuals with IGD showed decreased activation in DLPFC than controls when viewing gaming-related stimuli and choosing larger monetary rewards (G. Dong, Liu, Zheng, Du, & Potenza, 2019; G. Dong et al., 2018; Y. Wang, Hu, et al., 2017; Zhang, Hu, et al., 2020). The DLPFC plays an important role in a variety of functions, including evaluation of reward value, emotion regulation, working memory and inhibitory control (Angius, Santarnecchi, Pascual-Leone, & Marcora, 2019; Golkar et al., 2012; Staudinger, Erk, & Walter, 2011). Also, studies found that lower activation of the DLPFC was correlated with larger craving induced by addiction-related stimuli in addicted individuals and the increased activation of the right DLPFC caused by transcranial direct current stimulation (tDCS) facilitated down-regulation of game craving in IGD subjects (G. Dong et al., 2019; Kober & Mell, 2015; Kober et al., 2010; Wu et al., 2020). These studies indicated the important role of the DLPFC in regulation of craving in addicted population.

Further, weaker FC between the left DLPFC and right putamen in the IGD subjects than the RGU subjects during positive events was identified in the present study, which was consistent with the studies examining the FC in IGD subjects during resting-state (H. Dong et al., 2021; Han, Wang, et al., 2018; Han, Wu, et al., 2018; D. Lee et al., 2021; M. Wang, Dong, Zheng, Du, & Dong, 2020; Yuan et al., 2016). The putamen, one part of the dorsal striatum, is known to be implicated in habitual behaviors (automatic responses to stimuli) and is commonly activated by positive rewards and addiction-related stimuli. Its activation correlated positively with the craving induced by addiction stimuli (Grodin, Courtney, & Ray, 2019; Nora D Volkow et al., 2006; Wong et al., 2006). Moreover, previous studies evidenced that weaker FC between the putamen and the prefrontal cortex was associated with larger game craving in subjects with IGD (H. Dong et al., 2021; M. Wang, Zheng, Zhou, et al., 2022). Studies on other addiction indicated that reduced craving caused by cognitive strategies or intranasal Oxytocin elicited increased activation in prefrontal regions and decreased activation in craving-related regions including caudate, putamen and midbrain in addicted individuals (Kober et al., 2010; Striepens et al., 2016). And the negative association between the activation of prefrontal regions and craving was fully mediated by the activation of striatum revealed by a mediation analysis (Kober et al., 2010). These findings demonstrated the crucial role of FC between the DLPFC and putamen in regulation of craving in addicted population. Therefore, the lower activation of the DLPFC and weaker FC between the DLPFC and putamen in the IGD subjects might suggest their deficient regulation of game craving when experiencing positive events during real gaming. This inference was further supported by the results that lower activation of the DLPFC and weaker FC between the DLPFC and putamen was associated with higher addiction severity of IGD.

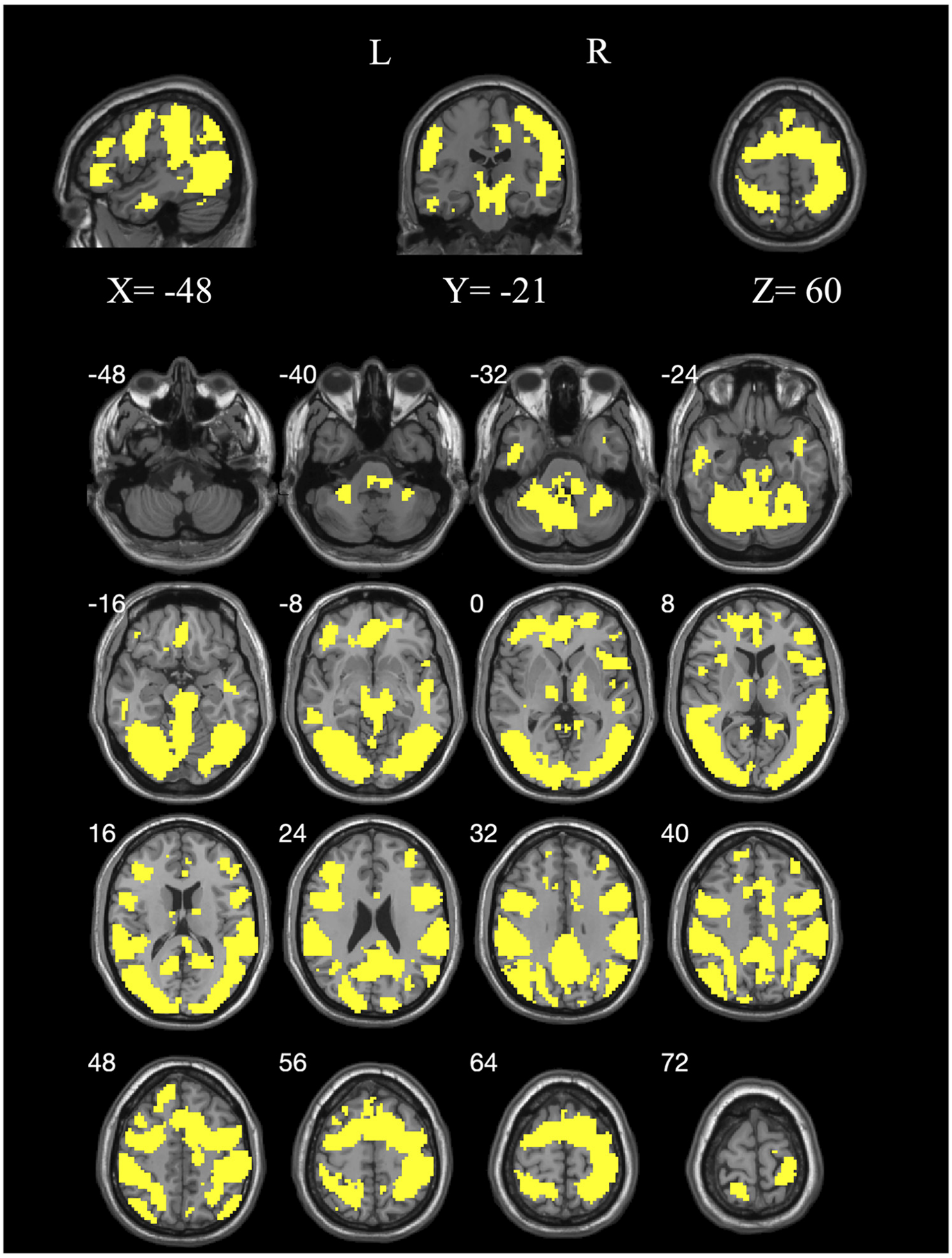

Fig. 4. **Regions showing significant activation during negative events among the IGD or RGU subjects**
The images were obtained after the FWE correction with a voxel-level threshold $p < 0.005$ and a cluster-level threshold $p < 0.05$.
Abbreviations: IGD, internet gaming disorder; RGU, recreational game use; L, left; R, right; MFG, middle frontal gyrus.

Notably, the current finding is consistent with the theoretical model of neural pathways in addiction proposed by (Brand, 2022). Specifically, the "feels better" path and the "must do" path are two driving paths to increase the engagement in online activities. Meanwhile, a "stop now" process mainly involving the DLPFC may regulate the two driving paths to addiction. The "must do" path includes habitual behaviors and especially compulsive behaviors, which mainly involved the dorsal striatum (putamen and caudate). The present finding that weaker FC between the DLPFC and putamen in the IGD subjects during real gaming provides direct evidence for the imbalance between the driving path ("must do") and "stop now" process in individuals with internet addiction expressed by this model. Accordingly, the present result might also suggest the deficient regulation of habitual and compulsive gaming responses to positive events during gaming in the IGD subjects, which may underlie their maladaptive persistence of gaming behavior despite its negative consequences.

IGD subjects show deficient regulation of negative emotions compared to RGU subjects during gaming

In response to negative events (i.e., the subjects suffer passively from the enemy's attack and are unable to effectively return the attack), brain activity in the left MFG was

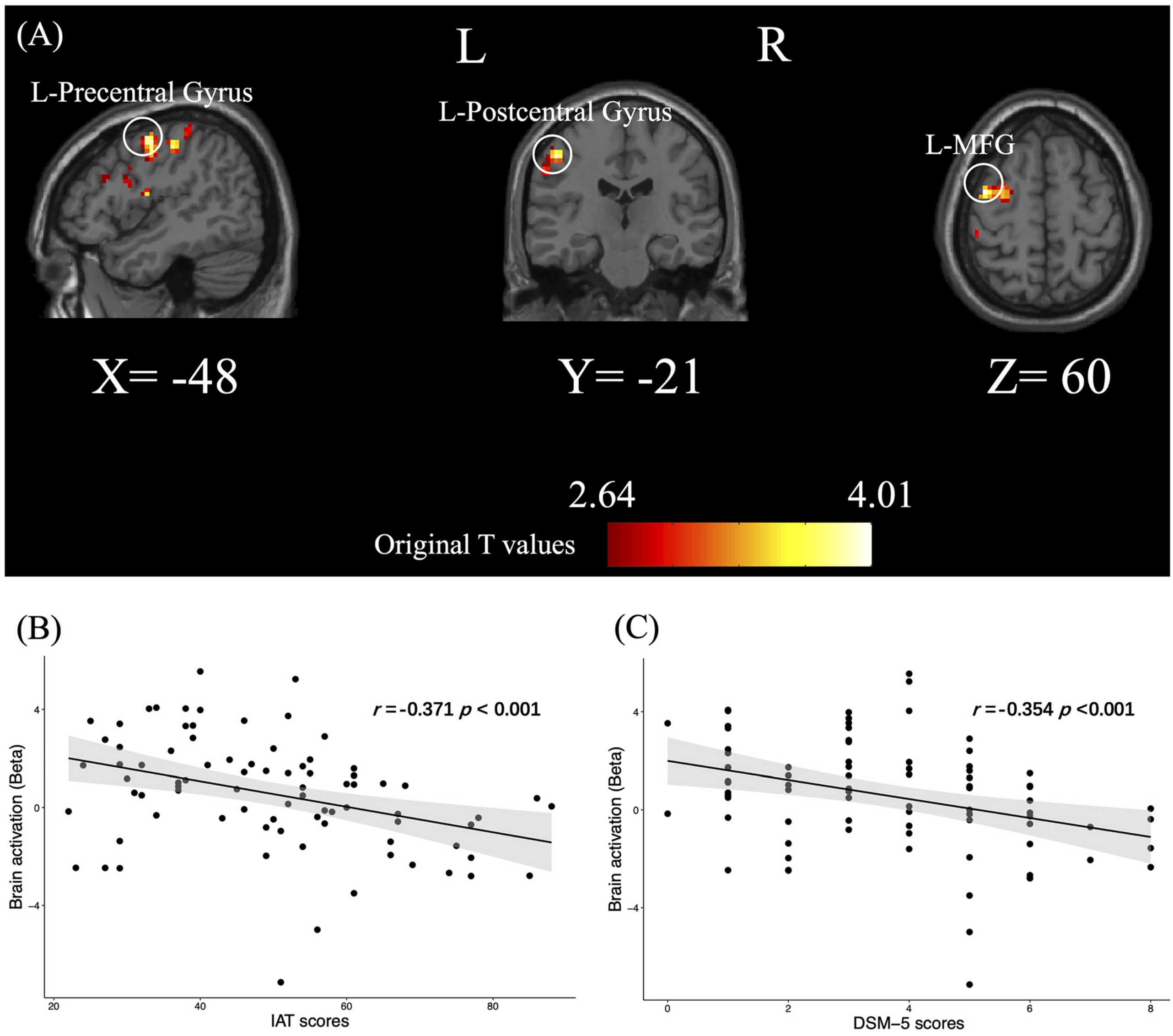

Fig. 5. **Regions showing group differences (IGD vs. RGU) in activation during negative events and correlations between brain activation and severity scores**

Subplot (A) illustrating the regions showing decreased activation in the IGD group compared to the RGU group during negative events (negative minus baseline). Subplot (B) illustrating the negative correlation between the brain activation of the left MFG and the IAT scores. Subplot (C) illustrating the negative correlation between the brain activation of the left MFG and the DSM-5 scores.

Abbreviations: IGD, internet gaming disorder; RGU, recreational game use; L, left; R, right; MFG, middle frontal gyrus; IAT, internet addiction test; DSM-5, the fifth edition of Diagnostic and Statistical Manual of Mental Disorders.

significantly lower in the IGD subjects than in the RGU subjects. The left MFG belongs to the prefrontal network and is involved in multiple functions, such as emotional regulation, reorientation of attention and inhibitory control (Blair et al., 2007; Japee, Holiday, Satyshur, Mukai, & Ungerleider, 2015; Munakata et al., 2011; Winecoff, LaBar, Madden, Cabeza, & Huettel, 2011). Similarly, individuals with IGD showed lower brain response in MFG to negative stimuli compared to controls, suggesting their emotional regulation ability (Yip et al., 2018). The correlational result, that is, lower activation of the MFG correlated with greater addiction severity of IGD, further suggested the clinical relevance of this neural activity.

Moreover, the IGD subjects showed weaker FC between the left MFG and the right amygdala than the RGU subjects during negative events. The amygdala is known to be responsible for the perception and arousal of negative emotions in response to negative stimuli (Adolphs, Russell, & Tranel, 1999; Tranel, Gullickson, Koch, & Adolphs, 2006). The dynamic interplay between the prefrontal cortex and amygdala enables individuals to react to significant stimuli and modulate emotional responses to adapt to different situations (Ochsner & Gross, 2005; Pessoa, 2008; Quirk & Beer, 2006). In particular, individuals who were better able to down-regulate negative emotion showed stronger FC between the prefrontal regions and amygdala

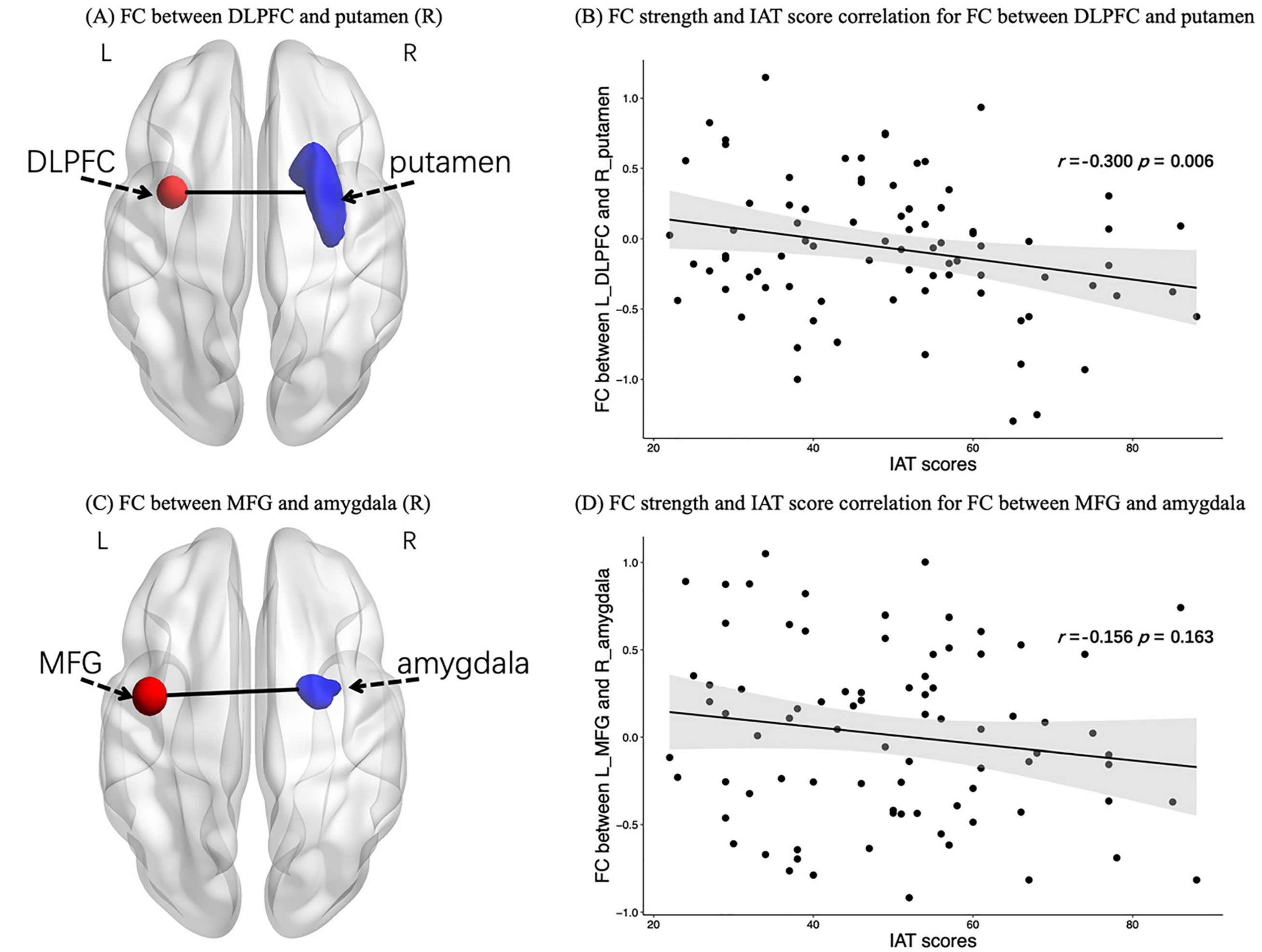

Fig. 6. **The results of the functional connectivity analysis and correlation analysis**

Subplot (A) showing the ROIs investigated in the FC analysis during positive events. Subplot (B) showing that the FC strength of the DLPFC-putamen under positive events is significantly negatively correlated with IAT scores. Subplot (C) showing the ROIs investigated in the FC analysis during negative events. The subplot (D) shows that the FC strength of the MFG-amygdala during negative events is negatively correlated with IAT scores.

Abbreviations: FC, functional connectivity; L, left; R, right; DLPFC, dorsolateral prefrontal cortex; MFG, middle frontal gyrus; IAT, internet addiction test; ROIs, regions of interest.

Table 4. Differences in functional connectivity between IGD and RGU group

Events	ROIs	x, y, z	Connected regions	*t*	*p*
IGD < RGU					
Positive					
	DLPFC (L)	−54, 3, 33	Putamen (R)	−2.37	0.020*
Negative					
	MFG (L)	−42, −3, 60	Amygdala (R)	−2.11	0.038*

Table notes: we listed the significant FCs of decreased activation in the IGD group compared to the RGU group in different events.
* indicates $p < 0.05$ after FDR correction.
Abbreviations: IGD, internet gaming disorder; RGU, recreational game use; ROIs, regions of interest; DLPFC, dorsolateral prefrontal cortex; MFG, middle frontal gyrus; L, left; R, right; FC, functional connectivity.

(H. Lee, Heller, Van Reekum, Nelson, & Davidson, 2012). And weaker FC between the amygdala and MFG is proved to be a neurobiological marker in patients with major depressive disorder, a typical emotional disorder that is bad at regulating negative emotions (Qiao et al., 2020). Therefore, the lower activation of the MFG and weaker FC between the MFG and amygdala in the IGD subjects might suggest their deficient regulation of negative emotions when experiencing negative events during real gaming.

As stated in the theoretical model of neural pathways in addiction proposed by (Brand, 2022), the “feel better” driving path includes both positive and negative reinforcement experiences. Not only pleasure and reward are the motivation to persistently engage in online activities in individuals with internet addiction, but also reduction of stress and negative mood. Based on the negative reinforcement in addiction, researchers have demonstrated the impaired regulation of negative emotions in individuals with IGD using questionnaire survey, resting-state fMRI and emotional regulation tasks (Z. Wang, Song, et al., 2022; Yen et al., 2018; Yip et al., 2018; Zhang, Dong, et al., 2020). The present finding that deficient regulation of negative emotions in the IGD subjects during real gaming provides direct evidence for the imbalance between the driving path ("feel better") and "stop now" process in individuals with internet addiction expressed by this model.

IGD subjects exhibit impaired audiovisual and sensorimotor functions compared to RGU subjects during gaming

During positive events, subjects with IGD showed decreased activity in the middle and inferior temporal gyrus compared with the individuals with RGU. This result was consistent with previous findings from IGD (G. Dong, Huang, & Du, 2012; G. Dong & Potenza, 2016). These regions are considered responsible for auditory and visual functions (Rezk et al., 2020; Robins, Hunyadi, & Schultz, 2009). The inferior temporal gyrus is one component of the higher levels of the ventral stream of audio and visual processing and is associated with the representation of complex object features (Allison, McCarthy, Nobre, Puce, & Belger, 1994; Lewald, Staedtgen, Sparing, & Meister, 2011). The middle temporal gyrus is highly specialized to process visual motion (Sulpizio et al., 2022; Tootell et al., 1995). The decreased activity in those regions might suggest that the audiovisual function of the subject with IGD is impaired. During negative events, the lower activation of the postcentral gyrus and precentral gyrus was consistent with previous studies on the cue reactivity of individuals with IGD (L. Wang, Wu, et al., 2017). Moreover, these two brain regions significantly predicted the severity of IGD (Jin et al., 2016; Ye, Wang, Yang, Dong, & Dong, 2020). The postcentral and precentral gyrus play a key role in the sensorimotor network to integrate sensorimotor information and coordinate body movement (Desmurget et al., 2014; Porro et al., 1996). The lower activation of these two regions might indicate that the sensorimotor function of the IGD subjects is broken. Overall, the current results might suggest that prolonged and compulsive game playing had negative impacts on the audiovisual and sensorimotor functions in IGD subjects.

Limitations

Three limitations should be noted. First, the female subjects were fewer than the male subjects in the present study due to the higher prevalence of IGD in males than in females. Although the number of females and males was balanced between the IGD and RGU groups, the results might be biased. Future studies to explore the sex effect in IGD during game-playing are needed. Second, in the present study, we avoided the effects of gaming experiences between the IGD and RGU groups to the greatest extent, including similar gaming time, gaming history, familiarity to the game (LOL) and performance during gaming among the two groups, however, the level of game skills of the subjects was not recorded. The final results may be biased by the possible differences in game skills between the two groups. Future studies are expected to examine the current studies after controlling the level of game skills and explore its effect to IGD. Third, the correlations between the brain activity and the IAT, DSM-5 scores only among the IGD subjects were not significant in the present study, which may be caused by the relatively small range of IAT scores and DSM scores and the small sample size of the IGD group (n = 30). Most of the IGD subjects scored between 50 and 70 for IAT, scored between 5 and 6 for DSM. The small difference in addiction severity among these IGD subjects and the small sample size make it difficult to detect a significant trend between addiction severity and brain activity among the IGD group. To tackle this limitation, we performed correlations among all the subjects. The IAT and DSM scores of RGU subjects also reflect their degree of issues and symptoms related to internet gaming. Accordingly, to some extent, the significant correlations between IAT, DSM scores and brain activity among all the subjects could also indicate the important role of brain activation of those regions (Table 3) in the severity of internet gaming problems. Studies with using a larger sample size of IGD subjects with a wider range of IAT scores and DSM scores was expected to examine the current correlational results.

CONCLUSION

The current study overcame the limitations of previous findings on IGD during experimental tasks and provided the direct detection of the brain responses during game playing in IGD subjects. This study revealed decreased activity in the prefrontal regions and weaker FC between these regions and regions associated with craving/emotion processing in subjects with IGD during real-time gaming. Furthermore, these abnormalities in neural activation and FC were significantly negatively correlated with the subjects' addiction severity (IAT and DSM-5 scores). In addition, the current study found decreased activity in audiovisual and sensorimotor brain regions in subjects with IGD during real-time gaming. These results mainly reveal that individuals with IGD show deficient regulation of game-craving/habitual gaming behaviors and negative emotions, as well as audiovisual and sensorimotor function deficits during real gaming. These findings provide insights into the neural mechanisms activated during real-time gaming in subjects with IGD and explain why subjects with IGD show strong craving, maladaptive habitual gaming behaviors and impaired emotional regulation when playing games. An important and efficient approach for the treatments and preventative measures for IGD would be to use the neural abnormalities identified in the current study as targets.

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Authors' contribution: Mr. Zhang conducted the statistical analysis and wrote the manuscript. Dr. L Wang and Dr. Dong collected the research data and modified the manuscript. Dr. Du contributed to the data collection. Miss S Wang contributed to statistical analysis. Dr Qi contributed to the revision of the manuscript. All authors have full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors have approved the final manuscript.

Conflict of interest: The authors declare no conflict of interest.

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