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Dissociable neural processes during risky decision-making in individuals with Internet-gaming disorder☆

Lu Liu[a], Gui Xue[b,c], Marc N. Potenza[d,e], Jin-Tao Zhang[b,*], Yuan-Wei Yao[b], Cui-Cui Xia[a,f], Jing Lan[a], Shan-Shan Ma[b], Xiao-Yi Fang[a,*]

[a] Institute of Developmental Psychology, Beijing Normal University, Beijing 100875, China
[b] State Key Laboratory of Cognitive Neuroscience, Learning and IDG/McGovern Institute for Brain Research, Beijing Normal University, Beijing 100875, China
[c] Center for Collaboration and Innovation in Brain and Learning Sciences, Beijing Normal University, Beijing 100875, China
[d] Departments of Psychiatry and Neuroscience, the Child Study Center, the National Center on Addiction and Substance Abuse, Yale University School of Medicine, New Haven, CT 06519, USA
[e] Connecticut Mental Health Center, New Haven, CT 06519, USA
[f] Students Counseling Center, Beijing Normal University, Beijing 100875, China

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ABSTRACT

Risk-taking is purported to be central to addictive behaviors. However, for Internet gaming disorder (IGD), a condition conceptualized as a behavioral addiction, the neural processes underlying impaired decision-making (risk evaluation and outcome processing) related to gains and losses have not been systematically investigated. Forty-one males with IGD and 27 healthy comparison (HC) male participants were recruited, and the cups task was used to identify neural processes associated with gain- and loss-related risk- and outcome-processing in IGD. During risk evaluation, the IGD group, compared to the HC participants, showed weaker modulation for experienced risk within the bilateral dorsolateral prefrontal cortex (DLPFC) ($t = -4.07$; $t = -3.94$; $P_{FWE} < 0.05$) and inferior parietal lobule (IPL) ($t = -4.08$; $t = -4.08$; $P_{FWE} < 0.05$) for potential losses. The modulation of the left DLPFC and bilateral IPL activation were negatively related to addiction severity within the IGD group ($r = -0.55$; $r = -0.61$; $r = -0.51$; $P_{FWE} < 0.05$). During outcome processing, the IGD group presented greater responses for the experienced reward within the ventral striatum, ventromedial prefrontal cortex, and orbitofrontal cortex (OFC) ($t = 5.04$, $P_{FWE} < 0.05$) for potential gains, as compared to HC participants. Within the IGD group, the increased reward-related activity in the right OFC was positively associated with severity of IGD ($r = 0.51$, $P_{FWE} < 0.05$). These results provide a neurobiological foundation for decision-making deficits in individuals with IGD and suggest an imbalance between hypersensitivity for reward and weaker risk experience and self-control for loss. The findings suggest a biological mechanism for why individuals with IGD may persist in game-seeking behavior despite negative consequences, and treatment development strategies may focus on targeting these neural pathways in this population.

1. Introduction

Internet gaming disorder (IGD) is characterized by persistent gaming online despite negative consequences (e.g., poor academic performance, impaired social interaction, insomnia) (King and Delfabbro, 2014; Petry et al., 2014). This particular feature is a criterion of IGD that has been considered central to the disorder (Petry et al., 2014), and one reflecting maladaptive risky decision-making in real life. Behavioral studies have shown that individuals with IGD select risky options more often than do healthy participants (Dong and Potenza, 2015; Yao et al., 2015a; Yao et al., 2015b), Risk-taking also has been associated with substance-use and gambling disorders (Noël et al., 2013). These observations together suggest that impairments in risky decision-making may be core features shared by different kinds of addictions.

Risky decision-making, as a complex process, involves both risk evaluation and outcome processing (Gowin et al., 2013; Xue et al., 2009). Previous studies of IGD or Internet addiction disorder (IAD) have revealed neural alterations underlying reward/outcome processing including ones involving the medial prefrontal cortex (MPFC),

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* Correspondence to: Jin-Tao Zhang, State Key Laboratory of Cognitive Neuroscience and Learning and IDG/McGovern Institute for Brain Research, Beijing Normal University, Beijing 100875, China. Xiao-Yi Fang, Institute of Developmental Psychology, Beijing Normal University, Beijing 100875, China.
E-mail addresses: zhangjintao@bnu.edu.cn (J.-T. Zhang), fangxy@bnu.edu.cn (X.-Y. Fang).

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orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), and the posterior cingulate cortex (PCC); these regions have been implicated in affective/motivational responses, reward-value processing, aversive processing and attentional/motor control, respectively (Dong et al., 2013b; Dong et al., 2011; Lorenz et al., 2013). Studies have also identified altered neural function related to risk evaluation and impulse control including the inferior frontal gyrus (IFG), anterior insula, ACC and the inferior parietal lobule (IPL) individuals with IGD as compared to those without (Dong et al., 2013a; Dong and Potenza, 2015; Lin et al., 2015), with the ACC along with the anterior insula implicated in conflict monitoring and aversive processing, the IFG in inhibition processing, and the IPL in uncertainty processing. However, few studies have assessed dysfunction of specific facets of decision-making to investigate systematically decision-making deficits and their neural correlates in IGD.

Risk evaluation and outcome processing underlying decision-making may require different processes for assessing potential gains versus losses (Levin et al., 2011; Weller et al., 2007). Individuals with substance-use disorders (SUDs) have been shown to make more disadvantageous choices for potential rewards related to impaired risk evaluation (Brevers et al., 2014; Brevers et al., 2012), to demonstrate greater reward sensitivity associated with hyper-activation of reward circuitry (Jia et al., 2011), and to show hypersensitivity to loss outcomes (Gowin et al., 2016). Moreover, individuals with IGD made more disadvantageous choices for potential losses due to insensitivity to levels of uncertainties and outcome magnitudes (Yao et al., 2015a). In addition, neural studies suggest enhanced reward sensitivity and decreased neural response to monetary loss in IGD (Dong et al., 2013b; Dong et al., 2011). However, since previous decision-making tasks mostly framed mixed prospects (combining gain and loss within one trial as potential outcomes), such as a reality-simulated guessing task, the balloon analog risk task (BART) and the game of dice task (GDT) (Dong et al., 2013b; Qi et al., 2015; Yao et al., 2014), they do not provide optimal insight into risk perceptions and outcome processes under separate valences (potential gains versus losses) in IGD. Thus, it is promising to further distinguish features of these two processes in potential gains versus losses, which may contribute to an improved understanding of the pathophysiology of IGD and ultimately to the development of more effective interventions for IGD.

Previous work has identified several neural regions involved in processes of risky decision-making (Goldstein and Volkow, 2002; Schonberg et al., 2011). Specifically, the ventromedial prefrontal cortex (vmPFC), OFC and ventral striatum (VS), within the mesolimbic dopaminergic (DA) system, are neural structures involved in reward anticipation and outcome processing (Gowin et al., 2013; McClure et al., 2004; Xue et al., 2009). Data suggest altered responsiveness within these regions to reward- versus loss- or control-outcomes in individuals with SUDs and behavioral addictions (Balodis and Potenza, 2015). Meanwhile, the DLPFC, related to risk-taking and self-control, functions differently during risky decision-making in individuals with and without SUDs (Kohno et al., 2014; Paulus et al., 2003). Similarly, the IPL, implicated in processing uncertainty (Vickery and Jiang, 2009), has been found to function differently during decision-making in individuals with and without IGD (Dong and Potenza, 2015). In addition, the insula, OFC and ACC have been implicated in risk representation (Naqvi et al., 2014; Schonberg et al., 2011), the abnormal activation of which has been related to impaired risk-taking in addicted populations (Brevers et al., 2015; Gowin et al., 2014; Paulus et al., 2008). Taken together, these central brain structures may contribute importantly to impaired decision-making in IGD.

In the current study, we used a decision-making task, the cups task, which can separately assess gain and loss domains and has been used in studies of lesions and addictions (Levin et al., 2011; Weller et al., 2007), as well as in healthy samples (Xue et al., 2009), to systematically investigate behavioral and neural alterations underlying impaired risky decision-making in individuals with IGD. Based on previous findings summarized above, we hypothesized that IGD participants, compared to healthy comparison (HC) participants, would: (1) choose more risky options in both gain and loss trials; and, (2) show greater responses in mesocorticolimbic regions for gain-related outcome processing, and decreased activation within risk- and control-related regions for risk evaluation. We also hypothesized that within IGD participants, the observed between-group differences in behavior and brain activations would relate to individual risk preferences and severity of IGD.

2. Materials and methods

2.1. Participants

Forty-five individuals with IGD and 30 HC participants were recruited via the Internet and advertisements posted at local universities and selected through an online questionnaire and telephone screening.

Participants were recruited according to their weekly Internet gaming time and scores on the Chinese Internet Addiction Scale (CIAS) (Chen et al., 2003), which consists of 26 items on a 4-point Likert scale. The reliability and validity of the CIAS among college students has been demonstrated previously (Chen et al., 2003). Inclusion criteria for the IGD group were: (1) a score > 67 on the CIAS (Ko et al., 2009); (2) > 20 h per week engaged in Internet gaming, for a minimum of one year; and, (3) endorsement of Internet gaming as their primary Internet activity. Inclusion criteria for HC participants were: (1) a score of 60 or lower on the CIAS; and, (2) never having spent > 2 h per week engaged in Internet gaming. Participants who reported current or a history of use of illegal substances and any gambling experience (including online gambling) were excluded given the illegality of gambling in China. Additional exclusion criteria were assessed through a semi-structured personal interview, consistent with previous studies in IGD (Yao et al., 2015b; Zhang et al., 2016). Exclusion criteria included: (1) any self-reported history of any psychiatric or neurological illness; and, (2) current use of any psychotropic medication.

Given the higher prevalence of IGD in males versus females (Ko et al., 2009; Meng et al., 2014), only male participants were included. Four IGD and three HC subjects were excluded due to excessive head motion during scanning (defined as motion in excess of one voxel); thus, the final dataset was comprised of 41 individuals with IGD and 27 HC individuals.

2.2. Questionnaires

Current status of depression and anxiety was assessed using the Beck Depression Inventory (Beck et al., 1961) and the Beck Anxiety Inventory (Beck et al., 1988), respectively. Cigarettes and alcohol use was recorded, and the Fagerstrom Test for Nicotine Dependence (FTND) (Fagerström, 1978) and alcohol consumption questions from the Alcohol Use Disorders Identification Test (AUDIT-C) (Bush et al., 1998) were used to assess tobacco and alcohol use disorders, respectively. Exclusion criteria are detailed in the Methods section of Supplementary Materials.

2.3. The cups task

To assess the neural mechanisms of risky decision-making in gain and loss domains, we used a computerized version of the cups task (Xue et al., 2009). The cups task includes a gain domain and a loss domain. Subjects were instructed to win as much money as possible in the gain domain and to lose as little money as possible in the loss domain. For both gain-domain trials and loss-domain trials, subjects were required to choose between a risky option and a safe option. The safe option is to win or lose $1 for sure, whereas the risky option could lead to a probability (0.20, 0.33, or 0.50) of a larger win ($2, $3, or $5) or

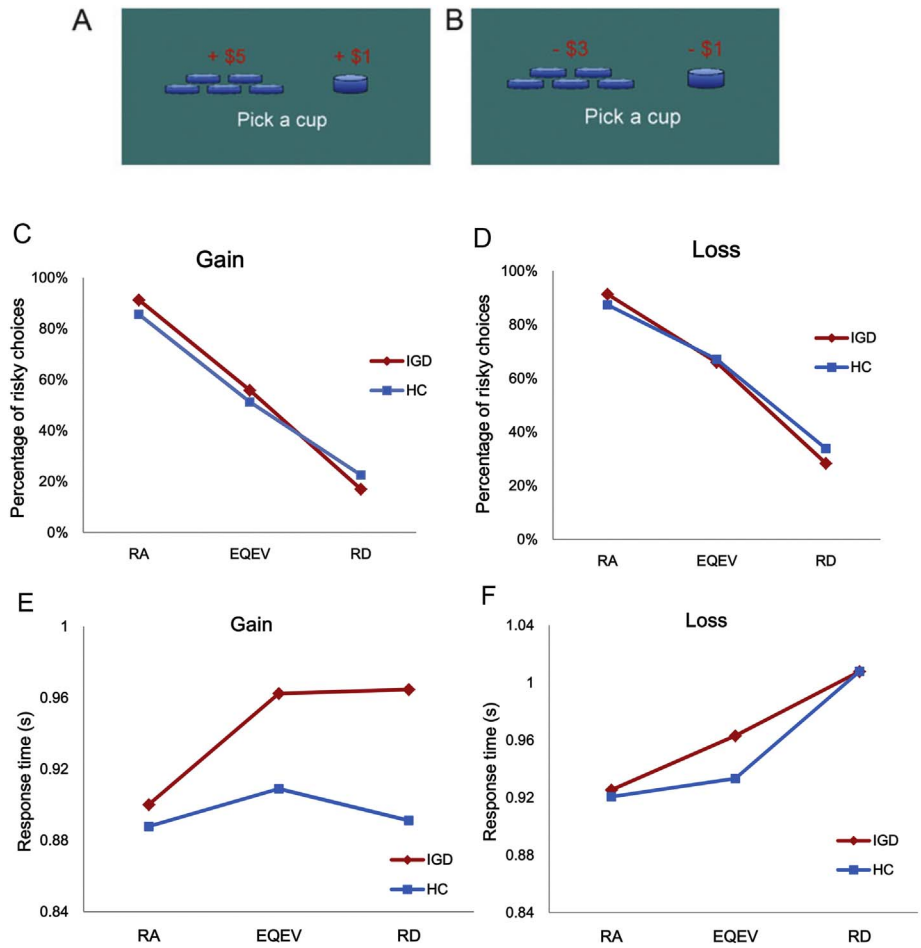

Fig. 1. The cups task and behavioral performance among IGD and HC participants. The cups includes a gain domain (A) and a loss domain (B). Each trial consists of a safe option with $1 in one cup, and a risky option with a probability of 1/2–1/5 (as determined by the number of cups) of larger gain or loss (± $2 to ± $5). In some trials, the EV of the safe option is equal to that of the risky choice (i.e., EQEV), whereas other combinations could be RA or RD (see Methods section). Mean percentage of risky choices made in the gain domain (C) and loss domain (D), as a function of EV level and group, are displayed. Mean response times (RTs) during decision-making in the gain domain (E) and loss domain (F) are also displayed. IGD = Internet gaming disorder; HC = healthy comparison; EV = expected value; RA = risk advantageous; EQEV = equal expected value; RD = risk disadvantageous.

winning nothing otherwise in the gain domain, and to a possibility of losing more ($2, $3, or $5) or losing nothing otherwise in the loss domain (Fig. 1). Within each domain, probability and outcome magnitude of the risky option were manipulated such that some combinations of probability and outcome magnitude create equal expected value (EQEV) for the risky and safe options: 0.20 × 5, 0.33 × 3, and 0.50 × 2 on both gain and loss trials. This approach provides a measure of participants' risk preference. Some combinations are slightly risk advantageous (RA), meaning that the expected value (EV) is more favorable for the risky option than for the safe option: 0.33 × 5, 0.50 × 3 in the gain domain; 0.20 × 3, 0.33 × 2 in the loss domain. Some combinations are slightly risk-disadvantageous (RD), meaning that the EV is more favorable for the safe option: 0.20 × 3, 0.33 × 2 in the gain domain; 0.33 × 5, 0.50 × 3 in the loss domain. The 2 combinations with the biggest differences in EV between risk and safe options (i.e., 0.20 × 2 and 0.50 × 5) were excluded in the current study because of their insensitivity to individuals' attitude toward risk, evident from healthy young adults (Xue et al., 2009) (see the Methods section of Supplementary Materials for further details on task and experimental methods).

2.4. Behavioral data analysis

Between-group comparisons of demographic, clinical characteristics, and task performance measures were conducted using mixed-model ANOVAs, independent-sample *t*-tests or Chi-square tests as appropriate in SPSS 20.0.

2.5. fMRI acquisition and analysis

Data were acquired using a SIEMENS Trio 3.0 T scanner in the Beijing Normal University Imaging Center for Brain Research. Image acquisition and analysis methods are detailed in Supplementary Materials. Imaging data were preprocessed using SPM8 (Welcome Department of Cognitive Neurology, London, UK, http://www.fil.ion.ucl.ac.uk/spm/spm8). Functional data were slice-timed, realigned, coregistered with the structural images, segmented for normalization to the standard MNI Space (ICBM152), and smoothed with a 5-mm Gaussian kernel at full width at half maximum (FWHM). To remove low-frequency signal drift, a high-pass filter (280 Hz) was applied.

Statistical analysis of individual participant imaging data was performed using both *categorical analysis* and *parametric analysis* of a general linear model (GLM) (Friston et al., 1995). For the category analysis, the following events were modeled based on participants' responses: Risky Loss_Gain-domain, Risky Win_Gain-domain, NoRisk_-Gain-domain, Risky Loss_Loss-domain, Risky Win_Loss-domain, and NoRisk_Loss-domain. To quantify the brain activation for each type of choice and outcome, we sorted the trials into 6 different categories according to the task domain (gain vs. loss), subjects' choice (risky vs. safe) and the outcome (win vs. loss). To reveal the domain-related differences, contrast images for decision (subjects' choices) and outcome were created separately in gain and loss trials.

The parametric analysis was used to further quantitatively describe the relationship between brain activation and decision parameters. The following 5 parameters were generated for each trial and entered into a GLM model: the magnitude (Mag, the possible outcome of the risky choice), the probability (Prob, the number of cups), the relative EV of the risky option, the experienced risk and the experienced reward. The relative EV of the risky option is calculated by subtracting the EV of the safe choice from that of the risky choice ($1 or −$1 for the Win and Loss domain, respectively). As previously (Preuschoff et al., 2006; Tobler et al., 2007; Xue et al., 2009), risk was defined as the variance of the outcome and calculated as follows: Risk = [(1 − Prob) × (0 − EV)^2 + Prob × (Mag − EV)^2]. The experienced risk reflects the outcome uncertainty that is generated only by taking a risky choice. In order to examine the experienced risk, we multiply the decision risk parameter by the subject's response (coded 1 for the risky choice and 0 for the safe). We mainly focused on the 2 parameters associated with experienced risk and experienced reward which due to the factorial design and nature of the task, were largely orthogonal, and the use of a GLM allowed us to examine their unique contributions.

A fixed effect model was used to create cross-run contrasts for each subject for a set of contrast images. These contrast images were entered into a second-level random-effects analysis using a two-sample *t*-test design to investigate between-group effects. We report significant brain activations at the whole-brain level corrected by means of Gaussian Random Field Theory (GRFT) with voxel-level $P < 0.005$ and cluster-level $P < 0.05$ to result in a family-wise error rate of 5%. For confirmatory purposes, a more stringent criterion (corrected by means of GRFT with voxel-level $P < 0.001$ and cluster-level $P < 0.05$) was also conducted in whole-brain analyses (see Table S1). The results were visualized using DPABI (http://rfmri.org/dpabi).

2.6. Exploratory analysis: voxel-wise regressions

In order to probe whether group differences in risk evaluation and outcome processing were related to addiction severity or altered risk preference behavior, we conducted voxel-wise regression analyses for the IGD participants of brain responses within voxels, finding significant differences between IGD and HC participants in risk-experience and outcome-processing (masks with clusters survived at voxel-level $P < 0.005$ and cluster-level $P < 0.05$) and of the self-report CIAS scores, rate of risk-taking as well as response time for decision-making under the EQEV trials (potential gains and losses separately). According to previous studies on risky decision-making (Tom et al., 2007; Xue et al., 2009), risk-taking under the EQEV trials provides a sensitive estimation of individuals' risk preferences. For exploratory purpose, regions of interests (ROIs) analyses were also conducted including the vmPFC, VS, and OFC using bilateral masks derived from the Harvard-Oxford atlas (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases; we applied the Harvard-Oxford atlas to MNI space with DPABI). We report significant brain activations within the ROIs that corrected by means of GRFT with voxel-level $P < 0.001$ and cluster-level $P < 0.05$ ($P_{SVC\text{-}FWE} < 0.05$).

3. Results

3.1. Demographic and behavioral characteristics

Demographic characteristics of IGD and HC participants are shown in Table 1. IGD and HC groups did not differ significantly in age or years of education. Consistent with the inclusion criteria, IGD participants had significantly higher CIAS scores, with 26.94 (SD = 9.81) hours of time on Internet games weekly. Thirty of the 41 IGD participants and 15 of the 27 HC participants were occasional alcohol drinkers (non-dependent drinkers), with no group difference in AUDIT-C scores. Three IGD and no HC participants reported current cigarette smoking. Participants with IGD scored higher than HC participants on the BDI, with a trend toward higher scores on the BAI.

Table 1
Demographic characteristics between IGD and HC subjects.

Variable	IGD (n = 41) Mean (SD)	HC (n = 27) Mean (SD)	Test statistics
Age	21.93 (1.88)	22.74 (2.35)	$t = -1.58$, $P = 0.12$
Years of education	15.73 (1.86)	16.22 (1.93)	$t = -1.05$, $P = 0.30$
Time spent on Internet gaming (hours per week)	26.94(9.81)	1.33 (0.58)[a]	$t = 16.32$, $P < 0.001$
CIAS score	79.66 (8.45)	40.22 (9.44)	$t = 17.98$, $P < 0.001$
Alcohol use (at least once per month)	30	15	$\chi^2 = 2.26$; $P = 0.13$
AUDIT-C score	3.20 (1.90)[b]	2.33 (1.29)[c]	$t = 1.58$, $P = 0.12$
Cigarette use (at least once per month)	3	0	
FTND score	2 (0.00)[d]	–	
Depression severity (BDI score)	8.63 (4.90)	3.41 (5.43)	$t = 4.12$, $P < 0.001$
Anxiety severity (BAI score)	4.41 (4.20)	2.63 (3.62)	$t = 1.81$, $P = 0.08$

SD = standard deviation; IGD = Internet gaming disorder; HC = healthy comparison; CIAS = Chen Internet addiction scale; AUDIT-C = alcohol use disorder identification test; FTND = Fagerstrom test for nicotine dependence; BDI = Beck Depression Inventory; BAI = Back Anxiety Inventory.
[a] n = 3.
[b] n = 30.
[c] n = 15.
[d] n = 3.

3.2. Risk-taking preference

Risky preference reflects an individual's tendency to choose the risky option over the safe option at each of the three EV levels (RA, EQEV, RD) calculated separately for the gain and loss domains. A 2–by-3-by-2 repeated-measures ANOVA involving domain (gain, loss), EV level (RA, EQEV, RD) and group (IGD participants, HC participants) was conducted. There were significant main effects of domain ($F_{1, 66} = 19.07$, $P < 0.001$, partial $\eta^2 = 0.22$) and EV level ($F_{2, 132} = 244.59$, $P < 0.001$ partial $\eta^2 = 0.79$), but no significant main effect of group ($F_{1, 66} = 0.02$, $P = 0.89$, partial $\eta^2 < 0.001$) or interactions (Fig. 1C, D).

Although individual tendencies to choose the risky option at each EV level did not vary significantly between groups, interesting differences were found in response times for decision-making. In the gain domain, responses took longer for RD and EQEV trials than for RA trials within the IGD group ($F_{2, 132} = 17.66$, $P < 0.001$), and this effect was not found in HC participants ($F_{2, 132} = 1.97$, $P = 0.14$). In the loss domain, responses took longer for RD and EQEV trials than for RA trials in both the IGD ($F_{2, 132} = 16.94$, $P < 0.001$) and HC ($F_{2, 132} = 18.61$, $P < 0.001$) groups. In addition, there were a significant domain-by-EV-level interaction ($F_{2, 132} = 14.55$, $P < 0.001$, partial $\eta^2 = 0.18$) and a trend toward a domain-by-group interaction ($F_{2, 132} = 3.59$, $P = 0.06$, partial $\eta^2 = 0.05$) (Fig. 1E, F).

3.3. fMRI results

3.3.1. Alterations in IGD participants processing risks

3.3.1.1. Gain domain. No group differences were found in the gain domain.

3.3.1.2. Loss domain. Whole-brain-corrected group comparisons of the parametric analysis for experienced risk revealed decreased modulation of bilateral DLPFC (MNI: −42, 54, 18, $t = -4.07$; MNI: 33, 21, 51, $t = -3.94$) and IPL (MNI: −45, −54, 48, $t = -4.08$; MNI: 33, −63, 57, $t = -4.08$) in IGD participants compared to the HC group (Fig. 2A

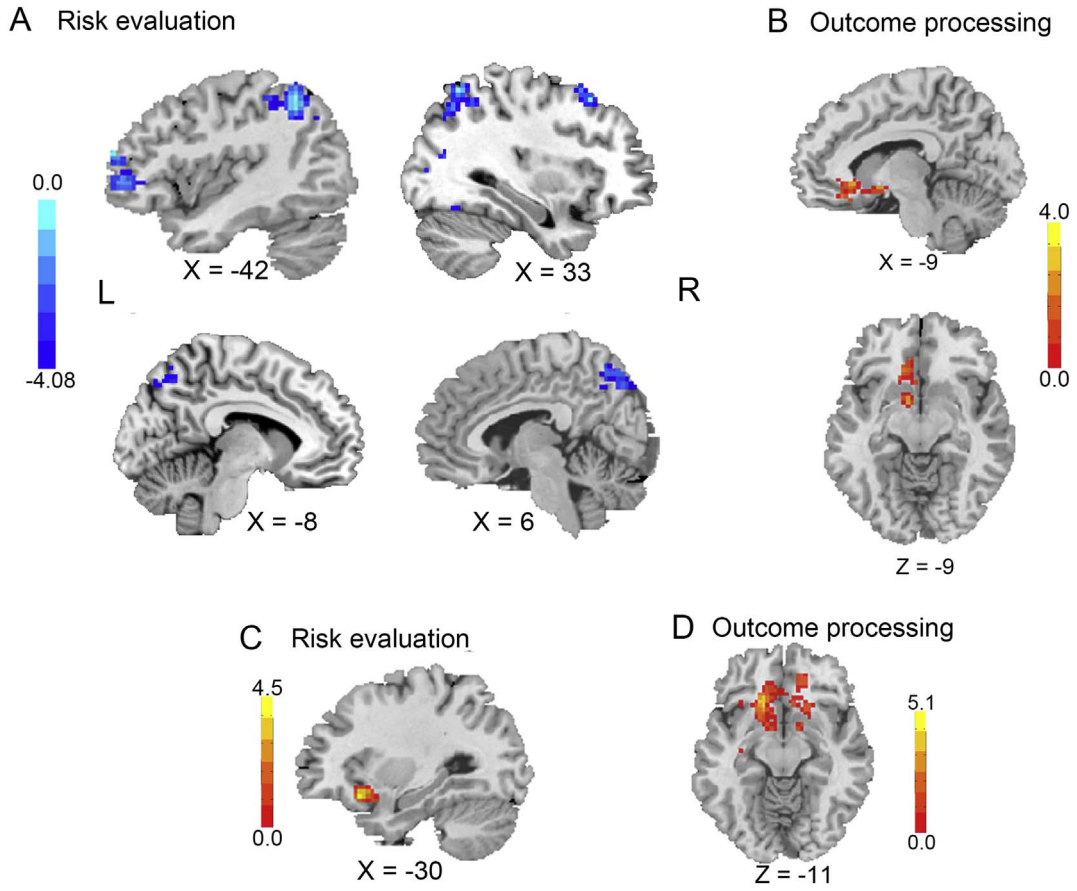

Fig. 2. Group differences in fMRI findings using parametric (panel A and B) and categorical analysis (panel C and D). Group differences of sensitivity to experienced risk under loss conditions (A) and experienced reward (B) are displayed. Group differences of participants' responses to risky versus safe for potential losses (C) and to win versus loss for potential gains (D) are displayed. The color bars reflect *t* values. The 2D activation maps are overlaid on a T1 image using DPABI. (voxel-level $P < 0.005$ and cluster-level of $P < 0.05$, whole-brain corrected). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 2
Whole-brain analyses comparing risk-related BOLD responses between IGD and HC participants (voxel-level $P < 0.005$ and cluster-level of $P < 0.05$).

Hemisphere	Brain regions	BA	Cluster size	Peak MNI (mm)			Peak *t* value
				X	Y	Z	
IGD > HC							
Loss domain - parametric analysis							
L	MFG/IFG	46, 47, 10	172	− 42	54	18	− 4.07
L	IPL/Precuneus/SPL/Angular	40, 39, 7	492	− 45	− 54	48	− 4.08
R	MFG/SFG	8, 9, 46	144	33	21	51	− 3.94
R	IPL/Angular/Precuneus/SOG	7, 39, 40	270	33	− 63	57	− 4.08
R	IOG/Fusiform Gyrus/MOG	19	132	39	− 75	− 15	− 3.82
Loss domain - categorical analysis							
L	Insula/OFC	47, 38	122	− 30	21	− 15	4.49

BOLD = blood oxygen level dependent; IGD = Internet gaming disorder; HC = healthy comparison; BA = Brodmann's area; R = right; L = left; MFG = middle frontal gyrus; IFG = inferior frontal gyrus; SFG = superior frontal gyrus; IPL = inferior parietal lobule; SPL = superior parietal lobule; SOG = superior occipital gyrus; IOG = inferior occipital gyrus; MOG = middle occipital gyrus; OFC = orbitofrontal cortex.

and Table 2). That is, there was a weaker relationship between activation of the identified brain regions (DLPFC, IPL) and the experimental parameter (experienced risk) in the IGD as compared to the HC group.

Whole-brain-corrected group comparisons of risky choices > safe choices showed higher brain activations in the left insula extending into the lateral OFC (MNI: − 30, 21, − 15, $t = 4.49$) in the IGD group compared to the HC group (Fig. 2C and Table 2).

3.3.2. Alterations in IGD participants processing outcomes

3.3.2.1. Gain domain. Whole-brain-corrected group comparisons of the parametric analysis for the experienced outcome revealed increased modulation of the VS, which extended to the vmPFC and OFC (MNI: − 9, 3, − 9, $t = 3.94$) in IGD participants compared to the HC group (Fig. 2B and Table 3).

Similarly, categorical analysis of win- > loss-outcomes showed higher brain activations in the bilateral VS (MNI: − 15, 24, − 9, $t = 5.04$) and the right OFC (MNI: 27, 24, − 21, $t = 4.54$) extending into the vmPFC (Fig. 2D and Table 3).

3.3.2.2. Loss domain. In the loss domain, no group differences were found.

Table 3
Whole-brain analyses comparing outcome-related BOLD responses between IGD and HC participants (voxel-level $P < 0.005$ and cluster-level of $P < 0.05$).

Hemisphere	Brain regions	BA	Cluster size	Peak MNI (mm)			Peak *t* value
				X	Y	Z	
IGD > HC							
Gain domain - parametric analysis							
L	VS/ACC/vmPFC/OFC/Rectus	25, 11	115	− 9	3	− 9	3.94
Gain domain - categorical analysis							
L/R	VS/vmPFC/Caudate/ACC/Putamen/OFC	11, 25, 38, 47	276	− 15	24	− 9	5.04
R	OFC/VS/Caudate/vmPFC/Rectus	11, 48, 25	216	27	24	− 21	4.54

BOLD = blood oxygen level dependent; IGD = Internet gaming disorder; HC = healthy comparison; BA = Brodmann's area; R = right; L = left; VS = ventral striatum; vmPFC = ventromedial prefrontal cortex; ACC = anterior cingulate cortex; OFC = orbitofrontal cortex.

3.3.3. Relationship between brain activities, individual risk preference and IGD characteristics

3.3.3.1. Risk-processing in the loss domain. Among the IGD group, whole-brain regression analyses revealed significant negative associations between severity of IGD and modulation of the left DLPFC-activation-experienced risk (MNI: − 42, 45, 6, $r = -0.55$; small-volume-corrected (SVC)) and the modulation of bilateral IPL (MNI: − 42, − 54, 57, $r = -0.61$; MNI: 45, − 57, 45, $r = -0.51$; SVC) (Fig. 3A).

Small-volume regression analyses revealed a significant negative association between HC participants' risk preference and risk-related activity within the left IFG (risk > safe contrast, MNI: − 45, 12, 24, $r = -0.68$; SVC).

3.3.3.2. Outcome-processing in the gain domain. Among IGD participants, ROI-based regression analyses revealed a positive association between severity of IGD and right OFC activation in win vs. loss outcomes (MNI: 39, 21, − 21, $r = 0.51$; SVC) (Fig. 3B). The HC group showed a positive association between individual risk preference and this reward-related activity within the right vmPFC (MNI: 9, 51, − 15, $r = 0.63$; SVC).

3.3.4. Functional dissociations of risk and outcome processing among HC participants

When contrasting the risky choices with the safe ones and the win trials with the loss ones for whole trials, this study replicated results among HC participants for differentially modulated dorsal and ventral MPFC activation by risk estimation and outcome processing (Xue et al., 2009) (see Supplementary Results).

4. Discussion

By combining functional MRI and a task which isolates decision-making for gain and loss domains as well as separates two decision-making processes that support the evaluation of risk versus the evaluation of outcomes, our study detected different mechanisms for processing potential gains versus losses during risky decision-making in individuals with IGD. Specifically, our results suggest that individuals with IGD may be overly sensitive to reward-outcomes in gain conditions, with relatively increased activations within the vmPFC, VS and OFC; in contrast, this population showed less activation in the DLPFC and IPL during risk perception and evaluation of potential losses. Consistent with theories in individuals with substance-use (Goldstein

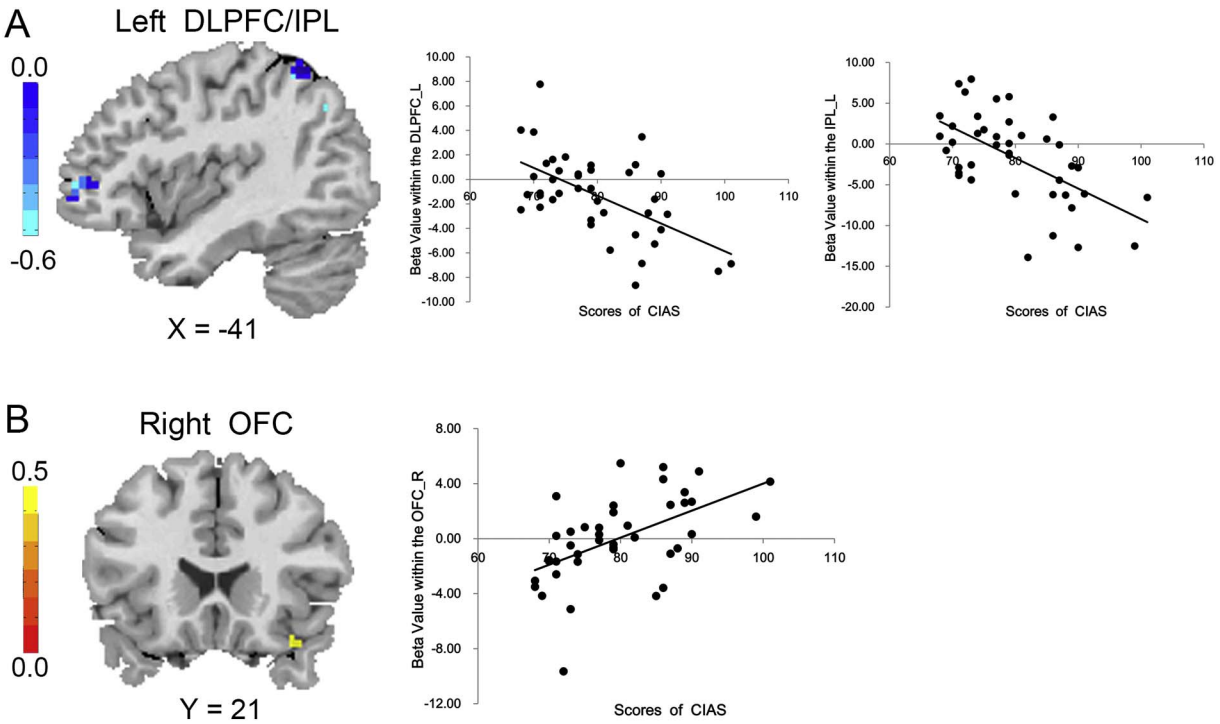

Fig. 3. fMRI correlations of IGD participants addiction severity with regions surviving in group comparisons. Regions show significant negative correlation between Internet-addiction severity of IGD and modulation of the left DLPFC and IPL activation for experienced risk (A); and a significant positive association between severity of IGD and the right OFC activation in the risky vs. safe choices contrast (B). Scatterplots are shown of correlations between addiction severity and beta values for each cluster surviving in the left DLPFC, IPL, and right OFC, respectively. (voxel-level $P < 0.001$ and cluster-level of $P < 0.05$; small-volume corrected).

and Volkow, 2011) and Internet-use (Brand et al., 2016; Dong and Potenza, 2014) disorders displaying enhanced reward-related drives and affective-related sensitivities in conjunction with reduced executive function/inhibitory, our data further suggest such an imbalance underlying impaired risky decision-making in individuals with IGD. Such an imbalance may promote persistent gaming behavior despite negative consequences.

4.1. Risk processing for potential losses

Consistent with findings from substance-using populations (Kohno et al., 2014; Paulus et al., 2003; Paulus et al., 2008), and from IGD subjects (Qi et al., 2015), between-group differences identified weaker modulation of activity in the DLPFC for risk evaluation for potential losses. Given its role in risk avoidance and self-control (Schonberg et al., 2011), blunted DLPFC sensitivity to risk in IGD subjects may reflect impaired risk processing for potential losses, which may further explain previous behavioral findings regarding IGD participants' insensitivity to uncertainty (Yao et al., 2015a). The IPL, implicated in uncertainty processing and risk-taking in decision-making (Krain et al., 2006; Vickery and Jiang, 2009), showed weaker modulation in this region among IGD subjects, further supporting a characteristic linked to insensitivity regarding uncertainty within this population. Consistently, previous studies showed decreased response within the IPL for decision-making among IGD subjects (Dong and Potenza, 2015). Moreover, the negative associations between modulation in the DLPFC and IPL and Internet-addiction severity further link possible dysregulation of these brain structures to risk sensitization in IGD.

Increased activations of the left anterior insula and lateral OFC among IGD versus HC participants were found in the loss condition. Similarly, previous studies using different decision-making tasks showed increased activation of the insula in individuals with IGD (Dong et al., 2013a) and substance addictions (DeVito et al., 2013; Gowin et al., 2014); and increased activation of the lateral OFC in seen in individuals with pathological gambling (Power et al., 2012). In healthy participants, the anterior insula and lateral OFC contribute to risk representation and risk-taking (Bechara, 2005; Naqvi et al., 2014; Schonberg et al., 2011). Further, the insula has been implicated in anticipatory and affective/motivational processes, as well as during harm avoidance (Craig, 2009; Ernst and Paulus, 2005). The insula is also hypothesized to exhibit alterations in psychiatric disorders at particular stages of decision-making (Ernst and Paulus, 2005). In the loss domain of the study, taking risky options could give subjects a chance to avoid losing even though it might be only $1 for the safe option. Individuals with IGD may experience higher anticipation to loss avoidance by exhibiting risk-taking in loss situations. In addition, given models of addiction emphasizing roles of the OFC in affective “hot” function and DLPFC in cognitive “cool” executive function in decision-making (Goldstein and Volkow, 2011), our findings suggest that abnormal risk preference mediated by OFC and insula function, combined with reduced sensitivity to risk relating to DLPFC and IPL function during loss conditions, may be a core deficit in IGD that underlies continued gaming behavior despite negative consequences.

4.2. Outcome processing for potential gains

Group comparisons using contrasts from parametric and categorical analyses both identified a greater outcome-related neural activation for gain trials in the vmPFC, which extended to the VS and OFC in IGD participants. These findings are consistent with studies that individuals with IGD show increased activation in the vmPFC/OFC during gain trials in a reality-simulated guessing task (Dong et al., 2011), and that heavy cannabis users demonstrated higher activity in the OFC during win versus loss evaluation during the Iowa gambling task (Cousijn et al., 2013), and that individuals with cocaine dependence than those without cocaine dependence show a greater response for rewarding outcome in the bilateral VS during a monetary incentive delay task (Jia et al., 2011). The vmPFC, OFC and VS are linked to reward anticipation and outcome processing during decision-making (Brand et al., 2014; Preuschoff et al., 2006) and may help encode both wins and losses by tuning up and down activations (Tom et al., 2007; Xue et al., 2009). Consistent with the theory proposed by Robinson and Berridge (2003) that posits that the possibility of drug-enhanced reward sensitivity may spillover to nondrug rewards (e.g., money rewards), our results, together with previous findings, suggest a generalized hypersensitivity in brain reward circuit among different addiction subtypes including IGD. Furthermore, the activity in the right OFC was positively associated with Internet-addiction severity within the IGD group, which is consistent with studies in IGD and heavy cannabis users (Cousijn et al., 2013; Dong et al., 2011). The increased response within these reward-related regions for rewarding outcomes may reflect hypersensitivity to reward finally leading to elevated reward-seeking (e.g., maladaptive gaming) despite negative consequences, although this interpretation remains speculative.

In addition, enhanced reward sensitivity is suggested by findings from response times (RTs) during decision-making. That is, the significantly increased RTs at RD and EQ levels for gain trials in IGD participants suggest that there may be more deliberation, conflict or hesitation when IGD participants, compared with HC participants, make decisions during trials when subjects' optimal actions are risk-averse versus risk-seeking.

Partially consistent with theoretical models of IGD and other types of Internet addictions (Brand et al., 2016; Dong and Potenza, 2014), findings in this study indicate that a dysfunctional interaction between poor executive control and enhanced generalized reward-seeking, perhaps as a result of addictive behaviors, may promote disadvantageous decision-making. This may reflect a bias toward affective and reward responses over executive control during decision-making in IGD that may promote this population's persistent gaming behavior despite negative consequences. These models, based on theories of substance addictions (Goldstein and Volkow, 2011), may apply to non-substance addictions in non-addiction-related situations, or at least to IGD in monetary risky decision-making, although further investigation is needed to verify this possibility.

In seeming contrast to previous studies of IGD (Yao et al., 2015a; Yao et al., 2015b), no group differences on risk-taking preference were observed in this study. Contrary to previous studies with larger amounts of money for winning or losing (possible outcomes: 200 yuan, 300 yuan, or 400 yuan), the smaller amounts of money and the exclusion of options with the biggest differences in EV (see Methods section of Supplementary Materials) in this study may have blunted the detection of group differences. This version of the cups task, in return, may be more sensitive to individuals' attitude toward risk and the detection of group differences in brain responses.

4.3. Limitations and future directions

Since our data are cross-sectional, it is not possible to make causal conclusions related to altered brain activations and risky decision-making. Longitudinal (including intervention) research is needed to further characterize the relationship between altered brain activations in impaired decision-making and the course of IGD. The extent to which the identified behavioral and neural differences in IGD relate to other clinically relevant measures (e.g., individual differences in treatment outcome that may subsequently be helpful for developing and targeting interventions) warrants additional study. Given that theoretical models of IGD consider decision-making impairments in combination with reward sensitivity and executive functioning, it would be important in future studies to investigate such interactions of cognitive functions (e.g., level of reward sensitivity and inhibitory control) and brain activity (e.g., activation in the OFC and DLPFC) in IGD. In addition, IGD participants were oversampled in the current study. Thus, there exists

an imbalance in the IGD and HC groups. Despite these limitations, the use of a task that parses specific aspects of decision-making is strength and provides insight into the neural correlates of these processes in IGD.

5. Conclusions

This study provides new insights into the neurobiological foundation for decision-making deficits in individuals with IGD. By combining fMRI and a task which isolates decision-making for gain and loss domains as well as risk- and outcome-processing, the results of our study suggest that individuals with IGD may be hypersensitive to reward-outcomes in gain conditions with relatively increased activations within the vmPFC, VS and OFC; and this population may be weaker in risk experience and self-control of potential losses relating to less activation in the DLPFC and IPL. Such findings implicate a biological mechanism for why individuals with IGD may persist in game-seeking behavior despite negative consequences.

Authors contribution

XYF and JTZ were responsible for the study concept and design. LL, YWY, CCX, JL, and SSM contributed to the acquisition of MRI data. LL, JTZ, MNP and GX assisted with data analysis and interpretation of findings. LL drafted the manuscript. JTZ, MNP and XYF provided critical revision of the manuscript for intellectual content. All authors critically reviewed and approved the final version of the manuscript submitted for publication.

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Appendix A. Supplementary data

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