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Research Article

Associations between levels of Internet Gaming Disorder symptoms and striatal morphology–replication and associations with social anxiety

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Abstract

Background: Brain structural alterations of the striatum have been frequently observed in internet gaming disorder (IGD); however, the replicability of the results and the associations with social-affective dysregulations such as social anxiety remain to be determined.

Methods: The present study combined a dimensional neuroimaging approach with both voxel-wise and data-driven multivariate approaches to (i) replicate our previous results on a negative association between IGD symptom load (assessed by the Internet Gaming Disorder Scale-Short Form) and striatal volume, (ii) extend these findings to female individuals, and (iii) employ multivariate and mediation models to determine common brain structural representations of IGD and social anxiety (assessed by the Liebowitz Social Anxiety Scale).

Results: In line with the original study, the voxel-wise analyses revealed a negative association between IGD and volumes of the bilateral caudate. Going beyond the earlier study investigating only male participants, the present study demonstrates that the association in the right caudate was comparable in both the male and the female subsamples. Further examination using the multivariate approach revealed regionally different associations between IGD and social anxiety with striatal density representations in the dorsal striatum (caudate) and ventral striatum (nucleus accumbens). Higher levels of IGD were associated with higher social anxiety and the association was critically mediated by the multivariate neurostructural density variations of the striatum.

Conclusions: Altered striatal volumes may represent a replicable and generalizable marker of IGD symptoms. However, exploratory multivariate analyses revealed more complex and regional specific associations between striatal density and IGD as well as social anxiety symptoms. Variations in both tendencies may share common structural brain representations, which mediate the association between increased IGD and social anxiety.

Keywords: internet gaming disorder; social anxiety; source-based morphometry; gray matter; MRI; replication

Introduction

Gaming disorder (GD, also referred to as Internet Gaming Disorder, IGD) has recently been included in the most recent International Classification of Diseases (ICD-11, 11th version) system of the World Health Organization (WHO). In 2013, the DSM-5 (American Psychiatric Association, APA) included a research diagnosis called IGD, hence focusing on online gaming, as a research diagnosis. The present work focuses on the older APA framework, which means that five out of nine criteria must be fulfilled to reach the full diagnosis (for overlap and similarities between the DSM-5 and ICD-11 frameworks see Montag *et al.*, 2019; Montag, Schivinski, *et al.*, 2021). While most gamers engage for recreational purposes in online games, a significant minority of vulnerable individuals will progressively escalate their engagement in gaming and ultimately develop IGD symptoms such as preoccupation with gaming, loss of control over behavior, craving, and withdrawal symptoms, including anxiety and irritability (Zhao *et al.*, 2017). Accumulating evidence suggests that the development of the IGD symptoms is accompanied—or maybe facilitated—by behavioral and emotional dysregulations, including increased levels of depression and anxiety (Andreassen *et al.*, 2016), as well as changes in brain structure and function (Klugah-Brown *et al.*, 2021; Yu *et al.*, 2021). The dysregulations on the symptomatic, behavioral, and brain level are partially similar to dysregulations observed in substance-based addictions (Brand *et al.*, 2019; Klugah-Brown *et al.*, 2020; Taebi *et al.*, 2022; Zhou *et al.*, 2018; Zimmermann *et al.*, 2018).

Accumulating evidence from recent neuroimaging meta-analyses suggests that excessive and problematic engagement in internet gaming might be accompanied by changes in the structural architecture of the brain, particularly in terms of the integrity of gray matter (Gao *et al.*, 2021; Klugah-Brown *et al.*, 2021; Qin *et al.*, 2020; Solly *et al.*, 2022). These meta-analyses included the numerous previous studies that employed a retrospective

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cross-sectional design comparing gray matter volumes (GMV) between participants with disordered gaming/internet use and healthy controls. However, the limitations of the conventional retrospective case control designs in neuroimaging of mental disorders have been increasingly acknowledged (e.g. Etkin, 2019). These limitations include, for instance, generally high comorbidity with elevated levels of depression or neuroticism (for associations between neuroticism and gaming disorder see Montag, Kannen, *et al.*, 2021), which per se associated with gray matter changes (e.g. Liu *et al.*, 2021, 2022, but see also a critical review on personality neuroscience by Chen & Canli, 2022), progressive gray matter changes with the duration of the disorders, drug use or interventions (e.g. Han *et al.*, 2021; Kendrick *et al.*, 2021), and variations in gray matter that precede the onset of the disorder and thus may represent predisposing vulnerability markers (Becker *et al.*, 2015). To partly address these issues and to capture gray matter changes that align with dimensional disorder models as proposed, for instance, in the Research Domain Criteria approach (Krueger & DeYoung, 2016) dimensional neuroimaging approaches have been increasingly used. These models aim to determine associations between individual variations in pathology relevant traits or symptom dimensions and variations in the structural or functional organization of the brain.

Initial studies have begun to successfully employ this approach to determine transdiagnostic GMV alterations in behavioral and substance use addictions (Yip *et al.*, 2018) and an increasing number of studies have used this approach to map GMV changes as a function of problematic and escalating internet use in comparably large population samples spanning the entire range of internet use behavior (e.g. for social media and messenger engagement see e.g. Montag *et al.*, 2017, 2018; for general screen media engagement see Paulus *et al.*, 2019; for general disordered internet use see e.g. Pan *et al.*, 2018; Sadeghi *et al.*, 2021; Yu *et al.*, 2022). Capitalizing on the dimensional neuroimaging approach, our group recently reported that higher levels of IGD symptoms according to both the WHO and APA frameworks associated with lower striatal volume in a group of 82 healthy male individuals with a broad range of internet gaming symptom load (Zhou *et al.*, 2020). However, recent studies indicate limited robustness and replicability of associations between psychological variables and GMV variations (Masouleh *et al.*, 2019; Zhou *et al.*, 2022), and an increasing number of studies have reported sex differences with respect to IGD-related brain changes (Wang *et al.*, 2022; Zeng *et al.*, 2021). The replicability of the association and the generalization to women thus remains to be determined.

Moreover, the role of emotional dysregulations in developing and maintaining addictive disorders including IGD has received increasing attention (Brand *et al.*, 2019; Zhao *et al.*, 2020; Zimmermann *et al.*, 2018). In addition to domains such as depression, social anxiety has been proposed as a conceptually derived and plausible risk factor for the development and maintenance of IGD (see Marino *et al.*, 2020 or González-Bueso *et al.*, 2018 for a more detailed discussion). However, empirical support for an association between social anxiety and IGD remained inconsistent (e.g. Gentile *et al.*, 2011; Wei *et al.*, 2012; Yen *et al.*, 2007; see also Marino *et al.*, 2020). Furthermore, while individual variations in both IGD and social anxiety have been associated with functional and structural brain variations (e.g. Luo *et al.*, 2018; X. Zhou *et al.*, 2020), the possibility of common neurobiological pathways remains to be explored. The current study thus employed a dimensional approach to determine associations between variations in IGD and brain structure as well as to explore associations between IGD with social anxiety and the underlying brain structural pathways using both novel source-based morphometry (SBM) analyses and voxel-based morphometry. We employed SBM as a novel data-driven multivariate approach to brain structural analyses shown to have demonstrable advantages over conventional univariate analysis techniques such as voxel-based morphometry, including a higher sensitivity (Gupta *et al.*, 2019). SBM uses a mixing matrix containing the linear combinations of the sources generated from pathological and normal variation among individuals to identify associations between individual phenotypical variations.

Considering that an increasing number of recent studies suggests (i) a low replicability of conventional analyses of GMV associations with psychological variables, (ii) sex-differences in associations between IGD symptoms (again in the literature now studies on DSM-5 and ICD-11 frameworks can be found) and the brain, (iii) a potential higher robustness and specificity of multivariate—compared to the conventional univariate GMV—analyses (Zhou *et al.*, 2022), and (iv) accumulating evidence for a role of social anxiety in IGD and associations between social anxiety (Wang *et al.*, 2018) and striatal volume, the present study extended our previous exploratory results of negative associations between level of IGD as assessed by the Internet Gaming Disorder Scale-Short-Form (IGDS9-SF) and lower striatal volume in men (Zhou *et al.*, 2020) with respect to the following aspects: (i) we recruited an independent sample of $n = 157$ individuals to replicate our previous findings, and (ii) the new data additionally included female individuals to test whether the associations between IGD symptoms and brain structure generalize to women. Next, we examined (iii) the robustness of the results using a novel multivariate analytic approach (SBM) that examines gray matter density (GMD) and (iv) tested a potential role of social anxiety in IGD and the determined brain structural alterations by combining a multivariate analysis technique of brain structural data with neuroimaging mediation models. Because both approaches depend on sample size and power, we combined data from the two independent samples, which constitute part of a larger project on IGD (total $n = 239$), to determine the multivariate robustness of the results and examine common neurostructural signatures between IGD and social anxiety.

Methods

Participants and Assessment of Symptom Load

A total of 157 healthy young individuals underwent structural MRI acquisition and provided self-report data on IGD and social anxiety symptom load. These participants were part of a larger project on the effects of social media and internet use (e.g. see also Wang *et al.*, 2022) and served as independent replication dataset for our previous results reported in (Zhou *et al.*,2020). For further multivariate and mediation analyses, the data were pooled with the $n = 82$ individuals from the Zhou *et al.*,2020 sample leading to a total of $n = 239$ participants ($n = 82$ from the previous study, $n = 157$ from an independent dataset, age 21.8 ± 2.8 years). IGD load was assessed with the Chinese version of the IGDS9-SF. The APA framework is used to quantify IGD in the IGDS9-SF (using 9 items that are answered on a Likert scale from 1 = never to 5 = very often). The 24-item Liebowitz Social Anxiety Scale (LSAS) (Liebowitz, 1987) was included to evaluate individual variations in social anxiety. The study and its procedures were approved by the local ethics committee and adhered to the most recent version of the Declaration of Helsinki. All participants were required to provide informed consent. Further details are provided in our previous publication with the discovery sample (Zhou *et al.*, 2020). Of

note, while in the previous study we excluded participants with an elevated level of subclinical depression or high autism trait scores, we did not exclude individuals based on these criteria in the new sample to increase the generalizability of the findings (see also limitations in Zhou *et al.*, 2020). In line with the previous study, these variables were included as covariates in the analyses.

MRI Data Acquisition

The data were acquired on a 3.0 T GE MR750 system (General Electric Medical Systems, Milwaukee, WI, USA). T1-weighted high-resolution anatomical images were acquired with a spoiled gradient echo pulse sequence, repetition time (TR) = 6 ms, echo time (TE) = 2 ms, flip angle = 98, field of view (FOV) = 256 × 256 mm, acquisition matrix = 256 × 256, thickness = 1 mm, and number of slices = 156.

Brain Structural Data Preprocessing and Analysis Approach

Preprocessing

Structural MRI data were preprocessed with CAT12 implementing the computational anatomy approach (http://dbm.neuro.uni-jena.de/cat). The process involved the following steps: first, T1-weight images were bias-corrected, segmented into gray matter (GM), white matter, and cerebrospinal fluid, and spatially normalized to the standard Montreal Neurological Institute space. Second, GM images were smoothed with a Gaussian kernel of 8 mm full-width at half-maximum for subsequent statistical analysis, and the total intracranial volume (TIV) was estimated to correct for individual differences in brain size.

Replication of previous results in independent replication sample

Our independent replication sample comprised $n = 157$ and was used to examine the replicability of our previous work. After the tissue segmentation, we obtained GM images, and linear regression models were applied in the Statistical non-Parametric Mapping Toolbox (SnPM13, http://www.warwick.ac.uk/snpm) based on 10 000 random permutations, using the smooth GM maps as dependent variables, and IGDS9-SF as independent variables. In both linear regression models, age, education level, BDI-II, Autism-Spectrum Quotient, and TIV were also included as covariates (in line with Zhou *et al.*, 2020). Consistent with the region-specific *a priori* hypothesis on striatal associations, the analyses were restricted to the bilateral striatum (in line with the discovery study by Zhou *et al.*, 2020). Within the striatal mask, a voxel-level threshold of $P < 0.05$ was applied with small volume correction using FWE multiple comparison corrections. We next explored whether the findings generalize to male and female participants by splitting the data accordingly and performing a second linear regression to examine the associations within the sexes.

Multivariate analysis in combined sample

Multivariate analyses have received increasing attention in neuroimaging and may reveal more robust brain structural characterizations of biologically plausible variations (e.g. Zhou *et al.*, 2022) but at the same time, may require larger samples to warrant sufficient power. We, thus, capitalized on the comparably larger sample ($n = 239$) to explore the robustness of the results using a data-driven multivariate approach. Given that it has been proposed that social anxiety may represent a vulnerability factor as well as a consequence of excessive gaming (Gentile *et al.*, 2011; Wei *et al.*, 2012), we performed a mediation strategy that tested both directions. The details of the SBM analysis are as follows: GMD was analyzed by using independent component analysis (http://mialab.mrn.org/software/gift/). The independent component analysis was used to extract features reflecting relationships among GMD regions. The number of components was estimated using the minimum description length. Then through ICASSO and visual inspection, intrinsic components (ICs) were selected to ensure the removal of artifactual components, primarily those exhibiting high values in ventricles, white matter, and/or showing less stability across runs. To examine which ICs associated with individual variations in IGD and social anxiety symptom load, a multiple linear regression model between "loading coefficients" of the selected ICs as dependent and IGDS9-SF or LSAS as independent variables was used. In this analysis, age, educational level, Beck Depression Inventory-II (BDI-II), Autism-Spectrum Quotient, and TIV were included as covariates, and significance tests were thresholded at $P < 0.05$.

Mediation Analysis

For our mediation analysis and to further examine whether the brain changes mediate the association between IGD and social anxiety, we estimated a single-level mediation model (Wager *et al.*, 2009). Briefly, the mediation model examines whether a third variable (the mediator) can explain the effect of predictor and outcome. To this end, IGDS9-SF served as a predictor of the LSAS served as the outcome and vice versa. The SBM loading coefficients of the significant component were included as the mediator.

Results

Demographic Characteristics of Participants

The combined sample included $n = 167$ males and $n = 72$ females aged between 19 and 28 years (age 21.8 ± 2.8 years). The IGD symptom load covered a wide range of engagement in problematic internet gaming (IGDS9-SF; range 9–40; mean = 17.7, SD = 7.21). Social anxiety assessed by the LSAS had a mean = 52.45, SD = 24.8 (range 5–119). The mean score for depression according to the BDI-II was 7.58 ± 8.32. We also computed the reliability of the questionnaires using Cronbach's Alpha, which indicated a good reliability of the IGDS9-SF ($\alpha = 0.92$) and LSAS (fear: $\alpha = 0.95$, avoidance: $\alpha = 0.94$), respectively. For further demographic details, see also Zhou *et al.* (2020).

Correlation Among all Behavioral Measures

We first examined the correlation among all behavioral measures within the sample to ascertain whether there is a statistical significant association between each pair of scores obtained in the present sample. Table 1 shows the significant values thresholded at $P < 0.05$ for a two-sided Spearman correlation. In line with our hypothesis, a significant positive association between the level of IGD and social anxiety was observed in the entire sample ($p = 0.034$, $r = 0.133$).

Replication of Previous Findings in the Independent Sample

The voxel-wise analysis was restricted to the bilateral striatum and revealed significant associations between the regional volume of the bilateral dorsal striatum (caudate) and IGD (left caudate: $x = -18$, $y = 18$, $z = 18$; right caudate: $x = 18$, $y = 24$, $z = 15$,

Table 1: Correlation analysis among all behavioral measures for both male and female.

	Age	IGDS9_SF	LSAS1	LSAS2	Total_LSAS	TIV	BDI
Males							
Age	1	−0.081	−0.011	0.002	−0.001	−0.024	−0.052
IGDS9_SF	−0.081	1	0.202*	0.225*	0.230*	0.156*	0.284*
LSAS-anxiety	−0.011	0.202*	1	0.725*	0.937*	0.043	0.305*
LSAS-avoidance	0.002	0.225*	0.725*	1	0.913*	0.040	0.308*
Total_LSAS	−0.001	0.230*	0.937*	0.913	1	0.053	0.332*
TIV	−0.024	0.156*	0.043	0.040	0.053	1	−0.054
BDI	−0.052	0.284*	0.305*	0.308*	0.332*	−0.054	1
Female							
Age	1	−0.030	0.089	0.120	0.108	0.036	−0.073
IGDS9_SF	−0.030	1	0.008	0.091	0.066	0.091	0.093
LSAS-anxiety	0.089	0.008	1	0.744*	0.949*	0.002	0.393*
LSAS-avoidance	0.120	0.091	0.744*	1	0.902*	0.092	0.339*
Total_LSAS	0.108	0.066	0.949*	0.902	1	0.041	0.418*
TIV	0.036	0.091	0.002	0.092	0.041	1	0.050
BDI	−0.073	0.093	0.393*	0.339*	0.418*	0.050	1

*Significant two-tailed at $P < 0.05$, LSAS1 = anxiety, LSAS2 = avoidance.

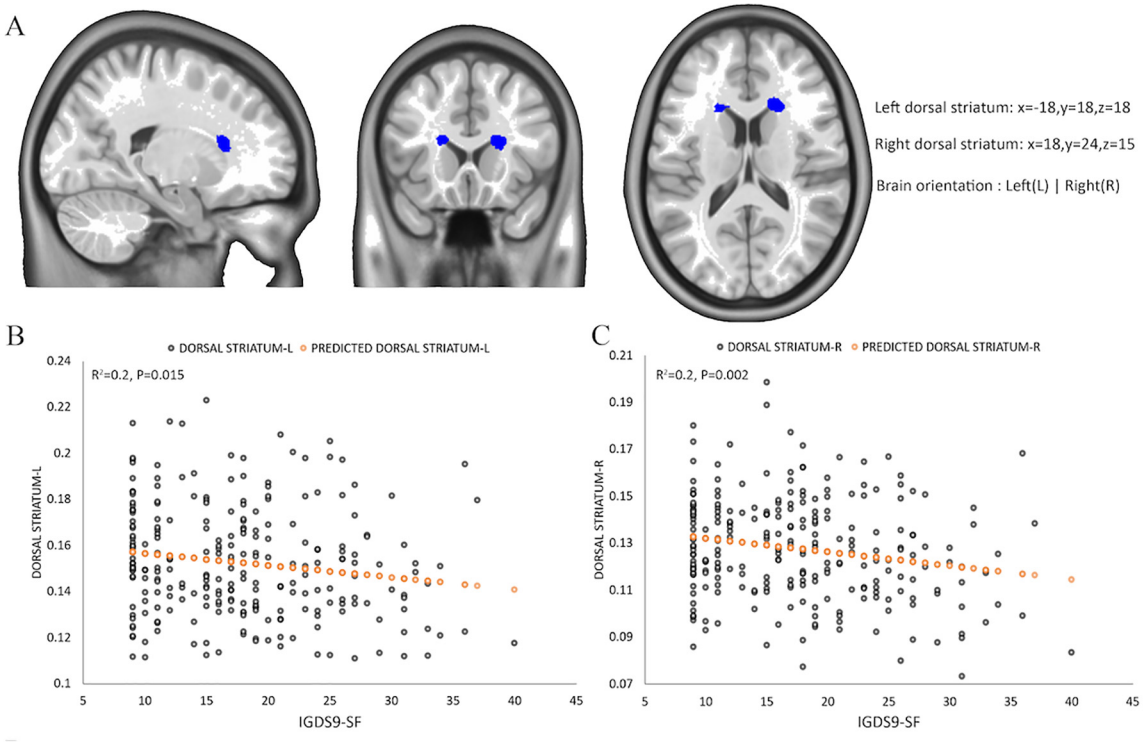

Figure 1: Volumetric changes and associations. (A) The reduced dorsal striatal region associated with IGD. (B and C) The negative associations between Internet gaming symptom loads (IGDS9-SF) and the left and right dorsal striatum (caudate), respectively. Significant results reported at pFWE < 0.05.

see Fig. 1A). Plotting the extracted parameter estimates from these regions revealed a negative association reflecting that IGD symptom loads were associated with reduced caudate volume (Fig. 1B and C). In addition, exploring the associations in the male and female participants separately revealed that IGD symptom loads were significantly negatively associated with right caudate volume in both male ($P = 0.003$) and female ($P = 0.04$) participants. A similar pattern was observed for the left caudate, but the negative associations in both male and female participants reached only a marginal significance level ($P = 0.054$ or 0.055, respectively) (Fig. 2).

Exploratory Analysis Using the Multivariate Approach

Nine ICs were estimated and selected based on their high quality (voxels located on gray matter and low spatial overlap of the maps). Loading coefficients were extracted from all nine ICs. The multiple regression revealed only one component significantly associated with IGDS9-SF and LSAS. Figure 3A shows the localization of the significant IC1, encompassing both increase ($x = -5$, $y = 11$, $z = -5$) and decrease ($x = -11$, $y = 10$, $z = 11$) in GMD in the ventral striatum; the increased regions were specifically localized in the nucleus accumbens (NAcc). In addition, we found positive

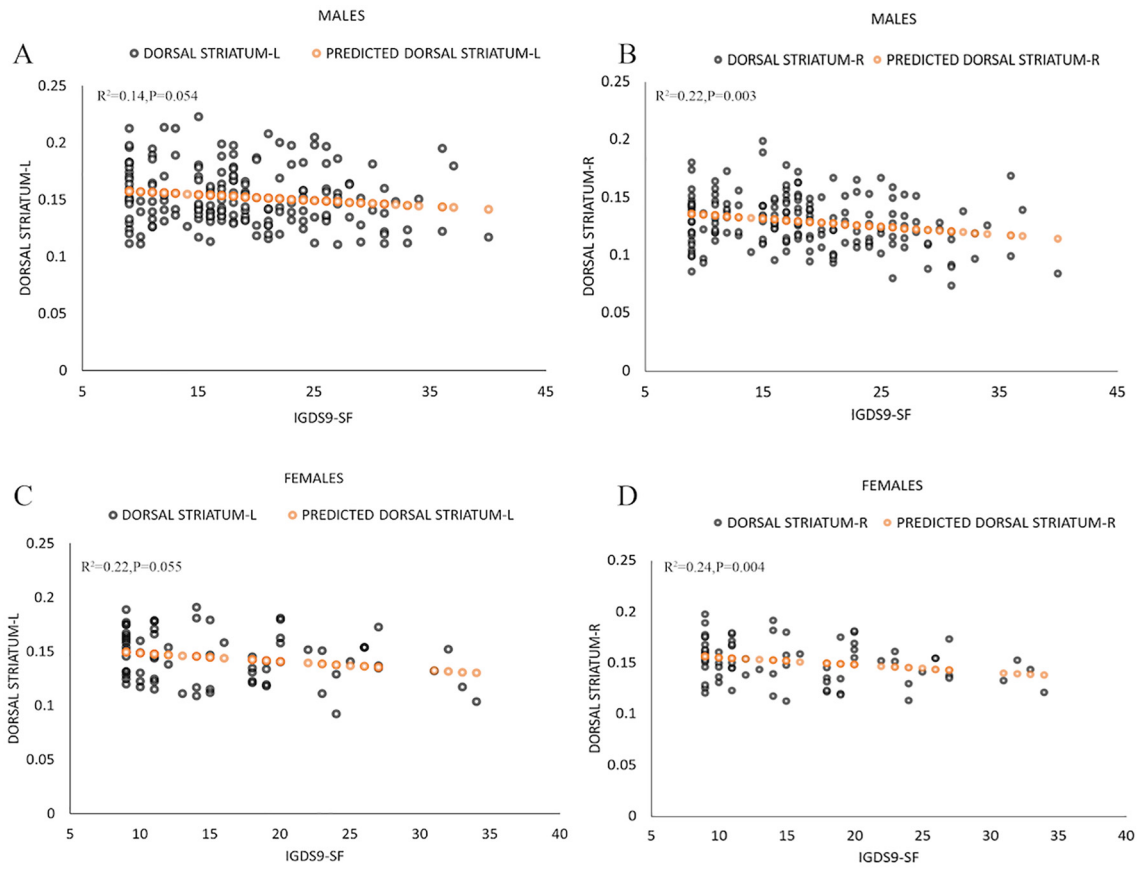

Figure 2: Separate analyses for the sexes showing the association between IGD and brain volume in male and female participants separately. (A and B) The association between IGD symptom loads and the left and right dorsal striatum (caudate) in the male subgroup. (C and D) The association between IGD symptom loads and the left and right dorsal striatum(caudate) in the female subgroup. All statistical significance values were threshold at $P < 0.05$.

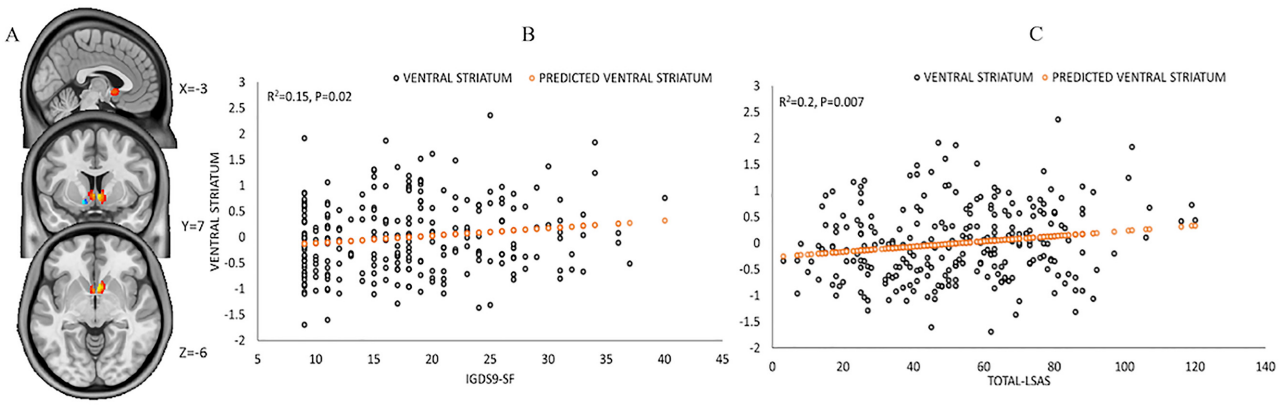

Figure 3: Significant component and association with behavioral scores. (A) The significant component showing ventral striatum (NAcc). (B and C) The positive prediction of GMD values (loading coefficients) and its association with IGDS9-SF and LSAS.

associations between the altered striatal region, the IGD symptom loads, and the social anxiety scores, respectively (Fig. 3B, C).

Significant path effects were observed for the mediation analysis computed for the entire sample, as demonstrated in Fig. 4 A and B, Table 2. Paths *a* effectively demonstrated that GMD is associated with higher IGD symptom loads independent of GMD and social anxiety (path *b*, $P < 0.05$). a, initial variable (IGDS9-SF/LSAS in I and II, respectively); b, outcome (LSAS in I or IGDS9-SF in II); c, simple a to b effect when we do not control for the mediator ; *c'*, *x* to *y* effect when we do control for the mediator; a∗b, mediation effect (indirect). That is, Path *b* effectively describes the GMD alterations that predict social anxiety. Path a∗b (product or "mediation effect") indicates that variations in GMD significantly mediate the association between levels of IGD (IGDS9-SF) and social anxiety. The effects were significant at $P = 0.0016$ (10 000 permutations). Together, these findings indicate that variations in striatal density mediate the bidirectional association between IGD and social anxiety.

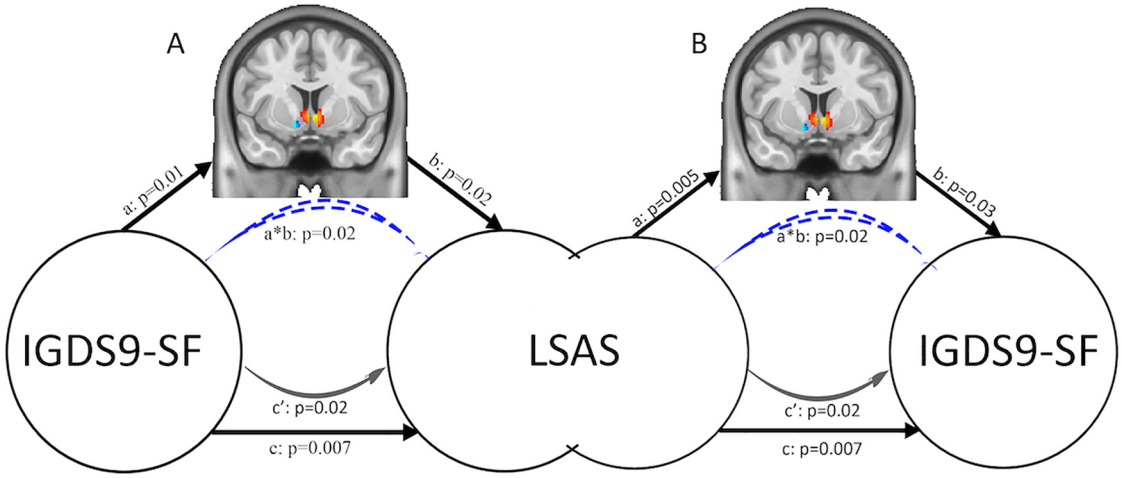

Figure 4: Mediation analysis in the entire sample. (A and B) The mediation analysis between IGDS9-SF and LSAS. a, initial variable; b, outcome; c, simple a to b effect when we do not control for the mediator; c′, x to y effect when we do control for the mediator; a*b, mediation effect (indirect) shown in blue dotted arrow from the IGDS9-SF to the LSAS (A) and from LSAS to the IGDS9-SF in (B), both mediated by the brain structure component.

Table 2: The paths between IGD symptom loads, social anxiety, and GMD variation.

	I. Paths of effect (IGDS9-SF as a predictor)				
	a	**b**	**c′**	**c**	**a*b**
Coefficient	0.01	5.04	0.53	0.6	0.07
Standard error	0.01	2.1	0.22	0.22	0.05
P-value	0.01	0.02	0.02	0.007	0.02
	II. Paths of effect (LSAS as a predictor)				
	a	**b**	**c′**	**c**	**a*b**
Coefficient	0	1.24	0.05	0.05	0.01
Standard error	0	0.59	0.02	0.02	0
P-value	0.005	0.03	0.02	0.007	0.0208

Discussion

Here, we used a dimensional neuroimaging strategy in combination with a replication design and a data-driven multivariate analytic approach to examine brain structural changes associated with IGD and to explore the neural basis of associations between IGD and emotional problems, i.e. social anxiety. To improve the strength of our analysis, we adopted a three-step approach: first, we replicated and extended our previous findings of an association between higher levels of IGD-symptom load as measured by the IGDS9-SF that is based on the current diagnostic criteria for IGD and brain structural variations in the striatum using an independent sample. Second, we extended the independent data to include female participants and conducted a separate analysis to examine whether the association generalizes between men and women. Finally, we capitalized on the data from the comparably large entire sample to test the robustness of the findings using a data-driven multivariate approach and to further explore associations with social-affective dysregulations (social anxiety). In line with the findings in the discovery study, we observed a negative association between IGD and volumes of the bilateral caudate. The association was comparable in both the male and the female subsamples. Further examination using the multivariate approach revealed that while the GMD of the caudate showed a negative association, the GMD of the nucleus accumbens showed a positive association with IGD symptom load suggesting that multivariate analyses may reveal more complex patterns of brain behavior associations. While we did not observe a positive association with the nucleus accumbens using the univariate approach multivariate findings underscore a potentially more complex association between IGD and fine-grained variations in striatal morphology.

Furthermore, we explored the contribution of social anxiety. As expected, IGD was highly associated with social anxiety in the entire sample. This association was mediated by striatal variations, suggesting that striatal variations may mediate both tendencies.

Our present study replicated our previous results on a negative association between of IGD and striatum volumes in a sample of healthy young individuals with a broad range of IGD symptom loads. An early study by Kühn *et al.* (2011) found that participants who regularly engage in video games had altered left striatal GMV and enhanced activity in the left striatum. Subsequent studies including our dicovery study furthermore reported that the GMV of the caudate was inversely correlated with the severity of IGD (Seok & Sohn, 2018; Zhou *et al.*, 2020). These findings align with an increasing number of studies reporting an association between prolonged and excessive engagement in internet gaming and morphological and functional alterations of the striatum. Of note, several previous and recent studies that examined associations between the levels of generalized disordered internet use and brain volume reported associations with the volume of frontal or parietal regions. In contrast, a recent study found significant associations specifcially with striatal GMV when accounting for the symptom-dimensions of loss of control/time management and craving/social problems in the domain of general disordered internet use (e.g. Pan *et al.*, 2018; Sadeghi *et al.*, 2021; Yu *et al.*, 2022).

Although our replication results confirm the relative robustness of the association in IGD using a dimensional approach, neuroimaging meta-analysis in participants with IGD and behavioral addiction reflect the inconsistent involvement of the striatum, with some meta-analyses reporting striatal volumetric alterations in IGD, while others did not find robust alterations in this region (e.g. Qin *et al.*, 2020; Yao *et al.*, 2017). These

findings may suggest a high heterogeneity within the assessments of symptoms of behavioral addictions and the samples recruited that might together underlie the inconsistent findings. In contrast to accumulating evidence for sex-differential alterations in addictive disorders, including brain volumetric alterations in association with excessive internet use (e.g. Sadeghi *et al.*, 2021), we observed a negative association between levels of IGD and caudate volume in both men and women. In terms of statistical significance, the effects in men and women were more pronounced in the right dorsal striatum, although the left dorsal striatum showed a similar and marginal significant association in both sexes. Together these findings may suggest that progressive dorsal striatal changes represent a vulnerability marker or a use-associated change that accompanies excessive internet gaming in both sexes.

The multivariate analyses further documented the robustness of the findings; however, they provided a more complex picture between the structural topography of the striatum and IGD as well as its associations with emotional dysregulations in the domain of social anxiety. First, IGD and social anxiety were associated with a single component encompassing striatal regions, thus confirming the regional specificity of the brain–behavior associations. Second, the IGD association in the component encompassed a pattern of positive GMD in the nucleus accumbens and a negative GMD in the caudal part of the striatum. This partly aligns with our replication study's results, but in addition to these findings, it emphasizes that subtle changes in the nucleus accumbens may contribute to IGD. In line with these results, some studies in young adults with IGD reported increased nucleus accumbens volume (NAcc) and decreased functional connectivity with brain regions involved in reward (Wee *et al.*, 2014), as well as increased volumes of both the ventral striatum (nucleus accumbens) and dorsal striatum (Park *et al.*, 2017; Yu *et al.*, 2022). While these changes have not been observed in our previous study or the present sample using the conventional univariate analyses approach, the multivariate approach in combination with the larger sample size may have contributed to determining the additional associations in the nucleus accumbens. While the methodological differences require further detailed examination, the multivariate findings may reflect the complex functional involvement of the striatum in processes ranging from reward, cognitive control, and habit formation (e.g. Everitt & Robbins, 2016; Huang *et al.*, 2018; Zhuang *et al.*, 2021), and in turn the multifaceted role of this region in addictive disorders.

Convergent evidence from animal and human studies suggests that neuroplastic changes in the striatal system accompany the escalation of drug use and transition to compulsive and addictive substance use (e.g. Everitt & Robbins, 2016; Huang *et al.*, 2018). Changes in the complex functional organization of the striatum may underpin different behavioral symptoms and stages of the addictive process, such that growing evidence from studies in substance-dependent addictions suggest that changes in the ventral regions such as the nucleus accumbens may mediate early alterations in reward and motivation while progressive changes in more dorsal parts of the striatum may mediate the development of habitual and compulsive use (in humans see, e.g. Vollstädt-Klein *et al.*, 2010; Zhou *et al.*, 2018; Zhou *et al.*, 2019). Accumulating evidence suggests that neuroplastic changes in these regions may play a critical role in escalating online game involvement, and longitudinal designs need to disentangle the separate roles of striatal subregions in the progressive behavioral and cognitive changes that accompany the development of IGD.

Finally, we found that the multivariate striatal component was not only associated with IGD but also with the level of social anxiety as assessed by the LSAS. Previous studies have reported an overlapping brain structural signature in anxiety disorders with striatal alterations being reported in generalized anxiety disorders and fear-related anxiety disorders, including social anxiety disorder (Hilbert *et al.*, 2015; Liao *et al.*, 2014; Wang *et al.*, 2018) and further suggest that structural changes in the striatal-thalamic systems may distinguish social anxiety from other anxiety disorders (Wang *et al.*, 2021). The application of a dimensional neuroimaging approach allowed us, for the first time, to demonstrate that individual variation in the symptom load of both IGD and social anxiety maps onto individual variations in the structural integrity of the striatum. Levels of IGD were related to higher levels of social anxiety in our sample, confirming earlier findings, and the relevance of brain structural changes to this association could be further assessed using a mediation technique. In particular, the level of IGD as an independent variable significantly predicted the brain structural component (mediator). In contrast, the loading coefficients significantly predicted levels of social anxiety, implying that brain structural alterations mediate the relationship between higher levels of IGD and social anxiety.

Although the findings need to be interpreted cautiously, the mediation results provide initial evidence that gaming-related brain structural alterations in these regions are linked to increased social anxiety. Also, the findings of the present study must be considered in the context of a number of limitations. The retrospective nature of the study design does not allow us to draw clear conclusions regarding the direction of the association between social anxiety, IGD symptomatology, and striatal volumes. Prospective longitudinal studies are needed to disentangle the association between higher excessive gaming, social anxiety, and variations in brain structure. The separate samples used to examine sex differential alterations were comparably small and require further validation in larger samples. Finally, future studies should also consider the WHO framework for Gaming Disorder to validate whether the findings generalize across diagnostic frameworks . Unfortunately the Gaming Disorder Test (Pontes et al., 2021), assessing individual differences in Gaming Disorder according to the WHO criteria, was only filled in by a subsample of the present participants and therefore not focus of the present study.

Author's contribution

B.K.-B. conceptualized, conducted formal analysis, and wrote the draft. X.Z. conducted and validated the data processes. B.Biswal and C.M. reviewed and revised the manuscript. B. Becker conceptualized the study, interpreted data, and revised the manuscript. X.Z., L.W., X.G., R.Z., X.L., X.S., W.Z., and F.Y. implemented the experiments and collected data. B. Biswal revised the manuscript. All authors contributed to and approved the final version of the manuscript and take responsibility for the integrity of the data and the accuracy of the data analysis.

Conflict of interest

The authors declare no conflict of interest. However, the authors, Dr. Benjamin Becker, and Bharat Biswal are the editorial-board members of *Psychoradiology*. They were blinded from reviewing or making decisions on the manuscript.

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