Brain morphology, harm avoidance, and the severity of excessive internet use

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Abstract
As the previous studies have mainly focused on the reward system and the corresponding brain regions, the relationship between brain morphology and excessive internet use (EIU) were not clear; the purpose of the study was to investigate if the brain regions other than the reward system were associated with EIU. Data were acquired from 131 excessive internet users. Psychological measures included internet use, life quality, personality, mental illness symptoms, impulsivity, and thought suppression. The brain was scanned with 3T magnetic resonance imaging (MRI) and six types of brain morphological indexes were calculated. Lasso regression methods were used to select the predictors. Stepwise linear regression methods were used to build the models and verify the model. The variables remaining in the model were left precentral (curve), left superior temporal (surface area), right cuneus (folding index), right rostral anterior cingulate (folding index), and harm avoidance. The independent variable was the EIU score of the worst week in the past year. The study found that the brain morphological indexes other than the reward system, including the left precentral (curve), left superior temporal (surface area), right cuneus (folding index), right rostral anterior cingulate (folding index), and harm avoidance, can predict the severity of EIU, suggesting an extensive change in the brain. In this study, a whole-brain data analysis was conducted and it was concluded that the changes in certain brain regions were more predictive than the reward system and psychological measures or more important for EIU.
1 | INTRODUCTION

Excessive internet use (EIU) has become a health concern, especially among teenagers and young adults. The negative consequences of EIU include the long-term lack of sleep, deterioration of physical health, difficulty concentrating on work, and reduced close relationships with family members (Young, 2004), which negatively affect the quality of life (Cheng & Li, 2014).

EIU is usually associated with changes in brain structures and microstructures (Yuan, Qin, Liu, & Tian, 2011). A positron emission tomography study observed a reduced availability of dopamine D2 receptors in the striatum of EIU (Kim et al., 2011). Functional magnetic resonance imaging (fMRI) studies have shown that people who regularly play online games have insufficient participation of the reward system and decreased activity of the ventral striatum when expecting small or large monetary rewards (Hahn et al., 2011). Internet game disorder was suggested to share typical neurobiological changes of addiction to a large extent, such as activation of brain regions related to rewards, cue exposure, craving research, and dopamine-mediated participation in the reward mechanism (King & Delfabbro, 2014). In a large sample of habit internet users, there was a negative correlation between excessive internet use and gray matter changes and functional connection changes in the frontal-striate circuits (Kuehn & Gallinat, 2015). There was a significant negative correlation between the Internet Addiction Test score and the gray matter volume of the right frontal pole. The functional connection between the right frontal pole and the left ventral striatum was positively correlated with a higher internet addiction score. The internet addiction score was positively correlated with the low-frequency fluctuation (ALFF) of the bilateral ventral striatum (Kühn & Gallinat, 2015). Voxel-based morphometry analysis found a significant negative correlation between the absolute value of gray matter of the orbitofrontal cortex and internet use problems (Altbacker et al., 2016). Other studies have shown gray matter volume reduction in the prefrontal brain area, including the orbitofrontal cortex (Jin et al., 2016; Wang et al., 2018), dorsolateral prefrontal cortex, anterior cingulate gyrus cortex, supplementary motor area (Jin et al., 2016), and temporal–parietal area (Wang et al., 2018). Decreased cortical thickness was found in the orbitofrontal cortex and temporal–parietal regions of EIU (Wang et al., 2018). In addition, a diffusion tensor imaging study found that the structural connectivity between the ventral tegmental region and the nucleus accumbens region in EIU participants was low (Wang et al., 2019). These studies have suggested that EIU is driven by neuronal circuits related to addiction or the brain reward system.

However, in a 3-year follow-up study with a large sample of children (11.2 ± 3.1 years; range 5.7–18.4 years), a higher frequency of internet use decreased language intelligence and was related to a smaller increase in the volume of the gray matter and white matter of a wide range of brain areas. These areas involved areas related to language processing, attention and executive function, emotion and reward processing (Takeuchi et al., 2018). The study suggested a more comprehensive cognitive and brain change other than the reward system under EIU. Reduced activity in the brain regions related to impulse control and impaired decision-making (Verdejo-Garcia, Garcia-Fernandez, & Dom, 2019) and reduced functional connections involving cognitive control, executive function and motivation in the brain network have been found (Sussman, Harper, Stahl, & Weigle, 2017). Excessive use of the screen activated the brain regions related to cognitive, motor, and sensory functions that were not directly involved in addiction (Elman & Borsook, 2015).

Therefore, brain regions other than the reward system are involved in EIU, but the investigation is insufficient. The relationship between brain morphology and the severity of EIU has been reported, but the quantitative relationship is understudied. In addition, internet addiction and mental illness usually coexist, including affective disorders (depression), anxiety disorders (general anxiety disorder and social anxiety disorder), and attention deficit hyperactivity disorder (Yen, Ko, Yen, Wu, & Yang, 2007). Personality traits (Eksí, 2012), parenting and family factors (Ko, Yen, Yen, Lin, & Yang, 2007), and drinking and social anxiety (Lam, Peng, Mai, & Jing, 2009) have also been found to be related to EIU. The influence of these factors on the relationship between brain morphology and EIU was not clear. Therefore, the purpose of the study was to reveal (1) the relationship between brain morphological indexes and the severity of EIU; (2) the influence of the cofounding factors on the relationship; and (3) the relative advantages of the reward system and other relevant brain regions for EIU prediction. The work has been registered in the Open Science Foundation (https://osf.io).

2 | METHODS AND MATERIALS

The experimental approach is summarized in Figure 1. For more details, see the supplementary experimental procedure.

2.1 | Participants

Data were acquired from 131 excessive internet users. Participants who used the internet for at least 12 months and continued internet use daily in the past 3 months, beyond the purpose of work or study, were recruited. They had no history of current neurological or psychiatric disorders, including substance use, medicine use, or substance abuse, in the past 3 months.

2.2 | Psychological measures

Psychological traits were measured with the Excessive Internet Use Questionnaire (EIU; Sun et al., 2009), Symptom Checklist 90-Revised...
2.3 | Magnetic resonance imaging

MRI data were acquired using two identical 3-T Siemens Magnetom Trio scanners (Siemens, Erlangen, Germany). Functional images were acquired with a T2-weighted gradient echo-planar imaging sequence (TR = 2 s, TE = 30 ms, FOV = 240 mm, matrix, 64 × 64) with 33 axial slices (3.7 mm thickness, no gap), covering the whole brain. High-resolution T1-weighted spin-echo images were also collected for anatomical overlay.

The imaging data were processed with the analysis of functional neuroimages (AFNI; Version 20.3.00 “Vespuccia”). We used FreeSurfer software, a set of automated tools for reconstruction of the brain cortical surface (Fischl & Dale, 2000). Cortical surface reconstruction was performed with standard procedures provided by the software (http://surfer.nmr.mgh.harvard.edu/fswiki). We obtained an array of anatomical measures, including cortical thickness, surface area, and curvature at each region on the cortex, within the Desikan-Killiany atlas (Desikan et al., 2006).

2.4 | Lasso regression

There was often multicollinearity between variables. When the correlation between variables was high, good prediction results were often difficult to obtain. In this case, we used Lasso regression analysis (with SPSS 24) to select the best predictors in each category separately and then ran Lasso regression for the second time with all the selected factors for the overall selection.

2.5 | Linear regression

Stepwise linear regression was used to predict the EIU scores and test whether the selected factors were significant for the prediction. Six types of brain structural indexes (curvature index, folding index, Gaussian curvature, gray matter volume, surface area, and average thickness) were entered as independent variables, and four types of EIU scores were entered as dependent variables (see the EIU scale in the supplemental materials).

2.6 | Verification of the model

A model was established through stepwise regression analysis, and then we used the enter method plus bootstrap sampling to test the validity of this model by sampling 1,000 times in the same sample. To test the influence of the confounding factors on the regression relationship, we entered the selected psychological measures as the covariates into the final linear regression model and compared the models with and without covariates.

To test whether the brain reward system can predict the severity of EIU, the variables were screened in the reward system with Lasso regression, and the regression model was built using linear regression.

To test whether the psychological measures can predict the severity of EIU, the variables in the psychological measures were entered stepwise backwards, and the regression model was built using linear regression.

3 | RESULTS

3.1 | Samples and psychological measures

One hundred thirty-one participants took part in the study, mean age = 19.74, SD = 2.83, all males. The mean and standard deviation of each item in the questionnaires are presented in Table S1, and the
correlations between the psychological measures are presented in Table S2. In addition, the EIU score (of the worst week in the past year) was positively correlated with hunting in personality, attention in the BIS and motivation in the BIS, Pearson’s coefficients = 0.283, 0.228 and 0.261, respectively, ps < .05.

3.2 | Identifying potential predictors

With a penalty coefficient of 0.30–0.34 and regularized R square of 0.74, the significant factors in the questionnaire measures were psychosis, psychological health, and harm avoidance. They were later used in the stepwise regression analysis.

Six types of brain morphological indexes were used: brain curvature index, folding index, integrated rectified Gaussian curvature, gray matter volume, surface area, and average thickness. The indexes were calculated for 34 brain regions for each hemisphere. Lasso regression analysis was used separately for each type of index. The best predictive factors were selected and are listed in Table 1, with penalty coefficients and regularized R square listed as well.

The factors in Table 1 were entered into a Lasso regression analysis for the second time, and we found that the left precentral (curve), left parsopercularis (folding), left lateral occipital (surface), left superior temporal (surface), right cuneus (folding), and right rostral anterior cingulate (folding) were better predictive factors than others, with penalty coefficients of 0.52–0.68 and regularized R square of 0.39.

3.3 | Building a predictive model

To build a predictive model, we used a backwards stepwise linear regression method. The selected predictive variables were left precentral (curve), left parsopercularis (folding), left lateral occipital (surface), left superior temporal (surface), right cuneus (folding), right rostral anterior cingulate (folding), psychosis, psychological health, and harm avoidance. The independent variables were EIU scores. We found that in step 4, the model was significant at p < .05. The variables remaining in the model were left precentral (curve), left superior temporal (surface), right cuneus (folding), right rostral anterior cingulate (folding), and harm avoidance. The independent variable was the EIU score of the worst week in the past year, F(5,84) = 2.55, p = .03. See Table 2 and Figure 2 for Model I.

3.4 | Verification of the model

Self-sampling was used to check the reliability of the model. After 1,000 self-samplings, it was found that the model formed by these five variables still tends to be significant, with a small change in the variable coefficients. The left precentral (curve), left superior temporal (surface area), and right cuneus (folding index) were negatively correlated with EIU scores. The right rostral anterior cingulate (folding index) and harm avoidance were positively correlated with the EIU score (see Table 2). When the stepwise procedure was repeated after removing these five variables, no other variant significantly contributed to the EIU scores. Five variables continued to be significant factors in the ANCOVA, which included hunting in personality, attention in BIS, and motivation in BIS as covariates.

3.5 | Other predictive models

To test whether the brain reward system can predict the severity of EIU, the variables were screened and entered into the linear regression. Among the caudal anterior cingulate, medial orbitofrontal lobe, parahippocampal, parsopercularis, and rostral anterior cingulate, we found that the rostral anterior cingulate (thickness), parahippocampal (gray matter volume), parsopercularis (folding), parahippocampal (curve),

| TABLE 1 | Brain morphological factors selected by Lasso regression |
|---------------------------------|---------------|---------------|---------------|
| Index name                      | Left hemisphere | Right hemisphere | Penalty coefficient R^2 | Right hemisphere | Penalty coefficient R^2 |
| Brain curvature index           | Lateral occipital pars orbitalis precentral | Entorhinal middle temporal pars orbitalis | 0.44–0.56 | R^2 = 0.24 | 0.44–0.52 |
| Folding index                   | Lateral occipital pars opercularis pars orbitalis | Cuneus frontal pole rostral anteriorcingulate | 0.52–0.58 | R^2 = 0.14 | 0.64–0.66 |
| Integrated rectified gaussian curvature | Bank of ssts posterior cingulate transverse temporal | Inferior parietal Para hippocampal Supramarginal | 0.36 | R^2 = 0.07 | 0.40–0.46 |
| Gray matter volume              | Lateral occipital Parahippocampal pars triangularis | Fusiform lateral occipital superior frontal superior temporal | 0.36 | R^2 = 0.07 | 0.36–0.38 |
| Surface area                    | Lateral occipital Precuneus superior temporal | Bank of ssts Medialorbitofrontal Parstriangularis Supramarginal | 0.30–0.36 | R^2 = 0.22 | 0.32 |
| Average thickness               | Caudal anterior cingulate posterior cingulate rostral anteriorcingulate | Entorhinal Pericalcarine rostral middle frontal | 0.36–0.44 | R^2 = 0.20 | 0.34–0.48 |

Verification of the model

Self-sampling was used to check the reliability of the model. After 1,000 self-samplings, it was found that the model formed by these five variables still tends to be significant, with a small change in the variable coefficients. The left precentral (curve), left superior temporal (surface area), and right cuneus (folding index) were negatively correlated with EIU scores. The right rostral anterior cingulate (folding index) and harm avoidance were positively correlated with the EIU score (see Table 2). When the stepwise procedure was repeated after removing these five variables, no other variant significantly contributed to the EIU scores. Five variables continued to be significant factors in the ANCOVA, which included hunting in personality, attention in BIS, and motivation in BIS as covariates.
and caudal anterior cingulate (thickness) can effectively predict the EIU score, $F_{(5,123)} = 4.357$, $p = .001$ (see Table 3 and Figure 3 for Model II).

To test whether the psychological measures can predict the severity of EIU, the variables in the psychological measures were entered into the backwards stepwise linear regression. Among TABLE 2 The stepwise linear regression model and the self-sampling model

|                      | Model I (step 4) |          |          | Self-sampling |          |          |
|----------------------|------------------|----------|----------|--------------|----------|----------|
|                      | Standardized coefficient | $t$ | $p$      | Standardized coefficient | $t$ | $p$      |
| Constant             | 3.026            | 0.003    |          | 3.429        | 0.001    |          |
| Left precentral (curve) | $-0.145$        | $-1.243$ | 0.217    | $-0.132$     | $-1.339$ | 0.183    |
| Left superior temporal (surface area) | $-0.093$        | $-0.818$ | 0.416    | $-0.073$     | $-0.737$ | 0.462    |
| Right cuneus (folding index) | $-0.246$        | $-2.131$ | 0.036    | $-0.192$     | $-1.905$ | 0.059    |
| Right rostral anterior cingulate (folding index) | 0.015          | 0.134    | 0.894    | 0.049        | 0.478    | 0.634    |
| Harm avoidance       | 0.121            | 1.142    | 0.257    | 0.104        | 1.150    | 0.253    |

$F_{(5,84)} = 2.552$
$p = .032$

$F_{(5,117)} = 2.213$
$p = .061$

FIGURE 2 Factors in the linear regression model, scatter plots and fitted lines

TABLE 3 Model II and Model III

|                      | Standardized coefficient | $t$ | $p$ |
|----------------------|--------------------------|-----|-----|
| Model II             |                          |     |     |
| Constant             | 0.094                    | .925|     |
| Left caudal anterior cingulate (thickness) | 0.097        | 0.970| .334|
| Left parahippocampal (gray matter volume) | $-0.118$        | $-1.305$ | .194|
| Left parahippocampal (curvature) | $-0.117$        | $-1.242$ | .217|
| Left parsorbitalis (folding) | $-0.214$        | $-2.487$ | .014|
| Left rostral anterior cingulate (thickness) | 0.166        | 1.720| .088|

$F_{(5,123)} = 4.357$
$p = .001$

|                      | Standardized coefficient | $t$ | $p$ |
|----------------------|--------------------------|-----|-----|
| Model III            |                          |     |     |
| Constant             | 0.079                    | .937|     |
| Harm avoidance       | 0.220                    | 1.759| .082|
| Thought suppression  | $-0.226$                | $-1.958$ | .054|
| Attentional BIS      | 0.218                    | 1.569| .121|
| Motivated BIS        | 0.244                    | 1.948| .055|
| Unplanned BIS        | $-0.204$                | $-1.390$ | .168|

$F_{(5,79)} = 2.701$
$p = .026$

Abbreviation: IS, Barratt impulsiveness scale.
personality, impulsiveness, and thought suppression, we found that unplanned, motivated, attentional, avoidance, and suppression can predict the EIU score, $F_{(5,79)} = 2.701$, $p = .026$ (see Table 3 and Figure 4 for Model III).

4 | DISCUSSION

The study evaluated the effectiveness of multiple factors in predicting the severity of excessive internet use and investigated their relative strength in the prediction. The study revealed the relationship between excessive internet use and brain morphological indexes through whole-brain analysis and comprehensive regression analysis, including Lasso regression and stepwise linear regression. We found that the strongest impact factors on the severity of EIU were brain morphological indexes and harm avoidance. The predictive factors were the left precentral (curve), the left superior temporal (surface area), the right cuneus (folding index), the right rostral anterior cingulate (folding index), and harm avoidance; they effectively predicted the EIU score of the worst week in the past year. The cofounding factors did not affect the predictive power of these five predictors in the model (Model I).

Harm avoidance is a feature of internet gaming disorder (Howard, Kivlahan, & Walker, 1997; Lee et al., 2018). Young adults with problematic internet use had worse scores on harm avoidance, novelty seeking, and reward dependence than normal controls (Pettorruso et al., 2020). Consistently, the study revealed a positive relationship between harm avoidance and the EIU score.

Using the variables in the reward system and the variables in the psychological measures, we obtained two models (II and III), respectively, and both models showed significance, indicating the accuracy of the two models and usefulness of these variables. This was consistent with the results of a large number of previous studies. The reward system is an important participant in behavioral addiction, and psychological measures must be closely related to behavioral addiction. However, when the number of collected variables increased, there might be many features that were not important (coefficients were small). Lasso regression can compress the coefficients of these unimportant variables to 0, which not only achieves more accurate parameter estimation but also selects the variables (dimensionality reduction). Therefore, when we put all the measured variables, including six types of morphological indexes and psychological measures, into Lasso regression, the variables were ranked according to their importance, and the unimportant variables were filtered out. This means that the variables in Model I were more important than the variables in Models II and III.

As long as the interference variables or intermediary variables are put into the model, the influence of key factors may decrease or even disappear (the p value becomes larger and the significance decreases). There are many reasons for this change, one of which is that the
interference variable precedes the independent and dependent variables and affects both, and the mediating variable refers to the intermediate factor through which the independent variable has an impact on the dependent variable (Flannely, Flannely, & Jankowski, 2014). In addition, the presence of complementary explanatory factors and competing explanatory factors makes single-class predictors, such as those in Models II and III, misleading. This explained why Models II and III appear to be more predictive; in fact, the factors in them were likely to be influenced by more important factors, which were the factors in Model I.

Overall, the study found that the brain morphological indexes other than the reward system, the left precentral (curve), the left superior temporal (surface area), the right cuneus (folding index), and the right rostral anterior cingulate (folding index), can predict the severity of EIU, suggesting an extensive change in the brain other than addiction-related changes. In this study, a whole-brain data analysis was conducted and it was concluded that the changes in certain brain regions were more predictive than the reward system and psychological measures or more important for EIU.

Since the study only collected EIU data and did not include healthy internet users, the lack of contrast between the two groups was a limitation of this study. As internet use and EIU are becoming increasingly common in human society, future work should conduct extensive discussion on the behavior but not just in the context of addiction. Although the study revealed the relationship between morphological change and EIU, the causal relationship between them remained unclear, and a longitudinal study was suggested to clarify the chronological sequence of a series of changes in the brain after EIU.

AUTHOR CONTRIBUTIONS

LW conceptualized and wrote this article. RZ, YL, and JR contributed to the data collection and MRI data processing. QZ and HZ contributed to data analysis and reference check. All the authors contributed to interpretation of the data, drafting of the manuscript, approval of the final manuscript, and were responsible for the decision to submit the manuscript. All the authors report no biomedical financial interests or potential conflicts of interest.

DATA AVAILABILITY STATEMENT

Data and code is available upon request.

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