STUDY PROTOCOL
https://doi.org/10.30773/pi.2021.0383

Print ISSN 1738-3684 / On-line ISSN 1976-3026
OPEN ACCESS

Structural and Functional Neural Alterations in Internet Addiction: A Study Protocol for Systematic Review and Meta-Analysis

Jun-Li Liu[1]*, Jing-Ting Sun[2,3]*, Hui-Lin Hu[4], Hao-Yuan Wang[5], Yun-Xi Kang[1], Tian-Qi Chen[6], Zhu-Hong Chen[3], Yu-Xuan Shang[3], Yu-Ting Li[3], Bo Hu[3] ✉, and Rui Liu[7] ✉

[1]Xi'an Technological University, Xi'an, China
[2]Shaanxi University of Chinese Medicine, Xianyang, China
[3]Department of Radiology, Tangdu Hospital, Fourth Military Medical University, Xi'an, China
[4]Arizona State University, Tempe, AZ, USA
[5]McMaster University, Ontario, Canada
[6]Institution of Basic Medicine, Fourth Military Medical University, Xi'an, China
[7]Department of Rehabilitation, Tangdu Hospital, Fourth Military Medical University, Xi'an, China

A growing number of neuroimaging studies have revealed abnormal brain structural and functional alterations in subjects with internet addiction (IA), however, with conflicting conclusions. We plan to conduct a systematic review and meta-analysis on the studies of voxel-based morphometry (VBM) and resting-state functional connectivity (rsFC), to reach a consolidated conclusion and point out the future direction in this field. A comprehensive search of rsFC and VBM studies of IA will be conducted in the PubMed, Cochrane Library, and Web of Science databases to retrieve studies published from the inception dates to August 2021. If the extracted data are feasible, activation likelihood estimation and seed-based d mapping methods will be used to meta-analyze the brain structural and functional changes in IA patients. This study will hopefully reach a consolidated conclusion on the impact of IA on human brain or point out the future direction in this field.
Psychiatry Investig 2023;20(1):69-74

Keywords Internet addiction; Smartphone; Social media; Voxel-based morphometry; Resting state functional connectivity.

INTRODUCTION

With the widespread use of the internet around the world, the way of communication has changed tremendously. By the end of January 2022, there are over 5.2 billion active internet users, accounting for 66.2% of the global population (http://www.internetworldstats.com/stats.htm). The internet has become an indispensable role in modern life, however, while it has brought unprecedented benefits, internet addiction (IA) has also become a major problem plaguing the public.

Received: December 16, 2021 **Revised:** May 18, 2022
Accepted: July 4, 2022

✉ **Correspondence:** Rui Liu, MD, PhD
Department of Rehabilitation, Tangdu Hospital, Fourth Military Medical University, 569 Xinsi Road, Xi'an 710038, Shaanxi, China
Tel: +86-29-84777756, **E-mail:** tdliurui@fmmu.edu.cn

✉ **Correspondence:** Bo Hu, MD, PhD
Department of Radiology, Tangdu Hospital, Fourth Military Medical University, 569 Xinsi Road, Xi'an 710038, Shaanxi, China
Tel: +86-29-84778689, **E-mail:** rayhb@foxmail.com

*These authors contributed equally to this work.

IA refers to internet users' obsession with the internet due to their long-term use, involving smartphone addiction, social media addiction, and internet gaming addiction (IGD).[1] These phenomena will eventually lead to various negative effects, such as craving,[2,3] impulsiveness,[4] response inhibition,[5] emotional disturbance,[6] reduced executive function,[7] and even cognitive disorders.[8,9] Besides, it also exposes people to sleep disorders,[10] attention deficit hyperactivity disorder, depression, and anxiety.[11-13] Ultimately, concerns about IA increase over time.

Currently, magnetic resonance imaging (MRI), as a non-invasive neuroimaging tool, has been widely used to study brain characteristics. As the attention on IA increased, related neuroimaging studies have also emerged, especially voxel-based morphometry (VBM) studies and resting-state functional connectivity (rsFC) studies. VBM can reflect the gray matter (GM) structure of the brain, such as the significantly reduced volume of GM in the anterior cingulate cortex (ACC),[4] dorsolateral prefrontal cortex (DLPFC),[14] and supplemental motor area (SMA)[15] of patients with IA. rsFC is effective in detecting cerebral large-scale network dysfunction. Studies in this domain demonstrated that the rsFC was increased in insula,[16] posterior cingulate cortex (PCC),[17] and precuneus[18] of IA patients, while the rsFC was decreased in SMA,[18] inferior parietal lobule,[19] and superior frontal gyrus (SFG).[20] These studies suggest that IA not only affect the overall function of the brain but also lead to abnormalities in brain structure. However, not all results across these studies are consistent, therefore, a meta-analysis is needed to synthesize all current research to find a consistent conclusion.

At present, activation likelihood estimation (ALE) and seed-based mapping (SDM) are the two most used methods in the meta-analysis of neuroimaging.[21,22] ALE is easy for operation and strict for multiple comparison correction. However, it cannot synthesize both negative and positive outcomes. SDM can synthesize both positive and negative results, providing multimodal analysis, but the correction is not as strict as ALE. Considering both methods have advantages and disadvantages, conclusions obtained by using only one method may be biased.

Therefore, this protocol aims to comprehensively explore structural and functional brain alterations in individuals with IA by combining ALE and SDM. This study was registered in PROSPERO (CRD42021277662).

METHODS

The meta-analysis that integrates the latest neuroimaging studies will be conducted through ALE and SDM to synthesize the brain functional and structural changes associated with IA to better understand the effects of IA on the human brain, enabling targeted early intervention and treatment.

Criteria of selection for study

Criteria for inclusion

1) Diagnoses of IA in each study were based on Diagnostic and Statistical Manual of Mental Disorders-fifth edition, other quantitative assessment tools or both.
2) VBM studies or seed-based rsFC studies.
3) IA patients were compared with healthy controls (HCs).
4) Results were reported as coordinates in Montreal Neurological Institute (MNI) or Talairach space.

Criteria for exclusion

1) Not VBM study.
2) Not seed-based rsFC approach.
3) Studies only reported region of interest findings.
4) Longitudinal or intervention studies that did not compare with baseline state.
5) No HCs.

Search methods

Electronic searches

From the inception dates to August 2021, the following databases will be searched: PubMed, the Cochrane Library, and Web of Science. The searching strategy of the PubMed database is presented in Table 1.

Searching other resources

Additional studies will be further identified based on a list of all identified publications, including previous reviews and meta-analyses, as well as a reference list of the selected studies.

Data collection

Selection of studies

The study selection process will be consulted before publication selection. After an electronic search, the results will be output to a database created with Endnote software. Publications obtained from other sources will also be entered into the same database. Two authors will screen the included articles independently, any differences will be settled in consultation with a third researcher. First, the investigators will screen

Table 1. Search strategy for PubMed database

Study	Search strategy
Voxel-based morphometry	"internet addiction disorder" OR "social media addiction" OR "smartphone addiction" OR "internet gaming disorder" OR "gaming addiction" OR "mobile phone dependence" OR "internet communication addiction" OR "problematic smartphone use") AND ("voxel-based morphometry" OR "VBM" OR "gray matter" OR "grey matter"
Resting state functional connectivity	"internet addiction disorder" OR "social media addiction" OR "smartphone addiction" OR "internet gaming disorder" OR "gaming addiction" OR "mobile phone dependence" OR "internet communication addiction" OR "problematic smartphone use") AND ("magnetic resonance imaging" OR "functional magnetic resonance imaging" OR "fMRI") AND ("functional connectivity"

This search strategy was modified to be suitable for other electronic databases. VBM, voxel-based morphometry; fMRI, functional magnetic resonance imaging studies in the title/abstract, and then within the full text to determine whether to include them. The selection diagram for the study is shown in Figure 1. All reasons for exclusion will be listed in this report.

Data extraction

Information about the identified studies will be extracted, including the following data: first author name; published year; sample size for each group; comorbidity; mean age; diagnostic criteria; machine information; application of multiple comparison correction and coordinates of abnormal brain regions.

Quality assessment

Currently, there is no consensus on the quality assessment criteria for neuroimaging studies. Previous reviews of neuroimaging systems usually set quality assessment tools based on their studies. For this meta-analysis, we will use the Newcastle-Ottawa Scale (http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm) as the basis for quality assessment and checked systematically for data acquisition, experimental design, diagnostic criteria, multiple comparison correction.

Data analysis

ALE meta-analysis

Brain regions with structural abnormalities and brain regions with functional abnormalities will be analyzed separately using the ALE technique, which is a voxel-based method for finding convergence across neuroimaging experiment coordinates.[23,24] First, the coordinates reported in Talairach space will be transformed into the MNI space using the "convert foci" option implemented in the Ginger ALE toolbox.[25-27] Then, the coordinates of MNI space will be input into ALE software. Based on recommendations,[28] ALE maps will be set with a threshold at $p<0.05$ using a cluster level family-wise error (FWE) with a cluster forming threshold at voxel level $p<0.001$. The p-values in our analysis will be generated from 5,000 permutations.

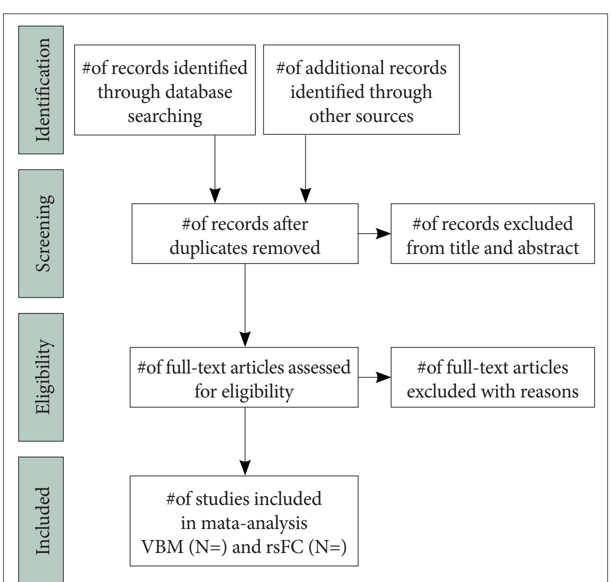

Figure 1. Flow diagram of study selection process. VBM, voxel-based morphometry; rsFC, resting-state functional connectivity.

SDM meta-analysis

SDM technology emerged after the ALE method. It is a common method for coordinate-based meta-analysis. Anisotropic effect size seed-based d mapping (AES-SDM) software has been used in many meta-analyses in the past.[29,30] To improve the reliability of the results and to compare the consistency of the SDM and ALE methods, we will investigate the VBM study and the rsFC study separately by using not only the latest version of the ALE software but also the latest version of the SDM software: seed-based d mapping with permutation of subject images (SDM-PSI). First, the peak coordinates of significant clusters and the related t-values will be extracted. If the original study reported z-scores or p-values, we will convert them to t-values using the online tools available on the SDM website.[31] Second, as a pre-processing step, the lower and upper effect-size bounds will be estimated. SDM-PSI calculates an image of the lowest potential effect size of each voxel and an image of the largest potential effect size of each voxel. A 20 mm full-width half maximum (FWHM) anisotropic Gaussian kernel and 2 mm voxel size will be used for preprocessing.[31] Third, the maximum likelihood estimation (MLE) of the most likely effect size and its standard error will be performed. The MLE will be performed according to standard SDM-PSI parameters.[31] Fourth, FWE correction based on threshold-free cluster enhancement will be used to thresholding the significant results.[31] The corrected p-value threshold will be 0.05, and the minimum cluster will be 10 voxels.

Heterogeneity, sensitivity, and published bias

Between-study heterogeneity was examined to find the heterogeneous brain regions with Q statistics. To verify the stability and reliability of the study results, we performed a jackknife sensitivity analysis, discarding each dataset in turn and repeating the combined analysis with other datasets. To test the possible publication bias, we will establish a funnel plot based on SDM-PSI software, which calculates effect sizes through Hedge's g.[32] If there is no obvious publication bias, the scatter plot will resemble a symmetrical inverted funnel.[33]

Subgroup analyses or meta-regression

If sufficient studies are included, we will examine potential confounding factors using subgroup analyses or meta-regression. For example, individuals were divided into IGD, smartphone addiction, social media addiction, etc.

DISCUSSION

Although IA has not been recognized by the World Health Organization, there is a rising trend of IA among the younger generation, and the prevalence of IA among adolescents and young adults is alarming. The results of the current systematic review show that IA as a complex problem is closely related to age, gender, region, and other variables (e.g., increased individualism, decreased sociability, and enculturation).[34,35] IA deserves wider attention in more fields. IA is a behavioral addiction, similar to substance addiction, mainly related to abnormal reward system.[36,37] Previous research has shown that addiction leads to disruption or rewiring of neural circuits in the reward system.[38] This process mainly involves dopamine (DA) pathways in the mesolimbic region. Dopaminergic neurons are located in the ventral tegmental area and project to the nucleus accumbens (NAs).[39] Certain addictive behaviors, including IA, increase DA in NAs, therefore the development of IA is associated with dopaminergic involvement.[40] The purpose of this study is to design an objective and accurate method for systematic review and meta-analysis to investigate the structural and functional abnormalities of the brain in patients with IA.

IA, as neurological dysfunction, has been explored in a large number of neuroimaging studies. The resting state is a functional brain imaging method used to assess interactions between brain regions when subjects are not performing specific tasks. Existing resting-state MRI studies show that brain abnormalities in IA patients are mainly concentrated in the default mode network (DMN), executive control network, and salience network compared to HCs. Studies of IGD have shown a significant decrease in the amplitude of low frequency fluctuations (ALFF) in the left SFG and posterior cerebellar lobe, while the ALFF in the superior temporal gyrus was increased.[41,42] In patients with smartphone addiction, the ALFF in the ACC, indicates reduced activity in the ACC.[43] This may be a neural correlate of impaired self-awareness and emotion regulation in IA patients. IGD also showed low rsFC between the left SFG and the PCC, the right angular gyrus, and the right DLPFC.[41] In addition, IGD participants showed decreased rsFC between the DLPFC and the caudate nucleus, left dorsal putamen, and left medial prefrontal cortex, and increased rsFC between the PCC and DLPFC.[18,44,45] These brain regions are associated with executive function and decision-making. These alterations may be potential biomarkers reflecting inhibitory function in patients with IA. Meanwhile, previous studies demonstrated that IA subjects revealed increased local functional connectivity density (lFCD) values in the right DLPFC, left parahippocampal gyrus, and cerebellum, and the bilateral middle cingulate cortex and superior temporal pole, as well as decreased lFCD values in the right inferior parietal lobe, and bilateral calcarine and lingual gyrus.[46] These regions involve cognitive control networks, DMN, and visual attention networks, which may be potentially linked to lack of attention and uncontrolled network use in individuals with IA.[46] In further, it has been indicated that using resting-state features can classify IA and HC, reveal brain alterations after intervention, and even efficacy assessment, for example, using functional connectivity density (FCD) can successfully distinguish IA from HC with an accuracy of 82.5%, while using the FCD change ratio can successfully assess the efficacy of cognitive behavior therapy with a correlation efficient of 0.59.[47] And related studies have used rsFC to display IA brain changes in patients before and after acupuncture treatment.[48] MRI studies also revealed structural disorders in the prefrontal striatum circuit in IGD patients.[49] Subjects with IGD have reduced gray matter volume in brain regions associated with executive control, such as the ACC and SMAs,[4,15] similar to drug addiction.[50] Besides, task-state functional magnetic resonance imaging studies can be used to estimate which areas of the brain are activated by the stimuli associated with IA. A study showed greater activation in the cortical-limbic system during cue-inducing tasks, with the left orbitofrontal cortex and ventral striatum associated with cue responses in computer game players.[51] Compared to controls, participants with online game addiction made more errors in the Go/No Go task and showed reduced activation in the dorsolateral prefrontal and superior parietal lobes, suggesting that IGD leads to impaired response inhibition.[5] In a reward-related task, internet addiction disorder patients also showed increased activation in the orbitofrontal cortex on gain trials and decreased activation in the ACC on loss trials, implying enhanced reward sensitivity and reduced loss sensitivity.[52] Positron emission computed tomography studies found that patients with IGD showed low metabolism in the ACC, temporal lobe, frontal lobe, parietal lobe, and striatum, and low metabolic connectivity between temporal and limbic regions and motor and occipital regions.[53] Patients with IA had reduced levels of striatal dopamine receptors compared to controls.[54] These findings above are consistent with mechanisms of addiction, but specific neurobiological markers are uncertain and more research on IA is urgently needed.

However, inconsistencies remain and reliable conclusions cannot be drawn. For example, in a study of IGD, the rsFC of the posterior insula and SMA was weakened compared to HC.[20] But an opposite situation was found in another IGD study that the rsFC of posterior insula and SMA was increased.[55] These inconsistencies are partly due to differences in research methods and limited sample sizes. Therefore, meta-analysis is required to synthesize these research results to draw the most credible conclusions.

Availability of Data and Material

Data sharing not applicable to this article as no datasets were generated or analyzed during the study.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Rui Liu, Bo Hu. Data curation: Hui-Lin Hu. Formal analysis: Jing-Ting Sun. Funding acquisition: Rui Liu. Investigation: Jun-Li Liu, Jing-Ting Sun. Methodology: Jun-Li Liu, Hui-Lin Hu, Hao-Yuan Wang. Project administration: Hao-Yuan Wang. Resources: Jun-Li Liu. Software: Yun-Xi Kang, Tian-Qi Chen. Supervision: Zhu-Hong Chen, Yu-Xuan Shang. Validation: Yun-Xi Kang, Tian-Qi Chen. Visualization: Yu-Ting Li. Writing—original draft: Jun-Li Liu, Jing-Ting Sun. Writing—review & editing: Rui Liu, Bo Hu.

ORCID iDs

Jun-Li Liu	https://orcid.org/0000-0002-6184-0439
Jing-Ting Sun	https://orcid.org/0000-0001-9384-2714
Hui-Lin Hu	https://orcid.org/0000-0002-7218-0480
Hao-Yuan Wang	https://orcid.org/0000-0002-9221-1627
Yun-Xi Kang	https://orcid.org/0000-0002-6279-6572
Tian-Qi Chen	https://orcid.org/0000-0001-9737-1745
Zhu-Hong Chen	https://orcid.org/0000-0001-9366-513X
Yu-Xuan Shang	https://orcid.org/0000-0003-0637-2895
Yu-Ting Li	https://orcid.org/0000-0001-9334-5582
Bo Hu	https://orcid.org/0000-0002-1135-0669
Rui Liu	https://orcid.org/0000-0002-9746-9280

Funding Statement

This work was supported by the Major Theoretical and Practical Issues in Philosophy and Social Sciences of Shaanxi Province research Project (2021ND0187 to RL) and 2020 Project of the 13th Five-Year Plan of Education Science of Shaanxi Province (SGH20Y1098 to RL).

Acknowledgments

The authors would like to thank Drs. Wu-Xun Cui, Si-Jie Xiu, from the Department of Radiology of Tangdu Hospital for their outstanding technique support. Our gratitude also goes for Profs. Jin-Lian Li, Liang-Wei Chen, and Jun-Ling Zhu from the Department of Radiology of Tangdu Hospital for helpful comments on the manuscript.

REFERENCES

1. Uncapher MR, Lin L, Rosen LD, Kirkorian HL, Baron NS, Bailey K, et al. Media multitasking and cognitive, psychological, neural, and learning differences. Pediatrics 2017;140(Suppl 2):S62-S66.
2. Dong G, Wang L, Du X, Potenza MN. Gender-related differences in neural responses to gaming cues before and after gaming: implications for gender-specific vulnerabilities to internet gaming disorder. Soc Cogn Affect Neurosci 2018;13:1203-1214.
3. Ma SS, Worhunsky PD, Xu JS, Yip SW, Zhou N, Zhang JT, et al. Alterations in functional networks during cue-reactivity in internet gaming disorder. J Behav Addict 2019;8:277-287.
4. Lee D, Namkoong K, Lee J, Jung YC. Abnormal gray matter volume and impulsivity in young adults with internet gaming disorder. Addict Biol 2018;23:1160-1167.
5. Liu GC, Yen JY, Chen CY, Yen CF, Chen CS, Lin WC, et al. Brain activation for response inhibition under gaming cue distraction in internet gaming disorder. Kaohsiung J Med Sci 2014;30:43-51.
6. Karaer Y, Akdemir D. Parenting styles, perceived social support and emotion regulation in adolescents with internet addiction. Compr Psychiatry 2019;92:22-27.
7. Yao YW, Wang LJ, Yip SW, Chen PR, Li S, Xu J, et al. Impaired decision-making under risk is associated with gaming-specific inhibition deficits among college students with internet gaming disorder. Psychiatry Res 2015;229:302-309.
8. Loh KK, Kanai R. How has the internet reshaped human cognition? Neuroscientist 2016;22:506-520.
9. Cudo A, Zabielska-Mendyk E. Cognitive functions in internet addiction - a review. Psychiatr Pol 2019;53:61-79.
10. Aledavood T, Torous J, Triana Hoyos AM, Naslund JA, Onnela JP, Keshavan M. Smartphone-based tracking of sleep in depression, anxiety, and psychotic disorders. Curr Psychiatry Rep 2019;21:49.
11. Jorgenson AG, Hsiao RC, Yen CF. Internet addiction and other behavioral addictions. Child Adolesc Psychiatr Clin N Am 2016;25:509-520.
12. Weinstein A, Lejoyeux M. Internet addiction or excessive internet use. Am J Drug Alcohol Abuse 2010;36:277-283.
13. Wang BQ, Yao NQ, Zhou X, Liu J, Lv ZT. The association between attention deficit/hyperactivity disorder and internet addiction: a systematic review and meta-analysis. BMC Psychiatry 2017;17:260.
14. Wang Y, Zou Z, Song H, Xu X, Wang H, d'Oleire Uquillas F, et al. Altered gray matter volume and white matter integrity in college students with mobile phone dependence. Front Psychol 2016;7:597.
15. Jin C, Zhang T, Cai C, Bi Y, Li Y, Yu D, et al. Abnormal prefrontal cortex resting state functional connectivity and severity of internet gaming disorder. Brain Imaging Behav 2016;10:719-729.
16. Ko CH, Hsieh TJ, Wang PW, Lin WC, Yen CF, Chen CS, et al. Altered gray matter density and disrupted functional connectivity of the amygdala in adults with internet gaming disorder. Prog Neuropsychopharmacol Biol Psychiatry 2015;57:185-192.
17. Seok JW, Sohn JH. Altered gray matter volume and resting-state connectivity in individuals with internet gaming disorder: a voxel-based morphometry and resting-state functional magnetic resonance imaging study. Front Psychiatry 2018;9:77.
18. Lee D, Namkoong K, Lee J, Jung YC. Dorsal striatal functional connectivity changes in internet gaming disorder: a longitudinal magnetic resonance imaging study. Addict Biol 2021;26:e12868.
19. Ding WN, Sun JH, Sun YW, Zhou Y, Li L, Xu JR, et al. Altered default network resting-state functional connectivity in adolescents with internet gaming addiction. PLoS One 2013;8:e59902.
20. Zhang Y, Mei W, Zhang JX, Wu Q, Zhang W. Decreased functional connectivity of insula-based network in young adults with internet gaming disorder. Exp Brain Res 2016;234:2553-2560.
21. Cortese S, Castellanos FX, Eickhoff CR, D'Acunto G, Masi G, Fox PT, et al. Functional decoding and meta-analytic connectivity modeling in adult attention-deficit/hyperactivity disorder. Biol Psychiatry 2016; 80:896-904.
22. Pezzoli S, Sánchez-Valle R, Solanes A, Kempton MJ, Bandmann O, Shin JI, et al. Neuroanatomical and cognitive correlates of visual hallucinations in Parkinson's disease and dementia with Lewy bodies: voxel-based morphometry and neuropsychological meta-analysis. Neurosci Biobehav Rev 2021;128:367-382.
23. Turkeltaub PE, Eden GF, Jones KM, Zeffiro TA. Meta-analysis of the functional neuroanatomy of single-word reading: method and validation. Neuroimage 2002;16(3 Pt 1):765-780.
24. Raimo S, Cropano M, Trojano L, Santangelo G. The neural basis of gam-

bling disorder: an activation likelihood estimation meta-analysis. Neurosci Biobehav Rev 2021;120:279-302.
25. Eickhoff SB, Laird AR, Grefkes C, Wang LE, Zilles K, Fox PT. Coordinate-based activation likelihood estimation meta-analysis of neuroimaging data: a random-effects approach based on empirical estimates of spatial uncertainty. Hum Brain Mapp 2009;30:2907-2926.
26. Eickhoff SB, Bzdok D, Laird AR, Kurth F, Fox PT. Activation likelihood estimation meta-analysis revisited. Neuroimage 2012;59:2349-2361.
27. Turkeltaub PE, Eickhoff SB, Laird AR, Fox M, Wiener M, Fox P. Minimizing within-experiment and within-group effects in activation likelihood estimation meta-analyses. Hum Brain Mapp 2012;33:1-13.
28. Eickhoff SB, Nichols TE, Laird AR, Hoffstaedter F, Amunts K, Fox PT, et al. Behavior, sensitivity, and power of activation likelihood estimation characterized by massive empirical simulation. Neuroimage 2016; 137:70-85.
29. Wollman SC, Alhassoon OM, Hall MG, Stern MJ, Connors EJ, Kimmel CL, et al. Gray matter abnormalities in opioid-dependent patients: a neuroimaging meta-analysis. Am J Drug Alcohol Abuse 2017;43:505-517.
30. Wang X, Cheng B, Wang S, Lu F, Luo Y, Long X, et al. Distinct grey matter volume alterations in adult patients with panic disorder and social anxiety disorder: a systematic review and voxel-based morphometry meta-analysis. J Affect Disord 2021;281:805-823.
31. Albajes-Eizagirre A, Solanes A, Vieta E, Radua J. Voxel-based meta-analysis via permutation of subject images (PSI): theory and implementation for SDM. Neuroimage 2019;186:174-184.
32. Albajes-Eizagirre A, Solanes A, Fullana MA, Ioannidis JPA, Fusar-Poli P, Torrent C, et al. Meta-analysis of voxel-based neuroimaging studies using seed-based d mapping with permutation of subject images (SDM-PSI). J Vis Exp 2019;153:e59841.
33. Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ 2011;343:d4002.
34. Lozano-Blasco R, Robres AQ, Sánchez AS. Internet addiction in young adults: a meta-analysis and systematic review. Comput Hum Behav 2022;130:107201.
35. Lozano-Blasco R, Latorre-Martínez M, Cortés-Pascual A. Screen addicts: a meta-analysis of internet addiction in adolescence. Child Youth Serv Rev 2022;135:106373.
36. Hammond CJ, Mayes LC, Potenza MN. Neurobiology of adolescent substance use and addictive behaviors: treatment implications. Adolesc Med State Art Rev 2014;25:15-32.
37. Goodman A. Neurobiology of addiction. An integrative review. Biochem Pharmacol 2008;75:266-322.
38. Joffe ME, Grueter CA, Grueter BA. Biological substrates of addiction. Wiley Interdiscip Rev Cogn Sci 2014;5:151-171.
39. Volkow ND, Wang GJ, Fowler JS, Tomasi D. Addiction circuitry in the human brain. Annu Rev Pharmacol Toxicol 2012;52:321-336.
40. Volkow ND, Michaelides M, Baler R. The neuroscience of drug reward and addiction. Physiol Rev 2019;99:2115-2140.
41. Sun Y, Wang Y, Han X, Jiang W, Ding W, Cao M, et al. Sex differences in resting-state cerebral activity alterations in internet gaming disorder. Brain Imaging Behav 2019;13:1406-1417.
42. Lin X, Jia X, Zang YF, Dong G. Frequency-dependent changes in the amplitude of low-frequency fluctuations in internet gaming disorder. Front Psychol 2015;6:1471.
43. Horvath J, Mundinger C, Schmitgen MM, Wolf ND, Sambataro F, Hirjak D, et al. Structural and functional correlates of smartphone addiction. Addict Behav 2020;105:106334.
44. Zhang JT, Yao YW, Potenza MN, Xia CC, Lan J, Liu L, et al. Altered resting-state neural activity and changes following a craving behavioral intervention for internet gaming disorder. Sci Rep 2016;6:28109.
45. Yuan K, Yu D, Cai C, Feng D, Li Y, Bi Y, et al. Frontostriatal circuits, resting state functional connectivity and cognitive control in internet gaming disorder. Addict Biol 2017;22:813-822.
46. Wang Y, Qin Y, Li H, Yao D, Sun B, Li Z, et al. Abnormal functional connectivity in cognitive control network, default mode network, and visual attention network in internet addiction: a resting-state fMRI study. Front Neurol 2019;10:1006.
47. Wang Y, Qin Y, Li H, Yao D, Sun B, Gong J, et al. Identifying internet addiction and evaluating the efficacy of treatment based on functional connectivity density: a machine learning study. Front Neurosci 2021;15: 665578.
48. Wang Y, Qin Y, Li H, Yao D, Sun B, Li Z, et al. The modulation of reward and habit systems by acupuncture in adolescents with internet addiction. Neural Plast 2020;2020:7409417.
49. Weinstein AM. An update overview on brain imaging studies of internet gaming disorder. Front Psychiatry 2017;8:185.
50. Volkow ND, Wang GJ, Fowler JS, Tomasi D, Telang F, Baler R. Addiction: decreased reward sensitivity and increased expectation sensitivity conspire to overwhelm the brain's control circuit. Bioessays 2010;32: 748-755.
51. Lorenz RC, Krüger JK, Neumann B, Schott BH, Kaufmann C, Heinz A, et al. Cue reactivity and its inhibition in pathological computer game players. Addict Biol 2013;18:134-146.
52. Dong G, Huang J, Du X. Enhanced reward sensitivity and decreased loss sensitivity in internet addicts: an fMRI study during a guessing task. J Psychiatr Res 2011;45:1525-1529.
53. Kim H, Kim YK, Lee JY, Choi AR, Kim DJ, Choi JS. Hypometabolism and altered metabolic connectivity in patients with internet gaming disorder and alcohol use disorder. Prog Neuropsychopharmacol Biol Psychiatry 2019;95:109680.
54. Kim SH, Baik SH, Park CS, Kim SJ, Choi SW, Kim SE. Reduced striatal dopamine D2 receptors in people with internet addiction. Neuroreport 2011;22:407-411.
55. Zhang JT, Yao YW, Li CS, Zang YF, Shen ZJ, Liu L, et al. Altered resting-state functional connectivity of the insula in young adults with internet gaming disorder. Addict Biol 2016;21:743-751.