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META-ANALYSIS



Neural mechanisms of behavioral addiction: An ALE meta-analysis and MACM analysis

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ABSTRACT

Background and aims: Behavioral addictions (BAs) represent complex and multifaceted disorders often associated with maladaptive neural alteration. To deepen our understanding of the essence of BAs, this study focuses on the neural mechanisms underlying its three stages: reward seeking, self-control, and decision-making. The aim of the current meta-analysis is to investigate the brain regions and neural networks involved in BAs. **Methods:** Adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we systematically searched for relevant articles published before September 1, 2024, in the Web of Science and PubMed databases, and supplemented our search with Google Scholar. We conducted analyses using activation likelihood estimation (ALE) meta-analysis and meta-analytic connectivity modeling (MACM) analyses. **Results:** A total of 50 functional magnetic resonance imaging studies involving 906 participants were included. The findings showed that individuals with BAs exhibited hyperactivation in the right inferior frontal gyrus (IFG), bilateral caudate and left middle frontal gyrus (MFG), and a high degree of connectivity was found between the right caudate, left caudate, and right IFG. These findings indicated that BAs were associated with the fronto-striatal circuits. Individuals with BAs demonstrate specific neural activation patterns in the reward seeking, self-control, and decision-making stages, characterized by differences in activation and functional connectivity of brain regions associated with these stages. **Discussion and conclusions:** This study verifies the pivotal role of the fronto-striatal circuits in BAs and highlights the specific patterns of brain activity in different stages of addictive behavior. These findings expand our understanding of neural mechanisms underlying BAs and supports and provide partial support for the I-PACE model.

KEYWORDS

behavioral addiction, activation likelihood estimation, meta-analytic connectivity modeling

INTRODUCTION

Behavioral Addictions (BAs) are defined as the condition in which an individual experiences an intense and uncontrollable urge for a particular behavior, persisting in engaging in this behavior despite being cognizant of potential adverse outcomes to their psychological and social functioning (Grant, Potenza, Weinstein, & Gorelick, 2010; Mei et al., 2024). These addictions primarily include gambling disorder (GD) which was included in the fifth revision of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), internet gaming

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disorder (IGD) with Gaming Disorder being the official term according to the WHO and recognized as an emerging condition in DSM-5 (American Psychiatric Association, 2013), and other type of BAs with insufficient evidence and criteria, such as buying-shopping disorder (BSD), and problematic pornography use (PPU) (Starcke, Antons, Trotzke, & Brand, 2018). In recent years, BAs have increasingly emerged as a prominent public health concern. Globally, it is reported that around 5% of the population suffers from IGD using the American Psychiatric Association (APA) framework (Pontes, Schivinski, Kannen, & Montag, 2022), 0.1%–6% suffer from gambling disorder (Calado & Griffiths, 2016), and 3%–7% suffer from compulsive shopping (Maraz, Griffiths, & Demetrovics, 2016). Additionally, an increasing number of individuals with BAs have comorbid mental disorders, such as attention-deficit/hyperactivity disorder (ADHD) (Michael & Seymour, 2023; Wang, Yin, Wang, King, & Rost, 2024; Wartberg, Kriston, Zieglmeier, Lincoln, & Kammerl, 2019) or depression and anxiety disorders (Qu et al., 2024; Teng, Pontes, Nie, Griffiths, & Guo, 2021). Despite the development of various treatment interventions, clinical treatment outcomes for BAs still require further improvement. BAs are complex and multifaceted, influenced by various factors including neurobiology, environment, cognition, genetics, among others. Therefore, it is essential to investigate the cognitive neural mechanisms of BAs to further understand their nature and provide theoretical support for improving personalized treatment strategies and enhancing intervention effectiveness.

Due to potential similarities between BAs and substance use disorders (SUDs), some studies have applied research methods from SUDs to BAs research, leading to some overlapping observations. Individuals with BAs exhibit typical addictive symptoms, such as intense craving for a certain stimulus (Limbrick-Oldfield et al., 2017), difficulty controlling their behavior (Ioannidis et al., 2019), and excessive engagement despite negative consequences (Dong, Hu, & Lin, 2013). Similarly, BAs are also associated with the maladaptive neural modulation in the frontal cortex and the limbic system. Compared to non-addicted individuals, those with BAs show reduced gray matter (GM) in the left anterior cingulate cortex (extending to the left medial superior frontal gyrus and bilateral orbitofrontal gyrus), right putamen and right supplementary motor area (Qin et al., 2020), along with increased activation in the midcingulate cortex (Le, Potvin, Zhornitsky, & Li, 2021). Moreover, functional connectivity between the frontoparietal network (FPN) and the affective network (AN) is enhanced, while connectivity between the FPN, salience network (SN), and default mode network (DMN) is decreased in individuals with BAs (Zeng, Han, Zheng, Jiang, & Yuan, 2023). Previous neuroimaging studies and meta-analyses have primarily concentrated on specific types of BAs, and the results of these studies have suggested that the brain regions exhibiting abnormal activity among various types of BAs are not entirely consistent (Quaglieri et al., 2020; Zheng et al., 2019). Consequently, the question of whether these different BAs share a common

neural basis remains unresolved. To clarify this issue, it is essential to perform a comprehensive meta-analysis of existing neuroimaging studies. This analysis aims to identify most crucial neural changes in individuals with BAs.

While existing studies have investigated brain regions involved in abnormal activation among individuals with BAs, the role of irregular activation at different stages of addictive behavior remains uncertain. Brand, Young, Laier, Woelfling, and Potenza (2016) proposed the Interaction of Person-Affect-Cognition-Execution (I-PACE) model based on relevant theories and empirical findings of BAs. Initially designed to explain the development and maintenance of internet use disorders (formerly known as Internet addiction), this model has been expanded by Brand et al. to incorporate gambling, gaming, shopping, and compulsive behaviors, broadening the explanatory scope of the I-PACE model to include BAs. According to this model, the development of addictive behaviors results from the interplay of emotional and cognitive responses (such as craving) to specific stimuli, impaired self-control, and adverse decision-making (Brand et al., 2019). In more detail, the motivations associated with seeking rewards and alleviating stress, the behavioral control related to executive inhibition, and the decision-making process that involves weighing the pros and cons of motivated behaviors are also key factors influencing individual addictive behavior (Dong & Potenza, 2014). In addition, this model helps us understand how addictive behaviors develop. Specifically, addicted individuals are stimulated by external or internal cues related to the addictive stimulus, generating motivation to obtain pleasure or alleviate stress and discomfort, and exhibiting craving for the addictive stimulus. Subsequently, as self-control starts to take effect, individuals regulate their desires and cravings for the addictive stimulus through self-control. However, self-control is lowered in BAs. When such individuals arrive at the decision-making stage, deciding whether to engage in a particular addictive behavior, it is difficult for those with BAs to achieve a balance between immediate rewards and long-term adverse consequences. Consequently, the occurrence of individual addictive behaviors can be divided into three distinct stages: reward seeking, self-control, and decision-making.

Reward seeking

In reward seeking, individuals experience a strong craving for the addictive stimulus. Through operant conditioning, various addiction-related cues become associated with the rewarding properties of pleasure or relief from stress and discomfort. This association leads to significant activation of the dopamine system (Pollard et al., 2023). As the frequency of conditioned cues triggering conditioned emotional/motivational responses (i.e., cue reactivity) increases, the individual's neural system gradually sensitizes. This sensitization makes addiction-related cues more salient and further leads to manifesting of craving for the addictive stimulus (Robinson & Berridge, 1993, 2008). Research often employs cue reactivity paradigms to investigate the excessive attention

paid by individuals with BAs towards addiction-related cues (Starcke et al., 2018).

Research on relevant neural mechanisms suggest a close association between addiction-related cues and activation of specific brain regions in the prefrontal cortex (PFC), parietal cortex, and limbic system of individuals with addiction. A meta-analysis indicated significant hyperactivation of the bilateral anterior cingulate cortex (ACC) and bilateral precuneus, while the insula showed significant hypoactivation in IGD during cue-reactivity tasks (Zheng et al., 2019), accompanied by stronger connectivity between the dorsal striatum and medial frontal gyrus in IGD (Dong, Dong, et al., 2021). Research by Schmitgen et al. (2020) suggested that problematic smartphone users exhibit greater activation in the medial prefrontal cortex (MPFC), occipital, temporal, and ACC, specifically in temporoparietal regions, and cerebellum compared to healthy controls (HC). However, current findings at the moment are overall inconclusive (Montag & Becker, 2023). A study on buying-shopping disorder showed hyperactivation in the extrastriate cortex region specifically when facing shopping-related cues (Trotzke, Starcke, Pedersen, & Brand, 2021).

Brain abnormalities among individuals with BAs are also observable at the network level. For instance, in cue-reactivity tasks, those with GD showed enhanced functional connectivity between the nucleus accumbens and left mid-insula (Limbrick-Oldfield et al., 2017). Furthermore, Ma et al. (2019) identified abnormalities in the temporo-occipital, temporal-insular, frontal-parietal networks, and dorsal limbic network among individuals with IGD. These findings underscore the critical role played by the PFC, parietal cortex, and limbic system during the reward seeking phase of addiction.

Self-control

In self-control, the individual's inhibitory control plays a primary role. This is shown as the ability to restrain desires and manage the extent of engaging in reward seeking behaviors (Dong & Potenza, 2014). In essence, atypically altered inhibitory control is a hallmark of addiction. Existing research suggests that deficits in inhibitory control among addicts lead to difficulties in regulating their addictive-related behaviors (Kräplin et al., 2020). Compared to HC, individuals with BAs performed worse on inhibitory control tasks such as Stroop and Go/No-Go tasks (Chen et al., 2021; Yan, Chen, Liu, & Zheng, 2021). At the neural level, the impaired inhibitory control in BAs primarily occurs in the frontal lobe. Qin et al. (2020) found that the severity of BAs was positively associated with decreases in gray matter (GM) in the left ACC and right supplementary motor area (SMA). Abnormalities in BAs are also reflected in brain region activity. Compared to HC, individuals with IGDs were significantly hyperactive in the left superior medial frontal gyrus, right ACC, right superior/middle frontal gyrus, left inferior parietal lobule (IPL), left precentral gyrus, and left precuneus and cuneus (Ding et al., 2014). Likewise, the individuals with PPU showed hypoactivation in the right

IFG (Seok & Sohn, 2020). Furthermore, those with GD also exhibited abnormalities in prefrontal regions, specifically increased activation in the dorsolateral prefrontal cortex (dlPFC) and decreased activation in the ventromedial prefrontal cortex (vmPFC) (de Ruiter, Oosterlaan, Veltman, van den Brink, & Goudriaan, 2012). Moreover, abnormal activity in brain regions associated with cognitive control—particularly the IFG, ACC, and primary motor cortex—is also correlated with the severity of addiction among individuals (Wang, Yang, Zheng, Li, Qi, et al., 2021).

Furthermore, BAs shows abnormal connectivity between brain regions. Previous work found that, compared to HCs, individuals with PPU had decreased functional connectivity between the IFG and pre-supplementary motor area (pre-SMA) during inhibitory control tasks (Seok & Sohn, 2020). Individuals with IGD also exhibited lower functional connectivity within the executive control network compared to HCs (Dong, Lin, & Potenza, 2015). Another study based on functional brain connectivity in IGD patients showed significantly increased functional connectivity between the left midline nucleus (MN) and right postcentral gyrus, as well as between the pulvinar and medial frontal gyrus. Inhibitory control scores were negatively correlated with functional connectivity between the left MN and postcentral gyrus (Zhou et al., 2021). These results indicate that impaired self-control in individuals with BAs is closely associated with abnormal activation in prefrontal regions and disrupted functional connectivity between different prefrontal areas.

Decision-making

Individuals with BAs exhibit less consideration of negative consequences when making decisions. Moreover, when making decisions between participating in instant rewards (e.g. playing game) and long-term return (e.g. using the time spent on games to perform activities related to long-term career success), addicted individuals tend to choose instant rewards (Miedl et al., 2015; Wang et al., 2017). In previous research the decision-making processes of addicted individuals were investigated using risk decision paradigms, which typically provide subjects with feedback on wins and losses through simulated real-world guessing and gambling tasks (Zheng et al., 2019). Neurobiological studies have found that during decision-making, BAs primarily activate the striatum and frontal lobe regions. Compared to HCs, problematic internet users were more inclined to take risks for high rewards and exhibit stronger activation in the striatum (including the nucleus accumbens and caudate) (Wang, Yang, Zheng, Li, Wei, et al., 2021). Similarly, individuals with PPU exhibited increased activation in the ventral striatum when predicting rewards associated with their addiction (Gola et al., 2017). Gamblers showed greater activity in the ventral striatum, vmPFC and dlPFC and ACC when faced with rewards (Schmidt et al., 2021), and exhibited decreased activation in the right striatum and medial prefrontal cortex when facing losses (Romanczuk-Seifert, Koehler, Dreesen, Wüstenberg, & Heinz, 2015).



These findings suggest that increased sensitivity to rewards and reduced sensitivity to losses in individuals with BAs are linked to abnormal activation in the striatal and prefrontal regions.

At the level of brain networks, research has found that internet gaming addicts exhibited higher task-related activity in the DMN and less engagement in the executive control network (ECN) during delay discounting tasks (Wang et al., 2016). Zhang, Zheng, Zhou, and Dong (2023) found that individuals with IGD exhibited increased effective connectivity between the orbitofrontal cortex (OFC) and dlPFC/OFC, as well as between the OFC and occipital lobe when faced with difficult choices. Conversely, they showed decreased effective connectivity between the occipital lobe and OFC. Additionally, individuals with GD demonstrated abnormal increases in functional connectivity within the frontal-striatal regions (van Holst, Chase, & Clark, 2014). A resting-state fMRI study reported similar results. This study found that individuals with IGD had higher functional connectivity in the bilateral amygdala with the contralateral insula and functional connectivity between the left amygdala and dlPFC was negatively correlated with impulsivity (Ko et al., 2015). These findings suggest that impulsive decision-making in individuals with BAs is closely related to abnormal connectivity between subjective evaluation systems and executive control systems.

Previous functional magnetic resonance imaging (fMRI) studies on BAs have provided preliminary evidence on brain regions involved in the stages of reward seeking, self-control, and decision-making in BAs. However, the shared brain regions and functional connectivity anomalies across different stages, as well as the stage-specific characteristics, remain unclear. Furthermore, previous studies have faced limitations such as small sample sizes and inconsistent experiment paradigms, which may have influenced their outcomes due to factors like sample characteristics and research methodologies. Therefore, a meta-analysis is necessary to elucidate the shared and specific neural mechanisms across the stages of reward seeking, inhibitory control, and decision-making in BAs. This study aims to explore the neural mechanisms of BAs from the perspective of the individual addiction process, thereby enhancing our understanding of the underlying neurobiology of BAs.

Activation Likelihood Estimation (ALE) is one of the most commonly used meta-analytic methods in the field of neuroimaging. The basic principle of ALE is to compute the likelihood of activation for each voxel in each experiment under a certain condition and then perform statistical analysis on it (Chein, Fissell, Jacobs, & Fiez, 2002). Using activation likelihood as an indicator, the ALE method calculates the likelihood of activation across experiments for each voxel and conducts hypothesis testing on this likelihood, thereby obtaining consistency in brain activation across multiple experiments (Turkeltaub et al., 2012). Meta-Analytic Connectivity Modeling (MACM) is an extension of Activation Likelihood Estimation (ALE). This method enhances ALE results by revealing significant co-activations across all experiments that activate specific seed regions,

allowing for a comprehensive evaluation of the functional connectivity patterns associated with these seed areas (Krall et al., 2015). By doing so, we can broaden our understanding of the reliable functional connectivity patterns in brain regions related to BAs. It provides deeper insights into the neural mechanisms underlying this condition.

This study employed ALE to explore the neural mechanisms of BAs from the perspective of brain activation and functional connectivity, investigating brain activity characteristics across different stages of addiction and comparing these features. Additionally, to further elucidate the connectivity among regions associated with BAs, seed regions will be defined from ALE analysis, and MACM analysis will be utilized to examine the patterns of co-activation of regions engaged in BAs.

Based on previous research findings, we propose the following hypotheses: (1) Compared to HCs, individuals with BAs exhibit hyperactivation in the PFC and limbic system regions. (2) There are shared brain regions across the three stages of BAs, such as hyperactivation observed in the PFC region in all three stages. (3) Different stages have specific neural activation patterns, manifested by differences in activation and functional connectivity of brain regions associated with stage-specific features.

METHODS

Literature search

The Web of Science and PubMed databases were systematically reviewed for relevant articles published in English before September 1, 2024, and Google Scholar was used to supplement our search. The keywords were set as (“gambling disorder” or “pathological gambling” or “gambling” or “virtual addiction” or “smartphone addiction” or “problematic smartphone use” or “problematic hypersexual behavior” or “problematic pornography use” or “internet addiction” or “problematic Internet use” or “internet gaming disorder” or “shopping” or “pathological use”) and (“fMRI” or “neuroimaging” or “functional magnetic resonance imaging”). A total of 2,147 articles were retrieved. One researcher assessed the quality of the included studies and reassessed the included studies three months later. Once the articles had been preliminarily included, another researcher conducted a quality check on them. Following this, two researchers independently extracted and coded the data, which then underwent cross-validation. In cases of disagreement, a third party resolved the issue, or the matter was discussed within the group. The extracted data included study characteristics (author and publication year), participant information (age and sample size), task performance (referring to the task paradigm), and imaging results (spatial coordinates of peak and the standard space template). This process adhered to the literature selection methods recommended by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Study selection

The inclusion criteria for the studies were as follows: (1) Studies examining the potentially addictive behaviors in the area of internet use, smartphone use, gaming, shopping, pornography-related items, gambling; (2) The study was empirical, peer-reviewed, and published in an English-language journal; (3) The study compared BAs with HC; (4) The study conducted whole-brain analysis of task based fMRI results for tasks and reported using either standard Montreal Neurological Institute (MNI) or Talairach coordinates. (5) Participants of all ages and genders were included.

Studies were excluded if they met any of the following criteria: (1) Protocols, abstracts, reviews, or case reports; (2) Duplicate articles or overlapping subjects; (3) Studies unrelated to BAs; (4) Studies focused on structural imaging, resting-state or brain functional connectivity; (5) studies that concentrated on regions of interest (ROI) analysis; (6) data could not be extracted, for instance, when the coordinates for BA > HC were not explicitly reported, or when the coordinate space used was not clearly specified. Additionally, due to the absence of co-activated clusters in BA < HC during preprocessing, only activation points with BA > HC were retained for specific analysis. For detailed screening processes and results, see Fig. 1.

We excluded eating/food disorder in the research for the following reasons: Firstly, eating/food disorder involves the consumption of food, which is a main difference to the other behavioral addictions. Behavioral addiction reflects dependence on a behavior or feeling brought about by an action, as opposed to a substance (Alavi et al., 2012), while food addiction clearly involves food intake. Secondly, eating/food disorder is a separate diagnostic category I in both DSM-5 and ICD-11.

Hoarding disorder was also excluded. Hoarding disorder is listed in the subcategory of obsessive-compulsive disorders in both DSM-5 and ICD-11. It is also a separate diagnostic category. Therefore, it was not included in this study.

Criteria for paradigm classification

According to the I-PACE model and the stages of BAs development, we categorized fMRI studies into three types. (1) Reward Seeking: Studies included in this category measured neural activity in individuals with BAs using cue-reactivity tasks, with cues containing both addiction-related and neutral stimuli. (2) Self-Control: Studies included in this category measured neural activity in individuals with BAs using inhibition control paradigms, including go/no-go tasks, Stroop tasks, and Stop Signal Tasks (SST). (3) Decision-making Stage: Studies included in this category measured decision-related neural activity in individuals with BAs using risk decision-making paradigms, including guessing tasks, risky decision tasks, delay discounting tasks, Wisconsin Card Sorting Test (WCST), odd-even pass tasks, cup tasks, and gambling tasks.

Activation likelihood estimation

In the current study, the meta-analysis was conducted by using GingerALE 3.0.2 (<http://brainmap.org/ale>) (Eickhoff et al., 2009; Turkeltaub et al., 2012) as the tool for coordinate-based meta-analysis. Prior to data analysis, it was necessary to extract the coordinates of reported activation enhancements from the literature included in the meta-analysis, namely, extracting coordinates where differences exist between individuals with BAs and HCs. Since the meta-analysis was conducted in the Montreal Neurological Institute (MNI) standard space, coordinates reported in

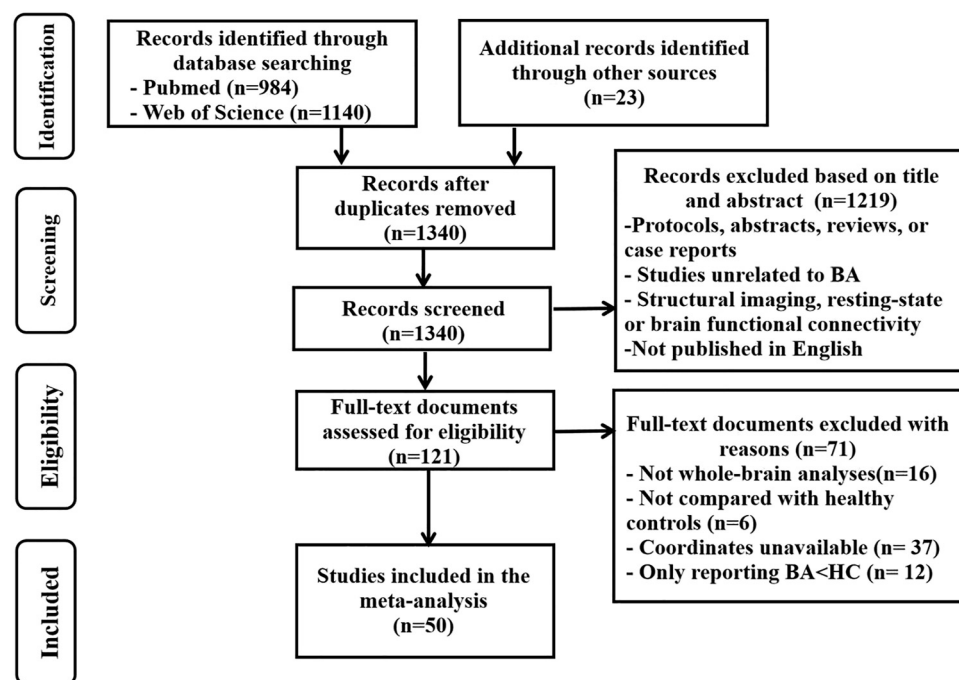


Fig. 1. Flow diagram of the literature search used in this meta-analysis

Talairach space were transformed into MNI standard space using the conversion tool provided in the software.

Meta-analyses were initially conducted on individuals with BAs and HC. Subsequently, subgroup analyses were performed on three stages, creating distinct ALE maps for each domain of interest, acquiring activation regions for reward seeking, self-control, and decision-making. According to previous work (Gou et al., 2023), a significance threshold of uncorrected $p < 0.001$ was employed to control for type I error, with a minimum volume set at 250 mm^3 , which had been proved to be reliable (Sulpizio, Del Maschio, Fedeli, & Abutalebi, 2020; Yuan et al., 2022). Results were reported using Mango (<http://ric.Uthscsa.edu/mango/>) and Brainnet Viewer (Xia, Wang, & He, 2013).

In addition, a jackknife sensitivity analyses was performed to test robustness of the results by removing one dataset at a time. Specifically, we excluded one study at a time and conducted repeated meta-analyses on the remaining data (Yuan et al., 2022). This approach supports the robustness of our findings, ensuring that results are not unduly influenced by any single study (Eickhoff et al., 2016). This method has also been employed in prior research to demonstrate reliability of the results (Yuan et al., 2022; Zeng, Han, Zheng, Jiang, & Yuan, 2023).

Contrast and conjunction analyses

The ALE method was also employed to statistically compare ALE maps obtained by the single meta-analyses. We conducted three discriminability analyses to ascertain whether differences exist in brain activation between each stage and the others. Each analysis yielded brain regions that are specifically activated for reward seeking, self-control, and decision-making stages.

Based on previous studies (Cona, Santacesaria, & Scarpazza, 2023), this research amalgamated coordinates from each pair of the three stages' activation coordinates. We obtained the ALE maps by the single meta-analyses, and contrasted the ALE map of the three stages with each other, to understand whether there are shared and specific brain regions in the three stages. Specifically, ALE maps for reward seeking were contrasted with those derived from the consistency analysis of self-control and decision-making activations (Reward seeking > Self-control + Decision-making). Self-control ALE maps were compared with those derived from reward seeking and decision-making (Self-control > Reward seeking + Decision-making). Decision-making ALE maps were contrasted with those derived from reward seeking and combined coordinates of self-control (Decision-making > Reward seeking + Self-control). Following recommendations from the ALE manual, the parameters were set at uncorrected $p < 0.01$ and a minimum cluster size greater than 200 mm^3 (10,000 permutations) (Gavazzi et al., 2023) for contrast and conjunction analyses in this study. In addition, to investigate the impact of participants' age on the results, we conducted subgroup analyses for adults (aged 18 and older) and adolescents (aged less than 18).

MACM analyses

To further explore the neural circuits of the three stages, the present study employed a brain connectivity meta-analysis model to identify coactivation patterns across the three stages. Brain area characteristics related to BAs, reward seeking, self-control, and decision-making were identified at the brain network level using BrainMap's Sleuth 3.0.4 (<http://brainmap.org/sleuth>) software and GingerALE 3.0.2 (<http://brainmap.org/ale>). Firstly, regions of interest (ROIs) with a radius of 12 mm were created based on the results of meta-analysis and subgroup analysis: four ROIs were defined for BAs, five ROIs for reward seeking, two ROIs for self-control, and five ROIs for risk decision-making.

Region-specific functional connectivity was applied by utilizing the feature database of the BrainMap Sleuth 3.0.4 software. Following recommendations from prior studies (Huang, Huang, Li, Lin, & Zou, 2023) and the Ginger ALE manual, the following search terms were employed: (i) "Locations: Rectangular ROIs" for defining corresponding ROIs in MNI space, (ii) "Experiments: Activations, Activations only", (iii) "Experiments: Context, Normal Mapping". Upon searching each pre-defined ROI based on the aforementioned criteria, experiment coordinates meeting the criteria were automatically exported as a text file and transformed into MNI space. Subsequently, GingerALE was employed for meta-analysis of the activated coordinates, with parameters set at uncorrected $p < 0.001$ and minimum volume set to 250 mm^3 .

Network modeling for MACM analysis was conducted using methods consistent with prior research (Huang et al., 2023; Kotkowski, Price, Fox, Vanasse, & Fox, 2018; Meier, Ray, Mastan, Salvage, & Robin, 2021). To summarize this procedure, Mango was used to visualize the uncorrected MACM overlay for each seed coordinate on an MNI template (Colin27_T1_seg_MNI.nii). The uncorrected p -values for meta-analytic connectivity were extracted and recorded for each seed region and all other specified nodes.

The p -values for multiple comparisons between nodes were corrected using a Bonferroni correction ($p = 0.05/\text{number of nodes}$). The corrected p -values represent the covariance statistics between nodes (i.e., each seed point used in MACM) and projections (i.e., connectivity between MACM seed points and other ROIs), which are used to generate edges in meta-analytic connectivity modeling. Connections between identified peak regions are mapped to display unidirectionality (arrows indicating unidirectional covariance), bidirectionality (darker edges indicating bidirectional covariance), or nodes with no significant connections to each other.

RESULTS

Characteristics of each study

In Table 1, we provide the main characteristics of each study.



Table 1. Summary of recent whole brain analysis task study of BAs

Classification	Task	Study	Addictive Behavior	Sample	Age (SD or range) years	Space
Reward seeking	Cue-reactivity task	Schmitgen et al. (2020)	SPA	SPA: 21 HC: 21	SPA: 22.57 (3.04) controls: 22.52 (3.01)	MNI
	Cue-reactivity task	Liu, Yip, et al. (2017)	IGD	IGD: 39 HC: 23	IGD: 22.64 (2.12) HC: 23.09 (2.13)	MNI
	Cue-reactivity task	Ko et al. (2009)	IGD	IGD: 10 HC: 10	IGD: 22.00 (1.49) HC: 22.70 (1.34)	Talairach
	Cue-reactivity task	Sun et al. (2012)	IGD	IGD: 10 HC: 10	IGD: 20.40 (1.506) HC: 20.30 (0.675)	Talairach
	Cue-reactivity task	Ko et al. (2013)	IGD	IGD: 15 HC: 15	IGD: 24.67 (3.11) HC: 24.47 (2.83)	Talairach
	Cue-reactivity task	Han, Hwang, and Renshaw (2010)	IGD	IGD: 10 HC: 10	IGD: 21.5 (5.6) HC: 20.3 (4.1)	Talairach
	Cue-reactivity task	Trotzke et al. (2021)	BSD	BSD: 18 HC: 18	BSD: 47.74 (8.62) HC: 49.67 (10.12)	MNI
	Cue-reactivity task	Zhang, Yao, et al. (2016)	IGD	IGD: 40 HC: 19	IGD: 21.95 (1.84) HC: 22.89 (2.23)	MNI
	Cue-reactivity task	Nasser et al. (2020)	PIGU	PIGU: 15 HC: 15	PIGU: 22.2 (0.86) HC: 21.67 (1.18)	MNI
	Cue-reactivity task	Seok and Sohn (2015)	PHB	PHB: 23 HC: 22	PHB: 26.3 (3.4) HC: 26.1 (4.1)	MNI
	Cue-reactivity task	Lorenz et al. (2013)	PCGPs	PCGPs: 8 HC: 9	PCGPs: 25 (7.4) HC: 24.8 (6.9)	MNI
	Cue-reactivity task	Goudriaan, De Ruiter, Van Den Brink, Oosterlaan, and Veltman. (2010)	PG	PG: 17 HC: 17	PG: 35.3 (9.4) HC: 34.7 (9.7)	MNI
	Cue-reactivity task	Crockford, Goodyear, Edwards, Quickfall, and El-Guebaly (2005)	PG	PG: 10 HC: 10	PG: 39.3 (7.6) HC: 39.2 (8.3)	Talairach
	Cue-reactivity task	Potenza et al. (2003)	PG	PG: 10 HC: 11	PG: 36.20 (11.95) HC: 30.09 (7.71)	Talairach
	Cue-reactivity task	Liu et al. (2016)	IGD	IGD: 19 HC: 19	IGD: 21.4 (1.0) HC: 20.8 (1.1)	Talairach
	Cue-reactivity task	Limbrick-Oldfield et al. (2017)	PG	PG: 20 HC: 22	PG: 31 (27–51) HC: 28 (25–52)	MNI
Self-control	The classical color–word Stroop task	Shen, Li, Sheng, Zhou, and Wang (2023)	PMVG	PMVG: 28 HC: 30	20.71 (1.71)	MNI
	The classical color–word Stroop task	Dong et al. (2014)	IA	IA: 15 HC: 15	IA: 21.2 (3.2) HC: 22.1 (3.6)	MNI
	The classical color–word Stroop task	Dong et al. (2013)	IA	IA: 15 HC: 15	IA: 23.8 (3.7) HC: 24.1 (3.3)	MNI
	The classical color–word Stroop task	Dong, DeVito, Du, and Cui (2012)	IA	IA: 12 HC: 12	IA: 23.6 (3.5) HC: 24.2, (3.1)	Talairach
	Stroop Match-to-Sample task.	Lee et al. (2015)	IGD	IGD: 18 HC: 18	IGD: 13.6 (0.9) HC: 13.4 (1.0)	MNI
	Addiction Stroop task	Zhang, Lin, et al. (2016)	IGD	IGD: 19 HC: 21	IGD: 22.2 (3.1) HC: 22.8 (2.4)	MNI
	Go/No go	Ko et al. (2014)	IGD	IGD: 26 HC: 23	IGD: 22.2 (3.08) HC: 22.8 (3.6)	MNI
	Go/No go	Ding et al. (2014)	IGD	IGD: 17 HC: 17	IGD: 16.41 (3.20) HC: 16.29 (2.95)	MNI
Decision-making	Incentive Delay Task	Gola et al. (2017)	PPU	PPU: 28 Control Sub: 24	PPU: 30.49 (7.55) Control Sub: 30.96 (6.51)	MNI
	Monetary Incentive Delay task	Schmidt et al. (2021)	GD	GD: 25 HC: 28	GD: 26.8 (5.8) HC: 27.9 (9.3)	MNI
	Roulette task	Wang, Yang, Zheng, Li, Qi, et al. (2021)	IGD	IGD: 27 HC: 26	IGD: 27.9 (9.3) HC: 26.8 (5.8)	MNI

(continued)

Table 1. Continued

Classification	Task	Study	Addictive Behavior	Sample	Age (SD or range) years	Space
Other	The cups task	Liu, Xue, et al. (2017)	IGD	IGD: 41 HC: 27	IGD: 21.93 (1.88) HC: 22.74 (2.35)	MNI
	Card-Deck paradigm	Brevers et al. (2015)	GD	GD: 10 HC: 10	GD: 36.20 (12.95) HC: 34.00 (8.53)	MNI
	Decision-making task	Dong et al. (2013)	IA	IA: 16 HC: 15	IA: 21.4 (3.1) HC: 22.1 (3.6)	MNI
	Reality-simulated guessing task	Dong, Huang, and Du (2011)	IA	IA: 14 HC: 13	IA: 23.4 (3.3) HC: 24.1 (3.2)	MNI
	Reality-simulated guessing task	Dong et al. (2013)	IA	IA: 16 HC: 15	IA: 21.4 (3.1) HC: 22.1 (3.6)	MNI
	Incentive delay task	Sescousse, Barbalat, Domenech, and Dreher (2013)	PG	PG: 18 HC: 20	PG: 34.1 (11.6) HC: 31 (7.3)	MNI
	Iowa Gambling Task	Power, Goodyear, and Crockford (2012)	PG	PG: 13 HC: 13	PG: 42.4 (10.8) HC: 41.0 (11.0)	MNI
	Monetary incentive task	Choi et al. (2012)	GD	GD: 15 HC: 15 OCD: 13	GD: 27.93 (3.59) HC: 26.60 (4.29)	MNI
	WCST	Han, Kim, Bae, Renshaw, and Anderson (2016)	IGD	IGD: 60 HC: 42	IGD: 20.2 (3.2) HC: 20.2 (2.9)	MNI
	Probability discounting	Lin, Zhou, Dong, and Du (2015)	IGD	IGD: 19 HC: 21	IGD: 22.2 (3.08) HC: 22.8 (3.5)	MNI
	Gambling task	Gelskov, Madsen, Ramsøy, and Siebner (2016)	PG	PG: 14 HC: 15	PG: 29.43 (6.05) HC: 29.87 (6.06)	MNI
	Slot machine task	Sescousse et al. (2016)	GD	GD: 22 HC: 22	GD: 35.7 (8.8) HC: 32.2 (11.1)	MNI
	Delay discounting and Probability discounting task	Miedl, Peters, and Büchel (2012)	PG	PG: 16 HC: 16	PG: 35 (2) HC: 38 (2)	MNI
	guessing task	Dong, Li, Wang and Potenza (2017)	IGD	IGD: 18 HC: 19	IGD: 21 (2.83) NFLGU: 21 (3.67)	MNI
	Two-stage task	Kwon, Choi, Park, Ahn, and Jung (2024)	IGD	IGD: 22 HC: 30	IGD: 23.73 (23.33, 24.13) HC: 22.6 (22.14, 23.06)	MNI
	a modified version of the 2-armed bandit task	Zuo et al. (2024)	IGD	IGD: 29 HC: 33	IGD: 21.62 (2.48) HC: 21.73 (2.13)	MNI
	Display words	Chun, Choi, Cho, Lee, and Kim (2015)	IGD	IGD: 16 HC: 19	IGD: 13.63 (1.03) HC: 13.37 (0.90)	MNI
	Self-concept task	Choi et al. (2018)	IGD	IGD: 12 HC: 15	IGD: 13.83 (2.69) HC: 15.33 (0.98)	MNI
	Self-retrieval paradigm	Leménager et al. (2016)	IGD	IGD: 19 HC: 19	IGD: 25.68 (6.69) HC: 27.68 (7.95)	MNI
	Simple and complex calculation tasks	Kim, Han, Lee, Kim, and Renshaw (2012)	IGD	IGD: 13 HC: 10	IGD: 14.5 (1.1) HC: 14.2 (1.3)	Talairach
	ball-throwing animation task	Kim, Son, et al. (2012)	IA	IA: 17 HC: 17	IA: 13.76 (0.83) HC: 13.76 (0.83)	Talairach
	a right–left discrimination test	Kim et al. (2014)	IA	IA: 15 HC: 15	IA: 13.87 (0.83) HC: 13.87 (0.83)	Talairach
	downregulation of negative emotions in a Cognitive Reappraisal Task	Navas et al. (2017)	GD	GD: 17 HC: 21	GD: 32.94 (7.77) HC: 31.00 (4.60)	MNI

Abbreviations: SPA = smartphone addiction; IGD = internet gaming disorder; BSD = buying-shopping disorder; PIGU = problematic Instagram use; PHB = problematic hypersexual behavior; PCGPs = pathological computer game players; PG = pathological gambler; PMVG = Problematic mobile video gaming; IA = internet addiction; PPU = problematic pornography use; GD = gambling disorder; HC = healthy control; WCST = Wisconsin Card Sorting Test.



Neural activations of behavioral addiction

The ALE meta-analysis was conducted on the peak activations of all selected articles to explore neural mechanisms of BAs. It comprised 50 experiments involving 906 participants and 401 foci. The results showed that across all studies, brain regions exhibiting increased activation intensity compared to HC included the bilateral caudate, right IFG (Brodmann area 9) and left MFG (Brodmann area 6) (Table 2, Fig. 2). The jackknife sensitivity analyses showed that most of the brain regions identified were highly reliable, and at least 47 out of the 50 dataset combinations were reproducible (see Table S1).

Subgroup analysis

To further elucidate the neural mechanisms of BAs, subgroup analyses were conducted on studies showing enhanced activation. These studies were categorized into three groups based

on stages of BAs - reward seeking, self-control, and decision-making - each subjected to univariate analysis. Furthermore, to explore the commonalities and specificities of activated brain regions across different stages of BAs, this study additionally conducted contrast and conjunction analyses on ALE maps for each stage.

Reward seeking

A meta-analysis was conducted for reward seeking, encompassing 181 foci from 12 experiments involving a total of 189 participants. The results indicated that, compared to HCs, BAs exhibited significant hyperactivation in the bilateral IFG (Brodmann area 9), right precuneus (Brodmann area 19), left MFG (Brodmann area 6), and left lingual gyrus (Brodmann area 19) during reward seeking (see Table 3, Fig. 3). Similar regions were found when contrasted with self-control and decision-making (see Table 3, Fig. 3).

Table 2. Results of general ALE meta-analysis on behavior addiction

Cluster	Volume	Brain regions	Hemisphere	Brodmann area	MNI coordinates			ALE ($\times 10^{-2}$)
					X	Y	Z	
1	1,320	Caudate	L	/	−8	14	−4	2.44
		Lentiform Nucleus	L	/	−8	4	−6	1.85
		Lentiform Nucleus	L	/	−10	0	2	1.59
2	1,288	Inferior Frontal Gyrus	R	9	58	10	22	2.73
		Middle Frontal Gyrus	R	9	46	16	26	1.84
3	552	Caudate	R	/	12	10	−2	1.73
4	488	Middle Frontal Gyrus	L	6	−18	−14	52	1.65

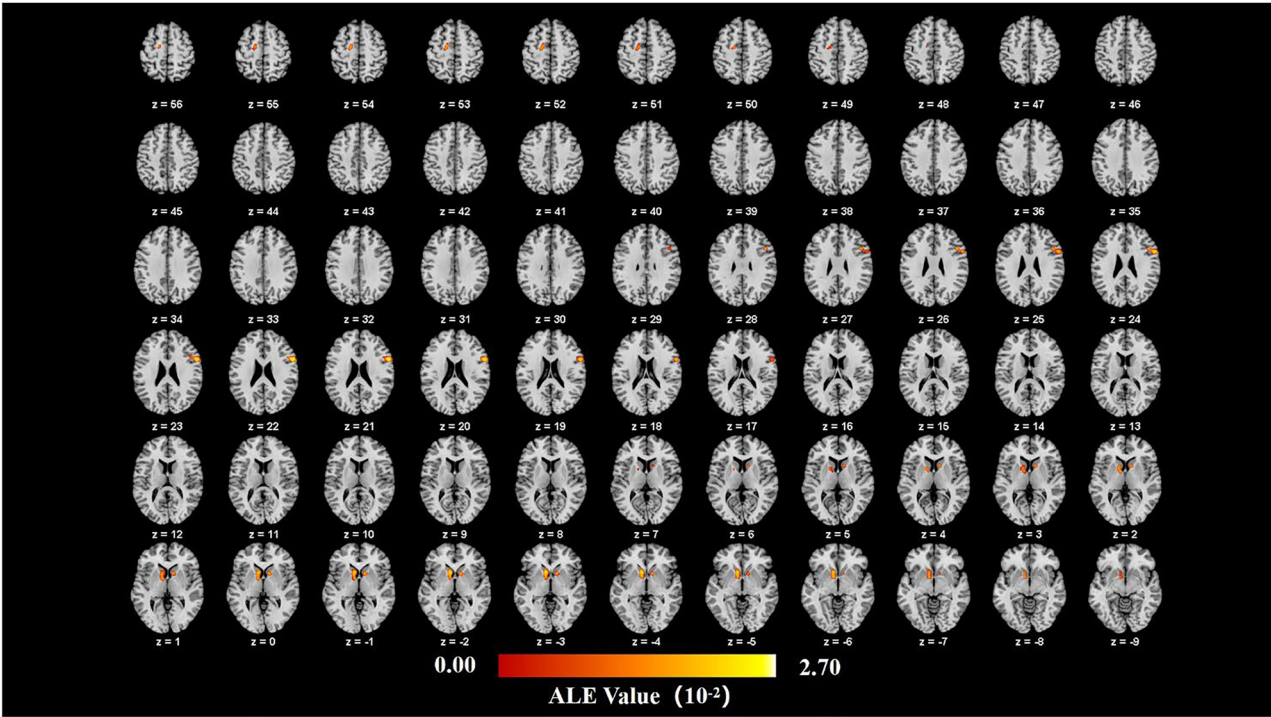


Fig. 2. Neural activations of BAs compared with HCs in all studies



Table 3. Locations of clusters of activation in each stage (BAs > HC)

Cluster	Volume	Brain regions	Hemisphere	Brodmann area	MNI coordinates			ALE ($\times 10^{-2}$)
					X	Y	Z	
Reward seeking								
1	1,352	Middle Frontal Gyrus	R	9	46	16	26	1.78
		Inferior Frontal Gyrus	R	44	52	16	14	1.06
2	472	Inferior Frontal Gyrus	L	9	−40	8	24	1.18
		Inferior Frontal Gyrus	L	9	−48	14	24	1.06
3	392	Precuneus	R	19	40	−80	40	1.65
4	336	Middle Frontal Gyrus	L	6	−50	6	40	1.18
5	264	Lingual Gyrus	L	19	−32	−70	−2	1.38
Reward seeking > Self-control + Decision-making								
1	936	Inferior Frontal Gyrus	R	45	52	18	14	
		Middle Frontal Gyrus	R	9	48	18	22	
		Inferior Frontal Gyrus	R	9	42	14	24	
		Middle Frontal Gyrus	R	9	46	19.5	26	
2	344	Inferior Frontal Gyrus	L	9	−42	12	26	
		Inferior Frontal Gyrus	L	9	−48.8	14.4	26	
Self-control								
1	528	Middle Frontal Gyrus	R	9	30	32	28	1.42
2	304	Medial Frontal Gyrus	L	6	−16	−12	54	0.98
Self-control > Reward seeking + Decision-making								
No activation								
Decision-making								
1	2,232	Caudate	L	/	−8	14	−4	2.44
			L	/	−8	4	−6	1.72
2	424	Middle Frontal Gyrus	R	6	34	22	50	1.48
3	392	Caudate	R	/	10	20	−8	1.13
			R	/	6	26	−2	1.07
4	384	Caudate	R	/	10	10	−2	1.26
5	264	Superior Frontal Gyrus	L	8	−6	46	42	1.15
Decision-making > Reward seeking + Self-control								
1	2,088	Caudate	L	/	−7.2	13.6	0.8	
		Caudate	L	/	−14	16	0	
		Caudate	L	/	−11.5	10	−3.5	
		Lentiform Nucleus	L	/	−11.3	4	−6.7	
		Caudate	L	/	−10	8.5	−4	
		Lentiform Nucleus	L	/	−6	2.7	−8	
Conjunction analysis								
No activation								

Self-control

The meta-analysis on self-control included 37 foci from 8 experiments, comprising a total of 152 participants. Results revealed significant hyperactivation in the right MFG (Brodmann area 9) and left medial frontal gyrus (Brodmann area 6) in individuals with BAs compared to HCs (see Table 3, Fig. 3). When contrasted with reward seeking and decision-making tasks, no specific regions were found to be activated (see Table 3, Fig. 3).

Decision-making

The meta-analysis of decision-making included 122 foci from 19 experiments, with a total of 401 participants. Results showed significant hyperactivation in the bilateral caudate, right MFG (Brodmann area 6) and left superior frontal gyrus (SFG) (Brodmann area 8) (see Table 3, Fig. 3). When compared to

reward seeking and self-control, hyperactivation was found in the caudate in decision-making (see Table 3, Fig. 3).

Conjunction analysis

In order to ascertain common activation regions among the reward seeking, self-control, and decision-making, we conducted a conjunction analysis of the individual ALE results from these three stages. The findings revealed no overlapping brain regions activated across the three stages (see Table 3).

Subgroup analysis based on age

The subgroup analyses based on age indicated that adults demonstrated hyperactivation in the bilateral caudate, right IFG, and left MFG. In contrast, adolescents showed hyperactivation in the left middle temporal gyrus (MTG), left postcentral gyrus, and left precentral gyrus (Table S2).



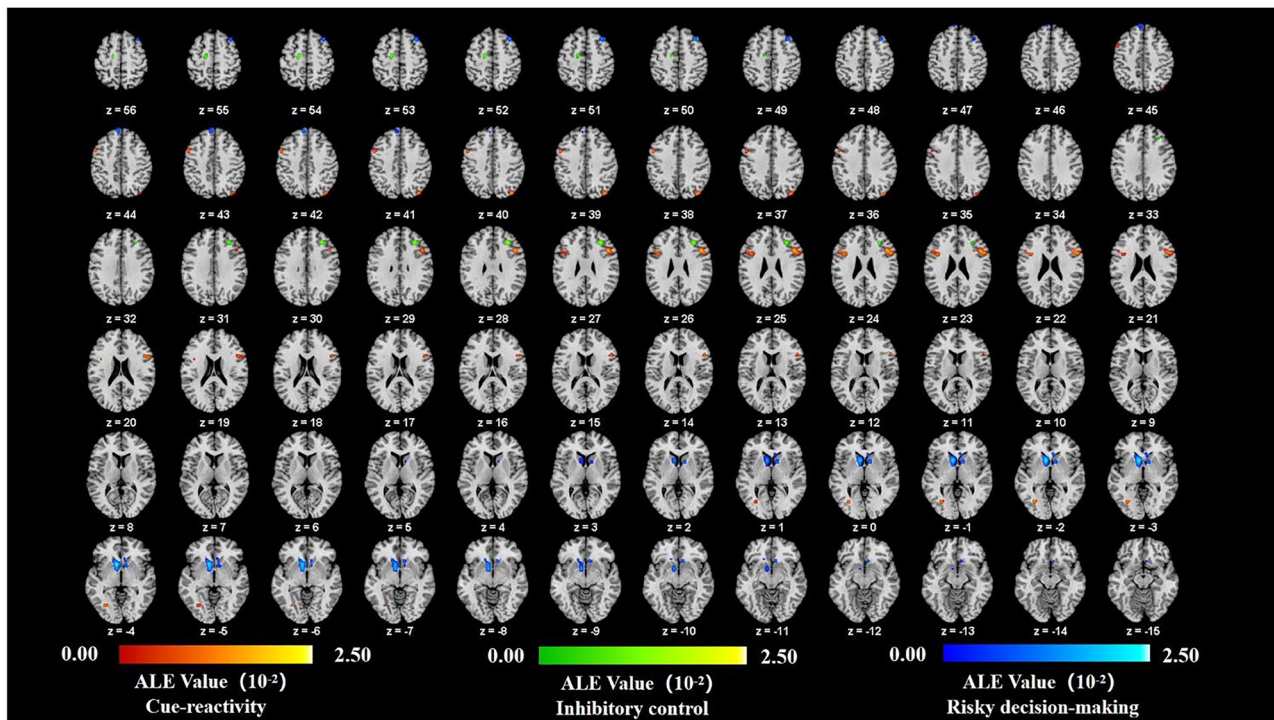


Fig. 3. Neural activations of three stages

MACM results

To further comprehend neural patterns of the three stages at the brain network level, we conducted MACM analysis on the extracted ROIs from ALE analyses of the reward seeking, self-control, and decision-making.

Neural network of behavioral addiction

From the ALE analysis of all studies, four regions of interest (ROIs) were extracted for MACM analysis. We found that significant bidirectional functional connectivity existed between the bilateral caudate and right caudate with the left IFG. Additionally, significant unidirectional functional connectivity was observed between the left caudate and right IFG. This was specifically evidenced by connections from the right caudate to right IFG and from the left caudate to right IFG (see Fig. 4).

Subgroup analysis

For reward seeking, five ROIs were extracted from the ALE analysis for further analysis. We found that significant bidirectional functional connectivity existed between the bilateral IFG, left MFG, and right IFG, as well as between the left and left IFG. Moreover, significant unidirectional functional connectivity was observed between the left lingual gyrus and left MFG, as well as between the left lingual gyrus and right IFG, specifically manifesting as connections from the left lingual gyrus to left MFG and right IFG (see Fig. 5). For self-control, two ROIs were extracted from the ALE analysis for MACM analysis, and no significant functional connectivity was found to exist (see Fig. 5). For

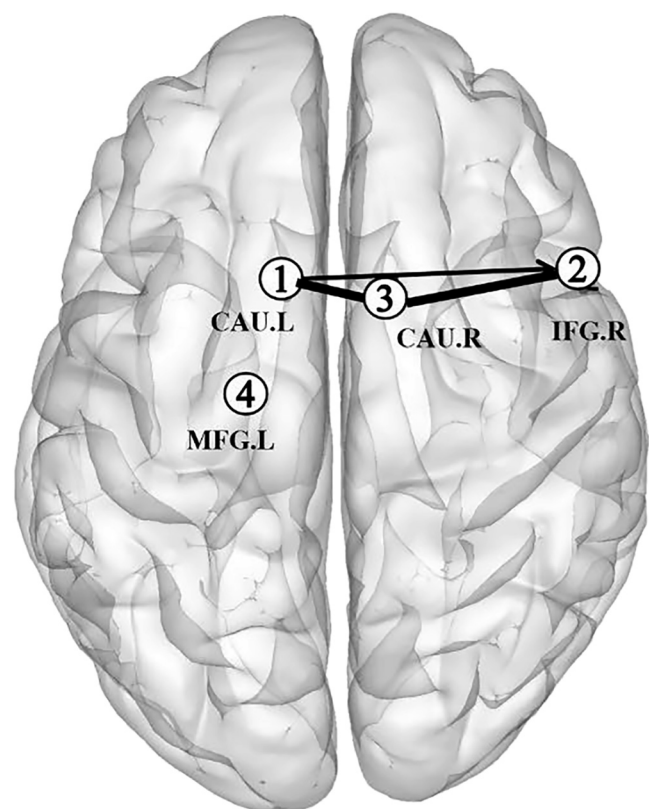


Fig. 4. Meta-analytic model of connectivity of BAs
Abbreviations: CAU.L = Left Caudate; IFG.R = Right Inferior Frontal Gyrus; CAU.R = Right Caudate; MFG.L = Left Middle Frontal Gyrus.

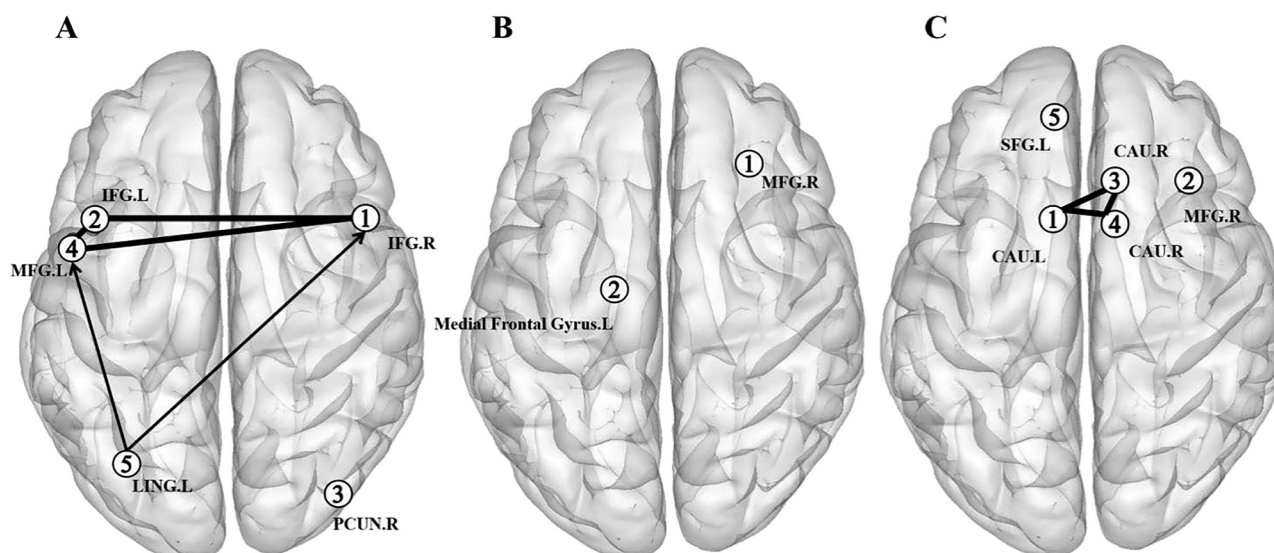


Fig. 5. Meta-analytic model of connectivity of reward seeking, self-control and decision-making

Abbreviations: IFG.R = Right Inferior Frontal Gyrus; IFG.L = Left Inferior Frontal Gyrus; PCUN.R = Right Precuneus; MFG.L = Left Middle Frontal Gyrus; LING.L = Left Lingual Gyrus; Medial Frontal Gyrus. L = Left Medial Frontal Gyrus; CAU.R = Right Caudate; CAU.L = Left Caudate; SFG.L = Left Superior Frontal Gyrus.

decision-making, five ROIs were extracted for analysis from the ALE analysis, revealing significant bidirectional functional connectivity between the bilateral caudate (see Fig. 5).

DISCUSSION

This study utilized ALE meta-analysis to investigate the neural mechanisms of BAs. The results found hyperactivation in the striatum and frontal regions of individuals with BAs. Furthermore, we analyzed the neural mechanism of different addiction stages and found that there were no shared brain regions across the three stages but rather specificity in activation patterns. Finally, based on the ALE results, this study explored the functional connectivity networks of brain regions implicated in BAs and their three stages.

Neural mechanism of behavioral addiction

In previous studies, the PFC, striatum, and other brain regions showed abnormalities in individuals with BAs (Le et al., 2021; Qin et al., 2020). Similar results were obtained in this study, where ALE analysis confirmed hyperactivation in the bilateral caudate, right IFG and left MFG among individuals with BAs. The caudate is part of the limbic system, associated with the reward system. Additionally, activation was found in the right IFG among individuals with BAs, consistent with previous research findings (Dong, Dong, et al., 2021; Luijten, Meerkerk, Franken, van de Wetering, & Schoenmakers, 2015; Yao et al., 2017). The IFG is part of the FPN, implicated in individual's executive control abilities (Osaka et al., 2004; Yao et al., 2017). This finding suggests

that anomalies in both the reward system and executive function system are potential neural mechanisms underlying BAs.

The I-PACE model was supported to a certain extent by our results. The I-PACE model posits that imbalances between the fronto-striatal circuits, particularly between the ventral striatum, amygdala, and dlPFC, are associated with the individual's process of BAs (Brand et al., 2019). Previous studies have indicated decreased functional connectivity between the orbitofrontal cortex and dorsolateral striatum in individuals with IGD compared with HC (Kim et al., 2019). The severity of addiction in IGD individuals is negatively correlated with functional connectivity between the striatum and prefrontal regions (Li et al., 2015). In our study, brain regions hyperactivated in BAs, identified through ALE, were subjected to MACM analysis. The results showed a high degree of connectivity between the right caudate, left caudate, and right IFG, supporting the significant role of the fronto-striatal circuits in BAs.

This study also provides evidence for similarities and specificities in the neurobiological mechanisms between SUDs and BAs. Our findings indicate that individuals with BAs and those diagnosed with SUDs share similarities in atypical brain regions. Previous studies have shown that individuals with SUDs exhibit abnormalities in the dorsal striatum, including the caudate and putamen as well as the prefrontal, limbic and insular cortex, including inferior, superior, and medial frontal regions as well as ACC and the anterior insula (Klugah-Brown et al., 2020). Additionally, a meta-analysis investigating aberrant brain regions in SUDs and IGD revealed common alterations in the prefrontal regions, specifically in the medial frontal gyrus spreading into the adjacent ACC and IFG (Klugah-Brown et al., 2021). In our study, we also observed hyperactivation in the prefrontal

regions. Combining the findings of previous studies, it can be inferred that the PFC, particularly the orbitofrontal region, may serve as a crucial brain area in addiction, which is associated with executive control abilities. This suggests that the fundamental cause of addictive behaviors may be attributed to impaired executive control abilities.

Although BAs and SUDs share common brain regions, their neurobiological mechanisms are not identical. In our study, no abnormal activation of the ACC was observed in individuals with BAs, in contrast to findings in SUDs research (Klugah-Brown et al., 2020, 2021; Zheng et al., 2019; Zheng et al., 2019). One possible explanation is that the activation pattern of the ACC may exhibit specificity across different types of BAs. While most studies in addiction have reported abnormalities in the ACC (Zhao et al., 2021), the specific activation pattern remains controversial. A meta-analysis investigating SUDs and BAs noted potential opposite activation patterns in the ventral and dorsal aspects of the ACC across these two addiction types (Hüpen, Habel, Votinov, Kable, & Wagels, 2023). A recent study also found that the activation patterns in the ACC differ between SUDs and BAs. SUDs showed reduced low-frequency fluctuation amplitude (ALFF), while BAs demonstrated increased ALFF in the ACC (Zheng et al., 2024). Furthermore, some studies on BAs did not find activation in the ACC (Trotzke et al., 2021). These findings suggest the need for further refinement of the functional regions within the ACC in future research to explore their roles in different types of addictive behaviors. Our study also found abnormalities only in the FPN and limbic network in BAs, which differs from previous research on substance addicts' abnormal brain networks (Taebi et al., 2022). This result reflects the specificity of BAs in terms of brain activation patterns compared to SUDs.

Reward seeking

In reward seeking, significant hyperactivation was observed in the precuneus of individuals with BAs, consistent with previous research findings (Dong, Wang, Du, & Potenza, 2017). The precuneus, located in the posterior medial part of the parietal lobe, is recognized as a critical component of the reward system. And its activation will increase, when individuals are faced with rewards (Huo, Chen, Zhang, Xu, & Feng, 2024). Additionally, activation of the precuneus is related to self-referential processes. It not only promotes internally guided self-relevant processes, but can also promote detection of self-relevant information in the environment. This result supports the hypothesis that self-referential processes may play an important role in the initial stages of BAs such as excessive gaming (Yu et al., 2021). Furthermore, hyperactivation was observed in bilateral IFG and the left MFG, in line with prior studies (Dong, Wang, et al., 2021). The IFG and MFG are part of the FPN associated with executive control function (such as working memory) (Osaka et al., 2004; Yao et al., 2017). These regions are involved in the detection of cues, where increased activation enhances the significance of cues

(Hampshire, Chamberlain, Monti, Duncan, & Owen, 2010; Starcke et al., 2018). This indicates that presentation of addiction-related cues prompts individuals to recall previous rewarding experiences, thus establishing a link between addiction-related cues and rewarding experiences.

Furthermore, hyperactivation was found in the lingual gyrus area among individuals with BAs in this study. The lingual gyrus is a visual area that reflects the individual's selective visual attention processes (Ceh et al., 2021). Hyperactivation in this area indicates an attention bias towards addiction-related cues among individuals with BAs.

The result of MACM analysis showed a high degree of connectivity between the bilateral IFG, left MFG, and left lingual gyrus. This result is consistent with previous research (Ma et al., 2019). This finding suggests that abnormal neural processes in individuals with addiction, induced by addiction cues, partly reflect the dopamine-regulated reinforcement learning process in reward seeking. This process is characterized by the repeated strengthening of connections between addiction cues and reward experiences (Robinson & Berridge, 1993, 2008). Thus, the neural activity of individuals with BAs in reward seeking may involve the participation of multiple brain networks, such as the precuneus involved in the reward system, FPN involved in executive control, and lingual gyrus in selective attention.

Self-control

In self-control, the individual's ability for inhibitory control is utilized to regulate the individual's craving for addictive behaviors or substances, thereby reducing impulsive behaviors (Dong & Potenza, 2014). However, as addiction severity deepens, the individual's inhibitory control weakens, leading to an increased likelihood of habitual behaviors (Wang, Dong, Zheng, Du, & Dong, 2020). Previous studies have indicated a correlation between addiction and decreased inhibitory control (Kräplin et al., 2020), with greater impairment of response inhibitory observed in IGD (Shen et al., 2023) and functional abnormalities identified in the prefrontal regions (Ding et al., 2014). Abnormal activation in the right MFG and the left medial frontal gyrus area were also observed in BAs during inhibitory control tasks in this study. Both regions, located in the PFC, are crucial for regulating individual impulsivity and might be involved in neural circuits for autonomous regulation of impulsive behavior (Ding et al., 2014; Sweitzer, Allen, & Kaut, 2008). The hyperactivation of these regions indicates impaired inhibitory control in individuals. This finding further supports the I-PACE model. However, no common activation was detected between the right MFG and left medial frontal gyrus in the MACM analysis. One possible explanation is that the MACM method calculates shared activation between brain regions based solely on coordinates obtained from previous studies, and these coordinates may provide less information. This could affect the results about functional connectivity between the right MFG and left medial frontal gyrus area. Further investigation of this result is warranted in future research endeavors.

Decision-making

When faced with two or more possibilities, decisions need to be made by individuals. The decision-making process of addicted individuals typically manifests as “myopia”, wherein more emphasis is placed on immediate pleasure derived from the behavior while overlooking potential long-term negative consequences (Miedl et al., 2015; Wang et al., 2017). In the I-PACE model, adverse decisions are considered as the result of dysfunction between reward seeking and executive functions during cue-reactivity periods (Brand et al., 2019). Hence, in this sub-analysis, various types of decision-making paradigms were included to explore the neural mechanisms underlying decision-making in addicted individuals.

This study found that in decision-making, hyperactivation was observed in the bilateral caudate, right MFG and left SFG in individuals with BAs. The caudate is a component of the reward system within the insular cortex (Zeng, Wang, Dong, Du, & Dong, 2022), and the hyperactivation in these regions reflects changes in the reward system of individuals with BAs. Additionally, excessive activation was found in the PFC region in individuals with BAs, which may reflect inhibitory control deficits. Both the PFC and caudate are critical parts of the prefrontal-striatal circuit (Ko et al., 2015), and hyperactivation in these two regions may be related to an imbalance in the fronto-striatal circuit. This hyperactivation indicates that the decision-making process in individuals with BAs involves cognitive activities across multiple brain networks. It necessitates the involvement of neural networks including the DMN, visual network, sensorimotor network (SMN), limbic network (LIN), and FPN. This is consistent with previous research (Niu et al., 2023; van Holst et al., 2014). A meta-analysis demonstrated significant hyperactivation in the visual and limbic networks of individuals with IGD, while the SMN, attention network, frontoparietal control network, and DMN exhibited significant hypoactivation (Zheng et al., 2019).

The MACM analysis was conducted on five brain regions based on ALE, revealing significant functional connectivity among the bilateral caudate regions. This result is consistent with previous research (Niu et al., 2023; van Holst et al., 2014) and further supports the significant role of the caudate in decision-making among BAs. We infer that abnormal functional connectivity within the caudate contributes to the imbalance of the fronto-striatal circuitry. Moreover, this finding supports the I-PACE model, suggesting that an imbalance between reward seeking and inhibitory control functions during cue reactivity leads to maladaptive decision-making in individuals with BAs.

Differences in the neurocognitive mechanisms among the three stages

The conjunction analysis found that there was no shared brain region between the reward seeking, self-control, and decision-making. This result indicates the specificity of neural activity across these three stages. In reward seeking, specific activation was observed in the bilateral IFG of individuals

with BAs, a region integral to the FPN and is associated with individual executive control capabilities (Osaka et al., 2004). This result suggests a potentially greater role of executive control functions in reward seeking. Previous studies have indicated that the IFG is involved in the detection of significant cues (Hampshire et al., 2010), with activation in this region reflecting a salience for addiction-relevant cues (Starcke et al., 2018). Therefore, we infer that the significant abnormal activation of this region may be attributed to individuals with BAs in reward seeking associating addiction-related cues with rewarding experiences. In decision-making, significant hyperactivation was found in the caudate region of individuals with BAs, a crucial component of the fronto-striatal circuitry (Quaglieri et al., 2020). This finding indicates that dysfunctional caudate functionality might be a primary contributor to the imbalance within the fronto-striatal circuitry in decision-making. However, significant hyperactivation regions were not identified in self-control in this study, possibly due to the involvement of self-control-related brain regions primarily located in the PFC, which are engaged across various stages of addictive behavior (Ding et al., 2014; Romanczuk-Seiferth et al., 2015; Schmitgen et al., 2020) and thus did not exhibit specific activation during the ALE comparative analysis. Further validation of these findings is warranted in future research.

Additionally, subgroup analyses for both adult and adolescent revealed differences in hyperactivated brain regions. Adults showed hyperactivation in the PFC and caudate, while adolescents exhibited abnormal activation in the precentral and postcentral gyrus, as well as the temporal lobe. The precentral and postcentral gyrus are part of the SMN, which plays a crucial role in motor planning and conduction (Nock, Dimitropoulos, Tkach, Frasure, & von Gruenigen, 2012). Damage to these regions could lead to abnormalities in receiving, processing, and integrating bodily signals (Pan et al., 2018). This might make individuals more sensitive to addiction-related cues (Xie et al., 2024) and ultimately contributing to addictive behaviors. The hyperactivation in the temporal lobe has been associated with auditory impairments (Feng et al., 2013; Zhang, Wang, et al., 2023). These differences in brain activation might be due to adolescents being in a critical period of neural development, making them more susceptible to environmental influences. Future research could explore the differences in neural mechanisms between adults and adolescents with BAs. This could help develop personalized prevention and treatment plans tailored to BAs of different ages, thereby enhancing intervention effectiveness.

These findings are also crucial for precise diagnosis and personalized treatment. Clinically, observing the activity of core brain regions allows for more accurate assessment of addiction severity and treatment efficacy. Moreover, the study provides directions for the development of non-pharmacological treatments, such as using techniques like transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) to directly modulate neural activity in corresponding brain regions, thereby enhancing self-control capabilities (Jeong et al., 2024).



Finally, understanding the patterns of core brain region activity can also help identify high-risk individuals, facilitating targeted prevention and relapse management.

Limitations

ALE analysis and MACM analysis were employed in this study to investigate the patterns of neural activation during various stages of BAs. However, shortcomings exist within this study. Firstly, the meta-analysis of peak and effect sizes utilized published data rather than raw data, potentially compromising the accuracy of the results (Radua et al., 2012). Secondly, because there is currently no unified standard for categorizing the severity of BAs, this study did not group individuals on the severity of addiction. Previous research indicates that there may be differences in neural mechanisms between individuals in early and late stages of addiction (Brand et al., 2019), which may also manifest across different developmental stages. Therefore, further exploration of this aspect can be pursued in future studies. Thirdly, the limited number of articles included in the subgroup analysis may have affected validity of our results. In the future, if more studies are available, more stringent correction methods can be used to further validate robustness of the results in our study. Additionally, heterogeneity among subjects in the literature, such as differing diagnostic criteria, diverse control conditions, and gender ratios, warrants further investigation in future research to understand the impact of these factors. Lastly, this study conducted a preliminary exploration of the core brain regions and specific neural activation patterns related to different stages of behavioral addiction. However, due to the limited number of articles, it did not examine the neural mechanisms underlying BAs subtypes. Future research could investigate these neural mechanisms and further explore the similarities and differences among various behavioral addiction subtypes in the reward seeking, self-control, and decision-making stages. Additionally, future research could also consider incorporating more potential subtypes of behavioral addictions, such as work addiction, exercise addiction, and compulsive sexual behavior, to provide a more comprehensive understanding of the neural mechanisms underlying behavioral addictions.

CONCLUSION

This study employed ALE and MACM analyses to broaden our understanding of the neural mechanisms of BAs. It conducted subgroup analyses to explore specific neural activation patterns across different stages of addictive behaviors. The results revealed aberrant activation in the frontal regions and striatal areas in BAs, as well as significant hyperactivation in the bilateral IFG in reward seeking and left caudate in decision-making. These findings partially support our hypothesis and validate the significant role of the fronto-striatal circuit in BAs, providing some support for the I-PACE model. However, this study did not find shared

brain regions across different stages, indicating stage-specific neural mechanisms. Additionally, this research has clinical implications by providing objective physiological indicators for the diagnosis and treatment of BAs. Understanding the activity patterns in core brain regions may also aid in identifying individuals at high risk, enabling targeted prevention and relapse interventions.

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Conflict of interest: All authors declare that they have no conflicts of interest with this study. However, outside the scope of the present paper, the authors report the following: HY notes that he is a paid full-time faculty member at Tianjin Normal University. ZL notes that he is a doctoral student at Tianjin Normal University. CM notes that he is a paid, full-time faculty member at Ulm University. JDE notes that he is a paid, full-time faculty member at University of Toledo and has received grant research funding from the U.S. National Institutes of Health.

SUPPLEMENTARY MATERIAL

Supplementary data to this article can be found online at <https://doi.org/10.1556/2006.2024.00082>.

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