ORIGINAL ARTICLE



Structural and functional neural substrates underlying the concreteness effect

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Received: 9 January 2023 / Accepted: 13 June 2023 / Published online: 30 June 2023 © The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2023

Abstract

The concreteness effect refers to the advantage in speed and accuracy of processing concrete words over abstract words. Previous studies have shown that the processing of the two types of words is mediated by distinct neural mechanisms, but these studies were mainly conducted with task-based functional magnetic resonance imaging. This study investigates the associations between the concreteness effect and grey matter volume (GMV) of brain regions as well as resting-state functional connectivity (rsFC) of these identified regions. The results show that the GMV of left inferior frontal gyrus (IFG), right middle temporal gyrus (MTG), right supplementary motor area and right anterior cingulate cortex (ACC) negatively correlates with the concreteness effect. The rsFC of the left IFG, the right MTG and the right ACC with the nodes, mainly in default mode network, frontoparietal network and dorsal attention network positively correlates with the concreteness effect. The GMV and rsFC jointly and respectively predict the concreteness effect in individuals. In conclusion, stronger connectivity amongst functional networks and higher coherent engagement of the right hemisphere predict a greater difference in the verbal memory of abstract and concrete words.

Keywords Concreteness effect · Grey matter volume · Resting-state functional connectivity

Introduction

Differences in the representation and processing of concrete and abstract words have attracted attention from almost all branches of psycho- and neuro-linguistic research, providing insights into the cognitive and neural representations of words in the brain (Dove et al. 2020; Henningsen-Schomers and Pulvermüller 2021). Behaviourally, concrete words are processed and recalled more easily than abstract words by healthy adults (Pexman et al. 2007) as well as by people with disorders (Malhi et al. 2019). This advantage of processing concrete words over that of abstract words is regarded as the concreteness effect (Paivio 1991).

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Theories have been proposed to explain this phenomenon. The dual-coding theory argues that concrete words are processed in both verbal and imaginal systems and thus elicit activation in both the left and right hemispheres whilst abstract words are represented only in the verbal system and activate just the left cerebral hemisphere (Paivio 1991). The context availability theory (Schwanenflugel et al. 1988; Schwanenflugel and Stowe 1989) proposes that the advantage of concrete words originates in the supportive strength of the context (Schwanenflugel 1991). This theory argues against a causative explanation from the right hemisphere as there are no obviously distinct processing systems for the two types of words. More recently, the theories of "embodied language" have proposed a neural mechanism subserving the human concepts that are grounded in sensory, motor, social or emotional experiences (Buccino et al. 2019; Barsalou et al. 2008; Borghi et al. 2011; Wilson-Mendenhall et al. 2013). Adequate empirical evidence has been found to testify the embodiment of concrete words (Kiefer and Pulvermüller 2012), but abstract words pose a challenge due to their lack of physical and identifiable referents (Connell and Lynott 2012; Guan et al. 2013). Weakly embodied theories, such as Affective Embodiment Account and Words as Social

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Tools, acknowledge that concepts could be embodied in the experiences of action and perception as well as emotion, introspection and situation, and highlight that abstract words are also embodied in linguistic information which is symbolic to access to concepts (Vigliocco et al. 2014; Borghi et al. 2019; Barsalou and Wiemer-Hastings 2005). Strongly embodied theories claim that both abstract and concrete concepts were sub-served by the same mechanisms, and the difference lies in the complexity of the underlying grounding (Glenberg et al. 2008; Buccino et al. 2019), and abstract meaning is effector-unspecific, multi-systemic and dynamic in terms of neural mechanism (Buccino et al. 2019).

Neuroimaging studies on the healthy population have found that distinct brain regions are activated for concrete and abstract words during task performance, most of which are based on the activation contrast (Fiebach and Friederici 2004; Noppeney and Price 2004; Wang et al. 2018; Yan et al. 2023). In a verbal memory paradigm, contrastive analysis showed that abstract words elicit stronger activations in the Broca's region and the right lateral occipital gyrus during mnemonic tasks whilst concrete words elicit stronger activations in the left inferior frontal gyrus anterior of Broca's region, the bilateral posterior inferior parietal, the lower right parietal lobe and the precuneus (Jessen et al. 2000). Memory of abstract words relies more on linguistic and visual models, and concrete words on image-related associative region. Meta-analysis found that abstract concepts elicit greater activation in the left middle temporal gyrus, the inferior frontal gyrus, the medial frontal cortex and the bilateral temporal poles whilst concrete concepts elicit greater activation in the left fusiform gyrus, bilateral posterior cingulate, left parahippocampal gyrus and precuneus (Bucur and Papagno 2021; Del Maschio et al. 2022). The results show that abstract concepts are more supported by the verbal system and concrete concepts are more grounded in visual, imagery and spatial representations (Wang et al. 2010). The consensus regarding the neural mechanism underlying the concreteness effect has not been reached even for regional activation due to the variation in task types, complexity and modality (Fiebach and Friederici 2004; Noppeney and Price 2004). However, the inferior frontal gyrus was consistently found to be involved more in processing of abstract than concrete concepts. Traditionally regarded as a core region for language processing, it is also part of sensory-modality-general network for integrating multisensory information (Li et al. 2020). Greater involvement of inferior frontal gyrus may imply the complexity of processing abstract concepts.

Clinical evidence has also shown an association between atrophy of grey matter in some brain regions and patients' semantic memory. For example, atrophy of grey matter in the left anterior temporal lobe in persons with semantic dementia is associated with inefficiency of semantic memory (Mummery et al. 2000). This region stores and processes

visual semantic features (Bonner et al. 2009). In another study of patients with semantic dementia, grey matter reduction in the left temporal pole and the temporal gyri is associated with the impairment of semantic memory, whilst grey matter reduction in hippocampus is associated with episodic memory deficits (Bernard et al. 2001). These studies on brain structure manifested the relationship between grey matter volume (GMV) and individual difference in semantic processing. Regarding the concreteness effect, patients with semantic-variant primary progressive aphasia (svPPA) and those with behavioural-variant frontotemporal degeneration (bvFTD) have provided the anatomical evidence. Patients with svPPA show progressive decrease in the concreteness effect and grey matter atrophy, mainly in the left ventral and inferior temporal cortices. Degradation of areas where visual feature knowledge is stored, such as the left parahippocampal gyrus and left anterior inferior temporal cortex, associated with decrease in the concreteness effect (Cousins et al. 2017). In contrast, patients with bvFTD showed impairment of abstract words processing. They suffered loss of grey matter in the bilateral inferior frontal gyrus, right insula, right anterior middle temporal gyrus and right superior temporal gyrus, areas that support semantic selection and control (Cousins et al. 2017). However, few anatomical studies on grey matter have been conducted to investigate the concreteness effect to date. Related studies concerning healthy people investigated association between semantic memory and GMV of the elderly, and found that GMV of anterior temporal lobes (Taki et al. 2011), temporolimbic cortical (Seubert et al. 2020), and left and right lateral prefrontal cortex (Becker et al. 2015) of older adults associated with semantic memory. No studies up till now have investigated the relation between GMV and the concreteness effect of healthy population.

In addition to the local activation of brain regions, the concreteness effect can also be explained by the involvement of networks in the processing of the two types of words. Semantic processing could be supported to a greater extent by the connectivity of regions than by the activation of any single region. An independent components analysis of resting-state functional connectivity showed that the anterior temporal lobe, the posterior middle temporal gyrus, the inferior parietal lobe, the inferior frontal gyrus, the medial prefrontal cortex, the angular gyrus and the medial temporal lobes form a broad neural network that sub-serves the semantic representation and control (Binder et al. 2009; Jackson et al. 2019). This finding was corroborated by a psychophysiological interactions (PPI) analysis, which identified a core semantic network including the anterior and posterior middle temporal gyrus, the inferior frontal gyrus, the anterior temporal lobe and the angular gyrus that is active in both the resting and task states (Jackson et al. 2016). The spontaneous activities of functional connectivity implicate that words are commonly embodied in these regions and both concrete and abstract words were modulated by this semantic network. However, former study found that the processing of concrete words is more supported by task-based functional connectivity amongst widespread brain regions than that of the abstract words (Weiss and Müller 2013). The connectivity of three pairs of networks is stronger for concrete imagery than for abstract imagery. One network, for example, consisted of the inferior frontal gyrus and superior temporal gyrus pairs with the precentral gyrus, postcentral gyrus and insula (Hemati and Hossein-Zadeh 2018). To our knowledge, few studies have investigated the concreteness effect in terms of resting-state functional connectivity. Such an approach could provide compelling intrinsic evidence of difference in processing between these two types of words. Researchers have previously proposed that the spontaneous connectivity between different brain regions for cognitive tasks is rooted in a longstanding history of co-activation (Dosenbach et al. 2007). This hypothesis is supported by studies which found that language maps extracted from resting-state functional magnetic resonance imaging (fMRI) data spatially correspond to their task-based homologues (Branco et al. 2020; Vidaurre et al. 2017).

The concreteness effect has been widely studied with event-related potentials (ERP), transcranial magnetic stimulation (TMS) and event-related functional magnetic resonance imaging (fMRI) (Dalla Volta et al. 2014; Yan et al. 2023; Jessen et al. 2000). As far as we know, no studies have investigated the concreteness effect with intrinsic neuroanatomical and functional features, such as GMV and restingstate functional connectivity (rsFC). We believe that study from this perspective may contribute to a more comprehensive understanding of the neural mechanism sub-serving the concreteness effect and explore how the individual variation of brain structure and spontaneous neural activity could predict the performance. The GMV and rsFC have been regarded as valid neuro-markers of behaviour and associate with semantic processing and episodic memory (Duarte et al. 2006; Bizzo et al. 2017; Palacio and Cardenas 2019; Reinke et al. 2013; Pexman et al. 2007; Xie et al. 2020). In this study, we collected GMV, rsFC and behavioural data of verbal memory of concrete and abstract words. The difference in the accuracy of recognition memory for these two types of words was tested to indicate the strength of the concreteness effect. To explore the neuroanatomical features and intrinsic functional architectures underlying the concreteness effect, we identified the regions whose GMV was correlated with the concreteness effect using voxel-based morphometry (VBM), analyzed the rsFC with the identified regions as seed regions, and estimated the predictive power of GMV and rsFC for individual behaviours of concreteness effect. We hypothesize that individual concreteness effect may associate with GMV of the regions for executive control like IFG and semantic representation like MTG, which are consistently found to be crucial for the concreteness effect regardless of modality and task types, according to the metaanalyses of task-based neural activities for abstract and concrete words (Bucur and Papagno 2021; Del Maschio et al. 2022; Wang et al. 2010). We also hypothesize that individual concreteness effect may associate with rsFC between the regions identified by the VBM analysis and other regions in the networks, such as the hetero-modal default mode network (DMN) and the executive control network of frontoparietal network (FPN), for the concrete words processing was found to elicit more synchronized and integrated brain activities (Hemati and Hossein-Zadeh 2018; Thomas Yeo et al. 2011).

Materials and methods

Subjects

Seventy-two students from the University of Electronic Science and Technology were originally recruited for this experiment. All the subjects are right-handed, with normal or corrected-to-normal vision, and none of them reported psychiatric disorders or contraindications to MRI scans. Data from two subjects were discarded because their reaction times were either less than or more than triple standard derivation from the mean. The data of seventy subjects were then analyzed (30 females; mean age 20.7 years, standard deviation 1.8 years). This study was approved by the local committee for the Ethics Committee for Protection of Human Subjects of the University of Electronic Science and Technology of China and was conducted in accordance with the Declaration of Helsinki. All the subjects signed written informed consent forms.

Stimuli and procedure

The memory task consisted of two sessions, memory encoding and recognition. Thirty-six concrete and thirtysix abstract words were prepared for the encoding session. Seventy-two abstract and seventy-two concrete words were prepared for the recognition session; half of them were old words presented previously in the encoding session and the rest were new words added.

All stimuli were two-character Chinese words selected from the "Dictionary of Usage Frequency of Modern Chinese Words" (Liu 1990) with similar word frequencies between 100 and 500 occurrences per million words. Fifteen volunteers who did not participate in the experiment rated the concreteness of these words with a 7-point Likert scale. Words with mean score below 2 were labelled as concrete words (mean 1.2412, SD 0.28323), and words with mean score above 4 were labelled as abstract words (mean: 4.8776, SD: 0.58782). The independent-samples *t* test showed that the concreteness of these two groups of words was significantly different (t=37.49, p < 0.000). As to the visual complexity of word stimuli, the mean number of strokes of the concrete words was 17.5278 and the standard deviation was 5.07957, and for the abstract words 17.0556 and 4.45601. The independent-samples *t* test showed that there was no significant difference in the numbers of strokes between the two types of words (t=0.593, p=0.439). The English translation of the stimuli is attached in the appendix. The stimuli were randomly displayed using E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA) on a computer monitor (41 × 23 cm²) with a 1366 × 768 pixel resolution and a refresh rate of 60 Hz.

The paradigm was adapted from a previous mnemonic study (Dresler et al. 2017). Before the memory encoding session started, the subjects were instructed explicitly to memorize the words presented in this session for the subsequent recognition task. The encoding session began with a word shown in the middle of the screen for 2000 ms, followed by a 2000 ms fixation cross and then the presentation of another word. Thirty-six abstract and thirty-six concrete Chinese words were presented randomly. The recognition session began an hour later. Seventy-two old words which were presented in the encoding session together with thirtysix new concrete words and thirty-six new abstract words were displayed randomly. The subjects were instructed to judge if the presented word was old or new by pressing the corresponding buttons. Each word was presented for 2000 ms at most, and participants were required to response as soon as possible. Once the subject pressed a button, the screen automatically and immediately progressed to the fixation cross. The accuracy and reaction time were collected by E-Prime 2.0. The encoding and recognition processes are illustrated in Fig. 1.

Image acquisition

The MRI data were acquired by a 3.0-T GE Sigma scanner (General Electric, Milwaukee, WI, USA) with an 8-channel phase-array head coil in the MRI Brain Imaging Center at the University of Electronic Science and Technology of China. The high-resolution T1-weighted images, GMV data, were attained with the following parameters: $TE = 1.96 \text{ ms}; TR = 5.96 \text{ ms}; FOV = 256 \times 256 \text{ mm}^2;$ matrix size = 256×256 ; slice thickness/gap = 1.0 mm/ no gap: $FA = 9^{\circ}$: voxel size = 1 × 1 × 1 mm³: number of slices = 176. The resting-state fMRI data were collected with a gradient echo-planar imaging (EPI) sequence with following parameters: TE = 30 ms; TR = 2000 ms; $FOV = 240 \times 240 \text{ mm}^2$; matrix size = 64×64 ; slice thickness/gap = 3.75 mm/0.6 mm; FA = 90° ; voxel size = $3.75 \times 3.75 \times 3 \text{ mm}^3$; slices = 43. During the MRI scan, subjects were told to relax with their eyes closed, not to think of anything in particular, and not to fall asleep.

Behavioural data analysis

Accuracy and reaction times (RTs) were collected to measure individual behaviour for the concrete effect. Only the trials with correct responses were included in the analysis. Trials with RTs more than triple standard derivation were discarded (Munneke et al. 2008). Further analyses were based on accuracy. Here, the strength of the concreteness effect in terms of RTs was computed by subtracting the RTs of concrete words from the RTs of abstract words: concreteness effect = $RT_{(abstract)} - RT_{(concrete)}$. The strength of the concreteness effect in terms of accuracy was computed by subtracting the accuracy of concrete words: Concreteness effect = $accuracy_{(concrete)} - accuracy_{(abstract)}$. These measurements reflected the relative advantage of concrete word memory over that of abstract words.





Fig. 1 Encoding and recognition processes

Structural imaging data analysis

The high-resolution T1-weighted images were preprocessed with the Statistical Parametric Mapping toolbox (SPM12, https://www.fil.ion.ucl.ac.uk/spm/) and the Computational Anatomy Toolbox (CAT12, http://dbm.neuro.uni-jena.de/ cat12/). According to the default settings in the CAT12 toolbox, the steps for preprocessing were as follows: checking artefacts and the visual orientation of raw images visually; segmenting white matter, grey matter and cerebrospinal fluid: inter-subject registration and modulation: spatial normalizing to the Montreal Neurological Institute space $(1.5 \times 1.5 \times 1.5 \text{ mm}^3)$ with high-dimensional DARTEL normalization; and spatial smoothing with 8 mm Gaussian kernel. Multiple regression analyses were conducted to explore brain regions whose GMV correlated with individual concreteness effect, with age and sex as covariates of noninterest (Becker et al. 2019; Weise et al. 2019). The results for voxelwise analysis were corrected for multiple comparisons with a threshold of p < 0.001 (uncorrected) and a cluster size > 30 voxels (Xie et al. 2020; Zhang et al. 2022).

Functional imaging data analysis

The resting-state fMRI data were preprocessed with SPM12 and the Data Processing Assistant for Resting-State fMRI toolbox (DPARSF, http://rfmri.org/DPARSF). First, we discarded the first five images of every subject for the signal stabilization, and conducted head motion correction and slice timing. Then, we made a regression of nuisance covariates for Friston-24 motion parameters and three other confounding signals, that is, white matter, cerebrospinal fluid and global signals. After that, we performed spatial normalization to the Montreal Neurological Institute space and resampling to $3 \times 3 \times 3$ mm³, removed the linear trends, and filtered temporal bandpass (0.01–0.08 Hz). Finally, we conducted spatial smoothing with a 6 mm full-width-halfmaximum Gaussian kernel.

The seed-based voxel-wise rsFC was analyzed with DPARSF. We first defined regions of interest (ROIs), according to the VBM analysis, by creating 6 mm spheres surrounding the peak coordinates of the brain regions whose GMV significantly associated with concreteness effect. Then we extracted and averaged the time courses of all voxels within the seed regions, and calculated the Pearson correlation between the mean time courses of the ROIs and the other voxels over the whole brain to establish rsFC maps. In order to improve the data distribution normality and statistical effect, we converted the rsFC maps into *z*-maps by Fisher's *r*-to-*z* transformation. Finally, we conducted multiple regression analyses to explore the ROIs whose rsFC is correlated with individual concreteness effect. The multiple comparisons were corrected with a false discovery rate

(FDR) at the voxel level (p < 0.05, corrected), and an additional cluster-level threshold of cluster size > 30.

Prediction analysis with cross-validation

We further explored whether the GMV of the ROIs or the rsFC between the ROIs and other regions could reliably predict the concreteness effect in a novel subject. The internal cross-validation was analyzed with the Pattern Recognition for Neuroimaging Toolbox (PRoNTo v2.1, http://www.mlnl. cs.ucl.ac.uk/pronto/) (Schrouff et al. 2013). Sex and age were regressed out as covariates of noninterest. Centring of the training data was conducted by subtracting the voxel-wise mean from each data vector. The predictive power was evaluated with the Pearson's correlation analysis of the predicted and actual data. Permutation testing without replacement was performed 5000 times to stabilize the statistical significance of the correlation.

Regression models assessing the contributions of GMV and rsFC

To evaluate the individual and joint contributions of the GMV and rsFC of the defined regions to explain the variation in the concreteness effect, we conducted multiple linear regression analyses. The dependent variable was the individual concreteness effect. The two independent variables were the GMV of the defined regions associated with the concreteness effect and the rsFC when these regions were regarded as seeds. The GMV and rsFC were first included in the regression model separately to evaluate their individual contribution, and then they were included simultaneously to evaluate their joint contribution. The individual (GMV or rsFC) and joint contributions (GMV and rsFC) were determined by the proportion of variance explained (adjusted R²) by the model.

Results

Behavioural results

Independent-sample *t* tests were conducted to compare the recognition accuracy and RTs of the concrete and abstract words. A significant difference was found in accuracy between the abstract and concrete words (mean_(concrete) = 0.8345, SD_(concrete) = 0.0705; mean_(abstract) = 0.7984, SD_(abstract) = 0.0904; *t* = 5.163, *p* < 0.001). However, there was no significant difference in RTs (mean_(concrete) = 936.6235, SD_(concrete) = 221.6606; mean_(abstract) = 963.7981, SD_(abstract) = 235.4666; *t* = -1.503, *p* = 0.137). Thus, the concreteness effect was reflected in the significant difference in accuracy.

Exploratory analysis

The regions whose GMV significantly correlated with the concreteness effect were identified, controlling sex and age as the covariates of no interest. The whole-brain VBM analysis showed that the concreteness effect negatively correlated with GMV of the left inferior frontal gyrus (IFG) (x, y, z=-54, 32, 24), right middle temporal gyrus (MTG) (x, y, z=42, -60, 12), right anterior cingulate cortex (ACC) (x, y, z=12, 48, 9) and right supplementary motor area (SMA) (x, y, z=15, -8, 68) (Table 1 and Fig. 2). GMV did not positively correlate with the concreteness effect in any brain region analyzed.

Correlation of the concreteness effect and rsFC

We further assessed the relationship between intrinsic functional connectivity and the concreteness effect by conducting seed-based rsFC analysis. The seeds were centred on the regions identified by the VBM analysis with a 6 mm sphere surrounding the peak coordinates. The regions of interest (ROIs) were the left IFG (x, y, z = -54, 32, 24), the right MTG (x, y, z = 42, -60, 12), the right ACC (x, y, z = 12, 48, 9) and the right SMA (x, y, z = 15, -8, 68). Controlling for sex and age, multiple regression analyses (FDR-corrected, p < 0.05; clusters > 30 voxels) revealed a significant association of the concreteness effect with the rsFC of the left IFG, the right MTG and the right ACC, but not the right SMA. The results are shown in Tables 2, 3 and 4.

To analyze the clusters connected to the three identified regions in a large-scale network, we calculated the ratio of significant voxels which fell into the seven-network parcellations (Thomas Yeo et al. 2011), including the default mode network (DMN), the fronto-parietal network (FPN), the dorsal attention network (DAN), the ventral attention network (VAN), the sensorimotor network (SMN), the limbic (LN) and visual network (VN). Amongst the voxels connected to the left IFG (x, y, z= – 54, 32, 24), 36.5% were in the DMN,

Table 1Brain regions whoseGMV negatively correlated withthe concreteness effect

Regions	Cluster	Peak MNI coordinates			T value	r _{cluster}
R middle temporal gyrus	110	42	- 60	12	4.15	- 0.472**
R supplementary motor area	36	15	- 8	68	3.73	- 0.416**
R anterior cingulate cortex	40	12	48	9	3.46	- 0.371**
L inferior frontal gyrus	161	- 54	32	24	3.38	- 0.388**

 r_{cluster} : the correlation coefficient between the averaged GMV within the significant clusters and the concreteness effect

MNI Montreal Neurological Institute, L left, R right

The significance level was set at p < 0.001 (uncorrected) and the minimum cluster size was 30 voxels. **p < .01



Fig. 2 Negative correlations between the individual concreteness effect and GMV of the left IFG, the right MTG, the right ACC, and the right SMA

 Table 2
 Brain regions with

 significant correlations between
 the concreteness effect and rsFC

 with the left IFG
 the concreteness effect and rsFC

 Table 3
 Brain regions with

 significant correlations between
 the concreteness effect and rsFC

with the right MTG

Regions	Cluster	Peak MNI coordinates			T value	r _{cluster} ^a
L middle cingulate cortex	248	- 6	- 45	33	5.25	0.529**
L precuneus		0	- 45	39	4.56	
R posterior cingulate cortex		9	- 39	30	4.40	
R middle temporal gyrus	521	42	- 6	39	4.97	0.583**
R middle occipital gyrus		48	- 81	3	4.64	
L rectus	534	- 9	42	- 18	4.91	0.604**
R superior frontal gyrus		15	63	- 18	4.88	
L anterior cingulate cortex	82	- 9	39	15	4.84	0.511**
R anterior cingulate cortex		6	39	6	3.95	
L middle frontal gyrus	62	- 36	18	33	4.74	0.496**
R middle temporal pole	47	48	15	- 36	4.64	0.457**
R middle temporal gyrus		54	6	- 30	3.75	
L precuneus	225	- 12	- 78	45	4.37	0.607**
L calcarine		- 18	- 63	18	4.04	
R inferior temporal gyrus	41	66	- 12	- 30	4.30	0.467**
R middle temporal gyrus		69	- 9	- 15	3.28	
R superior frontal gyrus	55	15	51	21	3.78	0.44**
R middle frontal gyrus		27	54	21	3.25	
L middle temporal gyrus	90	- 54	- 72	3	3.73	0.446**
L middle occipital gyrus		- 33	- 81	3	3.48	
R middle frontal gyrus	31	39	15	39	3.65	0.412**

MNI Montreal Neurological Institute, L left, R right

The significance levels were set at p < 0.05 (FDR-corrected) and a minimum cluster size of 30 voxels. **p < 0.01

^aThe correlation coefficient between the average resting-state functional connectivity within the significant clusters and the strength of the concreteness effect

Regions	Cluster	Peak MNI coordinates			T value	r_{cluster}^{a}
L inferior temporal gyrus	36	- 57	- 51	- 15	5.21	0.521**
L inferior frontal gyrus	130	- 54	24	27	5.17	0.56**
R angular gyrus	172	36	- 57	36	4.86	0.557**
R superior parietal lobule		36	- 60	51	4.76	
L middle occipital gyrus	55	- 27	- 69	39	4.68	0.513**
L angular gyrus		- 36	- 60	36	3.70	

MNI Montreal Neurological Institute, L left, R right

The significance levels were set at p < 0.05 (FDR-corrected) and a minimum cluster size of 30 voxels. **p < 0.01

^aThe correlation coefficient between the average resting-state functional connectivity within the significant clusters and the strength of the concreteness effect

21.3% were in the VN, 8.8% were in the FPN, 6.9% were in the LN, and 2.4% were in the DAN. Amongst the voxels connected to the right MTG (x, y, z = 42, -60, 12), 45.5% were in the FPN, 17.4% were in the DAN, and 9.0% were in the DMN. Amongst the voxels connected to the right ACC (x, y, z = 12, 48, 9), 41.1% were in the FPN, 13.0% were in the DAN, 4.1% were in the VAN, and 3.1% were in the SMN (Fig. 3).

Predictive analysis

The predictive power of the GMV of the identified ROIs and the predictive power of the rsFC with seeds set as the left IFG, the right MTG and the right ACC for the individual concreteness effect were assessed with internal cross-validation. Figure 4 shows the strength of the concreteness effect observed and the strength predicted Table 4 Brain regions with significant correlations between the concreteness effect and rsFC with the right ACC

Dagions	Cluster	Dook N	INI coordinat	Typluo	a	
Regions	Cluster	r cak N		.05	1 value	cluster
R inferior frontal gyrus	302	45	18	24	6.33	6.33**
R middle frontal gyrus		36	21	21	5.75	
R middle frontal gyrus	42	36	45	- 6	4.37	4.36**
R insula	46	33	- 15	9	4.35	0.432**
R putamen		30	- 6	6	4.23	

MNI Montreal Neurological Institute, L left, R right

The significance levels were set at p < 0.05 (FDR-corrected) and a minimum cluster size of 30 voxels. ***p*<0.01

^aThe correlation coefficient between the average resting-state functional connectivity within the significant clusters and the strength of the concreteness effect

by the GMV and rsFC which displayed significant correlation. The measured strength of the concreteness effect showed significant correlations with that predicted by the GMV (r=0.267, p<0.05) (Fig. 4a). Similarly, the measured strength of the concreteness effect displayed significant correlations with that predicted by the rsFC of the left IFG (r=0.513, p<0.001) (Fig. 4b), the right MTG (r = 0.585, p < 0.001) (Fig. 4c) and the right ACC (r = 0.556, p < 0.001) (Fig. 4d).

Individual and joint contributions of GMV and rsFC

GMV and rsFC have been demonstrated to be associated with the individual concreteness effect, but their contributions to the individual concreteness effect may differ. We further assessed the individual and joint contributions by the GMV and rsFC of the regions identified in the VBM analysis. In the regression model, GMV and rsFC explained 58.6% of the variation in the strength of the concreteness effect (GMV and rsFC, adjusted $R^2 = 0.586$, p < 0.001). The variance inflation factor of multicollinearity between GMV and rsFC is 1.072. In addition, we also tested their individual contributions using hierarchical multiple regression analysis. When GMV entered the model before rsFC, the addition of rsFC significantly raised the explanatory power of the regression model (adjusted $R^2 = 0.227 \rightarrow 0.586$, p < 0.001). Conversely, when rsFC stepped into the model before GMV, the inclusion of GMV also improved the explanatory power of the model (adjusted $R^2 = 0.491 \rightarrow 0.586$, p < 0.001) (Table 5).

Discussion

In this study, we investigate the relationships of the concreteness effect with GMV of brain regions as well as rsFC of these identified regions. The results show that, first, the verbal memory of concrete words was stronger than that of Brain Structure and Function (2023) 228:1493-1510

abstract words. Second, the GMV of identified regions in the frontal and temporal cortices negatively correlated with the strength of the individual concreteness effect. Third, the rsFC of the left IFG, the right MTG and the right ACC positively correlated with the strength of the individual concreteness effect. Specifically, subjects with a stronger concreteness effect have stronger rsFC between the left IFG and brain regions in the DMN, VN, and FPN, between the right MTG and regions in the FPN and DAN, and between the right ACC and regions in the FPN and DAN. Finally, we found that GMV and rsFC jointly explain 60.3% of individual variations in the strength of the concreteness effect. Overall, these findings highlight the importance of brain structure and interregional interactions in the resting state with regard to the advantage of verbal memory of concrete words over that of abstract words.

Structural substrates underlying the individual concreteness effect

First, we find that individual variations in the verbal memory of abstract and concrete words correlate with individual differences in GMV of regions in the frontal and temporal cortices, which play crucial roles in language processing and semantic executive control. Greater GMV of these regions correlates with less difference in processing between these two types of words, indicating that memory of abstract words may rely more heavily on regions responsive to executive, linguistic and emotional processing, as semantic retrieval of abstract words is based on the extent of executive demand (Scott 2004). On the one hand, the frontal cortex, including the IFG, SMA and ACC, is generally involved in semantic retrieval, context integration, context tracking and other higher-order cognitive functions (Hertrich et al. 2016; Badre and D'Esposito 2007). This finding is also in line with meta-analytical studies on the neural correlates of abstract and concrete words, which consistently identified the greater activation of the IFG and MTG for abstract > concrete contrast (Bucur and Papagno 2021; Del Maschio et al. 2022).



Fig. 3 a Brain regions whose rsFC with the left IFG positively correlated with the concreteness effect and their proportion of voxels overlapping with the seven-network parcellation, **b** Brain regions whose rsFC with the right MTG positively correlated with the concreteness

effect and their proportion of voxels overlapping with the seven-network parcellation, **c** Brain regions whose rsFC with the right ACC positively correlated with the concreteness effect and their proportion of voxels overlapping with the seven-network parcellation



Fig.4 Models predicting the concreteness effect by GMV and rsFC maps. **a** Predicted strength of the concreteness effect according to GMV; **b** predicted strength of the concreteness effect by the rsFC of the left IFG; **c** predicted strength of the concreteness effect by the

rsFC of the right MTG; **d** predicted strength of the concreteness effect by the rsFC of the right ACC. The scatter plots and line charts show a clear correlation and consistency between the observed (black line) and predicted (red line) strength of the concreteness effect

 Table 5
 Linear regression

 models including GMV
 and/or rsFC, illustrating

 both individual and joint
 contributions

Variables included in the models	Adjusted R^2	F	Р	ΔR^2	Sig. F change
GMV	0.227	21.229	< 0.001	_	_
rsFC	0.491	67.539	< 0.001	_	_
GMV + rsFC	0.586	49.8	< 0.001	_	_
$GMV \rightarrow [GMV + rsFC]$				0.36	< 0.001
$rsFC \rightarrow [GMV + rsFC]$				0.1	< 0.001

On the other hand, the temporal cortex, including the MTG, is generally involved in semantic storage, and executive and cognitive control (Kaneda and Osaka 2008; Leshinskaya and Thompson-Schill 2020; Cousins et al. 2017; Chen and Lin 2012). According to an fMRI study of word processing, both abstract and concrete words elicit activation in the anterior cingulate, middle temporal gyrus, and inferior frontal gyrus (Kiehl et al. 1999), suggesting that these regions support processing of both two types of words. Although inferior frontal gyrus and middle temporal gyrus are conventionally regarded to perform semantic control, anterior cingulate cortex and supplementary motor area are not classical semantic hubs. Involvement of conventional language systems could not fully explain the difference in processing the two types of words. It could be assumed that the difference might not lie in the distinct distribution of information, for abstract and concrete concepts are represented in a continuum, but instead may be rooted in the complexity of associated grounding experiences (Buccino et al. 2019). Inferior frontal gyrus and supplementary motor area are parts of a sensory-modality-general network recruited to integrate multisensory information, indicating that these two areas subserve representations with complex modalities (Li et al. 2020). Besides, right middle temporal gyrus is a hub area for associative coding of events (Leshinskaya and Thompson-Schill 2020), and anterior cingulate cortex is an area where emotion and cognition are juxtaposed (Allman et al. 2001). These areas may help integrate complex information which is embodied in the experiences in varied modalities.

In the frontal lobe, GMV of three brain regions, the left IFG, right ACC and right SMA, negatively correlates with the advantage of verbal memory of concrete words over that of abstract ones. According to the results, larger GMV of the left IFG, right ACC and right SMA predicts smaller difference in the verbal memory accuracy of abstract and concrete words. The IFG plays an important role in general semantic memory processing for both abstract and concrete words, and its involvement increases with increasing demands on semantic executive control (Sabsevitz et al. 2005; Binder et al. 2005; Kumar 2016). A positive correlation between activity in the prefrontal cortex and GMV in the IFG has been found during memory retrieval (Rugg et al. 2008; Brassen et al. 2009). Children with attention-deficit/hyperactivity disorder have reduced GMV (Batty et al. 2010) and older

adults with better associative memory performance have higher GMV of the prefrontal cortex (Becker et al. 2015).

The left IFG is conventionally regarded as an area for semantic control, and it could be that the verbal memory of abstract words imposes greater retrieval and selection demands on executive control, thereby eliciting greater activation of the IFG (Hoffman et al. 2015; Rugg et al. 2002). However, memory of concrete words also involves left IFG as well for semantic processing and executive control (Gnedykh et al. 2022). Left inferior gyrus was found to be activated more by abstract words and nonwords than concrete words, possibly indicating that processing of abstract words is more grounded in phonological representation due to the acquisition experiences (Binder et al. 2005; Borghi et al. 2019). Mirror neurons were first found in the area F5 of a macaque monkey with tasks of performing a hand action and observing others perform similar action (Matelli et al. 1985), and human counterparts were identified in Broca's area in the left IFG (Rizzolatti et al. 1996). This mirror-neuron system is activated for observation, imagination, recognition and imitation of actions, processing audio-visual representations of almost all biological effectors (Gallese et al. 1996; Nishitani and Hari 2000; Rizzolatti et al. 2001; Kohler et al. 2002). Broca's area, primarily considered as a pure speech area, converges multimodal representations for complex cognition, integrating sounds and actions (D'Ausilio et al. 2009). Greater GMV of the left IFG may predict better performance of abstract words memory, possibly because this area sub-serves processing of complex grounding information, matching with the multidimensional characteristics of abstract concepts.

The SMA, located in the medial premotor cortex, is connected with inferior frontal language areas as a part of an expanded network to perform semantic control (Dick et al. 2014). Reduced executive control is related to decreased GMV of the SMA, as shown in patients with internet gaming disorder (Lee et al. 2018). Abstract words focus on the social and introspective aspects of situations that are more complex and involve more events and actions (Barsalou and Wiemer-Hastings 2005; Connell and Lynott 2012). Not only the sensorimotor and mental states but also related scenarios are simulated to facilitate the association of abstract concepts (Borghi et al. 2019). SMA, not a conventional language area, sub-serves sequences for action, temporal and spatial processing, working memory, and integrates them into superordinate representations (Cona and Semenza 2017). And for memorizing words, SMA regulates sequence operations in cognitive activities by maintaining early elements and integrating later elements into higher-order representations (Cona and Semenza 2017), as in a timely introspective simulation process of experiences in sensory and motor modalities (Naghibi et al. 2023). Greater GMV of SMA may facilitate the sequential representation for association of complex abstract concepts, thus reducing the difference in memorizing abstract and concrete words.

The ACC is a region for attentional control. It modulates and supports semantic processing heterogeneously, with wide connexions with sensorimotor cortices (Margulies et al. 2007; Zhao et al. 2017; Kaneda and Osaka 2008). To meet task demands, it evaluates competing information and monitors and suppresses irrelevant and obstructive information (MacDonald et al. 2000). Abstract verbal memory demands greater mental effort due to its vague representation, and thus may elicit greater activation of the ACC. The ACC not only supports cognitive control, but also receives inputs from the orbitofrontal cortex and amygdala, thereby serving to process and regulate emotion for both linguistic and non-linguistic stimuli (Rolls 2019; Etkin et al. 2011). The ACC is responsive more to abstract words than concrete words (Vigliocco et al. 2014), possibly because abstract concepts are grounded in affective experience and have greater emotional valence than concrete concepts (Vigliocco et al. 2014; Skipper and Olson 2014) (Palomero-Gallagher et al. 2008). The affective embodiment account proposes that abstract words evoke more emotion, because emotion accompanies and facilitates the acquisition of them (Kousta et al. 2011). A fMRI study, with 2 (abstract/concrete) $\times 2$ (neutral/valence) factorial design, found that ACC is activated by emotional valence rather than abstractness and that activation to abstract and concrete words overlap with that to emotional words (Skipper and Olson 2014). Not only abstract words but also concrete words evoke ACC in case the words are emotional. And it might be inferred from this study that abstract concepts are not represented in an amodal way, but grounded in the experiences with varied complex modalities. Greater GMV of ACC may predict better processing of abstract words and thus reduce the concreteness effect because abstract words are more grounded in emotion than concrete ones.

In the temporal lobe, the GMV of the MTG negatively correlated with the advantage of verbal memory of concrete words over that of abstract words; in other words, greater GMV of this area predicts a smaller difference between abstract and concrete verbal memory (Bucur and Papagno 2021). It was found that MTG are involved in social cognition, emotion, semantic and auditory processing, and is long regarded as a traditional language area (Xu et al. 2019). As part of the hetero-modal network, the MTG where the outputs from different processes converge plays a significant role in representing and integrating information with different modalities (Ferreira et al. 2015; Fahimi Hnazaee et al. 2020; Zhao et al. 2017). It responds to perceptual and associative coding as well as relational categories, processing both specific and general attributes (Leshinskaya and Thompson-Schill 2020). Besides, MTG is consistently detected to retrieve from memory the information of action and relations between elements. The neural mechanism of MTG could support the complex concepts relying on multimodal representations and memory. Greater GMV in the MTG may facilitate the processing of multimodal information of abstract concepts which are mainly embodied in emotional, situational and social experiences (Barsalou 2008; Vigliocco et al. 2014; Borghi et al. 2019).

The greater GMV of the IFG, SMA, ACC and MTG could be a biomarker of reduced concreteness effect. All concepts, except proper nouns, involve abstraction, with abstract and concrete words represented in continuum rather than dichotomy (Dove 2018). Not only concrete word, such as "knife", but also abstract word, such as "love", may reenact visual, tactile, emotional, situational and other experiences concerning them and evoke corresponding neural activities. The characteristics of abstract words are multidimensional with greater complexity and flexibility (Conca et al. 2021), so their processing is more supported by areas sub-serving multimodal representations, such as IFG, SMA and MTG. Since compared to concrete words, abstract words are represented in multiple modalities, their association for memory will probably involve switch between modalities, which causes more modality-switching cost. A study showed that verifying property for concepts in different modalities cost more reaction time than those in the same modality (Pecher et al. 2003). The complexity in representational modalities of abstract words would incur more modality-switching cost which could be manifested as the concreteness effect.

Functional substrates underlying the individual concreteness effect

After applying a seed-based rsFC analysis, we found that the individual concreteness effect correlates with distinct patterns of rsFC and the rsFC of the left IFG, the right MTG and the right ACC efficiently predicts the individual concreteness effect. The positive correlation between the seedbased rsFC and the concreteness effect indicates that the stronger the functional connectivity, the greater the concreteness effect is. These three ROIs exhibit rsFC with nodes mainly in the DMN, FPN, DAN and VN, which partially overlap areas activated in a task-based fMRI study on the network connectivity of language processing. Similarly, edges of the vocabulary comprehension network are mainly located in the DMN and FPN (Tomasi and Volkow 2020).

First, the individual concreteness effect positively correlates with the rsFC between the left IFG and brain regions mainly in the DMN (36.5%) and the VN (21.3%), indicating that interregional and internetwork interactions contribute to this effect. This finding is partially supported by a study which claims that the brain is more integrated and synchronized in response to concrete word imagery with stronger connexions between brain areas than in response to abstract words (Hemati and Hossein-Zadeh 2018). A meta-analysis of abstract and concrete words has found that concrete words elicited greater activation in the temporo-parieto-occipital regions (Bucur and Papagno 2021; Del Maschio et al. 2022). The DMN, a hetero-modal network storing various representations of concrete words from sensorimotor areas, is considered more strongly activated by concrete words processing than by abstract words processing (Lanzoni et al. 2020; Binder et al. 2005; Wang et al. 2010). The visual imagery of concrete words is supported by the functional connectivity between the precuneus, the crucial node of the DMN and the frontotemporal network (Jefferies 2013; Wang et al. 2010). Specifically, the left IFG which is highly involved in executive control modulates the activity of the DMN by optimizing memory retrieval (Osaka et al. 2004). Therefore, the coupling of the left IFG and precuneus may facilitate the verbal memory of concrete words to a greater extent than abstract words. Another important region in the DMN coupling with IFG is posterior cingulate cortex. The functional connectivity at rest between them is stronger in the subjects who perform semantic tasks more efficiently, with the executive control region (IFG) regulating the retrieval of memory stored in the posterior cingulate cortex (Krieger-Redwood et al. 2016). The VN, a complex system contributing to memory, visuospatial processing, multimodal sensory integration and attention, exhibits rsFC with the left IFG in our study. Predominantly located in the bilateral cingulum, the related areas in the VN facilitate cognitive tasks demanding executive effort, especially tasks for requiring accuracy rather than speed (Bush et al. 2000). Specifically, the bilateral middle temporal gyri may contribute to the integration of emotional information from audio-visual modalities (Dong et al. 2022; Beauchamp et al. 2004). Besides, the middle occipital gyrus sub-serves visual-spatial processing, especially for face/tool processing, and modulates category-selective attention (Tu et al. 2013). The above-mentioned regions coupling with the IFG in temporo-parieto-occipital regions mainly encompass the areas where visual, spatial, auditory information is embodied. Concrete words are usually grounded on these physical representations, so the stronger functional connectivity between IFG and these regions may facilitate the memory of concrete words more than abstract words.

Second, the individual concreteness effect positively correlates with the rsFC between the right MTG and brain regions mainly in the FPN (45.5%) and the DAN (17.4%). The MTG, a crucial region to represent and integrate semantic features, is a part of the dorsal attention network and collaborates strongly with the FPN, especially the left IFG, indicating that collaborations within and between networks may be related to semantic executive control (Corbetta and Shulman 2002). The FPN modulates representational memory between visual and associative areas, and greater cortical thickness in the FPN may predict better complex attentional control (Babiloni et al. 2004; Schmidt et al. 2016). The left IFG and the posterior MTG are both recruited when semantic retrieval must be steered away from automatically retrieved aspects of concepts towards more unusual features or associations. The coupling of the posterior MTG and left IFG may facilitate goal-directed executive control over semantic memory retrieval (Davey et al. 2016). The DAN focuses the task-related top-down attentional control on the encoding load of a series of items to be processed (Majerus et al. 2018). The angular gyrus and the superior parietal lobule are part of a dynamic buffering system to integrate multi-modal information, especially sensory-motor and spatial information (Humphreys et al. 2021; Passarelli et al. 2021). This system supports the verbal memory of concrete words more than abstract words because concrete words are embodied mainly in these representations. The integration and synchronization of the attention and executive control networks better predict concrete verbal memory compared to abstract verbal memory, indicating that the whole brain exhibits greater coordination to process concrete words.

Third, the individual concreteness effect positively correlates with the rsFC between the right ACC and regions mainly in the FPN (41.1%) and the DAN (13%). Similar to the rsFC of the right MTG, the nodes were mainly distributed in the FPN and the DAN. The ACC has been assumed to support response inhibition, target detection and response selection (Carter et al. 1998). The FPN may support executive control on a trial-by-trial basis, whilst the DAN may exhibit sustained activity to maintain and integrate ongoing cognition (Dosenbach et al. 2007). Specifically, amongst these nodes, the right middle frontal gyrus elicits greater activations during concrete word processing than during abstract word processing (Sabsevitz et al. 2005), and the right IFG exhibits modality-independent perceptual processing of the nonlinguistic features of words (Baumgaertner et al. 2013). The correlation of changes in activation between the ACC and the IFG is significantly stronger under concrete conditions than under abstract conditions (Kaneda and Osaka 2008). The activation of the right hemisphere may be elicited by nonlinguistic processing, such as by imagery features, of the word stimuli. The nodes with functional connectivity to the right ACC are all located exclusively in the right hemisphere, supporting the role of the right hemisphere in concrete word processing. This finding is in accordance with dual-coding theory which emphasizes the joint role of the right hemisphere in supporting concrete word processing (Paivio 1991).

The rsFC results show that the stronger connectivity between regions predicted a stronger concreteness effect, indicating that the verbal memory of concrete words may benefit more from synchronization and integration between brain regions. Task-based functional connectivity and rsFC exhibit similar synchronized patterns (Vidaurre et al. 2017), implying that stronger connexions amongst resting-state functional networks could facilitate faster processing of concrete words (Hemati and Hossein-Zadeh 2018). In addition, the results of this study also indicate that greater coherence of engagement of the right hemisphere predicts a greater difference in verbal memory of the two types of words. Compared to GMV, rsFC has greater predictive power regarding the strength of the concreteness effect, which indicates that rsFC is a more reliable biomarker for assessing the strength of the concreteness effect because brain connexions determine brain functions (Thiebaut de Schotten and Forkel 2022).

Our study contains some limitations. First, the subjects in our study are college students. Further research should examine children, i.e. subjects in the process of cognitive development, as well as older individuals, i.e. subjects exhibiting verbal memory deterioration. Second, we investigate whether rsFC explains the variation in the individual concreteness effect using seeds derived from anatomical analysis; thus, we cannot exclude the possibility that other sites might be responsible for this variation. Finally, this study examines the association between verbal memory performance and intrinsic brain characteristics (GMV and rsFC). Modulation via brain stimulation, such as transcranial magnetic stimulation or transcranial direct current stimulation, may help identify the roles of the ROIs from this study and alterations in rsFC in the strength of the concreteness effect.

Conclusion

This study investigates the structural and functional neural substrates underlying the concreteness effect. We find that the GMV of the left IFG, the right MTG, the right ACC and the right SMA negatively correlates with the strength of the concreteness effect. The rsFC of the left IFG, the right MTG, and the right ACC, with nodes mainly in the DMN, FPN and DAN, positively correlates with the strength of the concreteness effect. The GMV and rsFC jointly and individually predict the strength of the concreteness effect in individuals.

Appendix

Concrete words		Abstract words	
Letter	White clouds	Violence	Aid
Beer	Garden	Delight	Resources
Photo	Soybean	Virtue	Interests
Egg	Judge	Ability	Link
Pigeon	River bank	Presentation	Effect
Store	Nursery garden	Fame	Remnants
Plum blossom	Stretcher	Wealth gap	Reform
Couplet	Gemstone	Philosophy	Riot
Planet	Tomato	Representation	Sensibility
Straw	Rose	Intension	Illusion
Raincoat	Paint	Talent	Opportunity
Moon	Stool	Happiness	Mood
Snowflake	Lantern	Setback	Security
Chalk	Nurse	Rumor	Warfare
Newspaper	Liver	Authority	Predicament
Sparrow	Porcelain	Impressions	Idea
Breast	Beard	Ending	Ambition
Cloud	Island	Suffering	Supply
Flame	Engine room	Enthusiasm	Trouble
Bulb	Secretary	Beginning	Force
Train	Floor	Outside	Aspiration
Band	Rubber	Dignity	Example
Father	Pointer	Expectation	Bias
Honey	Wadded jacket	Utility	Miracle
Red star	Tube	Increase	Reputation
Sculpture	Willow	Noema	Ending
Walnut	Dock	Esteem	Microscale
Dessert	Crab	Disadvantage	Limit
Throat	Beach	Effort	Vital part
Glacier	Flower	Knowledge	Target
Rice	Banana	Public order	Courage
Lamp	Eyebrow	Question	Attainments
Pineapple	Parcel	Progress	Accumulation
Mine	Drug	Duty	Difficulty
Shoulder pole	Bullet	Manners	Taste
Record	Spider	Decision	Experience

English translations of the Chinese concrete and abstract words used in the task.

Author contributions JY and WL wrote the main manuscript text. WL collected data and prepared all the figures and tables. JY, WL, TZ, JZ, ZJ and LL reviewed and editted the manuscript. LL supervised the whole study.

Funding This research was supported by grants from the National Nature Science Foundation of China (62176045), the Sichuan Science and Technology Program (2023YFS0191, 2022014), the 111 project

(B12027), and the Fundamental Research Funds for the Central Universities (ZYGX2020FRJH014).

Availability of data and material (data transparency) The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Code availability (software application or custom code) The code used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest The authors declare that they have no competing interests.

Ethics approval We obtained written informed consent of each subject prior to participation. The experimental procedures were carried out in accordance with the Declaration of Helsinki and were approved by the Institutional Review Board of the University of Electronic Science and Technology of China.

Consent to participate and Consent for publication Informed consent was obtained from all participants included in the study.

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