



The divided brain: Functional brain asymmetry underlying self-construal

Gen Shi^a, Xuesong Li^{a,*}, Yifan Zhu^a, Ruihong Shang^a, Yang Sun^b, Hua Guo^b, Jie Sui^{c,*}

^a School of Computer Science and Technology, Beijing Institute of Technology, Beijing, PR China

^b Center for Biomedical Imaging Research, Department of Biomedical Engineering, School of Medicine, Tsinghua University, Beijing, PR China

^c School of Psychology, University of Aberdeen, Aberdeen, UK

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ABSTRACT

Self-construal (orientations of independence and interdependence) is a fundamental concept that guides human behaviour, and it is linked to a large number of brain regions. However, understanding the connectivity of these regions and the critical principles underlying these self-functions are lacking. Because brain activity linked to self-related processes are intrinsic, the resting-state method has received substantial attention. Here, we focused on resting-state functional connectivity matrices based on brain asymmetry as indexed by the differential partition of the connectivity located in mirrored positions of the two hemispheres, hemispheric specialization measured using the intra-hemispheric (left or right) connectivity, brain communication via inter-hemispheric interactions, and global connectivity as the sum of the two intra-hemispheric connectivity. Combining machine learning techniques with hypothesis-driven network mapping approaches, we demonstrated that orientations of independence and interdependence were best predicted by the asymmetric matrix compared to brain communication, hemispheric specialization, and global connectivity matrices. The network results revealed that there were distinct asymmetric connections between the default mode network, the salience network and the executive control network which characterise independence and interdependence. These analyses shed light on the importance of brain asymmetry in understanding how complex self-functions are optimally represented in the brain networks.

1. Introduction

The quest to understand the self and its role in guiding human behaviour is long-standing in psychology and other disciplines. From the beginning of scientific psychology and psychiatry, researchers distinguished different dimensions of the self (Freud, 1915). Since then, the self has been broadly defined concerning other people, identity, social contexts and cognitive capacities (Bandura, 1991; Conway and Pleydellpearce, 2000; Morris, 1979; Oyserman et al., 2002; Sedikides and Skowronski, 1997; Shavelson et al., 1976; Triandis et al., 1988). One critical dimension to define the self is its relationship to society and cultural contexts (Sui et al., 2021), initially termed self-construal and consisting of independence and interdependence (Markus and Kitayama, 1991), or known as individualism versus collectivism (Triandis et al., 1988). Individuals who hold a strong independent self-construal are prevalent in Western cultures where people tend to maintain independence from others and emphasize their unique inner attributes. In contrast, individuals in Eastern cultures tend to hold an interdependent self-construal that stresses links to other people, especially close others (e.g., families and friends), collectivist values, social norms and duties. A primary distinction between independence and interdependence is the relationship to other people, that is, defining

the self from a 'me' or 'us' perspective (Oyserman and Lee, 2008). Although this self-concept was initially developed from research on cross-cultural differences, considerable evidence demonstrated that orientations of independence and interdependence may be held within individuals, characterised the dynamic nature of the culture and self-relationship (Hong et al., 2000; Singelis et al., 1995). This multicultural minds in individuals are associated with individual variations in the brain (Kitayama and Uskul, 2011; Li et al., 2018; Wang et al., 2017). Therefore, the neural bases underlying self-functions of independence and interdependence has become an important topic in neuroscience because it may provide a propitious window to understanding how the brain deals with complex social information and concepts shaped by environmental forces in individuals.

A wide range of brain regions linked the orientations of independence and interdependence from the frontal regions (e.g., orbitofrontal cortex, OFC; ventral and dorsal medial prefrontal cortex, vMPFC, dMPFC; dorsolateral prefrontal cortex, DLPFC; inferior frontal gyrus, IFG), the anterior and posterior cingulate cortex (ACC, PCC), parietal and temporal regions, such as the inferior parietal lobule, precuneus, and temporoparietal junction (TPJ) to occipital areas, including the fusiform gyrus and calcarine sulcus (Han and Ma, 2014; Kitayama et al., 2017; Wang et al., 2017), using different methods (Kitayama and Uskul, 2011). Evidence from anatomical structural anal-

* Corresponding authors.

E-mail addresses: lixuesong@bit.edu.cn (X. Li), jie.sui@abdn.ac.uk (J. Sui).

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yses demonstrated that cultural experiences shape individuals' brain structures (Chee et al., 2011; Draganski and May, 2008; May and Gaser, 2006). Although some researchers argued that these changes in anatomical structures were not solely attributed to cultural experiences, accumulated evidence showed that higher independent self-construal scores were associated with increased grey matter volume in the frontal lobe, including the vMPFC and DLPFC, and right rostrolateral prefrontal cortex, parietal-occipital areas in the right fusiform cortex and left post-central cortex (Li et al., 2018; Wang et al., 2017). These regions reflect high-level self-evaluation, mentalizing the mental states of oneself and others, a sense of agency, and low-level self-perception. Higher interdependent self-construal scores, on the other hand, are associated with decreased grey matter volume in the OFC, which reflects reduced self-interest (Kitayama et al., 2017), and increased volume in the occipital regions, including the bilateral calcarine regions extending to the lingual gyrus, which reflect enhanced global attention to the environment as a whole rather than local objects (Nisbett et al., 2001; Wang et al., 2017), and increased volume in the occipital regions, including the bilateral calcarine regions extending to the lingual gyrus, which reflect enhanced global attention to the environment as a whole rather than local objects (Nisbett et al., 2001; Wang et al., 2017). The voxel-based morphometry analysis in these studies has widely been used to identify the neural localization of self-functions (e.g., orientations of independence and interdependence). Such results are also consistent with task-relevant functional magnetic resonance imaging (fMRI) studies that examined the functions of specific brain regions related to self-construals (Chiao et al., 2009; Harada et al., 2020; Ray et al., 2009; Sui and Han, 2007). It should be noted that these critical regions associated with self-construal from existing voxel-based morphometry and fMRI studies are part of well-established networks such as the default mode network (DMN, e.g., MPFC) and the executive control network (ECN, e.g., DLPFC) (Molnar-Szakacs and Uddin, 2013; Scalabrini et al., 2021). It therefore seems that the connections of these regions' associated networks may also be necessary for self-construal (Liang et al., 2015; Uribe et al., 2020).

Functional connectivity approaches have previously been used to investigate the roles of neural networks in self-referential processing (Enzi et al., 2009; Grigg and Grady, 2010; Johnson et al., 2002; Wuyun et al., 2014; Yang et al., 2013). Especially, because brain activity related to self-related processes are intrinsic, resting-state functional magnetic resonance imaging (rs-fMRI) have received great attention in self research (Biswal et al., 2010; Schneider et al., 2008). For example, the resting state brain activity are presumed to be spontaneous and intrinsic, and have been demonstrated in several brain function networks (e.g., DMN) (D'Argembeau et al., 2005; Northoff et al., 2011). The DMN is thought to reflect self-referential processing in a bottom-up fashion (Humphreys and Sui, 2016; Rahman et al., 2020). It interacts with other brain regions and networks such as the ECN and salience network (SN) for control of human behaviour (Sui and Gu, 2017). Yang and his colleagues found that autobiographic memory retrieval, rather than semantic memory retrieval, correlates with active coupling between the DMN and the hippocampus (corresponding to memories), because retrieval of autobiographic memory not only includes self-referential processes, but also evokes concrete self-relevant facts and memories (Yang et al., 2013). Using task-irrelevant resting-state rs-fMRI analyses, Grigg and Grady found that the DMN functional connectivity as an integrated whole was influenced by preceding self-referential tasks in which participants judged whether a personality trait appropriately described themselves or a familiar other (Grigg and Grady, 2010). Moreover, neuropsychological evidence in patients with chronic stroke revealed that brain damage in the vMPFC and insula led to a reduced self-referential processing (Sui, 2016; Sui et al., 2015), consistent with a loss of self-influence after brain damage in the DMN and the SN. In contrast, brain damage in the dorsal frontoparietal regions led to an enhanced self-referential processing, suggesting the release of attentional control extragrating self-processing after brain lesions in the ECN (Sui et al.,

2015). Collectively, these findings indicate the functional roles of these key neural networks in self-referential processing.

However, little is known about the contribution of functional connectivity specifically to self-construal. Only one study to date has evaluated the role of functional connectivity in self-construal using rs-fMRI (Li et al., 2018). In seed-based functional connectivity analysis, the authors found that the connectivity within the DMN (e.g., PCC/PCU and MPFC) and within the ECN (e.g., TPJ) positively correlated with the independent (vs. interdependent) scores, whereas the negative connectivity between the DMN (E.G., PCC/PCU) and the ECN (e.g., TPJ) negatively correlated with independence (vs. interdependence) (Li et al., 2018). The results indicate the importance of network synchronization for self-construal, and the interaction within and between the DMN and the ECN might reflect the complex engagement of different levels of self-referential processing such as the bottom-up reflexion and inference-based control processes (Johnson et al., 2002; Northoff et al., 2006; Sui, 2016; Sui and Gu, 2017; Uddin et al., 2007). This study provides the first confirmation of the relationship between functional connectivity and self-construal. However, as this study involved a small sample ($n = 51$) and the main results of functional connectivity came from seed-based analyses, it requires further validation.

It has been suggested that machine learning techniques are useful to learn the neural connectivity patterns with no seed selection bias (Al-Jarrah et al., 2015; Anticevic et al., 2015; Hoerl and Kennard, 1970; Huynh-Thu et al., 2012; Qiu et al., 2016; Uddén et al., 2019). A hypothesis-free and whole-brain analysis may reveal more global properties related to self-construal, involving a more complex combination of activity throughout the brain (Beucke et al., 2013; Gruner et al., 2014). We therefore set out to test the whole-brain functional connectivity related to self-construal using the machine learning approach in a large sample of participants ($n = 307$). There are five possible connectivity combinations to define the whole-brain functional connectivity, including brain Asymmetry Matrix measured by the connectivity asymmetry across different regions of the two hemispheres, two Hemisphere specialization Matrix by the intra-hemispheric (left or right) connectivity, Global connectivity Matrix by the sum of the two intra-hemispheric connectivity, and Interactive Matrix by inter-hemispheric interactions (see Section 2.5.1). Through examining and comparing all these possible matrices in predictive efficiency for self-construal, our study thus aimed to assess which connectivity matrix best predicts self-construal without a prior bias and to delineate neural networks associated with orientations of independence and interdependence by mapping the best predictive matrix to the three key neural networks including the DMN, the SN, and the ECN (Andrews-Hanna et al., 2014; Anticevic et al., 2012; Bressler and Menon, 2010).

Specifically, in contrast to the traditional static functional connectivity method that assumes temporal stationarity of the entire scan period, we used a dynamic connectivity method in rs-fMRI analysis (Li et al., 2019). It has been suggested that functional connectivity within and across neurocognitive networks (i.e., DMN, ECN and SN) is not stationary but rather fluctuate (Douw et al., 2016; Marusak et al., 2017). Recent studies have demonstrated the advantages of the dynamic method over the conventional static method in predicting psychological traits (Abrol et al., 2017; Chen et al., 2016; Li et al., 2019; Liegeois et al., 2017; Liegeois et al., 2019; Mash et al., 2019). For example, Mash et al. found that the dynamic connectivity method, in comparison to the static connectivity method, better predicted the differences between autism spectrum disorders (ASD) and typically developing (TD) individuals.

2. Materials and methods

2.1. Participants

There were three hundred and fifty-nine participants who were undergraduate or graduate students. All participants were right-handed. Informed consent was obtained from participants prior to the study ac-

ording to procedures approved by the Ethics Committee of the School of Medicine at Tsinghua University. Thirty-six participants with a mean frame-wise displacement value that exceeded the mean >0.5 mm or maximum frame-wise displacement >1 mm were excluded from data analyses as their results may be contaminated by head movements. Also, sixteen participants with uncompleted data were excluded from data analysis. Thus, a dataset of 307 participants was derived for further analysis (156 males, 151 females, ages 18–37 years, mean age 22.70 ± 3.05 years).

2.2. Measurements of independence and interdependence orientations

The participants completed a widely used measurement of independence and interdependence, the self-construal Scale with Chinese translation (Singelis, 1994). It consists of thirty items, half of which assess independence, and the remaining items assess interdependence. Participants were instructed to rate how much they agreed with each item using a 7-point Likert-type scale that ranged from 1 (strongly disagree) to 7 (strongly agree). Larger scores indicated a relatively larger orientation towards independence (mean value 72.61 ± 9.71) or interdependence (mean value 76.22 ± 9.34). The Cronbach's alpha reliabilities for the independence and interdependence subscales in this study were .76 and .78, respectively, consistent with previous studies (Fernández et al., 2005; Kitayama et al., 2017; Singelis and Sharkey, 1995).

2.3. Image acquisition

Brain imaging data were acquired at the center of Bio-Medical Imaging Research (CBIR), Tsinghua University using a 3T Philips Achieva MRI scanner (Philips Healthcare, Best, The Netherlands) with a 32-channel head coil. The gradient coil and the slew rate applied in the current study were 40 mT and 200 mT/m/s. There was a MRI QC test including the SNR and TSNR test in the morning on a daily basis. Head motion was controlled using a tight but comfortable foam padding. Resting-state fMRI images were acquired using a T2-weighted echo-planar imaging sequence: repetition time (TR) = 2300 ms, echo time (TE) = 35 ms, flip angle (FA) = 90° ; slice thickness = 2.5 mm with gap = 1.0 mm; slice orientation is transverse; voxel size = 2.5 mm \times 2.5 mm \times 2.5 mm; acquisition matrix = $96 \times 96 \times 37$; field of view (FOV) = 240×240 mm², 37 ascending slices. During the functional scan, the participants were instructed to open their eyes, not to think of anything, and not to fall asleep. The total duration of the scan was 508.3 s. High-resolution T1-weighted spoiled gradient-echo structural images were also obtained at a slice thickness of 1 mm with no gap in coronal view (TR = 8.1 ms, TE = 3.7 ms, 160 contiguous sagittal slices, flip angle. = 8° , FOV = 240×240 mm², acquisition matrix = $240 \times 240 \times 160$, voxel size = $1 \times 1 \times 1$ mm).

2.4. Data preprocessing and dynamic network construction

Functional images were preprocessed using the GRETNA (Wang et al., 2015) (www.nitrc.org/projects/gretna) and SPM12 toolkits (www.fil.ion.ucl.ac.uk/spm) with the following steps: (1) the first 10 volumes of images discarded to ensure magnetization equilibrium; (2) slice timing correction with the first slice; (3) head-motion estimation and correction with a 0.01–0.10 Hz frequency bandpass; and (4) the first scan of fMRI time series co-registered to the T1-weighted images then normalized to the Montreal Neurological Institute (MNI) template space and spatially smoothing with a 4 mm full-width at half-maximum Gaussian kernel. The results without Global signal regression (GSR) procedure are reported because they may include valuable information (Chen et al., 2012; Liu et al., 2017; Nalci et al., 2017; Scalabrini et al., 2020) (results with GRS are reported in Supplementary Material Section S.1.6).

Based on the construction of the dynamic functional connectivity using GRETNA software, we used a constant-step and constant-size win-

dow to capture the time-change feature of the functional connectivity for the 246 ROIs. As machine learning models typically benefit from the large number of available input features, we therefore used a fine-grained human Brainnetome Atlas, with 210 cortical and 36 subcortical subregions, which contains information on both anatomical and functional connection (Fan et al., 2016). Then we divided the time series data into 22-TR windows. The window was step-wise by 1 TR with the 221-TR length scan. There were 200 consecutive windows across the entire scan. We computed the nodal efficiency of each ROI for each window. There was an array of 200 windows for every ROI and a 246×246 nodal efficiency matrix for each participant. We computed Pearson's R-value between each array of nodal efficiency for all ROIs. The dynamic connectivity matrix (shape 246×246 for each subject) was acquired using this method. Each row of the matrix (shape 1×246) represents the dynamic connection between one ROI with the whole ROIs. Hence, the connectivity matrix characterizes the ROI connections in whole-brain at the global level, and then used for feature selection and model prediction analysis.

2.5. Data analysis

2.5.1. Definition of connectivity matrices

There were five possible matrices to measure the whole-brain functional connectivity including brain Asymmetry Matrix, left Hemisphere specialization Matrix, right Hemisphere specialization Matrix, Global connectivity Matrix, and Interactive Matrix. Specifically, we used the adjacent matrix to characterize the weighted network of whole-brain functional connectivity.

Functional asymmetry was defined by the Asymmetric matrix between the Left and Right intra-hemispheric matrix - the absolute value of the Left-brain matrix minus the Right-brain matrix (Fig. 1f). The Sum of the intra-hemispheric connectivity in the two hemispheres was measured as the Global matrix - the Left-brain matrix concatenating the Right-brain matrix (Fig. 1a). The inter-hemispheric communication between hemispheres was indexed as the Interactive matrix, the connectivity between the left and right hemispheres (Fig. 1b). The left or right Hemisphere Specialization Matrix referred to brain connectivity in each hemisphere (Fig. 1c and d).

2.5.2. Feature selection

We examined the linear relationships between self-construal (orientations of independence and interdependence) and the functional connectivity measured by the edges of every input connectivity matrix (e.g., Asymmetric matrix or Interactive matrix) using Pearson correlation analysis. Functional connections with p -values <0.05 in the correlations were kept for further analysis. We then concatenated the notable edges as a vector for every input connectivity matrix. In this work, there were 5 connectivity measures (Asymmetric Matrix, Interactive Matrix, Global Matrix, Left hemisphere specialized Matrix, Right hemisphere specialized Matrix) and 2 scores (independence, interdependence). Thus, there were 10 combinations in total.

2.5.3. Model prediction

We performed model prediction using three widely used linear machine-learning models to avoid bias for model selection, the Ridge (Hoerl and Kennard, 1970), Lasso (Tibshirani, 1996), and Support Vector Machine model (Boser et al., 1992) with linear kernel. In contrast to traditional statistics, these machine-learning computational analyses enabled us to discover multivariate patterns in self-functions without prior assumptions. Fig. 2a shows the flow of parameter selection for each model: (1) identification of the approximate global optimal parameter using the cross-validation method in a large parameter space; (2) sampling the parameters 50 times using a normal distribution (mean value = global optimal parameter, variance = square root of the optimal value, the sampling parameter with a negative

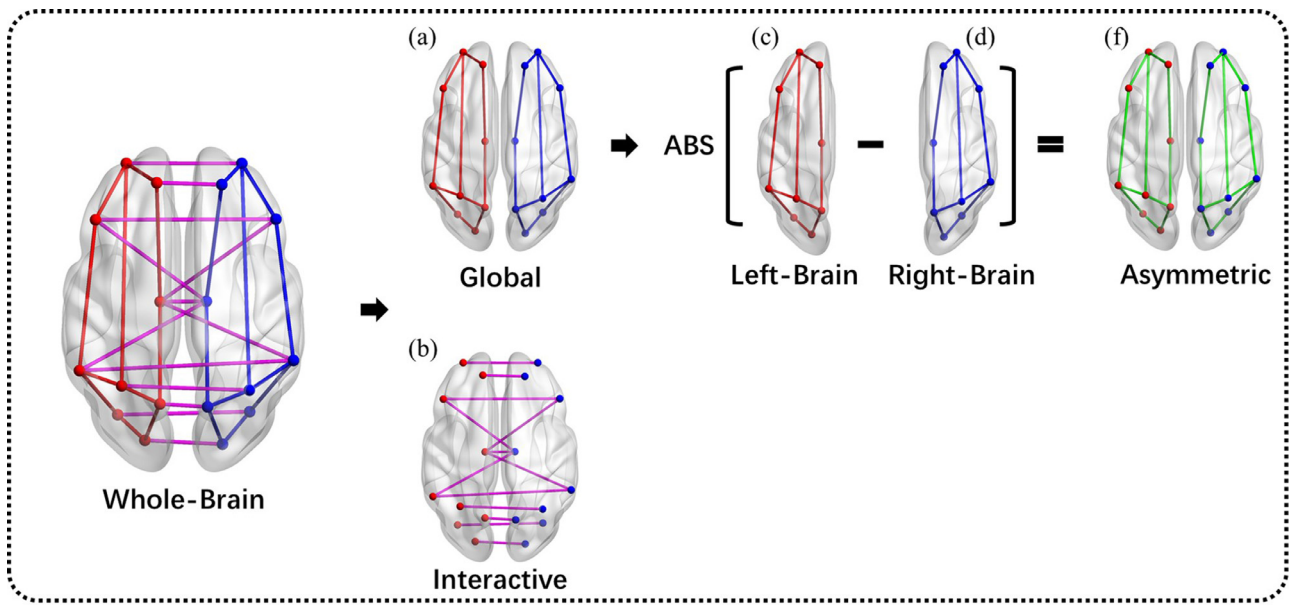


Fig. 1. Illustration of the functional connectivity asymmetry (the Asymmetry Matrix) (f), the whole-brain connectivity (the Global Matrix) (a), and the inter-hemispheric communication (the Interactive Matrix) (b), the left or right Hemisphere Specialization Matrix (c and d).

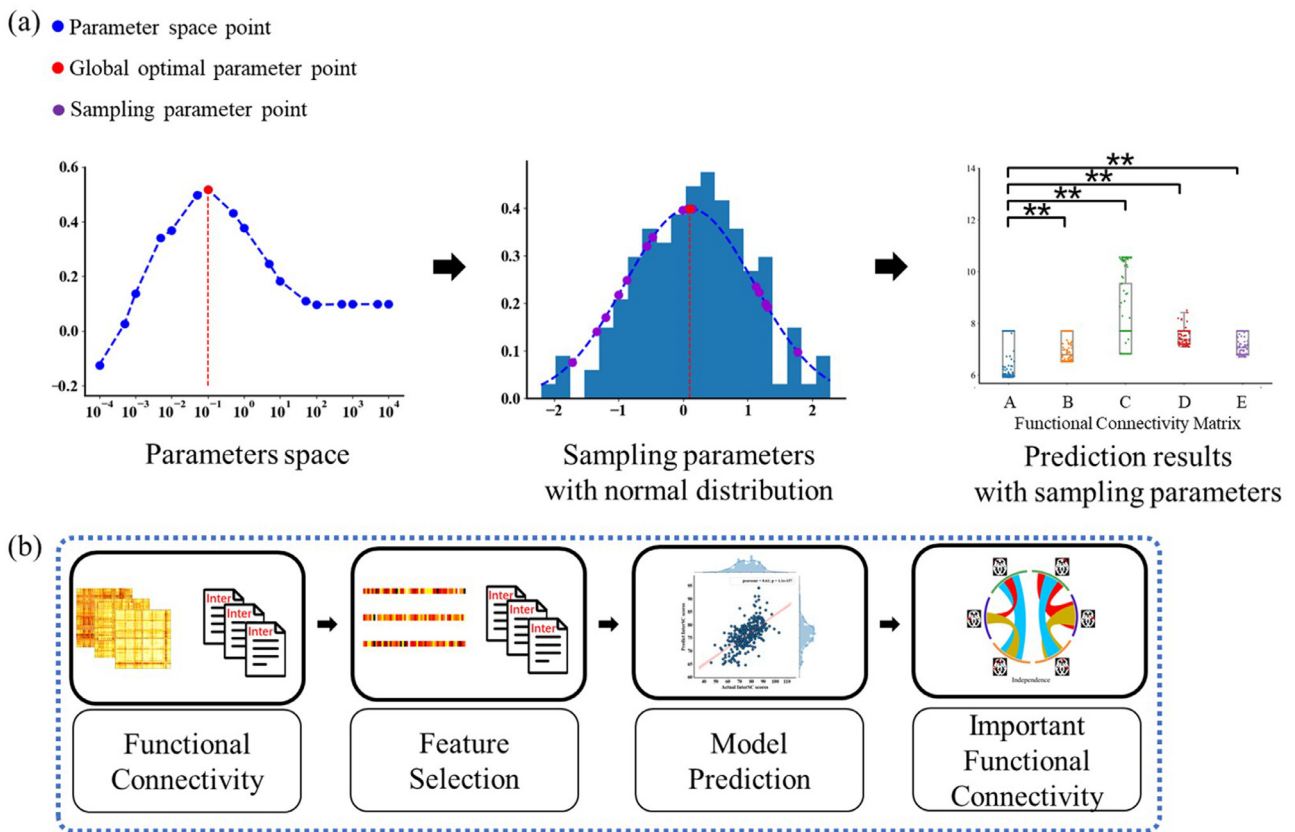


Fig. 2. (a) The flow of parameter selection for each machine-learning model. (b) The schematic pipeline of prediction tests with functional connectivity.

value replaced with its absolute value); (3) evaluation of the performance of model prediction in which the root mean square error (RMSE), mean square error (MAE), and Pearson correlation coefficient R-value of predicting self-construal scores and the real values were computed, and the cross-validation method was used by taking 10-fold cross-validation with 30 samples as the testing dataset and the remaining

samples as the training set to measure the out-of-sample prediction performance.

Fig. 2b shows the pipeline of the prediction task. The feature selection process yielded the vector representation from the functional connectivity matrix. The subsequent process predicted the independent and interdependent self-construal scores of the three machine-learning

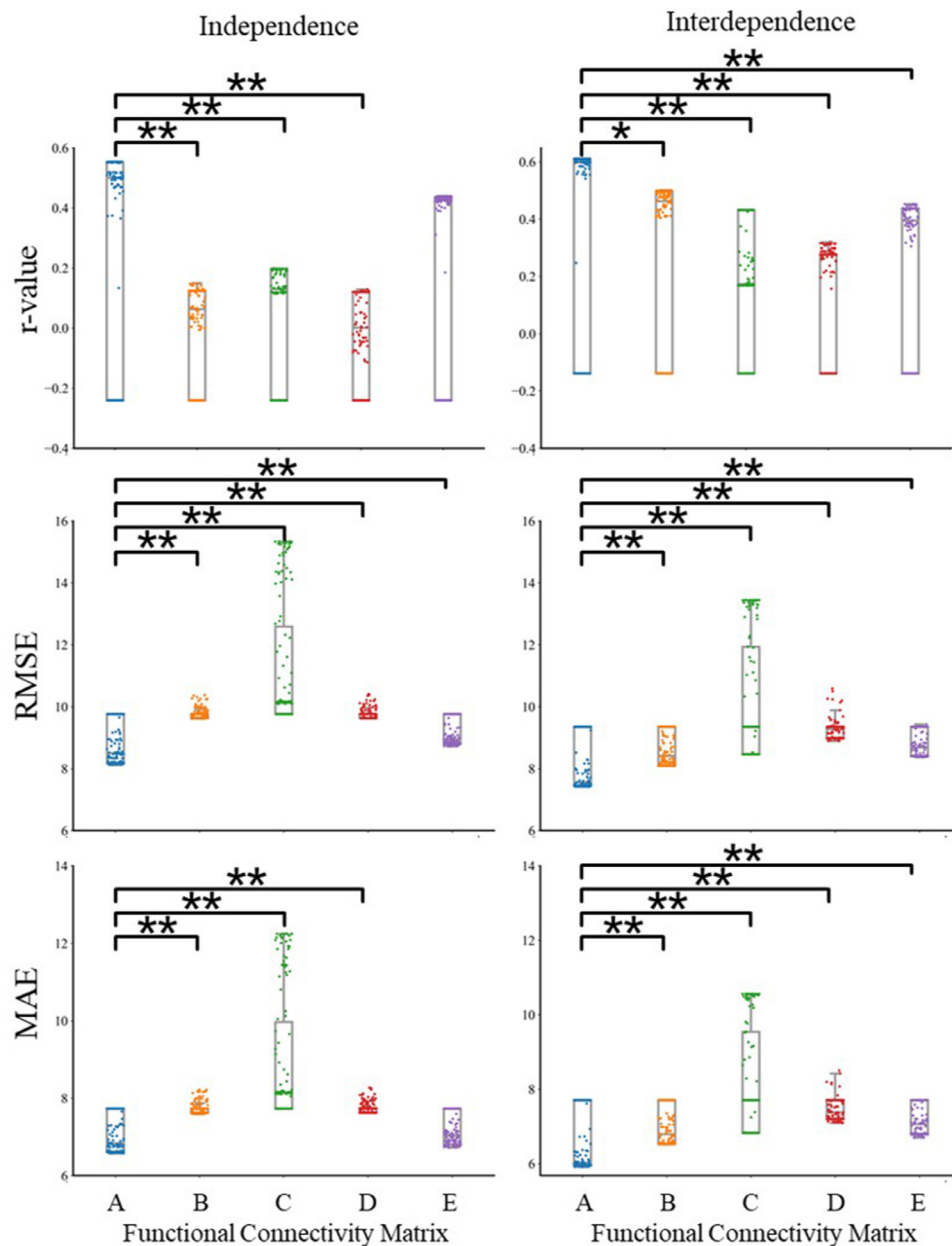


Fig. 3. The prediction results of each connectivities (A-Asymmetric, B-Interactive, C-Global, D-Left, E-Right matrices) for orientations of independence and interdependence. * if $p < 0.05$ and ** if $p < 0.001$ for permutation test. R value: Pearson correlation r value, RMSE: root mean squared error, MAE: mean absolute error

models with sampling the parameters 50 times in each model. We compared the 150 times prediction performance for each matrix (5 matrices for independent self-construal, 5 for interdependent self-construal). We examined which connectivity matrix out of 5 possible matrices better predicted independent and interdependent self-construals. Experimental comparison between different machine-learning models with the random sampling parameters was used to avoid a biased result from manually selected models and parameters.

To verify the above results, we repeated the primary analyses on feature selection and model prediction using the Individualism and Collectivism Scale (Singelis et al., 1995) in the same population ($n = 304$). The results that the asymmetric matrix, compared to other connectivity matrices, best predicted self-construals, were reproduced (see the Supplementary Materials, Section S.1.5).

Finally, we delineated the critical functional connectivity, specifically associated with independent and interdependent self-construals from the best prediction models. To reduce parameter estimation bias, we selected the top 5 prediction models for orientations of independence and interdependence each (Rubin et al., 2018; Xie et al., 2017). We re-

ported the top 200 functional connectivities with high weights among these models. These connections were then mapped to the three networks (i.e., ECN, SN, DMN) (Yeo et al., 2011), representing orientations of independence and interdependence separately.

3. Result

3.1. Functional asymmetry predicts independence

Experimental comparison showed that *Asymmetric Matrix*, in comparison to the *Global Matrix*, the *Interactive Matrix*, the *left and right Hemispheric Specification Matrices*, better predicted independence (Fig. 3). The results were consistent between the three types of prediction metrics, r value, RMSE, and MAE. Permutation tests revealed more accurate predictions from the Asymmetric matrix than all other matrices.

To verify the above results, we compared the top 5 performances for each prediction. We calculated the correlation R-value between the true scores and the predicted scores (see Table 1, Fig. 4). The result showed that compared to other matrices, the *Asymmetry Matrix* best predicted

Table 1
Prediction values and improvement from the 5 functional connectivity matrices.

FC matrix	Independence			Interdependence		
	R-value	RMSE	MAE	R-value	RMSE	MAE
Interactive Matrix	0.15	9.62	7.60	0.50	8.09	6.51
Sum/global Matrix	0.20	10.25	8.12	0.43	8.41	6.81
Left Matrix	0.12	9.64	7.63	0.32	8.91	7.10
Right Matrix	0.44	8.91	7.10	0.45	8.38	6.74
Asymmetric Matrix	0.55	8.16	6.60	0.61	7.45	5.96
Improvement Rate	20.00%	9.20%	7.58%	18.03%	8.59%	9.23%

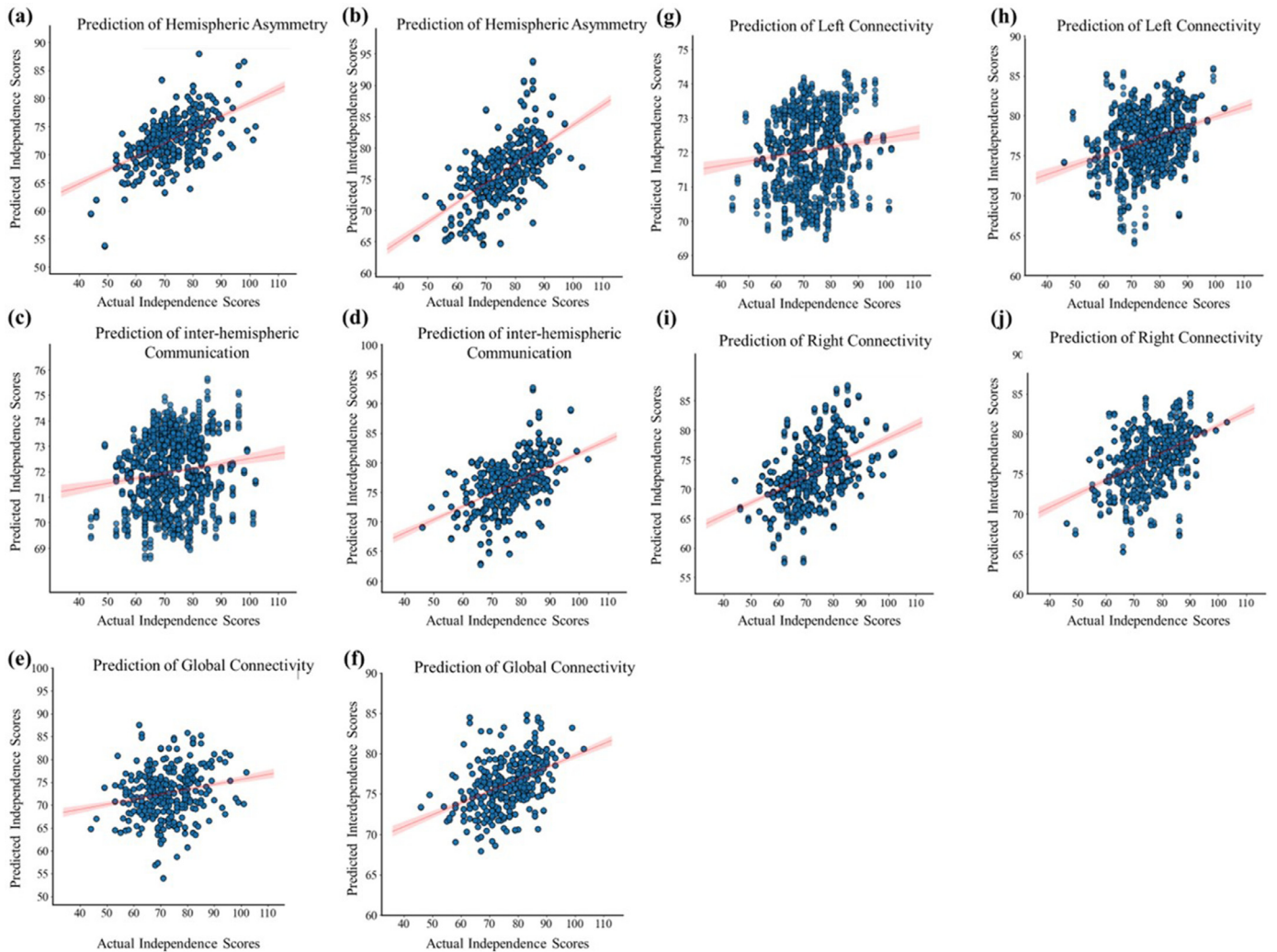


Fig. 4. The top 5 prediction performances of each task. (a) Asymmetric-Independence, (b) Asymmetric-Interdependence, (c) Interactive-Independence, and (d) Interactive-Interdependence, (e) Global-Independence, (f) Global-Interdependence, (g) Left-Independence, (h) Left-Interdependence, (i) Right-Independence, (j) Right-Interdependence

independence. In particular, although the *Global Matrix* contained the same initial information as the *Asymmetric Matrix*, the model comparison showed that the prediction performance improved at least 10% in the *Asymmetric Matrix* over the *Global Matrix*. The results were statistically tested by the ANOVA method (see the S.1.3 section).

3.2. Functional asymmetry predicts independence

In line with the results in independence, permutation tests showed that *Asymmetric Matrix* was the best predictive matrix for interdependence (Fig. 3). The results were robust among the three types of prediction metrics, r value, RMSE, and MAE. Again, the model comparison

revealed that the prediction performance improved at least 10% in the *Asymmetric Matrix* over the *Global Matrix*. The analysis of the top 5 performances for each prediction verified these results. The *Asymmetric matrix* more accurately predicted independence than other connectivity matrices (Table 1, Fig. 4, the S.1.3 section).

3.3. Network connectivity in independence and interdependence

To determine the roles of neural networks in orientations of independence and interdependence, we mapped the crucial functional connections from our best predictive models (i.e., the asymmetry connectivity

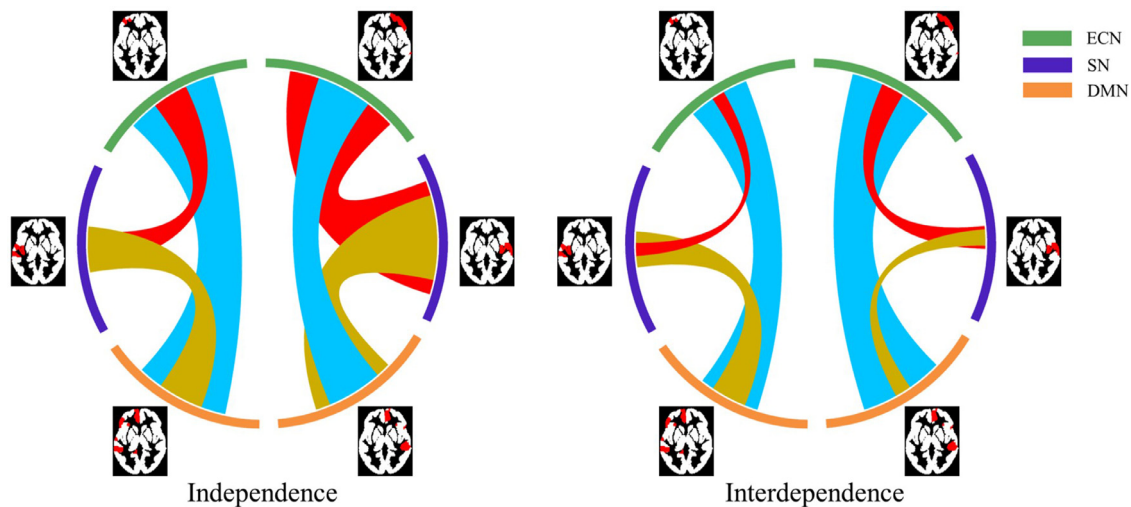


Fig. 5. Crucial inter-connections between 3 neurocognitive networks obtained from machine learning models for orientations of independence and interdependence respectively. The width of ribbons represents the mean connection strength across subjects between neurocognitive networks. The colour of the ribbons is just to distinguish each other.

matrix) to the DMN, SN, and ECN. Figs. 5 and 6 illustrate the connectivity asymmetry among the three networks.

For independence, there were stronger functional connections between the DMN and the ECN in the left brain than in the right brain, via the intra-frontal and frontal-temporal connectivity (SFG₅-MFG₂₁, MFG₂₃-IFG₃₁, IFG₃₅-IFG₃₁, OrG₄₁-SFG₁, SFG₁-pSTS₁₂₁, MFG₁₉-MTG₈₃, MFG₂₁-MTG₈₃, MFG₂₁-pSTS₁₂₁). The functional connectivity between the DMN and the SN showed the opposite pattern; there were greater DMN-SN connectivity in the right hemisphere than in the left hemisphere, via the frontal-parietal connectivity (PoG₁₆₀-SFG₁₄, PoG₁₆₀-OrG₄₂), parietal-temporal connectivity (PoG₁₆₀-STG₈₀, PoG₁₆₀-MTG₈₈) and frontal-temporal connectivity (PCL₆₆-MTG₈₄, STG₇₄-MTG₈₄); a similar pattern was observed in the connectivity between the ECN and the SN, mainly via the intra-frontal connectivity (OrG₄₆-PrG₅₄, OrG₄₆-PrG₅₈, OrG₄₆-PrG₆₀, MFG₂₈-PCL₆₆, MFG₂₀-PCL₆₆).

For interdependence, the functional connectivity between the DMN and the ECN showed the right hemispheric dominance, via the intra-frontal connectivity (MFG₂₀-SFG₆, MFG₂₈-OrG₄₄), frontal-parietal connectivity (MFG₂₄-IPL₁₄₄, MFG₂₈-IPL₁₄₄). In contrast, the DMN-SN connectivity demonstrated the left hemispheric dominance, via PrG₅₇-ITG₉₅, STG₇₅-ITG₉₅, PoG₁₆₁-CG₁₇₉, INS₁₇₁-OrG₄₁. There was a weak asymmetry pattern in the ECN-SN connectivity in the right brain, via the frontal-temporal connectivity (OrG₄₆-SFG₁₀, OrG₄₆-STG₇₆).

4. Discussion

Previous work has identified that self-construals are associated with a wide range of regions distributed across the two sides of the brain. However, the roles of connections of their associated networks have received little attention. Using the functional connectivity approaches, the current study revealed that orientations of independence and interdependence were underpinned by distinct asymmetric connectivity between the three networks (i.e., DMN, SN, ECN). First, the precise prediction of independence and interdependence was examined using input-based ablation experimental comparisons between all possible functional connectivity matrices with no a priori bias towards any measurement. Dynamic functional connectivity analyses revealed that the best prediction performance for self-construal came from the brain Asymmetry Matrix over the Global Matrix, the Interactive Matrix, and the Left/Right Hemisphere Specialization Matrix. Second, to identify which connections of the three networks were associated with self-construal,

we mapped the best predictive Asymmetric Matrix models to the three networks. Independence correlated with enhanced DMN-ECN connectivity in the left hemisphere and increased DMN-SN connectivity in the right hemisphere. In contrast, there were the opposite patterns for interdependence; the DMN-ECN connectivity showed a left hemispheric dominance and the DMN-SN connectivity with a right hemispheric dominance. The ECN-SN connectivity showed a right hemispheric dominance for both independent and interdependent self-construals.

Previous studies have emphasized hemispheric specialization in self-referential processing. For example, studies in neuropsychiatric and neurological patients that were related to brain lateralization (e.g., hallucinations, split-brain), revealed hemispheric specialization in self-recognition (Den Heuvel et al., 2009; Keenan et al., 2001; Sperry et al., 1979; Turk et al., 2002). Turk et al. (2002) found a left-hemisphere dominant for self-recognition in a split-brain patient. The authors claimed that brain networks in the left hemisphere are associated with a self-memory system that guides self-recognition. In contrast, Keenan et al. (2001) reported a right-hemispheric dominance for the retrieval of self faces compared to celebrity's faces in a recall task in five patients undergoing hemispheric specific anaesthesia (the WADA test). The approaches in these studies assessed the neural patterns of self-referential processing in each hemisphere and provided a qualitative difference of the two hemispheres in self-functions. Instead, the current study has proposed a quantitative approach to investigate functional connectivity for self-construal across the whole brain and link it to well-established cognitive neural networks. Our results showed that the Asymmetric connectivity Matrix best predicted independent and interdependent self-construals. The results may imply that individuals develop self-construal through social interactions with the environment and accumulated knowledge, which may benefit from the involvement of the two hemispheres and each of which dominates in different aspects of self-referential processes. The mixed results in previous patient studies may reflect different accessible aspects of self-referential processing in a given context (Kong et al., 2020). The current results support the view that brain asymmetry can effectively characterize psychological functions (Chen et al., 2019; Gotts et al., 2013; Kann et al., 2016).

Evidence from human to animal studies has showed that brain asymmetry is associated with various connections across the occipital, temporal, parietal and frontal circuits (Li et al., 2018; Vingerhoets, 2019). One important question is which circuit asymmetries are associated with independent and interdependent self-construals. Li et al. (2018) have reported that when the left PCC/PCu (part of the DMN) was selected

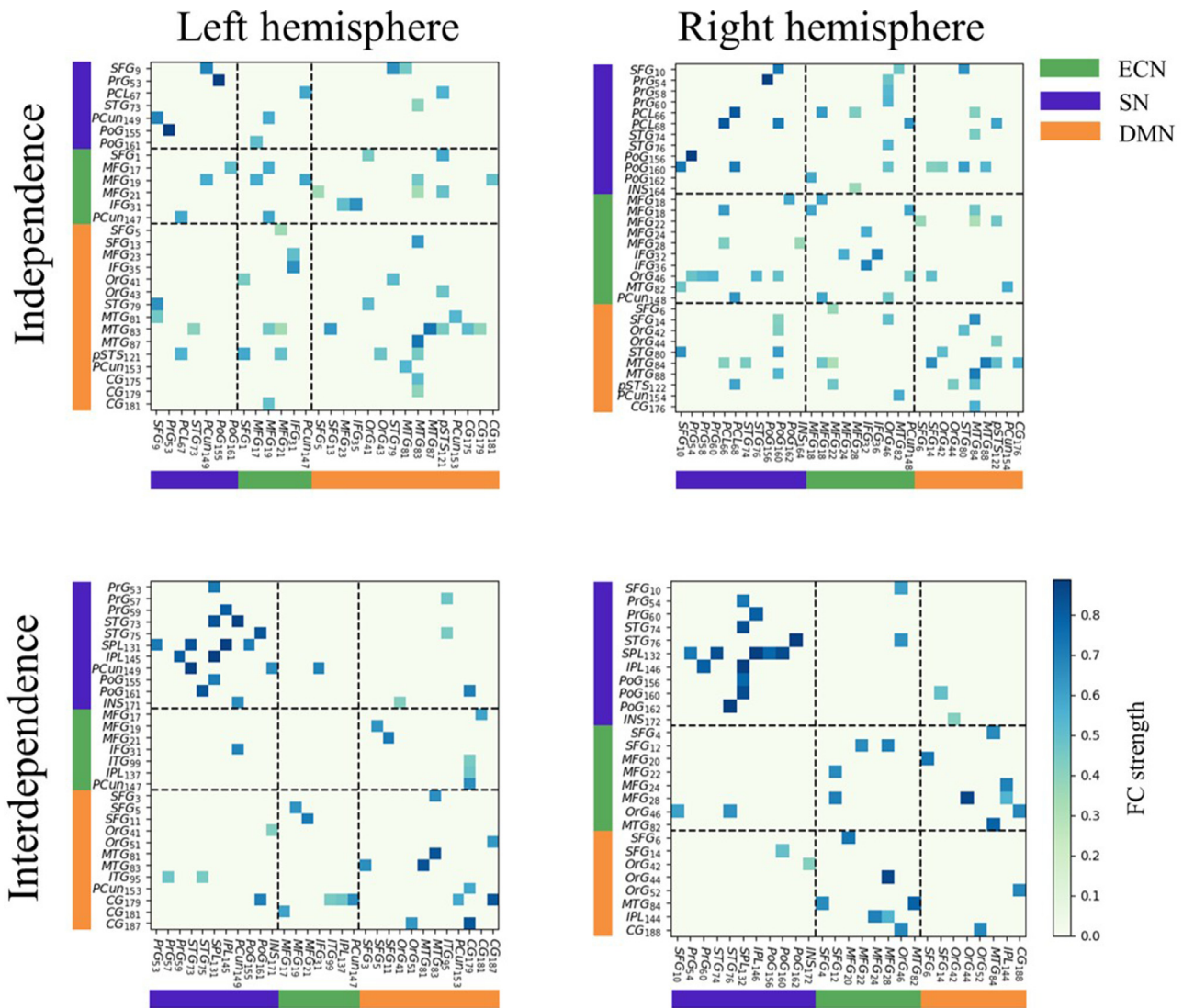


Fig. 6. Detailed crucial connections for orientations of independence (a) and interdependence (b), respectively. SFG-Superior Frontal Gyrus, MFG-Middle Frontal Gyrus, IFG-Inferior Frontal Gyrus, OrG-Orbital Gyrus, PrG-Precentral Gyrus, PCL-Paracentral Lobule, STG-Superior Temporal Gyrus, MTG-Middle Temporal Gyrus, ITG-Inferior Temporal Gyrus, FuG-Fusiform Gyrus, PhG-Parahippocampal Gyrus, pSTS-posterior Superior Temporal Sulcus, SPL-Superior Parietal Lobule, IPL-Inferior Parietal Lobule, Pcun-Precuneus, PoG-Postcentral Gyrus, INS-Insula Gyrus, CG-Cingulate Gyrus, MVOCc-MedioVentral Occipital Cortex, LOcc-lateral Occipital Cortex, Amyg-Amygdala, Hipp-Hippocampus, BG-Basal Ganglia.

as a seed, the connections between the seed and the left IFG and the right TPJ correlated with independence (vs. interdependence). When the right PCC/PCu was selected as a seed, the connections between the seed and the bilateral MPFC and the right TJP were associated with independence (vs. interdependence). A similar pattern was observed when the left IFG (part of the ECN) was used as a seed region. Li et al. (2018) measured functional connectivity between the ROIs, while our best predictive model came from the functional asymmetric matrix (the left-brain connectivity matrix minus the right-brain connectivity matrix). Although for this reason it is impossible to compare the two studies, the overall connectivity patterns, specifically for the connections through the DMN, appear to be similar. By mapping the best predictive matrix to the three networks without seed selection bias, the distinct functional asymmetry for independent self-construal occurred in the left DMN-ECN connections. The result is in line with previous fMRI studies demonstrating that enhanced coupling between the DMN (e.g., vMPFC) and the left ECN (e.g., pSTS) leads to a large self-bias in the perceptual matching task (Sui et al., 2013). In addition, our finding that the DMN-SN connectivity showed a right hemispheric dominance for independence

might reflect the direct linkage between self-referential processing and emotion processing, which has been observed in previous fMRI studies (Molnar-Szakacs and Uddin, 2013; Uddin et al., 2017; Yankouskaya and Sui, 2021). Therefore, the current results are consistent with the theoretical idea that the independent self-construal may reflect more on the personal and affective aspects of the self (Markus and Kitayama, 1991; Sui and Gu, 2017).

On the other hand, interdependence was associated with stronger DMN-ECN connections in the right brain but greater DMN-SN connectivity in the left brain. It is not clear why there are enhanced DMN-SN connections in the left hemisphere related to interdependence. One possibility is that individuals with higher interdependent self-construal scores may be more sensitive to socially salient stimuli in the environment (Sui et al., 2015), which requires increased activity in the left temporoparietal junction (Samson et al., 2004). The asymmetric networks were connected through the frontal regions, which have been found in previous MRI/fMRI studies in interdependence (Kitayama et al., 2017; Ray et al., 2009; Wang et al., 2013). The authors have argued that the involvement of these regions (e.g., bilateral OFC and TPJ, MPFC,

and the right middle frontal cortex) may reflect reduced self-interest (Kitayama et al., 2017) and enhanced theory of mind in more interdependent individuals (Ray et al., 2009; Sui and Han, 2007), as those individuals have a greater self-awareness in interpersonal relations. Therefore, our results of interdependence can be interpreted through the ‘we’ perspective (Oyserman and Lee, 2008).

Furthermore, we found a common ECN-SN connectivity pattern for independent and interdependent self-construals. The connectivity showed a right hemisphere dominance over the frontal and temporal regions. These regions have been argued to play a critical role in maintaining a sense of the self and mentalizing the mental states of others (Gallagher and Frith, 2003; Schurz et al., 2014; Sui and Gu, 2017). According to the previous work, our result might reflect that individuals, no matter with a greater independent or interdependent self-construal, have a strengthened sense of the self when they interact with the environment. Future research might focus on the relationship between self-construals and the functional connectivity between the ECN and SN.

It is not surprising that orientations of independence and interdependence were better predicted by brain asymmetry than brain communication and global connectivity. From an evolutionary perspective, the lateralized functions of two brains increased with evolution (Duboc et al., 2015). However, the development of brain asymmetry associated with complex self-functions may be linked to genetic and environmental variations (Jahanshad et al., 2010; Liu et al., 2009). An important unknown in the research of brain asymmetry is how functional connectivity asymmetries arise and interact with genetic factors to contribute to complex self-functions. One solution may be to combine the current methods with genetic approaches to test the development of neural asymmetry. For example, why are some circuit asymmetries distinct to independence or interdependence?

One limitation of the current study is that we investigated only linear relationships between the whole-brain functional connectivity matrices and self-construal. Self-construal is a complex cultural-related concept that may contain nonlinear influence from the environment. Future research should consider non-linear models to estimate the impact of cultural experience in the brain. Also, the sample of participants from a single culture can control for possible confounding components such as language and genetic factors. However, it limits the generalizability of the current findings. Another limitation of the current study is its correlative nature, preventing an inference on the necessary role of a connectivity for self-construals. Although data based reverse inferences were regarded as a useful method to generate new and novel hypotheses (Poldrack, 2011), the current findings need to be examined in future investigations, particularly in studies with a longitudinal design, task-based manipulations, and/or patients whose functional connectivity may be disrupted (Northoff and Gomez-Pilar, 2020; Qin and Northoff, 2011; Wade-Bohleber et al., 2021). In addition, due to the relatively long TR used in data acquisition procedure, short-term distortions such as head motion cannot be fully corrected (Mikl et al., 2008; Uddén et al., 2019; White et al., 2001). The current results also need to be validated in future studies with anatomical connectivity data (Zhong et al., 2021).

In conclusion, functional connectivity analyses revealed that brain asymmetry precisely predicted the orientations of independence and interdependence. The present findings are consistent with previous neuroimaging and neuropsychological studies showing that self-construals are associated with core regions of the DMN, SN, and ECN. Our findings indicate that self-construals were underpinned by functional connectivity between these networks, providing initial evidence that functional asymmetry may be a critical principle underlying the complex self-functions of independence and interdependence in the brain. Given the significance of understanding the self and others in social environments, the present results provide a useful way to understand individual variations of how social cultural contexts shape the neural expression of complex self-functions.

Credit authorship contribution statement

Gen Shi: Methodology, Writing – original draft. **Xuesong Li:** Supervision, Writing – review & editing. **Yifan Zhu:** Methodology, Visualization. **Ruihong Shang:** Visualization. **Yang Sun:** Data curation. **Hua Guo:** Data curation, Validation. **Jie Sui:** Writing – review & editing, Data curation.

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Data and code availability statements

Both data and code are available. Please contact the corresponding author and promise that the data will be used in a confidential manner and that the code will not be used for commercial applications.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.neuroimage.2021.118382](https://doi.org/10.1016/j.neuroimage.2021.118382).

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