Human Brain Functional Homotopic Affinity Atlas

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Abstract

Spatially corresponding regions in the left and right hemispheres of the human brain, also known as homotopic brain regions, often exhibit functional similarity, namely functional homotopy. To understand the functional homotopy patterns and mechanisms underlying human psychological behavior, this study proposes a novel method for investigating human brain functional homotopy based on the two-factor generative theory of brain connectomics: functional homotopy affinity. This method quantifies the functional affinity of homotopic brain regions by computing the cosine distance of their whole-brain functional connectivity patterns. Utilizing whole-brain functional magnetic resonance imaging databases from the US and Chinese Human Connectome Projects, we first mapped a functional homotopy affinity atlas with spatiotemporal precision of "700 milliseconds-2 millimeters" and evaluated its test-retest reliability for individual differences. Second, systematic analysis of this atlas identified three specific regions in the human temporoparietal junction, revealing their characteristic patterns of hemispheric lateralization and uncovering their functional associations with attention, language, and social cognition. Finally, through multimodal brain atlas correlation analyses, we further explored the relationships between human brain functional homotopy affinity and patterns of genetic, evolutionary, structural, and functional organizational distributions. In summary, the functional homotopy affinity method we propose can provide a high-reliability and high-validity measurement atlas of human brain function for population neuroscience research.

Full Text

Human Brain Mapping of Homotopic Functional Affinity

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Abstract

Homotopic brain areas, defined as spatially corresponding regions across the left and right hemispheres, often exhibit functional similarity—a phenomenon known as functional homotopy. To understand the principles and mechanisms underlying functional homotopy in human psychology and behavior, we propose a novel method termed Homotopic Functional Affinity (HFA) based on the dual-factor generative theory of the connectome. This method quantifies the functional affinity between homotopic regions by computing the cosine distance of their whole-brain functional connectivity profiles. Leveraging resting-state fMRI databases from the US and Chinese Human Connectome Projects, we first mapped HFA at high spatiotemporal resolution (700 ms–2 mm) and evaluated its test-retest reliability for individual differences. Second, systematic analysis of these maps identified three distinct subregions within the human temporo-parietal junction (TPJ), revealing characteristic patterns of hemispheric lateralization and their functional associations with attention, language, and social cognition. Finally, through multimodal brain map correlation analyses, we further explored how HFA relates to genetics, evolution, and the organizational distributions of structural and functional architecture. In summary, the proposed HFA method provides a high-validity neuroimaging measure for population neuroscience research.

Keywords: homotopic brain area, functional homotopy, affinity, connectome, temporo-parietal junction, cultural neuroscience

Introduction

Homotopic brain areas refer to mirror-symmetric regions across the left and right hemispheres, a bilateral organization rooted in evolutionary processes [1]. The corpus callosum provides direct structural connectivity for information integration between homotopic areas, resulting in high functional similarity and manifesting as functional homotopy [2, 3]. Meanwhile, distinct connections between each homotopic region and other functional networks facilitate hemispheric lateralization of information processing [4]. This hemispheric functional organization is crucial for the evolution of cognitive functions [5, 6]. Both the integrative and specialized properties of homotopic areas play indispensable roles in basic sensory perception, higher-order cognition, and behavior. Primary sensory cortices demand greater interhemispheric integration, exhibiting stronger functional homotopy, whereas higher-level cognitive processing shows

pronounced hemispheric preferences and thus lower functional homotopy [7-9]. Clinical studies have further revealed abnormal functional homotopy in brain disorders related to cognitive and psychiatric conditions, highlighting its potential applications for brain health [10, 11].

Functional homotopic connectivity [12] quantifies interhemispheric functional coordination by directly computing Pearson correlations between time series of homotopic areas in resting-state fMRI data. This approach has demonstrated considerable reliability [13, 14] and provided preliminary evidence for the cognitive and health significance of interhemispheric coordination and lateralization [15-17]. However, this method is purely data-driven and lacks theoretical guidance from connectome models. The dual-factor generative theory of the connectome [18]—based on extensive empirical observations across species and age groups—identifies two key factors shaping connectivity patterns: spatial distance between connected regions (geometric properties) and pattern homogeneity (topological properties) [19, 20]. Traditional functional homotopic connectivity only emphasizes the spatial geometric property of homotopic locations while neglecting network topological homophily, thus failing to capture the complete similarity of connectivity patterns between homotopic areas and limiting precise quantification and interpretation of functional homotopy.

Large-scale studies of human brain functional networks have demonstrated the systematic neuroscience value of characterizing homogeneity in inter-regional connectivity patterns. Yeo and colleagues defined macroscale cortical functional networks and a series of functionally homogeneous parcels by revealing the organizational architecture of the human resting-state functional connectome [21-23]. Building on this work, they further developed a homotopic template for brain function [24], providing prior functional information for homotopic areas. Finn and colleagues introduced the functional fingerprinting approach for the human connectome [25], defining each brain region' s connectivity pattern as its "functional fingerprint" and revealing unique fingerprints across individuals and regions, thereby offering new insights for comparing functional homogeneity across brain areas [26]. Subsequently, Margulies and coworkers defined the similarity of functional fingerprints between brain regions as "affinity" and investigated the whole-brain affinity matrix (i.e., network connectivity pattern homogeneity matrix) through dimensionality reduction of the functional connectome, uncovering the intrinsic dimensionality of functional organization in the adult brain—namely, the functional connectivity gradient [27]. Further research has demonstrated that gradient features of human functional connectivity organization correlate with phenotypes related to evolution, development, behavior, and psychopathology [28, 29].

Grounded in the dual-factor generative theory of the connectome, we propose a computational method for human brain functional homotopic affinity that characterizes functional homotopy through affinity of functional fingerprints between homotopic areas. Using high spatiotemporal resolution resting-state fMRI data from the US and Chinese Human Connectome Projects, we first computed

whole-brain homotopic affinity maps at 700 ms–2 mm resolution. We then evaluated the test-retest reliability of individual difference measurements using linear mixed models to demonstrate the reliability of HFA for assessing individual variability. Finally, we validated the effectiveness of HFA through region-of-interest cognitive association analyses and multimodal whole-brain map correlation analyses. This method enriches the methodological toolkit for functional homotopy research and provides a more reliable and valid neuroimaging measure of individual differences in brain function for population neuroscience studies.

Methods

Datasets

Human Connectome Project (HCP) Dataset We utilized resting-state fMRI data from 339 unrelated participants (157 males/182 females, age = 28.64 ± 3.70 years) in the HCP dataset [30], along with task-fMRI data from language processing and social cognition paradigms. Data were acquired on a customized 3T Siemens Skyra Connectome scanner with the following parameters: TR = 720 ms, TE = 33.1 ms, FOV = 208 mm × 180 mm, 72 slices, flip angle = 52°, voxel size = 2 mm × 2 mm × 2 mm. Each participant underwent four resting-state fMRI scans across two days (two scans per day with opposite phase-encoding directions: left-to-right and right-to-left). Each resting-state scan comprised 1,200 time points (14.4 minutes). Task paradigms are described in Section 1.2; each task included two fMRI runs with opposite phase-encoding directions. The language processing task lasted approximately 3.8 minutes (316 time points) per run, and the social cognition task lasted approximately 3.3 minutes (274 time points) per run [31].

Chinese Human Connectome Project (CHCP) Dataset The CHCP dataset is a multimodal neuroimaging dataset directly comparable to HCP, based on Chinese populations [32]. The current study included resting-state fMRI data from 217 participants (109 males/108 females, age = 22.37 ± 2.88 years), with task-fMRI data available for 185 participants (90 males/95 females, age = 22.57 ± 2.99 years). Data were acquired on a 3T Siemens Prisma scanner using a protocol similar to HCP: TR = 710 ms, TE = 30 ms, FOV = 212 mm × 212 mm, with identical slice number, flip angle, and voxel size. Resting-state scans were conducted over two days with two runs per day (opposite phase-encoding directions: anterior-to-posterior and posterior-to-anterior). Each run contained 634 time points (7.5 minutes). The language processing and social cognition tasks used paradigms consistent with HCP but adapted for Chinese participants. Each task included two runs with opposite phase-encoding directions. Scan durations were nearly identical to HCP: the language processing task contained 316 time points per run.

Task Paradigms

Language Processing Task The language processing task assessed phonological and semantic processing across two runs (two scans). Each run consisted of alternating blocks of story and arithmetic tasks (four blocks each), with each block lasting approximately 30 seconds. In story blocks, participants listened to 5–9 sentence adaptations of Aesop' s fables and selected the theme from two options. In arithmetic blocks, participants heard arithmetic operations and performed addition or subtraction to select the correct answer from provided options [33]. The arithmetic task served as a control condition with similar auditory and speech input but without semantic processing, requiring attention but not language comprehension.

Social Cognition Task The social cognition task, adapted from Castelli et al. [34] and Wheatley et al. [35], assessed theory of mind through video stimuli across two runs. Each run included five blocks of animated shape videos (two social interaction videos and three random motion videos, or vice versa) and five 15-second fixation blocks. In each video block, participants watched approximately 20-second animations featuring geometric shapes (squares, circles, triangles) and then judged whether the shapes' movements showed social interaction (options: "yes" —movements appeared to consider others' feelings and thoughts; "uncertain" ; or "no" —movements were random without interaction).

fMRI Data Preprocessing

All MRI data were preprocessed using standardized pipelines from the HCP and CHCP teams and are publicly available [32, 36]. Here we provide a brief overview. Both resting-state and task fMRI data were processed through the HCP minimal preprocessing pipeline [36]. This included distortion correction and motion correction, establishment of individual-to-standard space mappings, projection to standard 32k grayordinate space, and cortical surface smoothing with a 2 mm FWHM Gaussian kernel. Resting-state data were high-pass filtered at 2,000 s to remove slow temporal drifts and denoised using independent component analysis. Task fMRI data were processed for individual task activation estimation with high-pass filtering at 200 s (see [31, 32, 36] for detailed preprocessing information and inter-dataset comparisons).

Resting-State fMRI Time Series Concatenation

To reduce random noise and improve computational efficiency for large datasets, we concatenated preprocessed time series across participants using an incremental group-PCA approach [37] prior to HFA calculation, following HCP' s resting-state functional connectivity processing pipeline. This yielded total time series per vertex slightly shorter than the sum of individual scan time points. For group-level maps, all resting-state data from all participants were concatenated. For test-retest reliability analyses, each participant' s two scans from the same day were concatenated separately, yielding two measurements per participant

(one per day). Additionally, all four resting-state runs per participant were concatenated to create an average time series for subsequent analyses linking HFA with cognitive task activation.

Homotopic Functional Affinity Map Calculation

The HCP standardized grayordinate system provides a spatially symmetric brain template for homotopic calculations, where vertices with identical indices across hemispheres are homotopic. As illustrated in Figure 1 [Figure 1: see original paper], we first computed whole-brain functional connectivity patterns (functional fingerprints) for each homotopic vertex, quantifying temporal synchrony (positive connectivity) and asynchrony (negative connectivity) with all other vertices. We then calculated the cosine distance between these connectivity fingerprints to quantify functional affinity, defined as the homotopic functional affinity at that vertex. Higher affinity indicates stronger functional homogeneity between homotopic vertices, while lower affinity indicates greater functional heterogeneity. Notably, when computing cosine distance, intra-hemispheric and inter-hemispheric connectivity fingerprints must be properly aligned between homotopic vertices. Using concatenated time series, we computed group-level homotopic affinity maps for HCP and CHCP, individual test-retest maps, and individual maps (based on four-run concatenation). All individual-level maps were smoothed with a 5 mm FWHM Gaussian kernel to enhance spatial smoothness and signal-to-noise ratio.

Figure 1 Homotopic functional affinity calculation. Given a pair of homotopic vertices on the cerebral cortex (black circled vertex in the left and right hemispheres with opposite horizontal coordinates), their full-brain functional connectivity patterns (functional fingerprints) were calculated respectively to quantify their temporal synchrony (positive correlation) and asynchrony (negative correlation) with other vertices. The connectivity fingerprints of homotopic vertices were then concatenated in the order of intra-hemispheric and inter-hemispheric connectivity (as shown in the figure) respectively, and the cosine distance between the concatenated fingerprints was calculated as the homotopic affinity of the vertex.

Test-Retest Reliability Assessment

We evaluated test-retest reliability using linear mixed-effects models [38-40]. Age and sex were included as covariates to assess between-subject and within-subject variance components. We computed intraclass correlation coefficients (ICC) for whole-brain mean ( ) and standard deviation (σ) of HFA, as well as vertex-wise ICCs. Vertex-level ICCs required within-subject standardization of HFA values. For vertex k, the standardized HFA value hkz was computed as the raw value hk minus the individual' s whole-brain mean , divided by whole-brain standard deviation σ.

Region-of-Interest Analysis

ROI Localization and Validation Based on whole-brain HFA distribution patterns and vertex-wise test-retest reliability, we selected the temporo-parietal junction (TPJ)—a region showing high reliability and pronounced regional differentiation (low affinity)—as the ROI for further analysis. Using the HCP group-level HFA map, we performed edge detection near the TPJ to localize three distinct subregions: anterior TPJ (TPJa), central TPJ (TPJc), and posterior TPJ (TPJp). We extracted their whole-brain functional connectivity fingerprints across datasets to parse the sources of functional homotopic differentiation. Meta-analyses using the Brainmap database (https://www.brainmap.org) [41-43] examined cognitive-behavioral associations of these TPJ subregions in each hemisphere. Finally, we standardized individual HFA maps, extracted mean standardized HFA within each subregion, and computed Pearson correlations with task activation levels, applying multiple comparison corrections to assess consistency with meta-analytic results.

Whole-Brain Multimodal Map Association Analysis Using the Neuromaps resource [44], we extracted maps for gene expression [45], cortical evolutionary expansion [46], cross-species functional homology index [47], cortical myelination [48, 49], functional connectivity principal gradient [27], and cognitive association principal map [50]. These were transformed to standard 32k grayordinate space to model spatial relationships between mean hemispheric maps and HFA maps.

Results

High-Resolution Whole-Brain HFA Maps

HFA maps from HCP (Figure 2a [Figure 2: see original paper]) and CHCP (Figure 2b) showed highly consistent spatial distributions. Overall, functional affinity between homotopic areas gradually decreased along a "primary cortex–association cortex" gradient: visual, somatomotor, and auditory networks exhibited the highest HFA, while default mode and frontoparietal control networks showed the lowest, with ventral and dorsal attention networks falling in between.

Figure 2 Group-level homotopic functional affinity of human cortex. The homotopic functional affinity maps of both HCP (a) and CHCP (b) were derived and projected onto the hemispheric cortical surface. For the seven large-scale functional connectivity networks in the human brain [22], a series of Gaussian models were used to fit their homotopic affinity distributions across cortex.

Test-Retest Reliability of Individual Differences in HFA

Intraclass correlation coefficients (ICC), ranging from 0 to 1, can be categorized into five reliability levels: slight (0.0–0.2), fair (0.2–0.4), moderate (0.4–0.6),

substantial (0.6–0.8), and almost perfect (0.8–1.0) [51]. Whole-brain mean and standard deviation of HFA showed moderate reliability (HCP ICC = 0.59 and 0.56; CHCP ICC = 0.50 and 0.39). Vertex-wise ICC maps are shown in Figure 3 [Figure 3: see original paper]. In HCP, 73.58% of vertices showed moderate or higher test-retest reliability, compared to 53.56% in CHCP, reflecting differences in measurement design (primarily scan duration). However, the spatial distribution patterns of ICC maps were highly similar across datasets, with higher reliability in association cortices than primary cortices. Regions with limited BOLD signal (central sulcus, orbital frontal cortex, insula) showed lower ICCs, though HCP reliability was generally higher than CHCP in these areas.

Figure 3 Test-retest reliability maps of measuring individual differences in homotopic functional affinity. Linear mixed models are employed to model individual differences in cortical functional homotopic affinity and calculate its test-retest reliability quantified by intraclass correlation coefficients, which are rendered onto the cortical surfaces for (a) HCP and (b) CHCP, respectively.

ROI Analysis of TPJ Subregions

Localization and Functional Connectivity Fingerprints Edge detection on the HCP group-level HFA map localized three TPJ subregions: anterior TPJ (TPJa), central TPJ (TPJc), and posterior TPJ (TPJp). Figure 4 [Figure 4: see original paper] shows their spatial boundaries and positions within the seven large-scale functional networks [22], along with whole-brain functional connectivity fingerprints for left and right hemisphere subregions.

Left TPJa (lTPJa) showed predominantly synchronous connectivity, with strong connections among default mode, frontoparietal control, and auditory networks. Its right homolog (rTPJa) showed strongest synchrony with ventral attention network and strongest asynchrony with default mode network. Left TPJp (lTPJp) exhibited strongest synchrony with default mode and frontoparietal control networks and strongest asynchrony with ventral attention network, while rTPJp showed less asynchrony with default mode network but maintained strongest synchrony with default mode and frontoparietal control networks. TPJc displayed transitional connectivity fingerprints between TPJa and TPJp. Left TPJc (lTPJc) showed synchronous patterns similar to lTPJa but without network asynchrony, whereas rTPJc exhibited synchronous patterns resembling rTPJp with partial overlap in asynchrony patterns with rTPJa.

In CHCP, bilateral TPJa and TPJp fingerprints were consistent with HCP, but central subregions differed markedly: bilateral TPJc connectivity patterns diverged in opposite directions (lTPJc resembled lTPJp, rTPJc resembled rTPJa), and both showed asynchrony patterns, resulting in lower fingerprint similarity that prevented separation from TPJa and TPJp based on HFA values (see Supplementary Material 1 for detailed CHCP TPJ fingerprints).

Figure 4 Homotopic affinities and functional connectivity fingerprints of the Temporo-Parietal Junction (TPJ) subregions. Based on the homotopic func-

tional affinity map derived from HCP, we used an edge detection algorithm to locate the three TPJ subregions: anterior TPJ (TPJa), central TPJ (TPJc), and posterior TPJ (TPJp). The central panel shows the human brain functional affinity map, the boundaries of the three TPJ subregions, and their positions within the seven large-scale functional networks [22]. The left panel demonstrates the whole-brain functional connectivity fingerprints of the left TPJ subregions, and the right panel is for their homotopic positions.

Cognitive Functions of TPJ Subregions Meta-analytic results revealed cognitive functions associated with the three TPJ subregions (Figure 5 [Figure 5: see original paper]). Left hemisphere TPJ subregions showed stronger functional specificity than right hemisphere subregions, where cognitive processes were more equally weighted. Like connectivity fingerprints, cognitive associations showed transitional properties across subregions. TPJa was most strongly associated with inhibition, attention, and executive control, with right TPJa also showing somatosensory associations. TPJc primarily involved social cognition, with right TPJc also related to somatosensation. TPJp showed strongest associations with language (left hemisphere) and social cognition (right hemisphere).

Figure 5 Word cloud maps of cognitive association with the three TPJ subregions. The central panel depicts the human brain functional affinity map, the boundaries of the three TPJ subregions, and their positions within the seven large-scale functional networks [22]. The left panel demonstrates the word clouds derived from the meta-analysis on cognitive function of the left TPJ subregions, and the right panel is for their homotopic positions.

Correlation Between TPJ HFA and Task Activation Correlations between HFA and task activation in the three TPJ subregions further revealed their cognitive functions (Table 1). In HCP, during the "story–arithmetic" contrast of the language task, activation in lTPJa and rTPJp showed significant but opposite correlations with HFA. Bilateral TPJc activation showed significant opposite correlations that corresponded to the patterns observed in lTPJa and rTPJp. Similar relationships were observed for the "story" condition, but no significant correlations emerged for the "arithmetic" condition. In the social cognition task, rTPJc and rTPJp activation showed significant negative correlations with HFA for both "social interaction" and "random" conditions.

In CHCP, the "story–arithmetic" contrast showed HFA-activation relationships consistent with HCP. The "story" condition revealed significant negative correlations between left hemisphere activation and HFA across all three subregions. The "arithmetic" condition showed significant correlations for rTPJc and rTPJp. Social cognition task results showed the same trend as HCP but were non-significant.

Table 1 Associations between homotopic functional affinity and cognitive task activation within the three TPJ subregions.

Subregion	Task Contrast	Left Hemisphere	Right Hemisphere
TPJa	Story-Arithmetic	-0.18**	-0.36**
TPJa	Story	-0.25**	-0.36**
TPJa	Arithmetic	-0.21*	0.20**
TPJc	Story-Arithmetic	-0.20*	0.16*
TPJc	Story	0.24**	-0.26**
TPJc	Arithmetic	0.22**	-0.21*
TPJp	Story-Arithmetic	0.28**	-0.17*
TPJp	Story	0.28**	0.17*
TPJp	Social-Random	-0.16*	-0.15*
TPJp	Random	-0.27**	0.17*

* $p < 0.05$, ** $p < 0.01$, FDR-corrected within each dataset.

Multimodal Map Associations of Cortical HFA

HFA maps showed significant correlations with all six multimodal maps (Figure 6 [Figure 6: see original paper] shows HCP results; correlation topographies for both datasets are in Supplementary Material). HFA exhibited the strongest association with the functional connectivity principal gradient (HCP: r = -0.77; CHCP: r = -0.73), where higher HFA correlated with lower functional hierarchy. Evolutionary cortical expansion also negatively correlated with HFA (HCP: r = -0.53; CHCP: r = -0.45), indicating that less expanded regions showed higher HFA. Positive correlations emerged between HFA and gene expression, cross-species functional homology index, and cortical myelination (r = 0.53–0.60), suggesting that higher HFA regions have stronger genetic, evolutionary, and myelination constraints. The weakest correlation was with the Neurosynth cognitive activation map (HCP: r = 0.35; CHCP: r = 0.38), indicating that high-HFA regions have more defined cognitive associations, while low-HFA regions require further investigation.

Figure 6 Multimodal map association of HCP homotopic functional affinity map.

Discussion

We propose the HFA method and validate its reliability and validity for measuring individual differences. HFA serves as a reliable index of both functional integration and specialization between homotopic areas, with unique genetic, evolutionary, and functional organizational significance. Using HFA, we revealed the functional complexity of the TPJ and demonstrated its potential scientific value and applications for studying functional differentiation across brain regions, linking resting-state and task-based fMRI, and investigating cross-cultural brain mechanisms.

Reliability of the HFA Method

Despite widespread use of fMRI in brain function research, reproducibility remains challenging [52, 53], partly due to insufficient reliability of selected metrics [54]. Whole-brain mean HFA showed reliability > 0.5, with vertex-wise reliability generally > 0.4, outperforming typical resting-state functional connectivity and traditional task activation methods and approaching other highly reliable resting-state fMRI metrics [13, 14]. HFA thus provides a reliable measure of hemispheric integration and lateralization.

In association cortices such as the default mode and frontoparietal control networks, HFA reliability was consistently high across datasets, mirroring reliability distributions of other resting-state fMRI metrics [14, 55]. Association cortices show large inter-individual variability but relatively small intra-individual variability [56-58], making them effective for discriminating individuals [59]. In regions with limited BOLD signal (central sulcus, orbital frontal cortex, insula), HCP reliability exceeded CHCP reliability, likely due to longer scan duration in HCP (twice that of CHCP). Longer scans yield more stable time series, reduce random fluctuations, and improve test-retest reliability [60, 61].

Biological Significance of HFA Maps

HFA maps revealed that functional specialization between homotopic areas increases along a "primary–association"cortical gradient, a dominant axis in human brain organization across multiple dimensions [28, 62]. Our work validates this gradient' s role in shaping intrinsic functional representations from the perspective of hemispheric integration and specialization. Multimodal map associations further revealed the genetic, evolutionary, and cognitive significance of HFA distribution patterns.

Hemispheric lateralization of gene expression emerges during embryonic development [63]. In language networks showing prominent hemispheric specialization, genes related to electrophysiology and neurotransmitter circuits exhibit hemispheric preferences [64]. Primary cortices, which evolved earlier and support basic sensory functions, are assumed in our HFA framework to originate from a perfectly symmetric homotopic organization. During evolution, cortical expansion led to the emergence of association cortices and higher cognitive functions [65]. Regions with the greatest evolutionary expansion show the strongest functional specialization [4], and cognitive functions are tightly linked to hemispheric specialization [8]. Human language and frontoparietal control regions show greater lateralization than macaques [6], with lowest cross-species functional homology in these areas [47]. These findings support our theoretical assumptions and provide insights into the regulatory mechanisms and cognitive significance of hemispheric specialization.

Functional Specificity of the Temporo-Parietal Junction

The TPJ participates in multiple complex cognitive functions and occupies a unique position in the human brain [66]. No functionally equivalent region for human TPJ subregions has been identified in macaques [47]. HFA maps sensitively captured TPJ functional specificity, revealing fine-grained functional differentiation across subregions and hemispheres. Overall, TPJ cognitive functions transition from executive control to social cognition to language processing along a ventral-to-dorsal axis [67]. In the right hemisphere, rTPJa and rTPJc belong to ventral attention and parietal control networks. Meta-analytic associations with somatic pain and vision suggest intimate links between somatosensation and attentional orienting/executive control [68, 69]. Rajimehr et al. found that left-hemisphere activation in core language regions corresponds to right-hemisphere activation during social tasks [70]. Our meta-analysis of bilateral TPJp replicated this hemispheric complementarity between language and social cognition, offering important insights for understanding their interaction and neural mechanisms in related disorders. Furthermore, the pattern of correlations between HFA and task activation in TPJ subregions during language processing aligned with their resting-state connectivity fingerprints, demonstrating the potential of TPJ connectomes to predict intra- and inter-hemispheric information flow during language processing.

Cultural and Ethnic Differences in HFA Maps

We mapped HFA using high-resolution datasets from US and Chinese populations. Although overall patterns were highly similar, systematic differences emerged in certain brain regions. The relative HFA values of TPJc versus TPJa and TPJp differed between datasets. These differences likely reflect population distinctions, as substantial cultural and ethnic differences between Chinese and US populations influence cognition [71, 72]. TPJc is primarily associated with social cognition, and its differential HFA across datasets may reflect cultural and ethnic variations. Task activation correlations support this interpretation: significant HFA-activation associations during social cognition in HCP became non-significant in CHCP. Conversely, arithmetic condition correlations in CHCP were significant where HCP correlations were not. Different cultural backgrounds between East and West are known to influence learning styles [73, 74]. These results provide important reference points for understanding how cultural and ethnic differences manifest in human brain function.

Future Directions

Grounded in the dual-factor generative theory of human connectome development, we propose HFA as a novel method with important prospects for understanding emerging brain mapping approaches and deconstructing psychological and cognitive mechanisms.

Methodologically, HFA represents a subset of functional connectivity gradient

calculations. Our findings demonstrate high similarity between HFA maps and the principal functional gradient. Future work should investigate the weight of HFA in gradient computation, differences and similarities between HFA and principal gradient maps, and their respective cognitive implications. Additionally, since HFA incorporates whole-brain connectivity and different regions show varying preferences for intra- versus inter-hemispheric connections, differences in inter-hemispheric versus intra-hemispheric affinity warrant further investigation.

From evolutionary and developmental perspectives, our study reveals close links between HFA maps and human brain evolution. Future research should examine whether similar HFA maps exist across species and whether cross-species comparisons can provide further insights into human brain evolution. During development, the homophily factor strengthens while spatial constraints weaken in the dual-factor generative model [18, 19]. Since HFA is based on this theoretical framework, future studies should test whether individual HFA maps follow this developmental trajectory to further validate the biological validity of the method.

Finally, HFA reveals potential influences of sociocultural differences on TPJ function, demonstrating capacity to capture brain functional differences across racial and cultural populations. This highlights the need to consider cultural adaptation of behavioral paradigms in cross-cultural research and develop culturally appropriate protocols. Future studies should incorporate more cross-cultural datasets to validate current findings and leverage HFA to uncover additional brain mechanisms reflecting cultural and ethnic differences.

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