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Corresponding Author: David E. Oshei osher.6@osu.edu

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#### **RESEARCH**

# Connectivity and function are coupled across cognitive domains throughout the brain

Kelly J. Hiersche<sup>1,2</sup>, Zeynep M. Saygin<sup>1,2</sup>, and David E. Osher<sup>1,2</sup>

<sup>1</sup>Department of Psychology, The Ohio State University, Columbus, OH, USA, 43215 <sup>2</sup>Center for Cognitive and Behavioral Brain Imaging, The Ohio State University, Columbus, OH, USA, 43215

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#### **ABSTRACT**

Decades of neuroimaging have revealed that the functional organization of the brain is roughly consistent across individuals, and at rest, it resembles group-level task-evoked networks. A fundamental assumption in the field is that the functional specialization of a brain region arises from its connections to the rest of the brain, but limitations in the amount of data that can be feasibly collected in a single individual leave open the following question: Is the association between task activation and connectivity consistent across the brain and many cognitive tasks? To answer this question, we fit ridge regression models to activation maps from 33 cognitive domains (generated with NeuroQuery) using resting-state functional connectivity data from the Human Connectome Project as the predictor. We examine how well functional connectivity fits activation and find that all regions and all cognitive domains have a very robust relationship between brain activity and connectivity. The tightest relationship exists for higher order, domain-general cognitive functions. These results support the claim that connectivity is a general organizational principle of brain function by comprehensively testing this relationship in a large sample of individuals for a broad range of cognitive domains and provide a reference for future studies engaging in individualized predictive models.

# **AUTHOR SUMMARY**

The functional organization of the brain is similar across individuals, and a fundamental assumption of cognitive neuroscience is that functional specialization in a brain region arises from its connections to the rest of the brain. However, this relationship has been tested within only a handful of cognitive domains. Here, we utilize a large-scale database and meta-analytic data to comprehensively test the link between functional connectivity and functional activation across the entire brain for 33 different cognitive domains. We show that all regions and cognitive domains tested have a very robust relationship between brain activity and connectivity, therefore providing support for the assumption that connectivity is a general organizational principle of brain function and a reference for future studies engaging in individualized predictive modeling.

# INTRODUCTION

Decades of neuroimaging have revealed that the functional organization of the brain is roughly consistent across individuals, with, for example, the ventrotemporal cortex engaged  $\mathbf{Q}\mathbf{1}$ 

Connectivity fingerprint: The patterns of connections (either functional or structural) that can be used to predict a voxel's functional activation during task.

Ridge regression: Statistical method for fitting data that reduces overfitting by penalizing high-value coefficients. during visual perception (Grill-Spector & Weiner, 2014; Kanwisher, 2010), the frontotemporal cortex engaged for linguistic processing (Fedorenko et al., 2024; Malik-Moraleda et al., 2021), and the medial temporal cortex for episodic memory (Eichenbaum et al., 2012; Squire et al., 2004). Furthermore, the functional organization of the brain at rest is also roughly consistent across individuals (Ji et al., 2019), and these resting-state networks qualitatively resemble group-level task-evoked networks (Molloy & Osher, 2023; Thomas Yeo et al., 2011). A fundamental assumption in the field is that the functional specialization of a brain region arises from its connections to the rest of the brain (Passingham et al., 2002), but is the association between task activation and connectivity consistent across the brain and many cognitive tasks?

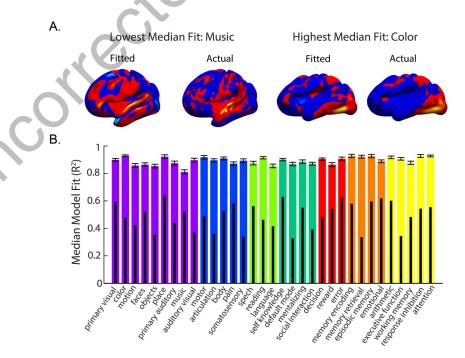
A large body of work has been dedicated to empirically testing the relationship between connectivity and function to predict individualized activation on a voxelwise scale. This has been done with structural connectivity in the temporal cortex (Saygin et al., 2012) and across the brain (Osher et al., 2016), as well as with functional connectivity, such that an individual's connectivity data can be used to predict their individual pattern of activation ("connectivity fingerprint" modeling; Bernstein-Eliav & Tavor, 2024; Mennes et al., 2010; Molloy et al., 2024; Osher et al., 2019; Tavor et al., 2016; Tobyne et al., 2018). More recent work has demonstrated generalizability, predicting individualized activation across tasks, ages, and scanner sites (Tik et al., 2023). However, despite this body of work dedicated to understanding the relationship between the idiosyncrasies of connectivity and task activation, their relationship across the broader landscape of cognition is still unclear. Does the prediction ceiling differ across different domains of processing? For example, perhaps unimodal, lower level sensory activation is better fit by connectivity, since these regions show strong relationships between structural connectivity and function (Valk et al., 2022). Furthermore, lower level cognitive tasks (e.g., vision, motor) also have lower interindividual variability (Mueller et al., 2013) and develop their functionality quite early in life without substantial environmental input (Bradley & Mistretta 1975), being instead determined by thalamic connections and being under strong genetic influence (Felleman & Van Essen, 1991; Hamasaki et al., 2004; O'Leary et al., 2007). Alternatively, perhaps higher level cognitive functions are those with the tightest link between functional activation and connectivity because they require years of coactivation and organization, leading to stronger coupling of these networks (Kelly & Castellanos, 2014; Tayoni et al., 2017). Higher level functions also integrate information across many regions (Cohen & D'Esposito, 2016; Khodaei et al., 2023; Shine et al., 2016). Furthermore, some cognitive functions are lateralized, showing greater activation in one hemisphere (e.g., language is lateralized to the left, whereas face and social processing are lateralized to the right; McCarthy et al., 1997; Ojemann, 1991; Rajimehr et al., 2022; Rossion et al., 2012). If repeated coactivations of regions drive a tighter relationship between resting-state connectivity and functional activation, we may expect connectivity and function to be more tightly linked in the dominant hemisphere for lateralized skills but show comparable associations across hemispheres for functions that recruit bilaterally.

The goal of this study is study is to provide a bird's eye view of the relationship between functional connectivity and functional activation across the entire brain for a broad sample of cognitive processing. To do this, we leveraged a large, publicly available database (Human Connectome Project, HCP; Van Essen et al., 2013) and NeuroQuery (Dockès et al., 2020), an online metanalytic tool that predicts brain maps (activation maps) based on semantic similarity among search queries and terms reliably associated with brain regions. We implemented ridge regression modeling to examine the association between functional connectivity and task activation to a broad range of cognitive domains across the entire brain. We find that all regions and all cognitive domains have a very robust relationship between brain activity

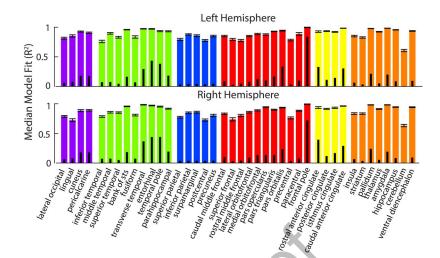
and connectivity, with the tightest relationship for higher order, domain-general cognitive functions. These results support the claim that connectivity is a general organizational principle of brain function by comprehensively testing this relationship in a large sample of individuals for a broad range of cognitive domains and provide a reference for future studies engaging in individualized predictive models.

### **RESULTS**

Functional activation was successfully modeled by resting-state connectivity across all domains and all regions (see two examples, fitted vs. expected activation maps in Figure 1A; see Supporting Information Figure S1 for all models fits), and each model's fit was higher than all random permutations. Model fits across all 2,706 models ranged from 0.35 to 0.9997, with a strong left skew, such that 1,292 models had a fit above 0.9, whereas only 26 models had a fit under 0.5, and the median fit across all models was 0.89. When examining the median model fit across all regions within a task, we see that the model fit remained high for all domains. The median fit (followed by the random permutation 99th percentile fit) was 0.88 (0.46) for the sensory domain, 0.90 (0.46) for somatosensory, 0.88 (0.46) for language, 0.88 (0.46) for social cognition, 0.89 (0.53) for decision-making, 0.91 (0.56) for memory, and 0.91 (0.51) for executive functioning (see Figure 1B for the fit by task). Model fit was also high when examining the median model fit for all tasks within a lobe: 0.88 (0.77) for occipital, 0.92 (0.14) for temporal, 0.83 (0.31) for parietal, 0.88 for frontal (0.35), 0.95 (0.30) for cingulate, and 0.93 (0.19) for subcortical (see Figure 2).



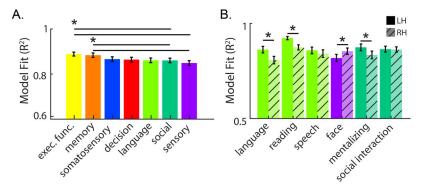
**Figure 1.** (A) Expected activation maps (from NeuroQuery, left) and connectivity-based fitted activation (right) for two sample cognitive domains. (B) Large colored bars show median fit (with standard error bars) for each domain across regions. Subset black bars show the 99th percentile performance of the permuted models for each domain. Sensory is in purple, somatosensory is in blue, language is in green, social is in blue-green, decision-making is in red, memory is in orange, and executive functioning is in yellow.



**Figure 2.** Large colored bars show the median fit (with standard error bars) for each region across domains. Subset black bars show the 99th percentile performance of the permuted models. The occipital lobe is in purple, temporal is in green, parietal is in dark blue, frontal is in red, cingulate is in yellow, and subcortical is in blue.

While all domains and regions show a tight relationship between connectivity and activation, we used a one-way analysis of variance (ANOVA) to examine differences in model fit across cognitive domains. A main effect of domain, F(6, 2699) = 7.28,  $p = 9.95 \times 10^{-8}$ ,  $\eta^2 = 0.0159$ , revealed significant differences in model fits, such that the executive function and memory domains outperformed both the social and sensory domains (see Figure 3A and Table 1).

Finally, we completed hypothesis-driven analyses to determine if lateralized functions were better fit for their dominant hemisphere (see Figure 3B). For the left hemisphere (LH), we tested language and reading, both of which are canonically left-lateralized, as well as speech, which shows bilateral activation, and found that connectivity significantly better fit functional activation in the LH for language, t(40) = 3.32, p = 0.0019, d = 0.45, and reading, t(40) = 6.08, p = 0.0019, d = 0.45, and reading, t(40) = 0.0019, d = 0.



**Figure 3.** Results of one-way analysis of variance and test of lateralized functions. (A) Main effect of category with mean model fit with standard error bars. \*p < 0.05, surviving Bonferroni-Holm multiple-comparisons corrections for 21 comparisons. (B) Hemispheric differences for lateralized functions. Mean model fit with standard error bars. \*p < 0.05, Bonferroni-Holm corrected for six comparisons.

**Table 1.** Results of post hoc two-tailed, independent-samples *t* tests to compare model fit across all seven cognitive domains

Category	Category	t (df)	р	d
Decision-making	Executive function	-2.62 (453)	0.0090	-0.215
Decision-making	Language	0.43 (490)	0.66	0.039
Decision-making	Memory	-2.32 (520)	0.02	-0.197
Decision-making	Sensory	1.73 (438)	0.08	0.126
Decision-making	Social	0.58 (515)	0.56	0.049
Decision-making	Somatosensory	-0.18 (507)	0.86	-0.015
Executive function	Language	3.17 (460)	0.0020**	0.260
Executive function	Memory	0.079 (653)	0.94	0.006
Executive function	Sensory	5.76 (997)	$1.10 \times 10^{-8}**$	0.344
Executive function	Social	3.67 (660)	$2.64 \times 10^{-4}$ **	0.274
Executive function	Somatosensory	2.89 (802)	0.0040	0.202
Language	Memory	-2.83 (527)	0.0050	-0.239
Language	Sensory	1.23 (447)	0.22	0.089
Language	Social	0.11 (521)	0.91	0.009
Language	Somatosensory	-0.67 (516)	0.50	-0.054
Memory	Sensory	4.88 (671)	$1.31 \times 10^{-6}**$	0.319
Memory	Social	3.21 (654)	0.0010**	0.251
Memory	Somatosensory	2.49 (702)	0.010	0.184
Sensory	Social	-1.24 (683)	0.22	-0.081
Sensory	Somatosensory	-2.317 (895)	0.021	-0.141
Social	Somatosensory	-0.87(707)	0.39	-0.064

Uncorrected p values listed and Cohen's d effect sizes. \*\*p < 0.05 after Bonferroni-Holm multiple-comparisons correction for 21 tests.

 $3.65 \times 10^{-7}$ , d = 0.63, whereas fit did not differ across the hemispheres for speech, t(40) = 1.28, p = 0.21, d = 0.12. We also tested mentalizing and face perception, which show right lateralized activation, as well as social interaction, which elicits bilateral activation. As expected, face perception was better fit in the right hemisphere (RH), t(40) = -2.83, p = 0.0072, d = -0.31, and social interaction was equally well fit across the hemispheres, t(40) = 0.30, p = 0.76, d = 0.025). Surprisingly, we found that mentalizing was better fit in the LH, t(40) = 3.01, p = 0.0045, d = 0.28, in contradiction with our hypothesis that functions would be better fit for their dominant hemispheres (mentalizing, similar to other social cognitive skills, is lateralized to the RH; Gupta et al., 2025; Rajimehr et al., 2022). All comparisons survived correction for six multiple comparisons.

#### **DISCUSSION**

Here, we provide substantial evidence that connectivity is a general organizational principle of brain function across the entire brain. Voxelwise functional activation for each region of the brain is well explained by its connectivity to other regions, and this is true across a broad array of cognitive domains and across the entire brain. Our analyses also reveal differences in model fits across cognitive domains and hemispheres, which we discuss below.

This study provides a bird's eye view of the functional connectivity and functional activation relationships across the entire brain for a broad sample of cognitive processing. Even with access to large-scale databases with many tasks and subjects, connectivity-function relationships have only ever been tested in as many as seven domains at a time (Tavor et al., 2016). This work demonstrates that connectivity-activation relationships are robust enough to emerge even when the data are representative of general brain activation and not explicitly measured in the same individuals. This provides quantitative evidence for a relationship that has been largely assumed in the past and tested in only a small sample of potential cognitive domains. Furthermore, we show that connectivity can explain expected activation not only in regions that are important for a task (e.g., language activation in temporal regions) but also in regions that are not involved in a task (occipital activation in speech). Given that the nuances of activation across all regions can modeled, regardless of a region's activation in a task, this paper provides a noise ceiling for the expected fit of connectivity and function for researchers involved in individualized predictive approaches. For example, our work suggests that the cerebellum is not well modeled when treated as a single anatomical region. Therefore, parcellations of the cerebellum, allowing for different models for different subregions, may be important for individuals attempting to predict cerebellar function based on its connectivity. Furthermore, given that this model allows us to examine the connectivity-function relationship across the whole brain, this model could be altered by "lesioning" particular regions (either typically involved or not in a task) to make predictions about the expected changes in functional activation. Additionally, these results provide a baseline for what might be considered the norm relationship between connectivity and function, allowing future work on individual differences to compare how an individual may vary from this average expected relationship. Finally, our study provides a reference for connectivity-function relationships in a young, healthy sample and a framework for assessing these relationships in other populations. Given that evidence suggests that connectivity patterns may be altered in aging and disease (barràs-Permanyer et al., 2019; Guimarães et al., 2017; Sala-Llonch et al., 2015; Zhang et al., 2010), future work can apply this approach to characterize alterations in the connectivityfunction relationship in aging populations, developmental samples, and disease.

Our planned analyses showed that lateralized functional activation (e.g., for language and faces) was better explained by connectivity in the dominant hemisphere, whereas bilateral functions within similar domains were equally well fit across the hemispheres. Lateralization of function is an interesting nuance of human cognition, and it indeed makes sense that connectivity patterns mimic this laterality. Certain functional lateralities develop quite early in development and may be driven by lateralized connectivity patterns that are genetically determined. For example, the language network tends to be left-lateralized by the age of 3 years, although this specialization and related lateralization continues to develop through early childhood (Hiersche et al., 2024; Olulade et al., 2020). Perhaps this early-developing functional laterality is biased or driven by connectivity (e.g., Li et al., 2020; Saygin et al., 2016), suggesting that the tight link between connectivity and function that we observe here with adults may reflect early developmental biases. However, we also observed stronger fits with

Lateralization: Stronger activation to a task in one hemisphere compared with another.

connectivity for mentalizing on the LH, despite greater RH activation. This result suggests that there may also be other factors that drive certain connectivity-function relationships, such as ongoing maturation and continued synchronization and strengthening of these networks, resulting in greater engagement of the LH in aspects of mentalizing that may require more effort and experience (Doricchi et al., 2022; Sun et al., 2023).

In line with this idea, executive function and memory domains that included arithmetic, attention, working memory, response inhibition, attention, episodic memory, and memory encoding and retrieval were the best fit by connectivity and significantly outperformed social and sensory domains. Executive function skills (and the networks that support them) show prolonged maturation, requiring many years to develop (Best & Miller, 2010; Gao et al., 2015; Sherman et al., 2014). This contrasts with cognitive skills and networks that are in place very early in development. For example, sensory networks are in place in utero and mature rapidly (Eyre et al., 2021), whereas higher order association networks are not always detectable or are weaker (Thomason et al., 2013). Thus, the stronger fit of connectivity and functional activation in these higher order domains may reflect the ongoing strengthening of disparate nodes of multimodal cortex and their connections through repeated coactivations (e.g., through interactive specialization; Johnson, 2011).

Resting-state functional connectivity: Refers to coactivation of brain regions (measured using correlation) during task-absent brain imaging.

By utilizing the large-scale data available through HCP and the meta-analysis tool Neuro-Query, this study examined the relationship between connectivity and function at a greater scale than any prior work. While aligning with prior showing that resting-state functional connectivity is strongly related to task activations (Cole et al., 2016), this method allowed us to examine a wider range of cognitive domains, testing the coupling of connectivity and function from low-level sensory activation to complex cognitive tasks, which is not feasible in any single dataset collected. However, this approach also has its limitations. The ideal case would be to have functional connectivity and task activation data in the same set of individuals, across many possible cognitive domains. Furthermore, while the cognitive domains selected do cover a breadth of terms studied by cognitive neuroscientists, we have not covered all possible terms; although given the consistency across all tested categories, it seems likely that the association between connectivity and function is strong for other domains as well. Furthermore, we provide the code for these analyses (see the Data and Code Availability section), allowing other researchers to expand upon the chosen domains for their own work, when applicable. Also, there is the possibility that NeuroQuery utilized studies implementing connectivitybased analyses when generating its predictive maps; therefore, there is potential that the relationship between connectivity and function could be mildly inflated, although given the number of papers that contributed to NeuroQuery (over 13,000) and the much greater prevalence of task-based fMRI research, likely many studies did not use this method. Furthermore, while we build upon the body work examining the connectivityfunction relationship (for review, see Bernstein-Eliav & Tavor, 2024), we were unable to examine individual variability of this connectivity-function relationship across domains with this meta-analytic approach. Despite this limitation, we hope that this study can be a helpful benchmark for estimating the potential of individualized predictive models across numerous domains and regions. Finally, this work does not consider or test the role of multivariate representations, which could reveal different aspects of information processing or more nuanced representations (e.g., differentiating exemplars of a particular category or domain of knowledge such as cats vs. dogs, or dynamic facial expressions) with differing relationships to connectivity.

Numerous questions remain. Future work should explore the contributions of structural connectivity, which has also been used to predict individualized activation (Osher et al.,

2016; Saygin et al., 2012), as well as cortical folding patterns that create subject-specific anatomical fingerprints (Duan et al., 2020). These anatomical measures will offer other potential mechanisms for complex mental function and likely interact with coactivations and functional connectivity in interesting ways (e.g., Bullmore & Sporns, 2009; Sporns, 2013). Furthermore, given that an individual's functional connectivity fingerprint may be genetically driven (Hu et al., 2022), genetic mechanisms of connectivity fingerprints should be explored to understand the influence of genetic versus experiential contributions to the link between connectivity and function. Finally, given the changes to functional connectivity across the lifespan (Betzel et al., 2014), future work should examine potential shifts in connectivity-function coupling across the lifespan. Longitudinal, developmental work can be used to further test whether connectivity-function coupling is strongest for tasks requiring greater environmental experience and determine the trajectory of the relationship between function and connectivity across the brain for different cognitive domains. This study provides the foundation for these next steps, allowing future work to further characterize the mechanisms supporting brain function.

#### **METHODS**

#### Resting-State fMRI Data

Each participant who completed all four runs of resting-state fMRI from the HCP (Van Essen et al., 2013) was included for connectivity analyses (N = 1,018; 546 females, 472 males). Four 15-min runs of resting-state data per individual were preprocessed following the HCP minimal preprocessing pipeline (Glasser et al., 2013). Additional preprocessing of the resting-state data included denoising with aCompCor (Behzadi et al., 2007), nuisance regression using the top five temporal principal components in white matter and cerebrospinal fluid separately, and surface smoothed using a Gaussian kernel with  $\sigma$  = 3 mm. Functional connectivity was computed for each subject, per run, as the Pearson correlation coefficient between each vertex and the mean time course of each region in the Desikan-Killiany atlas (Desikan et al., 2006). Data were Fisher-transformed and averaged across runs, and a final group average connectivity matrix was computed as the mean across all subjects. This matrix contained the average functional connectivity of each vertex to each cortical and subcortical region and was, thus, of size 91,282 vertices by 89 regions. The resulting matrix supplied the covariates of each multivariate model described below.

# NeuroQuery Activation Maps

We selected 33 cognitive domains of broad interest to cognitive neuroscientists, spanning seven categories (sensory, somatosensory, language, decision-making, social, memory, and executive function; see Figure 1). Each term was entered into NeuroQuery (a tool that uses search queries to generate maps of fMRI responses using information from 7,547 neuroimaging publications; Dockès et al., 2020) on February 9, 2025 or on December 19, 2024, and the resulting brain map was downloaded (these maps are available in volume space here; see the Data and Code Availability section, and Supporting Information Figure S2 shows activation on lateral surface for all categories). This map was examined by two experts in the field (authors Z.M.S. and D.E.O.) to confirm that expected brain regions were active for each term, to determine its category (e.g., to determine that "body" activated motor regions of the brain, placing it in the somatosensory category, and was not activating just high-level visual body regions in ventral temporal cortex), and to determine that the expected activation maps across domains were not highly overlapping (e.g., social interaction and mentalizing activate distinct regions of social processing, including faces, but not also facial expressions, as the maps were

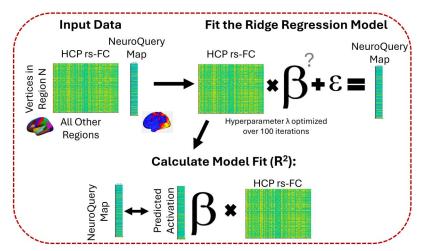
highly overlapping). Furthermore, each map was visually compared with multiple similar search terms in Neurosynth (Yarkoni et al., 2011), a commonly used meta-analytic tool for examining activation to cognitive domains across a wide range of peer-reviewed studies.

Results from NeuroQuery provide an expected activation (*z* statistic) for each 4-mm isotropic voxel in the MNI152 space. Each map was upsampled to 2 mm and then registered to the fsaverage\_LR32k template surface using Connectome Workbench (Marcus et al., 2011; https://github.com/Washington-University/workbench). These vertex-wise activation maps were the response variables of the multivariate models described below.

### Modeling Procedure and Analysis

In this study, we are assessing the goodness of fit of regression models that integrate restingstate connectivity with function (see Figure 4 for modeling procedure). Given that NeuroQuery only provides a single meta-analytic brain map, there is no out-of-sample data to predict. Therefore, we fit the average connectivity matrix across many subjects to the NeuroQuery expected activation in each region, using a separate model for each brain region and domain (33 domains × 82 regions). For each cognitive domain, connectivity and activation maps were extracted for each region separately, such that each vertex of a region is described by its degree of activation (scalar) and its connectivity pattern to each region of the brain (vector). To fit connectivity data to activation maps, we utilized ridge regression models (Hoerl & Kennard, 1970), similar to how we have previously performed connectivity fingerprinting analyses (Molloy et al., 2024; Osher et al., 2019). First, the hyperparameter (λ) was optimized for each model, using a fivefold cross-validation with 100 maximum number of objective function evaluations. Then, that optimal lambda was used to fit a ridge regression model (MATLAB R2020a, fitrlinear) to the HCP connectivity data and NeuroQuery meta-analytic map. We computed the coefficient of determination  $(R^2)$ , a commonly used within-sample measure for goodness of fit, which measures the percent variance in functional responses that is accounted for by each connectivity model.

Permutation testing determined if the relationship between functional connectivity and fitted activation for a particular region was significant. Each voxel was randomly assigned (within a region, without replacement) the functional activation of the same cognitive domain of another voxel while keeping its functional connectivity profile intact. With the permuted



**Figure 4.** Diagram outlining the model procedures for one domain and one region. This process was repeated for all 33 domains and 82 regions.

activation data (the dependent variable) but intact functional connectivity data (independent variables), we created 1,000 new regularized ridge regression models for each region and each domain to determine the relationship between "true" connectivity and "chance" expected activation. These permutation models utilized the same hyperparameters from the "true" model. For each permutation model, we calculated  $R^2$  to create a distribution of model fits to test whether our "true" model fits were likely the outcome of chance or represented a real relationship between functional connectivity and activation.

# Statistical Analyses

To examine the significance of each model fit, we compared the "true" model fit ( $R^2$ ) with the distribution of "random" fits calculated during permutation testing by determining the percentage of permutation models that outperformed our true model (sum permutation model  $R^2$  > "true" model fit divided by 1,000) and by calculating the 99% confidence level of the permuted models (analyzed in MATLAB R2020a). Distribution of model fit across domains and regions indicated primarily skewed distributions; therefore, median model fit is reported when collapsing across domains or regions.

To determine whether all cognitive domains were equally well fit by connectivity, we used a one-way ANOVA to examine differences in model fit ( $R^2$ ) across domains. The dependent variable ( $R^2$ ) was initially negatively skewed and was transformed (arcsine of square root) to represent a more normal distribution (examined with QQ plot), and a plot of fitted values verses residuals of the transformed data model showed a relative lack of relationship between fitted values and residuals, indicating homogeneity of variance. Two-tailed, independent-sample t tests were used for post hoc comparisons following a significant main effect, and all reported statistics survive multiple-comparison corrections for 21 comparisons. Cohen's d effect sizes are included for all t-test comparisons.

Finally, we conducted hypothesis-driven analyses (these analyses were not preregistered) based on the expected laterality differences in fit for a few select cognitive domains. Paired-samples, two-tailed t tests were used to compare fit across the hemispheres for reading, language, and speech, with the expectation that left-lateralized functions (language and reading) should show a tighter association between connectivity and function (and, therefore, higher model fit) in the LH compared with RH, whereas speech, which is more bilateral, should not show these differences. We also tested faces and mentalizing, which show right lateralized activation maps, as well as social interaction, which shows bilateral activation. All reported significant effects survive multiple-comparisons correction for the six tests performed.

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### SUPPORTING INFORMATION

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#### **AUTHOR CONTRIBUTIONS**

Kelly Hiersche: Conceptualization; Formal analysis; Visualization; Writing – original draft; Writing – review & editing. Zeynep M. Saygin: Conceptualization; Data curation; Funding acquisition; Methodology; Supervision; Writing – original draft; Writing – review & editing. David E. Osher: Conceptualization; Data curation; Formal analysis; Funding acquisition; Methodology; Supervision; Writing – original draft; Writing – review & editing.

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### **DATA AND CODE AVAILABILITY**

Brain maps, downloaded from NeuroQuery, along with all codes used for modeling and analysis are available here: https://github.com/CognitionBrainCircuitryLab/Connectivity-and-function-across-domains.

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