

1 **Title**

2 **Multi-hops functional connectivity improves individual**
3 **prediction of fusiform face activation via a graph neural**
4 **network**

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15

1 **Abstract**

2 Brain connectivity plays an important role in determining the brain region's
3 function. Previous researchers proposed that the brain region's function is
4 characterized by that region's input and output connectivity profiles. Following this
5 proposal, numerous studies have investigated the relationship between connectivity
6 and function. However, based on a preliminary analysis, this proposal is deficient in
7 explaining individual differences in the brain region's function. To overcome this
8 problem, we proposed that a brain region's function is characterized by that region's
9 multi-hops connectivity profile. To test this proposal, we used multi-hops functional
10 connectivity to predict the individual face response of the right fusiform face area
11 (rFFA) via a multi-layers graph neural network and showed that the prediction
12 performance is essentially improved. Results also indicated that the 2-layers graph
13 neural network is the best in characterizing rFFA's face response and revealed a
14 hierarchical network for the face processing of rFFA.

15

16 **Keywords:** Individual prediction, Multi-hops connectivity, Fusiform face function,
17 Graph neural network

18

1 **Introduction**

2 Brain connectivity acts as the pathway for transferring information between brain
3 regions and determines the information inflow and outflow of each cortical region.
4 Passingham et al. (2002) proposed that the function of each cortical region can be
5 determined by the region's input and output connectivity profiles. Mars et al. (2018)
6 further tested and extended this proposal via the neuroimaging of connectivity, and
7 showed that the connectivity space composed by each region's connectivity profiles
8 provides a powerful framework in describing a brain region's function.

9 The connectivity profile can be defined in terms of the white matter pathway
10 represented by tractography through diffusion magnetic resonance imaging (MRI), or
11 in terms of the temporal coupling between spontaneous fluctuations of resting-state
12 functional MRI (rfMRI) signal. Under the proposal of Passingham et al. (2002),
13 previous studies have utilized structural connectivity (Johansen-Berg et al. 2004;
14 Tomassini et al. 2007; Beckmann et al. 2009; Saygin et al. 2011a) or functional
15 connectivity (Cohen et al. 2008; Gordon et al. 2016) to characterize the boundary of
16 functionally distinct brain regions, or have utilized structural connectivity (Saygin et
17 al. 2011b; Osher et al. 2016; Saygin et al. 2016; Wu et al. 2020) or functional
18 connectivity (Tavor et al. 2016; Parker Jones et al. 2017) to predict the functional
19 activation information of brain regions at various task states.

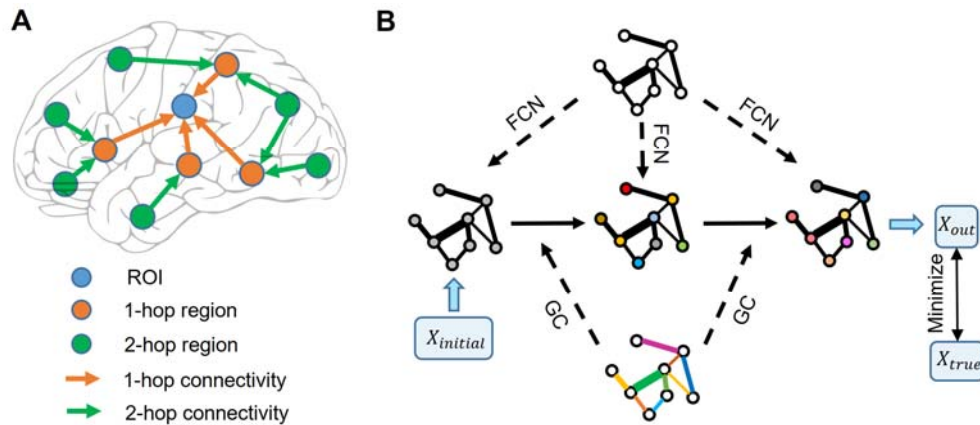
20 Though the proposal that a brain region's function is represented by the input and
21 output connectivity profiles is widely adopted in various studies, this proposal is
22 deficient in characterizing the individual brain region's function. Specifically, under
23 this proposal, a brain region's function can be represented by a linear combination of
24 the region's connectivity profiles, with the weight of the connectivity profiles viewed
25 as the functional information transferred from neighboring regions. However, the
26 weight of the linear model is the same for all subjects. This amounts to assume that
27 the functional information of neighboring regions is the same for different subjects. In

1 other words, the prediction model under this proposal neglects individual differences
2 in the functional information of neighboring regions and thus is deficient in predicting
3 individual brain region's function.

4 To overcome this problem, we proposed that more connectivity features in the
5 brain connectivity network should be considered. Explicitly, as shown in Fig. 1A, the
6 functional activation information of 1-hop regions is unknown, however, the
7 information of 1-hop regions is transferred from 2-hop regions through the
8 connections of 1-hop regions. According to this logic, when the functional activation
9 information of all brain regions is unknown, the connections of n-hop regions may
10 contain functional information of the region of interest (ROI). Denote the direct input
11 and output connections of the ROI as the 1-hop connections. The connections of the
12 1-hop regions amount to the 2-hop connections of the ROI. We then define the
13 ensemble of these 1-hop and 2-hop connections as the 2-hops connections relative to
14 the ROI. Using these terms, the previous proposal (Passingham et al. 2002) is
15 formulated as that a brain region's function is represented by the 1-hop connectivity
16 profiles. Separately, based on the above analyses, we proposed that a brain region's
17 function is represented by the multi-hops connectivity profiles.

18 To further test our proposal, we selected the right fusiform face area (rFFA) as the
19 ROI. We adopted the FACES-SHAPES (emotion task) and FACE-AVG (working
20 memory task) contrasts in the human connectome project (HCP) to define individual
21 subject's functional face selectivity, and utilized the rfMRI data to construct
22 individual brain functional connectivity network. Inspired by the fact that
23 computations in the graph neural network are analogous to the propagation of
24 functional information in the brain connectivity network, we designed a multi-layers
25 graph neural network (Fig. 1B). This graph neural network is well suitable for our
26 proposal because it includes both direct and indirect, single-step and multiple-step
27 connectivity features to characterize functional selectivity of the ROI. Finally, we
28 applied the graph neural network containing the multi-hops functional connectivity to

1 predict individual face selectivity of the rFFA.



2

3 Figure 1. Schematic illustration of graph neural network. (A) Functional information
4 of the ROI is transferred from the 1-hop neighboring regions via the 1-hop
5 connections, and the functional information of the 1-hop neighboring regions is
6 transferred from the 2-hop neighboring regions via the 2-hop connections. (B) Node
7 color represents the functional information of brain regions. Edge width represents the
8 strength of functional connectivity pathways. Edge color represents the coefficient of
9 graph convolution (GC), i.e. the extent to which each connection participates in the
10 functional information propagation. Initial functional information transfers within the
11 functional connectivity network (FCN) through the graph convolution network.
12 Coefficients of GC are trained by minimizing the error between the predicted output
13 and true functional activation information.

14 **Materials and Methods**

15 **Human Connectome Project data**

16 We used the minimally pre-processed data (Glasser et al. 2013) provided by the
17 HCP S1200 release. We selected all the 997 subjects that have the FACES-SHAPES,
18 FACE-AVG task contrasts, and resting-state fMRI acquisitions.

19 Task and resting-state fMRI data were projected onto 2 mm standard CIFTI
20 grayordinates space, and the multimodal surface matching (MSM) algorithm

1 (Robinson et al. 2014) based on areal features (MSMAll) was used for accurate
2 inter-subject registration. Acquisition parameters and processing are described in
3 detail in several publications (Barch et al. 2013; Smith et al. 2013). Briefly, resting
4 and task fMRI scans were acquired at 2 mm isotropic resolution, with a fast TR
5 sampling rate at 0.72 s using multiband pulse sequences (Ugurbil et al. 2013). Both
6 sets of functional data had already been registered to the MNI space (Glasser et al.
7 2013). Each subject had four 15-minute resting fMRI runs, with a total of 1,200 time
8 points per run. The resting fMRI data were further pre-processed by FIX to
9 automatically remove the effect of structured artifacts (Griffanti et al. 2014;
10 Salimi-Khorshidi et al. 2014).

11 **Functional Connectivity profile**

12 We calculated functional connectivity based on the HCP-MMP1.0 (Human
13 Connectome Project Multi-Modal Parcellation version 1.0) (Glasser et al. 2016) that
14 containing 360 brain regions. The functional connectivity was calculated from the
15 resting fMRI data. The four runs of individual resting-state time series data were
16 concatenated after being demeaned and variance-normalized along the time axis. We
17 did not apply global signal regression before calculating functional connectivity. The
18 time series for every vertex in the seed region was correlated with the averaged time
19 series for each of the remaining 359 target regions. The diagonal elements of the
20 functional connectivity matrix were set as ones.

21 **Gaussian-Gamma mixture model for determining activation threshold**

22 The HCP_MMP1.0 contains 360 brain regions. Using a connectivity matrix with
23 size 360×360 is likely to overfit the training dataset. Since some brain regions do not
24 involve in the face recognition process, removing these brain regions beforehand can
25 reduce the model complexity in a great deal. To prevent some individual differences
26 with opposite signs from canceling with each other, we calculated each brain region's

1 mean absolute activation across subjects. Then we used the Gaussian-Gamma mixture
2 distribution (Gorgolewski et al. 2012) to model the density distribution of the mean
3 absolute activation for the 360 brain regions. The Gaussian distribution is used to
4 model the random noise effect, and the Gamma distribution is used to model the
5 activation signal. We set the activation threshold as the point when the probability
6 density of Gamma distribution is higher than that of Gaussian distribution.

7 **Graph neural network for predicting functional face selectivity**

8 Graph neural network is widely used to process data with graph structures
9 (Defferrard et al. 2016; Kipf and Welling 2017; Veličković et al. 2018). We developed
10 a graph neural network that is adapted to process brain connectivity network data (Fig.
11 1B). The graph neural network with a single-layer can be represented in a matrix form
12 as follows:

$$13 \quad H_{n \times 1}^k = W_{n \times n}^k \odot A_{n \times n} X_{n \times 1}^{k-1} + B_{n \times 1}^k \quad (1)$$

14 k represents the k -th layer of the network. n represents the number of nodes in the
15 graph neural network, i.e. the number of brain regions. X and H respectively
16 represent the input and output of the graph neural network, i.e. the functional
17 activation of each brain region. B represents the bias term of the model. A
18 represents the adjacency matrix composed of functional connectivity. W represents
19 the functional information propagation coefficient of each functional connectivity
20 pathways. W exerts on A via the operation \odot that represents the element-wise
21 multiplication. A multi-layers computation can be achieved by applying formula (1)
22 repetitively. When one trains a multi-layers graph neural network, the vanishing
23 gradient effect usually occurs. Inspired by the residue neural network (He et al. 2016),
24 we added residue connections between neighboring layers to formula (1) and the
25 resulting model is:

$$26 \quad H_{n \times 1}^k = W_{n \times n}^k \odot A_{n \times n} X_{n \times 1}^{k-1} + B_{n \times 1}^k + X_{n \times 1}^{k-1} \quad (2)$$

1 To make the 1-layer graph neural network model consistent with the linear model
2 adopted by previous studies, the brain region's activation in the 0th layer is initialized
3 as all ones: $X_{n \times 1}^0 = [1, 1, \dots, 1]_{n \times 1}$. It is worth noting that model (2) doesn't involve
4 nonlinear activation functions but is nonlinear in the sense that the functional
5 connectivity feature A occurs in every computation layer. Therefore the resulting
6 multi-layers model contains nonlinear features that represent functional information
7 passing through multi-steps functional connectivity pathways.

8 **Metrics for assessing the model**

9 We used two metrics to assess the model performance on testing data. Denote the
10 target value by y and the prediction value by \hat{y} . The sum squared error
11 (SSE) = $\sum_i (y_i - \hat{y}_i)^2$ is widely used to assess the difference between the target and
12 prediction values. But in different divisions of the dataset, the variance of the target
13 value is different, thus the SSE cannot be compared across different divisions. We
14 divided the SSE by the sum squared total (SST) = $\sum_i (y_i - \text{mean}(y))^2$ and the
15 resulted normalized squared error (NSE) was used. We also adopted the Pearson
16 correlation to assess the similarity between the actual and prediction value, denoted
17 by r . Under the least squares condition, NSE represents the error proportion that
18 cannot be explained by the model, and r^2 represents the proportion of target data
19 that can be explained by the model. Since the least squares condition is not satisfied
20 by our model, these two metrics only serve as approximations.

21 Prediction similarity assessed by the Pearson correlation coefficient was Fisher's
22 z transformed when used for further statistical tests. Since the evaluation metrics for
23 different models were paired for each random division of the dataset, we performed
24 paired-sample t -tests using the custom Matlab command "ttest".

25 **Implementation details**

26 The whole dataset was randomly divided into a training set and a testing set with
27 a ratio of nine to one. Though the sample size 997 is relatively large in neuroimaging,

1 it is rather small compared to that of computer vision datasets in machine learning that
2 usually contain over ten thousand samples. The random splitting of a small dataset
3 can introduce random effects into the final results, i.e. the metrics for assessing the
4 model can vary widely across different divisions. To remove the random effect as
5 much as possible, we performed the prediction process 100 times with different
6 random divisions of the dataset and used the mean of the two metrics to assess the
7 model.

8 We implemented the graph neural network with PyTorch (<https://pytorch.org/>).
9 The parameters of the model were initialized by the Xavier normal distribution with a
10 gain of 0.1. The model was trained via the stochastic gradient descent optimizer with
11 a Nesterov momentum of 0.9 used. The training batch size was 128 and 500 training
12 epochs were used. The initial learning rate was 0.01 and a 0.1 multiplicative factor of
13 learning rate decay was set at 300 and 400 epochs respectively. To further overcome
14 the problem of overfitting caused by a small sample size, we added Gaussian random
15 noise to the individual connectivity features at each training step. The variance of the
16 Gaussian random noise was set equal to the variance of each connectivity feature
17 across subjects. This technique can be viewed as a kind of online data augmentation.
18 The graph neural network models were trained on an NVIDIA GeForce GTX 1080 Ti
19 graphic processing unit. The training time for each random separation lasts about 8
20 minutes, and the total training time for 100 random separations lasts about 13 hours.

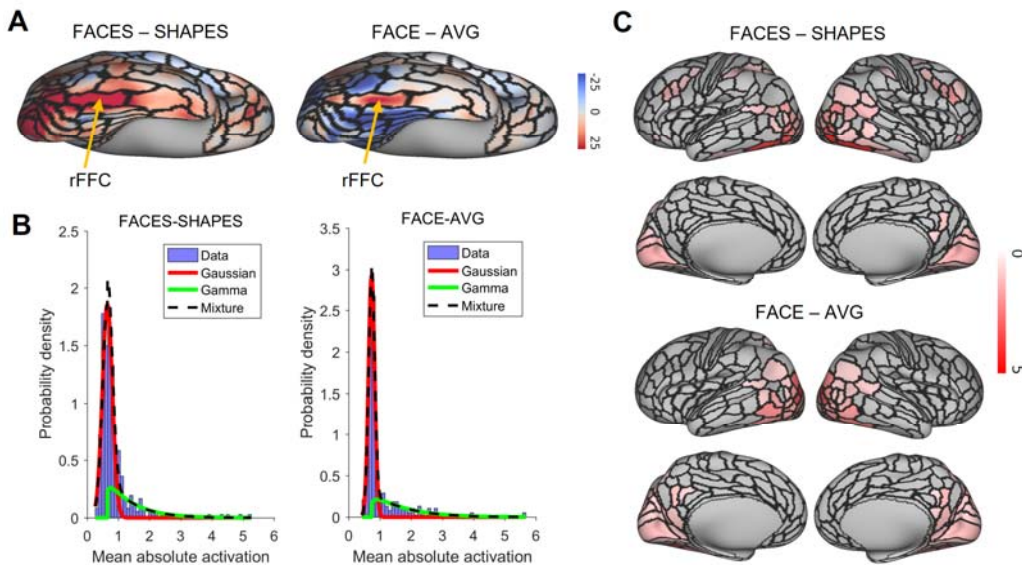
21 **Data availability**

22 The HCP S1200 data release is publicly available online at <https://www.human>
23 [connectome.org/](https://www.humanconnectome.org/).

1 Results

2 Functional face ROI localization

3 We selected the rFFA as the ROI, given that this region is the most selective in
4 the face processing network (Kanwisher et al. 1997). It is advantageous to study
5 individual differences by choosing a region that has a specialized function and is
6 reliably replicated across studies and participants. We identified the rFFA by the right
7 fusiform face complex (rFFC) region in the HCP-MMP1.0 (Glasser et al. 2016). The
8 FACES-SHAPES task contrast for the HCP emotion paradigm and the FACE-AVG
9 task contrast for the HCP working memory paradigm were separately used to identify
10 the functional face response. We showed the group average z -statistics of these two
11 task contrasts and the boundary of rFFC region in Fig. 2A. The rFFC region was
12 identified in both task contrasts, and the boundary of rFFC region coincided well with
13 that of the group average activation. The mean z -statistic within the rFFC region was
14 used to assess each subject's face selectivity.



15

16 Figure 2. Functional face ROI localization and network selection. (A) Voxel-wise
17 group average z -statistics of both contrasts were shown. The yellow arrow indicates
18 the area where the rFFC region locates. (B) The purple histogram indicates the density

1 distribution of the mean absolute activation for the 360 brain regions. A Gaussian (red
2 curve)-Gamma (green curve) mixture (black curve) model was used to fit the data. (C)
3 Mean absolute z -statistics of brain regions in the functional face activation network
4 were shown.

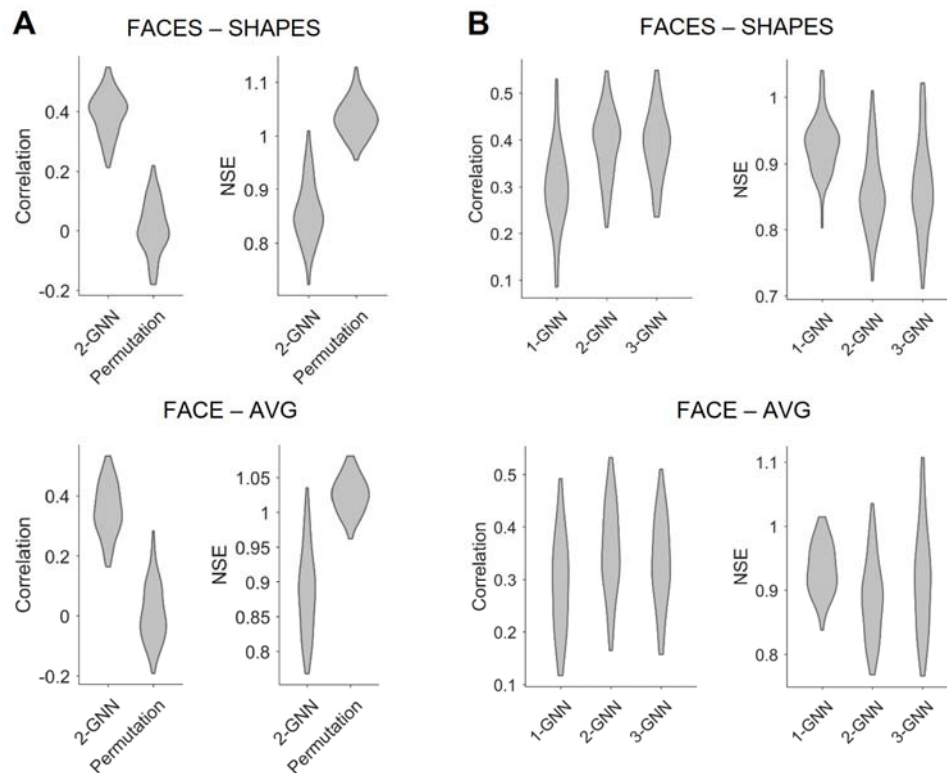
5 **Functional face activation network selection**

6 We next defined the functional face activation network in preparation for
7 constructing the graph neural network. Fig. 2B shows the density distribution of the
8 mean absolute activation for the 360 brain regions. We used a Gaussian-Gamma
9 mixture model to fit the density distribution. The threshold of the activation network
10 was chosen when the probability of Gamma distribution surpassed that of Gaussian
11 distribution. We showed the activation networks of both task contrasts in Fig. 2C.
12 Networks of both task contrasts mainly include brain regions in the visual cortices,
13 such as the primary and early visual cortices, dorsal and ventral stream visual cortices,
14 MT+ complex and neighboring visual areas. Both networks also include medial and
15 lateral temporal cortices, superior and inferior parietal cortices,
16 temporo-parieto-occipital junction, and posterior cingulate. In addition, the activation
17 network of FACES-SHAPES contrast also includes inferior frontal, orbital and polar
18 frontal, dorsolateral prefrontal, and premotor cortices. The activation network of
19 FACES-SHAPES contrast is broader than that of FACE-AVG contrast, because the
20 activation network of FACE-AVG contrast is mainly for basic face perception, while
21 the activation network of FACES-SHAPES contrast also includes emotional
22 processing of faces.

23 **Statistical validation of graph neural network prediction model**

24 After selecting the functional face activation network, we constructed graph
25 neural networks to predict individual face selectivity of the rFFC region. We first
26 compared the 2-layers graph neural network with the random permutation model to

1 validate the prediction model statistically. The random permutation model was
2 constructed with the same structure as the 2-layers graph neural network, except that
3 the pairings between the functional connectivity network and the response of rFFC
4 region was shuffled. We illustrated the comparison between the 2-layers graph neural
5 network and the random permutation model in Fig. 3A. For the FACES-SHAPES
6 contrast, the prediction error of the 2-layers graph neural network is significantly ($t(99)$
7 = -26.5, $p = 9.5 \times 10^{-47}$, paired-sample t -test) lower than that of the random permutation
8 model, and the prediction similarity of the 2-layers graph neural network is
9 significantly ($t(99) = 33.2$, $p = 1.7 \times 10^{-55}$, paired-sample t -test) higher than that of the
10 random permutation model. Results for the FACE-AVG contrast are similar (see
11 Supplementary Table S1). Hence, the 2-layers graph neural network can capture the
12 association between the individual functional connectivity network and the face
13 selectivity of rFFC region above random level.



14

15 Figure 3. Comparison of prediction metrics for different models. (A) Comparison
16 between the 2-layers graph neural network (2-GNN) and the random permutation

1 model with the same structure. The prediction performance of 2-GNN is better than
2 that of random permutation model in that the 2-GNN has a higher prediction
3 similarity (assessed by correlation) and a lower prediction error (assessed by NSE). (B)
4 Comparison of graph neural networks with different layers. The 2-GNN has a higher
5 ability to predict better individual differences than both the 1-GNN and 3-GNN.

6 **Comparison of graph neural networks with different layers**

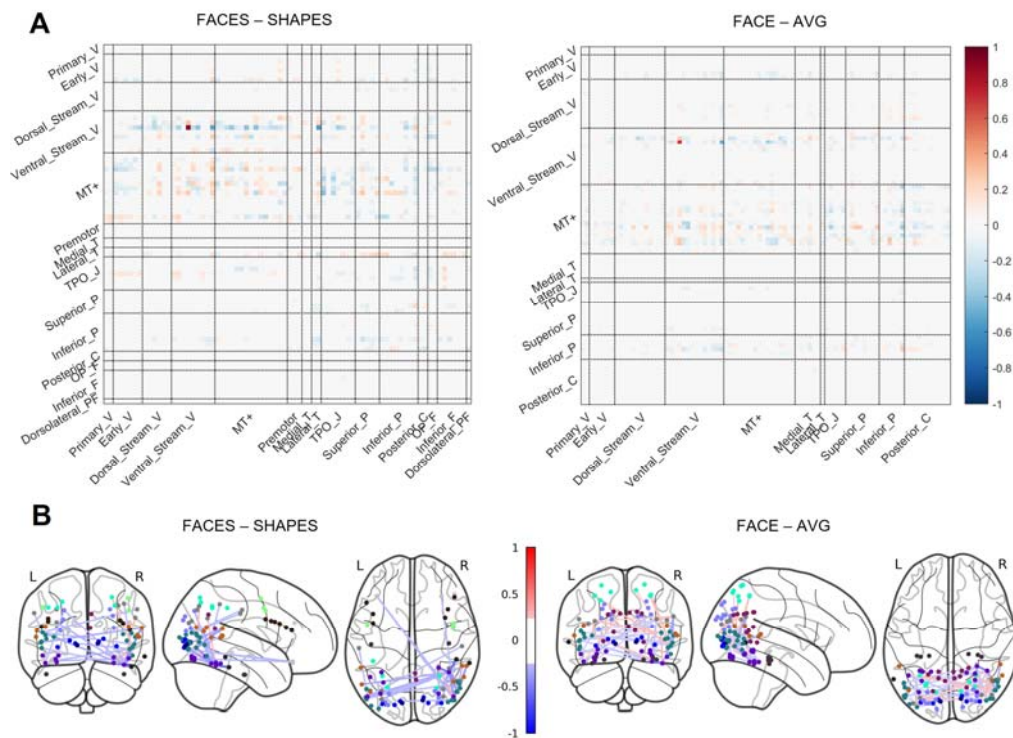
7 After validating the graph neural network statistically, we further tested our
8 proposed assumption by comparing graph neural networks with different layers. The
9 1-layer graph neural network corresponds to the linear prediction model adopted by
10 previous studies and utilizes the 1-hop (i.e., direct) functional connectivity of the
11 rFFC region to predict the rFFC region's individual functional face response. In the
12 2-layers graph neural network, the final layer corresponds to the 1-hop functional
13 connectivity representation of the rFFC region's face response, and the first layer
14 corresponds to the 2-hop functional connectivity representation of the rFFC region's
15 face response. Thus, the multi-layers graph neural network contains the representation
16 of the rFFC region's face response through multi-hops functional connectivity. If the
17 proposal that a brain region's function is represented by the multi-hops connectivity is
18 rational, using multi-hops functional connectivity should improve the prediction of
19 the rFFC region's face response. We determined the rational number of hops based on
20 the generalization ability of the graph neural networks with different number of layers
21 and showed the comparison results in Fig. 3B and Supplementary Table S1. For the
22 FACES-SHAPES contrast, the prediction error of the 2-layers graph neural network
23 (mean NSE = 0.857) is significantly ($t(99) = -16.0, p = 3.0 \times 10^{-29}$, paired-sample t -test)
24 lower than that of the 1-layer graph neural network (mean NSE = 0.927), but is not
25 very significantly ($t(99) = -2.09, p = 0.039$, paired-sample t -test) lower than that of the
26 3-layers graph neural network (mean NSE = 0.864). The prediction similarity of the
27 2-layers graph neural network (mean correlation = 0.392) is significantly ($t(99) = 13.5$,

1 $p = 2.8 \times 10^{-24}$, paired-sample t -test) higher than that of the 1-layer graph neural
2 network (mean correlation = 0.296), but is not significantly ($t(99) = 0.269$, $p = 0.788$,
3 paired-sample t -test) higher than that of the 3-layers graph neural network (mean
4 correlation = 0.391). Results for the FACE-AVG contrast are similar, except that the
5 differences between the 2-layers and 3-layers graph neural networks are significant
6 (see Supplementary Table S1). Since the evaluation metrics stopped improving, we
7 only tested graph neural networks with the number of layers up to 3. Overall, the
8 multi-layers graph neural network improves the prediction performance in individual
9 face selectivity of the rFFC region, and the 2-layers graph neural network possessed
10 the best prediction performance.

11 **Functional network pathways involving face selectivity**

12 In the previous section, we determined that the 2-layers graph neural network has
13 the best generalization ability, thus the functional network pathways containing the
14 rFFC region's 1-hop and 2-hop functional connectivity best characterize the
15 individual functional face selectivity of the rFFC region. Fig. 4 depicts the 2-hop
16 functional connectivity network involving face selectivity. The 2-hop functional
17 connectivity network also contains information about the 1-hop functional
18 connectivity, because the output of the first layer is subsequently used as the input of
19 the second layer. The 2-hop functional connectivity network is not symmetrical. The
20 rows represent brain regions that integrate functional information from neighboring
21 regions, and the columns represent brain regions that send functional information out.
22 In both task contrasts, connectivity coefficients with large absolute values mainly
23 concentrate in the rows of ventral stream visual cortices and MT+ complex visual
24 areas. This result indicates that brain regions in these two cortices mainly participate
25 in the computation of the following layer. Though some brain regions in other rows
26 do not have large absolute connectivity coefficients, these regions in the columns have
27 large absolute connectivity coefficients. This result indicates that some brain regions

1 do not integrate functional information for the following layer, but they send
2 functional information out to the regions that integrate functional information. The
3 whole results suggest a hierarchical functional face processing mechanism for the
4 rFFC region. The rFFC region first mainly integrates functional information from
5 regions in the ventral stream visual cortices and MT+ complex visual areas, then
6 regions in these two cortices integrate functional information from regions in other
7 cortices.



8
9 Figure 4. Visualization of connectivity pathways involving face selectivity. (A) The
10 functional network involving face selectivity is shown in a matrix plot. Color
11 represents the coefficient strength of each connection. Brain regions that belong to the
12 same cortex are grouped. Full names of cortices are included in Supplementary Table
13 S2. (B) The functional network is plotted on the glass brain. Only the connection with
14 the top 1% coefficient strength is shown to make the plot clean. Edge color represents
15 the coefficient strength of each connection. Node color represents the cortices that
16 each brain region belongs to (see Supplementary Fig. S1).

1 **Discussion**

2 In order to better characterize the brain region's function of individuals, our study
3 proposed that a brain region's function is represented by the multi-hops connectivity
4 profiles. The multi-layers graph neural network model was used to incorporate
5 multi-hops connectivity features in the functional connectivity network. We tested our
6 proposal by predicting the functional face response of the rFFC region via the rFFC
7 region's multi-hops functional connectivity. Our results showed that the 2-hops
8 functional connectivity profile has the best generalization ability in characterizing the
9 rFFC region's individual functional face response, and revealed a hierarchical
10 network for the rFFC region's functional face processing mechanism. The current
11 study provides new insights into understanding the brain region's function from a
12 network perspective.

13 Previous researchers proposed that a brain region's function is represented by the
14 1-hop connectivity profiles (Passingham et al. 2002). However, this proposal neglects
15 individual differences in the functional information of ROIs' neighboring regions.
16 Under our proposal that a brain region's function is represented by the multi-hops
17 connectivity profiles, individual differences in the 1-hop brain region's functional
18 information are taken into consideration via the 2-hop connectivity profiles. Our
19 proposal is also consistent with neuroscience findings. Researchers have suggested
20 that brain functions do not rely on the independent operation of a single brain region
21 or connectivity pathway, but derive from the brain network composed of multiple
22 brain regions and connectivity pathways (McIntosh 2000; Misic and Sporns 2016). In
23 addition, indirect connectivity features among other brain regions can also affect ROIs
24 via the brain network (Honey et al. 2009). Brain navigation efficiency is also due to
25 multi-hop brain connectivity pathways (Seguin et al. 2018). In a word, since the
26 multi-hop connectivity encodes the topological and geometrical properties of the brain
27 connectivity network, our proposal indicates that a brain region's function is encoded

1 in the topology of the brain connectivity network.

2 The multi-layers graph neural network perfectly matches our proposal, since the
3 multi-layers convolution computations characterize the propagation of functional
4 information among the brain connectivity network. Though some kinds of graph
5 neural network models have been developed to process brain network data (Ktena et al.
6 al. 2018; Parisot et al. 2018; Yang et al. 2019), our proposed graph neural network is
7 novel in the following aspect. As opposed to these graph neural networks (Ktena et al.
8 2018; Parisot et al. 2018; Yang et al. 2019) that impose parameters on node features,
9 our graph neural network directly imposes parameters on connectivity features instead.
10 Imposing parameters on connectivity features is especially beneficial when the
11 dimension of node features is very low, as it is the case that the node feature, i.e. the
12 brain activation statistic, has only one dimension in our study. Hence, our graph
13 neural network is well suitable for handling connectivity-driven problems, while the
14 others mainly aim at dealing with node-driven problems.

15 The functional connectivity network has also been verified to transfer functional
16 information across cortical regions (Cole et al. 2016; Ito et al. 2017). Under this
17 activity flow mapping, functional activation information is transferred to neighboring
18 brain regions via functional connectivity pathways. The activity flow mapping shares
19 certain similarities with our study in the sense that the functional information
20 propagates within the functional connectivity network. However, our study differs
21 from the activity flow framework mainly in that functional activation information of
22 all brain regions in our study is unknown, while only the ROI's functional activation
23 information is unknown in the activity flow framework. In this sense, our proposal
24 and study require less functional information of brain regions and thus has practical
25 implications in that one does not need to scan functional task contrasts beforehand to
26 get the functional information of some brain regions.

27 Our results showed that the 2-layers graph neural network containing 1-hop and
28 2-hop functional connectivity best characterizes the rFFC region's functional face

1 response, indicating that 2-hops connectivity information may be enough to estimate
2 the rFFC region's function. On the other hand, from the computation perspective, as
3 the number of layers in a graph neural network gets large, the parameters and
4 complexity of the model also enlarge. Since the sample size is relatively limited
5 compared to that of datasets in machine learning, models with large complexity are
6 also likely to overfit the data and thus have a poor generalization ability. Future work
7 involves utilizing datasets with a large sample size to test whether graph neural
8 networks with more layers can further improve the generalization ability.

9 We chose the rFFC region that has a specialized function and is reliably
10 replicated across studies to test our assumption primarily. However, the rFFC region
11 is specialized in the face selectivity function which has special meaning in the human
12 evolution process and has a specific neural mechanism (Tsao et al. 2006; Freiwald and
13 Tsao 2014). Whether our proposal can be generalized to brain regions beyond the
14 rFFC still remains to be solved, especially to brain regions that are more functionally
15 variable across individuals and flexible across tasks, i.e. the heteromodal association
16 cortices (Anderson et al. 2013; Mueller et al. 2013; Tei et al. 2017). Future work also
17 includes extension to brain regions involving a wide functional domains to test our
18 proposal.

19 We used undirected functional connectivity to construct the brain connectivity
20 network in this study. However, the propagation of functional information in the brain
21 is actually directional, and this directional information was not taken into account.
22 Effective connectivity should be considered in the future to capture the directionality
23 of information transfer. In addition, there are also other choices to construct the brain
24 connectivity network, such as the structural connectivity representing white matter
25 fiber pathways. Researchers can also explore the relationship between the multi-hops
26 structural connectivity network and the individual brain region's function.

27 In conclusion, we proposed that the multi-hops connectivity profile can improve
28 the prediction performance of individual differences in the brain region's function.

1 Results revealed that the 2-hops functional connectivity network best characterizes the
2 rFFC region's individual functional face response. This advancement contributes to
3 understanding the mechanism of individual brain region's function in terms of the
4 brain network and provides a new perspective on brain functional processing
5 mechanisms at the network level.

6

7 **Conflict of interest:** The authors declare that they have no conflict of interest.

8

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17

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