Gradual variation of anatomical connectivity in the macaque insula revealed by probabilistic tractography

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Background

Histological studies in the macaque insula evidenced a gradual transition in the cortical architecture, as well as in the anatomical connectivity, from agranular to granular cortical types. We aimed at finding evidence of a similar trajectory of connectivity variation by using the results of probabilistic tractography on diffusion-weighted MR images. The employed method of Laplacian Eigenmaps was able to display the expected gradient and to discriminate this situation from others in which segregated clusters were expected.

Image acquisition

Ex vivo high resolution diffusion-weighted magnetic resonance images (DW MRI) of an adult male fascicularis macaque brain were acquired at the Martinos Center for Biomedical Imaging at 4.7 Tesla in a 33 cm bore Oxford magnet, interfaced to a Bruker Biospec Avance console, a using a standard 72 mm i.d., birdcage coil (Bruker Biospin, Ettlingen, Germany) and the following acquisition parameters: 0.430 mm isotropic resolution, TE = 33 ms, 8 shots, TR = 350 ms, 120 isotropically distributed diffusion directions, b(max) = 8000, delta = 6.85, Delta = 10.8 ms, 27 hours total scan time). The brain was fixed with formalin and soaked for 28 days in a solution containing gadolinium (Gd-DTPA) MRI contrast agent to reduce the T1 relaxation time.

Probabilistic Tractography and estimation of the trajectory of connectivity variation

Probabilistic tractography: Two-fibers Bayesian estimation of diffusion parameters was performed on the DW data after motion correction using the FSL Fdt software. These parameters were used to perform probabilistic tractography by drawing 500 samples from the connectivity distribution from each seed voxel in the insula to the ipsilateral hemisphere. In addition, tractography was seeded in the medial motor wall to compare the results with those of the insula, in order to check for the presence of clusters. For each target voxel, the results of probabilistic tractography were corrected for the average distance to the seed and log transformed. The connectivity map for each seed voxel was vectorized, and the cross-correlation (CC) matrix of all connectivity vectors was calculated. A scaled euclidean anatomical distance matrix was then added to the CC matrix to correct for within-ROI distance of seed voxels.

Laplacian eigenmaps (LE): the graph laplacian of the resulting matrix was computed, using the smallest distance which led to a connected graph as a threshold to define nearest neighbours. The eigensystem of the graph laplacian was calculated, and its two smallest nonzero components were used to embed the original dataset, in order to recover a low-dimensional representation of the structure of connectivity variation. After removing the points >95% of the distribution of distances with each other points, a one-dimensional structure of variability became apparent. The distance of each point from one extreme of this structure was used to plot the results on the anatomical image

Results

Laplacian eigenmaps of the insula connectivity patterns recover a gradual one-dimensional trajectory of variation in the connectivity pattern of insular voxels, spanning from rostro-ventral to dorso-caudal territories, strongly resembling the one describing the variation of cortical types. Samples seeded in the antero-ventral insular cortex reach mostly regions in the paralimbic belt and in the prefrontal cortex, as well as in the inferior temporal lobe; on the other hand, samples from the dorso-caudal insular region mostly reach premotor, primary sensory and posterior parietal regions. Samples from the transitional zone in the insula feature a mixed connectivity pattern between the other two regions. These results appear to be in line with previous in vivo studies in macaque.

In order to assess the hypothesis of continuous variation vs. clustered connectivity, we also performed probabilistic tractography and build LE of the medial motor wall, in a region encompassin F1, F3 and F6, above the cingulate cortex. In this case, the LE also recovered a one dimensional trajectory of variability, but featuring two interruptions which delimited the three main functional regions of the medial motor wall. Importantly, the separation between F3 and F6 was found just rostral to the plane through the anterior commissure, where it was expected to be located.

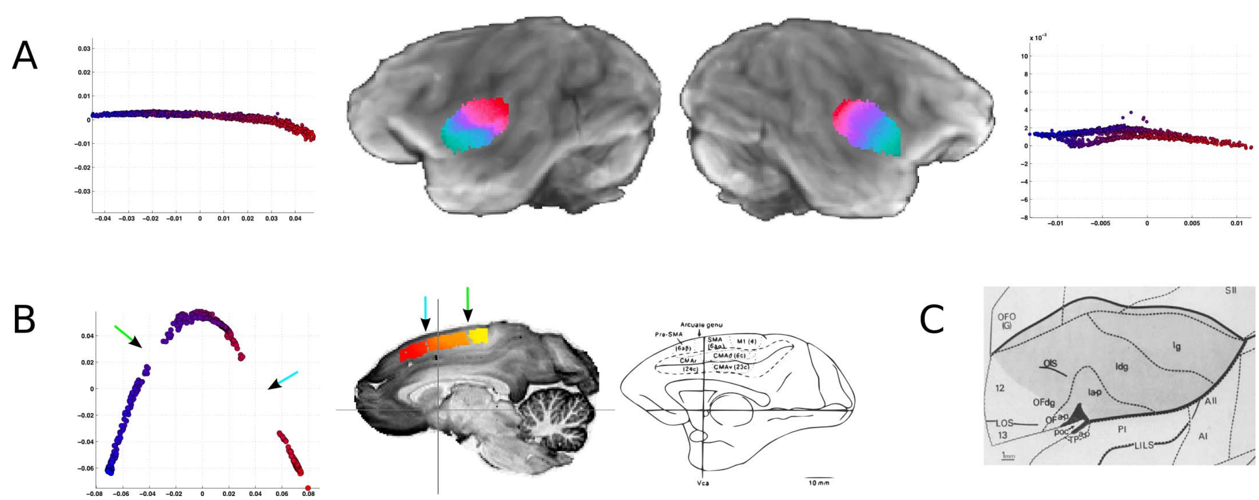

Fig 1: A Laplacian eigenmaps (LE) of the insular connectivity are shown on the sides, revealing a one-dimensional gradient of variation. Colors in the graphs refer to the distance of each point from the left extreme. In the middle, the values are overlaid onto the anatomy. **B**: in the medial motor wall LE suggested the presence of three clusters. **C** Location of different cortical types in the macaque insula.