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Cortical hierarchy relates to microstructural organization

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The neocortex is composed of an extensive recurrent network in which distinct feedforward and feedback inputs from other brain regions are integrated to generate coherent percepts and execute voluntary actions 1. In recent decades, research has begun to shed light on how the cortex performs these functions and constructs the cortical hierarchy based on a principle of hierarchical distance 2. However, the spatial patterning of cortical organization and circuit mechanisms of the human cortex remain unclear. The recently proposed regression dynamic causal model (rDCM) offers a powerful and reliable tool for assessing the effective connectivity in large networks based on functional magnetic resonance imaging (fMRI) data 3. This study characterizes the hierarchy of input-output asymmetry between cortical regions and assesses its associations with cytoarchitecture and cortical types.

In this work, we analyzed 7 Tesla (7T) movie fMRI data from 10 unrelated healthy adults at the group level. Specifically, our work (i) utilized rDCM and high-resolution 7T MRI to construct effective functional connectomes (FC), (ii) calculated the input-output asymmetry index for each region (input minus output) and cross-correlated these indices for all regions using the Spearman correlation coefficient to generate the asymmetry index similarity (AIS) matrix, (iii) captured the principal component of AIS using diffusion map embedding, and (iv) assessed associations between AIS and cytoarchitecture as cortical types.

The group-level parcel-wise effective FC matrix was generated using the Glasser atlas 4, revealing asymmetry between the input and output streams of each region (Figure 1A). We generated the AIS by cross-correlating parcel-wise asymmetry indices, and then estimated its first component (AISG1). AISG1 clusters regions with closer input-output asymmetry patterns together. We observed an axis stretching between the dorsal attention network and the cingulo-opercular network and mesial frontal lobe (Figure 1B). Examining the distribution of AISG1 across cortical hierarchy levels 5, we found the highest values in the paralimbic system and the lowest in the unimodal system (Figure 1C), indicating the difference of the input-output asymmetry patterns between these two systems. In terms of cortical types, AISG1 was higher in the agranular area and lower in the parietal area (Figure 1D). To further investigate the relationship between AISG1 and cytoarchitecture, we sampled layer-specific intensity profiles between the pial and white matter surfaces using histological data 6. We assessed the histological skewness, which indexes the balance of cellular density in infra- vs supragranular layers 7. Sensory areas exhibited lower skewness, while the paralimbic network showed higher skewness. Notably, we found a significant correlation between AISG1 and histological skewness ($rho=0.54$, $pspin<0.001$; Figure 1E).

Our findings point to a cortex-wide sensory-paralimbic differentiation of input-output asymmetry, which is associated with cytoarchitectural patterning. Our work provides new insights into macroscale interactions between cortical areas and how they are underpinned by cortical cytoarchitecture.

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