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A cross-modal, cross-species comparison of connectivity measures in the primate brain

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Abstract

In systems neuroscience, the term "connectivity" has been defined in numerous ways, according to the particular empirical modality from which it is derived. Due to large differences in the phenomena measured by these modalities, the assumptions necessary to make inferences about axonal connections, and the limitations accompanying each, brain connectivity remains an elusive concept. Despite this, only a handful of studies have directly compared connectivity as inferred from multiple modalities, and there remains much ambiguity over what the term is actually referring to as a biological construct. Here, we perform a direct comparison based on the high-resolution and high-contrast Enhanced Nathan Klein Institute (NKI) Rockland Sample neuroimaging dataset, and the CoCoMac database of tract tracing studies. We compare four types of commonly-used primate connectivity analyses: tract tracing experiments, compiled in CoCoMac; group-wise correlation of cortical thickness; tractographic networks computed from diffusion-weighted MRI (DWI); and correlational networks obtained from resting-state BOLD (fMRI). We find generally poor correspondence between all four modalities, in terms of correlated edge weights, binarized comparisons of thresholded networks, and clustering patterns. fMRI and DWI had the best agreement, followed by DWI and CoCoMac, while other comparisons showed striking divergence. Networks had the best correspondence for local ipsilateral and homotopic contralateral connections, and the worst correspondence for long-range and heterotopic contralateral connections. K-means clustering highlighted the lowest cross-modal and cross-species consensus in lateral and medial temporal lobe, anterior cingulate, and the temporoparietal junction. Comparing the NKI results to those of the lower resolution/contrast International Consortium for Brain Imaging (ICBM) dataset, we find that the relative pattern of intermodal relationships is preserved, but the correspondence between human imaging connectomes is substantially better for NKI. These findings caution against using "connectivity" as an umbrella term for results derived from single empirical modalities, and suggest that any interpretation of these results should account for (and ideally help explain) the lack of multimodal correspondence.

Keywords: connectomics, tract tracing, CoCoMac, resting state functional MRI, cortical thickness, structural covariance, diffusion-weighted MRI, hierarchical clustering, k-means clustering

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