Characterizing gradients in brain connectivity: Assessment and applications of manifold learning

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Background: Anatomical description of the human connectome has largely focused on delineating distinct cortical areas and network modules using various forms of categorical clustering. However, such approaches are limited in revealing the presence of: 1. broader gradations across distinct parcels; and, 2. gradual transitions between distinct areas, as previously demonstrated in cytoarchitectonic data. Evidence from gold-standard tract-tracing studies in the macaque monkey indicates the presence of stepwise gradations in patterns of connectivity. For example, direct projections occur predominantly between areas that are one level away in the architectonic hierarchy. In the frontal lobe, this pattern of progressive architectonic differentiation is spatially organized along orthogonal gradients spanning the dorso-ventral and rostro-caudal axes. Nonetheless, current applications of clustering methods to connectivity data acquired with MRI are not optimized to capture these overarching patterns. Previous studies have used MRI-based in vivo methods to investigate the similarity in the connectivity profiles of thousands of voxels simultaneously, and has shown the ability to identify boundaries between regions featuring a sharp transitions. However the presence of gradients of connectivity across regions has been thus far been neglected. Here we employed an original manifold learning method to recover complex connectivity structure, such as the overlapping gradients documented by the neuroanatomical literature.

Methods: Manifold learning (ML) refers to a family of non-linear dimensionality reduction techniques. Compared to linear methods (eg, singular value decomposition), ML reveals more complex geometrical structures generating the observed data without imposing shape constraints. Thus ML techniques are suitable for the detection of complex and potentially overlapping gradients of connectivity, which we demonstrate using a reduced simulation. We also apply diffusion maps (DM) to ADHD200 resting state functional connectivity data to characterize the underlying geometry, which we describe here as ‘connectivity gradients’.

Results: The simulation showed that DM can successfully detect overlapping gradients of connectivity present in the same brain structures. With ADHD200 data, DM consistently detected a gradient from DMN to FPN at individual subject-level and allowed for quantification of degree of separation between these networks.

Conclusions: We showed that diffusion embedding is able to unfold the presence of two overlapping gradients of connectivity. The ability to recover such complex organizations of brain connectivity is crucial to characterize the way in which they can be altered in different patients populations, as well as for the description of basic cortical parcellation.