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Feature Review

Comparative Connectomics

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We introduce comparative connectomics, the quantitative study of cross-species commonalities and variations in brain network topology that aims to discover general principles of network architecture of nervous systems and the identification of species-specific features of brain connectivity. By comparing connectomes derived from simple to more advanced species, we identify two conserved themes of wiring: the tendency to organize network topology into communities that serve specialized functionality and the general drive to enable high topological integration by means of investment of neural resources in short communication paths, hubs, and rich clubs. Within the space of wiring possibilities that conform to these common principles, we argue that differences in connectome organization between closely related species support adaptations in cognition and behavior.

Trends

In recent years, a growing number of connectomes of different species have been reconstructed, using a broad range of methodologies.

These connectome maps are being examined using a common set of tools, principally drawn from the mathematical field of graph theory.

Studies consistently report pronounced community structure, short communication paths, and the formation of hubs and rich clubs, features that appear to be universal across many species.

Overlapping topological network attributes may reflect common themes of wiring of nervous systems.

Differences in network architecture between closely related species may indicate specific adaptations in cognition and behavior.

Comparing Brains

Comparative biology and comparative neuroscience generally aim to discover common plans of organization while also accounting for diversity among species. A key objective of comparative studies of brain architecture is to achieve an understanding of the neurobiological basis for the emergence of complex brain structure and function. For example, several classic studies on the cellular composition of the primate cortex have addressed cross-species homologies [1–3] and contemporary comparative analyses have highlighted common cortical phenotypes and important roles of genetic and epigenetic interactions in development for creating cross-species diversity [4,5]. Together, these and many other comparative studies have laid the foundations for our understanding of mammalian brain anatomy and function.

One major focus has been on the growing size of brains from smaller to larger animals [6–9] and, in particular, the significant increase in volume required by the expansion of anatomical connections [10–12]. A seminal observation is that the proportion of brain mass spent on cortical white matter follows an **allometric scaling** (see Glossary) relation between body and brain size across the entire spectrum of simpler to higher-order mammalian species [13,14]. In small mammals, such as the mouse, only approximately 11% of total cortical volume comprises white matter, in contrast to 27% in the macaque monkey, 40% in chimpanzees, and 41% in humans (data from [13]). However, despite a larger volume of white matter, maintaining constant connection density among an increasing number of neurons and regions in larger brains will quickly outstrip the volume that can be allocated to long-distance neural wiring [15–17]. Thus, the scaling between brain size and white matter volume implies a lower proportion of directly connected neural elements in larger-sized brains [15,17,18], making it increasingly difficult for neural elements to communicate via direct connections. Maintaining fast and efficient neural communication brings significant benefits to brain function, arguably leading to a fundamental tension or tradeoff [19] between the conservation of neural resources that can be spent on long-distance connectivity and the promotion of efficient communication to support complex neural processing. These apparent opposing or competitive pressures highlight the importance of the **topological** organization of nervous systems that must provide an arrangement of neural

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elements and connections to balance the amount of neural resources used for connectivity while simultaneously enabling effective information transfer in the service of brain function.

Comparative Connectomics

The examination of brain network topology is a core element of the field of **connectomics** [20], the emerging science of structural and functional brain networks [21–24]. The increasing availability of connectomes of multiple animal species (Figure 1, Key Figure) provides a new opportunity for the comparative analysis of network architecture across species. In this review, we introduce '**comparative connectomics**', defined as the comparison of the topological layout of nervous systems across species, with the aim of identifying common principles and variations in network features. Comparative connectomics can provide insight into general principles of neural wiring that apply across species and can examine to what extent variations in connectivity between species may form the basis for differences in brain function. As we discuss, connectomes of different species reconstructed by a broad range of methodologies (Box 1) can be compared by applying a consistent set of network analysis measures and graph analytical

Key Figure

Connectomes across Species

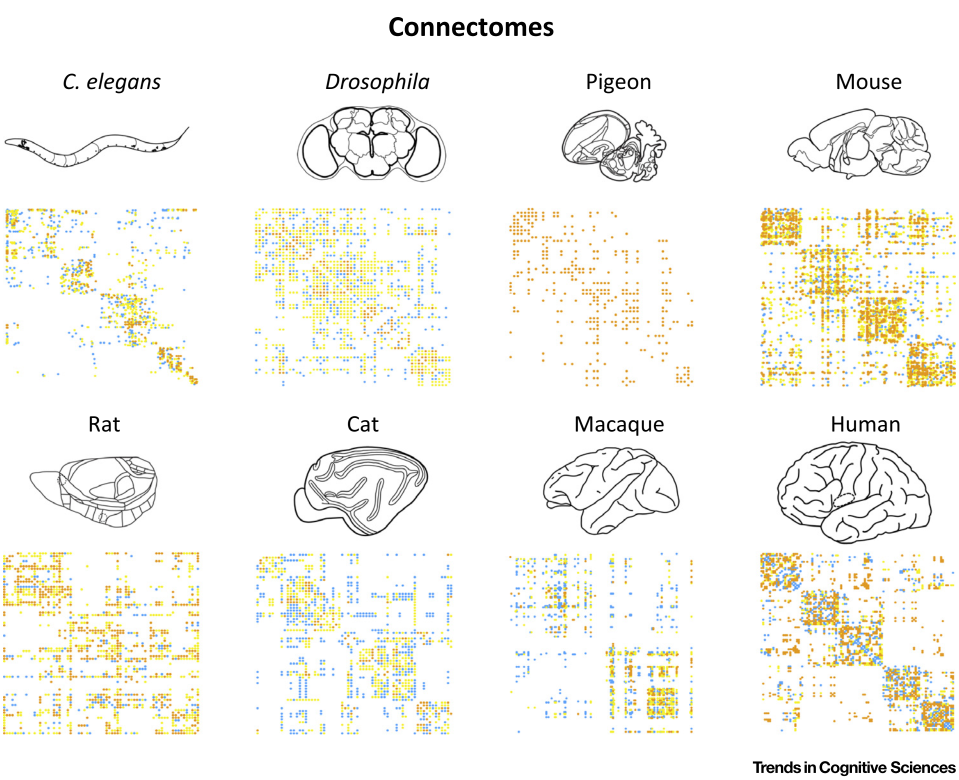

Figure 1. The Figure displays reconstructed connectomes of eight different species: *Caenorhabditis elegans* (roundworm) [26], *Drosophila* (fruit fly) [40], pigeon [44], mouse [45], rat [49], cat [51], rhesus monkey (macaque, FE91 atlas) [53,160], and human (Human Connectome Project data, [128]). Connectomes are represented as connectivity matrices with rows and columns depicting source and target regions (grouping regions participating in the same community together) and with the elements of the connectivity matrices showing the reconstructed projections. Pathways are grouped accordingly to whether they are weak (blue), medium (yellow), or strong (orange).

Glossary

Adjacency matrix: a systematic description of the absence or presence of a connection or edge between all pairs of nodes of a network, represented by a square matrix.

Allometric scaling: relation between body size and shape, morphometry, and function of brain parts across species where one or more of these measures change exponentially or nonlinearly.

Association matrix: a summary of the absence or presence (potentially including information about the strength of an association) of all pairwise associations of network nodes, represented by a square matrix.

Brain network: any set of structural or functional relations among brain elements.

Comparative connectomics: the quantitative study of cross-species commonalities and variations in brain network topology.

Connectivity: description of the anatomical projections (e.g., synaptic connections or axonal tracts) between brain network nodes (e.g., neurons or cortical areas).

Connectome: comprehensive network map of the neural connections of a nervous system.

Connectomics: a subfield of neuroscience that studies the reconstruction and analysis of connectomes.

Functional connectivity: statistical relation between time-series of physiological activity (e.g., fMRI or spike trains) of neural elements (e.g., neurons or brain regions).

Graph: a mathematical description of a network, comprising a collection of nodes (e.g., neurons or brain areas) and a collection of edges describing the pairwise relations between nodes (e.g., synaptic connections or macroscopic axonal projections) (Box 2).

Graph theory: a branch of mathematics that studies the topological organization of graphs.

Homology: properties of nervous system organization (e.g., cellular architecture or wiring organization) that are shared between species.

Morphospace: originally defined in evolutionary theory as the space of all possible body shapes or morphologies for a given group of organisms.