Mapping the human connectome at multiple scales with diffusion spectrum MRI

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Introduction

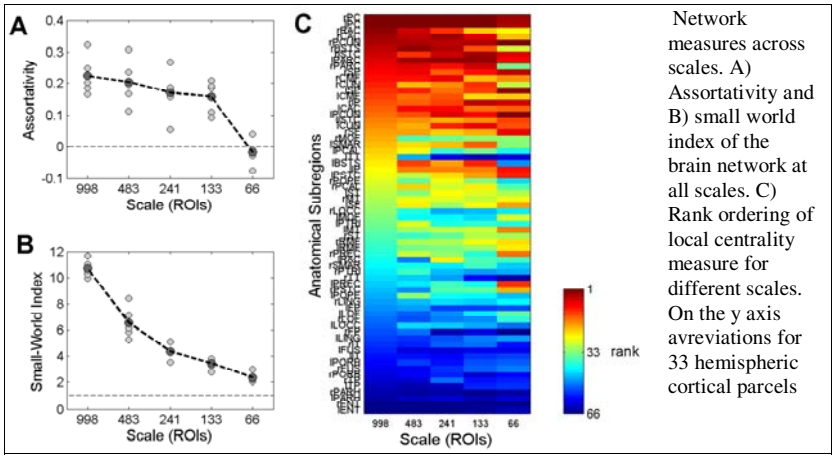
The aim of connectomics is to provide a comprehensive description of the complete structural connectivity of the entire brain (http://www.scholarpedia.org/article/Connectome). Given that such a description at the ultimate resolution of single cells is currently infeasible, one needs to adopt a multi-scale approach. At the level of the entire brain diffusion MRI represents a particularly interesting experimental avenue for in-vivo as well as ex-vivo studies. Very recently, we have used a methodology combining landmark-based registration and automatic cortical parcellation to build high resolution normalized connection networks [1] which has led to a detailed characterization of the human brain structural network [2]. In the present abstract we have extended this work by proposing a hierarchical parcellation scheme of the cerebral cortex in order to map the connection network of the brain at multiple scales. The motivation was not only to provide the end user with wiring maps corresponding to the scale needed for a specific application but also to ask whether network architectures at different scales would differ in the way they are organized. The latter finding would cast doubt on the generality across scales of any attempt to characterize cortical networks with the methods described in the present paper.

Material and Methods

Neuroimaging and Tractography : The path from diffusion MRI to multi-resolution structural connection matrices of the entire brain is a five step process very similar to that described in [1,2]: (1) diffusion spectrum [3] and high resolution T1-weighted MRI acquisition of the brain, (2) segmentation of white and gray matter [3], (3) white matter tractography [1,2], (4) segmentation of the cortex into 5 sets of ROIs (see details below) (5) network construction for the 5 different scales [1,2].
In step (4) 66 cortical parcels provided by Freesurfer software [4] served as the basis resolution and for the first network scale. Each of these parcels was then subdivided into a number of small and compact ROIs such that the total number of ROIs is 998 and each ROI measures ~1.5 cm^2. This latter partition served as the smallest scale and therefore generated the largest network made of 998 nodes. By pairing of spatially adjacent ROIs a network of 492 ROIs was created. This operation was repeated twice in order to get a cortical coverage with 242 and 138 ROIs. The end result of this procedure was 5 weighted networks of different scales for every subject of the study (5 right handed males). The anatomical positions of the ROIs are in register across subjects, allowing for averaging across individual networks.
Network Analysis: All network measures reported in this paper were computed from weighted undirected connection graphs obtained for individual subjects at all five scales. Briefly, degree is equal to the number of connections (edges) attached to each node (ROI); assortativity captures the cross-correlation of degrees across edges, with positive assortativity resulting from a tendency for nodes with matching degree to be connected to each other; clustering coefficients express how many neighbors of a node are also neighbors of each other, or the "cliquishness" of the neighborhood; path lengths record the length of the shortest path between a pair of nodes; and centrality is high for nodes that are located on many short paths in the network and low for nodes that do not participate in many short paths and are therefore more peripheral. For mathematical definitions of these measures see [2].

Results

Distributions of node degree as well as distributions of fiber densities (edge weights) were found to be consistent with exponential rather than scale-free distributions, as they were best fitted by straight lines in ranked distributions on a semilog scale (data not shown). Exponential scaling was found for all scale examined in this study. The assortativity was found to be positive across all scales with the exception of 66 ROIs (Figure A), indicating that highly connected nodes tended to connect to other highly connected nodes. This pattern is consistent with the existence of highly connected hub-like core, previously identified at the high resolution of 998 ROIs. Connection graphs across all scales exhibited robust small-world attributes, here expressed as the "small-world index", which captures the ratio of clustering to path length in comparison to equivalent populations (n=100) of random networks (Figure B). The small-world index increases sharply with the spatial resolution of the network, indicating that its constituent attributes are more highly expressed for more highly resolved cortical networks. Ranked distributions of node centrality per anatomical subregion are displayed in Figure C, for all five scales. Clearly, these distributions are correlated across scales (all pairwise correlation coefficients are > 0.75), with areas that are revealed as highly central at 998 ROIs generally remaining highly central also at the lowest resolution of 66 ROIs. Small anatomical subregions with few constituent ROIs tend to show the greatest discrepancies (e.g. transverse temporal cortex) across scales while regions with greater spatial extent are more consistently captured.



Network measures across scales. A) Assortativity and B) small world index of the brain network at all scales. C) Rank ordering of local centrality measure for different scales. On the y axis avreviations for 33 hemispheric cortical parcels

Discussion

Technology is now available in order to map the human connectome at the macro-scale in-vivo. More specifically in the present work we have developed the tools for the structural brain network to be measured at various scales, from large anatomical areas to small cortical patches in the centimeter square range. We showed that key network measures can be robustly estimated across multiple scales producing results that are consistent with previous single-scale investigations and thus confirm the reliability of the method. This technique will allow the end user to pick the scale that is most suitable for a specific application. Studies willing to evaluate differences in individual fiber bundles will probably use intermediate scales since those are most robust to registration errors. On the other hand, studies dedicated to the analysis of more global network properties or individual anatomical studies will probably use the finest scale available.

References [1] Hagmann P et al (2007)PLoS ONE 2: e597 [2] Hagmann P et al (2008) PLoS Biol 6(7): e159 [3] Wedeen VJ et al (2005) Magn Reson Med 54: 1377 [4] Freesurfer (surfer.nmr.mgh.harvard.edu).

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