Imaging the brain neuronal network with diffusion MRI: a way to understand its global architecture

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Introduction

Biological neuronal networks, and in particular the human brain, are remarkable natural systems capable of complicated patterns of behavior. To understand the emergence of higher level brain functions, the individual study of its components clearly seems insufficient. It is necessary to consider global properties of such complex systems. The backbone of complexity in the nervous system is composed by the large scale architectural characteristics of the neuronal network. We propose to study these properties by using DSI tractography. After having proposed a procedure to image the human long-range brain axonal network, we report on its small world and hierarchical architecture.

Material and Methods

We perform a whole brain study of a healthy volunteer on an Achieva 3T Philips scanner. We use a diffusion weighted single shot EPI sequence with the following timing parameters: TR/TE/Delta/delta = 3000/100/47.6/35 ms and b-max = 12000 mm^2/s. Q-space is sampled and the data reconstructed according to a standard DSI scheme [1]. The acquisition block was made of 32 slices of a 128x128 matrix with a spatial resolution of 2x2x3 mm3. DSI tractography is performed as described in [2] by initiating fibers uniformly over the whole brain. As opposed to the classical procedure of tract selection using manually chosen ROIs, in the present experiment we choose the ROIs differently. We place a 3D grid over the brain image. This corresponds to covering the brain with lots of small ROIs of size 8x8x8 mm^3 in study 1 and 4x4x4 mm^3 in study 2. Furthermore we identify the brain Gray Matter (GM) by using a T1w based segmentation algorithm and actually consider as ROIs only the boxes that contain GM. We construct a graph where the vertices represent the set of ROIs defined above. A weighted edge between two vertices is drawn if there is at least one fiber that has its origin and termination in the pair of different ROIs. The edge weight corresponds to the connection density between ROIs: it is the ratio number of fibers / (their average length * cortical surface in the ROI). This graph represents the brain long-range axonal connectivity between small cortical areas, in study 1 made of 748 and in study 2 of 4522 cortex positions. Now, we construct an unweighted version of this graph by setting an arbitrary threshold on the weight of edges, and keeping only the strongest connections, whose weight exceeded this threshold; the resulting graph is denoted by G_{brain}. This allows us to apply standard tools to study the large scale properties of the system. First, we test if the graph G_{brain} is a small world, which is an important property of many complex networks [3]. The small-world feature of a graph is assessed from two metrics: average path length L, and clustering coefficient C. L is the average number of hops between two randomly chosen nodes, and C captures the extent to which the network is clustered. As a reference point we take a random graph G_{rand} with the same number of vertices and edges as G_{brain}, but where the edges are thrown randomly. The graph G_{brain} can be declared a small world, if $L_{brain}/L_{rand}\approx 1$ and $C_{brain}/C_{rand}>>1$. Second we want to investigate the potential hierarchy of the data. We use hierarchical clustering, which is a way to investigate grouping in a data set, simultaneously over a variety of scales, by creating a cluster tree [4]. For the current application we simply define the distance d(i,j) as the length of the shortest path between nodes i and j. d(R,S) is the distance between two sets of vertices (1). The algorithm groups then successively the nodes by increasing distance.

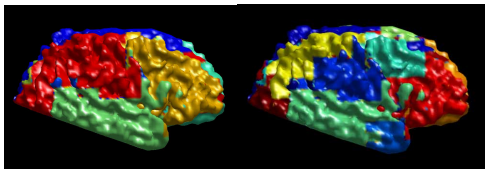
$$(1)\quad d(R,S)=\frac{1}{|R||S|}\sum_{i\in R}\sum_{j\in S}d(i,j)$$

A)

Vertex number	Average degree	L_{brain}	L_{rand}	C_{brain}	C_{rand}
748	51.5	2.34	1.96	0.031	0.0079
4522	25.3	3.33	2.89	0.011	0.00068

B)

C) D)



Hierarchical clustering subdivides the right hemisphere into temporal, parieto-occipital and fronto-prefrontal areas (Fig C). Lower levels of decomposition seen in Fig D compatible with functionally relevant areas.

Results

By varying the size of ROI we have constructed brain graphs G_{brain} of different sizes. In Tab. A, we present the average path length L and the clustering coefficient C obtained for the graphs with 748 and 4522 nodes. For both graph sizes, the average path length L_{brain} of the brain is comparable with the average path length L_{rand} of its random graph equivalent, whereas the clustering coefficient is higher for the brain. More importantly, with increasing refinement of the measures (and hence the number of nodes), the ratio C_{brain}/C_{rand} increases significantly, enhancing the small world characteristic. The application of the hierarchical clustering algorithm results in a structure that can be nicely summarized by a dendrogram in Fig.B. If we read it from top to bottom, we first notice that there are two main clusters. They are separated by a large linkage distance and clearly correspond to the left and right hemispheres. Considering the right hemisphere first, we notice next that a separation occurs between fronto-temporal and parieto-occipital cortices, which means that, in terms of White Matter (WM) axonal connectivity, fronto-temporal as well as parieto-occipital intra-connectivity is intense as compared to the looser fronto-parietal, fronto-occipital or temporo-parieto-occipital links (Fig C). Further decomposition of the lobes occurs into functionally significant areas. Similar decomposition occurs on the left hemisphere.

Discussion

The current approach distinguishes [5] itself from the standard tractography as it aims to study the global connective relationships between neuronal components and not the precise trajectories of specific links in 3D Euclidean space. Accordingly we combine conceptual models of neuronal networks with new brain measurement tools. The modeling part uses techniques provided by the fast growing field of complex networks, whereas the brain measurement tools are based on diffusion MRI, which is a unique technique that captures human brain connectivity at large scales and non invasively. Although there is a large resolution discrepancy between the true neuronal network (~10^{10} edges) and the imaged network (10^5 edges), it nevertheless provides us with exquisite information on the "coarse grain" topology of the network and may asymptotically reflect its real microscopic organization. As such our network imaging procedure is not very different from other imaging modalities, where resolution limitation amounts to average out the architecture. Our findings on the small world network organization of the human brain are further supported by various works on evolution theory [6] and confirm some basic evolutionary principles, such as minimal wiring length for maximal bandwidth. Furthermore, based on post-mortem tracing, studies in rat and macaque monkey brain regions reconstructed axonal connectivity graphs and found similar small world topologies for these brain parts, which again confirm our findings [7]. The identified groupings of cortical regions roughly agree with Brodmann's cytoarchitectonics and functional cortical subdivisions. At a certain "resolution" we segregate cortical lobes or lobes aggregates, whereas at another level of finer "resolution" sub-lobar entities of functional significance appear. We can recognize a segregation into visual, auditory, motoric and somato-sensory as well as associative prefrontal and parietal areas. Generally speaking, these results confirm experiments made on local brain regions of macaque monkey and cat that showed a highly structured connectivity among brain areas [7] and seem to be an essential feature for multisensorial integration and higher brain function.

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