The Structural Core of Human Cerebral Cortex and its relation to the brain's default network

P. Hagmann[1], L. Cammoun[2], X. Gigandet[2], R. Meuli[1], C. J. Honey[3], and O. Sporns[3]

[1]Department of Radiology, University Hospital Center and University of Lausanne, Lausanne, VD, Switzerland, [2]Signal Processing Institute, Ecole Polytechnique Fédérale de Lausanne, Lausanne, VD, Switzerland, [3]Department of Psychological and Brain Sciences, Indiana University, Bloomington, Indiana, United States

Introduction

In human cortex, the topology of functional connectivity patterns has recently been investigated [1], with the goal of characterizing key attributes of these patterns across different conditions of rest or cognitive load. The relationship between such functional connectivity patterns and the underlying large-scale neuroanatomy is not well understood, in part because comprehensive data sets of structural connection patterns of the human brain have been lacking. Recent advances in diffusion imaging and tractography methods permit the non-invasive mapping of white matter cortico-cortical projections yielding a connection matrix of inter-regional cortical connectivity [2]. In the present study, we apply network analysis techniques to identify regions of cortex that are both densely interconnected as well as topologically central, thus constituting a structural core. The structural core consists of several interconnected regions of the posterior medial cortex that have high topological centrality with respect to the rest of the cortex. Many of the components of the structural core we identify are members of the brain's default network, in particular the posterior cingulate region and the precuneus.

Material and Methods

Neuroimaging and Tractography : The path from diffusion MRI to a high-resolution structural connection matrix of the entire brain is a five step process: (1) diffusion spectrum [3] and high resolution T1-weighted MRI acquisition of the brain, (2) segmentation of white and gray matter, (3) white matter tractography [2], (4) segmentation into anatomical regions and subdivision into small Regions Of Interest (ROIs) and (5) network construction [2]. This methodology was applied to 5 healthy right handed male subjects.

The end result of this procedure was a weighted network of 998 ROIs, covering the entire cortex and grouped into 66 anatomical subregions. The anatomical positions of the ROIs are in register across subjects, allowing for averaging across individual networks.

Network Analysis : Network analyses were carried out for high-resolution connection matrices (N=998 ROIs), as well as for regional connection matrices (N=66 anatomical subregions). All networks covered both cerebral hemispheres but excluded subcortical nodes and connections. The data shown in this paper is based on the analysis of individual high-resolution connection matrices, followed by averaging across all 5 subjects. We used several network analysis tools to perform our analysis such as : 1) Modularity detection [4] to identify modules within each network. The algorithm generated a modularity matrix with an associated modularity score. 2) Hub Classification. Cluster assignment from the optimal modularity matrices provided the basis for the classification of network hubs into two groups. We calculated each node's participation index P [5], which expresses its distribution of extra- versus intra-module connections. We classified nodes with above average degree and a participation coefficient $P<0.3$ as provincial hubs, and nodes with $P>0.3$ as connector hubs. 3) Graph Theory Methods. Centrality of a node expresses its structural or functional importance. Highly central nodes may serve as waystations for network traffic or as centers of information integration. Other mappings such as connectivity backbone and k-core decomposition were performed (data not shown).

Results

Modularity and Hubs : We used spectral graph partitioning to identify clusters within the weighted high-resolution (998 ROI) network as well as within the weighted average regional (66 regions) network. Optimal modularity for the average regional connectivity matrix was achieved with 6 clusters (Fig. 1). Contralaterally-matched clusters localized to the frontal and temporo-parietal areas of a single hemisphere made up four of the clusters. The two remaining clusters were bilateral, one centered on the posterior cingulate and another more posterior on the precuneus and pericalcarine cortex. Knowledge of the distribution of connections within and between clusters enabled us to identify provincial hubs (hub regions that are highly connected within one cluster) and connector hubs (hub regions that link multiple clusters; Fig. 1). Without exception connector hubs are located within the anterior-posterior medial axis of the cortex, including bilaterally the rostral and caudal anterior cingulate, the paracentral lobule and the precuneus. Provincial hubs are members of the frontal, temporoparietal or occipital clusters (Fig 1).

Centrality : Regions with elevated betweenness centrality are positioned on a high proportion of short paths within the network. The spatial distribution of betweenness centrality measured for individual ROIs from a subject (Fig. 2) shows high centrality for regions of medial cortex such as the precuneus and posterior cingulate cortex, as well as for portions of medial orbitofrontal cortex, inferior and superior parietal cortex as well as the pars opercularis and right caudal middle frontal cortex.

Discussion

Cortical connectivity plays a crucial role in shaping spontaneous and evoked neural dynamics. In this paper we map structural cortico-cortical pathways in the human cerebral cortex at high spatial resolution and find evidence for the existence of a structural core composed of posterior medial cortical regions that are densely interconnected and topologically central. Many members of the structural core are also considered key members of the human default network. The most central components of the human default network are the posterior cingulate/ precuneus, lateral and medial parietal cortex and the medial prefrontal cortex [6]. Our structural results suggest that default network activity may be organized by highly coupled areas of the posterior medial cortex, additionally involving connected and highly central regions in other parts of the cortex, including medial orbitofrontal cortex, lateral parietal cortex and portions of temporal cortex.

Anatomical subregions (r = right, l = left) : BSTS = bank of the superior temporal sulcus, CAC = caudal anterior cingulate, CMF = caudal middle frontal, CUN = cuneus, ENT = entorhinal, FP = frontal pole, FUS = fusiform gyrus, IP = inferior parietal, IT = inferior temporal, ISTC = isthmus of the cingulate, LOCC = lateral occipital, LOF = lateral orbitofrontal, LING = lingual gyrus, MOF = medial orbitofrontal, MT = middle temporal, PARC = paracentral lobule, PARH = parahippocampal, POPE = pars opercularis, PORB = pars orbitalis, PTRI = pars triangularis, PCAL = pericalcarine, PSTS = postcentral gyrus, PC = posterior cingulate, PREC = precentral gyrus, PCUN = precuneus, RAC = rostral anterior cingulate, RMF = rostral middle frontal, SF = superior frontal, SP = superior parietal, ST = superior temporal, SMAR = supramarginal gyrus, TP = temporal pole, TT = transverse temporal.

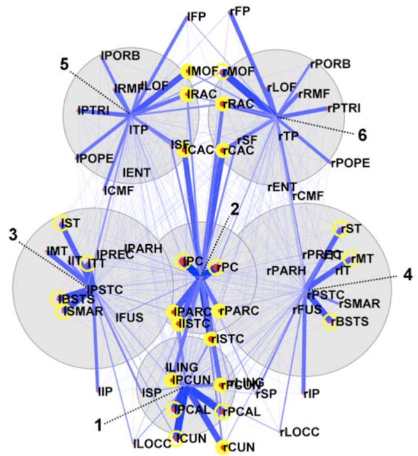

Fig 1: Modularity and hubs. 6 optimal modules identified by spectral clustering. Connector hubs (filled yellow circles) are exclusively spread along the medial line, while provincial hubs appear in the temporal as well as occipitals lobes.

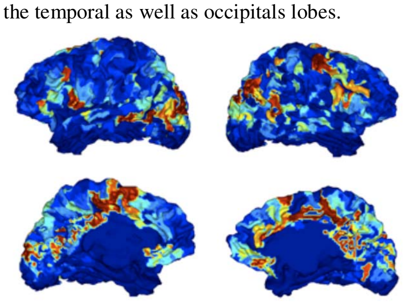

Fig 2: Centrality. Most central cortices are spread over the cingulated gyrus, cuneus and precueus as well as the parieto-temporal junction and inferior frontal gyrus.

References [1] Achard, S et al (2006) *J. Neurosci.* 26, 63-72. [2] Hagmann P et al (2007)PLoS ONE 2: e597. [3] Wedeen VJ et al (2005) Magn Reson Med 54: 1377-1386. [4] Alvarez-Hamelin, JI et al (2005) ECCS. [5] Newman, MEJ (2006) Proc. Natl. Acad. Sci. USA 103, 8577-8582. [6] Fox, M.D. et al (2005) *Proc. Natl. Acad. Sci. USA* 102, 9673-9678. **Acknowledgements:** This work was finacially supported by Mr Yves Paternot and Prof. Pierre Schnyder.