

Predicting Resting-State Functional Connectivity from Structural Connectivity

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Introduction

When participants are not performing any demanding task (the “resting state”), particular subsets of brain regions reliably exhibit correlated levels of activity; a collection of such mutually correlated areas is referred to as a “functional network”. A set of regions including posterior-medial, anterior-medial and lateral parietal cortices comprise the Default Mode Network (DMN), a functional network that is particularly robust across participants and cognitive states. The purpose of the present abstract is therefore to gauge how much of the resting state functional connectivity (rsFC, BOLD temporal correlation) across the cerebral cortex can be accounted for by structural connectivity (SC, inter-regional projection bundles). In addressing these questions, we employ anatomically informed computational models to generate simulated functional connectivity that is compared against empirical observations.

Material and Methods

5 participants were scanned on a 3T system with whole brain high-res T1w imaging, Diffusion Spectrum MRI (2x2x3mm voxels, b-max of 9000 s/mm², 129 diffusion gradient directions) and resting-state fMRI of 15 min (3.3x3.3x3.3 mm voxels, TE=30ms, TR=2000 ms).

Structural connectivity: The path from diffusion MRI to structural connection matrices of the entire brain is a five step process identical to that described in [1]: (1) diffusion spectrum [2] and high resolution T1-weighted MRI acquisition of the brain, (2) segmentation of white and gray matter [3], (3) white matter tractography [4], (4) segmentation of the cortex into 2 sets of ROIs (see details below) (5) network construction by computing the SC (#fibers connecting any pair of ROIs). In step (4) the 66 cortical parcels provided by Freesurfer software [3] served as the basis resolution. Each of this parcel was then subdivided into a number of small and compact ROIs such that the total number is 998 and measures ~1.5 cm². The anatomical positions of the ROIs are in register across subjects, allowing for averaging across individual networks.

Functional connectivity: Raw BOLD signals were registered and resampled onto the b₀ image of the diffusion scan using rigid body registration. Following slice time correction BOLD time series were then computed for each of the predefined 998 ROIs averaging across all voxels within the ROI mask, ROI BOLD time series were then piecewise-linearly detrended (every 50 seconds) and mean cortical, ventricular and white matters signals were regressed from each time series. Finally, Pearson correlations were calculated between all ROI-pairs constituting the rsFC.

Results

Having observed in [1] that SC is correlated with rsFC, we sought to capture a very wide range of network dynamic effects by using computational models. The models we employed were composed of nodes whose time evolution is governed by a set of differential equations, and a connection matrix that determines the couplings between these equations. Two models were employed to predict rsFC: a linear model for which the correlation structure in spontaneous dynamics can be calculated analytically [5], and a nonlinear neural mass model whose correlation structure was calculated from simulated time-series [6]. In both models, the empirically generated high-resolution SC determined the strength and topology of the inter-node couplings. The correlation between simulated rsFC and empirical rsFC at direct links in the high resolution network was slightly higher in the linear than the nonlinear model ($r = 0.55$ and $r = 0.43$ respectively), while the nonlinear model yielded a better prediction of the rsFC between indirectly connected nodes ($r = 0.36$ nonlinear versus $r = 0.26$ for the linear model). In the low resolution networks, the correlation for both linear and nonlinear models between simulated and empirical rsFC increased to $r = 0.70$ for directly linked pairs (Fig A). Indirectly linked pairs were again better captured in the nonlinear model ($r = 0.23$, versus $r = -0.03$ for the linear model). On an area-by-area basis (Fig B) correlations between simulated and empirical rsFC were highest for many regions located in the posterior medial cortex, including the precuneus and posterior cingulate cortex, as well as the medial orbitofrontal cortex. Surprisingly, lateral parietal cortex appeared to be not very well linked to the medial parietal cortex on the simulated data.

Discussion

Based on the observation of significant correlation between rsFC and SC [1], we attempted to model resting state functional activity running computational models on structural data in order to evaluate how much of the rsFC across the cerebral cortex can be accounted for by SC alone. We used two models, linear and non-linear, to compute cortical dynamics and showed that the rsFC of the entire cortex can be explained to a significant extent by SC and that some highly connected regions were matched with high fidelity. The rsFC of the posterior medial components of the default mode network was particularly well-captured in our nonlinear model and this is likely a consequence of the fact that there is a robust anatomical subnetwork linking DMN member regions. However, while modeled rsFC seeded in the DMN reproduced empirical rsFC patterns along the medial axis, the inclusion of the lateral parietal cortex was weak, probably related to fiber tracking difficulties in the posterior centrum semi-ovale where intricate fiber crossings occur. As a whole, the robust SC-rsFC relationship that we report via computational modeling provides compelling evidence that functional connectivity is reflective, at least in part, of interactions between distant neuronal populations.

References [1] Hagmann P et al (2008) PLoS Biol 6(7): e159 [2] Wedeen VJ et al (2005) Magn Reson Med 54: 1377 [3] Freesurfer (surfer.nmr.mgh.harvard.edu) [4] Hagmann P et al (2007) PLoS ONE 2: e597. [5] Galan et al (2008) PLoS ONE 3:e2148 [6] Breakspears et al (2003) Network 14:703

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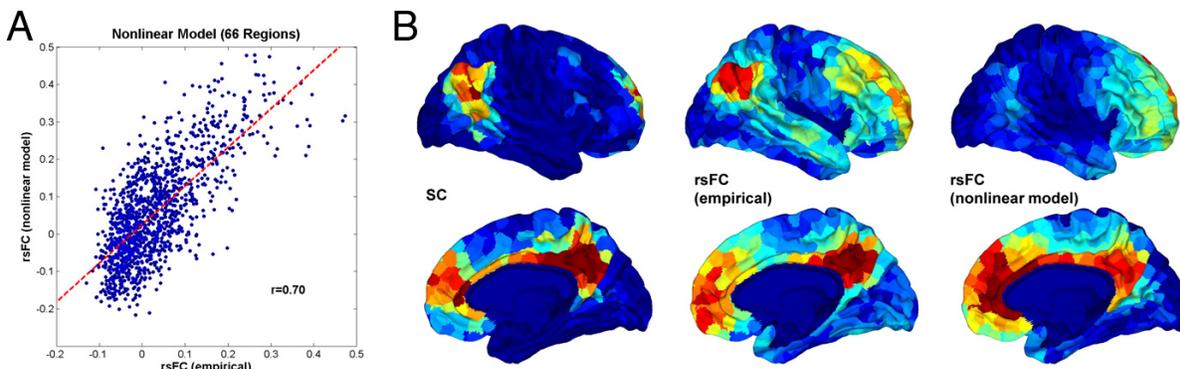


Fig: Modeling and prediction of functional connectivity. (A) Scatter plot of empirical rsFC versus simulated rsFC downsampled to 66 cortical regions. (B) Comparison of SC, rsFC (empirical) and rsFC (nonlinear model) for two single seed regions, the posterior cingulate in the right hemisphere and the precuneus in the left hemisphere.