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Linking human brain local activity fluctuations to structural and functional network architectures

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ABSTRACT

Activity of cortical local neuronal populations fluctuates continuously, and a large proportion of these fluctuations are shared across populations of neurons. Here we seek organizational rules that link these two phenomena. Using neuronal activity, as identified by functional MRI (fMRI) and for a given voxel or brain region, we derive a single measure of full bandwidth brain-oxygenation-level-dependent (BOLD) fluctuations by calculating the slope, α, for the log-linear power spectrum. For the same voxel or region, we also measure the temporal coherence of its fluctuations to other voxels or regions, based on exceeding a given threshold, Θ, for zero lag correlation, establishing functional connectivity between pairs of neuronal populations. From resting state fMRI, we calculated whole-brain group-averaged maps for α and for functional connectivity. Both maps showed similar spatial organization, with a correlation coefficient of 0.75 between the two parameters across all brain voxels, as well as variability with hodology. A computational model replicated the main results, suggesting that synaptic low-pass filtering can account for these interrelationships. We also investigated the relationship between α and structural connectivity, as determined by diffusion tensor imaging-based tractography. We observe that the correlation between α and connectivity depends on attentional state; specifically, α correlated more highly to structural connectivity during rest than while attending to a task. Overall, these results provide global rules for the dynamics between frequency characteristics of local brain activity and the architecture of underlying brain networks.

Introduction

Relating structure and function is fundamental to understanding the mechanisms of information processing in the brain. Non-invasive functional brain imaging, specifically MRI/fMRI, has played a pivotal role in demonstrating structure–function rules due to its capability to localize activity and relate it to structural features across the whole brain, on the scale of millimeters. Recent studies examining brain activity during rest demonstrate large-scale functional organizational rules, thus revealing intrinsic dynamical properties of the brain (Fox and Raichle, 2007). Likewise, functional connectivity (FC) of the brain during rest shows correspondences to structural connectivity (SC), although this relationship is intricate and not reciprocal — i.e., SC is highly indicative of FC, but not vice versa (Adachi et al., 2012; Greicius et al., 2009; Honey et al., 2009; Vincent et al., 2007). Still, rules with which structural and functional networks shape and constrain each other remain fundamental, unanswered questions in the field.

The power spectrum of brain activity signals is related to various network properties. This relationship has been captured across many studies using multiple methods such as fMRI (Ding et al., 2011; Tomasi and Volkow, 2011), EEG (von Stein et al., 1999), cultured neuronal networks (Jia et al., 2004; Muramoto et al., 1993), multi-unit activity (Konig et al., 1995), simultaneous single-unit recording and optical imaging (Tsodyks et al., 1999), and computational models (Steinke and Galan, 2011). These results have highlighted the central role of the spectral profile in understanding the structure–function interactions in the brain. However, most fMRI research has utilized only the low frequency component of the BOLD signal, assuming that frequencies above 0.1 Hz are contaminated with noise. On the other hand, BOLD frequencies above 0.1 Hz exhibit coherent patterns of activity (Niazy et al., 2011) and show an anatomically constrained distribution of power as a function of BOLD frequency (Baria et al., 2011). Therefore, it remains largely unknown how the full bandwidth properties of the BOLD signal relate to brain network properties. Here we aim to show that the architecture of synchronous brain networks and white matter networks (*structure*) is tightly related to the fluctuations of local BOLD activity (*function*).

In the frequency domain, the full bandwidth power spectrum of fMRI BOLD signal (approximately 0–0.24 Hz) roughly follows a straight

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line when viewed in log power versus frequency: $\log(P) = -\alpha(f)$. The value (α) offers a glimpse of the distribution of power across frequencies, and in a sense it provides some information about the heterogeneity of the informational content that is observed locally. The larger the absolute value of α, the higher the relative power at lower frequencies in the signal, whereas smaller values suggest that the fluctuations are more random, with less temporal redundancy, and are therefore more efficient in online information processing (He, 2011; Mandelbrot and Van Ness, 1968). Here we examine the relationship between α and FC, i.e., the presence of temporal coherence of BOLD activity, as well as α and SC, i.e., the presence of anatomical connectivity based on diffusion tensor imaging probabilistic tractography, for fMRI activity during either resting state or during a visual-motor attention task. We assess this relationship at different spatial resolutions and as a function of its underlying regional synaptic wiring. First, we test the hypothesis that the distribution of power in local fluctuations, at a per voxel basis, is related to the number of functionally connected voxels across the whole brain. Second, we parcel the brain into 3 anatomical regions of differing hodology that correspond to synaptic wiring and functional complexity (including unimodal, heteromodal, and limbic–paralimbic regions (Mesulam, 1998)), and we examine differential relations between the power of local fluctuations and FC. Third, to our knowledge, the MRI structure–function studies have solely relied on resting scan conditions, perhaps due to the growing evidence that functional networks during rest and task are spatially (Greicius et al., 2004; Smith et al., 2009) and dynamically (Tagliazucchi et al., 2011) similar. Previous work from our lab, however, counters this notion by demonstrating widespread shifts in BOLD frequency power between rest and task conditions (Baria et al., 2011). Here we demonstrate that BOLD power is differentially related to network architecture according to brain state, i.e., during rest versus attending to task. The significance of such an investigation lies in its potential to provide global rules for the dynamics between the spectral characteristics of local brain activity in relation to the architecture of underlying brain networks, as well as in relation to brain state.

Methods

Subjects

Thirty healthy participants (21 females, 40.2 ± 2.1 years old) were scanned for the high-spatial resolution voxel-wise mapping of α. A different set of 21 healthy subjects (18 females, 39.4 ± 2.4 years old) participated in a separate experiment that included a resting state scan, a task scan, and diffusion tensor imaging, for which analysis was performed at a lower spatial resolution at the level of brain regions that approximately equaled Brodmann areas (BAs). All subjects were right-handed and provided informed consent to procedures that were approved by the Northwestern University Institutional Review Board.

fMRI acquisition

Whole-brain functional MR data was acquired with a 3 T Siemens TIM Trio whole-body scanner with echo-planar imaging (EPI) capability. An 8-channel head coil optimized for prefrontal cortical activity was used. Multi-slice T2*-weighted echo-planar images were obtained with the following parameters: TR = 2.5 s, echo time TE = 30 ms, flip angle = 90°, slice thickness = 3 mm, in-plane resolution = 3.475×3.475 mm^2. The 36 slices covered the whole brain from the cerebellum to the vertex. Scans for the voxel-wise analysis were 300 volumes and lasted 12 min. Scans for the BA analysis lasted 10 min with 244 volumes.

For resting scans, participants were asked only to stay alert with their eyes open. Task scans required participants to rate the length of a bar fluctuating at ~0.01 to 0.05 Hz along an axis numbered 0 to 100. The bar was projected onto the screen in the scanner, and subjects continually rated its length as the bar moved by spacing their right thumb and forefinger, to which a voltage potentiometer recording device was attached with tape (Baliki et al., 2008). For example, if the bar reached a height of 100, subjects had their thumb and forefinger tips as far apart as possible. If the bar dipped to 0, their fingertips were touching. Prior to scanning, subjects were trained on the task. All subjects performed the task such that their finger movements were highly correlated with the visual bar movement ($r > 0.7$ for all subjects).

Anatomical scans

In addition to the functional scans, a T1-weighted anatomical MRI image was also acquired for each subject using the following parameters: TR = 2.1 s, TE = 4.38 ms, flip angle = 8°, FOV = 220 mm, slice thickness = 1 mm, in-plane resolution = 0.86×0.86 mm^2 and number of sagittal slices = 160.

DTI

Images were acquired using spin-echo EPI in one acquisition of 72 slices, covering the whole brain. DTI parameters were as follows: voxel size $2 \times 2 \times 2$ mm; TR, 5000 ms; TE, 87 ms; flip angle = 90°; in-plane matrix resolution, 128×128; field of view, 256×256 mm; b0, 1000 s/mm^2. Diffusion was measured in 60 distinct, non-collinear directions, separated in time, into seven groups by no-diffusion weighted volumes. A total of eight no-diffusion weighted volumes were acquired for the purposes of registration and head motion correction. Preprocessing of DTI images was performed using FDT version 2.0 (FMRIB diffusion toolbox), part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl), and included eddy current correction, head motion correction using affine registration to the reference volumes, and skull extraction.

BEDPOST (Bayesian Estimation of Diffusion Parameters Obtained using Sampling Techniques) was performed for each subject, which performs Markov-chain Monte Carlo sampling to establish distributions on the diffusion parameters at each voxel in the individual subject's space (Behrens et al., 2003). Probabilistic tractography was then performed for $6 \times 6 \times 6$ mm centers of brain regions identified by the standard Automated Anatomical Labeling (AAL) map (Tzourio-Mazoyer et al., 2002) and transformed into subject space. AAL regions are roughly equivalent to the classically defined BAs. We therefore refer to our brain regions as BAs. For each of the 21 subjects and from each BA, 5000 samples were drawn to build the a posteriori distribution of the whole brain connectivity distribution.

fMRI Data Preprocessing

Functional MRI data was preprocessed using FEAT (FMRI Expert Analysis Tool) Version 5.98, part of FSL. Preprocessing steps included: skull extraction, slice-timing correction, bulk head motion correction, spatial smoothing (Gaussian kernel of full-width-half-maximum 5 mm), and a high-pass (150 s) temporal filter, which removes artifacts associated with scanner drift at fluctuations less than 0.006 Hz. Peak to peak head motion was maintained at <3 mm for all subjects. Independent component analysis was performed using MELODIC, and temporal and spatial components associated with motion, cerebrospinal fluid, and white matter were identified and their time courses were regressed out of the BOLD signal as covariates of no interest. Global mean BOLD signal and head motion were also regressed from the BOLD signal, voxel-wise.

Connectivity analysis (voxel-wise)

Subject connectivity maps were created in subject space by calculating pairwise BOLD time-series Pearson correlations for every gray matter voxel in the brain and counting the number of correlations