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A REVIEW OF NEURAL BASIS OF RESTING-STATE FMRI CONNECTIVITY

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KEYWORDS :

Resting state functional magnetic resonance imaging (rs-fMRI) is an important modality for imaging the human brain. Capturing fluctuations in the blood oxygen level dependent (BOLD) signal while the brain is `at rest', rs- fMRI can detect distant, and often bilaterally-symmetric regions where activity is synchronized. Such regions are inferred to have `functional connectivity', and patterns of these networks have been found to be altered in a wide range of otherwise indistinguishable disease states. However, despite widespread use of rs-fMRI, interpretation of functional connectivity networks is limited by: 1) The dependence of fMRI BOLD signals on hemodynamic changes as a proxy for neural activity and: 2) A limited understanding of the mechanistic basis of functional connectivity networks in the context of cellular-level interactions and neural representations. [1]

Functional MRI has evolved from simple observations of regional changes in MRI signals caused by cortical activity induced by a task or stimulus, to the development of task-free acquisitions of time series of images in a resting state. Such resting state signals contain low frequency fluctuations which may be correlated between voxels, and strongly correlated regions are deemed to reflect functional connectivity within synchronized circuits. Resting state functional connectivity (rsFC) measures have been widely adopted by the neuroscience community, and are being used and interpreted as indicators of intrinsic neural circuits and their functional states in a broad range of applications, both basic and clinical.[2]

In the cerebral cortex, the activity levels of neuronal populations are continuously fluctuating. When neuronal activity, as measured using functional MRI (fMRI), is temporally coherent across two populations, those populations are said to be functionally connected. Functional connectivity has previously been shown to correlate with structural (anatomical) connectivity patterns at an aggregate level. [1]

In various studies, with the aid of computational modeling, it was observed whether systems-level properties of functional networks—including their spatial statistics and their persistence across time—can be accounted for by properties of the underlying anatomical network. Resting state functional connectivity was measured (using fMRI) and structural connectivity (using diffusion spectrum imaging tractography) in the same individuals at high resolution. Structural connectivity then provided the couplings for a model of macroscopic cortical dynamics. In both model and data, we observed (*i*) that strong functional connections commonly exist between regions with no direct structural connection, rendering the inference of structural connectivity from functional connectivity impractical; (*ii*) that indirect connections and interregional distance accounted for some of the variance in functional connectivity that was unexplained by direct structural connectivity; and (*iii*) that resting-state functional connectivity exhibits variability within and across both scanning sessions and model runs. These empirical and modeling results demonstrate that although resting state functional connectivity is variable and is frequently present between regions without direct structural linkage, its strength, persistence, and spatial statistics are nevertheless constrained by the large-scale anatomical structure of the human cerebral cortex.[2]

Dynamic fluctuations of neural signals in the resting brain generate patterns of FC that exhibit characteristic topography when measured with fMRI (3, 4). When recorded over long time periods, this spatial patterning of FC provides important information about the functional organization of intrinsic or resting-state networks (5, 6). The generative mechanisms that shape FC patterns and that can account for significant variations across healthy individuals and across disease states are therefore of great interest. Some papers explored the capacity of analytic measures that capture the network embedding of shortest paths, derived from the SC matrix, to predict FC. These measures, singly or in conjunction, were found to predict the strength of FC among both connected and unconnected node pairs, at levels that matched or significantly exceeded more conventional path length measures, Euclidean distance, as well as computational models of neural dynamics. Understanding the relationship between SC (the sparse network of axonal links among brain regions) and FC (the dense network of statistical couplings among their neural time series) remains a central challenge for computational cognitive neuroscience. Empirical studies have demonstrated a robust relationship between anatomical networks and networks of dynamic couplings at the macroscale of whole-brain activity (7, 8–10), the mesoscale of intraareal and interareal connectivity (11), as well as the microscale of neuronal circuits (12). Computational studies have built on these empirical data and delivered models of structurally constrained and endogenously driven neural dynamics that can reproduce key features of observed FC (8, 13, 14). Here, we addressed the relation between SC and FC by defining and assessing analytic measures of network communication. This approach is valuable because the degree to which these measures can predict FC may provide conceptual insight into aspects of dynamic interactions along structural connections among brain regions. Notably, the approach creates explicit links between communication processes unfolding within the SC matrix and the emergent pattern of FC, rather than relying on a phenomenological description of FC alone. In applications of graph theory to brain networks most studies have focused on shortest paths as the principal routes along which communication unfolds (15). Indeed, it seems plausible that interactions along such paths are dynamically favored (faster and less prone to noisy interference). However, accessing shortest paths requires information, due to the availability of vast numbers of less efficient alternatives. Hence, the contributions of shortest paths to neuronal communication should depend at least in part on how these paths are embedded within the global network. To capture some of the factors that promote dynamic interactions along shortest paths, it developed two measures that supplement the more standard measure of shortest path length (measured as either weighted distance or number of steps) by taking into account how such paths are embedded in the rest of the network. Search information quantifies the degree to which the shortest, and presumably most efficient, communication path is hidden within the network, here adapted for weighted networks. The principal findings were that search information predicted FC more strongly than path length alone, and that it remained predictive even when considering pairs of regions separated by an equal number of steps. Possible explanations involve increased common input onto nodes along the path, feedback loops that recurrently stabilize signals, or

recapturing of signals that have gone "off-path." The lack of directionality in human diffusion data precludes distinguishing these alternatives, but the question could be addressed in directed connectivity data from nonhuman primates. A corollary of some findings regarding path transitivity is that communication paths that use nodes with high matching index, such as those interconnected in dense subnetworks or modules, boost FC. The capacity of search information and path transitivity along shortest paths to predict whole-brain FC may provide some conceptual insight about the nature of the underlying communication process. If communication operates under a perfect routing policy, the degree to which the shortest path is hidden should be irrelevant to the efficiency by which signals propagate, because alternative (and less efficient) paths are excluded from access. In other words, perfect routing predicts no relationship between search information or path transitivity and the strength of FC. The fact that we observe such a relationship implies that neuronal interactions during spontaneous or resting-brain dynamics are not fully accounted for by perfect routing models and instead suggest diffusion or spreading dynamics or "greedy routing" strategies as potential candidate models for brain network communication. Specifically, our results demonstrate that the embedding of shortest paths within the network plays an additional important role, in particular the (weighted) degree sequence of the path and the availability of detours. Other generative models for FC have been proposed, focusing on the role of spatial distance along with simple topological measures and critical dynamics. A generative model based on the competition between a distance penalty and a tendency to link regions with matching inputs was able to reproduce key features of empirical resting fMRI FC. The findings point to a similar trade-off between the effects of network communication measures on FC. An important difference is that our measures are derived from the SC matrix, and that search information and path transitivity account for attributes of shortest paths that depend on the network context within which the path is embedded. Another generative model was based on Goñi et al. PNAS | January 14, 2014 | vol. 111 | no. 2 | 837 NEUROSCIENCE an analytically solvable Ising-spin attractor (20) and, in a low resolution version of the LAU1 dataset, demonstrated overlap between the empirical and modeled FC at a global SC coupling strength that places the system near a critical bifurcation point. The relationship between these near-critical dynamics and the network measures explored in the present study remains to be investigated in future work. Although the modeling approach presented in this paper has potential advantages, it also has limitations. One limitation is that analytic measures only predict the long-time covariance structure of communication processes unfolding on the SC matrix but cannot account for time-varying or non-stationary couplings, dynamic phenomena like noisy fluctuations around marginally stable states , or more complex measures of FC involving nonlinear coupling or partial correlation. Another limitation is that the model explored here assumes that FC is exclusively due to communication along shortest paths within the network, and excludes other factors that can boost FC, e.g., alternative (longer) paths, common input, or state-dependent modulation. Finally, model performance is subject to limitations inherent in neuroimaging data acquisition. These limitations include lack of directionality in SC, the quality of diffusion imaging data and the tractography reconstructions of fiber pathways, and run lengths and appropriate denoising of resting-state fMRI. Although our results are robust across three different datasets with varying acquisition parameters and techniques, the approach pursued in this paper will benefit from future methodological refinements that further improve sensitivity, spatial and temporal resolution. Further extensions include FC prediction within single subjects as well as use of data-driven (as opposed to atlas-based or random) parcellation schemes. With these limitations in mind, it was concluded that analytic graph based measures of network communication are capable of predicting patterns of resting-brain FC. Some findings lend support to the idea that, to a large extent, the long-time average of resting brain FC is shaped by the underlying SC, thus supporting a causal role of the connect o me in generating characteristic attributes of the brain's functional organization.

However, there has been relatively little work reported that validates whether inter-regional correlations in resting state fluctuations of MRI (rsfMRI) signals actually measure functional connectivity between brain regions, or to establish how MRI data correlate with other metrics of functional connectivity. In this mini-review, recent studies of rsFC within mesoscopic scale cortical networks (100µm-10mm) within a well defined functional region of primary somatosensory cortex (S1), as well as spinal cord and brain white matter in non-human primates, in which spatial patterns of resting state correlations were measured and validated their interpretation with electrophysiological signals and anatomic connections. Moreover, I emphasize that low frequency correlations are a general feature of neural systems, as evidenced by their presence in spinal cord as well as white matter. These studies demonstrate the valuable role of high field MRI and invasive measurements in an animal model to inform the interpretation of human imaging studies.[2]

In a recently published study, it demonstrated a new optical imaging technique capable of capturing both neural activity and hemodynamics across the bilaterally exposed superficial cortex of awake, behaving mice. This method revealed striking patterns of resting-state neural activity in the awake brain, exhibiting bilateral symmetry and features consistent with resting-state networks. Moreover, it demonstrated that this `neural network activity' was predictive of patterns of resting-state hemodynamics (via a linear convolution model), suggesting that we were visualizing the neural basis of resting state functional connectivity mapping. In the current proposal, the plan is to leverage this new view of neural network activity in the brain, to characterize its cellular dependencies, pathways, drivers, behavioral correlates and interactions with hemodynamics. Data will be acquired using novel measurement and circuit manipulation techniques in awake, behaving mice, in addition to analysis of human rs-fMRI, intracranial and intraoperative electrophysiology in patients undergoing epilepsy evaluation (data from ongoing trials) as well as new intraoperative simultaneous optical hemodynamic and electrocorticography recordings. A major aspect of this project will be the aggregation of this data to generate predictive mechanistic and mathematical models of 1) Neural network activity and its dynamic properties and representations across scales and modalities and 2) The coupling relationships between resting-state activity in specific cell types and hemodynamics. These models will be used to derive and test improved methods for rs-fMRI acquisition, analysis and interpretation. To perform this work, we have assembled a world-class interdisciplinary team consisting of neuroscientists, neuroengineers, neurosurgeons, statisticians and experts in resting state fMRI acquisition and analysis. With a sharper understanding of the properties of neural network activity, its dependencies, and how best to harness it in human rs-fMRI, the results of this work could ultimately provide a mechanistic basis for network dysfunctions and their cognitive and behavioral manifestations in disease, potentially yielding new targets for therapies and more robust rs-fMRI based disease detection.[1]

REFERENCE:

[1] Decoding the neural basis of resting-state functional connectivity mapping Hillman, Elizabeth M. C. Columbia University (N.Y.), New York, NY, United States

[2] https://www.researchgate.net/publication/313269700_ Biophysical_ and_neural_ basis_of_resting_state_ functional_connectivity_Evidence_from_non-h u m a n _ primates

[3] De Luca M, Beckmann CF, De Stefano N, Matthews PM, Smith SM (2006) fMRI resting state networks define distinct modes of long-distance interactions in the human brain. Neuroimage 29(4):1359–1367. 6. Fox [4]MD, et al. (2005) The human brain is intrinsically organized into dynamic, anticorrelated functional networks. Proc Natl Acad Sci USA 102(27):9673–9678

[5] Power JD, et al. (2011) Functional network organization of the human brain. Neuron 72(4):665–678. 32.

[6] Yeo BTT, et al. (2011) The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J Neurophysiol 106(3):1125–1165.

[7] Gong G, et al. (2009) Mapping anatomical connectivity patterns of human cerebral cortex using in vivo diffusion tensor imaging tractography. Cereb Cortex 19(3):

524–536
[8] Honey CJ, et al. (2009) Predicting human resting-state functional connectivity from structural connectivity. Proc Natl Acad Sci USA 106(6):2035–2040.
[9] van den Heuvel MP, Mandl RCW, Kahn RS, Hulshoff Pol HE (2009) Functionally linked resting-state networks reflect the underlying structural connectivity architecture of the human brain. Hum Brain Mapp 30(10):3127–3141.
[10] Hermundstad AM, et al. (2013) Structural foundations of resting-state and task-based functional connectivity in the human brain. Proc Natl Acad Sci USA 110(15):6169–6174.
[11] Wang Z, et al. (2013) The relationship of anatomical and functional connectivity to resting-state connectivity in primate somatosensory cortex. Neuron 78(6):1116–1126
[12] Pernice V, Staude B, Cardanobile S, Rotter S (2011) How structure determines correlations in neuronal networks. PLoS Comput Biol 7(5):e1002059.
[13] Honey CJ, Kötter R, Breakspear M, Sporns O (2007) Network structure of cerebral cortex shapes functional connectivity on multiple time scales. Proc Natl Acad Sci USA 104(24):10240–10245. 18.
[14] Deco G, Jirsa VK, McIntosh AR (2011) Emerging concepts for the dynamical organization of resting-state activity in the brain. Nat Rev Neurosci 12(1):43–56.
[15] Latora V, Marchiori M (2001) Efficient behavior of small-world networks. Phys Rev Lett 87(19):198701