Dynamics of resting-state functional connectivity: Methods and models

Tuesday, Jun 19: 8:00 AM - 9:15 AM
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Symposium
Tuesday - Symposia AM

Functional brain connectivity displays complex spatiotemporal dynamics that span multiple timescales. Characterising these dynamics with neuroimaging modalities is an active area of research that has given rise to several issues that remain contested, from the basic definitions of stationarity and dynamics, to the impact of head motion and physiological noise on time-resolved connectivity. Debate also continues about whether functional connectivity dynamics are most parsimoniously modelled as discrete connectivity states or a continuum of change. Our speakers will consider the merits of both discrete and continuous models, and demonstrate the utility of characterizing connectivity dynamics with resting-state fMRI data. To begin, Andrew Zalesky will provide an overview of the current state-of-the-art in connectivity dynamics and introduce the use of surrogate data to test hypotheses about stationarity. Mark Woolrich will then introduce a hidden Markov model (HMM) to characterize discrete transitions among putative brain states, while Raphael Liegeois will argue against the existence of discrete transitions and present a continuous autoregressive model of functional connectivity dynamics. To provide attendees with an understanding of potential neural mechanisms underlying connectivity dynamics, Joana Cabral will present a measure of switching dynamics and introduce the concept of multi-stability, as it relates to cognitive processing and behaviour. Attendees will gain an appreciation of the methods and models available to investigate dynamic functional connectivity, understand the limitations of studying these dynamics with fMRI and learn best practices for designing functional neuroimaging experiments to investigate dynamic changes in functional connectivity.

Why this topic is timely: Time-resolved analysis of functional neuroimaging data has gained significant prominence in the last few years. This area of neuroimaging is likely to give rise to a topical, timely and well-attended session. Updating the neuroimaging community about the current state-of-the-art and best practices for mapping dynamic changes in functional brain connectivity is timely and appeals to a broad cross-section of attendees. Our symposium appeals to both methodologists focussed on mapping network dynamics and neuroscientists interested in understanding the relation between cognition/behaviour and brain dynamics.

Objective

Attendees will be provided with the knowledge to:

1. Understand methods and models that are available to investigate dynamic functional connectivity and appreciate the key limitations and controversies of studying these dynamics with resting-state fMRI.

2. Understand basic definitions of dynamics, meta-stability and stationarity, as related to time-resolved functional connectivity.

3. Understand best practices for designing functional neuroimaging experiments to investigate dynamic changes in functional connectivity, particularly with respect to controlling for head motion, physiological noise and choosing appropriate null models to generate surrogate data.

Target Audience

Our symposium appeals to both neuroscientists interested in understanding neural dynamics and methodologists wanting an update on advances in functional connectivity dynamics. The breadth of talks will ensure the symposium has appeal to those without experience in functional neuroimaging or network modelling.

Co Organizer

Raphael Liegeois, National University of Singapore

Organizer

Andrew Zalesky, University of Melbourne

Presentations

Functional connectivity dynamics: Controversies, null models and clinical utility (index.cfm?do=ev.viewEv&ev=1601)

I will begin with an overview of the current state-of-the-art in methodologies and models for investigating functional connectivity dynamics with resting-state fMRI. I will specifically consider the choice of window length, mapping dynamics with instantaneous phase and whether dynamics are best represented as a continuum or discrete connectivity states. I will argue that it is important to establish whether dynamics in functional connectivity exceed expectations established under an appropriate null hypothesis. To this end, I will present an evaluation of various null models and test statistics that have been used to test whether functional connectivity dynamics can be distinguished from spurious fluctuations owing to sampling variation, physiological confounds and other noise sources. I will demonstrate that the choice of test statistic and null model to generate surrogate data is crucial. In the second part of my talk, I will demonstrate the potential clinical utility of resting-state functional connectivity dynamics in classifying schizophrenia patients from healthy comparison individuals. After controlling for head motion and physiological noise, I will show that utilizing spatial and temporal dynamics of resting-state fMRI can improve classification accuracy by more than 15% compared to static measures of connectivity. This work demonstrates the practical utility of functional connectivity dynamics, despite ongoing controversy about the core statistical properties of these dynamics.

Presenter

Andrew Zalesky, University of Melbourne

Time dynamics of resting brain networks (index.cfm?do=ev.viewEv&ev=1602)

The brain recruits multiple brain networks in a temporally coordinated manner in order to perform cognitive tasks. While much of the research has focused on the spatial nature of these networks, very little is known about the extent to which large-scale networks intrinsically exhibit their own organized temporal dynamics. Here, we use approaches based on the Hidden Markov Model (HMM) to investigate the nature of the temporal dynamics of large-scale networks when the brain is at rest. Using fMRI, we found that the brain spontaneously transitions between different large-scale networks, or brain states, in a relatively predictable manner [Vidaurre, PNAS]. Not only are some transitions more probable than others, but they also follow a hierarchical organization that is surprisingly simple: networks self-organise into two sets of states (referred to as metastates) such that the probability of cycling between networks within a metastate is much higher than transitioning between networks belonging to other metastates. The states belonging to one of these metastates primarily correspond to networks associated with higher-order cognitive functions, whereas the states belonging to the other metastate are mostly involved in perception and motor functions. Importantly, this organisation is specific to individuals in the sense that every person has a specific metastate profile that is very robust across sessions; is heritable, in the sense that members of the same family tend to have similar metastates profiles; and significantly relates to behaviour, in particular to intelligence, to happiness, and to the personality of the subjects. In a separate study, we used MEG and a version of the HMM capable of finding states with distinct spectral properties (including phase coupling between signals at different frequencies) to investigate the extent to which networks intrinsically exhibit phase-locking, consistent with the idea of communication-through-coherence being a key mechanism of communication in the brain. We found that resting cortical activity is indeed generally organised into networks that show transient increases in (phase-locking) coherence in specific frequency bands, but only when viewed at the very fast, subsecond time-scales accessible with the HMM [Vidaurre, bioRxiv]. This approach also revealed new insights into the organisation of the ubiquitous default mode network, which is revealed to be composed of two components, anterior and posterior, with very distinct temporal and spectral properties. These two separated components exhibit strong coherence with the posterior cingulate cortex, yet in very different frequency regimes. The operation of these large-scale cortical networks in very different frequency bands may reflect the different intrinsic timescales that they specialise in. Vidaurre, D., Smith, S. M., & Woolrich, M. W. (2017). Brain network dynamics are hierarchically organized in time. Proceedings of the National Academy of Sciences of the United States of America, 114(48)] Vidaurre, D., Hunt, L. T., Quinn, A. J., Hunt, B. A. E., Brookes, M. J., Nobre, A. C., & Woolrich, M. W. (2017). Spontaneous cortical activity transiently organises into frequency specific phase-coupling networks. bioRxiv

Presenter

Mark Woolrich, Oxford University

Dynamic and static resting-state functional connectivity encode complementary behavioral information (index.cfm?do=ev.viewEv&ev=1603)

Converging evidence suggests that static measures of resting-state functional connectivity (sFC) MRI are missing important information encoded in the temporal fluctuations of fMRI and FC time series. Our recent work suggests that a single first-order autoregressive (AR) model of fMRI time series is able to encode most of these temporal FC fluctuations. Here, we use the coefficient matrix of the AR model as a dynamic marker of FC (dFC). We then explore whether this dFC marker encodes behavioral information in a different way as compared to a classical sFC marker. Across 58 behavioral measures in 419 unrelated HCP subjects, we find that the proposed marker of dFC captures more behavioral information than sFC. Furthermore, dFC outperforms sFC in explaining task-performance measures (e.g., accuracy in a working memory task), whereas sFC and dFC explains self-reported measures (e.g., evaluation of social distress) equally well.

Presenter

Raphael Liegeois, National University of Singapore

The switching choreography of the functional connectome (index.cfm?do=ev.viewEv&ev=1604)

Growing evidence suggests that functional connectivity at rest is a multi-stable process exhibiting the transient activation of recurrent connectivity patterns. In other words, when evaluated over time, it appears that functional connectivity (FC) passes through multiple relatively stable network configurations rather than varying in a continuous sense. However, due to several methodological limitations, the best way to assess meaningful FC patterns and characterize the transitions between them remains under debate [1,2]. Recently, new methods have been proposed to capture FC from fMRI data at a quasi-instantaneous level, e.g. by computing the synchronization of BOLD signal phases [3], or the multiplication of BOLD temporal derivatives [4]. Although these methods allow for a higher temporal resolution, they are more susceptible to high-frequency noise fluctuations. Recently, we proposed a method to detect meaningful FC patterns from noisy instantaneous FC matrices by focusing on the leading eigenvector of the time resolved FC matrices [5]. The leading eigenvector captures the main mode of connectivity with substantially reduced dimension and therefore improves the detection of recurrent FC patterns using standard clustering algorithms. Notably, the use of the Leading Eigenvector Dynamics Analysis (LEiDA) has revealed consistent FC patterns that emerge recurrently within the same recording session and across large populations of participants. By characterizing the probabilities, lifetimes, and switching trajectories of each FC pattern, it is possible to obtain a full characterization of the FC switching profile for each fMRI session and evaluate differences between participant groups, brain states, or even medication. In this talk I will introduce the LEiDA as a promising measure to characterize the switching dynamics of the functional connectome, with emphasis on the assumptions made and its limitations. I will present published and submitted results where we have applied LEiDA to evaluate differences in the FC switching profiles of participants with different levels of cognitive skills [5], but also of participants under the effect of drug neuromodulation and participants with different degrees of neuropsychiatric diseases. The last part of the talk will end with an overview of the mechanistic scenarios proposed over the last decade for the emergence of transient FC patterns via computational models, including an extended discussion over the existence of multi-stability at the level of functional connectivity and its potential implications for effective cognitive processing and behavior. 1 Hutchison, R. M. et al. Dynamic functional connectivity: promise, issues, and interpretations. NeuroImage 80, 360-378, doi:10.1016/j.neuroimage.2013.05.079 (2013). 2 Cabral, J., Kringelbach, M. & Deco, G. Functional Connectivity dynamically evolves on multiple time-scales over a static Structural Connectome: Models and Mechanisms. NeuroImage, doi:10.1016/j.neuroimage.2017.03.045 (2017). 3 Glerean, E., Salmi, J., Lahnakoski, J. M., Jaaskelainen, I. P. & Sams, M. Functional magnetic resonance imaging phase synchronization as a measure of dynamic functional connectivity. Brain connectivity 2, 91-101, doi:10.1089/brain.2011.0068 (2012). 4 Shine, J. M. et al. Estimation of dynamic functional connectivity using Multiplication of Temporal Derivatives. NeuroImage 122, 399-407, doi:10.1016/j.neuroimage.2015.07.064 (2015). 5 Cabral, J. et al. Cognitive performance in healthy older adults relates to spontaneous switching between states of functional connectivity during rest. Scientific reports 7, 5135, doi:10.1038/s41598-017-05425-7 (2017).

Presenter

Joana Cabral, Pompeu Fabra University