Time-varying Connectivity in Resting-state fMRI: Methods, Interpretations, and Clinical Use

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1027
Educational Course - Half Day (4 hours)
SEC Armadillo
Room: Clyde Auditorium

Recent converging evidence suggests that a static representation of FC, e.g. based on the correlation between entire fMRI time series, misses important information encoded in fMRI data. Hence, various methods have been developed in recent years to exploit the information encoded beyond such static measures. The researcher interested in exploring time-varying FC properties has to select among the multitude of proposed methods, each one having different properties and underlying assumptions. The goal of this course is to provide guidance in the choice of an adequate time-varying FC method to address a specific neuroscientific question. In the first part of the course we will recall the definitions of the most important mathematical notions required to characterize temporal fluctuations of functional connectivity. Then, we will provide an overview of the main approaches used to explore functional connectivity beyond the classical static paradigm (e.g. brain states, co-activation patterns, autoregressive models, spatial vs temporal dynamics), including concrete examples of how these methods have been used in clinical applications. The second part of the course will be devoted to the interpretation of FC fluctuations. We will detail their links to micro-scale (i.e. neuronal) dynamics as well as their behavioral counterparts. We will conclude by summarizing the main remaining controversies and ongoing lines of inquiry in the field. In order to maximize learning outcomes for participants, we will discuss multiple-choice questions at the end of each talk, and take questions from the audience using the OHBM interactive tool.

We finally note that previous virtual course attendance was high (as was the last in-person meeting in OHBM-Rome). We believe this further reflects the interest of our community in the proposed course.

Objective

1. Definition of various terms important to the study of time-varying connectivity including ‘stationary’, ‘dynamic’, ‘static’, ‘time-varying’
2. Step-by-step explanation of popular methods used to explore the time-varying nature of FC (including null models and demos using popular toolboxes) and application to real datasets
3. Interpretation of the temporal fluctuations of FC in terms of (i) statistical significance, (ii) links to micro-scale (neuronal) dynamics and (iii) behavioral counterparts.

Target Audience

The target audience for this course are researchers interested in (the time-varying properties of) functional connectivity. While we will mainly discuss FC evaluated from fMRI data with some emphasis on multimodal studies as well. The proposed theoretical background and interpretations can be applied to any modality involving time series (e.g. MEG, EEG).

Presentations

On the (mis)use of null-models for time-varying functional connectivity

Null-models are widely used as a means to generate surrogate data and explore data properties. Various null-models have been proposed to characterize brain dynamics, but the interpretation of null-model testing should be cautious. In this talk, I will first introduce the basic theoretical foundations of null-model testing. In particular I will show that in most cases, more than one statistical property is attached to a given null-model. Therefore, the outcome of the corresponding tests might in general have multiple interpretations. I will then present the most popular null-models of neuroimaging data and detail which statistical properties they are testing for. I will conclude by emphasizing that instead of testing for the presence or absence of “time-varying” of “dynamic” functional connectivity, null-models should rather be used to characterize the nature of the temporal fluctuations of neuroimaging metrics.

Presenter

Raphael Liegeois, École Polytechnique Fédérale de Lausanne Geneve, Vaud
Switzerland

Time-varying connectivity: Data-driven approaches and clinical applications

The study of complex mental illness can greatly benefit from flexible analytic approaches. In particular, the advent of data-driven approaches to identify time-varying connectivity and activity has revealed a number of interesting clinically-relevant variation in the data which, when ignored, can provide misleading information. In this lecture I will provide a comparative introduction of a range of data-driven approaches to estimating time-resolved connectivity (trFC). I will also present detailed examples where studies of mental illness have been advanced by approaches designed to capture and estimate time-varying information in resting fMRI data. As part of this, I will review several exemplar data sets analyzed in different ways to demonstrate the complementarity as well as trade-offs of various modeling approaches to answer questions about complex mental illness. Finally, I will review and provide examples of strategies for validating trFC including simulations, multimodal imaging, and comparative prediction within clinical populations, among others. As part of the interactive aspect I will provide a hands-on guide to the dynamic functional network connectivity toolbox within the GIFT software, including an online didactic analytic decision tree to introduce the various concepts and decisions that need to be made when using such tools.

Presenter

Vince Calhoun, GSU/GATech/Emory
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United States

Terminology & Methodological Framework Overview

In this talk, I will first clarify the still existing
confusion about terminology when talking about time-varying functional connectivity (FC): what is meant by time-varying vs.dynamic, static vs. stationary, averaged vs. memoryless approaches. Basic concepts of FC and the simplest time-varying FC approach will
be then introduced, as in pairwise correlations between fMRI time courses of different brain regions, and their sliding-window variations. Then, the great deal of methodological effort performed in the last decade to ameliorate this simple methodology will
be summarized and elucidated in details with practical examples, concerning in particular: (1) the choice of the most suitable window characteristics; (2) overcoming parcellation limits; (3) alternative methods beyond the sliding-window; (4) the determination
of (time-varying or dynamic) FC states; (5) the link with brain structure. Limitations and pitfalls of each method will be outlined, to guide the audience towards the best choice in specific contexts.

Presenter

Maria Giulia Preti, École Polytechnique Fédérale de Lausanne Lausanne, Vaud
Switzerland

Resting-state activity from the perspective of Dynamical Systems Theory

Transiently and recurrently emerging patterns of connectivity are consistently detected across fMRI neuroimaging studies and their integrity has been implicated in a wide variety of neurological and psychiatric disorders. However, the principles governing the emergence and modulation of RSNs remain unclear, hindering the advance in therapeutic strategies targeted at rebalancing RSN dynamics.

In this workshop, I will describe novel methodological approaches to characterize the dynamical properties of resting-state activity borrowing tools used in Physics to characterize dynamical systems. In this mechanistic scenario, whole-brain activity can be decomposed into a discrete number of spatially-defined modes, whose power is modulated over time. I will describe different approaches to detect these modes, evaluate their overlap with known resting-state networks and verify their consistency across fMRI sessions. I will show how these modes can be characterized them in terms of occupancy, lifetime, stability and resonant properties. Finally, different statistical methods will be presented to evaluate differences between conditions and under different modulatory strategies. Ultimately, the implications of using dynamical systems theory to gain insight into the rules orchestrating brain activity and their physiological origin will be discussed.

A toolbox with the codes for analysis demonstrated in the workshop will be shared with attendees.

Presenter

Joana Cabral, Champalimaud Research, Champalimaud Centre for the Unknown
Life and Health Sciences Research Institute
Braga, Braga
Portugal

Biophysical models of dynamic functional connectivity: Linking scales and data modalities

The study of temporal dynamics in the natural world using dynamic systems has a long and successful history. Using these tools in neuroscience allows us to quantify intuitively appealing concepts such as metastability, chaos, recurrence and oscillations. In this talk, I briefly present the fundamental basis of modelling dynamic functional connectivity using dynamic systems theory and provide basic and clinical examples of its successful use. I will also overview the main toolboxes for exploring and employing dynamic models of large-scale brain dynamics.

Presenter

Michael Breakspear, University of Newcastle Newcastle, New South Wales
Australia

Common sources of variation in functional brain networks

Recent years have seen a surge in investigations into the time-varying nature of large-scale brain networks measured with fMRI. However, assessing the nature of these changes requires careful evaluation of the sources of variation in functional brain networks. In this educational symposium, I will take advantage of “precision” fMRI data to document evidence for how functional brain networks vary across different time scales within a person. The presentation will (a) discuss the size and characteristics of variation in functional networks during task states and rest and (b) review artifactual causes of variation including motion, respiration, and sampling variability. The presentation will touch on both more classic sliding-time window techniques and novel single timepoint ‘event’ analyses. I will close with a series of reflection questions and recommendations for studying variation in functional brain networks.

Presenter

Caterina Gratton, Northwestern University Evanston, IL
United States