NeuroImage xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Dynamic functional connectivity using state-based dynamic community structure: Method and application to opioid analgesia

Lucy F. Robinson [a,1,*], Lauren Y. Atlas [b,1], Tor D. Wager [c]

[a] Department Epidemiology and Biostatistics, Drexel University, 3215 Market St R, Philadelphia, PA 19104, USA
[b] Department of Psychology, New York University, 6 Washington Place, New York, NY 10003, USA
[c] Department of Psychology and Neuroscience, University of Colorado, Boulder, Muenzinger D244, 345 UCB, Boulder, CO 80309, USA

ARTICLE INFO

Article history:
Accepted 11 December 2014
Available online xxxx

Keywords:
fMRI
Functional connectivity

ABSTRACT

We present a new method, State-based dynamic community structure, that detects time-dependent community structure in networks of brain regions. Most analyses of functional connectivity assume that network behavior is static in time, or differs between task conditions with known timing. Our goal is to determine whether brain network topology remains stationary over time, or if changes in network organization occur at unknown time points. Changes in network organization may be related to shifts in neurological state, such as those associated with learning, drug uptake or experimental conditions. Using a hidden Markov stochastic block model, we define a time-dependent community structure. We apply this approach to data from a functional magnetic resonance imaging experiment examining how contextual factors influence drug-induced analgesia. Results reveal that networks involved in pain, working memory, and emotion show distinct profiles of time-varying connectivity.
© 2014 Elsevier Inc. All rights reserved.

Introduction

The explosion of several new topics in neuroimaging, including large-scale resting state studies (Van Dijk et al., 2012; Zuo et al., 2012; Smith et al., 2013), studies of psychopathology (Jafri et al., 2008; Greicius, 2008), and pharmacological functional magnetic resonance imaging (phfMRI) (Schwarz et al., 2007; Honey and Bullmore, 2004) has led to exciting innovations in methods for functional connectivity. Two emerging themes are the need for dynamic connectivity methods that allow for changes in connectivity over time, and network models that capture the complex structure of connectivity. In this paper we introduce a new method, State-based dynamic community structure (SDCS), that combines these approaches to identify distinct functional connectivity states with respect to the organization of networks of brain regions into communities of brain regions. This method is particularly well-suited for experimental contexts in which the timing of shifts between states cannot necessarily be specified *a priori*.

A growing body of work (Beckmann et al., 2005; De Luca et al., 2006; Damoiseaux et al., 2006; Ferrarini et al., 2009; Fair et al., 2009) has suggested that brain functional connectivity networks exhibit complex structure such that the whole-brain network can be represented as a collection of subnetworks, where each subnetwork is comprised of a set of spatially distributed brain regions. Recent work (Bassett et al., 2011a, 2011b; Bowman et al., 2012; Schwatz et al., 2009; Shen et al., 2010), (Meunier et al., 2009) has shown that these subnetworks can be illustrated as "communities" or modules of "nodes". Nodes within a community are highly connected and/or share some properties with respect to connectivity. Methods that estimate this network structure by partitioning a collection of brain regions into subgroups can provide complementary information to descriptive measures of the global properties of the functional connectivity network (Bullmore and Sporns, 2009) such as degree distributions (number of connections per node), clustering coefficients, and small world properties (Bullmore and Sporns, 2009; Rubinov and Sporns, 2010; Sporns et al., 2004; Simpson et al., 2013).

Several recent developments in fMRI analysis methods are motivated by the recognition that functional connectivity characteristics are dynamic, fluctuating over time with changes in mental states and other physiological processes (Hutchison et al., 2013). Recent work has incorporated temporal dynamics into the varied descriptions of functional connectivity properties, providing a flexible alternative to standard approaches that assume network behavior is static over time, or differs between task conditions with known timing. Changes in network characteristics include shifts in the strength of connection between a given pair or group of nodes, the degree distribution or clustering coefficient of the network as a whole, or other global network properties. Dynamic connectivity regression (Cribben et al., 2012) provides a method for detecting change points in an fMRI time series based on the connectivity graph of a group of selected regions. Dynamics of spatial activation components have been estimated using dynamic ICA (Allen et al., 2012) and dynamic principal components analysis (Leonardi et al., 2013). The characteristics of the functional connectivity network have been

* Corresponding author.
E-mail address: lucy.f.robinson@drexel.edu (L.F. Robinson).
[1] These authors contributed equally to this work.

http://dx.doi.org/10.1016/j.neuroimage.2014.12.034
1053-8119/© 2014 Elsevier Inc. All rights reserved.

Please cite this article as: Robinson, L.F., et al., Dynamic functional connectivity using state-based dynamic community structure: Method and application to opioid analgesia, NeuroImage (2014), http://dx.doi.org/10.1016/j.neuroimage.2014.12.034

UNCORRECTED PROOF

ARTICLE IN PRESS

shown to differ according to various task demands (Hutchison et al., 2013), and psychoactive drug conditions (Greicius, 2008; Boveroux et al., 2010). Of particular relevance to this paper, the dynamics of the modular structure of the functional connectivity network have been explored in resting state (Jones et al., 2012), learning (Bassett et al., 2011a, 2011b), and studies of emotion (Kinnison et al., 2012).

Recent developments in techniques for dynamic networks in neuroimaging data have occurred alongside new approaches to general dynamic network analysis problems, and in particular, work on dynamic community structure. Popular approaches include extensions of network partitioning algorithms based on modularity maximization or related "quality functions" to time-dependent networks, often by incorporating temporal smoothness into the quality function (Mucha et al., 2010; Kawadia and Sreenivasan, 2012; Chakrabarti et al., 2006; Chen et al., 2013). Other algorithms are based on incremental updates to estimates of community structure (Cazabet et al., 2010; Nguyen et al., 2011). Applications of Dynamic network models to fMRI data must address its particular characteristics, specifically low signal to noise ratio, relative lack of temporal resolution, and the related lack of observable instantaneous, or at least temporally identified, connections (*cf* EEG or email data). As will be discussed, we pursue an approach based on a stochastic generative model for network data, rather than an algorithmic method, and focus on identifying district states with respect to community structure.

In this paper, we introduce a dynamic network analysis technique, State-based dynamic community structure (SDCS),that identifies distinct temporal states with respect to community structure over time without *a priori* assumptions on the timing or type of changes in structure. Previous approaches to dynamic connectivity have largely used simple measures of connectivity, or have been confined to a small number of predefined regions and do not scale up easily to larger networks. As discussed in Hutchison et al. (2013), the sliding window approaches employed in many dynamic connectivity studies are difficult to interpret and induce spurious fluctuations under stable connectivity conditions. By contrast, the SCDS approach is able to capture complex changes, estimating the temporal and graphical structure of the network in an integrated manner. We characterize the organization of the network using the stochastic block model (Nowicki and Snijders, 2001), a statistical model for describing community structure. The goal of this approach is to estimate whether and how this network structure shifts over time in experiments with possible state-related changes in psychological activity. A change in the organization of the connectivity network could consist of, for example, a shift from a state in which connectivity is highly modular, *i.e.* connectivity is concentrated within subnetworks of regions, to a state in which the pattern of connectivity is less modular and more integrated throughout the network.

SDCS identifies state-based changes using a Hidden Markov model, a widely used method for identifying latent properties of time series data. Under this framework, we assume that there is an underlying, unobserved state property associated with the network at each point in time, and these states may shift at unknown times. The Hidden Markov model allows us to estimate the properties of the underlying states, and identify where likely shifts between states have occurred. Thus, we can assess whether the functional connectivity network is stationary in time with respect to structural organization, or whether there are shifts in structure, and identify the distinct structural patterns of the functional connectivity network. State-space models have been used previously in related fMRI problems, including studies of changes in effective connectivity for EEG/MEG data under a Dynamic Causal Model (Olier et al., 2013), and in multivariate state-space models for brain function (Janoos et al., 2013).

We apply the SDCS functional connectivity method to fMRI data acquired during a study of opioid- and expectancy-based pain modulation (Atlas et al., 2012). Our previous paper used voxel-wise event-related analyses to test whether opioid drug effects on pain-evoked responses differ as a function of belief (*i.e.* during Open, relative to Hidden, administration). In the present analysis, we use SDCS to examine the timecourse of connectivity within regions associated with psychological processes thought to underlie placebo effects and pain modulation: pain processing, emotion, and executive function/ working memory (Atlas and Wager, 2013). We build on our previous work by testing whether different networks have different timecourses of connectivity during Open Drug administration, irrespective of task design. Because our task involved changes on the order of minutes (due to the pharmacokinetics of the opioid analgesic) as well as shifts in context (baseline, instructions signaling onset and offset of drug infusion, post-infusion washout period), the present analysis can determine whether distinct functional networks and their within-network organization are differentially influenced by these factors.

Methods

The method for estimating time-dependent functional network structure consists of three stages. First, the total time interval is divided into a series of non-overlapping windows and the functional connectivity network is estimated independently in each window, as described in the section Network representation. Next, a hidden Markov model is fit to the sequence of estimated networks to identify possible distinct connectivity states and the most likely locations in time of meaningful shifts in community structure. The procedure for identifying connectivity states and the change points between them is described in the section Changes over time. Finally, the estimates of functional connectivity structure for each of the identified states are refined using MCMC. A schematic is shown in Fig. 1.

Network representation

Before estimating dynamic community structure, the brain regions comprising the network and the measure of connectivity must be defined, as well as the time windows on which the SDCS algorithm will operate. In this paper, we focused on connectivity within parcels of multi-voxel regions defined based on *a priori* functional and anatomical boundaries, examined 150-second windows (75 TRs), and used thresholded coherence as a measure of connectivity. We discuss each of these decisions and associated methods in more detail below. Though the application of our method involves making choices about how to define regions and the length of time windows to integrate over, the SDCS method is general and does not depend on particular choices of region definition and time windowing. Different choices will likely be optimal for different applications.

In network modeling of fMRI data, we have a choice in the definition of the nodes and edges. Voxels themselves can be used as nodes, as in ICA or seed region analysis, or voxels can be segmented into spatially contiguous groups, which are then treated as nodes in the functional connectivity network. While a single voxel approach has the advantage of introducing fewer assumptions on the network, a higher-level representation of connectivity can provide complementary information about patterns of connectivity which can't be attributed to spatial adjacency. In this work, we were primarily interested in brain networks involved in pain processing, working memory, or emotion, as each of these processes has been implicated in expectancy-based pain modulation (Atlas and Wager, 2013). We therefore used meta analyses to identify brain regions consistently activated by working memory (Wager and Smith, 2003) and emotion (Kober et al., 2008) as well as a mega-analysis of five previous studies of thermal pain to identify regions involved in pain processing (Atlas et al., 2010). We note that meta-analysis and mega-analysis provide ways to pool across previous studies to identify regions that are most likely to be activated by a given process. Thus they provide a principled way to identify functional networks *a priori* irrespective of specific experimental details such as fMRI field strength, study population, study location, *etc.* Details of these methods have been described in detail in previous work (Wager et al., 2007;

UNCORRECTED PROOF

Please cite this article as: Robinson, L.F., et al., Dynamic functional connectivity using state-based dynamic community structure: Method and application to opioid analgesia, NeuroImage (2014), http://dx.doi.org/10.1016/j.neuroimage.2014.12.034

Download English Version:

https://daneshyari.com/en/article/6025899

Download Persian Version:

https://daneshyari.com/article/6025899

Daneshyari.com