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Detection of functional brain network reconfiguration during task-driven cognitive states

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ABSTRACT

Network science offers computational tools to elucidate the complex patterns of interactions evident in neuroimaging data. Recently, these tools have been used to detect *dynamic* changes in network connectivity that may occur at short time scales. The dynamics of fMRI connectivity, and how they differ across time scales, are far from understood. A simple way to interrogate dynamics at different time scales is to alter the size of the time window used to extract sequential (or rolling) measures of functional connectivity. Here, in $n = 82$ participants performing three distinct cognitive visual tasks in recognition memory and strategic attention, we subdivided regional BOLD time series into variable sized time windows and determined the impact of time window size on observed dynamics. Specifically, we applied a multilayer community detection algorithm to identify temporal communities and we calculated network flexibility to quantify changes in these communities over time. Within our frequency band of interest, large and small windows were associated with a narrow range of network flexibility values across the brain, while medium time windows were associated with a broad range of network flexibility values. Using medium time windows of size 75–100 s, we uncovered brain regions with low flexibility (considered *core* regions, and observed in visual and attention areas) and brain regions with high flexibility (considered *periphery* regions, and observed in subcortical and temporal lobe regions) via comparison to appropriate dynamic network null models. Generally, this work demonstrates the impact of time window length on observed network dynamics during task performance, offering pragmatic considerations in the choice of time window in dynamic network analysis. More broadly, this work reveals organizational principles of brain functional connectivity that are not accessible with static network approaches.

Introduction

The use of network science in the field of neuroimaging has led to a better understanding of the brain as a complex system. This approach treats the brain as an interdependent network that displays both properties of local and distributed processing (Bassett and Bullmore, 2006, Bullmore and Sporns, 2009, Telesford et al., 2011). Network representations of neuroimaging data have been useful in understanding disease states including Alzheimer's disease (Supekar et al., 2008, Seeley et al., 2009), schizophrenia (Calhoun et al., 2009, Lynall et al., 2010), and epilepsy (Van Diessen et al., 2013, Khambhati et al., 2015). These diseases are now commonly characterized using graph theoretical properties that describe topological structure, such as community structure (Porter et al., 2009, Fortunato, 2010), core–periphery structure (Borgatti and Everett, 2000, Bassett et al., 2013b, Sporns, 2013), and network motifs (Milo et al., 2002). The study of these systems as networks enables a greater understanding of how patterns of interaction in the brain support human thought and behavior (Medaglia et al., 2015).

In practice, brain networks are represented as either *structural* networks, which include tract tracing (Honey et al., 2007) and diffusion tensor/spectral imaging (DTI/DSI) (Hagmann et al., 2003, 2007), or *functional* networks, which include functional magnetic resonance imaging (fMRI) (Eguíluz et al., 2005), electroencephalography (EEG) (Micheloyannis et al., 2006, Stam et al., 2007), magnetoencephalography (MEG) (Stam, 2004), and multielectrode array data (Srinivas et al., 2007). Across these neuroimaging modalities, network-based

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techniques can reveal differences between subject groups or between brain states (Simpson et al., 2013, Zalesky et al., 2012, Ginestet et al., 2011, Bassett et al., 2012).

Most network-based neuroimaging studies utilize a *static brain network* representation, which constructs a network using data from an entire scan session. In essence, these networks summarize the strength of functional connectivity between pairs of brain regions over the period of a scan session. However, many changes in the brain occur at shorter time scales on the order of milliseconds (for neuronal activity) or seconds (for cerebral blood flow) (Gonzalez-Castillo et al., 2014, De Zwart et al., 2005). Static network analyses are agnostic to these changes occurring at shorter time scales; however, recent interest in how networks change has led to the development of methods to examine dynamics in functional connectivity more generally (Hutchison et al., 2013a, Siebenhühner et al., 2013), and more specifically in brain networks (Bassett et al., 2011). The goal of the latter type of investigation uses a *dynamic brain network* representation to provide information about the time-evolving neurophysiological processes that underlie cognition.

To analyze dynamic networks, a neuroimaging scan session is subdivided into shorter time intervals or windows and functional brain networks are derived from each interval. Time windows can either be overlapping (Hutchison et al., 2013a) or non-overlapping (Bassett et al., 2011), depending on the desired temporal resolution of the analysis. Time window analyses have been used for a variety of dynamic functional connectivity studies in both rest (Sakoğlu et al., 2010, Hutchison et al., 2013b, Gonzalez-Castillo et al., 2014) and task (Bassett et al., 2011, Hutchison et al., 2013a, Siebenhühner et al., 2013) states, revealing transient reconfigurations of brain networks over time. Sliding time window analyses have also been used in independent component analyses (ICA) during tasks (Esposito et al., 2003) and rest (Kiviniemi et al., 2011). While there have been a variety of studies using a sliding window for ICA and functional connectivity, such studies in the context of whole-brain network analysis remain underexplored. In principal, dynamic network methods could significantly improve the sensitivity of whole-brain analyses to detect changes in network topology that capture changes in cognition and behavior (Braun et al., 2015).

Here, we examine the ability of dynamic network methods to uncover features of functional brain network reconfiguration across cognitive states. Specifically, we apply dynamic network analysis using a sliding window approach with non-overlapping time windows to fMRI data collected from a sample of 82 healthy adult subjects performing three different cognitive tasks: a strategic attention task and two recognition memory tasks with either faces or words as stimuli. These tasks required dynamic interaction among brain regions to integrate incoming sensory information with stored knowledge representations, providing rich spatiotemporal dynamics (Hermundstad et al., 2013). Given these task requirements, we were particularly interested in understanding the patterns of functional integration between brain regions and how they changed during task performance. To study these patterns, we built on recent work demonstrating that patterns of functional integration and segregation during task performance can be parsimoniously summarized in a network's modular architecture (Doron et al., 2012; Cole et al. 2014; Mattar et al., 2015). A module is a set of brain regions that are densely interconnected with one another (functional integration) and sparsely interconnected with brain regions in other modules (functional segregation). The dynamics of these modules can be studied using recently developed network-based clustering techniques (Mucha et al., 2010) that explicitly account for the fact that brain network dynamics in one time window are dependent on brain network dynamics in the preceding and following time windows. These temporal dependencies are represented in a multilayer network framework (Kivelä et al., 2014), where the functional brain network in one time window is linked with the networks in neighboring time windows (Bassett et al., 2011). This approach facilitates a statistical examination of temporal variation in functional connectivity patterns (Bassett et al., 2013b). Further, it enables us to study the dynamics of brain network function (Bassett et al., 2015), by identifying network communities or putative functional modules that are coordinated during task-driven cognitive states (Mattar et al., 2015).

To formalize our study, we implement an experimental approach in which we manipulate two independent measures (time window and cognitive state), and ask how they impact three metrics of network reconfiguration. The metrics of network reconfiguration are dependent measures of increasing abstraction, and include community size, flexibility, and core–periphery structure. Intuitively, the first statistic – the size of communities – reflects the spatial resolution of the underlying functional network architecture, and is a fundamental statistic of network dynamics. While the number of communities can provide information regarding functional grouping of nodes, the transient nature of communities is better understood using graph statistics that explicitly quantify community dynamics. Thus, the second statistic we study is the flexibility of community structure, which explicitly measures the magnitude of the change in community structure over the course of the experiment; by counting the fraction of times that a region changes its allegiance to a functional community. Flexibility has previously been shown to be an important correlate of learning (Bassett et al., 2011), cognitive flexibility (Braun et al., 2015), and working memory function (Braun et al., 2015). Finally, core–periphery analysis offers a statistically principled approach to identifying a set of regions that remain relatively rigid in their community allegiance throughout task performance (the *temporal core*), and a set of regions that remain relatively flexible in their community allegiance throughout task performance (the *temporal periphery*). In prior work, this notion of temporal core–periphery structure has offered fundamental insights into the task-general (*flexible periphery*) and task-specific (*rigid core*) reconfigurations required to produce successful task performance (Fedorenko and Thompson-Schill, 2014), and the role that rigid versus flexible regions play in behavioral adaptation (Bassett et al., 2013a,b).

We study these three dependent metrics of network reconfiguration by manipulating two independent measures. The first independent measure that we manipulate is the time window used to extract sequential (or rolling) measures of functional connectivity. The choice of time window is a key issue in dynamic network methods, and yet its role in observed properties of brain network reconfiguration is far from understood (Bassett et al., 2013b). The second independent measure that we manipulate is the task that the subjects are performing. Together, this experiment approach enables us to consider the effects of time window on observed features of functional brain network reconfiguration across multiple independent measurements of different brain processes, and to quantify our confidence in those observed features as well as to inform our understanding of how different cognitive tasks are instantiated in flexible versus rigid brain network dynamics.

Materials and methods

Participants and scanning protocol

The dataset has 82 participants (including 79 males, mean age 35 ± 4 (SD) years) taking part in three visual tasks, two recognition memory tasks and one strategic attention task (Aminoff et al., 2012, Hermundstad et al., 2013). Stimuli for the two recognition memory tasks were presented in a pseudo-block format. The stimuli were comprised of 360 stimuli of faces or words shown as mini-blocks with 6–9 stimuli shown in sequential trials with 1.5 s and 1 s inter-trial intervals, respectively. Participants studied 180 items and were tested on a 50/50 mixture of old and new items; 180 fixation trials were intermixed throughout the session, in which a '+' symbol was displayed onscreen for 2.5 s. The strategic attention task consisted of two 112 trial experimental blocks with random inter-trial intervals ranging from