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Are brain networks stable during a 24-hour period?

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ABSTRACT

Despite the widespread view of the brain as a large complex network, the dynamicity of the brain network over the course of a day has yet to be explored. To investigate whether the spontaneous human brain network maintains long-term stability throughout a day, we evaluated the intra-class correlation coefficient (ICC) of results from an independent component analysis (ICA), seed correlation analysis, and graph-theoretical analysis of resting state functional MRI, acquired from 12 young adults at three-hour intervals over 24 consecutive hours. According to the ICC of the usage strength of the independent network component defined by the root mean square of the temporal weights of the network components, the default mode network centered at the posterior cingulate cortex and precuneus, the superior parietal, and secondary motor networks showed a high temporal stability throughout the day (ICC>0.5). However, high intra-individual dynamicity was observed in the default mode network, including the anterior cingulate cortex and medial prefrontal cortex or posterior–anterior cingulate cortex, the hippocampal network, and the parietal and temporal networks. Seed correlation analysis showed a highly stable (ICC>0.5) extent of functionally connected regions from the posterior cingulate cortex, but poor stability from the hippocampus throughout the day. Graph-theoretical analysis using local and global network efficiency suggested that local brain networks are temporally stable but that long-range integration behaves dynamically in the course of a day. These results imply that dynamic network properties are a nature of the resting state brain network, which remains to be further researched.

Introduction

A recent trend in brain research can best be represented by the term “brain connectome” which describes the brain as a large complex network connected by local and inter-regional neurons (Sporns et al., 2005). Accordingly, a number of neuroimaging studies have investigated the anatomical and functional connectivity of the brain. Among methods for brain connectivity, the resting state functional MRI (fMRI) has vitalized the investigation of functional brain networks, such as a default mode network (DMN) (Raichle et al., 2001) and the global network (Bullmore and Sporns, 2009; Sporns and Zwi, 2004). While many studies have been based on this widespread view of the brain network, researches on its dynamicity or stability have been rarely found. Thus, how much brain networks remain stable or dynamic over the course of a day still remains to be explored.

As a typical example of brain dynamicity, circadian rhythms affect our cognitive system (Mecacci et al., 2004). Time of day is also consistently reported to influence cognitive performance in executive functioning, attention, and working memory (Anderson and Revelle, 1994; May et al., 2005; Schmidt et al., 2007). Both daily peak- and off-peak hours that vary widely among individuals exist for human cognitive functions (May et al., 2005). A positron emission tomography study showed highly variable glucose metabolism in the midline area of the brain between morning hours and evening hours (Buysse et al., 2004). Furthermore, a previous fMRI study demonstrated diurnal changes (Marek et al., 2010) and changes between night and afternoon in brain activation (Gorfine and Zisapel, 2009).

These findings raise a question regarding the dynamicity of resting state functional connectivity, known as resting state networks (RSNs), throughout a day. RSNs, including DMN, are driven from low frequency hemodynamic activity during the resting state, and are used to identify connectional changes in various groups such as blind and depressed patients (Liu et al., 2007; Sheline et al., 2009) and to evaluate the level of the consciousness in sleep state (Gujar et al., 2010) and in a non-communicative brain injury (Vanhaudenhuyse et al., 2010). Most RSN studies assume that intra-individual variability in RSNs is negligible compared to inter-individual variability, and that RSNs reflect the long-term intrinsic status of an individual brain, independent of dynamic brain phenomena.

Recent studies have documented the consistency of RSNs in terms of spatial distribution across multiple sessions, days, and subjects

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(Chen et al., 2008; Damoiseaux et al., 2006; Meindl et al., 2010). Of multiple sub-networks that comprise RSNs, the DMN has been mainly investigated. However, network dynamicity in the normal usage of each RSN sub-network within a one-day time period has not been investigated. Therefore, questions regarding the dynamic properties of all RSN sub-networks remain to be answered.

The purpose of this study is to examine the stability of RSN sub-networks by evaluating intra-individual variability of each RSN sub-network over the course of a day. For this purpose, we applied functional connectivity analysis to resting state fMRIs measured at three-hour intervals for 24 consecutive hours. We also analyzed the stability of the small world network (SWN) properties (Watts and Strogatz, 1998) which have been used to characterize large-scale topological properties of complex brain networks based on the graph theory. A network is called "small world network", if the connection structure in the network is more highly clustered compared to random networks and has a short average path length similar to random networks (Bullmore and Sporns, 2009). SWNs can be quantified by the local and global network efficiency based on the graph analysis. The detail concept and measures for a SWN are explained in the methods section.

Materials and methods

Subjects

Twelve healthy, right-handed participants (nine males and three females, mean age 25.42 ± 2.84 years) were recruited for the study. Handedness was assessed with a Korean version of the Annett handedness questionnaire (Annett, 1970). No participants had a history of neurological illness, sleep problems or psychiatric disorders. This study followed the human subject guidelines approved by the Institutional Review Board, and all participants gave informed consent before MRI examinations.

Image acquisition

All participants underwent fMRI scanning with a 3.0 Tesla MRI scanner (Siemens Tim Trio, Erlangen, Germany) to obtain T2* weighted single shot echo planar imaging (EPI) sequences. Each participant was axially scanned using the following parameters: voxel size, $3.0 \times 3.0 \times 3.3$ mm^3; slice number, 32 (interleaved); matrix, 64×64; slice thickness, 3.3 mm; repetition time (TR), 2000 ms; echo time (TE), 30 ms; and field of view, 192 mm. Each 330-sec scan produced 165 fMRI images, which is known to be sufficient to evaluate resting state functional connectivity (Van Dijk et al., 2010) and to obtain low frequency oscillation for the resting state functional connectivity (Biswal et al., 2010).

To facilitate later spatial normalization, a high-resolution structural data set was also obtained from each participant using a magnetization-prepared rapid acquisition gradient echo (MP-RAGE) three-dimensional T1-weighted sequence (voxel size, $0.9 \times 0.9 \times 1.0$ mm^3; TR, 2300 ms; TE, 3.08 ms). Foam pads were used to reduce head motion during EPI data acquisition. Each subject was scanned for approximately 5.5 min, while resting with eyes closed, for eight sessions at different times of day: 19:00 (1st day), 22:00, 1:00 (2nd day), 7:00, 10:00, 13:00, 16:00, and 19:00. We did not scan participants at 3:00 am (2nd day) in order not to disturb normal sleep.

Two participants underwent the examination as a group for a 24-hour period scanning day (total six groups). All participants stayed freely within the institute with a routine light exposure during the scanning day with an instruction of abstaining from highly demanding physical or mental works, alcohols, or nicotine. Participants were asked not to sleep during each scan. If a participant slept during a scan, the participant was rescanned. According to self-reports after scanning, no participants slept during each scan of 5.5 min. Since the purpose of the current study is to evaluate a routine RSN variability within a day rather than to find RSNs related to the circadian rhythm, we did not tightly control various factors associated with circadian oscillations or time-of-day effects.

Image preprocessing

Image preprocessing was conducted using statistical parametric mapping (SPM8, http://www.fil.ion.ucl.ac.uk/spm, Wellcome Department of Cognitive Neurology, London, UK) (Friston et al., 1995). After discarding the first 10 scans for stability issues, the 155EPI data were preprocessed by correction of the acquisition time delays between different slices and correction for head motion by realignment of all consecutive volumes to the first image of the session. The realigned images were co-registered to T1-weighted images, which were used to spatially normalize functional data into a template space using nonlinear transformation. Finally, all normalized images were smoothed using an 8 mm full-width half-maximum Gaussian kernel.

Statistical analysis

To examine the stability of RSN sub-networks, we applied both independent component analysis (ICA) (Bell and Sejnowski, 1995) and seed-ROI correlation analysis (Greicius et al., 2003) to resting-state fMRIs. ICA, a blind source separation method, is widely used to analyze functional data such as fMRI (McKeown et al., 1998) and EEG (Makeig et al., 1997), and is applied to identify brain sub-networks, for example, to study the DMN in resting-state fMRI time series (Beckmann et al., 2005; De Luca et al., 2006). ICA can decompose mixtures of time series fMRI signals from resting state underlying sources into maximally independent components (ICs), which we call functional sub-networks in this study (Beckmann et al., 2005).

We also evaluated variations in the SWN, originally described in social networks. Local and global efficiencies are most general metrics for SWN, which indicate the efficiency level of cerebral information flow (Achard and Bullmore, 2007). These metrics were used to identify altered SWN in disease groups (Liu et al., 2008; Rubinov et al., 2009; Wang et al., 2009).

The intra-individual stability of RSN parameters derived from these network analyses was tested using intra-class correlation (ICC), which has often been used to test reproducibility of fMRI time series (Caceres et al., 2009; Deuker et al., 2009; Friedman et al., 2008). All analysis procedures are described in Fig. 1.

1) Group ICA

We evaluated activities only at voxels within the masked region (total number of voxels $(V) = 275{,}814$), which were defined by a priori brainmask in SPM8. fMRI time series data were band-pass filtered (0.009–0.08 Hz) (Weissenbacher et al., 2009). All procedures for group ICA were based on previous studies (Calhoun et al., 2001; Calhoun et al., 2009; Zuo et al., 2010), which were composed of two steps: 1) to obtain group IC maps and 2) to derive individual IC maps and their time series for each subject from group IC maps.

To reduce redundancy in the temporal domain, a three-level principal component analysis (PCA) was applied before ICA (Calhoun et al., 2009). First, the 155 scan time points from each subject at each session were reduced to 30 principal components (PCs). Second, 30 PCs of the 12 subjects at each session were temporally concatenated and reduced to 30 group PCs. Although more than 50 components were estimated for each reduction level according to the minimum description length (MDL) criterion (Li et al., 2007), we chose 30 components for the first and second level since the use of 30 components sufficiently explained over 90% variance of data in each individual subject. Indeed, previous studies often have decomposed resting-state fMRI to 30 components (Chen et al., 2008; Jafri et al., 2008; Jann et al., 2010). Finally, data matrices of eight sessions were