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Effect of Resting-State fNIRS Scanning Duration on Functional Brain Connectivity and Graph Theory Metrics of Brain Network

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As an emerging brain imaging technique, functional near infrared spectroscopy (fNIRS) has attracted widespread attention for advancing resting-state functional connectivity (FC) and graph theoretical analyses of brain networks. However, it remains largely unknown how the duration of the fNIRS signal scanning is related to stable and reproducible functional brain network features. To answer this question, we collected resting-state fNIRS signals (10-min duration, two runs) from 18 participants and then truncated the hemodynamic time series into 30-s time bins that ranged from 1 to 10 min. Measures of nodal efficiency, nodal betweenness, network local efficiency, global efficiency, and clustering coefficient were computed for each subject at each fNIRS signal acquisition duration. Analyses of the stability and between-run reproducibility were performed to identify optimal time length for each measure. We found that the FC, nodal efficiency and nodal betweenness stabilized and were reproducible after 1 min of fNIRS signal acquisition, whereas network clustering coefficient, local and global efficiencies stabilized after 1 min and were reproducible after 5 min of fNIRS signal acquisition for only local and global efficiencies. These quantitative results provide direct evidence regarding the choice of the resting-state fNIRS scanning duration for functional brain connectivity and topological metric stability of brain network connectivity.

Keywords: resting state, connectome, functional connectivity, graph, scanning duration, fNIRS

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INTRODUCTION

As an emerging brain imaging technique, functional near infrared spectroscopy (fNIRS) is attracting increasing interests for studying human brain functional organization. The fNIRS technique possesses several unique advantages compared to functional magnetic resonance imaging (fMRI), such as simultaneous recording of signal changes in both oxygenated and deoxygenated hemoglobin concentration, higher temporal resolution, and better portability for use (Niu and He, 2013).

Recent advances allow fNIRS to acquire whole-brain resting-state signals and to construct entire cortical functional brain networks. Using modern graph theoretical approaches, fNIRS-derived brain networks can be further quantified to obtain topological characteristics representing network

organization configurations within the brain. Based on healthy adult data, our previous study revealed several important topological organizational principles from fNIRS brain networks, such as small-world property, modular structure, and highly connected hubs (Niu et al., 2012). The reproducibility and reliability of these network measures were also further validated based on our two-scanning-run resting-state data (Niu et al., 2013). In addition, in Fekete et al.'s study, the authors have also noted that the small-world properties of the prefrontal network derived from fNIRS-based data are associated with variability in young children's risk of developmental psychopathology (Fekete et al., 2014). To extend these studies to much wider applications, such as brain development and disease-associated studies, it is important for fNIRS data to be able to identify development/disease-associated changes in brain connectivity and topological metrics. Such changes may reflect functional markers of development/disease that could advance our understanding into brain nervous system function/dysfunction in the future.

It is generally necessary to perform several preprocessing procedures before constructing functional brain networks and computing graph theory metrics. These include collecting resting-state fNIRS time course data, preprocessing, estimating the correlation coefficient matrix, and analyzing the functional network using the graph theoretical method. Resting-state fNIRS data are typically collected for ∼7–10 min (Niu and He, 2013). However, the scanning length required to collect fNIRS data would be challenging for brain development studies associated with infants and young children. Certainly, such long scanning duration could also be problematic for constrained clinical patients, particularly for clinical imaging protocols that include additional task-related experimental designs. Previous fMRI–derived brain imaging studies have suggested that 5∼7 min (Van Dijk et al., 2010; Tomasi et al., 2016), or ≥9 min (Birn et al., 2013; Dawson et al., 2013; Laumann et al., 2015) BOLD data can yield stable correlation strengths and ∼2 min BOLD data can yield stable graph theoretical metrics (Whitlow et al., 2011). However, the length of time in which the resting-state fNIRS imaging data duration can generate stable, test-retest reproducible functional connection, and graph theory metrics of brain network connectivity remains unknown. Such conclusions would provide important information for human brain development and for the clinical implementation of fNIRS-based techniques.

In the present study, functional brain network connectivity and graph theoretical analyses were applied to a series of incrementally longer temporal epochs of resting-state fNIRS imaging data. We hypothesized that functional brain connectivity and the corresponding graph theory metrics would stabilize after a certain amount of time, requiring different durations of resting-state fNIRS imaging signal acquisition for optimal characterization. In this study, fNIRS data were collected from 18 healthy young subjects who underwent two resting-state scanning runs. For each participant, the hemoglobin signal was preprocessed using independent component analysis (ICA) to reduce physiological noise and other artifacts (e.g., instrumental noise, motion-induced artifacts, and physiological noises) from fNIRS measurement. Finally, we evaluated the influence of fNIRS signal scanning time on the stability and reproducibility of graph theory metrics of brain networks.

MATERIALS AND METHODS

Participants and Protocol

Twenty-one healthy right-handed subjects (mean age 24.5 years, 17 males and 4 females) participated in this study. Written informed consent was obtained from each subject prior to the experiment. Data collection was carried out according to the protocols approved by the Review Board at the State Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University. Resting-state fNIRS data of ∼11 min in length from each of two scanning runs (20-min intervals between them) were obtained from each subject. During the scanning, the subjects were asked to relax and remained still with their eyes closed but not to fall asleep. During the interval, the subjects were allowed to open their eyes and move their bodies and heads slightly. The data used in this study was same as in our previous studies that examined graph metrics reliability (Niu et al., 2013) and evaluated brain functional connectivity dynamics (Li et al., 2015).

Data Acquisition

A continuous wave near-infrared optical imaging system (CW6, TechEn Inc., MA, USA) was used to measure time courses of oxyhemoglobin (HbO) and deoxyhemoglobin (HbR) concentrations at a rate of 25 Hz. The system included 12 laser sources and 24 detectors, with each source including two wavelengths (690 and 830 nm) of near infrared light. The sources and detectors were systematically positioned on the participant's whole head, and the spatial separation between adjacent sources and detectors was set to be 3.2 cm. The configuration resulted in 46 measurement channels that covered the frontal, temporal, parietal, and occipital lobes (**Figure 1**) of the cerebral cortex. The positions of the probes were consistent with the international 10–20 system of electrode layout.

Data Preprocessing

We used the modified Beer-Lambert law (MBLL) (Cope and Deply, 1988) to compute concentration changes in hemoglobin signals from the attenuation of light through the head at two wavelengths. The time course of hemoglobin concentration was subsequently subjected to a temporal ICA analysis to remove motion-induced artifacts and systematic noise. The resulting data was then band-pass filtered (0.01∼0.1 Hz) to obtain low frequency hemodynamic fluctuations (Biswal et al., 1995; White et al., 2009; Sasai et al., 2012). Specifically, the ICA analysis was conducted with the following procedures: extracting steady hemoglobin concentration signals for all participants (e.g., 10 min scanning length in our study), reducing the dimensionality of the hemoglobin data using principal component analysis (PCA) for each participant, conducting ICA analysis on the reduced dimensional data, identifying typical noise components, removing the identified noise from the measured data, and computing "real" neural activity signals. The components related

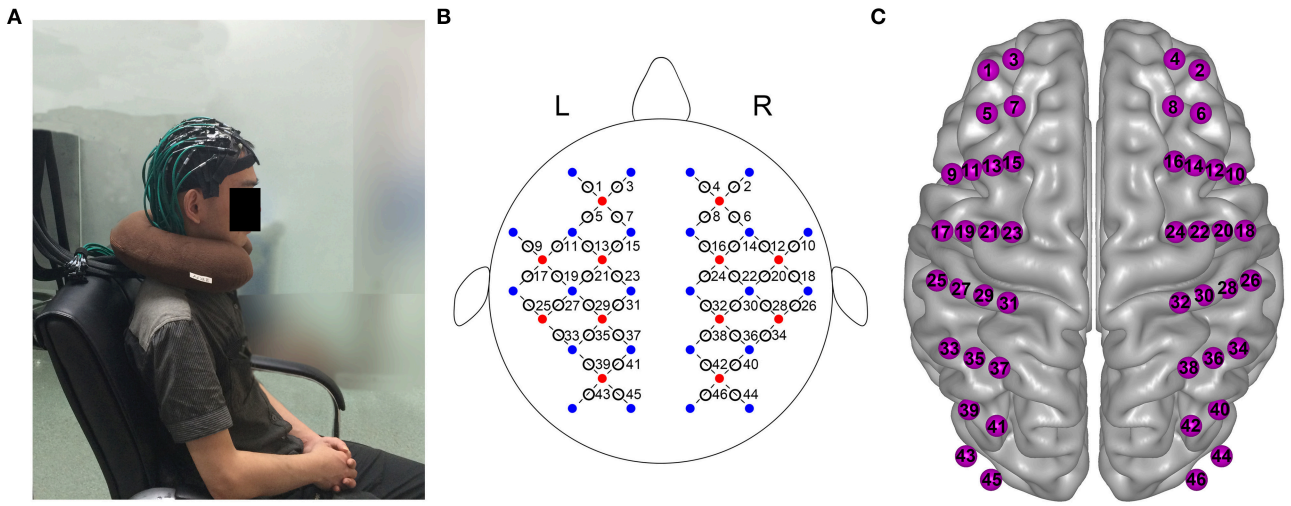

FIGURE 1 | Whole-head fNIRS measurement. **(A)** Photograph of whole-head fNIRS measurement on participant. **(B)** The schematic of whole-head imaging pad (12 sources, red, 24 detectors, blue). The sources and detectors were symmetrically placed on the left and right hemispheres and constituted 46 measurement channels, which allowed for the whole brain (i.e., frontal, temporal, parietal, and occipital lobes) to be measured. **(C)** Anatomical position of each measurement channel.

to noise and artifacts were identified from each individual subject based on the following three investigations: temporal profiles, spatial maps, and power spectra. A component would be considered noise if it met one of the following conditions (Zhang et al., 2010): (i) the temporal profile of the component included sudden jumps, slowly varied U or inverted U-shaped spike, or numerous inter-current quick spikes; (ii) the corresponding dominant frequency of the power spectra was outside the range of 0.01∼0.1 Hz; (iii) the spatial map of the component showed a global and spatially dispersive pattern. It has been pointed out that the spatial map with global and spatially dispersive pattern could represent systemic interference of superficial layer in the head (Kohon et al., 2007). After identifying these different kinds of noise components, the hemoglobin concentration signal that reflected "real" brain activity was reconstructed by eliminating the components identified as noise from the original hemoglobin time course, by assigning zero in the corresponding column of mixing matrix (Kohon et al., 2007). Finally, we truncated the ICA-based denoising data into 30-s time bins that ranged from 1 to 10 min in order to examine the effect of scanning duration on functional brain connectivity and network metrics. Of note, the procedures of ICA analysis used in here was consistent with our previous studies (Niu et al., 2013; Li et al., 2015) and Zhang et al.'s studies (Zhang et al., 2010, 2011), and it was conducted by using a publicly available software, FastICA v2.5 (http://www.cis.hut.fi/projects/ica/fastica/).

Functional Network Connectivity and Graph Theoretical Analysis

Functional Connectivity (FC) Definition

Pearson correlation and cross-correlation are the two most commonly used approaches for measuring inter-regional interactions or functional connectivity (FC) in the fNIRS community. In this study, we simultaneously evaluated the effect of different network construction approaches on the FC and graph metrics stability associated with different fNIRS acquisition durations (i.e., 1∼10 min in bins incrementally larger by 30 s). For given time series between any two nodal regions, the Pearson correlation or the cross-correlation was separately calculated to generate a 46 × 46 correlation matrix for each time series and subject. Considering the mean time course for one subject as $X = (x_i(t)_{t=1,2,\ldots N})$, where $x_i(t)_{t=1,2,\ldots N}$ is the mean time series of the ith region, we calculated these two connectivity metrics as follows:

Pearson's correlation:

$$r(x_i, x_j) = \frac{\sum_{t=1}^{N} [x_i(t) - \overline{x_i}][x_j(t) - \overline{x_j}]}{\sqrt{\sum_{t=1}^{N} [x_i(t) - \overline{x_i}]^2} \sqrt{\sum_{t=1}^{N} [x_j(t) - \overline{x_j}]^2}} \quad (1)$$

where $\overline{x_i}$ denotes the average of x_i.

Cross correlation:

$$r_{ij}(d_{ij}) = \frac{\sum_{t=1}^{N} [x_i(t) - \overline{x_i}][x_j(t - d_{ij}) - \overline{x_j}]}{\sqrt{\sum_{t=1}^{N} [x_i(t) - \overline{x_i}]^2} \sqrt{\sum_{t=1}^{N} [x_j(t - d_{ij}) - \overline{x_j}]^2}} \quad (2)$$

where d_{ij} denotes time delays between the mean time series of the ith and jth regions, and it ranges from 0 to N-1. The maximum $r_{ij}(d_{ij})$ in the series of calculation was considered as the functional connectivity strength of these two brain regions.

Network Thresholding

Because there is limited knowledge regarding selection of the network threshold in fNIRS imaging data, we adopted a widely used sparsity threshold, which is also similar to our previous

studies (Niu et al., 2012, 2013). Sparsity is defined as the number of existing edges divided by the maximum possible number of edges within a network. The range of the sparsity threshold was chosen from 0.17 to 0.5 (interval = 0.01) considering the small-worldness of human brain networks (Watts and Strogatz, 1998). Thus, for each subject at each time scanning duration, binarized adjacency networks were generated by using these chosen thresholds.

Network Measures

In graph theory, the metrics of network efficiency has been frequently proposed to characterize the capacity of information communication within a network (Latora and Marchiori, 2001, 2003). These related measures have been used to study normal development (Kaustubh et al., 2009; Wu et al., 2013; Cao et al., 2014) and a variety of clinically related brain diseases (Wang et al., 2009; Lynall et al., 2010; Rudie et al., 2012; Yu et al., 2016) because of their conceptual and technical advantages (Achard and Bullmore, 2007; Rubinov and Sporns, 2010). Here, we adopted three typical network efficiency metrics, i.e., nodal efficiency, network local efficiency, and global efficiency, to characterize the ability of information communication in fNIRS brain networks. Specifically, for each subject at each fNIRS signal acquisition duration, the nodal efficiency, network local efficiency, and global efficiency were separately computed by using an in-house FC-NIRS package (Xu et al., 2015) at each sparsity threshold. Furthermore, we also conducted similar calculation on the metrics of network clustering coefficient and nodal betweenness centrality in order to comprehensively examine the effect of fNIRS scanning duration on network metric stability. To exclude the impact of thresholds and to obtain a threshold-independent network evaluation, we further calculated the integral under the curve (AUC) of sparsity threshold values for each network metric (Wang et al., 2011; Niu et al., 2012, 2013) at each time epoch and subject. Specifically, the definitions of these network metrics are summerized as follows:

Nodal Efficiency

Nodal efficiency (E_{nodal}) is a measure that represents the capacity of a node to communicate with the other nodes of the network *G* and is generally defined as follows:

$$E_{nodal}(i) = \frac{1}{N-1}\sum_{i \neq j} \in G \frac{1}{d_{ij}} \tag{3}$$

where d_{ij} is the shortest path length between node i and node j, and N is the number of nodes in the network.

Nodal Betweenness

Nodal betweenness is a measure that characterizes the global role of a node in the brain functional network and is generally defined as follows:

$$b_i = \frac{1}{(n-1)(n-2)} \sum_{\substack{h,j \in N \\ h \neq j;\, h \neq i, j \neq i}} \frac{\rho_{hj}(i)}{\rho_{hj}} \tag{4}$$

where ρ_{hj} is the number of shortest paths between h and j, and ρ_{hj} (i)is the number of shortest paths between h and j that pass through i.

Network Clustering Coefficient

Network clustering coefficient is a global measure that characterizes the extent of local interconnectivity and cliquishness of a network and is generally defined as follows:

$$C = \frac{1}{n}\sum_{i \in N} C_i = \frac{1}{n}\sum_{i \in N} \frac{2t_i}{k_i(k_i - 1)} \tag{5}$$

where C_i is the clustering coefficient of node i, t_i is the actual number of edges between neighbors of node i, and k_i is the number of neighbors of node i.

Network Global Efficiency

Global efficiency is a global measure that characterizes information transferring ability in the entire brain network, and it is computed as the mean of nodal efficiency across all nodes of the network (Latora and Marchiori, 2001):

$$E_{glob}(G) = \frac{1}{N(N-1)}\sum_{j \neq i \in G} \frac{1}{d_{ij}} \tag{6}$$

where d_{ij} is the shortest path length between node i and node j, and N is the number of nodes in the network.

Network Local Efficiency

Network local efficiency represents the efficiency of information flow within the local environment, and it reflects the capability of a network to tolerate faults (Latora and Marchiori, 2001). The local efficiency of network *G* is computed as follows:

$$E_{loc}(G) = \frac{1}{N}\sum_{i \in G} E_{glob}(G_i) \tag{7}$$

where $E_{glob}(G_i)$ the global efficiency of G_i, the subgraph of the neighbors of node i. The neighbors of node i are defined as the nodes those connect with node i directly.

Stability Evaluation

To evaluate the stability of FC and network efficiency metrics associated with different fNIRS signal acquisition durations, a series of fNIRS data collection durations for FC and graph metric stabilization were contrasted with relatively longer 10-min data. For instance, for FC or the nodal efficiency metric, the linear correlation coefficient was calculated to demonstrate the similarity strength between spatial maps from each short duration data segment and that of the relatively longer 10-min data segments. For local and global efficiency metrics, a statistical analysis (paired *t*-test) was performed to determine the difference between the efficiency values of each short duration data segment and relatively longer 10-min data segments.

Between-Run Reproducibility Evaluation

We recomputed the FC and network efficiency metrics with the second scan data for all subjects. To assess the between-run