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Re ea ch A ic e

FC-NIRS: A Functional Connectivity Analysis Tool for Near-Infrared Spectroscopy Data

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Functional near-infrared spectroscopy (fNIRS), a promising noninvasive imaging technique, has recently become an increasingly popular tool in resting-state brain functional connectivity (FC) studies. However, the corresponding software packages for FC analysis are still lacking. To facilitate fNIRS-based human functional connectome studies, we developed a MATLAB software package called "functional connectivity analysis tool for near-infrared spectroscopy data" (FC-NIRS). This package includes the main functions of fNIRS data preprocessing, quality control, FC calculation, and network analysis. Because this software has a friendly graphical user interface (GUI), FC-NIRS allows researchers to perform data analysis in an easy, flexible, and quick way. Furthermore, FC-NIRS can accomplish batch processing during data processing and analysis, thereby greatly reducing the time cost of addressing a large number of datasets. Extensive experimental results using real human brain imaging confirm the viability of the toolbox. This novel toolbox is expected to substantially facilitate fNIRS-data-based human functional connectome studies.

1. Introduction

Functional near-infrared spectroscopy (fNIRS), a promising noninvasive imaging technique, has become an increasingly popular neuroimaging technique for brain function research in recent years [1–4]. This technique holds several advantages relative to functional magnetic resonance imaging (fMRI), namely, its instrument portability, high temporal sampling rate, and ability to perform long data acquisitions. Given the technique's specific strengths, fNIRS has been extensively used to localize brain activation during task states [5–10] and to identify functional connectivity (FC) during resting states in both normal and diseased populations [4].

For the study of resting-state fNIRS, one of its promising advances is the detection of resting-state FC [6, 11] and the characterization of the topological organization of the brain connectivity network [12]. The approaches of seed-based correlation analysis [6, 13, 14], whole-brain correlation analysis [15–17], and graph-theoretical topological analysis [12, 18] were primarily used to derive the resting-state FC and the brain network. Particularly, the seed correlation analysis calculates the resting-state FC by predefining a seed region and

subsequently computing the temporal correlation between it and other regions. With seed-based correlation analysis, researchers have observed a strong FC between the bilateral sensorimotor [11, 13], auditory [13], and visual system [19] in adults and connectivity changes during the normal development of early infancy [5, 15] and in neurological disorders [19, 20]. Similarly, whole-brain correlation analysis calculates resting-state FC by examining the temporal correlation of a time series between any two measurement regions in the whole-brain range. Using this approach, Homae et al. [15] found that the cerebral FC changed dynamically in infants from several days old to months old. Additionally, using this method, Zhang et al. [17] showed that the dominant frequency of FC within one functional system in adults can be identified by introducing a priori anatomical information. In contrast to the previous two methods, the graph-theoretical topological analysis models the brain as a complex network and then provides a straightforward but powerful mathematical framework for characterizing the topological properties of the brain networks. With the graph-theoretical network analysis approach, our group constructed the first whole-brain FC network using fNIRS brain data [12] and found that the fNIRS brain network was topologically organized in a nontrivial fashion, for example, with a small-world and modular architecture. Furthermore, our study [18] also showed that the graph theory metrics of the fNIRS brain network were reliable across different scanning sessions. In summary, this progress in FC and network analysis demonstrates the increasing interests in the study of functional brain connectivity and network organization using the fNIRS technique.

As an emerging analysis strategy for fNIRS data and considering the complexity of FC and network analysis, it is necessary and important to develop an easy-to-use and efficient FC toolbox to facilitate fNIRS researchers. There are already several available fNIRS toolkits, such as Homer [21], NIRS-SPM [22], fOSA [23], NINPY [24], and NAP [25], which have greatly assisted with the preprocessing of fNIRS data and activation detection based on task data. However, it must be noted that toolkits for assessing the FC and network analysis of resting-state fNIRS data are still lacking.

In this study, to facilitate human functional connectome studies in the fNIRS field, we developed a MATLAB software package for fNIRS-based connectivity analysis, which is called FC-NIRS (functional connectivity analysis for near-infrared spectroscopy data) and can be downloaded freely from the website http://www.nitrc.org/projects/fcnirs/ as an open-source package. The package's functions include preprocessing, quality control, FC calculation, and network analysis. Although the fNIRS collection has a chainless feature, it also easily leads to motion-head artifacts. At the same time, there are usually many sources and detectors placed on the head that are used for a whole-brain network study, which thus inevitably lead to a loss of contact between certain optodes and the scalp. Therefore, the two primary types of noise (i.e., motion artifacts [26, 27] and a low signal-to-noise ratio due to poor contact between the optodes and scalp [24]) need to be checked before performing FC and network analysis.

2. Materials and Methods

. . T b De e p e

. . . De e p e E i e . FC-NIRS was developed using MATLAB 2010b in a 64-bit Windows 7 environment. The data preprocessing and network analysis modules include two established packages, Hemodynamic Evoked Response (Homer) and Graph-Theoretical Network Analysis (Gretna), for fNIRS data processing and graph theory-based network analysis, respectively. This FC-NIRS toolbox has been successfully tested under different operating systems with MATLAB installed, such as Windows and Linux (Ubuntu and CentOS).

. . . Da a F a . Currently, FC-NIRS can process two file types: one type is in the .nirs format from the CW5/6 system (TechEn, Inc.) and the other type is in the .csv format from ETG4000/7000 (Hitachi Inc.). In fact, the .csv files can be easily transformed into.nirs files. Thus, in the following description, we mainly introduce the parameters that were included in .nirs files. (1) d: this variable was the actual raw data that were variable. This variable had the dimensions of ⟨number of measurements⟩×⟨number of time points⟩. The rows in d were mapped by the measurement list (the mL variable described below). The d variable could be complex (as in the case of sine-cosine demodulation for laser carrier frequencies). (2) t: this is a time variable describing the time length of the data collection. (3) SD: this variable was a structured variable that described the configuration of the probe (source-detector) geometry. Furthermore, during the stage of "processing," a ".proc" file could be brought out for each participant after clicking the "RUN" button. The ".proc" file was a MATLAB file with four fields: (1) RawData, which recorded the raw optical density information as in the .nirs file; (2) OD, which recorded optical density changes; (3) Conc, which recorded the time series of the relative concentration variations in oxyhemoglobin (HbO), deoxyhemoglobin (HbR), and the total hemoglobin (HbT); and (4) SD, which recorded the configurations of the sources, detectors, and measurement channels between the sources and detectors. The abundant information in the ".proc" file provided the convenience of processing batches for the subsequent FC calculation and network analysis in the toolbox.

. . . FC-NIRS A a i P ced e. The main procedure of FC-NIRS is shown in Figure 1, and it included four main function modules: (1) preprocessing, (2) quality control, (3) FC calculation, and (4) network analysis.

. . P ep ce i g. FC-NIRS provides a series of preprocessing methods in thds(l)-□□□(si-□.□-RS)-□□□(o)□□(S)-aaure□□□.□(p)□□

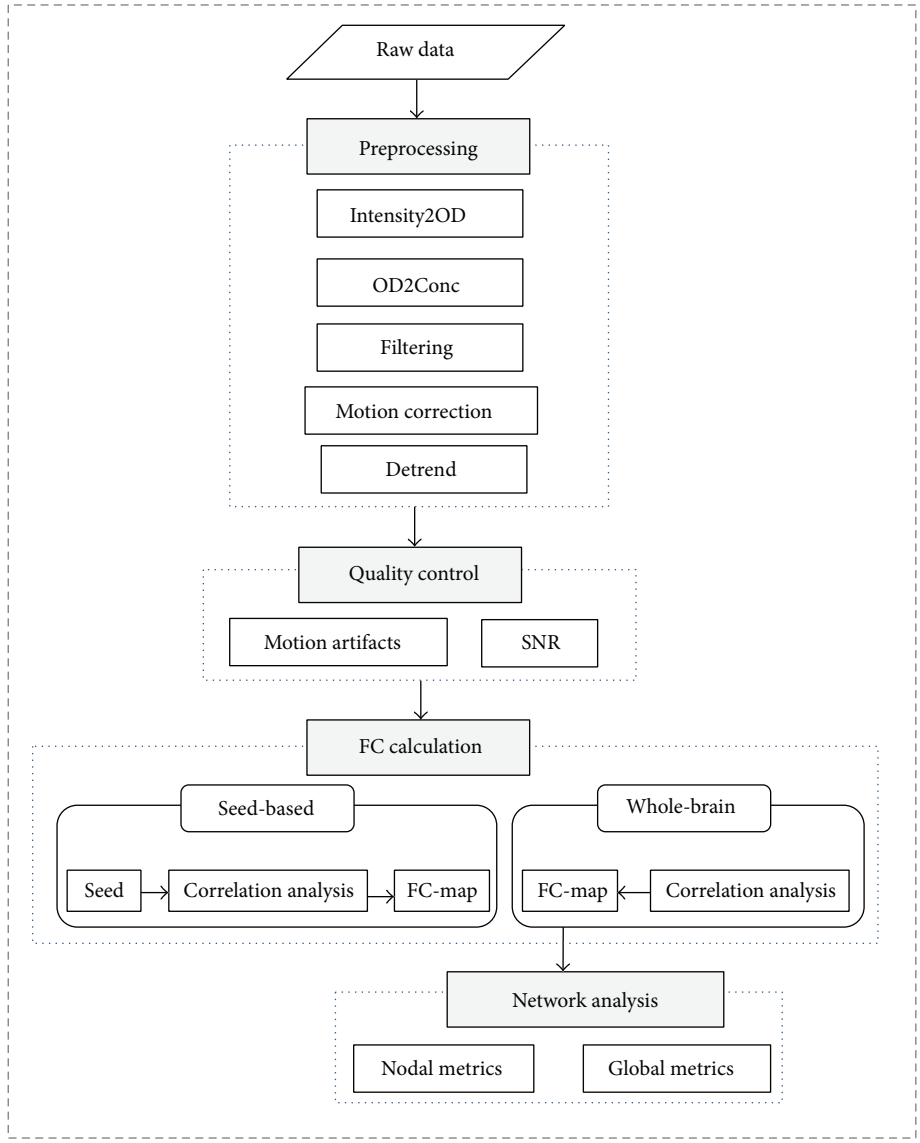


Figure 1: The main procedures for the processing of fNIRS datasets in FC-NIRS. The procedures contain four parts: (1) preprocessing, (2) quality control, (3) FC calculation, and (4) network analysis.

to read the raw data. Similarly, in the "out directory," the user also needs to provide an output directory to save the generated data. FC-NIRS also generated log files and kept track of the processing. After the operations and pressing the "RUN" button, FC-NIRS generated a ".proc" file for each subject in the output directory. For simplicity, FC-NIRS also provided some default preprocessing methods, which mainly included optical signal conversion, filtering, motion correction, and detrend. The details of the methods are as follows.

. . . Op ica Sig a C e i . Similar to Homer software [21], the raw optical intensity was first normalized as the optical density (OD) to provide a relative (percent) concentration change by dividing by the mean of the intensity. Then, the OD data were further converted to HbO, HbR, and HbT based on the modified Beer-Lambert law [28].

. . . Fi e i g. FC-NIRS uses a band-pass filter with third-order Butterworth, zero-phase digital filtering for low-pass and fifth-order Butterworth, zero-phase digital filtering for high-pass to remove low-frequency noise, and physiological interference sources. The filtering range for the band-pass filter could be defined by the users themselves according to their study objectives. In the FC-NIRS toolbox, for convenience, we provided a default band-pass range from 0.01 to 0.1 Hz, which represents the frequency range of hemodynamic signals that are thought to emanate from spontaneous neural activity.

. . . M i C ec i . To reduce the motion-induced artifacts, FC-NIRS provided a spline interpolation method [29] and a correlation-based signal improvement (CBSI) method [30], respectively. Specifically, the spline interpolation method detected the motion-induced artifacts by

the Institutional Review Board of Beijing Normal University Imaging Center for Brain Research. Of note, the data used in this study were obtained from a previous experiment that examined the test-retest reliability of the graph metrics of the resting-state fNIRS brain network [18].

... Da a Ac iii . A continuous-wave (CW) near-infrared optical imaging system (CW6, TechEn Inc., MA, USA) was used to measure the variations of the HbO and HbR concentration. The system generated two wavelengths (690 and 830 nm) of near-infrared light and collected the hemoglobin-dependent signals at a sampling rate of 25 Hz. Twelve light sources (each with two wavelengths) and 24 detectors were designed to configure 46 measurement channels to allow for the whole brain (i.e., frontal, temporal, parietal, and occipital lobes) to be covered bilaterally (Figure 8(a)). The spatial separation between any adjacent source and detector pair was 3.2 cm. The positioning of the probes was set according to the international 10–20 system.

... Da a P ep ce i g. The default procedures were used for data processing and analysis. These procedures included the conversion of the optical density to the hemoglobin concentration, band-pass filtering, detrending, and motion correction using CBSI. For each method, default parameters were used for data preprocessing.

... Q ai C . We checked the quality of the fNIRS data by examining the motion artifacts and SNR. We discarded the data from 3 participants that had large motion artifacts and low SNRs.

... FC Ca c ai . We adopted the seed-based correlation method to calculate the FC map in which the seed region was located in the right visual cortex region. Pearson's correlation was adopted to measure the FC strength between the seed and the other brain regions.

... Ne ₁ A a i . Graph-theoretical approaches were used to characterize the topological properties of the fNIRS brain networks. For simplicity, we only examined the small-world feature to verify the validity of the network analysis in FC-NIRS.

3. Results

.. T b De e p e

... D ₁ ad a d I a a i . The FC-NIRS toolbox is an open-source package, and its source code is freely available at the website http://www.nitrc.org/projects/fcnirs/. The toolbox can run under both Windows and Linux operating systems with MATLAB installed. The installation of FC-NIRS is similar to that of most MATLAB software packages. To run the package, type "FC-NIRS" in the command window of MATLAB after adding the FC-NIRS folder in the MATLAB search path. To facilitate users who do not have MATLAB installed, we generated an actual binary executable file (FC_NIRS.exe) for windows users. As shown in Figure 2, the four buttons preprocessing (Figure 3), quality control (Figure 4), FC calculation (Figure 5), and network analysis (Figure 6) are linked to four primary functional modules. In addition, a user-friendly manual is available within the packages, which provides a detailed guide for using FC-NIRS.

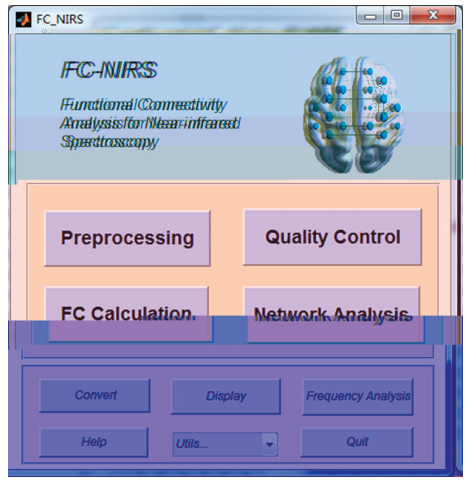


Figure 2: The main window of FC-NIRS. The four blue buttons are linked to four different functional modules, that is, preprocessing, quality control, FC calculation, and network analysis, which are shown in Figures 3, 4, 5, and 6, respectively.

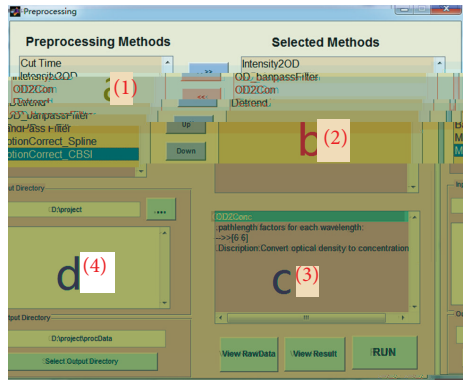
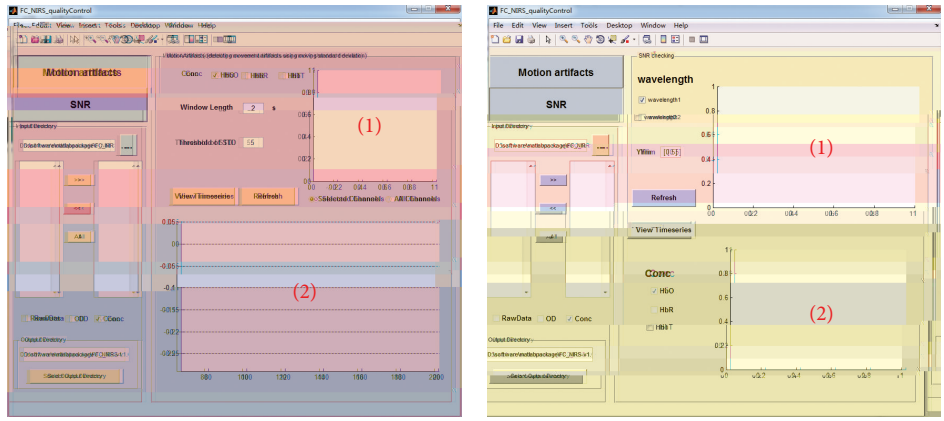


Figure 3: The preprocessing module of FC-NIRS. (1) Preprocessing methods provided by FC-NIRS; (2) preprocessing methods selected by users for data preprocessing; (3) parameter settings for selected methods; and (4) the input directory and output directory settings.

... Q ai C . Figure 4(a) shows the GUI of the motion artifact check, which includes two panels that display the probe geometry (Figure 4(a)(1)) and the moving standard deviation of the concentration signals at the selected measurement channels (Figure 4(a)(2)). The window length and the threshold of the moving standard deviation in the panel can be set by clicking the "Refresh" button. FC-NIRS also offers a quick way to check the time series in all of the channels by clicking the "View TimeSeries" button. Figure 4(b) shows the GUI of the SNR check, which also includes two panels that display the SNR values at all of the measurement channels (Figure 4(b)(1)) and the correlation matrix map calculated from the whole-brain time signals (Figure 4(b)(2)).



(a) (b)

FIGURE 4: The quality control module of FC-NIRS. (a) The motion check, in which "(1)" shows the probe geometry for the imaging pad and "(2)" shows the time series of the moving standard deviation for the selected channels. (b) The SNR check, in which "(1)" shows the SNR

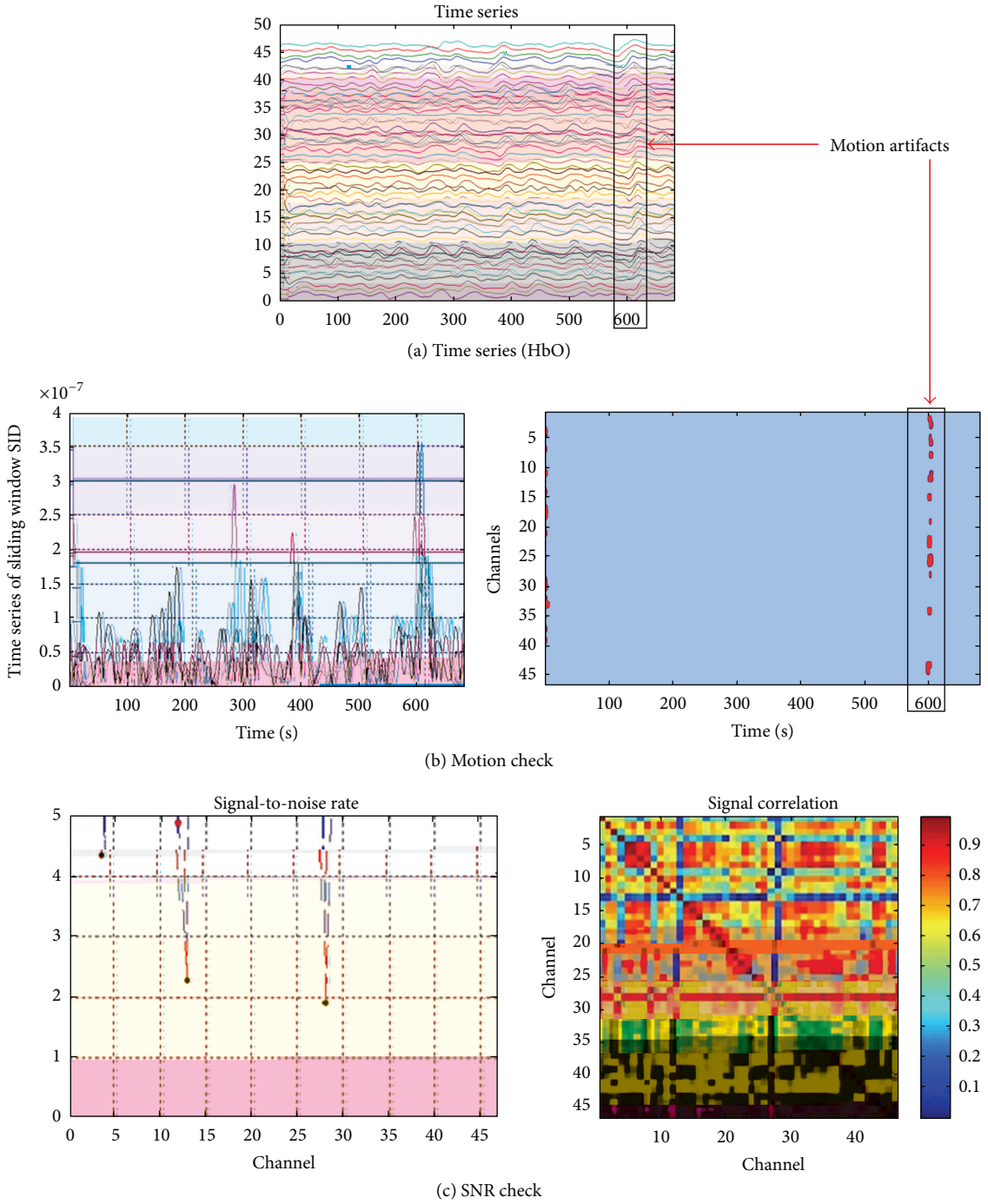
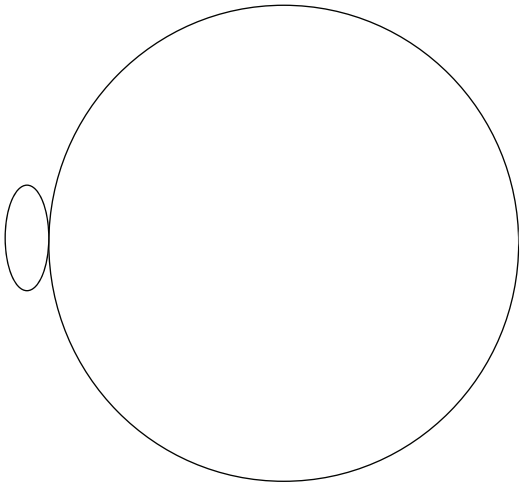
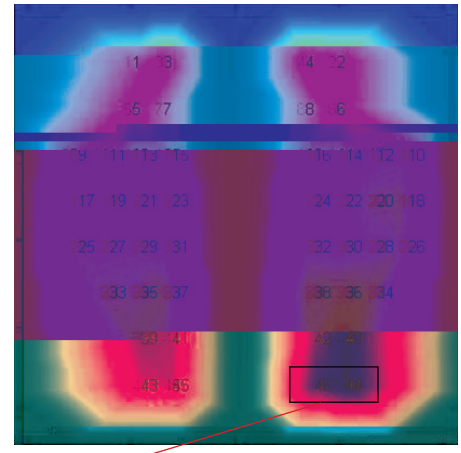


FIGURE 7: The experimental example for quality control of human brain data. (a) The time series of the hemoglobin concentration signals. A large fluctuation can be found at approximately 600 seconds. (b) The motion artifacts check. The window length is set to 2 s. The threshold is set to 5, which means that the values larger than five standard deviations from the mean are considered to be motion artifacts. (c) The SNR check. Channel 13 and channel 28 both have very low SNRs, which are computed as the mean signal intensity divided by the SD of the signal intensity over time compared with the other channels, and the corresponding signal correlation is very low. The low SNR of two channels can be caused by poor contact between the optodes and the scalp.

. . . FC Ca c a i . Seed-based (Figure 5(a)) and whole brain-based (Figure 5(b)) FC calculation methods can be selected by pressing the "Seed-based" or "Whole-brain" button. Figure 5(a) shows the GUI of the seed-based FC calculation. Within the panel, similar to the preprocessing procedure, the users must also set the input directory and the output directory in advance. To perform individual analyses, the user must input a seed channel and select a correlation



(a)



(b)

FC and networks [33], and fNIRS has been considered to be a promising technique for the study of functional connectome [4], especially during early childhood development and in unconscious patients. To handle the fNIRS-based connectome dataset, FC-NIRS has unique advantages, as it can process a large number of datasets in an efficient manner because of its batch processing strategies. Therefore, FC-NIRS can potentially make contributions to the study of the functional brain connectome in the future.

In the present study, we applied FC-NIRS to generate results for testing the resting-state FC in the bilateral visual cortex as well as network topological analysis at the whole-brain scale. Symmetrical FC was found in the bilateral visual system, which is highly compatible with previous findings [11, 34]. In addition, significant small-world features were observed in the whole-brain fNIRS network, which is also highly consistent with our previous results using the same dataset [12]. The present findings confirm the usability and validity of the FC-NIRS package.

In summary, FC-NIRS can facilitate and simplify the FC and network analysis in fNIRS-related studies and can provide optional FC definitions and network topological measures. However, some improvements in the software, such as providing statistical analysis for multiple comparisons and corrections for T-maps, are still required. Because FC-NIRS includes an extendable design framework, new functions for statistical analysis or new utilities can and will be added to future releases of the software.

Conflict of Interests

The authors declare that no conflict of interests exists.

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