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Abstract. Near-infrared spectroscopy (NIRS) is a developing and promising functional brain imaging technology. Developing data analysis methods to effectively extract meaningful information from collected data is the major bottleneck in popularizing this technology. In this study, we measured hemodynamic activity of the prefrontal cortex (PFC) during a color-word matching Stroop task using NIRS. Hemispheric lateralization was examined by employing traditional activation and novel NIRS-based connectivity analyses simultaneously. Wavelet transform coherence was used to assess intrahemispheric functional connectivity. Spearman correlation analysis was used to examine the relationship between behavioral performance and activation/functional connectivity, respectively. In agreement with activation analysis, functional connectivity analysis revealed leftward lateralization for the Stroop effect and correlation with behavioral performance. However, functional connectivity was more sensitive than activation for identifying hemispheric lateralization. Granger causality was used to evaluate the effective connectivity between hemispheres. The results showed increased information flow from the left to the right hemispheres for the incongruent versus the neutral task, indicating a leading role of the left PFC. This study demonstrates that the NIRS-based connectivity can reveal the functional architecture of the brain more comprehensively than traditional activation, helping to better utilize the advantages of NIRS. [DOI: 10.1117/1.JBO.19.5.057012]

Keywords: near-infrared spectroscopy; Stroop task; hemispheric lateralization; functional connectivity; effective connectivity.

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1 Introduction

Near-infrared spectroscopy (NIRS) is a developing and promising technology that monitors brain activity noninvasively and cheaply by measuring cerebral hemodynamic responses.[1,2] Because NIRS places fewer limitations on the subjects and environment than other functional neuroimaging methods such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET),[3,4] it has been widely applied in the cognitive and clinical research field.[5,6] However, the current application of NIRS in functional brain imaging is just the tip of the iceberg; the potential is far from fully exploited.[7,8] Current NIRS studies usually analyze only local changes in brain regions, with limited characterization of the brain's functional architecture. The development of data analysis methods will be a critical factor for promoting the application of NIRS technology.[7,9]

NIRS can provide high temporal resolution and reasonable spatial resolution in comparison to other traditional neuroimaging methods.[10] With the development of multichannel NIRS systems, it has become possible to measure interactions between brain regions other than traditional local brain activation to derive NIRS-based connectivity.[8,11] NIRS-based connectivity is a novel analysis tool for NIRS data from the perspective of functional integration,[12] which could be complementary to NIRS activation analysis.

Executive control, which refers to the ability to attend to relevant information, ignore distracting information, overcome conflict, and select the appropriate response, is a key cognitive function of human beings. The Stroop task is a prominent technique for measuring executive control during conflict.[13] Existing functional brain imaging studies demonstrate that the prefrontal cortex (PFC) is a predominant region involved in the Stroop task, which has functional hemispheric asymmetry.[14,15] However, current NIRS studies about hemispheric asymmetry in the Stroop task have focused on differences in activation, which can reveal only limited information about functional architecture of the brain.

In the present study, we aimed to fully examine the functional asymmetry of the PFC in executive control by employing traditional activation and NIRS-based connectivity analyses simultaneously. A color-word matching Stroop task that primarily activates the PFC was used.[14] Hemodynamic signals from the PFC were recorded by NIRS. Wavelet transform coherence (WTC) analysis was employed to assess the intrahemispheric functional connectivity for each side of the PFC. Granger causality (GC) analysis was used to evaluate effective connectivity between hemispheres. The relationship between behavioral performance and brain activity was examined through Spearman correlation analysis.

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2 Method

2.1 *Subjects*

Thirteen right-handed, paid volunteers (five females, aged 20–26 years, mean, 22.9 years) participated in the study. All volunteers reported that they were healthy with no psychiatric or neurological disorders, had normal color vision, and had normal or corrected-to-normal vision. Each subject gave his/her written informed consent before the experiment. The study was approved by the Human Subjects Institutional Review Board of Huazhong University of Science and Technology.

2.2 *Procedures*

A block design color-word matching Stroop task was employed in this study. Each stimulus consisted of two characters shown on a screen. The participants were asked to decide whether the meaning of the lower Chinese character was consistent with the color of the upper Chinese character [Fig. 1(a)]. If answer was "No," the participants pressed a button using the right index finger, and if answer was "Yes," they pressed the other button using the left index finger. Two types of stimulus conditions were displayed: incongruent and neutral. In the incongruent stimuli condition, the upper character was a color word (红, 黄, 蓝, 绿, 紫, meaning "red," "yellow," "blue," "green," and "purple") printed in a disparate color, and the lower character was a color word presented in white. In the neutral stimuli condition, the upper character was a noncolor word (涂, 贯, 华, 球, 奖, meaning "scrawl," "pass through," "China," "ball," and "prize") presented in red, yellow, blue, green, or purple [Fig. 1(a)]. For each stimulus condition, the trials were semirandomly mixed to avoid the consecutive appearance of more than three "Yes" or "No" trials.

The experiment was composed of four runs, and each run was composed of four neutral and four incongruent task blocks [Fig. 1(a)]. There were 20 trials in each block, and each trial contained a stimulus shown for 1200 ms and a blank screen that lasted 300 ms, hence each block lasted 30 s. There was a 15-s rest period between blocks, a 60-s rest period between runs, and a 60-s rest period before the first run and after the last run. A sound was played to cue subjects 1 s before each block. There was a practice session for each subject before the formal experiment.

2.3 *Near-Infrared Spectroscopy Data Collection*

The NIRS data were recorded using a homemade continuous-wave NIRS instrument.[16] The probe was supported by a piece of thermoplastic and held one source (850 and 785 nm) and eight detectors, so that there were eight NIRS channels for each probe. Two such probes were employed to cover the bilateral PFC. Channel L3, the third channel of the left probe, was over the F3 EEG electrode position, and the right probe was placed symmetrically [Fig. 1(b)]. The distance between the detector and the source of the same probe was 3 cm, and the acquisition rate was 70 Hz.

2.4 *Data Analysis*

The raw NIRS data were filtered <3 Hz to remove instrument noise, downsampled to 10 samples per second, and converted to change in optical density (ΔOD).

2.4.1 *Activation analysis*

The ΔOD data were bandpass filtered between 0.015 and 0.5 Hz (least-squares FIR filter with zero-phase distortion; order: 50) to eliminate slow signal drift and arterial pulsation. The modified Beer–Lambert law (MBLL) method was used to convert the ΔOD data into hemoglobin signals, with a 6.0 differential path-length factor (DPF) value of 785 nm and a 5.2 DPF value of 850 nm.[17] Finally, the hemoglobin signals were block averaged.

The mean value of the hemoglobin signal during the task period (0 to 30 s after the task began) was computed as the task hemodynamic response for each channel. The average task hemodynamic response across channels of the same hemisphere was obtained to indicate brain activation for each hemisphere.

2.4.2 *Functional connectivity analysis*

WTC measures the crosscorrelation of two data series as a function of time and frequency,[18] with the ability to detect locally phase-locked behavior, which might not be detectable using

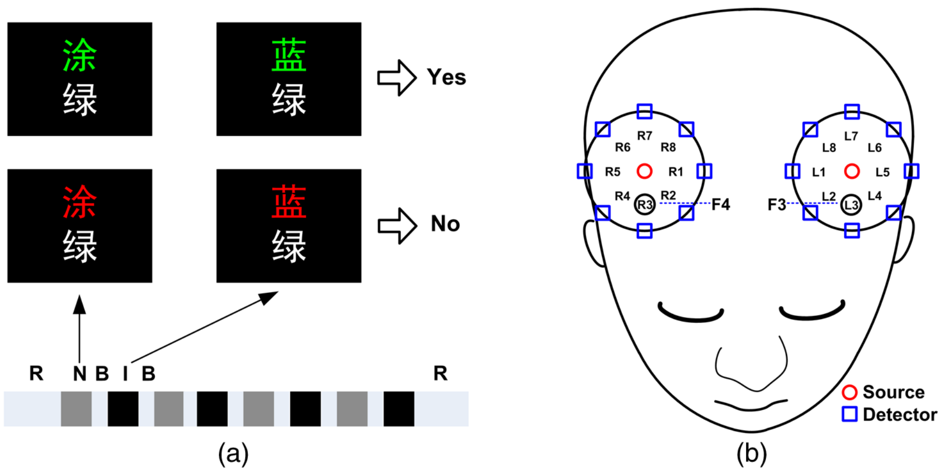

Fig. 1 (a) The task sequence in a run (bottom) and examples of the two stimulus conditions (top). R, 60 s rest; B, 15 s baseline; N, neutral block; I, incongruent block and (b) the NIRS probe locations. The numbers (R1–R8 and L1–L8) at the midpoints of the source-detector pairs denote the NIRS channels. Channel L3 was over the F3 electrode position, and Channel R3 was over the F4 electrode position.

traditional time series analysis methods.[19] More details about WTC were provided by Grinsted et al.,[20] and the WTC MATLAB package download from their website (http://noc.ac.uk/using-science/crosswavelet-wavelet-coherence) was employed to evaluate intrahemispheric functional connectivity for the left and the right PFCs separately.

The ΔOD data were converted into hemoglobin signals using the MBLL method, and the hemoglobin signals were block averaged. The WTC method was used to calculate pairwise coherences between all channels of the same probe to obtain the intrahemispheric functional connectivity for each side of the PFC. Frequency bands in which the coherence value changed between the neutral and incongruent tasks were identified as task-related bands.[19] The average coherence value for these frequency bands, which was between 0.071 and 0.5 Hz, was calculated to indicate functional connectivity for each channel pair.

2.4.3 *Correlation between behavioral performance and brain activity*

The response times (RTs) were recorded using presentation software. The average RT for each stimulus condition was computed for each subject, using only correct button press responses with RTs within three standard deviations of the mean value.

Because the focus of the paradigm was conflict-related processing, the Stroop effect (incongruent minus neutral) was used as the index to analyze the relationship between behavioral performance and brain activity. Spearman correlation coefficient was employed to examine the relationship between RT and brain activation and the relationship between RT and functional connectivity separately.

2.4.4 *Effective connectivity analysis*

GC was employed to evaluate effective connectivity between hemispheres.[12,21] Signal A is said to "Granger cause" signal B if information from the past of A helps to better predict B than only considering information from the past of B. Calculation of GC is based on an autoregressive model. Because the NIRS signal is an indirect measure of neural activity modulated by the hemodynamic response function (HRF), GC analysis of the NIRS signal should focus on the causality differences between brain regions and task conditions to minimize the impact of HRF variation.[22]

GC values were calculated for each homologous channel pair within the left/right PFC. Causality in the left to right direction minus causality in the right to left direction was defined as the differences of influence (DOIs), which corresponded to the net causality of left to right.[22] The DOI values were averaged over all homologous channel pairs for each task condition, and the differences of DOI (ΔDOI) between the incongruent and the neutral tasks (incongruent minus neutral) were then calculated. Positive ΔDOI values indicate increase information flow from the left to the right PFCs accompanying conflict processing.

The ΔOD data were filtered <0.5 Hz to eliminate arterial pulsation. The MBLL method was used to convert the ΔOD data into hemoglobin signals, and the hemoglobin signals were block averaged. GC analysis was implemented using the Granger causality MATLAB toolbox Granger causal connectivity analysis (GCCA, University of Sussex, Brighton, United Kingdom),[22] including data preprocessing, data stationarity check, model validity and consistency verification, and DOI calculation. Different time lags (1, 1.5, 2, 2.5, and 3 s) were used for the autoregressive models to validate that the results were robust.[23]

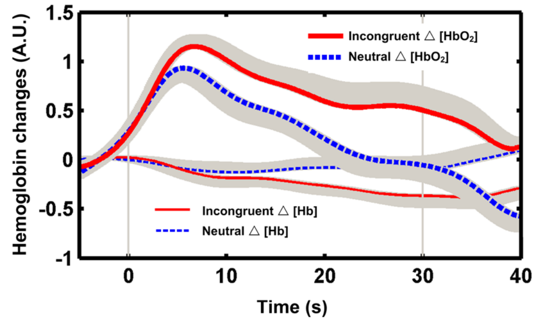

Fig. 2 The grand average hemoglobin signal for the two task conditions at NIRS channel L6. The gray area indicates standard error (SE). The gray vertical lines at 0 and 30 s indicate the start and end of the task. The hemoglobin changes were expressed in arbitrary units (A.U.).

3 Results

3.1 *Activation Results*

Figure 2 displays the grand average hemoglobin signal for the two task conditions at one typical NIRS channel. Figure 3 shows the grand average activation responses for the left and right hemispheres. The activation responses were greater for the incongruent task compared with the neutral task for both

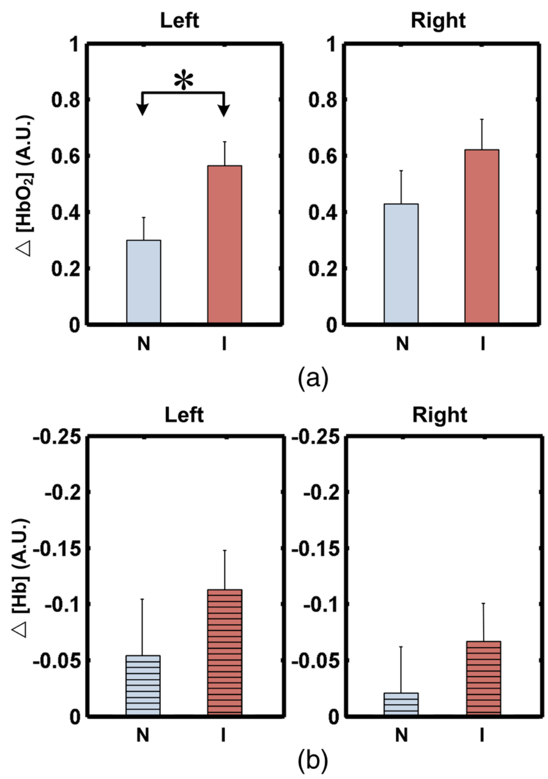

Fig. 3 The grand average activation responses on (a) HbO_2 signal and (b) Hb signal. Data are shown as mean values ± SE. N, neutral task; I, incongruent task. Black asterisk indicates $p < 0.05$, FDR correction.

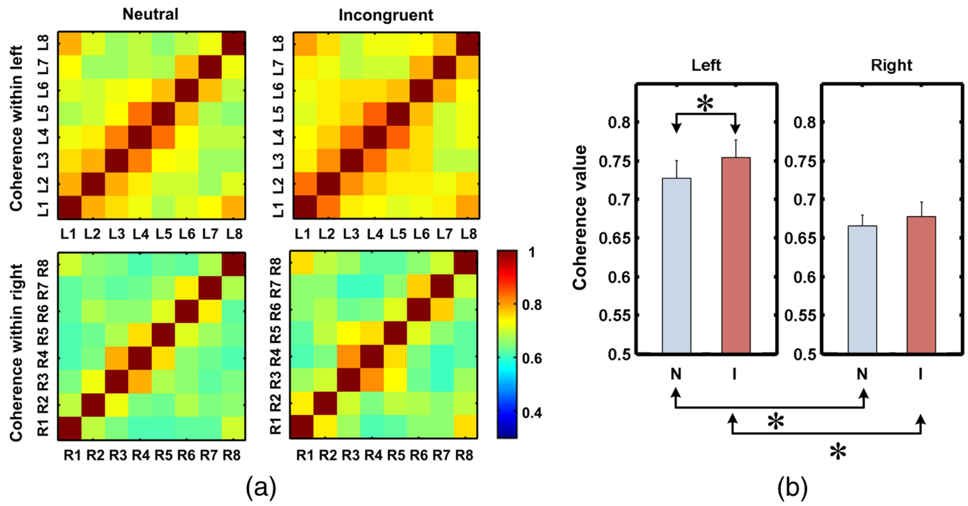

Fig. 4 (a) The average intrahemispheric functional connectivity matrices on HbO_2 signal across subjects and (b) the grand average intrahemispheric functional connectivity on HbO_2 signal. Data are shown as mean values ± SE. N, neutral task; I, incongruent task. Black asterisk indicates $p < 0.05$, FDR correction.

hemispheres, but only the left hemisphere showed a significant Stroop effect for HbO_2 signal. Before all the paired t-tests in this study, data were tested being normally distributed using Lilliefors test.

3.2 *Functional Connectivity Results*

Figure 4(a) shows the intrahemispheric functional connectivity matrices on HbO_2 signal averaged across subjects. Every matrix element was the coherence value for a NIRS channel pair (row coordinate and column coordinate). The mean value of the matrix elements was calculated for each matrix (except for elements of the secondary diagonal, which was the self-coherence of the channels) to indicate intrahemispheric functional connectivity for each hemisphere and each task [see Fig. 4(b)]. The intrahemispheric functional connectivities for both sides of the PFC were stronger for the incongruent task than for the neutral task, but only the left intrahemispheric functional connectivity showed a significant Stroop effect. In addition, for the incongruent or neutral tasks itself, the intrahemispheric functional connectivity of the left PFC was significantly stronger compared with that of the right PFC. Figure 5(a) shows the intrahemispheric functional connectivity matrices on Hb signal averaged across subjects, and Fig. 5(b) shows the grand average intrahemispheric functional connectivity on Hb signal. The left intrahemispheric functional connectivity on Hb signal showed a marginally significant Stroop effect. Fisher's z-transform was employed for coherence values before the paired t-test.[19]

3.3 *Correlation between Response Time and Activation/Functional Connectivity*

The results of correlation showed that there was a greater negative correlation between RT and the left PFC, compared with the right PFC (see Fig. 6). The negative correlation indicated

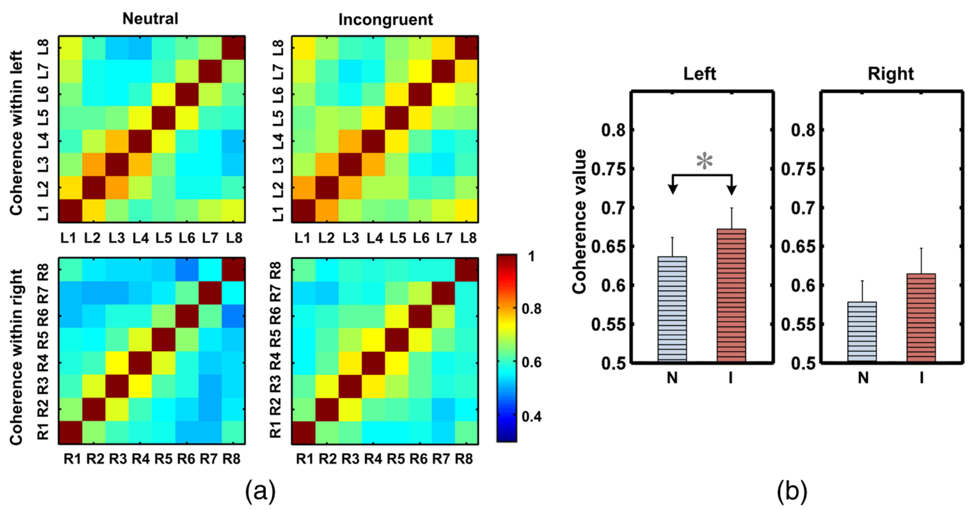

Fig. 5 (a) The average intrahemispheric functional connectivity matrices on Hb signal across subjects and (b) the grand average intrahemispheric functional connectivity on Hb signal. Data are shown as mean values ± SE. N, neutral task; I, incongruent task. Gray asterisk indicates $p < 0.1$, FDR correction.

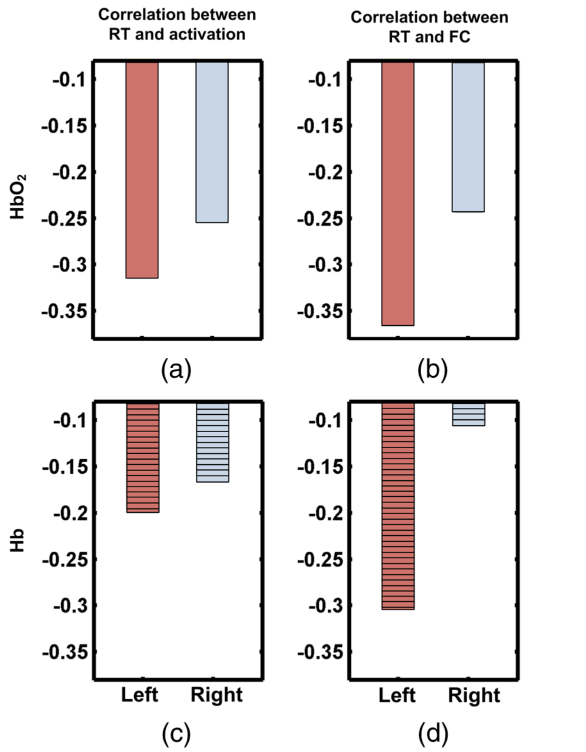

Fig. 6 The correlation between RT and activation for both sides of the PFC on (a) HbO_2 signal and (c) Hb signal. The correlation between RT and intrahemispheric functional connectivity for both sides of the PFC on (b) HbO_2 signal and (d) Hb signal.

that the stronger the brain activation/functional connectivity, the better the behavioral performance. Besides, both the correlations between RT and left intrahemispheric functional connectivity on HbO_2 signal and Hb signal were higher than activation.

3.4 *Effective Connectivity Results*

Figure 7 shows that the average ΔDOI values across subjects were positive for all time lags (subject 9 was excluded from the analysis for the 1-s time lag on HbO_2 signal because the values were more than three standard deviations from the mean value), and there were marginally significant differences between the incongruent and the neutral tasks for the 1-s time lag on HbO_2 signal and for the 1.5-s time lag on Hb signal. The effective connectivity results indicated that the flow of information from the left to the right PFCs increased accompanying conflict processing.

4 Discussion

This study employed traditional activation and novel NIRS-based connectivity analyses simultaneously to examine the functional asymmetry of the PFC in executive control. The results of both the NIRS activation and the NIRS-based connectivity analyses demonstrated a leftward lateralization for the Stroop effect and the correlation with behavioral performance. However, NIRS-based connectivity was more sensitive for hemispheric lateralization identification than activation analysis. Furthermore, NIRS-based connectivity can reveal and model the interaction between hemispheres, helping us to understand the functional organization of hemispheric asymmetry in the Stroop task more comprehensively. The results on HbO_2 and Hb are in consistency, with slightly better for results on HbO_2. Previous studies have demonstrated that, compared with Hb, HbO_2 had a better signal-to-noise ratio (SNR) and was the more sensitive indicator of changes in regional cerebral blood flow.[24,25] And the correlation between BOLD and HbO_2 was higher than Hb, which may because of the higher SNR of HbO_2.[26]

Compared with the neutral task, the activation responses were greater for the incongruent task for both sides of the PFC, and the left hemisphere showed a significant Stroop effect. The activation results indicated that the left PFC is dominant for Stroop interference processing, which is consistent with previous fMRI studies,[14] indicating that the design of this study was correct.

The functional connectivity results also demonstrated a left hemisphere dominance for Stroop interference processing. In addition to the Stroop effect, for the incongruent or the neutral tasks, there was also a leftward lateralization, which is in line with the verbal nature of the two types of tasks.[27] Previous studies have shown that, for right-handed subjects, the left hemisphere is more functionally specialized for verbal tasks than the right hemisphere.[28]

The results of both types of correlation analysis (RT and brain activation and RT and functional connectivity) indicated that the left PFC plays a primary role in affecting behavioral performance, in accordance with a previous study that reported poorer performance on the Stroop task in patients with left PFC lesions.[29] Compared with activation analysis, intrahemispheric functional connectivity of the left PFC had a greater correlation with RT, indicating that the functional connectivity could be

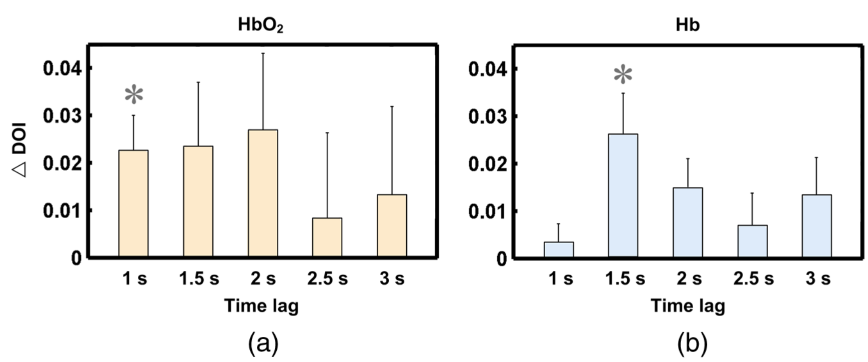

Fig. 7 The effective connectivity results. (a) The average ΔDOI values on HbO_2 signal and (b) the average ΔDOI values on Hb signal. Gray asterisk indicates $p < 0.1$, FDR correction.

more sensitive for identifying the primary brain regions that affect behavioral performance. The results also suggested that the functional connectivity could predict behavioral performance better than activation.

The reason that functional connectivity was more sensitive than activation for identifying hemispheric lateralization and predicting behavioral performance may be that there are uncertainties in quantifying hemoglobin change using the MBLL method.[7] Although some previous researches reported results in μM change,[7] it is not quantitatively accurate because the partial volume effect was not considered.[30,31] Additionally, DPF varies between different investigated areas and subjects. These two factors lead to errors in measured activation. However, the trend of hemoglobin change, on which functional connectivity analysis is based, is still correct.[7]

Executive control over conflict includes two steps: conflict detection and resolution.[13] The results of the effective connectivity analysis demonstrated increased information flow from the left to the right PFCs for the incongruent task versus the neutral task, indicating a leading role of the left PFC in regard to the right PFC during conflict processing. The results seem to show that the left PFC detected the conflict first and then aroused the right PFC for conflict resolution. The results support the viewpoint that the left PFC is involved in conflict detection, which is in line with a previous fMRI study that suggested that conflict detection is achieved by the left PFC.[32] The effective connectivity results illustrate that the NIRS-based brain connectivity can deliver more comprehensive information compared with traditional activation.

A meta-analysis about lateralized Stroop studies demonstrated that, although some studies showed a leftward lateralization, there are no significant differences between the hemispheres on the whole.[33] But the studies included in this meta-analysis were unilateral presentation Stroop experiments, and just employed reaction time as the dependent measure. Both the experimental paradigm and assessment indicator are different from ours, and these differences may lead to different conclusions.[33] What is more, instead of brain imaging technology, these studies used behavioral performance to assess the brain activity indirectly; thus, this assessment may be inappropriate. In the future, various task paradigms should be considered to further investigate the hemispheric lateralization during Stroop tasks. And multiple parameters, including brain activity and behavioral performance, should be obtained.

In addition, right dominance of PFC activity can be caused by the mental stress responses of the autonomic nervous system during mental stress tasks.[34] In this study, there was no mental-related information in the experiment materials. Before the formal experiment, there were practice sessions to familiarize the subjects with the task. Subjects reported that they were relaxed and peaceful during the formal experiment. Left dominance of PFC activity was observed in this study, indicating that the hemispheric lateralization was indeed caused by cognitive function.

In this study, due to the absence of reference channels, some approaches for reducing the interference of superficial layers, such as adaptive filtering technique, cannot be used here. For blind source separation, an estimation of the eigenstructure based on the prior information about the degree of noise or visual inspection with the step-by-step removal of eigenvectors is required. Then, subjective errors are likely introduced in the case that no reference channel is included.[35] In addition, the extent of the functional region is comparable with the spatial coverage of the probe in our study; PCA filters can negatively affect the estimate of the hemodynamic response.[36] It will be a similar situation for using global regression to reduce the influence. But what we focus on is the differences of task conditions in an experiment. And the evaluation of the differences itself would counteract the influence of task-unrelated signal components.[37]

5 Conclusion

This study analyzed hemispheric asymmetry using NIRS from multiple perspectives, including activation, functional connectivity, effective connectivity, and behavioral analysis. The results indicate that, compared with traditional activation, NIRS-based connectivity is more sensitive and delivers more comprehensive information that can help us to better understand the functional organization of the brain. This study demonstrates that, as a novel NIRS analysis tool, NIRS-based connectivity can exploit the capabilities of NIRS effectively, helping to promote the application of NIRS in neuroscience research, especially in clinical study.

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Biographies of the other authors are not available.