Site-specific effects of 800- and 850-nm forehead transcranial photobiomodulation on prefrontal bilateral connectivity and unilateral coupling in young adults

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Supplementary Material

Theoretical Foundation for Data Processing

Methods to quantify changes in concentrations of oxygenated hemoglobin (Δ[HbO]), deoxygenated hemoglobin (Δ[HHb]), and redox-state cytochrome c oxidase (Δ[CCO]) have been developed and reported [1, 2]. A brief review is provided below for general readers who wish to understand the theoretical foundation and processing methods in depth.

A broadband near-infrared spectroscopy (bbNIRS) system provides measurements of optical spectra at different times (t), as expressed $I(t, \lambda)$. A relative optical density spectrum, $\Delta OD(t, \lambda)$, can be defined and calculated at each wavelength λ as:

$$\Delta OD(t,\lambda) = log_{10}[\frac{I_0(t=0,\lambda)}{I(t,\lambda)}], \quad (1)$$

where $I_0(t=0, \lambda)$ can be the baseline spectrum at time t=0 or an average of several initial baseline spectral readings (i.e., the first two spectra collected in each experiment), and $I(t, \lambda)$ represent time-varying spectra acquired at each time point throughout the entire experiment. The estimations of Δ[HbO] and Δ[CCO] from raw spectral data taken with bbNIRS throughout the experiment were based on modified Beer-Lambert's law [3], which offers a quantitative relationship of $\Delta OD(\lambda)$ on $\Delta[HbO]$, $\Delta[HHb]$, *and* $\Delta[CCO]$ at each wavelength, λ, at each time point, with a wavelength-dependent path-length factor, $L(\lambda)$. Based on optical diffusion theory [4], $\Delta OD(\lambda)/L(\lambda)$ can be expressed as a sum of optical absorbance contributed by $\Delta[HbO]$, $\Delta[HHb]$, and $\Delta[CCO]$ components, as given below:

$$\begin{bmatrix} \frac{\Delta OD(\lambda_1)}{L(\lambda_1)} \\ \frac{\Delta OD(\lambda_2)}{L(\lambda_2)} \\ \frac{\Delta OD(\lambda_3)}{L(\lambda_3)} \\ \dots \\ \frac{\Delta OD(\lambda_n)}{L(\lambda_n)} \end{bmatrix} = \Delta[HbO]*\begin{bmatrix} \varepsilon_{HbO}(\lambda_1) \\ \varepsilon_{HbO}(\lambda_2) \\ \varepsilon_{HbO}(\lambda_3) \\ \dots \\ \varepsilon_{HbO}(\lambda_n) \end{bmatrix} + \Delta[HHb]*\begin{bmatrix} \varepsilon_{HHb}(\lambda_1) \\ \varepsilon_{HHb}(\lambda_2) \\ \varepsilon_{HHb}(\lambda_3) \\ \dots \\ \varepsilon_{HHb}(\lambda_n) \end{bmatrix} + \Delta[CCO]*\begin{bmatrix} \varepsilon_{CCO}(\lambda_1) \\ \varepsilon_{CCO}(\lambda_2) \\ \varepsilon_{CCO}(\lambda_3) \\ \dots \\ \varepsilon_{CCO}(\lambda_n) \end{bmatrix}, \quad (2)$$

where *Δ[HbO], Δ[HHb] and Δ[CCO]* are relative concentration changes of HbO, HHb and CCO respectively; $\varepsilon_{HbO}(\lambda)$, $\varepsilon_{HHb}(\lambda)$ and $\varepsilon_{CCO}(\lambda)$ represent the extinction coefficients at each wavelength of HbO, HHb and CCO, which can be found in ref. [1]; $L(\lambda)$ is a wavelength dependent factor that denotes the effective pathlength of the detected photons through tissues at each wavelength. Furthermore, according to the Modified Beer-Lambert Law [3, 5], $L(\lambda)$ can be expressed as:

$$\begin{bmatrix} L(\lambda_1) \\ L(\lambda_2) \\ L(\lambda_3) \\ \dots \\ L(\lambda_n) \end{bmatrix} = r*\begin{bmatrix} DPF(\lambda_1) \\ DPF(\lambda_2) \\ DPF(\lambda_3) \\ \dots \\ DPF(\lambda_n) \end{bmatrix}, \quad (3)$$

where r is a constant that denotes the source-detector distance. In this study, we used source detector separation of 3 cm, so r=3. The wavelength dependence of $L(\lambda)$ is caused by a wavelength-dependent differential pathlength factor, $DPF(\lambda)$. By substituting Eq. (3) into Eq. (2) for multiple wavelengths, the estimation of *Δ[HbO], Δ[HHb] and Δ[CCO]* can be expressed as follows:

$$\begin{bmatrix} \Delta[HbO] \\ \Delta[HHb] \\ \Delta[CCO] \end{bmatrix} = \frac{1}{r}*\begin{bmatrix} \varepsilon_{HbO}(\lambda_1) & \varepsilon_{HHb}(\lambda_1) & \varepsilon_{CCO}(\lambda_1) \\ \varepsilon_{HbO}(\lambda_2) & \varepsilon_{HHb}(\lambda_2) & \varepsilon_{CCO}(\lambda_2) \\ \dots & & \\ \varepsilon_{HbO}(\lambda_n) & \varepsilon_{HHb}(\lambda_n) & \varepsilon_{CCO}(\lambda_n) \end{bmatrix}^{-1} \begin{bmatrix} \frac{\Delta OD(\lambda_1)}{DPF(\lambda_1)} \\ \frac{\Delta OD(\lambda_2)}{DPF(\lambda_2)} \\ \dots \\ \frac{\Delta OD(\lambda_n)}{DPF(\lambda_n)} \end{bmatrix}. \quad (4)$$

In order to accurately solve *Δ[HbO], Δ[HHb] and Δ[CCO]* using Eq. (4), we would need to know *DPF(λ)* in the wavelength range of our measurements. It is known that appropriate or accurate selection/estimation of wavelength-dependent DPF is crucial for accurate estimation of chromophore concentrations [6]. In this study, DPF(λ) values were assumed to be time-invariant because of given stable brain optical properties. Based on diffusion theory with the semi-infinite boundary geometry [7], *DPF(λ)* can be determined by

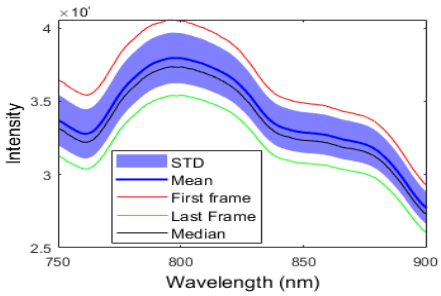
$$DPF(\lambda) = \frac{\sqrt{3\mu_s'(\lambda)}}{2\sqrt{\mu_a(\lambda)}} * \frac{r\sqrt{3\mu_a(\lambda)\mu_s'(\lambda)}}{r\sqrt{3\mu_a(\lambda)\mu_s'(\lambda)}+1} \quad (5)$$

where $\mu_a(\lambda)$ and $\mu_s'(\lambda)$ are the estimated absorption and reduced scattering coefficients across the wavelength range of interest.

Values of $\mu_a(\lambda)$ and $\mu_s'(\lambda)$ were measured using a tissue oximeter (OxiplexTS, ISS) that operates in the frequency-domain. This device provides readings of μ_a and μ_s' values at 750 nm and 830 nm, as well as absolute concentrations of [HbO] and [HHb]. However, to obtain $\mu_s'(\lambda)$ values across the entire range of wavelengths from 780-900 nm, we used Mie theory to interpolate and extrapolate the two measured μ_s' values at 750 nm and 830 nm. Mie theory is typically represented by $k\lambda^{-b}$, where k and b were determined by fitting this equation to both μ_s' values at 750 nm and 830 nm. In addition, absorption coefficients in the same wavelength range (780-900 nm) were estimated based on [HbO] and [HHb] measured by the same tissue oximeter [4].

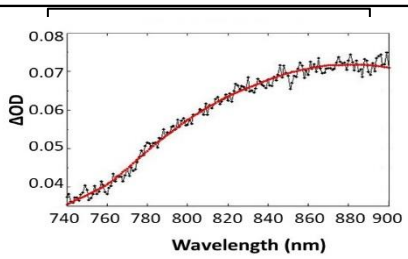
After combining the measured *ΔOD(λ)* values across the measurement period and empirical *μa(λ)* and *μs'(λ)* values of the human forehead [2], we were able to solve eq. (4) at each measurement time point using MATLAB, achieving temporal series of *Δ[HbO]*, *Δ[HHb]* and *Δ[CCO]* under respective experimental conditions, as shown in Fig. 4(b) in the main paper. Specifically, our calculations covered the spectral range of 780-900 nm with a total of 121 wavelengths. Figure S1 below illustrates the processing steps described above.

Step 1: bbNIRS data acquisition to form time-dependent optical spectra in the NIR range of 750-900 nm.



Step 2: Calculation of ΔOD spectra at each time point. t.

$$\Delta OD(t,\lambda) = log_{10}[\frac{I_0(t=0,\ \lambda)}{I(t,\lambda)}]$$



Step 3: Modified Beer-Lambert's law that associates measured ΔOD values over *n* wavelengths with changes of concentrations in *Δ[HbO]*, *Δ[HHb]* and *Δ[CCO]*.

$$\begin{cases} \Delta OD(\lambda_1) = r * DPF_{t0}(\lambda_1) * \{\Delta[HbO] * \varepsilon_{HbO}(\lambda_1) + \Delta[HHb] * \varepsilon_{Hb}(\lambda_1) + \Delta[CCO] * \varepsilon_{CCO}(\lambda_1)\} \\ \Delta OD(\lambda_2) = r * DPF_{t0}(\lambda_2) * \{\Delta[HbO] * \varepsilon_{HbO}(\lambda_2) + \Delta[HHb] * \varepsilon_{Hb}(\lambda_2) + \Delta[CCO] * \varepsilon_{CCO}(\lambda_2)\} \\ \Delta OD(\lambda_3) = r * DPF_{t0}(\lambda_3) * \{\Delta[HbO] * \varepsilon_{HbO}(\lambda_3) + \Delta[HHb] * \varepsilon_{Hb}(\lambda_3) + \Delta[CCO] * \varepsilon_{CCO}(\lambda_3)\} \\ \quad \vdots \\ \Delta OD(\lambda_n) = r * DPF_{t0}(\lambda_n) * \{\Delta[HbO] * \varepsilon_{HbO}(\lambda_n) + \Delta[HHb] * \varepsilon_{Hb}(\lambda_n) + \Delta[CCO] * \varepsilon_{CCO}(\lambda_n)\} \end{cases}$$

Step 4: Quantification of *Δ[HbO]* and *Δ[CCO]* by solving the following matrix at each time point after performing the pseudo-inversion of the *n*×3 ε matrix. Then, a time-dependent series of *Δ[HbO]* (and *Δ[CCO]*) can be formed, as demonstrated below on the right panel.

$$\begin{bmatrix} \Delta[HbO] \\ \Delta[HHb] \\ \Delta[CCO] \end{bmatrix} = \frac{1}{r} * \begin{bmatrix} \varepsilon_{HbO}(\lambda_1) & \varepsilon_{HHb}(\lambda_1) & \varepsilon_{CCO}(\lambda_1) \\ \varepsilon_{HbO}(\lambda_2) & \varepsilon_{HHb}(\lambda_2) & \varepsilon_{CCO}(\lambda_2) \\ \cdots & & \\ \varepsilon_{HbO}(\lambda_n) & \varepsilon_{HHb}(\lambda_n) & \varepsilon_{CCO}(\lambda_n) \end{bmatrix}^{-1} \begin{bmatrix} \frac{\Delta OD(\lambda_1)}{DPF(\lambda_1)} \\ \frac{\Delta OD(\lambda_2)}{DPF(\lambda_2)} \\ \cdots \\ \frac{\Delta OD(\lambda_n)}{DPF(\lambda_n)} \end{bmatrix}$$

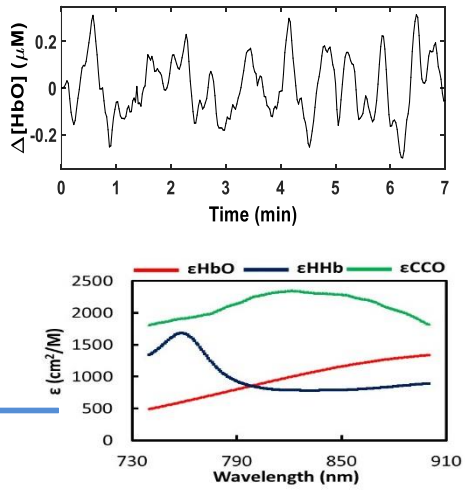


Fig. S1 A data processing flow chart used to quantify *Δ[HbO]* and *Δ[HHb]* from raw bbNIRS data.

References:

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