An Index Independent of Mean Path Length for Evaluation of Cerebral Blood Volume and Oxygenation in Continuous-Wave Near-Infrared Spectroscopic Measurements

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Abstract: Continuous-wave near-infrared spectroscopy (CWNIRS) is most commonly used in noninvasive near-infrared spectroscopy (NIRS), providing relative changes in concentrations of oxygenated hemoglobin (Δ[oxy-Hb]), deoxygenated hemoglobin (Δ[deoxy-Hb]), and total hemoglobin (Δ[total-Hb]). The CWNIRS device is portable and allows real-time monitoring, demonstrating that the device is very useful in measuring changes in oxygenation and hemodynamics. Although this system has yet to achieve absolute quantification of hemoglobin concentration, our previous study indicated that a ratio of Δ[deoxy-Hb] or Δ[total-Hb] to Δ[oxy-Hb] in CWNIRS measurements may be useful in evaluating cerebral oxygenation and hemodynamics. The purpose of this study is to theoretically clarify whether a ratio in oxygenation- and hemodynamic measurements, such as Δ[deoxy-Hb]/Δ[oxy-Hb] obtained using CWNIRS, is independent of mean path length and enables comparisons of measurements on cerebral oxygenation and hemodynamics among channels, subjects, or experiments.（J Jpn Coll Angiol, 2006, **46**: 11–13）

Key words: cerebral oxygenation, comparable index, continuous wave, near-infrared spectroscopy, theoretical analysis

Introduction

Near-infrared spectroscopy (NIRS) is a new noninvasive technique for measuring blood volume and oxygenation in the brain[1-3] and muscle.[4] With continuous light, continuous-wave NIRS (CWNIRS) measures the intensity of the transmitted or reflected light. The CWNIRS system is most commonly used in NIRS, providing relative changes in concentrations of oxygenated hemoglobin (Δ[oxy-Hb]), deoxygenated hemoglobin (Δ[deoxy-Hb]), and total hemoglobin (Δ[total-Hb]). The CWNIRS device is portable and makes real-time monitoring possible, demonstrating that the device is very useful in measuring changes in oxygenation and blood volume in the brain during a mental task.[2, 5] Although this system has yet to achieve absolute quantification of hemoglobin concentration, our previous study indicated that the ratio of Δ[deoxy-Hb] or Δ[total-Hb] to Δ[oxy-Hb] may be useful in evaluating cerebral oxygenation and hemodynamics.[6]

The purpose of this study is to theoretically clarify whether the ratio of Δ[deoxy-Hb] or Δ[total-Hb] to Δ[oxy-Hb] obtained by CWNIRS enables us to compare oxygenation and hemodynamics in the brain among channels, subjects, or experiments.

Principles and theoretical analysis

If a scattering change between two successive measurements at a wavelength is negligible, absorbance change for a scattering medium with absorber is described as follows, based on the modified Beer-Lambert law:[7-10]

$$\Delta A(\lambda) = \varepsilon(\lambda)\, L(\lambda)\, \Delta C \qquad (1)$$

where $\Delta A(\lambda)$ denotes absorbance change at wavelength λ;

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$\varepsilon(\lambda)$, extinction coefficient ($mM^{-1}\cdot cm^{-1}$) of the absorber at wavelength λ; $L(\lambda)$, mean path length (cm) of detected photons at wavelength λ; ΔC, concentration change (mM) of the absorber (**Fig. 1**). Here it should be noted that mean path length L is not known *a priori* and it depends on the absorption and scattering properties of the medium[9, 10] when the concentration varies greatly.

The following equation is derived from equation (1) assuming that light-absorbing heme proteins except for oxy-Hb and deoxy-Hb are absent or only present at insignificant concentrations and that the effects of cytochrome aa_3 are small; these assumptions are reasonable in the brain, which has no myoglobin, under the normal physiological conditions for the wave lengths employed:[11]

$$\Delta A(\lambda) = \varepsilon_a(\lambda)\, L_a(\lambda)\, \Delta[\text{oxy-Hb}] + \varepsilon_b(\lambda)\, L_b(\lambda)\, \Delta[\text{deoxy-Hb}] \quad (2)$$

where $\varepsilon_a(\lambda)$ and $\varepsilon_b(\lambda)$ represent extinction coefficients ($mM^{-1}\cdot cm^{-1}$) of oxy-Hb and deoxy-Hb at wavelength λ, respectively; $L_a(\lambda)$ and $L_b(\lambda)$, mean path lengths (cm) of detected photons in oxy-Hb and deoxy-Hb at wavelength λ, respectively; Δ[oxy-Hb] and Δ[deoxy-Hb], changes in concentrations (mM) of oxy-Hb and deoxy-Hb from initial values of measurements, respectively.

A CWNIRS system measures absorbance change ΔA at several wavelengths, determining Δ[oxy-Hb], Δ[deoxy-Hb], and Δ[total-Hb] (= Δ[oxy-Hb] + Δ[deoxy-Hb]) by solving equations based on equation (2) with Δ[oxy-Hb] and Δ[deoxy-Hb] as unknown variables. If measurements at two wavelengths λ_1 = 840 nm and λ_2 = 760 nm are made, the following equations are obtained:

$$\Delta[\text{oxy-Hb}] = K\{\Delta A(840) - (k_1'/k_2')\,\Delta A(760)\} \quad (3a)$$

$$\Delta[\text{deoxy-Hb}] = K\{(k_1/k_2')\,\Delta A(760) - (k_2/k_2')\,\Delta A(840)\} \quad (3b)$$

where the number in parentheses stands for wavelength (nm) used for measurements; $k_1 = \varepsilon_a(840)\, L_a(840)$, $k_1' = \varepsilon_b(840)\, L_b(840)$, $k_2 = \varepsilon_a(760)\, L_a(760)$, $k_2' = \varepsilon_b(760)\, L_b(760)$, and $K = (1/k_2)/(k_1/k_2 - k_1'/k_2')$. Hence, $k_1'/k_2' = \varepsilon_b(840)\, L_b(840)/\varepsilon_b(760)\, L_b(760)$, $k_1/k_2' = \varepsilon_a(840)\, L_a(840)/\varepsilon_b(760)\, L_b(760)$, $k_2/k_2' = \varepsilon_a(760)\, L_a(760)/\varepsilon_b(760)\, L_b(760)$, $k_1/k_2 = \varepsilon_a(840)\, L_a(840)/\varepsilon_a(760)\, L_a(760)$, and $k_1'/k_2' = \varepsilon_b(840)\, L_b(840)/\varepsilon_b(760)\, L_b(760)$.

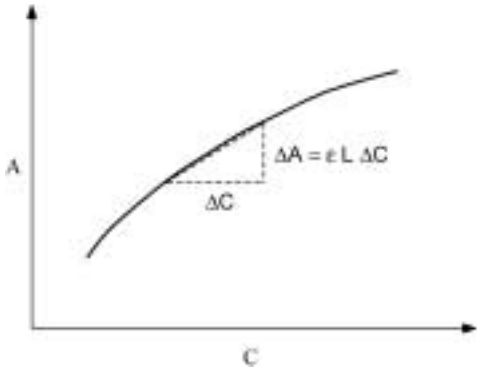

Figure 1 Schematic diagram of nonlinear relationship between concentration of absorber and absorbance of an absorbing and scattering medium.
C: concentration of the absorber
A: absorbance of the medium
ΔA: absorbance change
ε: extinction coefficient of the absorber
L: mean path length of detected photons
ΔC: concentration change

A study with a biological model consisting of milk, yeast, and red blood cells demonstrated that these quotients of the coefficients such as k_1'/k_2' remain almost constant when the change in concentration of red blood cells is less than 50% of the initial value.[12] On the other hand, K includes $1/k_2$ involving directly unknown mean path length L_a, which depends on the absolute concentration of oxy-Hb. This results in possible incorrect measurements of Δ[oxy-Hb] and Δ[deoxy-Hb], which are described using arbitrary unit in general CWNIRS systems, assuming tentatively that K is one.

However, if we employ a ratio of these measurements Δ[oxy-Hb], Δ[deoxy-Hb] and so on to cancel K, it is expected that the obtained ratios such as Δ[deoxy-Hb]/Δ[oxy-Hb] are independent of unknown mean path length, and depend only on measurable absorbance changes in the case of relatively small changes in concentration:

$$\Delta[\text{deoxy-Hb}]/\Delta[\text{oxy–Hb}] = \{(k_1/k_2')\,\Delta A(760) - (k_2/k_2')\,\Delta A(840)\}/\{\Delta A(840) - (k_1'/k_2')\,\Delta A(760)\} \quad (4)$$

where $k_1/k_2' = \varepsilon_a(840)\, L_a(840)/\varepsilon_b(760)\, L_b(760)$, $k_2/k_2' = \varepsilon_a(760)\, L_a(760)/\varepsilon_b(760)\, L_b(760)$, and $k_1'/k_2' = \varepsilon_b(840)\, L_b(840)/\varepsilon_b(760)\, L_b(760)$.

Both the numerator and denominator of the right side of equation (4) can be obtained from measurements using a

CWNIRS system, which generally assumes that K equals one as mentioned above. The calculated ratio of the right side of equation (4) does not contain K anymore, resulting in being unaffected by mean path length in the case of relatively small concentration changes.

The ratio of Δ[deoxy-Hb] to Δ[oxy-Hb] in equation (4) was calculated in our recent experiment at a low inspired oxygen concentration and seemed to vary depending on the concentration of carboxyhemoglobin in blood.[6] Hence, the ratio is most likely to reflect the body's ability to supply oxygen to tissues and to be useful in evaluating its ability. Moreover, the ratio is quite stable as compared to a similar ratio of Δ[oxy-Hb] to Δ[oxy-Hb] plus Δ[deoxy-Hb], which may have been used with an insufficient examination of relationship to mean path length in CWNIRS, during inhalation of a low concentration of oxygen.[6] Clinical studies and further research on the brain will help establish the usefulness of the ratio of Δ[deoxy-Hb] to Δ[oxy-Hb], etc. in CWNIRS measurements.

Conclusion

Although CWNIRS systems themselves include unknown mean path length in the measurements and are subsequently unable to provide absolute measurements of hemoglobin, it has been demonstrated that a ratio of CWNIRS measurements, such as Δ[deoxy-Hb]/Δ[oxy-Hb], is independent of mean path length and depends only on measurable absorbance changes. As a result, comparisons of measurements on cerebral oxygenation and hemodynamics among channels, subjects, and experiments can be possible.

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