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Research Paper

Noninvasive measurement of cerebral cortex hemoglobin oxygenation with Near-Infrared spectroscopy

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Abstract

Near-Infrared (NIR) is the region of light with wavelength from 650 nm to 1100 nm. In this region light can penetrate into higher depth compared to visible light in biological tissues. In NIR region there is a special optical window from 700 nm to 900 nm in which dominant absorber chromophores inside the brain are oxy-hemoglobin and deoxy-hemoglobin. non-invasive Functional Near-Infrared Spectroscopy (fNIRS) is a portable low-cost efficient method for monitoring hemodynamic change in cerebral cortex. Since fNIRS and Functional Magnetic Resonance Imaging (fMRI) both measure hemoglobin oxygenation, it is acceptable to compare these two methods for cortex related cognitive task studies and drug addiction studies. in cases that other diagnostic techniques like fMRI are not applicable and might be harmful for example in case of a patient with cardiac pacemaker, or when fMRI is not available or for claustrophobic patient an alternative method should be available. in many studies for specific tasks because of subject's positioning limits inside fMRI, an inexpensive method that allows data acquisition from a sitting or standing subject fNIRS is a reliable alternative. When it's about cerebral cortex fNIRS can be an alternative for fMRI considering that fNIRS price is much lower and for many cognitive task designs subject's mobility and position are important factors and with fNIRS we do not have to be that concerned about these issues. In this article Principles and equations for this technology will be described and as an example we designed a cognitive task and used fNIRS device to measure cerebral activity in left prefrontal cortex of healthy male adult to show accuracy and efficiency of this device for cerebral cortex activity monitoring. Also, Value of this method in attention & cognitive disorders specially in children thanks to higher depth of light penetration in their brain compared to adults will briefly be discussed.

Keywords: NIR-spectroscopy, hemodynamic monitoring, cognitive tasks, hemoglobin, fNIRS

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1. Introduction

Important absorbers when fNIRS is used on scalp are oxyhemoglobin, deoxyhemoglobin, water and melanin pigment in hair which causes noise in data. Rest of chromophores are usually considered negligible. Below 700 nm and in visible range of light, penetration depth of light inside biological tissue is limited and from 700 nm to 900 nm melanin pigment absorption continuously decreases which is an advantage for this optical window. above 900 nm absorption coefficient of water rises rapidly and water becomes the dominant absorber above 950 nm. Another advantage of 700 nm to 900 nm optical window is that water in tissue has less scattering in this region compared to visible light. These facts according to Fig-1 makes 700 nm to 900 nm optical window a special range for biological tissue. By using Near-Infrared sources and placing detector 3 to 4 cm in an ipsilateral arrangement on

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scalp we can measure change in optical density which can be related to change in chromophores and oxygenation in cerebral cortex[1] . the advantages of fNIRS compared to fMRI are portability, easy access, its lower price and ability for data acquisition during different subject positionings. The important difference is that fNIRS measures only changes in oxy and deoxy hemoglobin not the absolute values and for children thanks to high penetration of light into tissue its possible to measure changes in deep regions of brain but in adults depth of penetration is limited and by putting optical source and detector on adult scalp we can measure cerebral cortex activity which is approximately 1.5 cm below scalp [2].

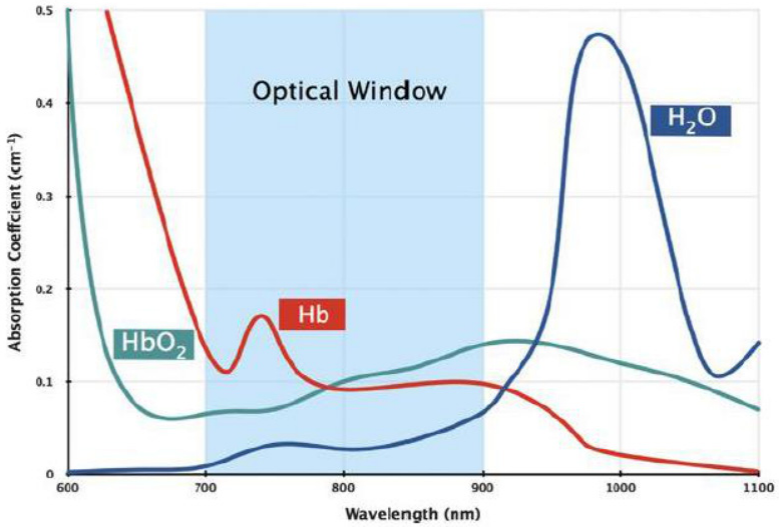

Fig 1: Absorption spectrum of water (H_2O) , oxyhemoglobin (HbO_2) and deoxyhemoglobin (Hb) in NIR region with focus on 700 nm to 900 nm optical window[3].

The measured fNIRS signal will be from banana-shaped path between source and detector inside tissue and the region with high sensitivity is the region in the middle of source-detector distance at the depth of 1.5 to 2 cm. By increasing the source-detector distance the banana-shaped path will be longer and from deeper regions of tissue but with lower signal intensity and higher noise. this trade-off means that this method for adults' brain is best only for cortex oxygenation monitoring. The most important chromophores in brain are oxyhemoglobin and deoxyhemoglobin. Compared to these two we can say cytochrome has lower concentration and lower percentage and sometimes is considered negligible. When it comes to change in chromophores in cerebral cortex the rest of chromophores can be ignored because of very low change in concentration during cerebral monitoring. If cytochrome is also ignored it's possible to use only two wavelengths to measure change in concertation of oxyhemoglobin and deoxyhemoglobin during a cognitive task or any cerebral activity preferably with limited patient movement. In most of brain studies because oxyhemoglobin and deoxyhemoglobin are predominant chromophores the signal from NIR spectroscopy is from these two and cytochromes is ignored because of its limited contribution [2].

This method is based on modified beer-lambert law. This equation in diffuse optics considers absorption and scattering of underlying tissue for NIR light passing through biological tissue. This equation is an empirical description of light passing through tissue and it includes overall attenuation of light in highly scattering mediums and also measurement geometry effect which is an added term known as G in equation[4]

$$OD = -\log\frac{I}{I_o} = \varepsilon CLB + G \qquad (1)$$

In this equation OD is optical density and considering that during brain activity or a cognitive task we assume that scattering loss is constant in the region of interest (cortical gray matter) and all the change in optical intensity is because of absorption due to change in oxy and deoxy hemoglobin concentrations it's fair to say OD represents absorption. I_0 is incident constant intensity from source (emitter) and I is intensity measured by detector.

ε is the extinction coefficient of a chromophore and C is concentration for that particular chromophore for example oxyhemoglobin. L is real linear distance between source and detector and is usually between 3 to 4 cm but in some cases a

second detector in much shorter distance from source like 0.7 cm is placed to reduce the noise by excluding some changes in optical intensity due to tissues above cortical gray matter. the actual path that light travels through tissue from source to detector is larger than source to detector distance. parameter B in this equation includes partial volume factor and Differential Path Factor. Partial volume factor is a parameter that excludes effect of extracerebral skin, skull and CSF layers because the only interesting volume in fNIRS is grey matter of brain and its only a fraction of measurement volume so an adjustment is necessary[1, 5]. These two parameters are not measured with continuous wave (CW) sources and usually references with advanced technologies are used in order to calculate these parameters. But for adults and children Differential Path factor is different but easy to estimate and there are equations for approximating its value and in this equations age is an important parameter [6]. to account for scattering which increases the distance traveled by light from source to detector effective distance is defined by total mean path length of detected photons. This parameter is Differential Path Factor (DPF) in equation [1].

all Calculation of changes in optical density are valid assuming the source is stable and has a constant intensity. Because the purpose is calculating changes and not absolute values, we use differential measurements and parameters like L and G remain constant at the same time and thanks to subtraction we can continue without the complicated G parameter. Although B and Ɛ are wavelength dependent but for a certain wavelength C (chromophores concentration) only changes due to cerebral activity or hemodynamic change. In other words, oxyhemoglobin and deoxyhemoglobin concentration change (ΔC) , in our equation causes change in optical density (ΔOD) and the rest of parameters for a certain wavelength are constant. Here are two chromophores are oxyhemoglobin ($\Delta[HbO_2]$) and deoxyhemoglobin (Δ[Hb]) concentration and these chromophores changes is what we can measure. calculating absolute values is much harder and requires costly technologies. Since we have ($\Delta[HbO_2]$) and (Δ[Hb]) by adding them we can have total change in hemoglobin concentration. During a brain activity there is an increase in local blood flow and cerebral blood volume due to neurovascular coupling and increased oxygen transported to the active region of brain usually exceeds the rate of oxygen consumption by local neurons. as a result during brain activity in a certain region we measure an increase in oxygenated hemoglobin [2].

$$\Delta OD = -\log \frac{I_{Final}}{I_{Initial}} = \varepsilon \Delta C L B \qquad (2)$$

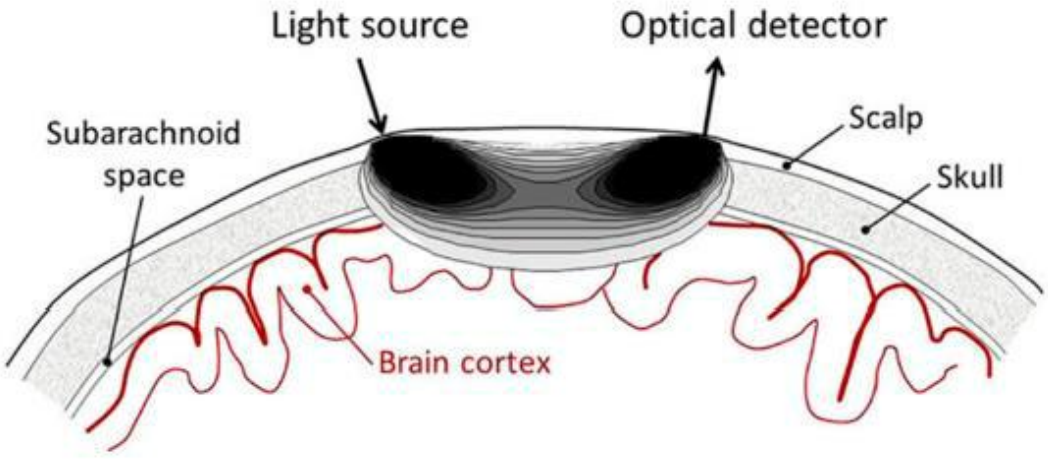

Fig 2: schematic representation of banana-shaped shaded area from source to detector in Near-infrared Spectroscopy of the human brain [5].

2. METHODOLOGY

Most researchers consider change in cytochrome compared to hemoglobin negligible and because we have two variables that are change in oxyhemoglobin ($\Delta[HbO_2]$) and change in deoxyhemoglobin (Δ[Hb]) for solving our equation we need a second wavelength for a second equation to be able to calculate both.

$$\Delta OD^{\lambda} = \left(\varepsilon^{\lambda}_{\mathrm{HbO_2}} \Delta[\mathrm{HbO_2}] + \varepsilon^{\lambda}_{\mathrm{Hb}} \Delta[\mathrm{Hb}]\right) B^{\lambda} L, \qquad (3)$$

It worth mentioning that in cerebral cortex studies that are usually expensive and have limited clinical applications a third wavelength is used for calculating change in cytochrome concentration plus the other two mentioned hemoglobin's with 3 equations and 3 unknowns.

B and Ɛ are wavelength dependent and we have two wavelengths (λ_1 & λ_2) and our detector can measure change in optical density of each wavelength separately. Two wavelengths in 700 to 900 nm range are chosen in a way to be far from 805 nm which is isosbestic point of oxy and deoxy hemoglobin which means at wavelengths close to 805 we cannot distinguish these two chromophores. For example 730 nm and 850 nm are good choices because extinction coefficient (Ɛ) for oxy and deoxy hemoglobin is different enough so we can separate these two chromophores[7].

$$\Delta[\mathrm{Hb}] = \frac{\varepsilon_{HbO_2}^{\lambda 2}\frac{\Delta OD^{\lambda 1}}{B^{\lambda 1}} - \varepsilon_{HbO_2}^{\lambda 1}\frac{\Delta OD^{\lambda 2}}{B^{\lambda 2}}}{\left(\varepsilon_{Hb}^{\lambda 1}\cdot\varepsilon_{HbO_2}^{\lambda 2} - \varepsilon_{Hb}^{\lambda 2}\cdot\varepsilon_{HbO_2}^{\lambda 1}\right)L}.$$

$$\Delta[\mathrm{HbO_2}] = \frac{\varepsilon_{Hb}^{\lambda 1}\frac{\Delta OD^{\lambda 2}}{B^{\lambda 2}} - \varepsilon_{Hb}^{\lambda 2}\frac{\Delta OD^{\lambda 1}}{B^{\lambda 1}}}{\left(\varepsilon_{Hb}^{\lambda 1}\cdot\varepsilon_{HbO_2}^{\lambda 2} - \varepsilon_{Hb}^{\lambda 2}\cdot\varepsilon_{HbO_2}^{\lambda 1}\right)L} \quad (4)$$

As an example, to show the validity and reliability of a noncommercial inexpensive CW fNIRS device we measured hemodynamic change in prefrontal cortex of a healthy adult subject during a cognitive task. Prefrontal cortex has been implicated in decision making and executive function. We considered cerebral activity during rest state as a reference point also known as a baseline. for oxyhemoglobin and deoxyhemoglobin and for 3 minutes before beginning of task the fNIRS device was on and the subject was asked to be relaxed and breath in a normal manner in order to avoid artifacts. each time for 30 seconds subject has to estimate complicated mathematical multiplication and after that he can relax for the next 30 seconds and we repeated this task continuously for 2 times on the subject.

First 30 seconds of data as shown in Fig-3 subject was relaxed but for the next 30 second (30 – 60 sec) subject was performing mathematical task. After that we repeated this procedure and data in Fig-3 is the real time data without further processing and it includes a few artifacts but the advantage of real time data is that researchers can monitor the subject during task which is an important factor. considering that subject should act according to demands and this real time data even with limited error has the advantage of operators monitoring the subject and data simultaneously. if the error is increased or there is an issue, operator can correct subject's behavior specially during cognitive tasks. For example, subject's attention, breathing pattern, movements or even if subject scratches his body as we know it can cause noise. the same as other modalities like Electroencephalography (EEG) we know operator controls the subject to avoid noises.

3. FINDINGS/RESULTS

Hemodynamic change of cerebral cortex with CW fNIRS during task as mentioned was measured.By using two independent optical detectors separated 2 cm on left prefrontal cortex we measured hemodynamic changes in two separated voxels of prefrontal cortex.

Signals in Fig-3 shows change in molar concentration as a function of time in two separated, independent voxels of left prefrontal cortex. In figure oxyhemoglobin (red), deoxyhemoglobin (blue) and summation of both known as total hemoglobin (green) are shown. On timeline 0 was beginning of procedure and for 30 seconds subject was relaxed and after that from 30 sec to 60 sec subject was calculating complicated multiplications and few seconds after subject started this calculations, amount of oxyhemoglobin shown in red color kept increasing until it reached its first oxyhemoglobin peak (in red) and simultaneously deoxyhemoglobin concentration decreased as expected. After that because subject was relaxing from 60 to 90 sec and oxyhemoglobin was decreasing and after that with few seconds lag when subject started mathematical calculations again the oxyhemoglobin increased until it reached the second peak.

The few seconds lag is inevitable and time scale because of delay should be large.

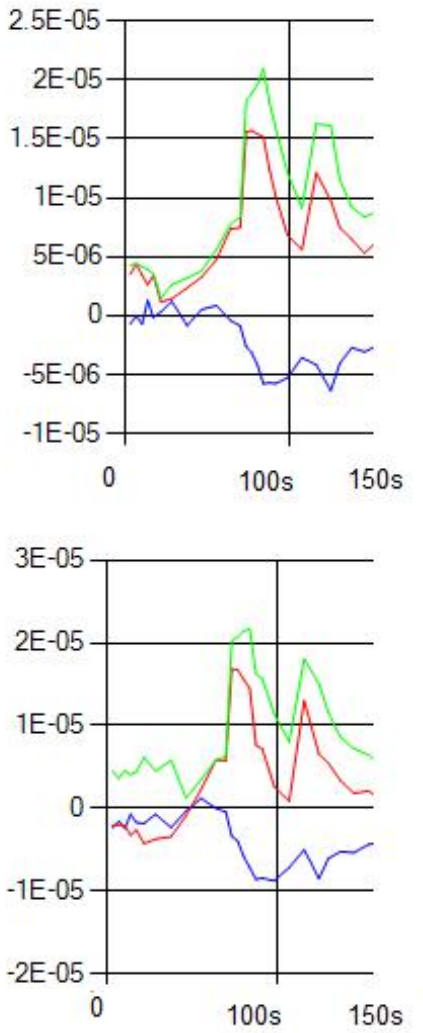

Fig 3: change in chromophores in molar as a function of time during task in two voxels on left prefrontal cortex.. Oxyheamoglobin is colored red , deoxyheamoglobin is in blue and summation of both is total heamoglobin colored in green .

The purpose of this example was to show efficiency of the least expensive version of this device. Correlation between signals in 2 separated, independent voxels acquired by 2 detectors represents accuracy and reliability of this method. thanks to many studies on continuous wave fNIRS in the last decade this method became more popular and its importance for physicians in hospital and researchers became obvious. subject populations including children and elderly that are traditionally difficult to study with confining fMRI are now easier subjects for fNIRS study. efficient, real time cerebral cortex hemodynamic measurements during task or for other goals without complicated signal processing with fNIRS is reliable. This method can be used widespread as a non-invasive option for studies in adults during activity in cerebral cortex and when it comes to children it's possible to use this device for grey matter and white matter thanks to higher penetration depth of light in children's skull[5].

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