

# SIMULTANEOUS MEASUREMENT OF CEREBRAL TISSUE OXYGENATION OVER THE ADULT FRONTAL AND MOTOR CORTEX DURING REST AND FUNCTIONAL ACTIVATION

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## 1. INTRODUCTION

Near-infrared spectroscopy (NIRS) has been shown to measure subtle haemodynamic changes in the human brain. Differential spectroscopy has been used to record changes in oxy-haemoglobin concentration  $\Delta[\text{HbO}_2]$  and deoxy-haemoglobin concentration  $\Delta[\text{HHb}]$ , following various kinds of stimulation including motor<sup>1</sup>, visual<sup>2</sup>, and cognitive<sup>3</sup>. NIRS based topography systems have also been used to map cerebral haemodynamic responses<sup>4,5</sup> around the evoked region. NIRS provides an alternative to more expensive techniques such as positron emission tomography and functional magnetic resonance imaging, in the understanding of brain function.

Using multiple closely spaced detectors, the technique of spatially resolved spectroscopy<sup>6</sup>, is based on the measurement of attenuation slope as a function of source detector separation. From these measurements it is possible to de-couple the absorption ( $\mu_a$ ) and scattering coefficients ( $\mu_s$ ), resulting in the calculation of scaled absolute haemoglobin concentrations, i.e.  $k \cdot [\text{HbO}_2]$  and  $k \cdot [\text{HHb}]$ . The Tissue Haemoglobin Index (THI) is defined as  $k \cdot [\text{HbO}_2] + k \cdot [\text{HHb}]$  while the Tissue Oxygenation Index (TOI) as  $(k \cdot [\text{HbO}_2] / (k \cdot [\text{HbO}_2] + k \cdot [\text{HHb}])) \cdot 100\%$ <sup>7</sup>. The constant  $k$  here is a scaling factor for  $\mu_s$ . TOI is a measure of oxygenation saturation in cerebral tissues whereas THI reflects the total amount of haemoglobin.

Using a continuous-wave type spectrometer with SRS capability and fast sampling rate of 6 Hz (NIRO 300, Hamamatsu Photonics KK), we aim to (1) establish the normal ranges of TOI and THI over both frontal and motor cortex, (2) compare the slow spontaneous oscillations ( $\sim 0.1\text{Hz}$ ) found in  $\Delta[\text{HbO}_2]$  signals simultaneously measured over both sites, and (3) investigate the responses of  $\Delta[\text{HbO}_2]$ ,  $\Delta[\text{HHb}]$ , TOI and THI in the resting and activated human adult brain.

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## 2. METHODS

### 2.1 Experiment

Simultaneous measurements of cerebral oxygenation were made over the right frontal cortex and left motor cortex of ten normal adult volunteers (median age=36±12 years) using a NIRO 300 spectrometer. An optode spacing of 5 cm was used for the optical probe over the frontal cortex while a smaller spacing of 4 cm was used for that over the motor cortex to optimise signal to noise ratio. Both optical probes were covered with a black cloth. Whilst seated in a quiet, dark room, with their eyes closed, subjects were asked to relax and 5 minutes of resting data were recorded. Subjects were then asked to perform a finger opposition task with their right hand. The task was performed for 43 seconds followed by a 30 second rest period and measurements were made for a total of ten task/rest repetitions. Respiration was measured using a capnogram and the pulse plethysmograph (PPG) was recorded from a pulse oximeter probe on the left earlobe (Novamatrix, USA). Raw data, including the optical densities at four wavelengths and attenuation slopes at three wavelengths, were collected from the spectrometer via the serial port onto a PC and other physiological signals recorded via an analogue-to-digital conversion card. The sampling rate was set to 6 Hz. All data were saved onto a hard disk for further analysis. The raw NIRS data were converted to  $\Delta[\text{HbO}_2]$ ,  $\Delta[\text{HHb}]$ , TOI and THI with a Matlab program (Mathworks Ltd.) written based on a SRS literature from the manufacturer<sup>7</sup>. A differential pathlength factor of 6.4 was used<sup>8</sup>.

## 3. RESULTS

### 3.1 TOI and THI in the resting brain

The mean and standard deviation of TOI and THI for 10 resting subjects over 5 minutes are shown in Table 1. TOI over the frontal cortex was found to be significantly higher than that over the motor cortex (paired t-test,  $p < 0.002$ ). THI over the frontal cortex was found to be significantly lower than that over the motor cortex (paired t-test,  $p < 0.003$ ).

### 3.2 Cross-correlation between $\Delta[\text{HbO}_2]$ measured over the frontal and motor cortex

The  $\Delta[\text{HbO}_2]$  signals measured over the frontal and motor cortex were found to contain signal components, including those due to heart beat (~1 Hz), respiration (~0.25Hz) and slow spontaneous oscillations (~0.1Hz), as previously reported<sup>9</sup>. The signals sometimes also contained a slow drift (<0.005Hz). One possible origin of the slow spontaneous oscillations is the vasomotion in the capillary level<sup>9</sup>. In order to investigate this signal component more closely, the slow drift was first removed (detrended) by subtracting the lowpass filtered  $\Delta[\text{HbO}_2]$  signal at a cut-off frequency of 0.005Hz from the raw  $\Delta[\text{HbO}_2]$  signal. The resulting signal was again lowpass filtered at a cut-off frequency of 0.5Hz to remove the strong heart beat signals. The filtering was carried out by a 5<sup>th</sup> order lowpass Butterworth digital filter in forward-backward directions to avoid introducing a phase delay. The filtered signals were dominated by the

slow spontaneous oscillations ( $\sim 0.1$ Hz). An example of the filtered  $\Delta[\text{HbO}_2]$  signals over the motor and frontal cortex is shown in Figure 1. For the 10 subjects at rest, a mean ( $\pm$  S.D.) correlation coefficient ( $r^2$ ) of  $0.57 \pm 0.18$  was found between the filtered  $\Delta[\text{HbO}_2]$  signals measured over the frontal and motor cortex.

### 3.3 Motor stimulation

The on-off period for the stimulation was 43-30 seconds, corresponding to approximately 0.014Hz. The NIRS signals, including  $\Delta[\text{HbO}_2]$ ,  $\Delta[\text{HHb}]$ , TOI and THI, were detrended and lowpass filtered at 0.08 Hz as described above so that effects of other signal components were minimised. The filtered NIRS signals were then ensemble averaged over 8 cycles. The response to the stimulation was calculated as the difference between the average of 10 seconds worth of data just before the onset of the stimulation, and the average of 30 seconds worth of data 10 seconds after the onset of the stimulation. For the 10 subjects, the mean and standard deviation of responses of the NIRS signals over the two sites are summarised in Table 2. The t-test was conducted to assess the significance of the responses in the NIRS signals. Using a significant level of 0.03 as a threshold, Table 3 shows that there are no significant responses in any of the NIRS signals measured over the frontal cortex, whereas all of the NIRS signals measured over the motor cortex show significant responses to motor stimulation. Using a p value of 0.05, the  $\Delta[\text{HbO}_2]$  response at the frontal cortex just achieved significance. To see if this could be due to a change in central circulatory parameters, the heart rate signals were examined. Figure 2 depicts the grand averaged heart rate signal. In the 10 subjects, the heart rates show significant increases during activation (mean =  $4.1 \pm 3.1$  beats/min., t-test:  $p < 0.003$ ). Figure 3 shows the grand averaged responses of the NIRS signals measured over the two sites for all subjects. It should be noted that although the grand averaged TOI and THI measured over the motor cortex showed responses starting slightly earlier than the stimulation, this behaviour can only be found in 5 of the 10 subjects and is likely due to variations unrelated to the stimulations.

## 4. CONCLUSIONS

It has been found that TOI and THI measured by the SRS based technique may be affected by the location of probes which prompts the need to specify the measurement site when these quantities are to be compared. The relatively high correlation coefficient found between  $\Delta[\text{HbO}_2]$  signals over the frontal and motor cortexes may suggest a centrally mediated system playing a role in the production of the slow spontaneous oscillations around 0.1Hz. It can be seen that the heart rate increases during stimulation which may cause a systemic change in the brain<sup>5</sup>. The slight (but barely statistically significant) response in the NIRS signals measured over the frontal cortex may be due to this systemic change. SRS based measures such as TOI and THI were also shown to be able to detect evoked responses over the motor cortex during motor stimulation experiments. The availability of two simultaneous measurements, the relatively high sampling rate of 6 Hz and the absolute TOI measurements offered by the spectrometer will allow more detailed analyses of spontaneous and activation related changes in cerebral haemodynamics.

**Table 1** Mean and standard deviation of raw TOI and THI for 10 resting subjects (recording duration = 5 minutes)

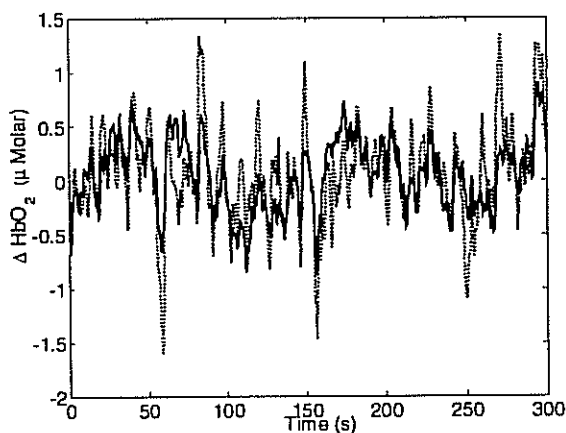
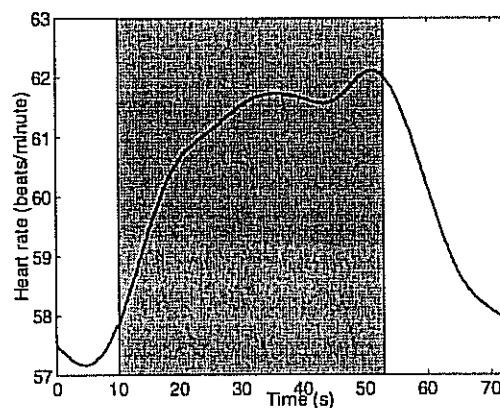
	TOI (%)		THI (a.u.)	
	(frontal)	(motor)	(frontal)	(motor)
Mean	68.49	59.25	37.65	91.27
S.D.	3.49	8.02	9.52	46.97

**Table 2** Responses of NIRS signals over the frontal and motor cortex during motor stimulation experiments (n=10)

	Over Frontal Cortex		Over Motor Cortex	
	Mean	S.D.	Mean	S.D.
$\Delta[\text{HbO}_2]$ ( $\mu$ molar)	0.112	0.177	0.571	0.289
$\Delta[\text{HHb}]$ ( $\mu$ molar)	-0.052	0.099	-0.228	0.182
TOI (%)	0.051	0.246	1.28	0.527
THI (a.u.)	0.052	0.218	0.628	0.438

**Table 3** Evoked responses found in NIRS signals measured over the motor cortex as determined by t-tests ( $H_0$ : response = 0,  $H_1$ : response > 0 (for  $\Delta[\text{HbO}_2]$ , TOI, THI) or  $H_1$ : response < 0 (for  $\Delta[\text{HHb}]$ )

	Over Frontal Cortex		Over Motor Cortex	
	p	Evoked response (p<0.03)	p	Evoked response (p<0.03)
$\Delta[\text{HbO}_2]$	0.04	×	<0.0001	√
$\Delta[\text{HHb}]$	0.07	×	0.0017	√
TOI	0.26	×	<0.0001	√
THI	0.24	×	<0.001	√

**Figure 1.** Filtered  $\Delta[\text{HbO}_2]$  signals measured over the frontal (solid line) and motor (dotted line) cortex.**Figure 2.** Grand averaged heart rate signal (n=10).

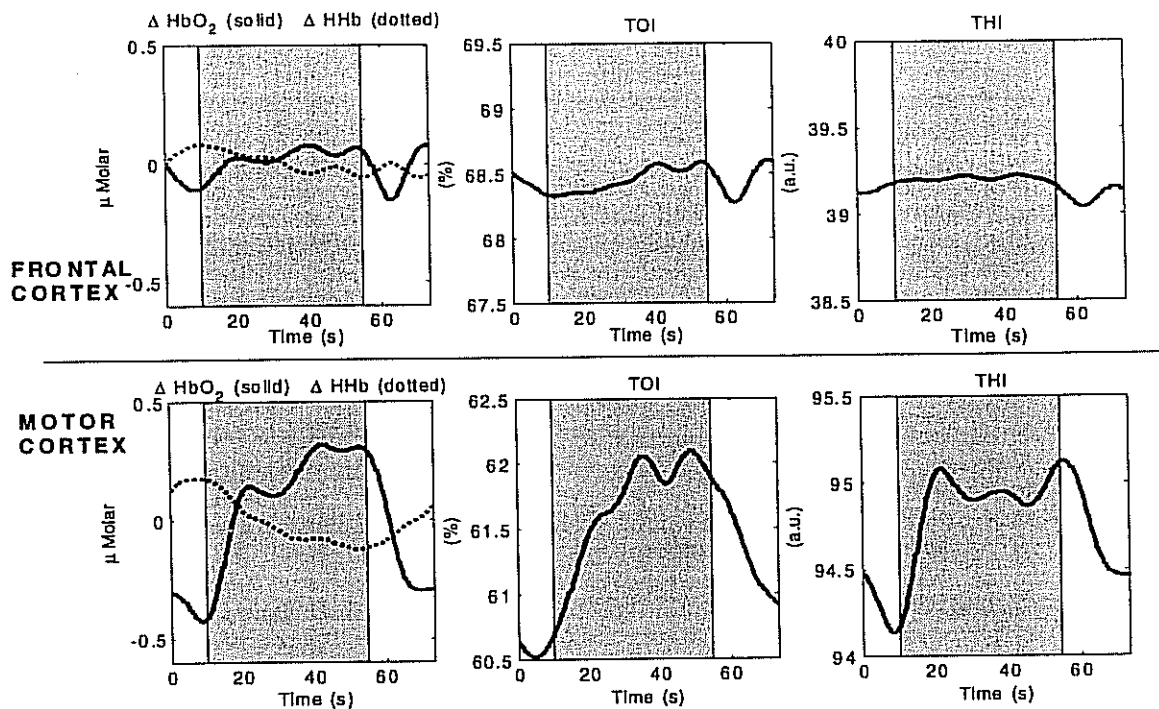


Figure 3. Grand averaged responses of NIRS signals in motor stimulation experiments (n=10).

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