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CEREBRAL TISSUE OXYGEN SATURATION CALCULATED USING LOW FREQUENCY HAEMOGLOBIN OSCILLATIONS MEASURED BY NEAR INFRARED SPECTROSCOPY IN ADULT VENTILATED PATIENTS

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Abstract: Oxy- (HbO₂) and deoxy- (HHb) haemoglobin signals measured by near infrared (NIR) spectroscopy over the human frontal lobes frequently contain respiratory and low frequency oscillations (LFOs). It has been suggested previously that venous oxygen saturation (S_vO₂) can be calculated from these respiratory oscillations. In this paper, we investigated the use of a Fourier transform based algorithm to calculate an oxygen saturation measure known as S_{osc}O₂ which may be a close estimate of the underlying S_vO₂. S_{osc}O₂ was calculated using three different frequency ranges, (1) respiratory oscillations only, (2) LFOs only, and (3) both respiratory oscillations and LFOs. At each frequency range S_{osc}O₂ was calculated using either 1) the modified Beer-Lambert law (MBL) or 2) spatially resolved spectroscopy (SRS). In total six different measurements of S_{osc}O₂ were investigated here. Experiments were performed in six adult ventilated patients with traumatic brain injury. The patients' inspired oxygen fraction (F_iO₂) was raised in two hyperoxic phases. The calculated S_{osc}O₂ values were compared with other cerebral oxygenation measures including an intraparenchymal catheter based brain tissue oxygen tension (PbrO₂) and the NIR based tissue oxygenation index (TOI). It was found that the S_{osc}O₂ calculated using the combined respiratory and LFO frequency range and the SRS method resulted in the highest detection rates of hyperoxic changes. This measure of S_{osc}O₂ may provide a viable, continuous, non invasive, bedside measure of cerebral venous oxygen saturation.

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1. INTRODUCTION

Measurements of cerebral S_vO_2 using non-invasive NIRS have previously been discussed in the literature. The central idea is to identify changes in blood volume which can be attributed to the venous compartment and then to calculate S_vO_2 based on the relative proportion of $\Delta[HbO_2]$ and $\Delta[HHb]$ within those changes. In adults and neonates, changes in venous blood volume can be initiated through head tilting¹ or jugular vein occlusion^{2,3}. They can also be associated with respiration⁴⁻⁶ which is one of the main focuses in this work. Respiration influences cardiovascular activities such as heart rate, stroke volume, arterial pressure, venous pressure and blood flow⁷. Strictly speaking, respiratory oscillations are associated with both arterial and venous blood volume changes. However, since the veins are much more compliant than the arteries⁸, it is expected that these oscillations occur predominantly within the venous compartment⁶. In this study, all patients were being ventilated using intermittent positive pressure, in which, inspiration generally causes an increase in intrathoracic pressure leading to a reduction of venous return and an increase in peripheral blood volume.⁵ The patients' ventilation rates were between 10 and 14 breaths/min (0.17 and 0.23 Hz).

Other types of oscillation often found in the cerebral haemodynamic signals ($\Delta[HbO_2]$ and $\Delta[HHb]$) in healthy humans occur at a frequency of around 0.1 Hz and are termed either vasomotion-waves or spontaneous low frequency oscillations⁹⁻¹². In this paper, we have adopted the term low frequency oscillations (LFOs). Similar oscillations can also be found in arterial blood pressure and heart rate^{13,14} and are known as Mayer-waves which are generally thought to be generated by baroreflex activity¹⁵.

In this paper we describe a cerebral oxygen saturation measure which utilises these respiratory and low frequency oscillations. We have termed this saturation, $S_{osc}O_2$ with the subscript "osc" indicating the oscillatory basis of the signals. The aim of this paper is to investigate whether $S_{osc}O_2$ can be used to measure cerebral S_vO_2 . We compare our $S_{osc}O_2$ value with other cerebral oxygenation measures such TOI and $PbrO_2$ during a hyperoxic study in six adult ventilated patients with traumatic brain injury. TOI is a mixed arterial and venous oxygen saturation measurement that is also dependent on the arterial to venous volume ratio (which in the brain is assumed to be 1:3). Another cerebral oxygenation measurement, which is invasive, and often used in the care of traumatic brain injury patients on the intensive care unit, is $PbrO_2$ which provides a local partial pressure of oxygen in the extra-cellular fluid of the brain tissue and reflects the availability of oxygen for aerobic metabolism. As such $PbrO_2$ can be thought of as reflecting the balance between oxygen delivery and consumption¹⁶.

2. METHODS

2.1 Experiments

The study was approved by the Joint Research Ethics Committee of the National Hospital for Neurology and Neurosurgery and the Institute of Neurology. We studied six adult ventilated patients with traumatic brain injury. An NIR monitor (NIRO300, Hamamatsu Photonics KK.) was used to measure $\Delta[HbO_2]$, $\Delta[HHb]$ and TOI in the less

injured frontal lobe. $PbrO_2$ was measured using a Licox PMO catheter inserted in the peri-contusional brain tissue. Arterial oxygen saturation (S_aO_2) was measured using a pulse oximeter (Novamatrix) placed on the finger. During the study, F_iO_2 was increased so that comparisons could be made between the baseline and two hyperoxic levels. We investigated which of the cerebral oxygenation measures, namely $S_{osc}O_2$, TOI and $PbrO_2$, could detect an increase (1) from baseline to hyperoxic phase 1, and (2) from hyperoxic phase 1 to 2. Baseline F_iO_2 was determined by the minimum level required to produce an arterial partial pressure of oxygen (p_aO_2) larger than or equal to 13 kPa. After 30 minutes of baseline, F_iO_2 was increased to 60% for 60 minutes (phase 1) and then 100% for 60 minutes (phase 2), before being returned to baseline for a further 30 minutes. If baseline F_iO_2 was larger than 60% then phase 1 was omitted.

2.2 Theory

An algorithm based on the Fourier transform of the data was used to estimate $S_{osc}O_2$:

$$S_{osc}O_2 = \frac{\sum_i \sqrt{P_{HbO_2}[i]}}{\sum_i \sqrt{P_{HbO_2}[i]} + \sum_i \sqrt{P_{HHb}[i]}} \times 100\% \quad (1)$$

where $P_{HbO_2}[i]$ and $P_{HHb}[i]$ are the power spectral densities (PSD) of the $\Delta[HbO_2]$ and $\Delta[HHb]$ signals, and the index i corresponds to different frequency ranges. Three frequency ranges have been used here, (1) the LFO range: from 0.018 to 0.1 Hz, (2) the ventilation/respiration range: a bandwidth of 0.02Hz around the ventilation/respiration frequency (different in each patient) and (3) the combined LFO and ventilation/respiration range: from 0.018 to 0.3 Hz.

The NIR spectrometer used in this work (NIRO300) is able to make measurements based on both the modified Beer Lambert law (MBL) and spatially resolved spectroscopy (SRS).¹⁷ The SRS measurements (i.e. $k[HbO_2]$ and $k[HHb]$ where k is a constant accounting for scattering) have previously been shown to be more sensitive to intracerebral changes than those based on MBL.¹⁸ Two versions of $S_{osc}O_2$ can thus be calculated, using either the MBL ($S_{osc}O_2^{MBL}$) or the SRS ($S_{osc}O_2^{SRS}$) in the three frequency ranges previously mentioned. The SRS version of $S_{osc}O_2$ was calculated simply by using $k[HbO_2]$ and $k[HHb]$ in calculating $P_{HbO_2}[i]$ and $P_{HHb}[i]$ in equation (1). In total six versions of $S_{osc}O_2$ were calculated for each set of data.

2.3 Data analysis

To implement equation (1), the $\Delta[HbO_2]/\Delta[HHb]$ (for MBL) or $k[HbO_2]/k[HHb]$ (for SRS) signals were first linearly detrended over 10 minutes. Their power spectral densities $P_{HbO_2}[i]$ and $P_{HHb}[i]$ were then estimated using the Welch spectral estimation method with a 1024 point Fast Fourier Transform, 50% overlap and a 1024 point Hanning windowing function. Subsequently, $S_{osc}O_2$ was calculated using equation (1). Each 10 minute block of data resulted in one value of $S_{osc}O_2$. Each calculation was then repeated on a block of data with the same length but shifted along by 1 minute. Altogether ten $S_{osc}O_2$ measurements were calculated for each phase (baseline, hyperoxic phase 1 and 2). For

hyperoxic phases 1 and 2, the initial 20 minutes of data after the increase of F_iO_2 were excluded to allow for stabilisation. The ten measurements from each patient were used to calculate the individual mean value in each phase. One averaged value of $PbrO_2$ and TOI was obtained per 10-minute block for each parameter and 10 values (separated by 1 minute) were calculated for each phase.

3. RESULTS

In the baseline phase, the mean value of F_iO_2 was measured at the mouth to be $32\pm 5\%$ (range: 24 to 39%). In the first hyperoxic phase, F_iO_2 was raised and the mean value was measured as $58\pm 1\%$ (range: 56 to 59%). In the second hyperoxic phase, F_iO_2 was raised further and the mean value was measured as $96\pm 3\%$ (range: 90 to 98%).

In this study, we found consistently strong LFOs at around 0.02 Hz in the $\Delta[HbO_2]$ and $\Delta[HHb]$ signals in all our patients with brain injury. The frequency was lower than those reported previously for healthy human subjects⁹.

Using spectral analysis, we often found high peaks in the LFO frequency range in the $\Delta[HbO_2]$ and $\Delta[HHb]$ amplitude spectra. The existence of a strong $\Delta[HHb]$ spectral peak is most interesting. It is expected that the LFOs in $\Delta[HbO_2]$ and $\Delta[HHb]$ are both due to blood volume and possibly flow changes in the arterial and venous sites. Arterial blood is highly oxygenated at around 98% which means that the amplitude of the $\Delta[HHb]$ LFOs should be very low in the arterial site. The strong LFOs found in $\Delta[HHb]$ are therefore most likely to arise from venous changes. Examples of the $\Delta[HbO_2]$ and $\Delta[HHb]$ signals and their amplitude spectra are shown in Figure 1.

The group mean and standard deviation of $S_{osc}O_2$, TOI and $PbrO_2$ for all the patients were calculated from the individual means (Table 1). Table 2 shows the number of patients whose $S_{osc}O_2$, TOI and $PbrO_2$ show statistically significant increases (1) from baseline to hyperoxic phase 1, and (2) from hyperoxic phases 1 to 2, based on the ten measurements in each phase. As mentioned earlier, there are six versions of $S_{osc}O_2$ in total each being calculated using the same method as described above.

Table 1: Group means and standard deviations of S_aO_2 , TOI and $S_{osc}O_2$ (6 versions) in the three phases of the hyperoxic experiments (n=6)

	S_aO_2 (%)	TOI (%)	$S_{osc}O_2^{MBL}$ (%)			$S_{osc}O_2^{SRS}$ (%)		
			LFO range	Resp. range	LFO & Resp. Range	LFO range	Resp. range	LFO & Resp. Range
Baseline	98±1	67±11	64±10	63±14	59±7	59±5%	58±7%	55±3%
Hyperoxic Phase 1	100±1	69±13	67±10	64±11	61±8	63±6%	59±7%	58±4%
Hyperoxic Phase 2	100±1	71±15	67±7	65±11	61±5	63±5%	62±8%	60±4%

LFO range: 0.018-0.1 Hz

Resp. range: Respiratory frequency with a bandwidth of 0.02 Hz

LFO & Resp. range: 0.018-0.3 Hz

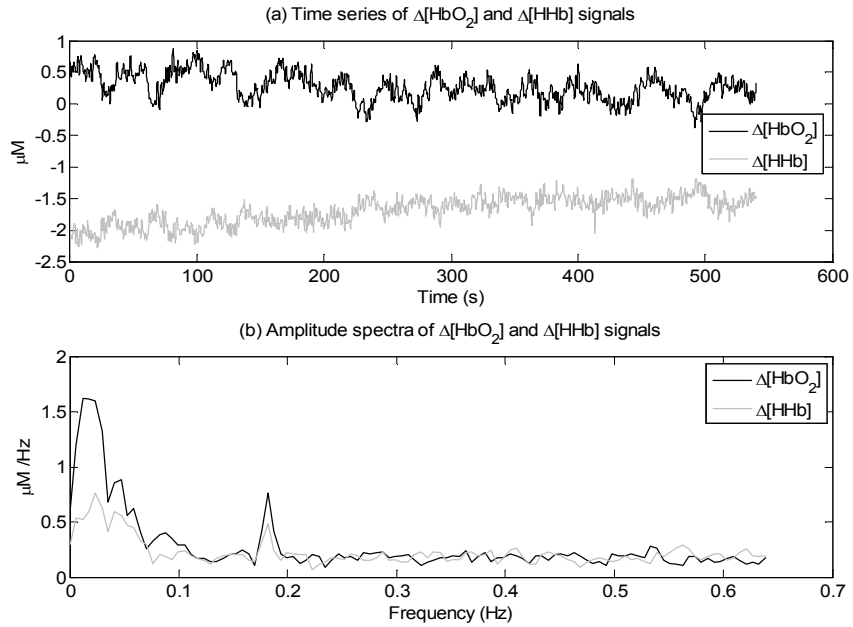


Figure 1: Time series and amplitude spectra of the $\Delta[\text{HbO}_2]$ and $\Delta[\text{Hb}]$ signals

Table 2: Number of patients (detection rate %) showing statistically significant increases (t-test, $p < 0.05$) over the previous phase (n=6)

	PbrO ₂	TOI	S _{osc} O ₂ ^{MBL}			S _{osc} O ₂ ^{SRS}		
			LFO range	Resp range	LFO & Resp. range	LFO range	Resp range	LFO & Resp. range
From Baseline to Hyperoxic Phase 1	6 (100%)	4 (67%)	6 (100%)	2 (33%)	5 (83%)	4 (67%)	2 (33%)	6 (100%)
From Hyperoxic Phase 1 to 2	6 (100%)	5 (83%)	2 (33%)	1 (17%)	3 (50%)	2 (33%)	3 (50%)	5 (83%)

LFO range: 0.018-0.1 Hz

Resp. range: Respiratory frequency with a bandwidth of 0.02 Hz

LFO & Resp. range: 0.018-0.3 Hz

4. DISCUSSION

The mean values of the six versions of $S_{osc}O_2$ were between 55 to 71% in the baseline phase. These values are comparable to S_vO_2 measured in a study in which the mean of the jugular venous saturation of normoxic subjects ($n=6$) was measured as 69%.¹⁹ All patients were in a stable condition when the studies were carried out and it is assumed that the cerebral metabolic rate of oxygen ($CMRO_2$) was constant during the experiment. In the first hyperoxic phase, S_aO_2 was increased from 98 to 100% and the underlying S_vO_2 was also expected to increase because of a stable metabolic rate. A small increase in dissolved oxygen in the plasma should also increase the underlying S_vO_2 . In the second hyperoxic phase, F_iO_2 was raised further. Although S_aO_2 was fully saturated at 100%, there should be a small increase in dissolved oxygen in the plasma and hence an increase in the underlying S_vO_2 . Therefore, any increase in $S_{osc}O_2$ during hyperoxic phase 1 to 2 is likely to represent this increase in S_vO_2 .

Table 2 shows that $PbrO_2$ increased in all patients during both hyperoxic phases, indicating an increased oxygenation at the tissue level. It is interesting to note however that other cerebral oxygenation measures such as TOI and $S_{osc}O_2$ do not always increase. As shown in Table 2, TOI increased from the baseline to hyperoxic phase 1 in only 4 out of 6 patients. This could be due to the fact that vasoconstriction occurred during hyperoxia which in turn lowered the arterial to venous volume ratio. While the underlying S_aO_2 and S_vO_2 may both slightly increase, the overall effect could be a lowered TOI. The same mechanism could also explain the fact that TOI increases from hyperoxic phase 1 to 2 in only 5 out of 6 patients.

The six versions of $S_{osc}O_2$ performed differently in the hyperoxic tests. Despite previously being used in both adults and neonates^{3,5}, $S_{osc}O_2$ based on the respiratory frequency range (both MBL and SRS versions) had low detection rates in the two hyperoxic phases as shown in Table 2. In fact, not all patients exhibit strong respiratory oscillations. In two patients, the spectral peaks at the respiratory frequency were very weak (just above the noise floor) in the $\Delta[HbO_2]/\Delta[HHb]$ (and $k\Delta[HbO_2]/k[HHb]$) PSDs.

By comparison, $S_{osc}O_2$ based on the LFO frequency range has higher detection rates (both MBL and SRS versions) in the two hyperoxic phases. This could be due to the fact that there are consistently higher spectral peaks in the LFO range in the $\Delta[HbO_2]/\Delta[HHb]$ and $k\Delta[HbO_2]/k[HHb]$ PSDs for all the patients and all phases.

Relatively high detection rates in the two hyperoxic phases were achieved by $S_{osc}O_2$ based on the combined respiratory and LFO range. In particular, those using SRS have the highest detection rates (100% for hyperoxic phase 1 and 83% for phase 2) compared with TOI and other versions of $S_{osc}O_2$. This may be explained by the fact that SRS measurements have been shown to have a higher sensitivity to intracerebral changes¹⁸. It is possible that $S_{osc}O_2$ is dominated by the venous blood and is thus less susceptible to changes in the arterial to venous volume ratio.

In this preliminary analysis, we have taken the empirical approach that $S_{osc}O_2$ can be calculated using equation (1). The use of this equation however has not been fully justified in this paper, especially for the LFOs. Previous studies⁵⁻⁶ have shown that this equation is only valid when the $\Delta[HbO_2]$ and $\Delta[HHb]$ oscillations (both respiratory and LFO) are caused by blood volume change alone. As shown in Figure 1, the $\Delta[HbO_2]$ and $\Delta[HHb]$ LFOs are sometimes out of phase, suggesting that a blood flow change may also

have occurred, violating this assumption. However we found that the $S_{\text{osc}}\text{O}_2$ values obtained in our studies consistently fall within the expected range of venous saturation values. We are currently working on a theoretical model to explain the behaviour of the $\Delta[\text{HbO}_2]$ and $\Delta[\text{HHb}]$ LFO signals which may in turn improve the calculation of $S_{\text{osc}}\text{O}_2$ as an estimate of the underlying $S_v\text{O}_2$.

5. ACKNOWLEDGMENTS

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