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The effect of scalp ischaemia on measurement of cerebral blood volume by near-infrared spectroscopy

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Abstract. Near-infrared spectroscopy (NIRS) is a noninvasive method of quantifying changes in cerebral haemodynamics from changes in the absorption of near-infrared light by oxyhaemoglobin and deoxyhaemoglobin. Measurement of neonatal cerebral blood volume (CBV) by NIRS was described in 1990 but it has been suggested that, in adults, scalp and skull blood content contribute a significant amount to the cerebral haemodynamic variables quantifiable by NIRS.

To investigate this, CBV was measured in nine adult subjects, in the frontal region of the head, before and after inflating a pneumatic tourniquet proximal to the measurement site. Because a change in scalp blood content could potentially alter the pathlength of light passing through the head and hence affect the measured CBV, the optical pathlength factor was therefore also measured before and after tourniquet inflation. Blood flow occlusion was confirmed by laser Doppler velocimetry. The results showed that tourniquet inflation had no effect on the estimated value of CBV or the differential pathlength factor.

We conclude that, provided the distance between light entry and exit on the surface of the scalp is sufficiently large, changes in scalp blood flow have no effect on NIRS measurement of cerebral haemodynamics.

Keywords: cerebral blood volume, near-infrared spectroscopy

1. Introduction

Near-infrared spectroscopy (NIRS) is a recently developed optical technique which has the potential to provide noninvasive assessment of cerebral haemodynamics and oxygenation at the bedside (Elwell *et al* 1993). Tissue is comparatively transparent to light in the near-infrared part of the spectrum and with recent advances in light detection systems tissue thicknesses of up to 8 cm can be transilluminated (Cope and Delpy 1988). The principles of near infrared spectroscopy were first described in 1977 (Jöbsis 1977) and subsequently developed by a number of groups (Ferrari *et al* 1986, Wickramasinghe *et al* 1990, Owen-Reece *et al* 1996). The results of preliminary studies in adults (Hampson *et al* 1990, Harris and Bailey 1993, Elwell *et al* 1994) and newborn babies (Edwards *et al* 1988, Wyatt *et al* 1990) have been published.

The possibility remains that scalp blood content causes significant contamination of the NIRS signals by its absorption and, to some extent, its scattering properties. The effect of

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scalp blood content on the measurement of regional cerebral oxygen saturation in adults has recently been examined using a related, but different, optical technique (Germon *et al* 1994). The aim of this study was to investigate the effect of temporary interruption of scalp blood flow on another derived variable, cerebral blood volume (CBV) in adult volunteers, and to examine a potential artefact in CBV measurement due to a change in optical pathlength in the head.

2. Methods

13 adult volunteers (ten males and three females) between the ages of 24 and 44 were recruited for study and informed written consent was obtained from each subject. With the subject in a recumbent position, an inflatable tourniquet 4 cm wide was placed around the head just above the ears and connected to an aneroid sphygmomanometer. Soft pads were placed between the tourniquet and the superficial temporal arteries in both temporal fossae in order to ensure complete occlusion of the arteries when the cuff was inflated. In each subject, at the beginning of the experiment, the cuff was inflated manually to a pressure such that the pulse at both the superficial temporal arteries disappeared to palpation, and the pressure was noted. Four of the subjects were excluded from further study because the temporal pulses did not completely disappear despite maximal inflation of the tourniquet.

In the remaining nine subjects the ends of fibre optic bundles (optodes) were positioned on the left side of the forehead in the frontal region with one optode placed close to the midline and one approximately 5 cm (3.5–6.5 cm) lateral (avoiding the temporal region). They were always spaced as far apart as was compatible with adequate light detection by the equipment. The optodes were positioned high up on the forehead, as close as possible to the hairline. They were held in place using double-sided adhesive rings (EME Ltd, UK) and a flexible bandage ('Coban', 3M Ltd, USA). The distance between the optodes was carefully measured using a tape measure and an opaque cloth was wrapped gently round the head to prevent extraneous light from reaching the optodes.

The fibre optic bundles were connected to a NIRS spectrophotometer (NIRO 1000 or 500, Hamamatsu Photonics, Japan). Near-infrared light at four (NIRO 500) or six (NIRO 1000) different wavelengths between 779 and 907 nm was conveyed to the head via one of the fibre optic bundles. The light which had been transmitted through the head was collected at the receiving optode and conveyed back to the spectrophotometer by the other optical fibre bundle. Changes in the optical attenuation at each wavelength were measured continuously and converted into changes in the concentrations (in micromoles per litre) of cerebral oxyhaemoglobin [HbO_2] and deoxyhaemoglobin [Hb] using an algorithm which has been described previously (Wray *et al* 1988, Cope *et al* 1991). Their sum [HbT] was taken as the total haemoglobin concentration; the only other form of haemoglobin commonly found in significant quantities in healthy caucasian adults is carboxyhaemoglobin, which has negligible absorption in the near infrared. The NIRS data were displayed instantaneously and recorded on computer disk for later analysis.

A transcutaneous P_{CO_2} electrode (Novametrix 850, Novametrix Ltd, USA) was applied to the inner surface of the arm to monitor changes in arterial carbon dioxide tension and arterial oxygen saturation (Sa_{O_2}) was measured using a pulse oximeter (Nellcor N200E, Nellcor, USA) modified for beat to beat measurement, with the oximeter probe applied to one earlobe.

A breathing circuit was set up using a modified anaesthetic machine in order to provide a variable mixture of oxygen and nitrogen. The subject breathed the gas mixture through

a mouthpiece and a clip was applied to the nose. The inspired oxygen concentration was monitored continuously using an in-line oxygen analyser. This study was approved by the UCL Hospitals Committee on the Ethics of Human Research.

2.1. Measurement of CBV

CBV was measured by observing the effects on [HbO_2] and [Hb] of a gradual change in Sa_{O_2} of approximately 5% within the range 90–98%, induced by slowly altering the inspired oxygen concentration over a period of about 5 min. This method has been previously described in newborn infants (Wyatt *et al* 1990) using oxyhaemoglobin as an intravascular tracer molecule.

The CBV was calculated using the formula

$$[\mathrm{HbT}] \times \Delta \mathrm{fSa}_{\mathrm{O}_2} = \Delta[\mathrm{HbO}_2].$$

Rearranging,

$$[\mathrm{HbT}] = \Delta[\mathrm{HbO}_2]/\Delta \mathrm{fSa}_{\mathrm{O}_2}$$

where $\Delta \mathrm{fSa}_{\mathrm{O}_2}$ represents the change in fractional arterial oxygen saturation and $\Delta[\mathrm{HbO}_2]$ the change in oxyhaemoglobin concentration measured by NIRS.

CBV (mL/100 g) can be calculated from HbT (μmol) once the subject's blood haemoglobin concentration, the molecular mass of haemoglobin and cerebral tissue density are taken into account.

Four measurements were made in each subject and the mean was calculated.

2.2. Measurement of differential pathlength factor (DPF)

DPF was measured on a subsequent occasion in nine of the subjects by a time of flight method in which the time taken for a pulse of infrared laser light to cross the head is used to calculate the distance travelled. We have described the technique, using a pulsed laser and streak camera, in more detail elsewhere (Delpy *et al* 1988). The mean DPF was calculated using the equation

$$\mathrm{DPF} = c\langle t \rangle / nd$$

where c is the velocity of light in a vacuum, $\langle t \rangle$ is the measured mean time of flight, n the refractive index of tissue and d the geometric spacing between the optodes.

2.3. Sequence of measurements

Measurements of CBV were obtained as described above, with the tourniquet fully deflated. The tourniquet was then inflated to a pressure 30 mm Hg greater than the pressure at which the temporal arterial pulsation had disappeared. Repeat measurements of CBV were obtained with the tourniquet inflated. Finally the cuff was deflated. The total duration of ischaemia was approximately 25–35 minutes. A sample of blood was removed by venesection for estimation of the blood haemoglobin concentration. For the DPF measurements the tourniquet was set up as described above and the optodes of the time of flight equipment attached in positions as similar as possible to those used in the previous study. Light of 800 nm wavelength was used. Five measurements of the time of flight were made before and five after inflation of the tourniquet.

In seven of the subjects a second experiment was performed to test the effectiveness of the tourniquet using laser Doppler velocimetry. The tourniquet was positioned exactly as

in the first studies and the laser Doppler probe (Moore Instruments Ltd, UK) was placed in turn at the two sites on the scalp where the transmitting and receiving optodes had been previously positioned. The probe was secured with a self-adhesive ring. At each site the blood flow in flux units was measured for 1 min before the cuff was inflated and for a further minute following inflation of the cuff to the same pressure as in the first experiment. The cuff was then deflated. Scalp perfusion was allowed to stabilize and the laser Doppler probe was then moved to the other optode site on the forehead. The measurement procedure was repeated.

Measurements were compared using a Wilcoxon rank sum test test. The subjects acted as their own controls.

3. Results

The values for CBV in each subject before and after inflation of the tourniquet are given in table 1. Median CBV (with interquartile range) for all nine subjects was 2.3 (2.1–2.7) mL/100 g before and 2.5 (2.1–2.8) mL/100 g after inflation of the tourniquet ($p > 0.05$, Wilcoxon rank sum test). The values for scalp blood flux are shown in table 2. The median value for scalp blood flux was 29 (13–31.5) flux units before cuff inflation and 12 (4.5–17.5) afterwards. The individual values for DPF are displayed in table 3. DPF measured before tourniquet inflation had a median value of 6.8 (6.4–6.9), and afterwards 6.7 (6.4–6.9).

Table 1. Changes in CBV before and during scalp blood flow occlusion.

Subject	Interoptode spacing (cm)	CBV (ml/100 g) before occlusion (SD)	CBV (ml/100 g) after occlusion (SD)
1	4.8	2.1 (0.4)	2.8 (0.2)
2	5.0	2.3 (0.7)	1.7 (0.2)
3	4.5	2.7 (0.3)	2.2 (1.3)
4	4.0	2.0 (0.0)	2.1 (0.3)
5	4.8	2.7 (0.3)	2.9 (0.3)
6	5.3	2.2 (0.3)	2.8 (0.2)
7	6.5	1.8 (0.5)	1.4 (0.4)
8	4.2	2.6 (0.2)	2.5 (0.5)
9	3.5	3.0 (0.4)	2.6 (0.5)
Median (interquartile range)	4.8 (4.2–5.0)	2.3 (2.1–2.7)	2.5 (2.1–2.8)

4. Discussion

We have shown that occlusion of scalp perfusion using an inflatable tourniquet caused no significant change in CBV measured by NIRS in adult volunteers, despite a significant fall in scalp blood flow measured by laser Doppler velocimetry.

The blood supply of the scalp comprises the supratrochlear and supraorbital, superficial temporal, posterior auricular and occipital arteries which can all be occluded with a tourniquet positioned as we have described. The effectiveness of the scalp tourniquet in our study was confirmed by the significant reduction in scalp perfusion measured by laser Doppler velocimetry. One of the seven subjects displayed no fall in scalp blood flux after tourniquet inflation despite these precautions but owing to the prospective design of the study the values for this subject were included in the overall mean. By isolating this pool

Table 2. Skin blood flux before and during blood flow occlusion.

Subject	Skin blood flow before occlusion (arbitrary flux units)	Skin blood flow during occlusion (arbitrary flux units)
1	30	12
2	13	4
3	13	5
4	12	4
5	29	15
6	33	20
7	55	50
Median (interquartile range)	29 (13–31.5)	12 (4.5–17.5)

Table 3. Pathlength factor before and during fast and slow cuff inflation.

Subject	Pathlength factor before flow occlusion	Pathlength factor fast flow occlusion	Pathlength factor slow flow occlusion
1	6.9	6.7	6.6
2	6.9	7.0	6.9
3	6.0	6.1	6.0
4	6.9	6.9	7.0
5	6.7	6.7	6.7
6	6.8	6.9	6.9
7	6.5	6.4	6.4
8	6.1	6.2	6.2
Median (interquartile range)	6.8 (6.4–6.9)	6.7 (6.4–6.9)	6.7 (6.4–6.9)

of blood in the scalp it is unable to take part in the reversible desaturation manoeuvre by which CBV is determined and therefore cannot contaminate the CBV estimation in this way. It would still be theoretically be possible for this blood to exert an influence on DPF by its scattering effect and we intended to detect this by measuring the DPF before and after scalp blood flow occlusion.

Our results are the opposite of those published by Germon *et al* (1994) who have recently shown (using near-infrared equipment operating on different principles) that occlusion of scalp blood flow significantly reduced regional cerebral oxygen saturation (rS_{O_2}) as displayed by their equipment (INVOS 3100, Somanetics, USA). Their study did demonstrate, however, that once scalp ischaemia was established rS_{O_2} varied with systemic arterial saturation. This contrasts with our data which were *not* affected by extracerebral changes in the form of a fall in scalp blood flow.

This discrepancy could be at least partly explained by the greater mean interoptode distance in our study. In general, as the optodes become closer together the relative contribution to the NIRS signals from extracerebral tissues is likely to increase. There is evidence suggesting that at a spacing of 2.5 cm or less the scalp and skull comprise a greater proportion of the interrogated field and that therefore their blood content will have a greater influence on measured CBV (or cerebral blood flow (CBF)) (van der Zee *et al* 1992). In our studies the optodes were positioned at a mean distance of 4.7 cm apart (SD = 0.9 cm). The equipment used in the study of Germon *et al* has two detectors spaced respectively 3 and 4 cm from the transmitter and this smaller average spacing may have

contributed to the greater influence of the extracerebral tissues on rS_{O_2} in their study than in ours.

It should be stressed here that the NIRS instrumentation used in our studies operates in a different manner from that employed by Germon *et al*, which measures regional cerebral oxygen saturation and which has also been in use for some years (McCormick *et al* 1991). The relative changes in haemoglobin concentration are not fully quantified by such equipment but are converted to a ratio or percentage saturation. This contrasts with the alternative approach, employed in our study, of incorporating the differential pathlength factor (DPF) and thereby quantitating haemoglobin changes in micromolar units. Furthermore, the geometric positioning of the source and detector in that system together with the different mathematical processing of the data to derive an estimate of haemoglobin saturation may lead to a different sensitivity to surface tissue haemoglobin signals than for the systems used in the study reported here.

Our results imply that errors due to absorption of light by blood in the extracerebral tissues are not of great importance provided that there is sufficient distance between the optodes. A much more significant source of error is likely to be the scattering of light by scalp and skull as it passes through them. This powerful scattering of light is an attribute of all biological tissue and, together with absorption, attenuates the light that emerges. This fixed scattering factor gives rise to the large increase in optical pathlength over the geometric distance between the optodes and hence the need to take the DPF into account when calculating CBV.

Recent work using mathematical modelling of light transport in the head (Hiraoka *et al* 1993) suggests that only 30–50% of the transilluminated tissue volume comprises brain, which is well perfused, the remainder consisting mainly of scalp, skull and meninges which are relatively devoid of blood (Friberg *et al* 1986). The total DPF takes no account of the interrogated region actually being partitioned into a cerebral and an extracerebral compartment, both of which scatter light equally strongly. The use of a total DPF means that the calculated blood volume of the cerebral compartment is then unavoidably attributed to the entire tissue volume. It follows that any quantification of CBV (or CBF) in the adult head using this DPF value will be only 30–50% of the expected value. We have published data supporting this hypothesis by measuring CBF on the scalp and then on the dura (in the same seven subjects) during neurosurgery. Before surgery CBF had a mean value of 23 mL/100 g min^{-1} whereas on the dura the value was 67 mL/100 g min^{-1} (Owen-Reece *et al* 1996). The modelling work mentioned previously has also shown that in the preterm infant head (where the skull and overlying tissues are very thin) the penetration of light into the cerebral tissue is greater. Although a direct extrapolation is not possible, this result is further supported by the good correlation between values for CBF measured simultaneously by NIRS and ^{133}xenon washout (Skov *et al* 1991) in neonates.

The NIRS method has not been directly compared with alternatives for quantifying CBV since this variable is difficult to measure (although it can be estimated by positron emission tomography (PET)). This gives a value for adult CBV of approximately 2.7 mL/100 g for white matter and 5.2 mL/100 g for insular grey matter (Leenders *et al* 1990). It can be seen that the results obtained in our NIRS study are significantly lower than this value, again supporting our hypothesis. Despite the absence to date of a direct comparison between CBV measurement by NIRS and by any other established method, we have several pieces of evidence that this is a useful variable to measure. The method described has theoretical validity, and in neonates the similarity between the values for CBV measured by NIRS and by PET lends further support (Altman *et al* 1993). In this study, CBV by NIRS has a low value as expected on the basis of the work described above. It will probably be possible in

future to account accurately for the contribution of extracerebral and cerebral compartments to the total light path and hence to improve the accuracy of the method.

For the reasons summarized above, the DPF is an essential part of the quantification of CBV by NIRS. Since blood itself scatters light as well as absorbing it, we wished to consider the possibility that a change of DPF might occur during scalp blood flow occlusion. A slow cuff inflation owould theoretically allow blood to accumulate in the scalp to a greater extent than a fast one and so we examined the effects of fast and slow cuff inflation on scattering by its effects on DPF. There was no significant effect under the conditions which we have quoted.

5. Conclusion

We conclude that, provided the distance between the points of light entry and exit on the surface of the head is large enough, changes in scalp blood flow have no effect on measurement of CBV by NIRS. Alteration of scalp blood flow has no effect on the measured DPF.

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