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Correlation between Cerebral Oxygen Saturation Measured by Near-infrared Spectroscopy and Jugular Oxygen Saturation in Patients with Severe Closed Head Injury

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Background: **Near-infrared spectroscopy has been used to monitor cerebral oxygen saturation during cerebral circulatory arrest and carotid clamping. However, its utility has not been demonstrated in more complex situations, such as in patients with head injuries. The authors tested this method during conditions that may alter the arteriovenous partition of cerebral blood in different ways.**

Methods: **The authors compared changes in measured cerebral oxygen saturation and other hemodynamic parameters, including jugular venous oxygen saturation, in nine patients with severe closed head injury during manipulation of arterial carbon dioxide partial pressure and after mean arterial pressure was altered by vasopressors.**

Results: **The Bland and Altman representation of cerebral oxygen saturation *versus* jugular oxygen saturation showed a uniform scatter. Values for changing arterial carbon dioxide partial pressure were: bias = 1.1%, 2 SD = ±21%, absolute value; and those for alterations in mean arterial pressure: bias = 3.7%, 2 SD = ±24%, absolute value. However, a Bland and Altman plot of *changes* in cerebral oxygen saturation *versus* changes in jugular oxygen saturation had a negative slope (alteration in arterial carbon dioxide partial pressure: bias = 2.4%, 2 SD = ±17%, absolute value; alteration in mean arterial pressure: bias = −4.9%, 2 SD = ±31%, absolute value). Regression analysis showed that changes in cerebral oxygen saturation were positively correlated with changes in jugular venous oxygen saturation during the carbon dioxide challenge, whereas correlation was negative during the arterial pressure challenge.**

Conclusions: **Cerebral oxygen saturation assessed by near-infrared spectroscopy does not adequately reflect changes in jugular venous oxygen saturation in patients with severe head injury. Changes in arteriovenous partitioning, infrared-spectroscopy contamination by extracerebral signal, algorithm errors, and dissimilar tissue sampling may explain these findings. (Key words: Brain; hemodynamics; spectroscopy; transcranial Doppler.)**

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NEAR-INFRARED spectroscopy (NIRS) is a method for continuous, noninvasive monitoring of cerebral oxygen saturation (Sc_{O_2}). Its accuracy depends on distinguishing the signal reflected by the brain from that reflected by other tissues (skin, muscle, bone).[1,2] Several studies have shown that when used in normal human subjects, NIRS responds rapidly to cerebral oxygen desaturation during marked cerebral hypoperfusion or systemic hypoxia.[3–5] However, because severe hypotension (*e.g.*, circulatory arrest) influences both cerebral and extracerebral compartments, such studies do not validate the technique or at least do not prove its value in more complex situations. For example, NIRS detects only a fraction of the pathologic events identified by parallel multimodal monitoring in human head injury.[6] Moreover, when NIRS is used in an intensive care setting, changes in cerebral blood flow (CBF) or vascular

tone may modify the arteriovenous (AV) distribution of blood in the brain differently from the distribution in scalp and in other extracerebral tissues. All of these phenomena may considerably distort ScO_2. The present study therefore examines the relations between NIRS ScO_2 and jugular venous oxygen saturation (Svj_{O_2}) during changes in arterial carbon dioxide partial pressure (Pa_{CO_2}) and blood pressure in adults with head trauma. Our working hypothesis was that these tests produced different effects on CBF and AV partition, thus identifying some of the limitations of NIRS in clinical use.

Materials and Methods

Materials

This study was approved by the ethics committee of the hôpital H. Mondor, Créteil, France, and informed consent was obtained from patients' next of kin. Nine patients with severe closed head injury (Glasgow Coma Scale < 8) and with multifocal contusions or diffuse brain swelling confirmed by computed tomography scan were studied within the first 10 days after injury. Patients with bilateral frontal contusions were not included. In order to be able to measure all signals on the same side, patients who had focal contusions on the side of the dominant jugular vein were also excluded. All patients were placed in the supine position with the head and thorax tilted upward at 30°. They were sedated with midazolam and fentanyl and were ventilated mechanically to achieve 100% arterial oxygen saturation (Sa_{O_2}) and moderate hypocapnia (Pa_{CO_2} 30–35 mmHg). Patients who had a mean arterial pressure (MAP) < 70 mmHg were given a norepinephrine infusion to maintain arterial pressure above this threshold before the start of the study. All patients had normal core temperature and blood hemoglobin level > 10 g/100 ml.

A retrograde jugular catheter (Opticath 5.5 French; Abbott, Rungis, France) was placed on the side corresponding to the dominant jugular vein, as assessed by intracranial pressure (ICP) increase during a compression test.[7] The position of the catheter in the jugular bulb was confirmed by radiograph. Sc_{O_2} was recorded by NIRS (Invos 3100; Somanetics, Troy, MI). This system used two wavelengths: 730 and 810 nm. The sensor contained a near-infrared light-emitting diode, and two light detectors located 30 and 40 mm from the light-emitting diode, to distinguish between the cerebral and extracerebral signals and thus monitor the Sc_{O_2} in the underlying area of the brain. The sensor was placed on the upper forehead, on healthy skin, 4–5 cm from the midline, ipsilateral to the jugular catheter. Background light was excluded by an opaque cap. The blood flow velocity in the middle cerebral artery (MCAv) was recorded unilaterally by pulsed Doppler ultrasound (Angiodyne; DMS, Montpellier, France), which was placed on the same side as the NIRS probe. The jugular catheter was always ipsilateral to both Sc_{O_2} and Doppler probes.

The following parameters were recorded at 200 Hz (Labview 4.0; National Instrument, Austin, TX) and averaged every 4 sec: ICP (ventricular catheter), MAP (radial catheter), end-tidal CO_2 ($P_{ET_{CO_2}}$; Merlin, Hewlett Packard, Les Ulis, France), MCAv, and Sc_{O_2}. All signals were stored for off-line analysis. Svj_{O_2} was determined by sampling blood *via* the jugular catheter.

CO_2 Challenges

Jugular blood samples were taken and Sc_{O_2} was simultaneously recorded at three levels of $P_{ET_{CO_2}}$: (1) during moderate hyperventilation (Pa_{CO_2}: 30–35 mmHg, T_0); (2) during intense hyperventilation (Pa_{CO_2}): 20–25 mmHg, T_1); and (3) during a short period of moderate hypercapnia induced by CO_2 inhalation (T_2). CO_2 inhalation was achieved by connecting the air inlet of the ventilator to a chamber (AGA, Toulouse, France) containing 5% CO_2 in 95% O_2. The inspiratory CO_2 could thus be changed by altering the setting on the ventilator for fraction of inspired oxygen without altering the rate of ventilation or the tidal volume. Svj_{O_2} was not allowed to decrease to $< 50\%$ during hyperventilation, and ICP was not allowed to increase to > 35 mmHg during CO_2 inhalation. To standardize the procedure, the order of changes in Pa_{CO_2} was the same in all patients.

Jugular blood samples were taken in the basal state (T_0), during hypocapnia (T_1), and during hypercapnia (T_2). Steady state was maintained for at least 2 min (range, 2–10 min) at T_0 and T_1. The rapid increase in ICP at T_2 made it impossible to reach steady state. All patients underwent two or three CO_2 challenges, with an interval of at least 24 h between each.

An equivalent of cerebral vascular resistance (Eq_{CVRI}) was estimated from the ratio of cerebral perfusion pressure (CPP) to MCAv as proposed by Aaslid *et al.*[8] Changes in each variable studied during CO_2 challenge corresponded to the difference between the reading after the test minus that measured before the test.

Changes in Systemic Arterial Pressure

A formal test of the response to change in arterial pressure was performed once in each patient and was started after 20 min of steady state after the end of the

first CO_2 challenge. Therefore, the systemic arterial pressure was pharmacologically modified under the same level of moderate hypocapnia as that achieved at T_0. This was performed once in each patient by starting or increasing the rate of norepinephrine infusion (n = 4) or by discontinuing or reducing in the rate of norepinephrine perfusion (n = 5). Increasing or starting norepinephrine was used in patients whose MAP corresponded to values close to the lower limit of the autoregulatory plateau. Conversely, we stopped or reduced norepinephrine infusion in patients whose MAP was close to the upper limit of the autoregulatory plateau. In all patients, ICP was continuously monitored, and norepinephrine infusion was stopped or restarted (as appropriate) if ICP reached 35 mmHg. We also continuously monitored Svj_{O_2} *via* the fiberoptic catheter to ensure that it did not decrease to < 50% during the test. Arterial and jugular blood samples were taken when a stable condition was achieved after a step change in norepinephrine.

Statistical Analysis

Results are expressed as means ± SD. Differences between the means of the parameters determined during the CO_2 challenge, at T_0, T_1, and T_2 were compared by two-way analysis of variance for repeated measurements. The Bland and Altman test[9] was used to compare the absolute values of Sc_{O_2} and Svj_{O_2} obtained from jugular blood samples. This test was also applied to changes in Sc_{O_2} (δSc_{O_2}) and changes in Svj_{O_2} (δSc_{O_2}). The relative δSc_{O_2} for T_0–T_1 and T_0–T_2, were compared with the corresponding δSvj_{O_2} by linear regression. Data of the pressure test were analyzed in the same way as for the CO_2 challenge.

Results

Carbon Dioxide and Arterial Pressure Challenges

The data (means ± SD) obtained during CO_2 challenge and during changes in MAP are shown in tables 1 and 2. Data of Sc_{O_2} and Svj_{O_2} were plotted according to Bland and Altman.[9] We saw a similar scatter of error for both tests (fig. 1): the mean of individual differences ($Sc_{O_2} - Svj_{O_2}$) for CO_2 and arterial pressure challenges were 1.1 and 3.7. Two SDs of these individual differences amounted to ±21% (absolute value) and ±24% (absolute value) for the CO_2 and arterial pressure challenges, respectively. Individual differences between δSc_{O_2} and δSvj_{O_2} are shown in figure 2. There was an apparent systematic decrease of individual differences between δSc_{O_2} and δSvj_{O_2} when (δSc_{O_2} + δSvj_{O_2})/2 increased. This seems to reflect a bias that is not randomly distributed.

Table 1. Values of all Variables during CO_2 Challenge (n = 9)

	T_0	T_1	T_2
Pa_{CO_2} (mmHg)	34 ± 7	26 ± 5†	43 ± 9*
MAP (mmHg)	90 ± 23	88 ± 26	87 ± 19
ICP (mmHg)	15 ± 6	10 ± 5†	29 ± 8*
CPP (mmHg)	74 ± 25	78 ± 28†	58 ± 20*
MCAv (cm/s)	69 ± 25	50 ± 22†	79 ± 27*
Sc_{O_2} (%)	74 ± 13	69 ± 12†	76 ± 13‡
Svj_{O_2} (%)	75 ± 13	61 ± 10†	80 ± 12*
Eq_{CVRI} (mmHg · cm^{-1} · s)	1.16 ± 0.44	1.77 ± 0.88†	0.77 ± 0.23*

Values are mean ± SD. Differences between means with $P < 0.05$ are considered to be statistically significant.

MAP = mean arterial pressure; ICP = intracranial pressure; CPP = cerebral perfusion pressure; MCAV = blood flow velocity in the middle cerebral artery; Sc_{O_2} = O_2 saturation in the brain; Svj_{O_2} = jugular venous saturation; Eq_{CVRI} = equivalent of cerebral vascular resistance.

* Significantly different from T_0 and T_1.

† Significantly different from T_0 and T_2.

‡ Significantly different from Svj_{O_2} at T_2.

To better understand this effect we performed a linear correlation between δSc_{O_2} and δSvj_{O_2} for both tests (fig. 3). The slopes were both significantly different from unity ($P < 0.05$, with an SE of the slope = 0.033 and 0.11 for the CO_2 and the pressure challenge, respectively). They were positive in the CO_2 challenge but negative in the arterial pressure challenge. Hence, regression shows, in addition to the Bland and Altman analysis, that both tests were not only different in terms of the magnitude of the response but the relationship between δSc_{O_2} and δSvj_{O_2} during CO_2 and pressure were opposite.

Discussion

The main finding of our study is that Sc_{O_2} assessed by NIRS does not adequately reflect changes in Svj_{O_2} in patients with severe head injury. Unlike "conventional" hypoxic challenges, we chose to examine effects that could result in changes in the AV partition of cerebral blood volume in a possible contamination by extracerebral signals, and by different tissue fields being monitored. Patients with head injuries were studied rather than normal volunteers. This setting introduced more complexity because any regional difference in cerebral perfusion regimen could increase the discrepancy between Svj_{O_2} and Sc_{O_2}.

Table 2. Variables during Changes in MAP

	Decreasing MAP (n = 5)		Increasing MAP (n = 4)	
	Baseline	Low MAP	Baseline	High MAP
MAP (mmHg)	101 ± 33	65 ± 13*	74 ± 9	121 ± 22*
ICP (mmHg)	15 ± 10	12 ± 7	15 ± 4	13 ± 4
CPP (mmHg)	87 ± 39	53 ± 14*	59 ± 5	108 ± 25*
MCAv (cm/s)	75 ± 28	56 ± 24*	55 ± 9	67 ± 8
Sc_{O_2} (%)	81 ± 14	79 ± 16	69 ± 12	61 ± 8*†
Svj_{O_2} (%)	86 ± 4	77 ± 7*	66 ± 9	78 ± 12*
Pa_{CO_2} (mmHg)	37 ± 3	35 ± 3	35 ± 4	36 ± 4
Eq_{CVRI} (mmHg · cm^{-1} · s)	1.24 ± 0.57	1.03 ± 0.38	1.07 ± 0.12	1.61 ± 0.20*

Values are mean ± SD.

MAP = mean arterial pressure; ICP = intracranial pressure; CPP = cerebral perfusion pressure; MCAv = blood flow velocity in the middle cerebral artery; Sc_{O_2} = oxygen saturation in the brain; Svj_{O_2} = jugular venous saturation; Eq_{CVRI} = equivalent of cerebral vascular resistance.

* Significantly different from baseline ($P < 0.05$).

† Significantly different from Svj_{O_2} at high MAP ($P < 0.05$).

Arterial Pressure Challenge

An arterial pressure challenge in normal patients should not alter CBF because of autoregulation. Svj_{O_2} should also not vary, as cerebral metabolic rate in oxygen ($CMRO_2$) was likely to be constant throughout the study. But autoregulatory vasoconstriction[10,11] could reduce arteriolar blood volume. Venous blood volume should be unaffected if CBF remains constant. Thus, an increase in MAP in a context of effective autoregulation should lead to a decrease in Sc_{O_2} at constant Svj_{O_2}. However, autoregulation is often impaired in patients with head injuries, as in our patients. Indeed, we observed that Svj_{O_2} and MCAv decreased with decreasing MAP during the hypotensive challenge, despite a 17% reduction in Eq_{CVRI}. Conversely, Svj_{O_2} and MCAv increased during norepinephrine infusion, and Eq_{CVRI} also increased by 50%. Hence, in this condition of partially altered autoregulation, arteriolar vasoconstriction was insufficient to increase cerebral vascular resistance proportionally to cerebral perfusion pressure, and this was accompanied by an increase in CBF. This condition should have led to a decrease in the capillary oxygen gradient, a greater capillary contribution to the arterial

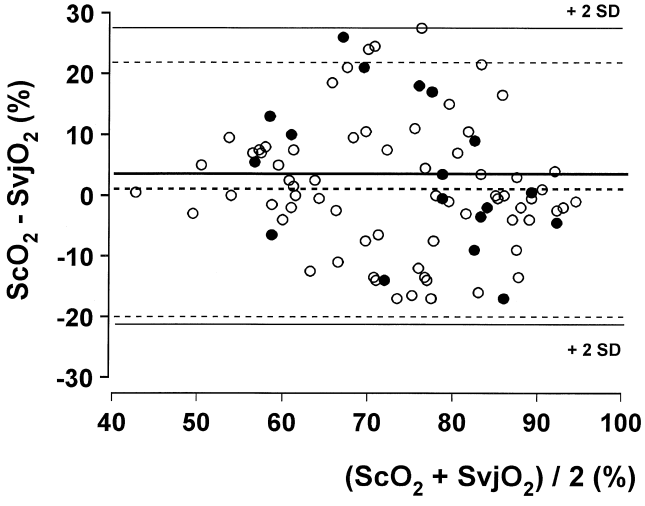

Fig. 1. Bland and Altman test with individual values of cerebral oxygen saturation (Sc_{O_2}) and venous jugular oxygen saturation (Svj_{O_2}). *Open symbols:* CO_2 test, with upper and lower dotted horizontal line corresponding to ± 2 SD. Middle dotted line represents the bias. *Closed symbols:* pressure test, with upper and lower solid horizontal line corresponding to ± 2 SD. Middle solid line represents the bias.

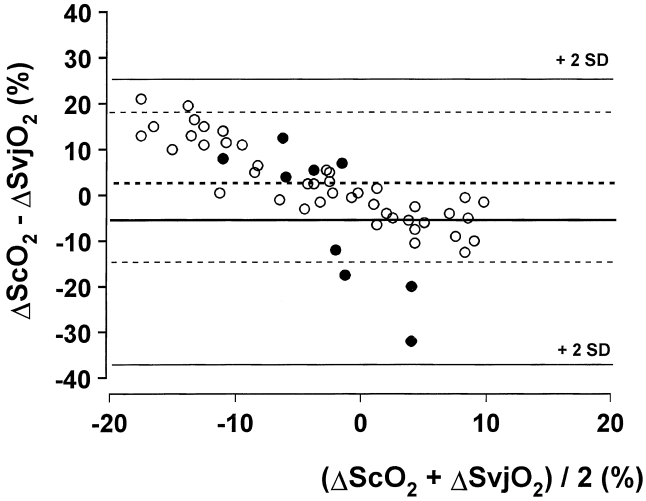

Fig. 2. Bland and Altman test with individual changes in cerebral oxygen saturation (δSc_{O_2}) and changes in venous jugular oxygen saturation (δSvj_{O_2}). *Open symbols:* CO_2 test, with upper and lower dotted horizontal line corresponding to ± 2 SD. *Closed symbols:* pressure test, with upper and lower solid horizontal line corresponding to ± 2 SD.

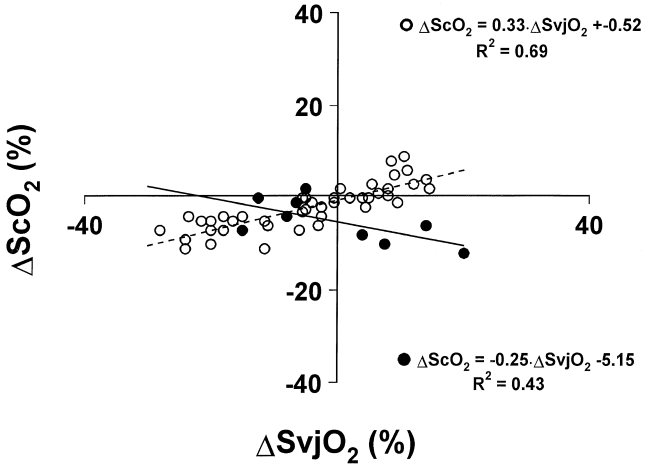

Fig. 3. Correlation between changes in cerebral oxygen saturation (δSc_{O_2}) and changes in venous jugular oxygen saturation (δSvj_{O_2}). *Open symbols:* CO_2 test. *Closed symbols:* pressure test. Dotted and solid lines represent the regression line of the CO_2 and pressure tests, respectively.

component of the Sc_{O_2} signal, but also to an increase in Svj_{O_2} and venous blood volume. The opposite phenomena was expected during vasodilation. We observed that δSc_{O_2} and δSvj_{O_2} correlated negatively when arterial pressure was changed. This tends to support the fact that changes in AV partition should have occurred with a larger increase in the venous compartment than the increase observed in the arteriolar one.

Carbon Dioxide Challenge

The decrease in cerebral vascular resistance in response to vasodilatation of the pial arterioles at T_2 was reflected in a 34% decrease in Eq_{CVRI} without change in MAP. Vasodilation should have allowed the volume of the arteriolar compartment to increase. The increase in blood flow at constant cerebral metabolic rate in oxygen should result in an independent increase in the oxygen saturation of the venous compartment and a passive increase in its volume.[12] Hence, hypercapnia, like a change in arterial pressure, may alter the AV partition. However, in contrast to the arterial pressure challenge, we observed a positive correlation between δSc_{O_2} and δSvj_{O_2} (fig. 3). Thus, the change in AV partition probably occurred during a CO_2 challenge different from that observed during an MAP change. One must also consider possible differential effects on extracerebral tissues. Moreover, Sc_{O_2}, which includes arteriolar blood, would be expected to be higher than Svj_{O2}. This was only true at T_2 in our study. All of these issues deserve comment.

First, Svj_{O_2} could be "artifactually high" compared with Sc_{O_2} because it incorporated deep brain structures that extract less oxygen than the neocortex structures monitored by NIRS. Second, the cerebral signal could be contaminated by a reflected signal from extracerebral structures (*e.g.*, bone, muscle) with unpredictable partition and O_2 saturation characteristics.

This contamination could account for most of the discrepancies observed between tests. The suggestion that the musculocutaneous territory makes a major contribution to NIRS signals is supported by recent experimental data, which indicate that the CBF measured by NIRS is three times greater when the probe is placed on the dura than when it is measured through the scalp.[13] Similarly, theoretical and experimental investigations of the propagation of light through the skull have shown that light is poorly absorbed by brain grey matter, as it accounts for only 15% of the total light absorbed.[14]

The impact of extracerebral tissues on Sc_{O_2} recording is critical. CO_2 dilates cerebral vessels, as well as those in the musculocutaneous territories such as the forehead and scalp.[15] There should therefore be a parallel between the changes in blood flow in both territories when Pa_{CO_2} is altered. The infusion of norepinephrine when autoregulation is disturbed should lead to a decrease in blood flow in the forehead and scalp and an increase in CBF as MAP increases. Although we did not measure velocity at the site of Sc_{O_2} measurement or in extracerebral tissues, we postulate that opposite responses by extracerebral tissues during changes in CO_2 and MAP, combined with changes in AV partition, could account for our findings. Such circumstances would not occur in studies based on hypoxic challenge because oxygen desaturation occurs simultaneously in all territories during such hypoxic experiments, including the musculocutaneous territory.[3] The same criticism can be made about measurements conducted after severe hypotension during ventricular fibrillation.[5] The inability of studies to cope with complex causes of inaccuracy may explain the persisting questions about the use of NIRS in clinical medicine.

Moreover, the physiology of our patients was not simple. Regional vascular variations may occur in patients with head injuries, with hypoperfused ischemic areas and hyperemic areas, leading to nonuniform oxygen extraction and venous saturation.[16] CBF–CO_2 reactivity and autoregulation may also be patchy.[17,18] Some investigators suggest that that these may account for the discrepancies between changes in Sc_{O_2} and Svj_{O_2}.[19,20] Metz *et al.*[21] showed, by bilateral Svj_{O_2} measurement in patients with head trauma, that unilateral Svj_{O_2} measure-

ment did not reliably reflect ischemic events. In contrast, the difference in Svj_{O_2} between each side did not change with time. Tateishi *et al.*[19] reached the same conclusion after reporting a fair correlation between δSvj_{O_2} and δSc_{O_2} during changes in Pa_{CO_2} in patients with acute brain disease. This suggests that interhemispheric inhomogeneity may not have had much effect in our study, which considered variations in Svj_{O_2} and in Sc_{O_2}. However, there may have been some intrahemispheric difference, especially between the anterior cerebral artery territory above which the NIRS sensor was placed and the middle cerebral artery territory, which was monitored by Doppler ultrasound. There is no reason to believe that this difference should be larger than the interhemispheric difference.

NIRS Technology

Apart from the problems originating from AV partitioning and the role of extracerebral tissue previously discussed, there may be other errors in the NIRS. The optical path length and light scattering may vary.[22] The technology we used includes a continuous wave and, thus, cannot correct for these sources of error. The limits of this method may also have been reached in our study, where different challenges may have induced differing effects on optical path length and light scattering in addition to the possible influences of the AV partition and extracerebral tissues.

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