Inconsistent detection of changes in cerebral blood volume by near infrared spectroscopy in standard clinical tests

D. Canova,1 S. Roatta,1 D. Bosone,2 and G. Micieli3

1Department of Neuroscience, Physiology Division, University of Torino, Torino; 2Neurovascular Laboratory and 3Department of Emergency Neurology, Istituto Di Ricovery e Cura a Carattere Scientifico, National Neurological Institute, C. Mondino Foundation, Pavia, Italy

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With the present study, we aimed to assess and document the role of extracranial circulation in disturbing NIRS monitoring of cerebral perfusion during three standard clinical tests, i.e., the Valsalva maneuver (VM), hyperventilation (HV), and head-up-tilt (HUT). These maneuvers, which are frequently adopted to investigate cerebrovascular reactivity and autoregulation, also, but differently, affect extracranial circulation. For this reason, they constitute a good model to reveal the possible influence of extracranial circulation on cerebral NIRS variables.

We have reported preliminary observations about incongruous indications by BL and SRS parameters, which occasionally detected changes in blood volume or in tissue oxygenation of the opposite sign, during neurovegetative tests (6). We hypothesized that the BL–SRS disagreement was due to a differential influence of extracranial circulation on the two sets of parameters, or, in other words, that extracranial circulation was potentially capable of reverting a putatively cerebral NIRS indicator during standard clinical examinations.
and the total hemoglobin index (THI), provided by SRS. Moreover, changes in blood volume occurring in the extracranial circulation were simultaneously monitored in different ways: by a second NIRS channel, the probe being applied on the cheek, and by a cutaneous photoplethysmographic device applied on the forehead. In a smaller number of subjects, a cutaneous laser Doppler flowmeter (LDF) applied to the forehead was also employed.

**METHODS**

**Subjects**

Twenty-nine healthy volunteers, aged between 23 and 40 yr (8 males and 21 females), were enrolled in the study after providing written informed consent. The study was conducted at the “C Mondino” Neurological Hospital after approval by the Local Ethical Committee.

**Protocols**

The study was performed in a quiet room at a constant ambient temperature (~23°C). The subjects were kept supine on an electrical auto-tilt table, were not allowed to speak during the experiment, and were asked to keep their eyes closed and relax. The three different maneuvers were performed sequentially in randomized order, separated by a resting period of 10–15 min during which the subjects remained in the supine position.

**VM.** The subjects performed VM by expiring through a closed mouthpiece connected to a manometer that they could read (33). They were requested to generate and hold a positive alveolar pressure of 40 mmHg for 15 s after a normal-size inspiration. A small leak in the tubing prevented the subjects from maintaining the pressure by closing the glottis (33).

**HV.** The subjects were asked to hyperventilate to achieve and maintain for 1 min an end-tidal carbon dioxide pressure (P$_{ETCO_2}$) of 20 mmHg. Visual feedback was obtained directly from the display of the capnograph (20).

**HUT.** Passive HUT to 70° for 5 min was performed. The bed was electrically operated by the experimenter, with up and down rotation being performed in ~20 s.

**Near Infrared Spectroscopy**

NIRS monitoring was performed by a two-channel NlRO 300 monitor (Hamamatsu Photonics). The NlRO 300 is a noninvasive bedside monitor that employs four pulsed laser diodes (emitter optode) emitting light at different wavelengths (775, 810, 850, and 910 nm) and collects scattered light by three closely placed photodiodes (receiver optode). The device simultaneously provides three parameters by conventional differential spectroscopy, based on a modified BL law (12) and on the information collected by a single photodiode, and two parameters based on SRS (3, 31) that takes advantage of all three photodiodes (4).

BL parameters measure concentration changes in oxyhemoglobin (O$_2$Hb), deoxyhemoglobin (HHb), and total hemoglobin (tHb = O$_2$Hb + HHb) and are all expressed in micromoles per liter; they do not provide a measure of the absolute concentration of the chromophores but of concentration changes with respect to an arbitrary value (31).

SRS measures tissue oxygenation by the tissue oxygenation index (TOI), expressed in percent, and total tissue hemoglobin concentration by the tissue hemoglobin index (THI), expressed in arbitrary units. These two parameters allow to assessment of relative changes in tissue oxygenation and tissue blood volume.

**Intracranial Measurements**

One NIRS channel was used for intracranial monitoring, the probe being placed high on left side of the forehead to exclude the temporalis muscle from the sampling volume and sufficiently lateral from the midline to exclude the superior sagittal sinus. NIRS optodes were set at a distance of 5 cm by a rubber holder secured to the skin by biadhesive foam and further stabilized by a crepe bandage around the head (2).

In addition, blood velocity in the left middle cerebral artery (V$_{MCA}$) was monitored using a 2-MHz transcranial Doppler ultrasoundanograph (Multi dop X; DWL), the Doppler probe being held by a headset for bilateral monitoring.

**Extracranial Measurements**

The second NlRO channel was used for extracranial monitoring, the probe being positioned on the left cheek.

In addition, extracranial circulation was monitored through an infrared plethysmograph transducer (MLT1020 IR Plethysmograph; PowerLab ADInstruments), detecting changes in blood volume from the cutaneous microcirculation (PPG), the probe being placed on the right side of the forehead. In a smaller group of subjects (n = 9), LDF (MBF3D; Moor Instruments) was also employed to monitor cutaneous blood flow at the forehead (right side). Application of LDF and PPG on the right side of the forehead, opposite to the intracranial NIRS monitoring, prevented possible interference with NIRS signals.

**Systemic Measurements**

Continuous noninvasive measurement of arterial blood pressure (ABP) was performed by photo-plethysmography (Finapres, Ohmeda 2300) applied to the right third finger. P$_{ETCO_2}$ was continuously recorded using a small nasal cannula connected to a capnograph (Ohmeda 4700 OxiCap).

**Signal Acquisition and Processing**

All NIRS signals from both channels, O$_2$Hbi, HHbi, tHbi, THli, TOli, O$_2$Hbe, HHbe, tHbe, THle, and TOle (“i” and “e” indicate the intracranial and extracranial monitoring, respectively) were continuously acquired and digitally transferred to PC by proprietary software (Hamamatsu Photonics; sampling frequency: 2 Hz) throughout the whole session. These data were subsequently exported in text files for off-line analysis under Microsoft Excel.

In addition, V$_{MCA}$, ABP, P$_{ETCO_2}$, PPG, and LDF, along with some of the NIRS signals (tHbi, THli, tHbe, and THle) were continuously acquired on PC (PowerLab ML 785; ADInstruments; sampling freq = 200 Hz) throughout the whole session.

The same software enabled off-line calculation of heart rate (HR) and was used to extract mean values and relative changes of the different signals throughout the different maneuvers.

**Data Analysis and Statistics**

The response to the different maneuvers was assessed by computing absolute or relative changes exhibited by the different variables with respect to the pretest (control) value. The control value was computed as the mean value over a 30-s interval immediately before the beginning of the test, whereas mean values elicited by each maneuver were computed over the phase II of the response to VM (46), over a 20-s interval starting 40 s after the beginning of HV, and over a 30-s interval starting 3 min after the beginning of HUT.

Inconsistency between BL and SRS parameters was assessed by detecting opposite changes in the blood volume indicators tHbi and THli in response to the different maneuvers. Data are presented as means ± SD.

Changes produced on the different variables (V$_{MCA}$, ABP, HR, TOli, THli, tHbe, TOle, THle, and PPG) with respect to the
RESULTS

Out of the 29 recruited subjects, two failed to complete the HUT, in 5 subjects the extracranial NIRS recording was not performed because of 1 probe being under scheduled maintenance, and in 2 subjects changes in extracranial NIRS variables during VM could not be assessed due to saturation of the signals.

VM

The response to VM from a representative subject is shown in Fig. 1. In the ABP trace, the different phases of the response are placed on the ABP trace (I, phase I; IIa-IIb, phase II; III, phase III; IV, phase IV). Disagreement between intracranial blood volume indexes is evidenced by a dashed circle; a.u., arbitrary units.

Table 1. Average changes produced by VM, HV, and HUT on the different variables

<table>
<thead>
<tr>
<th></th>
<th>VM</th>
<th>HV</th>
<th>HUT</th>
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</thead>
<tbody>
<tr>
<td>V&lt;sub&gt;MCA&lt;/sub&gt;, %</td>
<td>-6.75 ± 7.78†</td>
<td>-23.63 ± 14.46†</td>
<td>-6.23 ± 6.10*</td>
</tr>
<tr>
<td>ABP, %</td>
<td>4.84 ± 11.44</td>
<td>-4.10 ± 7.53*</td>
<td>3.71 ± 19.52</td>
</tr>
<tr>
<td>HR, %</td>
<td>32.42 ± 17.55†</td>
<td>40.25 ± 24.43†</td>
<td>21.41 ± 12.20†</td>
</tr>
<tr>
<td>TOI&lt;sub&gt;i&lt;/sub&gt;, %</td>
<td>-4.77 ± 2.96†</td>
<td>-5.18 ± 3.04†</td>
<td>-3.19 ± 4.22†</td>
</tr>
<tr>
<td>THI&lt;sub&gt;i&lt;/sub&gt;, %</td>
<td>2.30 ± 9.80</td>
<td>-3.90 ± 4.48*</td>
<td>-1.02 ± 14.61</td>
</tr>
<tr>
<td>tHbe, μM</td>
<td>6.73 ± 3.49†</td>
<td>0.48 ± 1.97</td>
<td>0.77 ± 3.68</td>
</tr>
<tr>
<td>TOI&lt;sub&gt;e&lt;/sub&gt;, %</td>
<td>6.25 ± 4.98†</td>
<td>3.41 ± 2.73†</td>
<td>-6.78 ± 3.33†</td>
</tr>
<tr>
<td>THI&lt;sub&gt;e&lt;/sub&gt;, %</td>
<td>33.85 ± 14.97†</td>
<td>2.80 ± 6.56</td>
<td>-11.61 ± 5.87†</td>
</tr>
<tr>
<td>tHbe, μM</td>
<td>16.13 ± 8.81†</td>
<td>1.17 ± 3.73</td>
<td>-4.75 ± 3.52†</td>
</tr>
<tr>
<td>PPG, arbitrary units</td>
<td>3.74 ± 3.02†</td>
<td>0.71 ± 2.07</td>
<td>-0.58 ± 3.30</td>
</tr>
<tr>
<td>LDF, %</td>
<td>-16.71 ± 37.00</td>
<td>32.89 ± 43.30</td>
<td>-27.47 ± 13.24†</td>
</tr>
</tbody>
</table>

Values are means ± SD. Relative changes are expressed in percent; absolute changes are expressed in the original units. VM, Valsalva maneuver; HV, hyperventilation; HUT, head-up tilt; V<sub>MCA</sub>, cerebral blood velocity; ABP, arterial blood pressure; HR, heart rate; TOI, tissue oxygenation index; THI, total hemoglobin index; tHb, total hemoglobin concentration; PPG, cutaneous plethysmography at the forehead; LDF, cutaneous Laser Doppler flowmetry at the forehead. The “i” and “e” indicate intracranial (at the forehead) and extracranial (at the cheek) near infrared spectroscopy monitoring. *P < 0.05. †P < 0.01.
values obtained from extracerebral monitoring. While LDF produced variable and nonsignificant results, both NIRS (cheek) and surface photoplethysmography applied to the forehead reported very significant increases in the blood volume indicators THIe, tHbe, PPG, and TOIe.

The scatter plots shown in Fig. 2 help to understand the correlation between the different variables, while all R values are summarized in Table 2. In particular, Fig. 2A underlines the agreement between THIe and tHbe, which never gave contradictory indications and exhibited a correlation of $R = 0.54$ ($P < 0.05$), which rises to 0.74 after removing one outlier. Conversely, a nonsignificant correlation was observed between tHbi and THIi (Fig. 2B). It is interesting to observe that a significant correlation resulted between tHbi and tHbe ($R = 0.48$; $P < 0.01$; Fig. 2C) and between tHbi and PPG ($R = 0.50$; $P < 0.01$; Fig. 2D).

Notably, cutaneous plethysmography at the forehead was not correlated with tHbe ($R = 0.15$), although they both increased in 100% of subjects, nor with LDF ($R = -0.03$). LDF and PPG showed concordant changes in 30% of the cases.

Table 2. Strength of the linear correlation (R) between changes exhibited by different pairs of variables in response to the three maneuvers

<table>
<thead>
<tr>
<th></th>
<th>VM</th>
<th>HV</th>
<th>HUT</th>
</tr>
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<tbody>
<tr>
<td>THIi vs. tHbi</td>
<td>0.27</td>
<td>0.47*</td>
<td>0.27</td>
</tr>
<tr>
<td>tHbi vs. tHbe</td>
<td>0.48*</td>
<td>0.57†</td>
<td>0.37</td>
</tr>
<tr>
<td>tHbi vs. PPG</td>
<td>0.50†</td>
<td>0.70†</td>
<td>0.55†</td>
</tr>
<tr>
<td>THIi vs. tHbe</td>
<td>0.10</td>
<td>0.10</td>
<td>0.41</td>
</tr>
<tr>
<td>THIi vs. PPG</td>
<td>0.37*</td>
<td>0.20</td>
<td>-0.11</td>
</tr>
<tr>
<td>THIe vs. tHbe</td>
<td>0.54*</td>
<td>0.73†</td>
<td>0.63†</td>
</tr>
<tr>
<td>PPG vs. tHbe</td>
<td>0.15</td>
<td>0.40</td>
<td>-0.068</td>
</tr>
<tr>
<td>LDF vs. PPG</td>
<td>-0.031</td>
<td>0.86†</td>
<td>0.079</td>
</tr>
<tr>
<td>THIi vs. VMCA</td>
<td>0.27</td>
<td>0.0087</td>
<td>0.092</td>
</tr>
<tr>
<td>tHbi vs. VMCA</td>
<td>-0.18</td>
<td>-0.32</td>
<td>-0.14</td>
</tr>
</tbody>
</table>

Values are means ± SD. Abbreviations are as in Table 1. *$P < 0.05$. †$P < 0.01$.

The response to HV of a representative subject is shown in Fig. 3. PETCO2 stabilizes at 20 mmHg during the maneuver, and VMCA exhibits a marked reduction with a latency of 10–15 s, while ABP exhibits a transient increase. In this subject, intracranial blood volume indicators exhibit opposite changes, while THIe and tHbe, as well as PPG, all indicate an increase in extracranial blood volume. On average (Table 1), HV produced a significant increase in HR (from 74.7 ± 10.4 to 104.2 ± 20.8 beats/min), a small decrease in ABP (from 85.8 ± 13.2 to 80.5 ± 15.4 mmHg), along with a marked and sustained decrease in VMCA (from 62.4 ± 13.11 to 46.5 ± 7.3 cm/s).

Blood volume in the extracranial compartment (cheek) exhibited changes of variable sign in the different subjects resulting in nonsignificant average change. However, a good correlation resulted between THIe and tHbe ($R = 0.73$; $P < 0.01$; Fig. 4A). At cerebral level, tHbi was not significantly affected, while THIi exhibited on average a significant decrease (it was reduced in 80% of the subjects). When looking at individual trials, the two parameters provided contradictory indications in 31% of the cases (Fig. 4B).

tHbi results significantly correlated with the extracranial indicators tHbe ($R = 0.57$; $P < 0.01$; Fig. 4C) and PPG ($R = 0.70$; $P < 0.01$; Fig. 4D), as well as with THIi ($R = 0.47$, $P < 0.05$; Fig. 4B).

With respect to VM, a lower agreement is here observed between extracranial blood volume changes at the cheek (tHbe) and at the forehead (PPG), exhibiting opposite sign in 50% of the cases, while a 78% agreement and a significant correlation is observed between LDF and PPG ($R = 0.86$; $P < 0.01$).

Notably, oxygenation indexes again show again opposite average changes at intracranial (increase) and extracranial (decrease) level.
**HUT**

The response to HUT in a representative subject is shown in Fig. 5. A slight decrease in \( V_{MCA} \), ABP, and \( P_{ETCO2} \), can be observed, particularly in the first minutes after the tilt-up. NIRS blood volume indexes exhibit discordant patterns at cerebral level with a decrease in tHbi and an increase in THIi. At the cheek level, no appreciable change in tHbe and a clear decrease in THIe are exhibited while forehead skin blood volume (PPG) decreased with a time course remarkably similar to tHbi. At variance with previous maneuvers, oxygenation indexes show concordant changes: a significant decrease in both TOIi and TOIe.

At the extracranial level, blood volume does not appear to be univocally affected. At the cheek level, both THIe and tHbe reveal a significant decrease (in 100% of the subjects) and a good correlation \( (R = 0.63; P < 0.01; \text{Fig. 6A}) \), while cutaneous blood volume index from forehead (PPG) evidences a greater response variability (8 increases out of 29 subjects), resulting in a nonsignificant change. In addition PPG variations were not correlated with changes in tHbe \( (R = -0.068) \), the two variables exhibiting changes of opposite sign in 30% of the cases.

With regard to the intracranial compartment, both THIi and tHbi showed a large variability and no significant changes on average; nevertheless, when looking at the individual trials, the two parameters yielded contradictory indications in 40% of the cases and resulted to be nonsignificantly correlated \( (R = 0.27; \text{Fig. 6B}) \).

At variance with what observed for VM and HV, the scatter plots here evidenced a nonsignificant correlation between changes in tHbi and changes in tHbe \( (R = 0.37; \text{Fig. 6C}) \). However, tHbi was still significantly correlated with PPG \( (R = 0.55; P < 0.01; \text{Fig. 6D}) \); in particular, it can be observed that large changes in PPG are associated with large changes in tHbi. This relationship also hold for responses to VM and HV (Figs. 2D, 4D, and 6D). PPG and LDF exhibited a 70% agreement and a nonsignificant correlation.

Figure 7 provides a summary of the correlations among the following variables: tHbi, THIi (intracranial variables), PPG, and tHbe (extracranial variables). To graphically emphasize the degree of correlation between two given variables, these have been connected by lines whose thickness is proportional to the \( R \) value. In addition, dashed instead of continuous lines have been used whenever the correlation was not statistically significant. By considering the three maneuvers all together, it can be observed that tHbi, the putative intracranial BL parameter, exhibits a stronger correlation with extracranial indicators, i.e., tHbe (2 out of 3 correlations are statistically significant) and PPG (all correlations are significant), than with THIi (only 1 correlation is significant). Conversely, THIi exhibits a weak correlation with the same extracranial indicators PPG (only 1 of the correlations is significant) and tHbe (none of the correlations is significant).

The correlations between \( V_{MCA} \) and the two intracranial NIRS parameters tHbi and THIi are always nonsignificant (Table 2).

**DISCUSSION**

The present study shows that tHbi and THIi, respectively, the BL and SRS NIRS indicators of cerebral blood volume, give contradictory information in a high percentage of cases, ranging between 31 and 46% (average 39%), during maneuvers routinely used in clinical investigations. Such inconsistency is observed to a much lesser extent in extracranial NIRS monitoring (occurrence of discordant indications between tHbe and THIe: 6.6%, on average).

The strong correlation observed between the tHbi and the extracranial indicators of blood volume, compared with the weak or absent correlation between THIi and the same parameters (Fig. 7), suggests that extracranial circulation is responsible for the observed inconsistency between BL and SRS. This interpretation is supported by the notion that BL parameters are intrinsically more sensitive than SRS parameters to extracranial circulation.

The results will be separately discussed for the different maneuvers before final considerations are drawn.

**VM**

VM produces a large increase in intrathoracic pressure, which hinders venous return and increases blood pressure in venous compartments (18, 33, 41, 46). The resulting marked
Increase of blood volume in extracranial compartments has been clearly detected by PPG, THhe, and tHbe.

The effect on blood volume at intracranial level is not as straightforward. In fact, cerebral blood volume can increase only if cerebrospinal fluid volume decreases (total volume of the cranium cannot change); however, both central venous pressure and central spinal fluid pressure are increased during the maneuver (22, 24, 33). A number of studies, employing

Fig. 4. Scatter plots illustrating the correlation between HV-induced changes in different variables. Explanation is as in Fig. 2.

Fig. 5. Response to head-up tilt (HUT) in a representative subject. Abbreviations are as in Fig. 1. Two leftmost vertical dashed lines indicate the tilt-up phase, while the rightmost indicate the tilt-down. Dashed circle evidences the contradictory information provided by the 2 intracranial indexes.
BL-based NIRS, report increased cerebral blood volume and oxygenation during VM (34, 36, 49). We also consistently observed an increase in tHbi (100% of cases); however, THIi decreased in 46% of subjects. This suggests that intracranial blood volume can possibly be reduced during VM and that the increased volume of extracranial compartments heavily affects the tHbi indicator. In addition, it cannot be excluded that also THIi could have been affected to a small extent, which would imply an overestimation of the intracranial blood volume change by THIi.

SRS-derived information about tissue oxygenation also deserves consideration. In fact, it is interesting to observe that, while TOIe was significantly increased (cheek level), TOIi consistently decreased at intracranial level. This is at variance with other studies (34, 36) in which a paradoxical increase in cerebral oxygenation was detected by BL-based NIRS. The VM-induced increase in central venous and intracranial pressures produces a decrease in cerebral perfusion pressure that impairs cerebral blood flow (10, 46). Such a situation fits well with the observed decrease in VMCA and the decrease in cerebral oxygenation, as detected by the SRS parameter TOIi. It is possible that, also in this case, the disagreement with BL-based data from the literature is due to the greater sensitivity of BL parameters to changes in extracranial circulation, compared with SRS.

HV

HV induces transient arterial hypocapnia and alkalosis provoking a rapid cerebral vasoconstriction, cerebral blood flow reduction (21, 30), and increased cerebral oxygen extraction (48). This results, as also observed in the present study, in both a marked reduction of VMCA (7, 39) and a decrease in cerebral oxygenation (TOIi; Refs. 5, 44, 48, 55).

A reduction of cerebral blood volume as detected by THIi (80% of subjects) is consistent with the occurrence of a marked cerebral vasoconstriction and is supported by previous studies (29, 35). On the other hand, tHbi is not significantly affected by HV and gives in 28% of the subjects opposite indication to THIi.

In extracranial compartments, information about perfusion changes in response to HV is scanty. In one study (40), increases in cutaneous blood flow have been reported. We here observe that both the NIRS signals from the cheek and cutaneous plethysmography (forehead) detected increase in blood volume in a large percentage of cases, all these signals being moderately correlated with tHbi. In particular, it can be observed from the scatter plots (Fig. 4, C and D) that largest PPG and tHbe increases are associated to the largest increases in tHbi, supporting the notion of extracranial interference on BL parameters (20, 51).

HUT

The response to HUT appears to be more complex. At the intracranial level, the postural change is considered to produce a decrease in cerebral perfusion pressure, which, together with the hyperventilation-induced hypocapnia induced by the hypertensive stimulus (45), may result in cerebral hypoperfusion, which, in turn, accounts for the reduction in VMCA and TOI (9, 26, 28, 39, 42), also observed in the present study.

In agreement with other studies from the literature (26, 27), significant changes in cerebral blood volume are neither detected by THIi nor by tHbi, which is possibly due to the prompt activation of local myogenic and metabolic compensatory mechanisms (25, 38).

Also, at the extracranial compartment, the response to HUT is not clear cut. Decreased transmural pressure at the venous...
side may decrease blood volume (venous collapse), but local and neural mechanisms may also intervene. In particular, the sympathetic activation driven by the orthostatic stimulus is known to increase vasoconstrictor tone in skeletal muscles but not in cutaneous tissues (52).

This may explain the consistent decrease in blood volume and oxygenation indicated by the NIRS channel positioned on the cheek, which likely reflects perfusion of underlying skeletal muscle layers. Conversely, forehead plethysmography, which mostly reflects cutaneous perfusion, results in a variable response, which poorly correlates with tHbe.

Notably, also in the HUT response a large percentage (38%) of inconsistent indications by THIi and tHbi was observed. At variance with what observed in the other maneuvers, tHbi was poorly correlated with tHbe but still rather correlated with PPG (Fig. 6, C and D).

Thus, also in this case, the occurrence of inconsistencies between cerebral blood volume indicators appears to be related to the influence of extracranial circulation on the BL parameter tHbi.

**General Considerations**

For the sake of simplicity, in the above discussion the assumption was made that measurements were collected at “steady state,” and we did not consider the possibility of different time course of the responses in the different tissues. However, this assumption does not undermine the main outcomes of the work.

The three maneuvers investigated in the present study elicit very different hemodynamic responses at intra- and extracranial levels. In particular: 1) VM provokes a marked increase in central venous pressure that results in a large increase in blood volume of extracranial compartments with minor changes at intracranial level, 2) HV produces a marked metabolic cerebrovascular regulation with minor changes at extracranial level, while 3) HUT affects the hydrostatic gradients and stimulates metabolic and neural regulation at both intra and extracranial levels.

The present results emphasize the notion that BL parameters are particularly sensitive to extracranial circulation (4, 51, 54), to the extent that extracranial interference may considerably alter the measured variables. This may occur not just in response to invasive interventions, like occlusion of external and internal carotid arteries, but also during the standard maneuvers commonly employed in the clinical routine, as well as in experimental investigations.

The inconsistency between tHbi and THIi represents a marker of extracranial interference on the putative cerebral NIRS monitoring. Such marker is quite easy to spot-out on the NIRO 300 that displays both SRS and BL variables at the same time; however, the following few issues deserve consideration: 1) the inconsistency may only occur if extra and intracranial circulations undergo opposite changes, which is not necessarily the rule. If, for example, both compartments exhibit a simultaneous increase in blood volume tHbi would overestimate intracranial changes but would probably not disagree with THIi; 2) the interference from the extracranial compartment was here evidenced on blood volume indicators but may equally affect BL assessment of tissue oxygenation; 3) although previous studies (4, 51, 54) and the present data quite clearly demonstrate that BL parameters can be affected by extracranial circulation, whether and to what extent SRS parameters can also be affected remains to be ascertained; and 4) although the present results, obtained with a specific NIRS device (the Hamamatsu Photonics, NIRO 300), cannot be readily extended to other devices, they suggest that uncorrected BL parameters should be interpreted with caution to infer hemodynamic changes at cerebral level.

In general, awareness of perfusion changes occurring in the extracranial compartment may be of good use in the interpretation of the NIRS recordings. Since NIRS is based on changes in hemoglobin concentration, surface plethysmography is to be preferred to flowmetry, also in consideration of the fact that blood flow and blood volume may not vary in a concordant way. This was well evidenced in the response to VM: besides large increases in forehead skin blood volume, a nonsignificant blood flow decrease was detected by LDF. In addition, we observed that plethysmographic monitoring of the extracranial compartment with a second NIRS channel placed on the cheek may not always be appropriate, possibly due to the different neural regulation of skin and muscle vascular beds, which makes the cheek (skin + muscle) not a good representation of the forehead (mostly skin). Surface plethysmography at the forehead proved to be better correlated to tHbi (particularly during HUT) and to better help in understanding the inconsis-
tency between tHbi and THI. On this basis, it is proposed as a valid and inexpensive measure to be included in the experimental-clinical setup.

The importance of specifically monitoring cutaneous circulation at the forehead is emphasized by the peculiar neural control of this area, which is profoundly affected by cognitive and emotional aspects (13, 50, 53). These factors are experimentally difficult to control and are likely to account for the observed variability of responses in the extracranial compartments.

Conclusions

In conclusion, the present study reveals that BL NIRS monitoring can be detrimentally affected by changes in extracranial circulation also in routine cardiovascular/neurovegetative tests and emphasizes its low reliability for the assessment of cerebral perfusion. Postural, mechanical, and neural changes, which may occur under most investigative maneuvers, alter blood perfusion or distribution in the extracranial compartment and affect BL NIRS variables to the extent that detected changes in cerebral tissue blood volume and oxygenation can be frequently reversed. On the basis of the present data, forehead cutaneous plethysmography is suggested as an additional measure to complement the hemodynamic monitoring and help in the interpretation of NIRS recordings.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

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