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Head-up tilt and hyperventilation produce similar changes in cerebral oxygenation and blood volume: an observational comparison study using frequency-domain near-infrared spectroscopy

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Abstract

Purpose—During anesthesia, maneuvers which cause the least disturbance of cerebral oxygenation with the greatest decrease in intracranial pressure would be most beneficial to patients with intracranial hypertension. Both head-up tilt (HUT) and hyperventilation are used to decrease brain bulk, and both may be associated with decreases in cerebral oxygenation. In this observational study, our null hypothesis was that the impact of HUT and hyperventilation on cerebral tissue oxygen saturation ($SctO_2$) and cerebral blood volume (CBV) are comparable.

Methods—Surgical patients without neurological disease were anesthetized with propofol-remifentanil. Before the start of surgery, frequency-domain near-infrared spectroscopy was used to measure $SctO_2$ and CBV at the supine position, at the 30° head-up and head-down positions, as well as during hypoventilation and hyperventilation.

Results—Thirty-three patients were studied. Both HUT and hyperventilation induced small decreases in $SctO_2$ [3.5 (2.6)%; P <0.001 and 3.0 (1.8)%; P <0.001, respectively] and in CBV [0.05 (0.07) mL·100 g^{-1}; P <0.001 and 0.06 (0.05) mL·100 g^{-1}; P <0.001, respectively]. There were no differences between HUT to 30° and hyperventilation to an end-tidal carbon dioxide ($ETCO_2$) of 25 mmHg (from 45 mmHg) in both $SctO_2$ (P = 0.3) and CBV (P = 0.4).

Discussion—The small but statistically significant decreases in both $SctO_2$ and CBV caused by HUT and hyperventilation are comparable. There was no correlation between the decreases in $SctO_2$ and CBV and the decreases in blood pressure and cardiac output during head-up and head-down tilts. However, the decreases in both $SctO_2$ and CBV correlate with the decreases in $ETCO_2$ during ventilation adjustment.

In patients with increased brain bulk, head-up tilt (HUT) and hyperventilation are often instituted to decrease intracranial pressure (ICP) or to improve operating conditions. However, these widely applied maneuvers can also have a negative impact on cerebral perfusion and oxygenation, i.e., HUT can severely compromise cerebral perfusion pressure, and hyperventilation can cause profound cerebral vasoconstriction.[1] There has been debate about the relative effects of HUT in maintaining cerebral blood flow (CBF) and decreasing ICP.[2–5] In contrast, the current point of view is that hyperventilation in head-injured patients can produce more harm than benefit, and it should be strictly limited to the emergent management of life-threatening intracranial hypertension pending definitive measures or to facilitate intraoperative surgery.[6] Recent advances in near-infrared spectroscopy (NIRS), such as frequency-domain (FD) and time-domain approaches, allow for absolute quantification of cerebral tissue oxy- and deoxyhemoglobin.[7,8] These newer quantitative NIRS technologies can assess not only cerebral tissue oxygen saturation ($SctO_2$) but also cerebral blood volume (CBV) based on total hemoglobin concentration (THC), the sum of oxy- and deoxyhemoglobin.[8,9] In this observational study, our null hypothesis was that HUT and hyperventilation cause similar changes in $SctO_2$ (an estimate of cerebral perfusion and oxygenation) and CBV (a contributor of intracranial mass and ICP). Our specific aim was to use FD-NIRS to compare the changes in $SctO_2$ and CBV caused by HUT and hyperventilation in propofol-remifentanil anesthetized non-neurosurgical patients.

Methods

Patients

After Institutional Research Board approval (HS#: 2010–7521; approved on: May 21st, 2010; Contact: Research Administration, 5171 California, Suite 150, Irvine, CA 92697) and informed verbal and written consent, patients scheduled for elective non-neurosurgical procedures at University of California Irvine Medical Center were recruited for this study. Exclusion criteria were: age ≤18 yr old, cerebrovascular disease, symptomatic cardiovascular disease, poorly controlled hypertension (systolic blood pressure ≥160 mmHg), and poorly controlled diabetes mellitus (blood glucose ≥200 $mg \cdot dL^{-1}$). The data presented here from our FD-NIRS study were acquired from the same patients we recruited to study the effects of vasopressor treatment. The result regarding the impact of vasopressor administration on $SctO_2$ and the result regarding the comparison of cardiac output (CO) measured by esophageal Doppler and Vigileo FloTrac have been previously published.[10,11] As each study has a unique hypothesis and paradigm, they have been reported separately. We took care to ensure vasopressor-induced hemodynamic changes returned to baseline values for at least five minutes before whole body tilt and ventilation adjustment.

Protocol

Following the patient's arrival in the operating room, a radial intra-arterial catheter, a bispectral index (BIS) monitor, and two FD-NIRS probes (left and right forehead) were placed in addition to the other routine monitors. Following anesthesia induction with fentanyl 1.5-2 $\mu g \cdot kg^{-1}$ and propofol 2–3 $mg \cdot kg^{-1}$, all patients' tracheas were intubated and maintained with total intravenous anesthesia using propofol 75–150 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and remifentanil 0.3–0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ to target a BIS of 30. Volume-controlled ventilation was used with a tidal volume of 8–10 $mL \cdot kg^{-1}$ and a respiratory rate of 8–10 $breaths \cdot min^{-1}$ to target an end-tidal carbon dioxide ($ETCO_2$) of 35 mmHg. The inspired oxygen was 50%. Muscle relaxation was maintained with cisatracurium. A 30° HUT (reverse-Trendelenburg position) and a 30° head-down tilt (Trendelenburg position) were performed and compared with the supine position (0°). The order of head-up and head-down tilts was randomized. Study measurements were recorded when mean arterial pressure (MAP) decreased to the lowest value with HUT and when MAP increased to the highest value with head-down tilt. After completion of the body tilt component and once tilt-induced hemodynamic changes receded, ventilation adjustment was conducted with the end point of hyperventilation at $ETCO_2$ of 25 mmHg and the end point of mild hypoventilation at $ETCO_2$ of 45 mmHg. The order of hyperventilation and mild hypoventilation was also randomized. Study measurements were recorded once the end points of hyperventilation and mild hypoventilation were reached. All measurements were obtained before the start of surgery.

Measurements

Cerebral tissue oxygen saturation and THC were measured by the Oxiplex TS cerebral oximeter (ISS Inc., Champaign, IL, USA), a non-invasive portable and quantitative FD-NIRS device.[7] It emits and detects near infrared (NIR) light at two wavelengths (690 nm and 830 nm). The emitted light is amplitude modulated (i.e., turned on and off) at 110 MHz. The spacing between the source and detector fibres on the optical probe (1.96 cm, 2.46 cm, 2.92 cm, and 3.45 cm) is sufficient for light to access the surface of the brain.[12] The measured optical properties characterize cerebral tissues and are not influenced appreciably by skin or surface contributions.[12,13] Cerebral blood volume is calculated via the following equation.[8,9]

$$CBV=(THC \times MW_{Hb} \times 10^{-5})/(HGB \times D_{bt} \times CLVHR)$$

Cerebral blood volume is in mL·100 g^{-1}; THC is in μMol; MW_{Hb} is the molecular weight of hemoglobin (64,458 g·Mol^{-1}); HGB is systemic blood hemoglobin concentration (g·dL^{-1}); D_{bt} is brain tissue density (1.0335 g·mL^{-1}); and CLVHR = 0.69 is the cerebral to large vessel hematocrit ratio.

Mean arterial pressure was monitored at the external ear canal level via a radial intra-arterial catheter system, Vigileo FloTrac (Edwards Lifesciences, Irvine, CA, USA). Cardiac output was monitored by both esophageal Doppler (CardioQ, Deltex Medical, UK) (CO_{ED}) and the third-generation Vigileo FloTrac (CO_{FT}). End-tidal carbon dioxide was determined by the gas analyzer built into the anesthesia machine (Aisys, GE Healthcare, Madison, WI, USA). Oxygen saturation by pulse oximetry was determined by pulse oximeter (LNOP Adt, Masimo Corp, Irvine, CA, USA). The depth of anesthesia was monitored via the BIS monitor (S/5™ M-BIS, GE Healthcare, Madison, WI, USA).

Statistical analyses

Sample-size determination for evaluating the impact of vasopressor treatment on $SctO_2$ was reported previously.[10] Since the observation we report in this article is a secondary outcome of the experiment, we did not carry out a separate sample-size determination. Data are expressed as mean standard deviation (SD). Ninety-five percent confidence intervals are reported. The *P* values reported for comparisons between head-up *vs* supine, head-down *vs* supine, and hyperventilation *vs* hypoventilation were compared by paired Student's *t* test. The *P* values reported for comparisons between HUT and hyperventilation were also compared by paired Student's *t* test. The *P* values reported for Pearson's correlations were calculated by Student's *t* test using linear regression analysis. The *P* values <0.001 (0.05/45 = 0.001) were regarded as significant, corresponding to the Bonferroni correction to control the familywise error rate at 0.05 for the 45 tests (comparisons) performed.

Results

Thirty-three patients [22 males, 11 females, aged 59 (13) yr, height 173 (9) cm, and weight 77 (13) kg] were recruited for this study. Among the 33 patients, three patients were categorized as American Society of Anesthesiologists' (ASA) physical status I, 22 patients were categorized as ASA II, and eight were categorized as ASA III. Due to their concern about low blood pressure, the attending anesthesiologists withdrew five patients from the tilt component of the study, and three from the ventilation component. The data from 28 patients were entered into the tilt analysis database, and data from 30 patients were entered into the ventilation analysis.

Individual MAP, $SctO_2$, and CBV measurements at different body positions are shown in Fig. 1. The physiological measurements at supine, head-up and head-down positions are summarized in Table 1. Compared with supine, the absolute (head-up - supine) and relative [(head-up - supine) / supine * 100%] decreases in $SctO_2$ induced by 30° HUT were 3.5 (2.6)% (*P* <0.001) and 5.1 (3.8)%, respectively, and the absolute and relative decreases in CBV were 0.05 (0.07) mL·100 g^{-1} (*P* <0.001) and 2.3 (3.0)%, respectively. In comparison, the absolute (head-down - supine) and relative [(head-down - supine) / supine * 100%] increases in $SctO_2$ induced by head-down tilt were 1.5 (2.3)% (*P* = 0.001) and 2.4 (3.6)%, respectively, and the absolute and relative increases in CBV were 0.11 (0.10) mL·100 g^{-1} (*P* <0.001) and 4.7 (4.1)%, respectively. Changes in $SctO_2$ and changes in CBV had no correlation with changes in MAP and CO induced by head-up and head-down tilts (*P* > 0.05) (Fig. 3). The correlations between changes in $SctO_2$ and CBV were not significant during HUT (*P* = 0.06) and head-down tilt (*P* = 0.04) (Fig. 5A, B).

Individual $ETCO_2$, $SctO_2$, and CBV measurements during hypoventilation and hyperventilation are shown in Fig. 2. The physiological measurements during hypoventilation and hyperventilation are summarized in Table 2. Compared with mild hypoventilation, the absolute (hyperventilation - hypoventilation) and relative [(hyperventilation - hypoventilation) / hypoventilation * 100%] decreases in $SctO_2$ caused by hyperventilation were 3.0 (1.8)% (P <0.001) and 4.3 (2.6)%, respectively, and the absolute and relative decreases in CBV were 0.06 (0.05) mL·100 g^{-1} (P <0.001) and 2.3 (1.7)%, respectively. Both changes in $SctO_2$ and CBV showed significant correlations with changes in $ETCO_2$ (P <0.001) (Fig. 4). The correlation between changes in $SctO_2$ and CBV caused by hyperventilation was also significant (P <0.001) (Fig. 5C).

In the 27 patients who received both interventions, the decreases in both $SctO_2$ and CBV showed no differences between HUT to 30° and hyperventilation to an $ETCO_2$ of 25 mmHg (from 45 mmHg) (P = 0.3 and P = 0.4, respectively).

Discussion

The unique aspect of this study is that it provides a direct comparison of changes in cerebral oxygenation and cerebral blood volume in the same patients due to hyperventilation and HUT. The major findings from this study using FD-NIRS in healthy surgical patients were that both HUT to 30° and hyperventilation to an $ETCO_2$ of 25 mmHg (from 45 mmHg) caused small but significant decreases in $SctO_2$ and CBV, and the decreases in both $SctO_2$ and CBV were not significantly different between the two conditions. We also found that changes in $SctO_2$ and changes in CBV had no correlation with changes in MAP and CO during head-up and head-down tilts. However, changes in both $SctO_2$ and CBV correlated well with changes in $ETCO_2$ during hyperventilation.

Our study based on 30° HUT in propofol-remifentanil anesthetized patients showed a small decrease in both $SctO_2$ [3.5 (2.6)%] and CBV [0.05 (0.07) mL·100 g^{-1}]. In awake healthy subjects, Hunt *et al.* found a decrease in $SctO_2$ of 2.6 (3.2)% and no change in CBV with 60° HUT using a NIRO 300 spectrophotometer,[14] and Suzuki *et al.* found a decrease in $SctO_2$ of 1.1 (1.0)% with 70° HUT using a PSA-III NIRS instrument.[15] In propofol-anesthetized healthy surgical patients, Lovell *et al.* found a decrease in THC (the measurement used to calculate CBV) of 0.70 (0.99) μMol with 18° HUT using a NIRO 500 spectrophotometer; however, changes in $SctO_2$ were not mentioned.[16] It is noteworthy that none of the above studies was based on FD-NIRS technology. We also observed a small decrease in both $SctO_2$ [3.0 (1.8)%] and CBV [0.06 (0.05) mL·100 g^{-1}] induced by hyperventilation. In propofol-anesthetized rabbits, Cenic *et al.* reported no change in both CBF and CBV based on contrast-enhanced computed tomography measurements when arterial blood carbon dioxide partial pressure ($PaCO_2$) was reduced from 41 to 27 mmHg via hyperventilation.[17] In a subsequent study, the same group confirmed that CBF and CBV reactivity to hyperventilation is absent in propofol but present in rabbits anesthetized with isoflurane.[18] Thus, although our findings are consistent with others in the literature, they may pertain only to patients anesthetized with propofol and remifentanil, and the results should not be extrapolated to patients receiving inhaled anesthetics.

Both HUT and hyperventilation are common interventions in neurosurgical patients to decrease brain bulk.[1,19] The intervention which causes the least decrease in $SctO_2$ and the greatest decrease in CBV would likely be more beneficial to the patient. In this FD-NIRS comparison study, we demonstrated that the decreases in both $SctO_2$ and CBV caused by 30° HUT did not differ significantly with those caused by hyperventilation to an $ETCO_2$ of 25 mmHg (from 45 mmHg). However, before extrapolating these findings to patients with intracranial pathology, a number of important factors should be considered. Our study was

conducted in healthy patients without intracranial disorders. Although the impact of HUT and hyperventilation on CBV is similar, their effects on ICP and brain bulk were not directly compared. In addition to CBV, cerebrospinal fluid (CSF) is another key contributor to intracranial volume and ICP. In addition to the decrease caused by CBV reduction, hydrostatic displacement of CSF (from the cranial cavity to the spinal subarachnoid space) induced by HUT—a property hyperventilation does not possess—might also help to decrease ICP.[20]

It is of interest that changes in $SctO_2$ and changes in CBV have no correlation with changes in both MAP and CO induced by HUT (Fig. 3). This observation differs from our published results where changes in $SctO_2$ correlated with changes in CO, but not MAP, after intravenous vasopressor administration.[10] In the vasopressor study, blood pressure increases while CO decreases after phenylephrine treatment; however, during HUT, both blood pressure and CO decrease. Therefore, it is possible that the insignificant correlation between $SctO_2$ and CO during HUT might be partially explained by the simultaneous hypotension, especially with the MAP lower than the lower limit of cerebral autoregulation [MAP = 43 (12) mmHg with HUT] (Table 1). It is difficult to distinguish the contributions of simultaneous low CO and significant hypotension to decreased cerebral perfusion and oxygenation. These observations imply that the impacts of HUT and vasopressor administration on cerebral hemodynamics are based on different mechanisms. In contrast, the decrease in both $SctO_2$ and CBV induced by hyperventilation correlates well with the decrease in $ETCO_2$ (Fig. 4). It is also interesting that changes in $SctO_2$ and CBV correlate with each other during hyperventilation, but not during head-up and head-down tilts (Fig. 5). A likely explanation is that the cerebral vasoconstriction caused by hyperventilation not only increases cerebrovascular resistance, thus causing a decrease in CBF and $SctO_2$, but also shrinks the cerebral vascular bed, at least the arterial side and perhaps secondarily the venous side, thus causing a decrease in CBV. During HUT, the negative impact on cerebral hemodynamics is mainly due to a reduction in blood pressure.[2,3] As blood pressure drops, cerebral vasodilation takes place in order to maintain a constant CBF.[21] Therefore, a dilated cerebrovascular bed may actually cause no change or an increase in CBV as a consequence. On the other hand, HUT-facilitated venous outflow from the brain may decrease CBV.[22,23] Operating together, these complicated mechanisms may be the reason why HUT-induced changes in $SctO_2$ and CBV do not correlate. In summary, the impacts of HUT and hyperventilation on cerebral hemodynamics are mechanistically different.

There are several methodological limitations to be considered. First, estimation of $PaCO_2$ by $ETCO_2$ has its limitations even though there are data that $ETCO_2$ is a reliable estimate of $PaCO_2$ and the change in $ETCO_2$ strongly approximates the change in $PaCO_2$.[24] For example, the use of the HUT position may significantly change the pulmonary blood flow, increasing the amount of zone 1 ventilation and causing significant dead space ventilation and an enlargement in the gradient between $ETCO_2$ and $PaCO_2$. Without knowing the PaCO2, the extent of hyperventilation is not known. Second, this study was conducted before surgical incision in order to avoid the impact of surgical stimulation on cerebral measurements. It was also done in non-neurosurgical patients with normal ICP in order to acquire “baseline” or normal brain information. Therefore, the clinical significance of the decreases in $SctO_2$ and CBV caused by HUT and hyperventilation was not directly addressed by this study.

The specific FD-NIRS technology used for this study provides a better estimate of absolute measurements than the commonly employed NIRS instruments based on continuous wave (CW) technology which provide only relative measurements.[25] Near infrared photons (~650–1000 nm) penetrate deeply (several centimetres) into tissues. At the wavelengths used in this study, the dominant absorbers (or chromophores) in tissue are oxy- and

deoxyhemoglobin. However, tissues also strongly scatter NIR light, and it is this dominant scattering of the signal that makes it difficult to measure tissue's hemoglobin absorbance accurately.[26] Frequency-domain near-infrared spectroscopy separates the contributions of absorption and scattering to the detected NIR signals, while CW-NIRS does not.[25] This may be important because studies have shown large intersubject variations in brain scattering based on measurements of optical path length in neonates, children, and adults.[27,28] For this reason, changes in hemoglobin saturation reported by CW-NIRS may be affected by factors such as the intersubject variation in tissue scattering. In contrast, FD-NIRS used in this study avoids this confounding factor by direct and continuous measurement of light scattering in the tissue.[7] Therefore, FD-NIRS is regarded as a quantitative method while CW-NIRS is considered a trend monitor only. An additional confounding factor is the contamination of the NIRS signal by extracerebral layers. Multiple studies show that the optode spacing distance determines the ability of NIRS to "see through" scalp and skull.[12,13,29,30] Studies using FD-NIRS in humans and with phantoms have found that extracerebral contamination is negligible when the source-detector spacing is larger than 2 cm.[12,13] Evidence also shows that NIRS measurements are consistent with those made by functional magnetic resonance imaging.[31] In summary, FD-NIRS is not only a quantitative technology by its ability to separate absorption and scattering, but it is also a technology which is likely less affected by the extracerebral tissue layers.

In conclusion, the significant but small decreases in both $SctO_2$ and CBV caused by HUT to 30° and hyperventilation to an $ETCO_2$ of 25 mmHg (from 45 mmHg) in normal healthy individuals are comparable. Changes in $SctO_2$ and CBV do not correlate with changes in MAP and CO during HUT; however, changes in both $SctO_2$ and CBV correlate with changes in $ETCO_2$ during hyperventilation.

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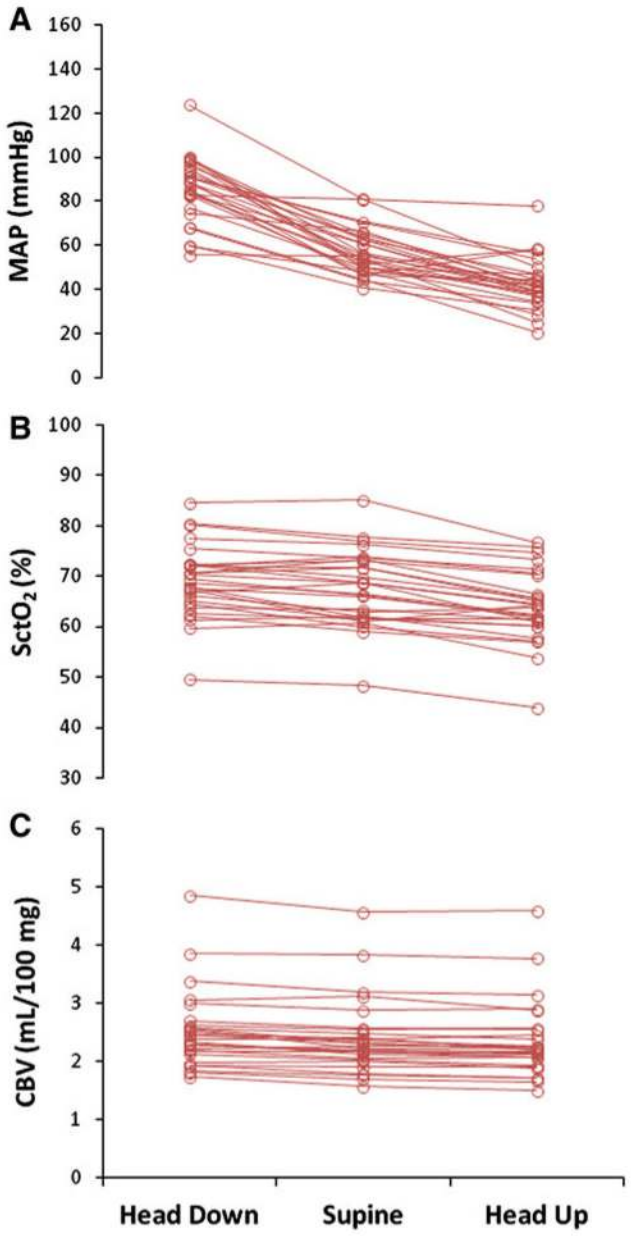

Fig. 1.
Measurements of mean arterial pressure (MAP), cerebral tissue oxygen saturation ($SctO_2$), and cerebral blood volume (CBV) at supine and at 30° head-up and head-down tilts

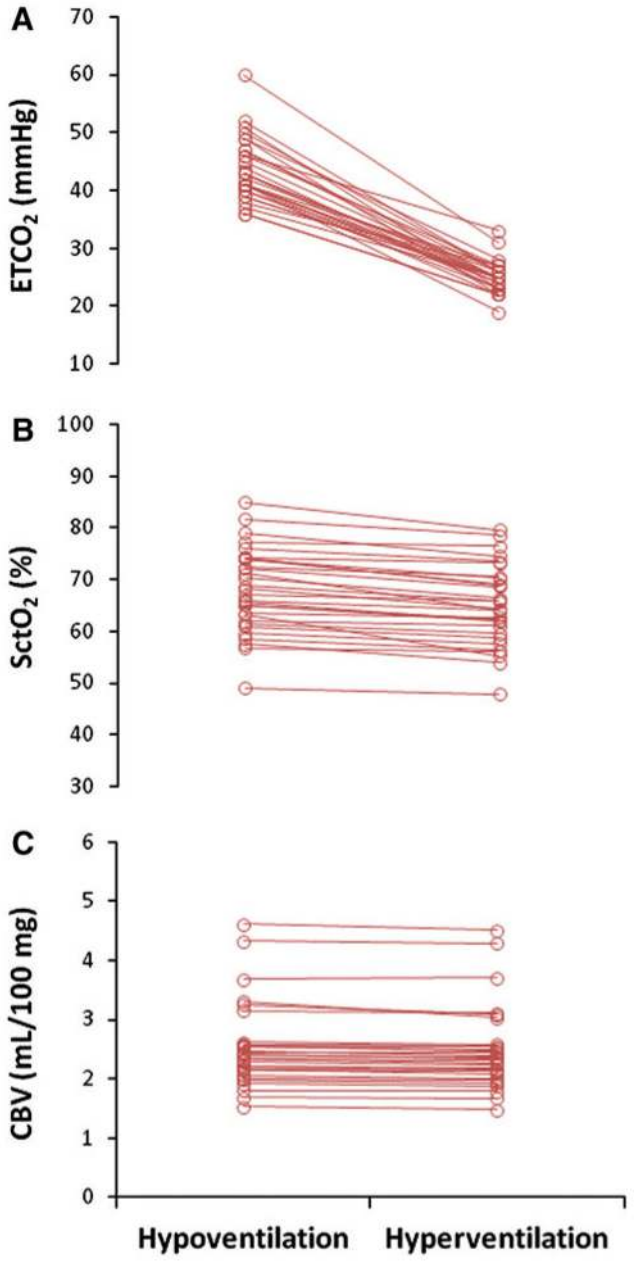

Fig. 2.
Measurements of end-tidal carbon dioxide ($ETCO_2$), cerebral tissue oxygen saturation ($SctO_2$), and cerebral blood volume (CBV) during hypoventilation and hyperventilation

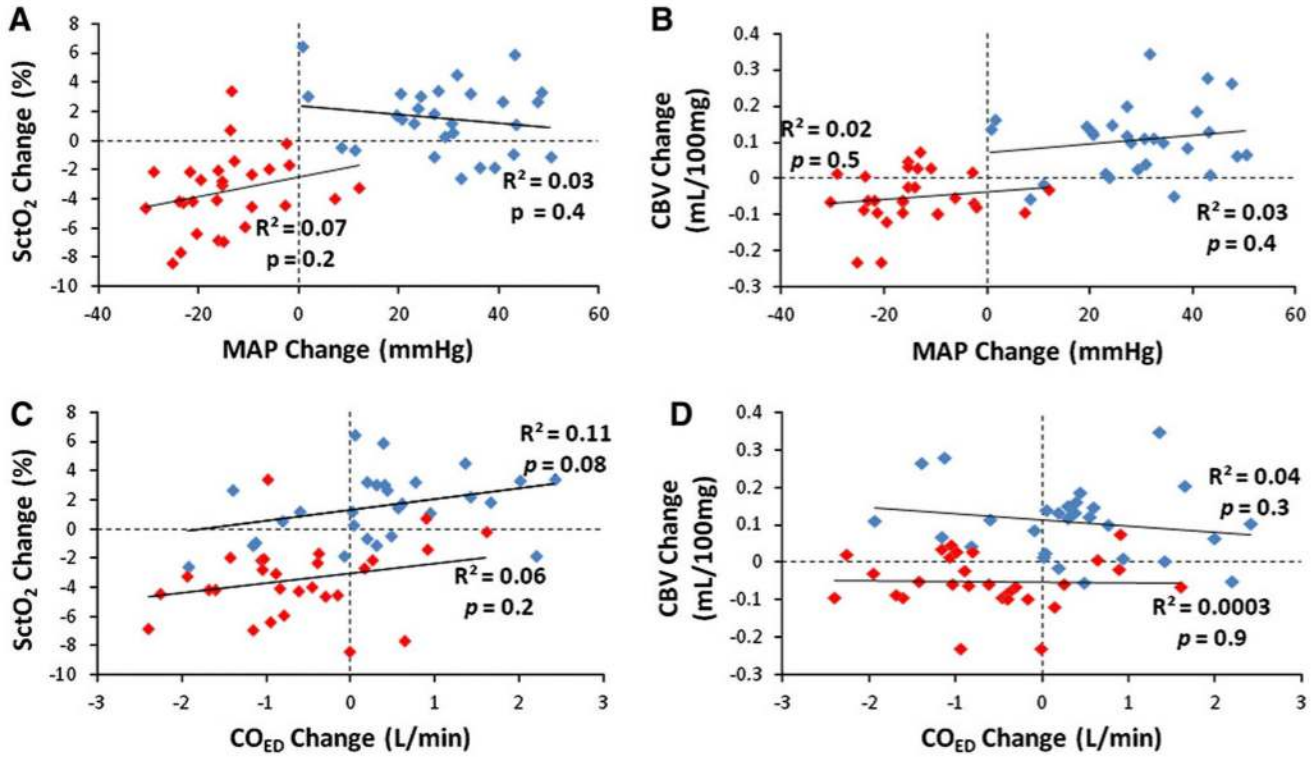

Fig. 3.

Correlations between changes in cerebral and global hemodynamic measurements induced by head-up and head-down tilts. $SctO_2$ = cerebral tissue oxygen saturation; CBV = cerebral blood volume; MAP = mean arterial pressure; CO_{ED} = cardiac output measured by esophageal Doppler; red = changes caused by head-up tilts; blue = changes caused by head-down tilts (Color figure online)

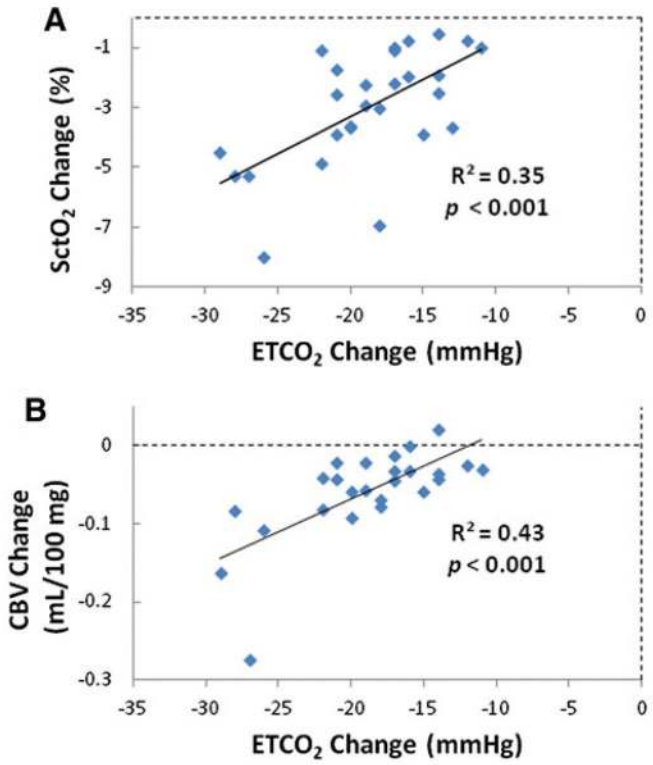

Fig. 4.
Correlations between changes in cerebral hemodynamic measurements and end-tidal carbon dioxide ($ETCO_2$) induced by ventilation adjustments. $SctO_2$ = cerebral tissue oxygen saturation; CBV = cerebral blood volume

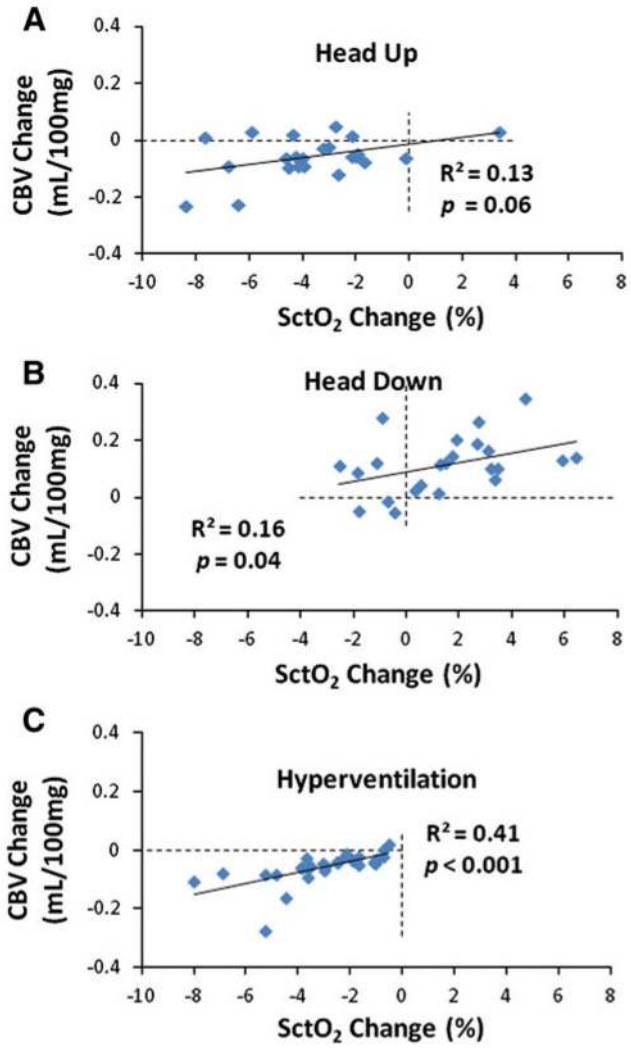

Fig. 5.
Correlations between changes in cerebral blood volume (CBV) and cerebral tissue oxygen saturation ($SctO_2$) induced by body tilts and ventilation adjustment

Table 1

Physiological measurements at supine, head-up, and head-down positions ($n = 28$)

	Supine[1]	Head Up				Head Down			
		Measurement	Change[2]	CI (95%)	*P* Value	Measurement	Change[2]	CI (95%)	*P* Value
MAP (mmHg)	57 (11)	43 (12)	−14 (10)	−18.1 to −10.6	<0.001	86 (15)	28 (14)	24.2 to 34.0	<0.001
CO_{ED} (L·min^{-1})	5.8 (1.3)	5.2 (1.5)	−0.6 (1.0)	−1.0 to −0.3	0.001	6.2 (1.8)	0.3 (1.0)	−0.05 to 0.7	0.1
CO_{FT} (L·min^{-1})	4.8 (1.4)	4.2 (1.5)	−0.6 (1.2)	−1.0 to −0.2	0.01	6.1 (1.8)	1.3 (1.0)	0.9 to 1.6	<0.001
HR (beats·min^{-1})	65.5 (10.7)	68.9 (16.0)	3.3 (9.8)	−0.2 to 7.1	0.1	63.2 (10.3)	−2.2 (6.8)	−4.8 to 0.3	0.1
SpO_2 (%)	99.2 (1.3)	98.7 (2.7)	−0.4 (1.7)	−1.1 to 0.2	0.2	99.1 (2.0)	0 (1.2)	−0.5 to 0.4	0.9
$ETCO_2$ (mmHg)	36 (4)	34 (4)	−2 (3)	−3.2 to −1.2	<0.001	36 (4)	0 (3)	−0.9 to 1.0	0.9
BIS	28 (9)	30 (9)	1 (4)	−0.4 to 2.7	0.2	27 (12)	−1 (9)	−4.4 to 2.2	0.5
$SctO_2$ (%)	67.5 (7.5)	64.0 (7.1)	−3.5 (2.6)	−4.4 to −2.5	<0.001	69.0 (7.1)	1.5 (2.3)	0.7 to 2.4	0.001
THC (μMol)	36.0 (9.0)	35.2 (9.0)	−0.8 (1.2)	−1.2 to −0.4	0.001	37.6 (9.4)	1.6 (1.5)	1.1 to 2.2	<0.001
CBV (mL·100 g^{-1})	2.38 (0.64)	2.33 (0.65)	−0.05 (0.07)	−0.08 to −0.02	<0.001	2.49 (0.66)	0.11 (0.10)	0.07 to 0.1	<0.001

Data are expressed as mean (standard deviation); [1] = averaged measurements before and after whole body tilt; Change[2] = head tilt - supine; CI = confidence interval; MAP = mean arterial pressure; CO_{ED} = cardiac output by esophageal Doppler; CO_{FT} = cardiac output by Vigileo FloTrac; HR = heart rate; SpO_2 = oxygen saturation by pulse oximetry; $ETCO_2$ = end-tidal carbon dioxide; BIS = Bispectral index; $SctO_2$ = cerebral tissue oxygen saturation; THC = total hemoglobin concentration (cerebral tissue); CBV = cerebral blood volume

Table 2

Physiological measurements during hypoventilation and hyperventilation ($n = 30$)

	Hypoventilation	Hyperventilation	Change[1]	CI (95%)	*P* Value
MAP (mmHg)	**74 (16)**	**73 (17)**	**−1 (7)**	**−3.6 to 1.5**	**0.4**
CO_{ED} (L·min^{-1})	6.4 (1.6)	6.2 (1.5)	−0.2 (1.1)	−0.6 to 0.2	0.3
CO_{FT} (L·min^{-1})	5.9 (1.7)	5.6 (2.0)	−0.3 (1.0)	−0.6 to 0.08	0.1
HR (beats·min^{-1})	61.3 (8.9)	64.5 (12.3)	3.2 (6.0)	1.1 to 5.3	0.006
SpO_2 (%)	98.9 (1.6)	99.3 (1.3)	0.4 (0.8)	0.2 to 0.7	0.005
$ETCO_2$ (mmHg)	44 (5)	25 (3)	−19 (5)	−20.1 to −16.9	<0.001
BIS	34 (9)	32 (8)	−2 (7)	−4.4 to 0.3	0.1
$SctO_2$ (%)	68.0 (8.1)	65.0 (7.7)	−3.0 (1.8)	−3.6 to −2.3	<0.001
THC (μMol)	37.9 (9.9)	37.1 (9.5)	−0.9 (0.9)	−1.2 to −0.6	<0.001
CBV (mL·100 g^{-1})	2.53 (0.71)	2.47 (0.70)	−0.06 (0.05)	−0.08 to −0.04	<0.001

Data are expressed as mean (standard deviation); Change[1] = hyperventilation - hypoventilation; CI = confidence interval; MAP = mean arterial pressure; CO_{ED} = cardiac output by esophageal Doppler; CO_{FT} = cardiac output by Vigileo FloTrac; HR = heart rate; SpO_2 = oxygen saturation by pulse oximetry; $ETCO_2$ = end-tidal carbon dioxide; BIS = bispectral index; $SctO_2$ = cerebral tissue oxygen saturation; THC = total hemoglobin concentration (cerebral tissue); CBV = cerebral blood volume