Title

Impact of stepwise hyperventilation on cerebral tissue oxygen saturation in anesthetized patients: a mechanistic study

Journal

Acta Anaesthesiologica Scandinavica, 57(5)

ISSN

0001-5172

Authors

ALEXANDER, BS

GELB, AW

MANTULIN, WW

et al.

Publication Date

2013-05-01

DOI

10.1111/aas.12054

Peer reviewed

Published in final edited form as:
Acta Anaesthesiol Scand. 2013 May ; 57(5): 604–612. doi:10.1111/aas.12054.

Impact of stepwise hyperventilation on cerebral tissue oxygen saturation in anesthetized patients: a mechanistic study

B. S. Alexander[1], **A. W. Gelb**[2], **W. W. Mantulin**[3], **A. E. Cerussi**[3], **B. J. Tromberg**[3], **Z. Yu**[4], **C. Lee**[5], and **L. Meng**[6]

[1]Irvine School of Medicine, University of California, Irvine, CA, USA

[2]Department of Anesthesia and Perioperative Care, University of California, San Francisco, CA, USA

[3]Beckman Laser Institute, University of California, Irvine, CA, USA

[4]Department of Statistics, University of California, Irvine, CA, USA

[5]Department of Anesthesiology and Perioperative Care, University of California, Irvine, CA, USA

[6]Department of Anesthesiology, Duke University Medical Center, Durham, NC, USA

Abstract

Background—While the decrease in blood carbon dioxide (CO_2) secondary to hyperventilation is generally accepted to play a major role in the decrease of cerebral tissue oxygen saturation ($SctO_2$), it remains unclear if the associated systemic hemodynamic changes are also accountable.

Methods—Twenty-six patients (American Society of Anesthesiologists I–II) undergoing nonneurosurgical procedures were anesthetized with either propofol-remifentanil (n = 13) or sevoflurane (n = 13). During a stable intraoperative period, ventilation was adjusted stepwise from hypoventilation to hyper-ventilation to achieve a progressive change in end-tidal CO_2 ($ETCO_2$) from 55 to 25 mmHg. Minute ventilation, $SctO_2$, $ETCO_2$, mean arterial pressure (MAP), and cardiac output (CO) were recorded.

Results—Hyperventilation led to a $SctO_2$ decrease from 78 ± 4% to 69 ± 5% (Δ = −9 ± 4%, P < 0.001) in the propofol-remifentanil group and from 81 ± 5% to 71 ± 7% (Δ = −10 ± 3%, P < 0.001) in the sevoflurane group. The decreases in $SctO_2$ were not statistically different between these two groups (P = 0.5). $SctO_2$ correlated significantly with $ETCO_2$ in both groups (P < 0.001). $SctO_2$ also correlated significantly with MAP (P < 0.001) and CO (P < 0.001) during propofol-remifentanil, but not sevoflurane (P = 0.4 and 0.5), anesthesia.

Conclusion—The main mechanism responsible for the hyperventilation-induced decrease in $SctO_2$ is hypocapnia during both propofol-remifentanil and sevoflurane anesthesia. Hyperventilation-associated increase in MAP and decrease in CO during propofol-remifentanil,

Address: *Lingzhong Meng* Department of Anesthesiology Duke University Medical Center Box 3094 Durham NC 27710 USA meng.lingzhong@gmail.com.

Conflicts of interest: The authors (W. W. M., A. E. C., and B. J. T.) consult for ISS, Inc., USA.

but not sevoflurane, anesthesia may also contribute to the decrease in $SctO_2$ but to a much smaller degree.

POSITIVE-PRESSURE ventilation is frequently adjusted in intubated patients. For example, hyperventilation is used in patients with elevated intracranial pressure or to facilitate neurosurgical procedures,[1,2] and hypoventilation ('permissive hypercapnia') is used in patients with acute respiratory distress syndrome as part of protective lung ventilatory strategy.[3] Cerebral blood flow (CBF) changes as a consequence to a change in blood carbon dioxide (CO_2) level.[4] If hemoglobin concentration, oxygen saturation, and cerebral metabolic rate are considered constant, a decrease in CBF will lead to a decrease in the amount of oxygen being delivered to the brain. As a consequence, cerebral oxygenation (the balance between cerebral oxygen demand and supply) will decrease. It has been shown that the change in cerebral oxygenation secondary to an adjustment in mechanical ventilation can be measured by cerebral tissue oxygen saturation ($SctO_2$) based on frequency-domain near-infrared spectroscopy (NIRS) technology.[5,6] However, it is not clear if the mechanism responsible for the change in $SctO_2$ is exclusively due to the change in blood CO_2 level or if changes in intrathoracic pressure and associated secondary changes in systemic hemodynamics, including blood pressure and cardiac output (CO), also contribute to the $SctO_2$ change. The influence of anesthetic choice, propofol-remifentanil vs. sevoflurane, is also uncertain, especially considering the fact that potent inhalational agents possess intrinsic cerebral vasodilatory effect while intravenous agents do not.[7] In this study, it was our hypothesis that the decrease in $SctO_2$ induced by stepwise hyperventilation is due to both changes in blood CO_2 level and changes in systemic hemodynamics. To test this hypothesis, we carried out this mechanistic study in which $SctO_2$, end-tidal CO_2 ($ETCO_2$), mean arterial pressure (MAP), and CO were continuously and simultaneously measured throughout a stepwise increase in minute ventilation from hypoventilation ($ETCO_2$ = 55 mmHg) to hyperventilation ($ETCO_2$ = 25 mmHg) in patients anesthetized with either propofol-remifentanil or sevoflurane.

Methods

The study was approved by the Institutional Research Board at the University of California, Irvine, California, USA. Nonneurosurgical adult patients with an American Society of Anesthesiologists (ASA) physical status I–II were recruited. Informed written consents for research were obtained. Exclusion criteria were: neurological disease, symptomatic cardiac and respiratory diseases, systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, and diabetes mellitus.

A quantitative frequency-domain NIRS device, Oxiplex TS cerebral oximeter (ISS Inc., Champaign, IL, USA), was used to measure $SctO_2$.[8] The specifics of this technology have been previously reported.[5,6,9] Minute ventilation and $ETCO_2$ were determined using the built-in spirometry and gas analyzer in the anesthesia machine (Aisys, GE Healthcare, Madison, WI, USA). MAP was monitored at the external ear canal level via a 20-gauge catheter placed in radial artery and connected to an arterial pressure transduction system (Vigileo-FloTrac, Edwards Lifesciences, Irvine, CA, USA). CO was monitored using esophageal Doppler (CardioQ, Deltex Medical, Chichester, West Sussex, UK). The depth of

anesthesia was monitored via the bispectral index (BIS) monitor (S/5™ M-BIS, GE Healthcare, Madison, WI, USA).

Following anesthesia induction with fentanyl (1.5–2 mcg/kg) and propofol (2–3 mg/kg), the patient was intubated, and anesthesia was maintained with either propofol-remifentanil or sevoflurane at the discretion of the attending anesthesiologist. The level of anesthesia was adjusted to maintain a BIS value between 30 and 50, and no further adjustment occurred during the formal study period. Muscle relaxation was maintained with cisatracurium. Pressure-controlled ventilation was used with the inspired oxygen percentage of 50% in an air-oxygen mixture, inspiratory to expiratory time ratio of 1 : 2, and positive end-expiratory pressure set to zero. During a stable intraoperative period, the formal study began with hypoventilation (ventilation pressure set between 8 and 12 cmH_2O and the respiratory rate set between 4 and 6 breaths per minute) to achieve a starting $ETCO_2$ of 55 mmHg. Once this end-point of hypoventilation was achieved and stabilized for 10 min, the first ventilatory adjustment was made by increasing the ventilation pressure 2 cmH_2O and respiratory rate one breath per minute. The same adjustment was repeated every 5 min to gradually increase minute ventilation until the end-point of hyperventilation, an $ETCO_2$ of 25 mmHg, was reached. Minute ventilation, $ETCO_2$, $SctO_2$, MAP, CO, BIS, cerebral tissue oxy-hemoglobin concentration, cerebral tissue deoxy-hemoglobin concentration, cerebral tissue total hemoglobin concentration, stroke volume, heart rate, and finger pulse oxygen saturation (SpO_2) were continuously monitored and recorded at least every 60 s throughout the study period.

Data were expressed as mean ± standard deviation. Demographics were analyzed to ensure age, gender, height, weight, and body mass index were not significantly different between propofol-remifentanil and sevoflurane groups. This was done using both unpaired Student's *t*-test and Mann–Whitney test for quantitative variables, and both Pearson's chi-square test and Fisher's exact test for qualitative variables. Both unpaired Student's *t*-test and Mann–Whitney test were used to analyze the difference of the changes in $SctO_2$ (from $ETCO_2$ of 55 to 25 mmHg) between propofol-remifentanil and sevoflurane groups. *P*-values reported are agreeable with both parametric and nonparametric analyses when applicable. A repeated measures general linear model (SPSS Version 20.0, IBM Corporation, Armonk, NY, USA) was used to determine the significance of hypocapnia, normocapnia, and hypercapnia on each physiologic parameter. Because our data are longitudinal, linear mixed-effects models were used to test whether there is a significant correlation between a measured variable and its explanatory variables. Specifically, we first fit a linear mixed-effects model with random effects for both intercept and slope; we then fit a reduced model with the slope removed. The significance of a correlation was determined by the likelihood ratio test that compares the likelihood of two models. A similar procedure was used to test the significance of a particular variant or a particular set of variants in our multivariate analysis. *P*-values less than 0.05 were regarded as significant. The statistical analysis was conducted using the R package (http://cran.r-project.org/).

Results

Twenty-six patients (n = 13 for both propofol-remifentanil and sevoflurane groups) were included in data analysis from a total of 28 patients recruited. One patient was excluded because of incomplete CO data; the other was due to unanticipated surgical position change. Patient's demographic and surgery data are summarized in Table 1. There were no significant differences in age, gender, height, weight, and body mass index between propofol-remifentanil and sevoflurane groups.

The infusion rates of propofol and remifentanil were 92 ± 3 mcg/kg/min and 0.4 ± 0.2 mcg/kg/min, respectively. The end-tidal sevoflurane level was 1.9 ± 0.4%. The hyperventilation protocol caused a continuous and consistent change in both minute ventilation and $ETCO_2$ from hypoventilation ($ETCO_2$ = 55 mmHg) to hyperventilation ($ETCO_2$ = 25 mmHg) in both propofol-remifentanil and sevoflurane groups. The time spent for the full range of change was 36 ± 7 min for both groups. The physiological data were summarized in Table 2 (propofol-remifentanil group) and Table 3 (sevoflurane group).

Throughout the stepwise increase in minute ventilation, $SctO_2$ gradually decreased from 78 ± 4% to 69 ± 5% (Δ = −9 ± 4%) in the propofol-remifentanil group (Fig. 1A) and from 81 ± 5% to 71 ± 7% (Δ = −10 ± 3%) in the sevoflurane group (Fig. 1B). Even though the decreases in $SctO_2$ from hypoventilation to hyperventilation were significant in both groups (P < 0.001, Tables 2 and 3), the absolute decreases in $SctO_2$ were not significantly different between these two groups (P = 0.5, −9 ± 4% vs. −10 ± 3%). Minute ventilation correlated significantly with $ETCO_2$ in both anesthetic groups (P < 0.001). Stepwise hyperventilation caused a consistent increase in MAP (Fig. 1C) and a consistent decrease in CO (Fig. 1E) in the propofol-remifentanil, but not the sevoflurane (Fig. 1D and F), group. Minute ventilation and BIS were not significantly correlated in both propofol-remifentanil (P = 0.7) and sevoflurane (P = 0.7) groups.

$SctO_2$ correlated significantly with $ETCO_2$ in both propofol-remifentanil (Fig. 2A) and sevoflurane (Fig. 2B) groups. $SctO_2$ also correlated significantly with both MAP (Fig. 2C) and CO (Fig. 2E) in the propofol-remifentanil, but not the sevoflurane (Fig. 2D and F), group. Further multivariate analysis of the propofol-remifentanil group revealed the following: When $ETCO_2$ and CO are taken into account, MAP is not significant (P = 0.3); when $ETCO_2$ and MAP are taken into account, CO is significant (P < 0.001); and when $ETCO_2$ is taken into account only, MAP and CO jointly are significant (P < 0.001).

Discussion

This study showed that stepwise hyperventilation, from $ETCO_2$ = 55 mmHg to $ETCO_2$ = 25 mmHg, caused a progressive decrease in $SctO_2$ in both propofol-remifentanil ($\Delta SctO_2 \approx$ −9%) and sevoflurane ($\Delta SctO_2 \approx$ −10%) anesthetized patients. As anticipated, $SctO_2$ correlated significantly with both minute ventilation and $ETCO_2$ in both groups. However, it also correlated significantly with MAP and CO during propofol-remifentanil, but not sevoflurane, anesthesia. This finding is in concordance with the result that the stepwise

hyperventilation in this study also caused a consistent increase in MAP and a consistent decrease in CO in propofol-remifentanil, but not sevoflurane, anesthetized patients.

We previously showed that hypoventilation correlated with a higher $SctO_2$ and hyperventilation correlated with a lower $SctO_2$ in propofol-remifentanil anesthetized patients.[5,6] Even though hyperventilation-induced hypocapnia may have played a major role in the $SctO_2$ decrement, the full extent of its influence (magnitude and mechanism) remained unclear. The mechanism responsible for the hyperventilation-induced decrease in $SctO_2$ has both theoretical and practical implications and needs to be carefully considered.

Cerebral oximetry based on frequency-domain NIRS technology quantitatively measures oxy- and deoxy-hemoglobin concentrations in pooled cerebral blood.[8] A decrease in NIRS-measured $SctO_2$ is attributed to one or a combination of the following mechanisms: (1) increased cerebral metabolic rate of oxygen; (2) decreased oxygen delivery to the brain; and (3) decreased arterial and/or increased venous blood contribution(s) to NIRS measurement. Mechanism 1 is unlikely to be true because this study was conducted during a stable intraoperative period in anesthetized patients. Moreover, the BIS measurement remained stable throughout the study period.

Mechanism 2, decreased oxygen delivery to the brain, is most likely the major cause of the observed decrease in $SctO_2$. Oxygen delivery to the brain must have been decreased because of the decrease in CBF as a consequence of the hyperventilation-induced hypocapnia. However, the potential contribution from hyperventilation-associated systemic hemodynamic changes cannot be ignored. Our data showed that stepwise hyperventilation caused a consistent increase in MAP and a consistent decrease in CO during propofol-remifentanil, but not sevoflurane, anesthesia. According to cerebral autoregulation,[10] an increased MAP will cause an increase in CBF if the cerebral perfusion pressure (CPP) is below the lower limit or if the autoregulatory mechanism is impaired; on the other hand, an increased MAP will not cause any change in CBF if the CPP is above the lower limit (and below the upper limit) and the autoregulatory mechanism is intact. Therefore, the increased MAP during propofol-remifentanil anesthesia in this study, no matter the resultant CPP is below or above the lower limit of cerebral autoregulation, is unlikely to have caused a decrease in CBF and contributed to the decrease in oxygen delivery to the brain (mechanism 2). However, the decreased CO during propofol-remifentanil anesthesia in this study may have contributed to the decrease in $SctO_2$ due to a decrease in oxygen delivery to the brain because it has been previously shown that a decrease in CO can cause a decrease in CBF.[11] Additionally, our published data have already demonstrated that $SctO_2$ decreases when CO is decreased, and there is a significant correlation between the decreases in $SctO_2$ and CO, after phenylephrine bolus treatment.[5,9]

Interestingly, the increase in MAP and decrease in CO throughout stepwise hyperventilation only occurred in patients anesthetized with propofol-remifentanil, but not sevoflurane. Our results imply that the systemic hemodynamic changes are due to an increased systemic vascular resistance (SVR) during propofol-remifentanil anesthesia (Table 2). However, it is not clear why the effects of hyperventilation on SVR during propofol-remifentanil or sevoflurane anesthesia are different. It is also difficult to quantify or apportion the

contributions from the decrease in CO_2 vs. the decrease in CO to the $SctO_2$ decrement in the propofol-remifentanil group. If the decrease in CO had made a major contribution to the decrease in $SctO_2$ during hyperventilation, we would have seen a lesser decrease in $SctO_2$ during sevoflurane anesthesia than propofol-remifentanil anesthesia because the former did not cause a decrease in CO. However, the decreases in $SctO_2$ are actually comparable between sevoflurane (≈ 10%) and propofol-remifentanil (≈ 9%). Therefore, we speculate that the contribution of the CO decrement to the decrease in $SctO_2$ during hyperventilation is minor under propofol-remifentanil anesthesia.

Mechanism 3, decreased arterial and/or increased venous blood contribution(s) to NIRS measurement, is also a possible contributor to the observed decrease in $SctO_2$. A decreased arterial blood contribution to NIRS measurement, and thus a decrease in $SctO_2$, may have occurred if hypocapnia-mediated cerebral vasoconstriction occurs mainly at the arteriolar vascular bed. There is evidence supporting this mechanism using positron emission tomography in awake volunteers.[12] Moreover, cerebral vasoconstriction must have occurred when MAP is progressively increased by stepwise hyperventilation during propofol-remifentanil anesthesia in order to maintain a constant CBF according to cerebral autoregulation. Therefore, a decreased arterial blood contribution to NIRS measurement may have also occurred if the autoregulatory vasoconstriction takes place primarily at the arterial/arteriolar vascular bed. It is worthwhile to emphasize that the decreased arterial blood contribution secondary to autoregulatory vasoconstriction does not occur during sevoflurane anesthesia because hyperventilation does not cause a consistent MAP increase in sevoflurane-anesthetized patients. Nonetheless, the contribution of the increased MAP to the decreased $SctO_2$ due to a decreased arterial blood contribution to NIRS measurement must be trivial, if any, because the arterial blood is a very small portion of the pooled cerebral blood targeted by NIRS.[13]

We did not measure jugular bulb oxygen saturation (SjO_2) in this study. Therefore, we cannot tell how SjO_2 would be decreased by stepwise hyper-ventilation. SjO_2 measures cerebral venous blood and is regarded as an invasive procedure. In contrast, $SctO_2$ measures an admixture of arterial, capillary, and venous blood and is regarded as a noninvasive technology. It is thus not surprising to see that the normal range of SjO_2 values is much lower than $SctO_2$ because of the lack of arterial blood contribution.[14,15] The poor agreement between changes in SjO_2 and $SctO_2$ in various clinical situations may also be mainly caused by the distinct targets (venous vs. mixed blood) being measured by SjO_2 and $SctO_2$.[16,17] In addition, we did not perform a power analysis at the outset of the study. As statistical power depends highly on sample size, the insignificant results in sevoflurane patients (correlations between $SctO_2$ and MAP or CO) could be due to the lack of statistical power of our current sample size. For example, using the effect size estimated from our data, the power for detecting a significant correlation between CO and minute ventilation in sevoflurane would increase from 18% to 90% if we increase the sample size from 13 to 130. However, Fig. 2F shows that the effect is unlikely to be clinically significant despite the fact that statistical significance could occur if we increase our sample size. Another limit was that our study was not randomized between propofol-remifentanil and sevoflurane anesthesia. This was due to that fact that, at the outset of the study, we were mainly aiming at a mechanistic exploration of the effects of progressive hyperventilation, not a comparison between

different agents. Even though the demographic characters were comparable between the two groups, randomization would have improved the quality of the study.

Clinical usage of cerebral oximetry based on NIRS technology is gaining popularity because of its potential value in improving patient's outcome.[18] Understanding the technical principles and the physiologic mechanisms behind the measured number is crucial for its appropriate clinical application. Among all factors which can affect $SctO_2$ measurement, ventilation adjustments are one of the most common. To the best of our knowledge, this study is the first to describe a continuous plot between minute ventilation and $SctO_2$ across the clinical $ETCO_2$ range from 25 to 55 mmHg. The information obtained in this study is helpful in managing ventilation and cerebral oxygenation in patients who are at high risk of cerebral ischemia and hypoxia. Even though the 9–10% absolute decrease in $SctO_2$ was well tolerated by the healthy patients in this study, it may impose significant risk in patients with marginal cerebral perfusion and oxygenation. The $SctO_2$ threshold of cerebral ischemia and hypoxia in various clinical situations is still under exploration. For example, Al-Rawi et al. found that a relative decrease in $SctO_2$ of 13% correlates with clinically significant cerebral ischemia in patients undergoing carotid artery surgery.[19]

In summary, this study shows that the main mechanism responsible for hyperventilation-induced decrease in $SctO_2$ is hypocapnia in both propofol-remifentanil and sevoflurane-anesthetized patients. Hyperventilation causes a consistent increase in MAP and a consistent decrease in CO during propofol-remifentanil, not sevoflurane, anesthesia. It is possible that hyperventilation-induced increase in MAP and decrease in CO may both have contributed to the decrease in $SctO_2$ based on different mechanisms; however, the contribution is most likely of small magnitude. The different responses of MAP and CO to stepwise hyperventilation during propofol-remifentanil or sevoflurane anesthesia may be due to their distinctive effects on SVR; however, the underlying mechanism is unknown.

Acknowledgments

We acknowledge the generous loan of the Oxiplex TX oximeter from ISS, Inc, USA. We also thank Guo Chen, MD (Chengdu, China), for her help in data collection.

Funding: Supported by the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH) through the following programs in the United States: the Institute for Clinical and Translational Science (ICTS) grant UL1 RR031985 (BJT, WWM); the Laser Microbeam and Medical Program [LAMMP, an NIH BRTP resource (P41-RR01192)] (BJT, AEC); the US Army SBIR Program (Contract W81XWH-09-C-0006, AEC); and the Laboratory for Fluorescence Dynamics (LFD) grant P41 RR03155 (WWM). Also supported by the Department of Anesthesiology and Perioperative Care, University of California, Irvine, California, USA.

References

1. Curley G, Kavanagh BP, Laffey JG. Hypocapnia and the injured brain: more harm than benefit. Crit Care Med. 2010; 38:1348–59. [PubMed: 20228681]
2. Gelb AW, Craen RA, Rao GS, Reddy KR, Megyesi J, Mohanty B, Dash HH, Choi KC, Chan MT. Does hyperventilation improve operating condition during supratentorial craniotomy? A multicenter randomized crossover trial. Anesth Analg. 2008; 106:585–94. table of contents. [PubMed: 18227320]
3. Ni Chonghaile M, Higgins B, Laffey JG. Permissive hypercapnia: role in protective lung ventilatory strategies. Curr Opin Crit Care. 2005; 11:56–62. [PubMed: 15659946]

4. Harper AM, Glass HI. Effect of alterations in the arterial carbon dioxide tension on the blood flow through the cerebral cortex at normal and low arterial blood pressures. J Neurol Neurosurg Psychiatry. 1965; 28:449–52. [PubMed: 5838479]
5. Meng L, Gelb AW, Alexander BS, Cerussi AE, Tromberg BJ, Yu Z, Mantulin WW. Impact of phenylephrine administration on cerebral tissue oxygen saturation and blood volume is modulated by carbon dioxide in anaesthetized patients. Br J Anaesth. 2012; 108:815–22. [PubMed: 22391890]
6. Meng L, Mantulin WW, Alexander BS, Cerussi AE, Tromberg BJ, Yu Z, Laning K, Kain ZN, Cannesson M, Gelb AW. Head-up tilt and hyperventilation produce similar changes in cerebral oxygenation and blood volume: an observational comparison study using frequency-domain near-infrared spectroscopy. Can J Anaesth. 2012; 59:357–65. [PubMed: 22234820]
7. Matta BF, Heath KJ, Tipping K, Summors AC. Direct cerebral vasodilatory effects of sevoflurane and isoflurane. Anesthesiology. 1999; 91:677–80. [PubMed: 10485778]
8. Fantini S, Franceschini MA, Maier JS, Walker SA, Barbieri B, Gratton E. Frequency-domain multichannel optical detector for noninvasive tissue spectroscopy and oximetry. Opt Eng. 1995; 34:32–42.
9. Meng L, Cannesson M, Alexander BS, Yu Z, Kain ZN, Cerussi AE, Tromberg BJ, Mantulin WW. Effect of phenylephrine and ephedrine bolus treatment on cerebral oxygenation in anaesthetized patients. Br J Anaesth. 2011; 107:209–17. [PubMed: 21642644]
10. Paulson OB, Strandgaard S, Edvinsson L. Cerebral autoregulation. Cerebrovasc Brain Metab Rev. 1990; 2:161–92. [PubMed: 2201348]
11. Ogoh S, Brothers RM, Barnes Q, Eubank WL, Hawkins MN, Purkayastha S, O-Yurvati A, Raven PB. The effect of changes in cardiac output on middle cerebral artery mean blood velocity at rest and during exercise. J Physiol. 2005; 569:697–704. [PubMed: 16210355]
12. Ito H, Ibaraki M, Kanno I, Fukuda H, Miura S. Changes in the arterial fraction of human cerebral blood volume during hypercapnia and hypocapnia measured by positron emission tomography. J Cereb Blood Flow Metab. 2005; 25:852–7. [PubMed: 15716851]
13. Watzman HM, Kurth CD, Montenegro LM, Rome J, Steven JM, Nicolson SC. Arterial and venous contributions to near-infrared cerebral oximetry. Anesthesiology. 2000; 93:947–53. [PubMed: 11020744]
14. Chieregato A, Calzolari F, Trasforini G, Targa L, Latronico N. Normal jugular bulb oxygen saturation. J Neurol Neurosurg Psychiatry. 2003; 74:784–6. [PubMed: 12754351]
15. Davie SN, Grocott HP. Impact of extracranial contamination on regional cerebral oxygen saturation: a comparison of three cerebral oximetry technologies. Anesthesiology. 2012; 116:834–40. [PubMed: 22343469]
16. Jeong H, Jeong S, Lim HJ, Lee J, Yoo KY. Cerebral oxygen saturation measured by near-infrared spectroscopy and jugular venous bulb oxygen saturation during arthroscopic shoulder surgery in beach chair position under sevoflurane-nitrous oxide or propofol-remifentanil anesthesia. Anesthesiology. 2012; 116:1047–56. [PubMed: 22421420]
17. Yoshitani K, Kawaguchi M, Iwata M, Sasaoka N, Inoue S, Kurumatani N, Furuya H. Comparison of changes in jugular venous bulb oxygen saturation and cerebral oxygen saturation during variations of haemoglobin concentration under propofol and sevoflurane anaesthesia. Br J Anaesth. 2005; 94:341–6. [PubMed: 15591331]
18. Vohra HA, Modi A, Ohri SK. Does use of intra-operative cerebral regional oxygen saturation monitoring during cardiac surgery lead to improved clinical outcomes? Interact Cardiovasc Thorac Surg. 2009; 9:318–22. [PubMed: 19447799]
19. Al-Rawi PG, Kirkpatrick PJ. Tissue oxygen index: thresholds for cerebral ischemia using near-infrared spectroscopy. Stroke. 2006; 37:2720–5. [PubMed: 17008623]

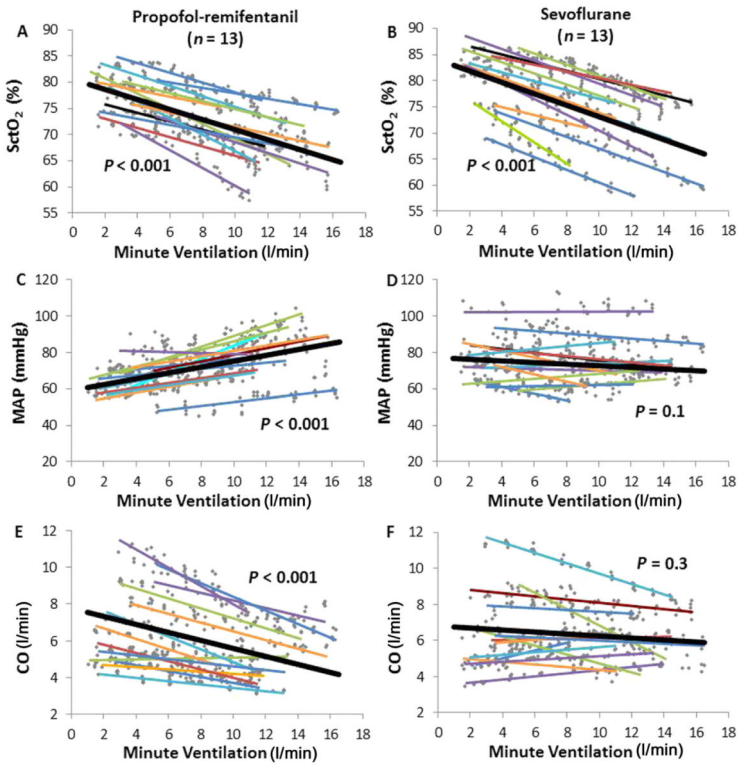

Fig. 1.

Correlations between minute ventilation and cerebral tissue oxygen saturation ($SctO_2$, A and B), mean arterial pressure (MAP, E and F), and cardiac output (CO, G and H) in patients anesthetized with propofol-remifentanil (A, C, and E) and sevoflurane (B, D, and F). Lightly colored lines are individual patients and the dark bold lines are the average. The interval between adjacent data points for each patient is 60 s.

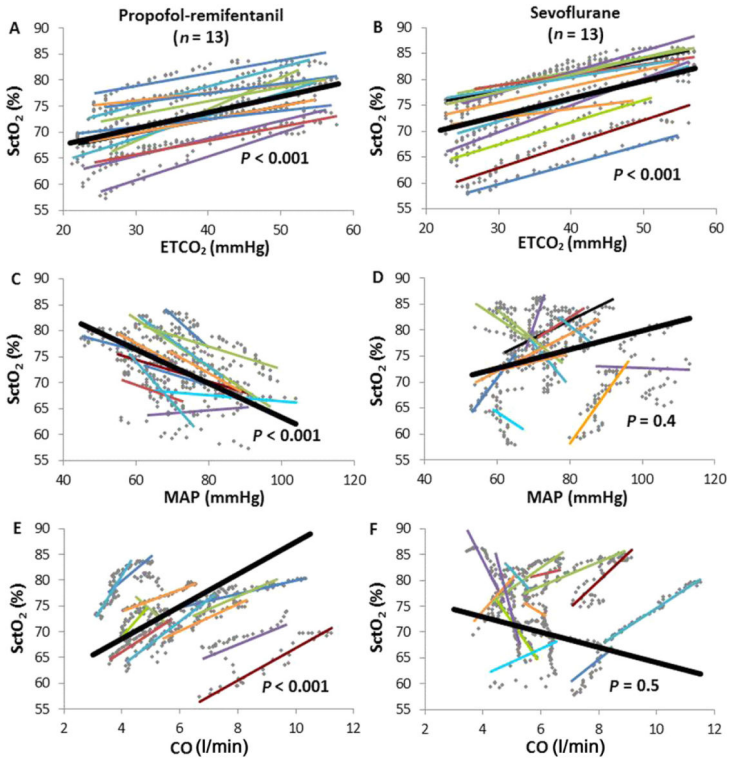

Fig. 2.

Correlations between cerebral tissue oxygen saturation ($SctO_2$) and end-tidal carbon dioxide ($ETCO_2$, A and B), mean arterial pressure (MAP, C and D), and cardiac output (CO, E and F) in patients anesthetized with propofol-remifentanil (A, C, and E) and sevoflurane (B, D, and F). Lightly colored lines are individual patients and the dark bold lines are the average. The interval between adjacent data points for each patient is 60 s.

Table 1

Demographic data.

	Propofol-remifentanil (*n* = 13)	Sevoflurane (*n* = 13)
Age (years)	39 ± 11	37 ± 15
Height (cm)	174 ± 8	172 ± 11
Weight (kg)	81 ± 17	87 ± 31
BMI	27 ±5	29 ± 8
Male : female (*n* : *n*)	9:4	8:5
Controlled hypertension (*n*)	1	1
Controlled type II DM (*n*)	1	0
ASA I (*n*)	6	6
ASA II (*n*)	7	7
Orthopedic surgery (*n*)	4	10
Gastrointestinal surgery (*n*)	3	1
Urological surgery (*n*)	4	1
Miscellaneous surgery (*n*)	2	1

Data are mean ± standard deviation.

BMI, body mass index; DM, diabetes mellitus; ASA, American Society of Anesthesiologists.

Table 2

Physiological data in propofol-remifentanil group.

	Hypocapnia ($ETCO_2$ = 25 mmHg)	Normocapnia ($ETCO_2$ = 40 mmHg)	Hypercapnia ($ETCO_2$ = 55 mmHg)
SctO2 (%)†	69 ±5	74 ±5	78 ± 4
THC (μMol)†	43 ± 11	44 ± 11	46 ± 11
Oxy-Hb (μMol)†	30 ±8	33 ±8	36 ± 8
Deoxy-Hb (μMol)†	13 ±4	12 ±4	10 ± 3
SV (ml/beat)†	73 ± 10	85 ± 12	96 ± 16
HR (beat/min)	68 ± 16	71 ± 17	73 ± 17
CO (l/min)†	5 ±1	6±2	7± 2
SVR [(dyne × s).cm^{-5}]†	1305 ± 381	985 ± 294	756 ± 232
MAP (mmHg)†	78 ± 12	71 ±9	63 ± 9
MV (l/min)†	12 ±2	7±2	3± 2
BIS	42 ± 12	41 ± 11	41 ± 12
SpO_2 (%)*	100 ± 0.4	99 ±1	99 ± 1

*$P < 0.05$;

†$P < 0.001$.

$SctO_2$, cerebral tissue oxygen saturation; THC, total hemoglobin concentration (cerebral tissue); Oxy-Hb, oxy-hemoglobin (cerebral tissue); Deoxy-Hb, deoxy-hemoglobin (cerebral tissue); SV, stroke volume; HR, heart beat; CO, cardiac output; SVR, systemic vascular resistance (SVR = 80*MAP/CO); MAP, mean arterial pressure; MV, minute ventilation; BIS, bispectral index; SpO_2, pulse oxygen saturation.

Table 3

Physiological data in sevoflurane group.

	Hypocapnia ($ETCO_2$ = 25 mmHg)	Normocapnia ($ETCO_2$ = 40 mmHg)	Hypercapnia ($ETCO_2$ = 55 mmHg)
$SctO_2$ (%)†	71 ±7	76 ±6	81 ± 5
THC (μMol)†	45 ± 10	47 ± 10	49 ± 10
Oxy-Hb (μMol)†	32 ±8	36 ±8	40 ± 9
Deoxy-Hb (μMol)†	13 ±4	11 ±4	9± 3
SV (ml/beat)	76 ± 20	78 ± 22	81 ± 27
HR (beat/min)	80 ± 11	81 ± 10	81 ± 10
CO (l/min)	6 ±1	6±2	7± 2
SVR [(dyne × s).cm^{-5}]	1013 ± 280	1018 ± 317	1053 ± 398
MAP (mmHg)*	73 ± 12	74 ± 12	76 ± 13
MV (l/min)†	12 ±3	7±2	3± 1
BIS	34 ± 12	34 ± 11	34 ± 11
SpO_2 (%)	99 ±1	99 ±1	99 ± 1

*$P < 0.05$;

†$P < 0.001$.

$SctO_2$, cerebral tissue oxygen saturation; THC, total hemoglobin concentration (cerebral tissue); Oxy-Hb, oxy-hemoglobin (cerebral tissue); Deoxy-Hb, deoxy-hemoglobin (cerebral tissue); SV, stroke volume; HR, heart beat; CO, cardiac output; SVR, systemic vascular resistance (SVR = 80*MAP/CO); MAP, mean arterial pressure; MV, minute ventilation; BIS, bispectral index; SpO_2, pulse oxygen saturation.