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Impact of phenylephrine administration on cerebral tissue oxygen saturation and blood volume is modulated by carbon dioxide in anaesthetized patients[†]

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Editor's key points

- Phenylephrine is known to reduce cerebral oxygenation.
- Fourteen patients received phenylephrine during normocapnia, hypocapnia, and hypercapnia.
- Hypocapnia intensified, and hypercapnia blunted, the phenylephrine-induced reduction in cerebral oxygenation.
- The study presents important data regarding interaction between CO_2 and phenylephrine and the effects on cerebral oxygenation.

Background. Multiple studies have shown that cerebral tissue oxygen saturation (Sct_{O_2}) is decreased after phenylephrine treatment. We hypothesized that the negative impact of phenylephrine administration on Sct_{O_2} is affected by arterial blood carbon dioxide partial pressure (Pa_{CO_2}) because CO_2 is a powerful modulator of cerebrovascular tone.

Methods. In 14 anaesthetized healthy patients, i.v. phenylephrine bolus was administered to increase the mean arterial pressure ∼20–30% during hypocapnia, normocapnia, and hypercapnia. Sct_{O_2} and cerebral blood volume (CBV) were measured using frequency domain near-infrared spectroscopy, a quantitative technology. Data collection occurred before and after each treatment.

Results. Phenylephrine caused a significant decrease in Sct_{O_2} during hypocapnia [$\Delta Sct_{O_2} = -3.4$ (1.5)%, $P < 0.001$], normocapnia [$\Delta Sct_{O_2} = -2.4$ (1.5)%, $P < 0.001$], and hypercapnia [$\Delta Sct_{O_2} = -1.4$ (1.5)%, $P < 0.01$]. Decreases in Sct_{O_2} were significantly different between hypocapnia, normocapnia, and hypercapnia ($P < 0.001$). Phenylephrine also caused a significant decrease in CBV during hypocapnia ($P < 0.01$), but not during normocapnia or hypercapnia.

Conclusion. The negative impact of phenylephrine treatment on Sct_{O_2} and CBV is intensified during hypocapnia while blunted during hypercapnia.

Keywords: carbon dioxide; cerebral blood volume; cerebral tissue oxygen saturation; modulation; phenylephrine

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Phenylephrine is one of the most commonly used vasopressors including in patients with acute neurological injury. There are a number of reports that cerebral tissue oxygen saturation (Sct_{O_2}) measured using near-infrared spectroscopy (NIRS) is decreased, even though arterial pressure is increased, after phenylephrine bolus and infusion administration in anaesthetized and awake humans.[1–4] Because cerebrovascular tone is powerfully modulated by carbon dioxide (CO_2), we hypothesized that the magnitude of the phenylephrine-induced decrease in Sct_{O_2} is influenced by arterial blood CO_2 partial pressure (Pa_{CO_2}). During hypercapnia, one may see a reduction in the decrease in Sct_{O_2} due to hypercapnia-mediated cerebral vasodilation, and during hypocapnia, the opposite effect may occur. Manipulation of Pa_{CO_2} is common in the operating theatre and intensive care unit. Within this context, a full understanding of how Sct_{O_2} is affected by phenylephrine administration at different Pa_{CO_2} levels will facilitate clinical decision making. This will be especially true in patients who are at an increased risk of cerebral ischaemia and hypoxia. In this study, it was our aim to determine whether the phenylephrine-induced decrease in Sct_{O_2}, measured using frequency domain (FD)-NIRS, is different at distinct Pa_{CO_2} levels in healthy anaesthetized surgical patients.

Methods

After Institutional Research Board approval, ASA I–II patients undergoing elective non-neurosurgical procedures at University of California Irvine Medical Center were recruited for this study (Table 1). Both verbal and written informed consents were obtained. Exclusion criteria were: age ≤18 yr old, cerebrovascular disease, symptomatic cardiac disease, symptomatic pulmonary disease, poorly controlled hypertension (systolic arterial pressure ≥140 mm Hg), and poorly controlled diabetes mellitus (blood glucose ≥160 mg dl^{-1}) or diabetes mellitus requiring insulin treatment. All patients received nothing by mouth 8 h before surgery.

Measurements

Sct_{O_2} and total haemoglobin concentration (THC, the sum of oxy- and deoxy-haemoglobin concentrations) were measured by the Oxiplex TS cerebral oximeter (ISS Inc., Champaign, IL, USA), a non-invasive, portable, and quantitative FD-NIRS device.[5] It emits and detects near-infrared light at two different wavelengths (690 and 830 nm). The 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, 2.46, 2.92, and 3.45 cm) is sufficient for light to access the surface of the brain.[6] The measured optical properties characterize cerebral tissue and are not appreciably influenced by extra-cerebral layers.[6 7] Cerebral blood volume (CBV) is calculated via the following equation:[8 9]

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

CBV is in ml 100 g^{-1}, THC is in µmol, MW_{Hb} is the molecular weight of haemoglobin (64 458 g mol^{-1}), HGB is systemic blood haemoglobin 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 haematocrit ratio.

Cardiac output (CO) was monitored using oesophageal Doppler (CardioQ, Deltex Medical, Chichester, West Sussex, UK). The CO values used for analysis were based on the average of every 10 successive stroke volumes. The mean arterial pressure (MAP) was monitored at the external ear canal level via an arterial pressure transducing system (Vigileo-FloTrac, Edwards Lifesciences, Irvine, CA, USA). End-tidal CO_2 (E'_{CO_2}) was determined by the gas analyzer built into the anaesthesia machine (Aisys, GE Healthcare, Madison, WI, USA). Pa_{CO_2} was analysed using a handheld blood analyzer (iSTAT, Abbott Laboratories, Abbott Park, IL, USA). Arterial blood oxygen saturation was determined by finger pulse oximeter (Sp_{O_2}) (LNOP Adt, Masimo Corp., Irvine, CA, USA). The depth of anaesthesia was monitored via the bispectral index (BIS) monitor (S/5™ M-BIS, GE Healthcare).

Protocol

After induction of anaesthesia with fentanyl (1.5–2 µg kg^{-1}) and propofol (2–3 mg kg^{-1}), all patients were intubated tracheally and maintained with total i.v. anaesthesia using propofol 75–150 µg kg^{-1} min^{-1} and remifentanil 0.2–0.5 µg kg^{-1} min^{-1} to target a BIS between 30 and 40. Muscle relaxation was maintained with cisatracurium. A radial intra-arterial catheter, a BIS monitor, an oesophageal Doppler probe, and two FD-NIRS probes (left and right forehead) were placed in addition to the other routine monitors. Pressure-regulated volume-controlled mechanical ventilation was used with the inspired oxygen fraction (F_{IO_2}) fixed at 50%, inspiratory to expiratory (I:E) time ratio fixed at 1:2, and positive end-expiratory pressure fixed at zero. The formal study was conducted during a stable intraoperative period.

Three different E'_{CO_2} levels were achieved via minute ventilation adjustments (Fig. 1). Normocapnia, defined as an E'_{CO_2} 5.1–5.3 kPa and confirmed with Pa_{CO_2}, was first achieved with a tidal volume (TV) of ∼6–10 ml kg^{-1} and a respiratory

Table 1 Patient characteristic and surgery data

Patient #	Age (yr)	Sex	Height (cm)	Weight (kg)	ASA	Co-morbidity	Major home medications	Surgery
1	49	M	178	73	I	None	None	Tibia fracture repair
2	55	F	155	58	II	Leiomyosarcoma	Gabapentin	Right femur radical resection
3	60	M	185	95	II	Controlled hypertension	Metoprolol	Robotic laparoscopic prostatectomy
4	41	M	173	73	I	None	None	Laparoscopic cholecystectomy
5	55	M	185	85	II	Kidney mass	None	Robotic laparoscopic nephrectomy
6	55	M	188	95	II	Prostate cancer	None	Robotic laparoscopic prostatectomy
7	27	F	160	61	I	Cervical cancer	None	Robotic laparoscopic hysterectomy
8	23	M	165	63	I	Retroperitoneal tumour	None	Retroperitoneal tumour resection
9	68	M	180	84	II	Controlled hypertension	Diovan	Abdominal hernia repair
10	37	F	165	103	II	Controlled diabetes	Lisinopril, glipizide	Hepatectomy
11	35	M	173	71	I	Humerus tumour	None	Humerus hardware removal
12	56	M	180	84	II	Controlled hypertension	Metoprolol	Robotic laparoscopic prostatectomy
13	22	M	183	83	I	Urethral stricture	None	Urethral stricture repair
14	31	M	183	95	I	None	None	Tibia fracture repair

Fig 1 Study protocol. E'_{CO_2}, end-tidal carbon dioxide.
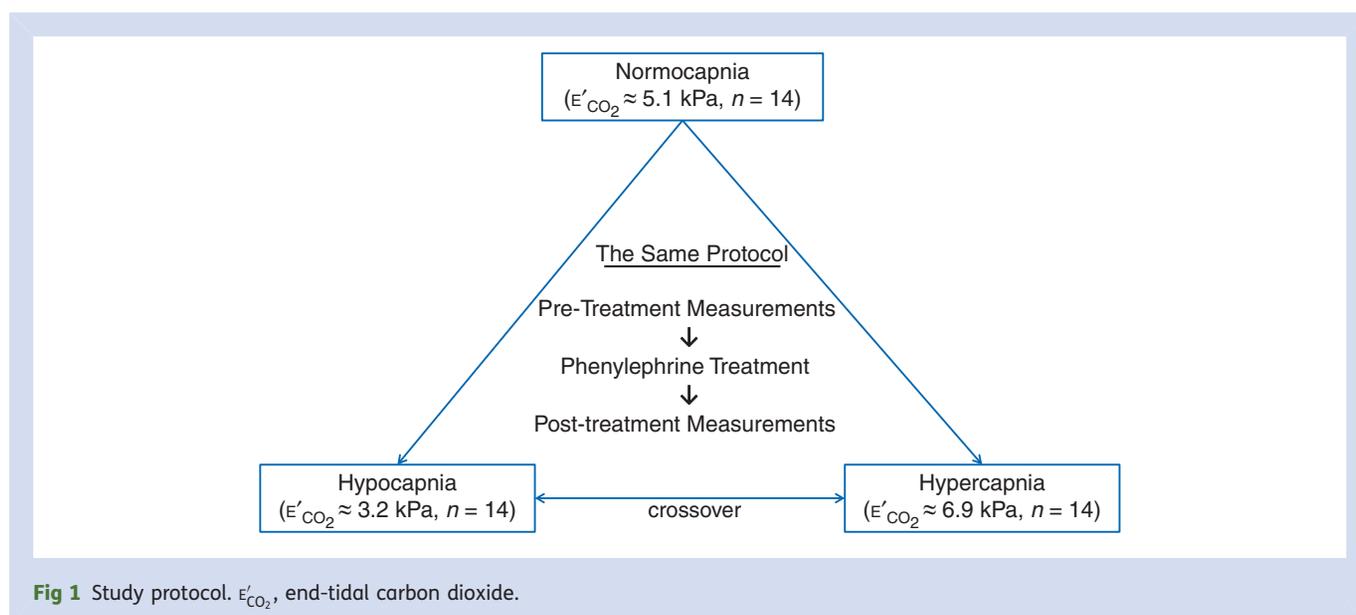
rate (RR) of ~8–10 bpm. Once the condition had remained stable for at least 5 min, an i.v. phenylephrine bolus was administered to increase MAP by ~20–30%. Physiological measurements were recorded immediately before and again after phenylephrine administration when the increase in MAP reached the highest level. The mean values of three successive recordings for each parameter were used for analysis. After the completion of the normocapnia study, both hypocapnia via an increase in TV and RR of ~40–50% and hypercapnia via a decrease in TV and RR of ~40–50% were achieved. Hypocapnia was defined as E'_{CO_2} 3.1–3.3 kPa (confirmed with Pa_{CO_2}) and hypercapnia as E'_{CO_2} 6.7–6.9 kPa (confirmed with Pa_{CO_2}). The same protocol used in the normocapnia study was used during both hypocapnia and hypercapnia studies. For any given patient, the same dose of phenylephrine was used at all CO$_2$ levels. However, the dose of phenylephrine varied (100, 150, or 200 µg) between patients due to inter-individual differences in body weight, response to vasopressor treatment, and extent of anaesthesia-related hypotension. The intervals between phenylephrine boluses were greater than 15 min.

Statistical analysis

Data are presented as mean (SD). Power analysis showed that a sample size of $n=10$ would be required (α level 0.05 and statistical power >80%) in order to detect an expected reduction in NIRS-determined Sct_{O_2} of 3 (3)%. Both one-way analysis of variance (ANOVA) with repeated measurements and the Friedman rank sum test were used to analyse the differences in pre-treatment measurements [E'_{CO_2}, Sct_{O_2}, CBV, MAP, CO, heart rate (HR), Sp_{O_2}, and BIS], post-treatment measurements (Pa_{CO_2}), and phenylephrine-induced changes ($\Delta E'_{CO_2}$, ΔSct_{O_2}, ΔCBV, ΔMAP, ΔCO, ΔHR, ΔSp_{O_2}, and ΔBIS) between hypocapnia, normocapnia, and hypercapnia. Both paired Student's t-test and Wilcoxon's signed-rank test

were used to analyse the differences between pre- and post-treatment measurements (E'_{CO_2}, Sct_{O_2}, CBV, MAP, CO, HR, Sp_{O_2}, and BIS) at each CO$_2$ level. P-values reported are agreeable with both parametric and non-parametric analyses. P-values reported for Pearson's correlations were calculated by Student's t-test using linear regression analysis. P-value <0.05 was regarded as significant.

Results

Out of 16 patients studied, complete data were obtained in 14 patients [11 males, three females, age 44 (15) yr old, height 175 (10) cm, and weight 80 (14) kg] (Table 1). Two patients were not included in analysis due to incomplete Pa_{CO_2} data secondary to either blood gas analyzer malfunctioning or blood sample mishandling.

Hypocapnia, normocapnia, and hypercapnia were successfully achieved via minute ventilation adjustments as demonstrated by E'_{CO_2} ($P<0.0001$) and confirmed by Pa_{CO_2} ($P<0.0001$; Table 2). The pre-treatment measurements of Sct_{O_2} were significantly different between hypocapnia, normocapnia, and hypercapnia ($P<0.0001$). The pre-treatment measurements of MAP were also significantly different between different CO$_2$ levels ($P<0.001$). However, the pre-treatment measurements of CBV, CO, HR, Sp_{O_2}, and BIS all showed no significant difference between different CO$_2$ levels ($P>0.05$).

Phenylephrine treatment induced significant increases in MAP during hypocapnia ($P<0.001$), normocapnia ($P<0.001$), and hypercapnia ($P<0.01$; Table 2). Sct_{O_2} was significantly decreased after phenylephrine treatment during hypocapnia ($P<0.001$), normocapnia ($P<0.001$), and hypercapnia ($P<0.01$). CBV was also significantly decreased during hypocapnia ($P<0.01$), but not during normocapnia and hypercapnia ($P>0.05$). Both CO ($P<0.001$) and HR ($P<0.01$) were also significantly decreased after phenylephrine treatment at all

Table 2 Measurements before (pre) and after (post) phenylephrine bolus treatments during hypocapnia, normocapnia, and hypercapnia. Data are presented as means (SD). Sct_{O_2}, cerebral tissue oxygen saturation; CBV, cerebral blood volume; THC, total haemoglobin concentration; OxyHb, cerebral tissue oxy-haemoglobin concentration; DeoxyHb, cerebral tissue deoxy-haemoglobin concentration; E'_{CO_2}, end-tidal carbon dioxide; Pa_{CO_2}, arterial blood carbon dioxide partial pressure; MAP, mean arterial pressure; CO, cardiac output; HR, heart rate; Sp_{O_2}, oxygen saturation per pulse oximetry; BIS, bispectral index; Δ=post–pre. *$P<0.001$, †$P<0.01$, and ‡$P<0.05$ (post *vs* pre)

	Hypocapnia			Normocapnia			Hypercapnia		
	Pre	Post	Δ	Pre	Post	Δ	Pre	Post	Δ
Sct_{O_2} (%)	70.6 (5.5)	67.1 (5.5)*	−3.4 (1.5)	73.2 (5.2)	70.7 (4.9)*	−2.4 (1.5)	75.7 (4.7)	74.3 (5.0)†	−1.4 (1.5)
CBV (ml 100 g^{-1})	3.0 (0.5)	2.9 (0.5)†	−0.05 (0.05)	3.0 (0.6)	3.0 (0.6)	−0.001 (0.05)	3.1 (0.6)	3.1 (0.5)	−0.0002 (0.04)
THC (μmol)	40.7 (9.7)	40.1 (9.4)†	−0.7 (0.6)	41.0 (9.7)	41.0 (9.4)	−0.02 (0.7)	43.0 (10.3)	43.0 (10.5)	0.01 (0.7)
OxyHb (μmol)	29 (8.2)	27.2 (7.6)*	−1.8 (1.0)	30.3 (8.2)	29.3 (7.7)†	−1.1 (1.0)	32.8 (8.9)	32.2 (8.8)‡	−0.6 (0.9)
DeoxyHb (μmol)	11.7 (2.5)	12.8 (2.5)*	1.2 (0.6)	10.7 (2.2)	11.8 (2.4)*	1 (0.7)	10.2 (2.1)	10.8 (2.2)†	0.6 (0.6)
E'_{CO_2} (mm Hg)	3.2 (0.3)	3.2 (0.3)	−0.01 (0.1)	5.1 (0.3)	5.2 (0.4)	0.05 (0.3)	6.8 (0.7)	7.1 (0.7)†	0.3 (0.1)
Pa_{CO_2} (mm Hg)	N/A	3.9 (0.5)	N/A	N/A	5.9 (0.5)	N/A	N/A	8.0 (0.7)	N/A
pH	N/A	7.5 (0.07)	N/A	N/A	7.4 (0.05)	N/A	N/A	7.3 (0.03)	N/A
MAP (mm Hg)	76 (15)	99 (12)*	23 (9)	73 (15)	100 (15)*	27 (13)	66 (11)	93 (9)†	27 (8)
CO (litre min^{-1})	4.8 (1.5)	3.2 (1.1)*	−1.5 (0.8)	4.8 (1.4)	3.2 (1.1)*	−1.6 (0.8)	5.2 (1.5)	3.7 (1.4)*	−1.5 (0.8)
HR (beats min^{-1})	63 (14)	50 (13)*	−13 (5)	59 (13)	47 (10)*	−12 (7)	59 (13)	52 (13)†	−7 (6)
Sp_{O_2} (%)	100 (0.6)	100 (0.6)	0 (0.4)	100 (0.8)	100 (0.7)	0.07 (0.3)	99 (1)	99 (1)	0.3 (1)
BIS	37 (9)	35 (9)	−2 (4)	35 (7)	35 (9)	0.8 (7)	36 (8)	37 (11)	0.4 (6)
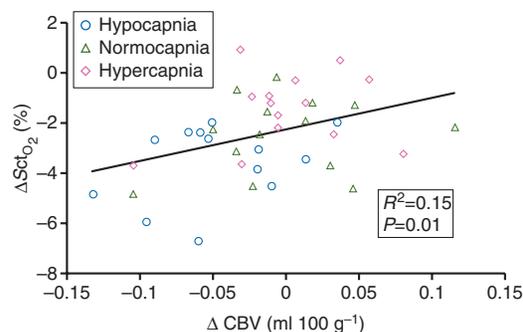
Fig 2 Pearson's correlation between changes in cerebral tissue oxygen saturation (ΔSct_{O_2}) and changes in CBV (ΔCBV).

CO$_2$ levels. Interestingly, E'_{CO_2} was significantly increased after phenylephrine administration during hypercapnia ($P<0.01$) even though the magnitude was small [2 (1) mm Hg], but not during hypocapnia and normocapnia ($P>0.05$). Changes in both Sp_{O_2} and BIS were not significant at any CO$_2$ levels ($P>0.05$).

Correlation between changes in Sct_{O_2} and changes in CBV was significant ($R^2=0.15$, $P<0.05$) (Fig. 2, pooled data).

Phenylephrine-induced changes in both Sct_{O_2} and CBV were significantly different between hypocapnia, normocapnia, and hypercapnia ($P<0.01$ and <0.05, respectively; Fig. 3 and Table 2). In contrast, changes in other physiological variables, including MAP, CO, HR, Sp_{O_2}, and BIS, showed no significant difference between different CO$_2$ levels ($P>0.05$).

Discussion

This is the first study to evaluate whether the negative impact of phenylephrine bolus treatment on Sct_{O_2} is modulated by CO$_2$. The results demonstrate that hypocapnia intensifies, while hypercapnia blunts, the phenylephrine-induced decrease in Sct_{O_2} in propofol–remifentanil-anaesthetized healthy patients. In addition, phenylephrine also causes a significant decrease in CBV during hypocapnia, but not during normocapnia and hypercapnia.

The Sct_{O_2}-decreasing effect of phenylephrine bolus and infusion administrations has been shown in both anaesthetized and awake humans.[1–4] Phenylephrine, a pure α_1-agonist, is one of the most commonly used vasopressors in the perioperative setting. A similar drug, norepinephrine, has also been shown to cause a decrease in Sct_{O_2} after its infusion administration.[10] How increased arterial pressure, and thus increased perfusion pressure, leads to a decrease in Sct_{O_2} needs careful consideration. Sct_{O_2} measures an admixture of arterial and venous blood per unit of cerebral tissue seen by light.[11 12] NIRS measurements show changes when the cerebral arterial to venous blood volume ratio (A:V ratio) changes. A hypothetical mechanism for how A:V ratio is affected by phenylephrine treatment is presented in Figure 4. We propose that the flow velocity in cerebral arterial bed (mainly arterioles) is increased by a phenylephrine-induced increase in perfusion pressure. At the same time, cerebral blood flow (CBF)-regulating vessels (mainly arterioles) constrict due to stretch or increased transmural pressure-mediated vasoconstriction. In accordance with autoregulation, CBF (velocity multiplied by cross-sectional area) is maintained because the increase in velocity is offset by the decrease in cross-sectional area. Cerebral
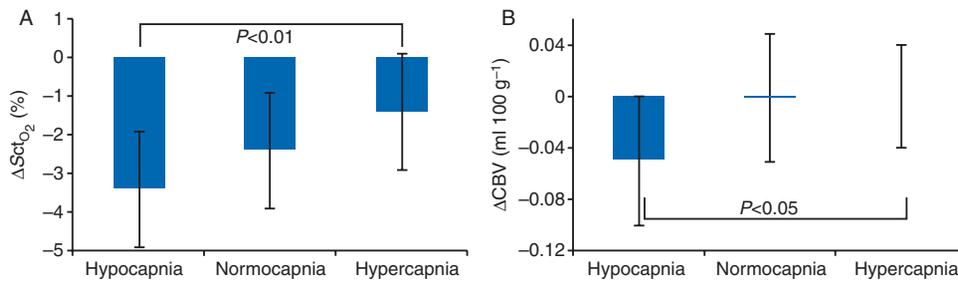
Fig 3 (A) Cerebral tissue oxygen saturation (Sct_{O_2}) and (B) CBV changes (Δ) during hypocapnia, normocapnia, and hypercapnia.
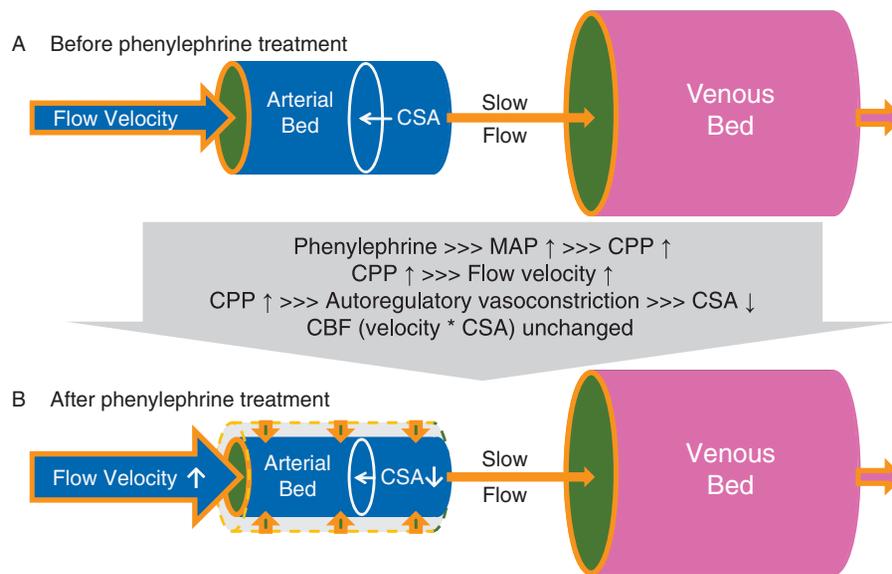
Fig 4 Hypothetical explanation of how phenylephrine treatment induces cerebral autoregulatory vasoconstriction. CSA, cross-sectional area; MAP, mean arterial pressure; CPP, cerebral perfusion pressure; CBF, cerebral blood flow.

vasoconstriction is an indirect autoregulation-mediated consequence, because phenylephrine does not cross the blood–brain barrier and it cannot constrict cerebral vessels directly.[13] A decreased arterial blood contribution secondary to cerebral arteriolar constriction may be partially accountable for the observed decrease in Sct_{O_2}. The findings that flow velocity measured by transcranial Doppler (TCD) is increased while cerebral oxygenation measured by NIRS is decreased after phenylephrine administration are consistent with the above proposed mechanism.[4] However, caution is needed here because it has been shown that the TCD-measured flow velocity is either slightly decreased or maintained during norepinephrine infusion, another vasopressor with some comparable features to phenylephrine.[10 14] Ito and colleagues' study using positron emission tomography demonstrated that changes in CBV during hypocapnia and hypercapnia are caused by changes in arterial blood volume without changing venous and capillary blood

volume.[15] This observation, even though it was based on Pa_{CO_2} manipulation and not vasopressor administration, supports our speculation that a decreased $A{:}V$ ratio may have occurred during cerebral vasoconstriction. The significant correlation between changes in CBV and Sct_{O_2} in this study also suggests a possible cause–effect relationship between changes in cerebral $A{:}V$ ratio and changes in Sct_{O_2} measured by NIRS. The above hypothetical explanation based on autoregulatory vasoconstriction is also supported by the CO$_2$'s modulating effect demonstrated by this study. Specifically, the worsening decrease in Sct_{O_2} during hypocapnia may merely reflect a more robust autoregulatory mechanism because it has been shown that an impaired autoregulation can be restored by hypocapnia.[16] Nonetheless, the mechanism of how phenylephrine induces cerebral vasoconstriction is complicated. The recent finding that sympathetic nerve activity (SNA) from the superior cervical ganglion is increased after pharmacologically (including phenylephrine) induced

rapid and large increase in arterial pressure suggests a role of SNA in cerebral circulation regulation.[17] [18] Increased SNA to the brain leads to cerebral vasoconstriction and prevents abrupt cerebral over-perfusion and haemorrhage.[17] [18] The biophysical change induced by this SNA mechanism is similar to the above proposed autoregulatory mechanism.

The results of this study agree with our previous findings in that both CO and Sct_{O_2} are consistently decreased after phenylephrine treatment.[1] These concordant changes imply that the decrease in CO is likely to account for the decrease in Sct_{O_2}. This is further supported by the observation that CBF estimated using transcranial Doppler is decreased when CO, but not MAP, is decreased via lower body negative pressure.[19] However, if the decrease in CO were solely responsible for the decrease in Sct_{O_2}, we would have observed similar decreases in Sct_{O_2} at different CO_2 levels, because this study shows that the decreases in CO at different CO_2 levels are comparable. Conversely, we have observed significantly different decreases in Sct_{O_2} at different CO_2 levels. This implies that while the decrease in CO may be responsible for the decrease in Sct_{O_2}, the other mechanisms such as the decreased $A{:}V$ ratio proposed above may also play a significant role.

The difference between FD-NIRS, the technology adopted by this study, and continuous wave (CW)-NIRS, the technology currently adopted by clinical practice has been described. In brief, FD-NIRS is regarded as a quantitative approach because it has the ability to differentiate between photon absorption and scattering while CW-NIRS is only regarded as a trend monitor due to its inability to differentiate between the two optical properties. Nonetheless, both technologies are similar in that they are not appreciably affected by the extracerebral tissue layers, if the spacing between optodes is optimized.[6] [7] [20] [21] For example, selective clamping of the external carotid artery in a patient with a defective Circle of Willis shows that FD-NIRS measurements are not affected during external carotid artery occlusion (Fig. 5A). Conversely, in the same patient, clamping of the internal carotid artery shows that pronounced changes in NIRS measurements occur (Fig. 5B). Clearly, the quantitative FD-NIRS result is both spatially and temporally responsive to changes in cerebral perfusion and oxygenation.

Even though phenylephrine causes a consistent decrease in Sct_{O_2}, the magnitude of the decrease is very small (~1.5–3.5% absolute change depending on CO_2 level) and seems unlikely to be clinically significant. Al-Rawi and colleagues found that a relative 13% decrease from baseline, which is approximately twice as great as that seen here, correlates with cerebral ischaemia in patients undergoing carotid artery procedures.[22] Importantly, the decrease in Sct_{O_2} may reflect, at least partially, a decreased arterial blood contribution to NIRS measurements due to cerebral vasoconstriction. Therefore, the phenylephrine-induced decrease in Sct_{O_2} may not represent real or significant cerebral ischaemia and hypoxia if it is partially attributed to a
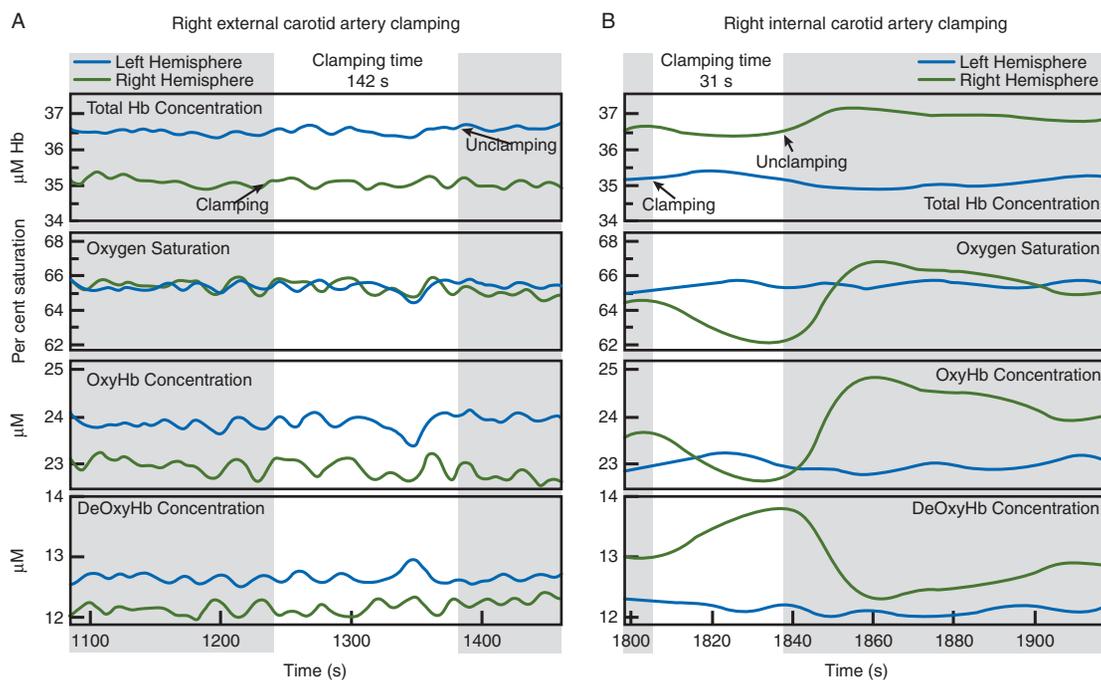
Fig 5 FD-NIRS measurements of THC (top panel), cerebral tissue oxygen saturation (second panel), oxy-haemoglobin concentration (third panel), and deoxy-haemoglobin concentration (bottom panel) during right external carotid artery clamping (A) and right internal carotid artery clamping (B) in a patient with defective collateral circulation through the Circle of Willis. Note that the time scales (s) are different between (A) and (B). (Courtesy of Fady T. Charbel, MD, FACS.)

functional pressure autoregulation mechanism. Caution is needed in extrapolating our results to clinical situations where autoregulation may be impaired. Caution is also needed when interpreting the CBV result because its changes are rather small and the study may be underpowered in detecting the small change. Propofol and remifentanil were used in this study to maintain general anaesthesia because they preserve cerebral autoregulation,[23] cerebrovascular CO_2 reactivity,[24] and CBF–cerebral metabolic rate of oxygen ($CMRO_2$) coupling[25] and they do not possess an intrinsic cerebral vasodilating effect, which may occur with inhalation anaesthetic agents.[26]

In summary, this study demonstrates that a phenylephrine bolus results in a consistent but small decrease in Sct_{O_2} and CBV, and this decrease is intensified by hypocapnia and blunted by hypercapnia. The decrease in CO may not be solely responsible for the decrease in Sct_{O_2}. A decreased $A{:}V$ ratio secondary to cerebral vasoconstriction may also account for the phenylephrine-induced decrease in Sct_{O_2}. The effect of phenylephrine treatment on Sct_{O_2} and CBV in individuals with injured nervous systems or receiving drugs that abolish autoregulation is not known.

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Declaration of interest

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