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ORIGINAL ARTICLE

The effect of continuous positive airway pressure on total cerebral blood flow in healthy awake volunteers

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Abstract
Purpose Continuous positive airway pressure (CPAP) is the gold standard treatment for obstructive sleep apnea. However, the physiologic impact of CPAP on cerebral blood flow (CBF) is not well established. Ultrasound can be used to estimate CBF, but there is no widespread accepted protocol. We studied the physiologic influence of CPAP on CBF using a method integrating arterial diameter and flow velocity (FV) measurements obtained for each vessel supplying blood to the brain.
Methods FV and lumen diameter of the left and right internal carotid, vertebral, and middle cerebral arteries were measured using duplex Doppler ultrasound with and without CPAP at 15 cm H_2O, applied in a random order. Transcutaneous carbon dioxide ($PtcCO_2$), heart rate (HR), blood pressure (BP), and oxygen saturation were monitored. Results were compared with a theoretical prediction of CBF change based on the effect of partial pressure of carbon dioxide on CBF.
Results Data were obtained from 23 healthy volunteers (mean±SD; 12 male, age 25.1±2.6 years, body mass index 21.8±2.0 kg/m^2). The mean experimental and theoretical CBF decrease under CPAP was 12.5 % ($p<0.001$) and 11.9 % ($p<0.001$), respectively. The difference between experimental and theoretical CBF reduction was not statistically significant (3.84±79 ml/min, $p=0.40$). There was a significant reduction in $PtcCO_2$ with CPAP ($p=<0.001$) and a significant increase in mean BP ($p=0.0017$). No significant change was observed in SaO_2 ($p=0.21$) and HR ($p=0.62$).
Conclusion Duplex Doppler ultrasound measurements of arterial diameter and FV allow for a noninvasive bedside estimation of CBF. CPAP at 15 cm H_2O significantly decreased CBF in healthy awake volunteers. This effect appeared to be mediated predominately through the hypocapnic vasoconstriction coinciding with PCO_2 level reduction. The results suggest that CPAP should be used cautiously in patients with unstable cerebral hemodynamics.

Keywords Continuous positive airway pressure · Cerebral blood flow · PCO_2 · Ultrasound

Introduction

Obstructive sleep apnea syndrome (OSAS) is characterized by repetitive episodes of upper airway obstruction during sleep and results in cessation (apneas) or reduction (hypopneas) in airflow which leads to awakening and the reduction of blood oxygen saturation (SaO_2). The most widely accepted treatment of OSAS is continuous positive airway pressure (CPAP). CPAP acts as a pneumatic "splint" by producing a positive pressure inside the airway thereby preventing upper airway collapse during sleep. Considering that a rise in intrathoracic pressure increases jugular venous pressure, CPAP could have an effect on cerebral blood flow (CBF) by reducing the cerebral perfusion pressure [1, 2].

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Moreover, decreased venous return due to increased intrathoracic pressure may decrease right (and left) filling pressure, which may in turn decrease cardiac output. CPAP use can also induce changes in partial pressure of carbon dioxide (PCO_2), which has a major impact on CBF, similar to the way in which hypocapnia constricts cerebral arteries and hypercapnia leads to a marked rise of CBF [3–5]. Changes in CBF induced by CPAP may have important clinical implications in patients for whom an optimal CBF is mandatory, such as acute stroke patients.

Published data about the effects of CPAP on cerebral hemodynamics are conflicting [6–8]. Various studies have reported an increase [8, 9], others a decrease [7, 10], and some an insignificant change [6] in CBF. The conflicting results may be due to inaccurate and/or insensitive CBF measurement methods. Furthermore, many of the studies that employed transcranial Doppler ultrasound (TCD) used only flow velocity (FV) and pulsatility index (PI) in the middle cerebral artery (MCA) to estimate total CBF [6–10]. However, TCD measurements do not take into account changes in artery diameter or in cerebral posterior circulation. As a result, it is unclear whether changes in MCA FV accurately reflect total CBF change. A method that takes into account both blood FV and the artery diameter of all vessels supplying blood to the brain is likely to be more accurate. Furthermore, in the previous studies [6–8] only end-tidal CO_2 level was monitored. This is an inaccurate measurement technique under the presence of CPAP considering that the expired CO_2 is diluted by incoming CO_2-free CPAP airflow.

The present study was performed to assess the effect of CPAP on total CBF measured by duplex color Doppler ultrasound (US) using a method, similar to that presented by Schoning et al. [11], incorporating FV and lumen diameter measurements obtained at the left and right internal carotid artery (ICA), vertebral artery (VA), and MCA. These measurements were obtained while transcutaneous carbon dioxide ($PtcCO_2$) level was monitored continuously.

Methods

Healthy, young, nonsmoking volunteers were invited to participate in the study by advertisement at the Centre Hospitalier Universitaire Vaudois and École Polytechnique Fédérale de Lausanne in Switzerland. Volunteers with a history of pulmonary, cardiac or cerebral disease were excluded. The study was carried out in accordance with the Declaration of Helsinki (1989) of the World Medical Association and was approved by the local ethics committee. All subjects gave their informed consent.

Ultrasound measurements

The US measurements were performed with and without CPAP (S8 AutoSet Spirit™ II, ResMed Inc, Poway, CA, USA) applied at 15 cm H_2O through a fitted full face mask MIRAGE QUATTRO ® (ResMed®, ResMed Inc, Poway, CA, USA) in a randomized order following a structured protocol. Randomization was accomplished by flipping a coin. The measurements were performed during the afternoon at atmospheric pressure at least 2 h after the last meal and drink with caffeine in a standard room with controlled temperature. All volunteers, who were studied in the supine position with a head tilt of 30°, tolerated CPAP at 15 cm H_2O well. The arteries were studied with and without CPAP in the following order: (a) right proximal ICA and VA, (b) left proximal ICA and VA, and (c) right and left MCA.

Peak systolic and end-diastolic FV and arterial diameter were obtained in M-mode [12] for three time points at the left and right ICA and VA using a 5–8 MHz duplex probe (Echograph Acuson Sequoia 512). Only FV was studied at the MCAs using a 2–4 MHz-pulsed TCD probe of the same manufacturer. $PtcCO_2$ level was monitored with a "Tosca 500" system (Radiometer Basel AG, Basel, Switzerland) using a single sensor applied to the chest. SaO_2 and heart rate (HR) were monitored with a finger pulseoximeter (Ohmeda) during the measurement period. Blood pressure (BP) was recorded before and after each test. US measurements under CPAP began after the $PtcCO_2$ level returned to baseline (±2 mmHg) or at steady state after at least 15 min of CPAP use. This time period was sufficient to ensure a steady state as changes in CBF caused by an alteration in PCO_2 level have been found to be completed within 30 s[13].

CBF calculations

A single investigator (CO) performed all of the US exams with the exception of two (LH). All velocity and diameter measurements, based on the US images, were performed by two investigators (CO, TY). Exams were reviewed by both investigators to assure that measurements were performed on the same M-mode screen and on the correct vessel within the region of interest. The mean value of both investigators' measurements was used for the calculations. The mean FV in each vessel was calculated by measuring the peak systolic, FV_{sys}, and end diastolic, FV_{dia}, FV for three cardiac cycles (Eq. 1)

$$FV = \frac{FV_{sys} + 2FV_{dia}}{3} \quad (1)$$

Mean diameter $\overline{D}$ of each vessel for three cardiac cycles was calculated based on the M-mode US measurements [12]

using a similar equation as Eq. 1, except with FV replaced with the systolic and diastolic diameter. An example of the FV and diameter measurement obtained at the right ICA is shown in Fig. 1.

Flow rate, Q (millimeter per minute), in each vessel was calculated by (Eq. 2) and total experimental CBF, CBF_{exp}, was determined by the sum of the flow in the left and right ICAs and VAs assuming a parabolic velocity profile[14] (Eq. 3).

$$Q = \frac{FV}{2} \times \frac{\pi \overline{D}^2}{4} \tag{2}$$

$$CBF_{exp} = Q_{ICAs} + Q_{VAs} \tag{3}$$

Vascular related results are presented as the average of the left and right vessel measurements for the 23 subjects (i.e., $FV_{ICA} = \frac{1}{23}\sum_{n=1}^{23}(FV_{ICAleft} + FV_{ICAright})/2$).

The following method was used to predict a theoretical change in CBF given an experimentally measured change in $PtcCO_2$ level. The relationship between CBF (ml/min/100 g brain tissue) and arterial CO_2 tension (millimeters of mercury) has been quantified in the literature (Fig. 2) [3, 15–21]. Table 1 summarizes the slope of the CBF to PCO_2 curve at baseline PCO_2 level based on Fig. 2 and other studies in the literature. The average slope was calculated to be 1.65, with a maximum and minimum slope value of 3.20 and 0.19, respectively (standard deviation=0.92). The average slope was used to determine a theoretical reduction in CBF in ml/min/100 g of brain tissue, $\Delta CBF_{theor100}$, based on the experimentally measured change in $PtcCO_2$ level with and without CPAP $\Delta CBF_{theor100} = -\text{slope} \times \Delta PtcCO_2$. The total theoretical change in CBF was determined ($\Delta CBF_{theor} = 14 \times \Delta CBF_{theor100}$) assuming that the human brain is approximately 14 times the weight of a Rhesus monkey [21].

The CBF_{exp} measurements were used to determine the experimental CBF reduction (ΔCBF_{exp}). Positive CBF reduction values were defined to indicate that total CBF decreased under CPAP, and vice versa. The average and standard deviation of ΔCBF_{exp} and ΔCBF_{theor} were determined for the 23 subjects based on both investigators measurements.

Statistical analysis

Statistical analysis was conducted with STATA software (version 11; College Station, TX, USA). The variable measured parameters were compared between conditions using a two-tailed paired t test and Mann–Whitney test, where appropriate. The level of significance was set at 95 %. Multivariate logistic regression, limited to two variables according to the total number of subjects, was performed with predictors with a univariate result of $p<0.1$. Agreement between investigators was calculated with the Lin's concordance correlation coefficient for agreement on a continuous measure.

Results

The study group was comprised of 23 subjects (12 male, 11 female) aged from 20 to 30 years (mean±SD; 25.1± 2.6 years) with a mean body mass index (BMI) of 21.8± 2.04 kg/m^2. Thirteen volunteers began the randomized measurement protocol with CPAP. Table 2 shows a summary of the hemodynamic data and results for the CBF calculations with and without CPAP.

With CPAP, FV decreased significantly in the ICA (0.05± 0.05 m/s, p=0.0002) and the MCA (0.038±0.06 m/s, p= 0.009), but not significantly at the VA (0.009±0.04 m/s, p= 0.25). Decrease in the ICA diameter was insignificant (−0.06± 0.2 mm, p=0.14), while decrease in VA diameter was significant (−0.12±0.12 mm, $p<0.001$). In a multivariate robust regression, with total CBF reduction as a dependant variable, only ICA FV ($p<0.001$) remained significant, whereas MCA FV was not significant (p=0.21).

A significant reduction in $PtcCO_2$ under CPAP (2.6± 2.4 mm Hg, $p=<0.001$) and an increase in mean BP (2.7± 3.6 mm Hg, p=0.0017) were measured. No significant change in SaO_2 (0.4±1.6 %, p=0.21) and HR (0.9565± 7.3173, p=0.62) was measured. Figure 3 illustrates the total CBF_{exp} reduction compared to the CBF_{theor} reduction for each of the 23 subjects and the average reduction for the entire study.

The mean CBF_{exp} decreased under CPAP by 12.5 % (66.6±63 ml/min, $p<0.001$), while the mean decrease in CBF_{theor} was 11.9 % (62.8±54.4 ml/min, $p<0.001$). There was no significant difference between experimental and theoretical CBF reduction (3.84±79 ml/min, p=0.40). No difference was found according to the sequence of measurements with or without CPAP, gender, height, weight, or BMI. No significant differences were found also between the left and right side US measurements of each arterial vessel. Agreement between final investigators results for CBF reduction in every subject was 87 % (95 % confidence interval 0.73–0.97).

Discussion

We observed that CPAP applied at 15 cm H_2O significantly decreased the total CBF in healthy awake volunteers. The change in CBF was studied using a method that integrates ultrasound measurements of blood FV and arterial lumen diameter obtained at the left and right ICA, VA, and MCA.

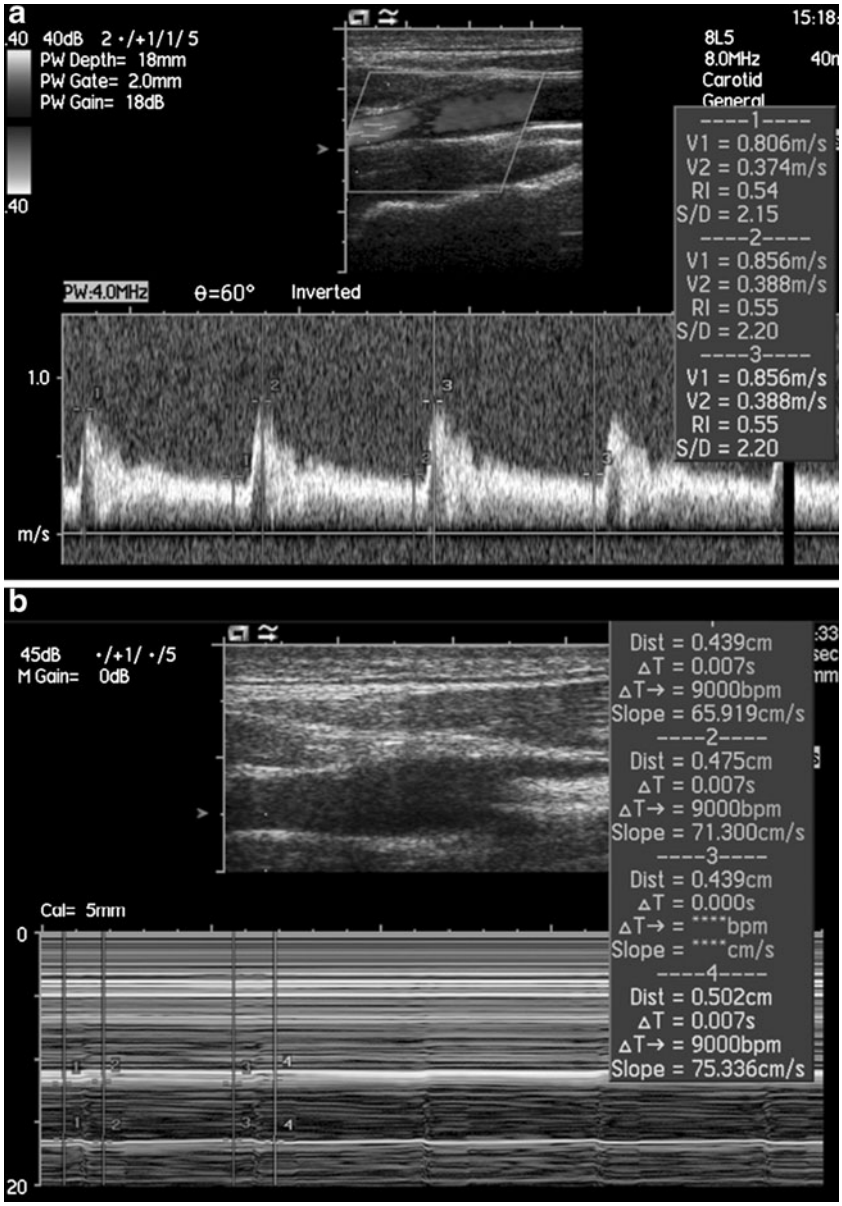

Fig. 1 Flow velocity (**a**) and vessel diameter in M-mode ultrasound (**b**) measured at the right ICA

Previous studies measured FV and PI in the MCA with the hypothesis that these parameters were a good indicator of total CBF [6–10]. Thus, the arterial diameter was assumed to remain stable [4]. Table 3 summarizes the main technical characteristics and results of the previous studies that investigated the effect of CPAP on CBF hemodynamics. We chose to evaluate total CBF based on the arterial diameter and FV measured in each of the primary vessels that supply blood to the brain (ICAs and VAs). Measurement of diameter and FV in these vessels has been proposed to be a more accurate and detailed method to help estimate total CBF [22].

In our study, we chose to monitor PCO_2 transcutaneously because it avoids the confounding dilution effect of end-tidal CO_2 measurements that occurs due to the mixing of expired CO_2 with incoming CO_2-free CPAP airflow. However, end-tidal PCO2 monitoring has also several advantages, such as the quick response under provocative conditions as well as the fact it provides detailed information about the breathing pattern (i.e., respiratory rate). In the case of end-tidal PCO2 monitoring, the problem of CO2 dilution in the mask under CPAP could be avoided by the insertion of a thin catheter into one nostril far from the expiratory port [7, 23].

The underlying physiological mechanism that results in CBF change due to CPAP usage is complex. A CPAP-induced increase in intrathoracic pressure may provoke hemodynamic effects (i.e., reduced cardiac output, reduced venous return, increased cerebral venous pressure) that could result in a decrease of cerebral perfusion pressure and CBF. On the other hand, it is well accepted that PCO_2

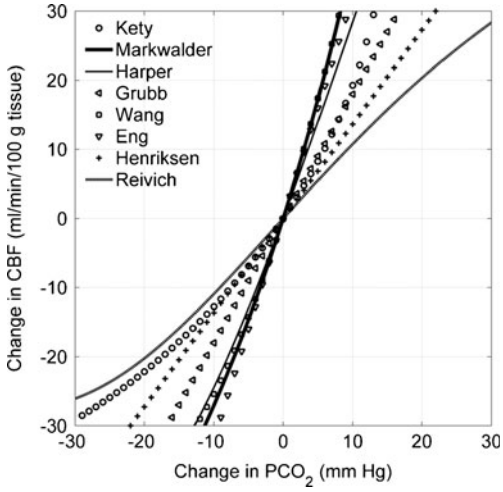

Fig. 2 Relation for change in CBF (ml/min/100 g brain tissue) given a change in PCO_2 (mm Hg) based on studies in the literature [3, 15–21]

affects the muscular regulation of the arterial wall, with hypercapnia leading to vasodilatation and hypocapnia to vasoconstriction. The relative contribution of CPAP-induced changes, such as intrathoracic pressure and PCO_2 level, to CBF change is unknown.

Our results supported that CBF reduction due to CPAP usage was primarily mediated through hypocapnic vasoconstriction. CPAP-induced intrathoracic pressure and venous hemodynamic changes did not appear to play an important role in CBF reduction. To determine the theoretical CBF effect of variation in PCO_2 level with and without CPAP, we used the average value of the slope of the CBF responsiveness to acute change in PCO_2 reported in the literature (Table 1). The difference between the theoretically predicted and experimentally measured change in CBF was not found to be significant (Fig. 3). This suggests that the theoretical prediction of the CBF decrease, which takes into account only the monitored $PtcCO_2$ level, was sufficient to capture the CBF changes that were observed. Thus, an increase in intrathoracic pressure alone did not appear to play a significant role in CBF alteration.

This study cannot conclude if CPAP pressure had a direct impact on total CBF. This is because the statistical calculation used to determine that intrathoracic pressure increase did not have a significant impact on total CBF was critically dependent on the assumed slope for change in CBF to PCO_2 level. A wide range of slope values have been reported in the literature (Table 1, slope=0.19–3.20) and thus it is possible that the theoretical predictions over or underestimated CBF change. For example, if the slope used to determine the theoretical change in CBF was chosen to be <1.1, the impact of CPAP pressure would have been found to be significant.

Table 1 Summary of CBF to PCO_2 slopes reported in the literature for different animal types and CBF measurement techniques (N_2O nitrous oxide, *NO* nitric oxide, Kr^{85} radioactive krypton, $H_2{}^{15}O$ transit diffusible tracer), Cerebral venous flowmeter (CVF), Intraarterial 133Xe

Investigator	Animal type	CBF measurement technique	Slope ($\Delta CBF/\Delta PCO2$) at baseline PCO_2
Kety [15]	Man	N_2O	1.47
Markwalder [3]	Man	Doppler	3.12
Wasserman [17, 30]	Man	N_2O	2.17
Eng [19]	Man	NO	3.20
Henriksen [20]	Man	^{133}Xe	1.36
White [31], Lambertsen [32]	Man	N_2O	1.34
Alexander [33]	Man	Kr^{85}	1.06
Pierce [34]	Man	N_2O	0.43
Grubb [17]	Monkey	$H_2{}^{15}O$	1.80
Reivich [21]	Monkey	Thermistor Flowmeter	1.11
White [31]	Monkey	CVF	1.11
Harper [16]	Dog	Kr^{85}	2.69
Raichle [37]	Dog	Kr^{85}	0.90
Fujishima [38]	Dog	N_2O	0.19
Smith [36]	Goat	Kr^{85}	1.79
James [35]	Baboon	Kr^{85}	1.22
Wang [18]	Rat	NO	3.10
			Ave 1.65
			Max 3.20
			Min 0.19
			SD, 0.92

Table 2 Hemodynamic results for the 23 volunteers with and without CPAP. All values are expressed as mean (SD)

	No CPAP (SD)	CPAP (SD)	*p* Value
BP (mmHg)	87.3 (6.6)	90 (7.1)	0.0017
HR	68.8 (10.6)	69.7 (12)	0.62
$PtcCO_2$ (mm Hg)	36.3 (5.3)	33.7 (6.2)	<0.001
SaO_2 (%)	97.5 (1.2)	97.9 (1.3)	0.21
FV_{ICA} (m/s)	0.48 (0.07)	0.43 (0.06)	0.0002
FV_{VA} (m/s)	0.31 (0.05)	0.30 (0.05)	0.25
FV_{MCA} (m/s)	0.65 (0.12)	0.62 (0.12)	0.009
PI_{ICA}	0.98 (0.18)	0.97 (0.22)	0.76
PI_{VA}	1.20 (0.18)	1.21 (0.18)	0.92
PI_{MCA}	0.78 (0.1)	0.82 (0.1)	0.12
$\overline{D}_{ICA}$ (mm)	4.13 (0.6)	4.07 (0.6)	0.14
$\overline{D}_{VA}$ (mm)	2.98 (0.4)	2.85 (0.4)	<0.001
CBF (ml/min)	535 (122.1)	468.5 (105.6)	<0.001

CPAP continuous positive airway pressure, *BP* blood pressure, *HR* heart rate, $PtcCO_2$ transcutaneous carbon dioxide level, SaO_2 oxygen saturation, *FV* flow velocity, *PI* pulsatility index, *D* diameter, *CBF* cerebral blood flow, *SD* standard deviation

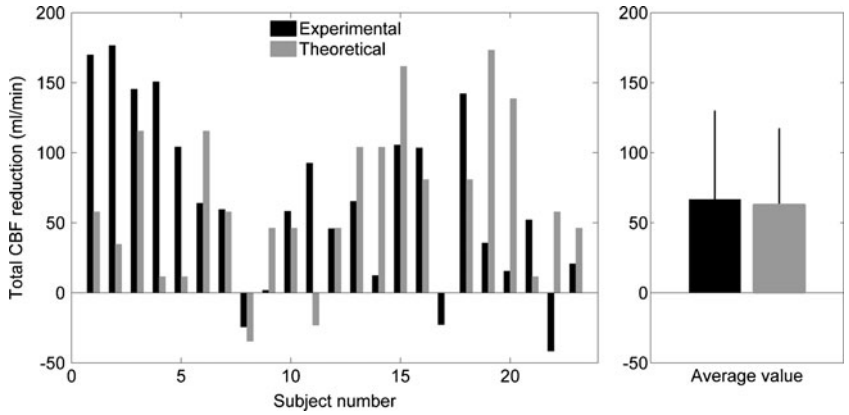

Fig. 3 Comparison of the total CBF reduction (millimeter per minute) under CPAP, ΔCBF_{exp}, with the predicted theoretical reduction in CBF, ΔCBF_{theor}, for each of the 23 subjects (*left*) and the average value for CBF reduction in all subjects (*right*)

To better understand the impact, if any, of intrathoracic pressure alterations brought on by CPAP usage on CBF, a study would need to be conducted with the PCO_2 level held constant while CPAP pressure is altered incrementally.

It appears that CPAP may decrease total CBF in healthy awake volunteers indirectly by modulating the PCO_2 level. However, the physiological mechanism for decrease of PCO_2 under CPAP is unclear. Our findings show a significant increase in BP under CPAP. This may be due to the autoregulation of systemic BP which seeks to maintain stable CBF [24]. Similarly, SaO_2 in the healthy range has little effect on the radius of blood vessels and subsequently on CBF [25]. One hypothesis for the change in total CBF is that CPAP improves the lung perfusion/ventilation ratio, which may increase CO_2 washout. Another explanation could be that the subjects experienced a mild hyperventilation due to anxiety induced by breathing against the CPAP. In our study, anxiety was not measured, but our measurements were obtained after an acclimatization period. It is also possible that anxiety had a direct influence on CBF.

Changes in CBF induced by CPAP could have important clinical implications in patients requiring an optimal and stable CBF such as acute stroke patients. The question of CPAP use in early stroke patients with OSAS remains open considering the positive effect of CPAP on apnea-induced oxygen deprivation versus possible negative effects of CPAP, such as reduction of total CBF. A specific study would need to be performed to examine the impact of CPAP pressure on CBF in stroke patients to validate these conjectures.

A primary limitation of this study is that the subjects who were tested were both healthy and awake. Subjects who are awake may react differently to CPAP than sleeping OSAS patients. However, these measurements could not be obtained on sleeping subjects, as these measurements would awaken them, and variable comorbidities (e.g., obesity, heart failure, medication) would make comparison between the subjects' results unreliable. Furthermore, our results

Table 3 Summary of the main technical features of the studies in the literature that investigated the impact of CPAP on CBF hemodynamics

Investigator	Level of CPAP (cm H_2O)	No of subjects/ health condition	Position of the subject/type of CPAP mask	US measurement technique	CBF measurement technique	PCO_2 measurement	Hemodynamic monitoring	Results
Bowie et al. [6]	5, 10	15 awake/healthy	Supine/mouthpiece	TCD	FV on MCA	End-tidal CO_2	BP	No significant change
Scala et al. [7]	5, 10, 15	25 awake/healthy	Supine/mouthpiece	TCD	FV on MCA	End-tidal CO_2	BP, HR, RR, SaO_2, anxiety score	Decrease of FV
Scala et al. [23]	Auto-CPAP mode (4–10) and increasing levels of 5, 10, 15	12 asleep and awake/acute stroke patients	Supine/nasal or facial	TCD	FV on MCA	End-tidal CO_2	BP, SaO_2	Decrease of FV
Haring et al. [8]	12	9 awake/healthy	Supine/mouthpiece	TCD	FV on MCA	End-tidal CO_2	BP, HR	Increase of FV
Present study	15	23 awake/healthy	Supine/mouthpiece	Duplex color Doppler US	FV and lumen diameter of ICA, VA and FV on MCA	Transcutaneous $PtcCO_2$	BP, HR, SaO_2	Decrease of CBF

CPAP continuous positive airway pressure, *BP* blood pressure, *HR* heart rate, *$PtcCO_2$* transcutaneous carbon dioxide level, *SaO_2* oxygen saturation, *FV* flow velocity, *CBF* cerebral blood flow, *RR* respiratory rate

suggest that non-invasive techniques that could be conducted during sleep, such as transcranial Doppler ultrasound obtained at the MCAs, may not be sufficient to measure the changes in CBF that were observed (Table 1). In our study, measurement of FV and diameter at all vessels supplying blood to the brain was needed to detect the CBF changes. In a multivariate robust regression with total CBF reduction as a dependent variable, only ICA FV remained significant. From a clinical point of view, this result justifies the fact that a bedside sampling of this parameter could more easily approximate total CBF, something that could be less time consuming especially in the case of patients such as acute stroke patients or OSAS patients with ischemic encephalopathy. It would be very interesting for future studies to examine this US approach on the aforementioned clinical population.

A secondary limitation of this study is that even though the assignment to spontaneous breathing or to CPAP was based on a randomized order following a structured protocol, a "breathing-machine effect" could not be excluded [26]. However, the protocol was set to evaluate the global impact of the CPAP (mask in combination with pressurized air) to cerebral hemodynamics as a mainstay therapy of OSAS. To further understand the effect of the CPAP mask and that of the CPAP mask and pressurized air using "sham ventilation", a separate study should be conducted focused on the potential effect of the mask itself on the breathing pattern independently from the pressurized air.

Another limitation of this study is that CPAP was adjusted at the high level of 15 cm H_2O. Haring et al. [8] and Droste et al. [27] submitted volunteers to CPAP 12 and 9 cm H_2O, respectively whereas Bowie et al. [6] and Scala et al. [7] studied the effects of different and increasing levels of CPAP on CBF. In our study, we applied CPAP of 15 cm H_2O in young healthy awake volunteers. This high level of CPAP is rarely used in controlling patients with sleep disordered breathing. CPAP at 15 cm H_2O was useful in the experimental setting of our study in order to underline the maximum physiological effects of CPAP on cerebral hemodynamics by minimizing possible bias. The level of CPAP was set at 15 cm H_2O on the machine. It is possible that this high pressure could have resulted in substantial air leaks and caused a gap between the applied and delivered mask pressure and subsequently increased subject discomfort [28, 29]. However, during the ultrasound measurements of our study the presence of air leaks was repeatedly assessed by the MD and adjusted when needed. All volunteers tolerated well the mask with CPAP at 15 cm H_2O.

Another limitation of this study is due to the operator dependence of the measurements used to determine CBF. To minimize operator-dependent error, both operators that conducted the vessel lumen measurements reviewed the US images together after the measurements were made. This review helped to assure that the correct vessel and the same acquisition period were used for the diameter measurements. With this precaution, a good agreement score was found.

In addition to operator-dependent error, our study utilized equations to calculate blood flow based on simplified hydrodynamics. To calculate total CBF, it was assumed that zero phase delay occurred between the arrival of the FV_{sys} at the ICA and VA and that a parabolic velocity profile was present to determine the true flow rate within the vessels [14]. To minimize measurement error, the mean flow in each vessel was approximated using the average of three sequential diastolic and systolic FV and diameter measurements. Even with these simplifications, the presented methodology is robust because it is sensitive to changes in CBF, the measurement of which was the primary objective of this study.

In conclusion, our study presents a noninvasive bedside method to evaluate total CBF in awake subjects using CPAP that could potentially be an improvement over other methods which only take into account FV at the MCA. The results suggest that CPAP at 15 cm H_2O significantly decreases CBF in healthy, awake volunteers. This effect seems to be mediated predominately through the hypocapnic vasoconstriction and likely, to a lesser extent, through the direct effect of CPAP on intrathoracic pressure and venous hemodynamics. These results suggest that CPAP should be cautiously used in patients with unstable cerebral hemodynamics.

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