The Impact of Increased Mean Airway Pressure on Contrast-Enhanced MRI Measurement of Regional Cerebral Blood Flow (rCBF), Regional Cerebral Blood Volume (rCBV), Regional Mean Transit Time (rMTT), and Regional Cerebrovascular Resistance (rCVR) in Human Volunteers

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Abstract: Contrast-enhanced magnetic resonance imaging (MRI) measurement of cerebral perfusion is a diagnostic procedure increasingly gaining access to clinical practice not only in spontaneously breathing patients but also in mechanically ventilated patients. Effects of increased mean airway pressure on cerebral perfusion are entirely possible. Therefore, the present study used continuous positive airway pressure (CPAP) (12 cm H₂O) to study the effects of increased mean airway pressure on cerebral perfusion in volunteers. CPAP significantly reduced regional cerebral blood flow (rCBF) and regional cerebral blood volume (rCBV) but increased regional mean transit time (rMTT) and regional cerebrovascular resistance (rCVR). Active vasoconstriction (e.g., arterial) and/or passive compression of capillary and/or venous vessel areas are the most likely underlying mechanisms. The number of interhemispheric differences in rCBF, rCBV, rMTT, and rCVR found at baseline rose when mean airway pressure was increased. These results, although obtained in volunteers, should be taken into consideration for the interpretation of contrast-enhanced MRI perfusion measurements in mechanically ventilated patients with an increased positive airway pressure. *Hum. Brain Mapping* 11:214–222, 2000. © 2000 Wiley-Liss, Inc.

INTRODUCTION

Increasing mean airway pressure, e.g. by administering positive end-expiratory pressure (PEEP) in mechanically ventilated patients to improve oxygenation by increasing pulmonary functional residual capacity, is clinical routine in intubated patients presenting for contrast-enhanced MRI perfusion measurements. It

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has previously been shown in human volunteers that increased mean airway pressure during CPAP breathing increases lumbar cerebrospinal fluid (CSF) pressure [Hormann et al., 1994] and reduces CSF peak velocity (CSFV_{Peak}) in the aqueduct of cerebri [Kolbitsch et al., 1999]. According to the concept of intracranial volume homeostasis, which is determined by CSF volume, brain tissue volume, and cerebral blood volume (CBV), these reported changes in CSF (e.g., volume) are most likely to be accompanied by changes in CBV. Indeed, a recent echo planar MR imaging and signal targeting with alternating radio frequency (EPSTAR) perfusion study found increases in regional cerebral hemodynamics, especially in white matter regions [Schocke et al., 1999].

However, the EPSTAR signal is simultaneously dependent on CBF and CBV [Buxton et al., 1998], while mapping of the functional organization of the human cortex requires selective measurement of CBF and CBV as, for example, is possible with contrast-enhanced MR perfusion. Therefore, it was the aim of the present study to investigate the influence of increased mean airway pressure not only on regional cerebral blood flow (rCBF) but also on regional CBV (rCBV) by means of contrast-enhanced MRI perfusion measurements. For a more detailed analysis of changes in rCBV, parallel changes in rCVR [Moyer et al., 1957] were calculated, and for analyzing relative changes in rCBV compared to rCBF, rMTT was used.

In order to avoid effects stemming from background medication (e.g., anesthetics, opioids), which influence cerebral hemodynamics in sedated and mechanically ventilated patients with PEEP, spontaneous CPAP breathing in human volunteers was used to increase mean airway pressure in the present study.

METHODS

Subjects and experimental design

After obtaining the approval of the local university ethics committee and written informed consent, 10 healthy, awake, male volunteers underwent MRI measurement of contrast-enhanced cerebral perfusion on two consecutive days. Wearing a tightly fitting face mask, the volunteers normoventilated (end-tidal CO₂ concentration [EtCO₂] = 40 mmHg; fraction of inspired oxygen [FiO₂] = 0.21) without CPAP (0 cm H₂O) during control measurement and at a CPAP of 12 cm H₂O in a randomized order. Before taking the readings, a minimum of 10–15 min was allowed at each level for stabilization. A high-flow CPAP device (CF-800, Draeger; Germany) was used to apply a con-

tinuous positive airway pressure of 12 cm H₂O (FiO₂ = 0.21). All airway pressure measurements were taken directly from the face mask. Flow adjustments provided an in- and expiratory pressure swing of no more than 1 cm H₂O. The volunteers had been trained to normoventilate (EtCO₂ = 40 mmHg) both by verbal instruction and by watching the capnographic trace of the monitor on the day prior to the MRI session. During the experiment breathing at a constant EtCO₂ (e.g., 40 mm Hg) was supported by voice command when necessary. FiO₂, EtCO₂, respiration frequency (RF), noninvasive mean arterial blood pressure (MAP) and hemoglobin oxygen saturation measured by pulsoxymetry (SpO₂) were monitored (Compact monitor, Datex, Finland) during execution of the experiment.

Magnetic resonance imaging (MRI) measurements

MRI measurements were performed on a 1.5-Tesla whole-body scanner [Magnetom VISION, Siemens, Germany) using a standard circular polarized head coil. Single-shot echo planar imaging (EPI) was performed with a repetition time (TR) of 2 sec and an echo time (TE) of 64 ms. An acquisition matrix of 64 × 128 (FOV 22 × 22 cm, inplane resolution 1.6 × 1.6 mm) was used. Slice thickness was set to 5 mm, and 15 slices were measured. A paramagnetic contrast agent Gd-DTPA (0.1 mmol/kg) was injected into an antecubital vein at a rate of 9 mL/s using an MR-compatible power injector (SPECTRIS, Medrad Inc., Pittsburgh, PA). Echo planar imaging (EPI) scans (n = 60) were performed at 2 sec intervals to cover the whole passage of the contrast agent through the brain. Six scans (6/60 scans) taken preinjection were used as the baseline.

Regional cerebral blood flow (rCBF), regional cerebral blood volume (rCBV), regional mean transit (rMTT) and regional cerebrovascular resistance (rCVR)

rCBV and rCBF were calculated in regions of interest (ROIs) outlined bilaterally in white and in (frontal, parietal, occipital, striatal and thalamic) grey matter (Figs. 1 and 2) by a blinded investigator.

The basic concept used to determine CBV and CBF was previously described by Ostergaard et al. [1996, 1998]. An improved gamma variate fit was used to reduce underestimation of the arterial input function (AIF), which otherwise leads to overestimation of CBV and CBF values [Ellinger et al., 1998]. CBF values are given in [mL · 100mL⁻¹ · min⁻¹] and CBV values in [mL · 100mL⁻¹].

Figure 1.

Representative CBV map showing regions of interest (ROIs) for evaluation of right hemispheric occipital (black), striatal (yellow), and thalamic (blue) grey matter CBV values during increased mean airway pressure (MPA = 12 cm H₂O). The sequence of colors black, red, green, and blue indicates increasing CBV values. The scale of the color bars is given in [mL/100 mL]. R = right hemisphere, L = left hemisphere.

Regional mean transit time (rMTT), which defines the average time that any particle of tracer (e.g., contrast media) remains within the region of interest [Young and Ornstein, 1994], was calculated with the equation:

$$rMTT = \frac{rCBV}{rCBF} \cdot 60 \quad (1)$$

rMTT is given in seconds (sec).

Regional cerebrovascular resistance (rCVR) was calculated with the equation [Moyer et al., 1957]:

$$rCVR = \frac{MAP}{rCBF} \quad (2)$$

rCVR is given in [mmHg · (mL · 100mL⁻¹ · min⁻¹)⁻¹].

Statistical analysis

Data are presented as mean ($\pm$ SEM) and mean ($\pm$ SD). Data were tested for normal distribution with the Kolmogorov-Smirnov Test. In the case of normal distribution analysis of variance (ANOVA) for repeated measurements with Bonferroni correction for

multiple testing was performed. Otherwise, the Mann-Whitney U-Test was employed. A $P \leq 0.05$ was considered statistically significant. The statistical computer package SPSS® 8.0.0 for Windows (95) was used for statistical analysis.

RESULTS

Ten male volunteers (mean [$\pm$ SD] age: 30 [$\pm$ 6] yr; weight: 81 [$\pm$ 11] kg; height: 186 [$\pm$ 8] cm) completed the study without complication. All volunteers were right-handed and nonsmokers. During CPAP breathing hemodynamic (heart rate, MAP) and respiratory parameters like SpO₂ and EtCO₂ remained unchanged (Table I), whereas respiration frequency decreased significantly.

Regional cerebral blood flow (rCBF)

rCBF ranged from 93.03 ($\pm$ 0.68) to 262.29 ($\pm$ 2.63) [mL · 100mL⁻¹ · min⁻¹] at baseline. Increasing mean airway pressure decreased rCBF in all regions studied (Fig. 3). The decrease was most pronounced in frontal and parietal and least pronounced in striatal grey matter independent of the hemisphere. White matter rCBF was

Figure 2.

Representative CBV map showing regions of interest (ROIs) for evaluation of right hemispheric white matter (yellow) as well as frontal (blue) and parietal (cyan) grey matter CBV values during increased mean airway pressure (MPA = 12 cm H₂O). The sequence of colors black, red, green, and blue indicates increasing CBV values. The scale of the color bars is given in [mL/100mL]. R = right hemisphere, L = left hemisphere.

TABLE I. Hemodynamic and respiratory parameters during baseline (MPA = 0 cm H₂O) and increased mean airway pressure (MPA = 12 cm H₂O)*

MPA (cm H ₂ O)	HR (beats/min)	MAP (mmHg)	SpO ₂ (%)	EtCO ₂ (mmHg)	RF (breaths/min)
0	68 (±8)	88 (±6)	96 (±1)	40 (±0.4)	15 (±5)
12	66 (±16)	90 (±7)	96 (±1)	40 (±1.7)	9 (±5) [†]

* Abbrev.: MPA, mean pressure airway; HR, heart rate; MAP, mean arterial blood pressure; SpO₂, hemoglobin oxygen saturation measured by pulseoxymetry; EtCO₂, end-tidal CO₂ concentration; RF, respiration frequency.

[†] significant to baseline (MPA = 0 cm H₂O) ($P \leq 0.05$); (n = 10).

lower than grey matter rCBF independent of hemisphere and increased mean airway pressure (Table II).

The number of interhemispheric differences in rCBF present at baseline rose when mean airway pressure was increased (Table III).

Regional cerebral blood volume (rCBV)

rCBV, which ranged from 7.37 (± 0.05) to 17.24 (± 0.25) [mL · 100mL⁻¹] at baseline, was decreased in all regions when increasing mean airway pressure (Fig. 4). Frontal grey matter rCBV decreased most, whereas white matter rCBV was least affected by increasing mean airway pressure (Table II). The number of interhemispheric differences in rCBV present at baseline rose when mean airway pressure was increased (Table III).

Figure 3.

Increased mean airway pressure (MPA = 12 cm H₂O) decreased regional cerebral blood flow (rCBF) bihemispherically. Abbrev: MPA(0), mean pressure airway 0 cm H₂O; MPA(12), mean pressure airway 12 cm H₂O; WM, white matter; GM_ST, striatal grey matter; GM_TH, thalamic grey matter; GM_FR, frontal grey matter; GM_PA, parietal grey matter; GM_OC, occipital grey matter.

Regional mean transit time (rMTT)

rMTT, which ranged from 3.63 (± 0.04) to 5.15 (± 0.04) (sec) at baseline, increased in all regions when CPAP was applied (Fig. 5). Grey matter showed occipitally the most and striatally the least pronounced increase in rMTT (Table II). The number of interhemispheric differences in rMTT present at baseline rose when mean airway pressure was increased (Table III).

Regional cerebrovascular resistance (rCVR)

At baseline rCVR ranged from 0.38 (± 0.00) to 1.19 (± 0.01) [mmHg · (mL · 100mL⁻¹ · min⁻¹)⁻¹]. Increasing mean airway pressure by CPAP breathing raised rCVR in all regions studied (Fig. 6), whereby frontal grey matter showed the greatest increase in rCVR, while white matter, followed by striatal grey matter, showed the least increase (Table II). The number of interhemispheric differences in rCVR was increased (Table III).

DISCUSSION

Increasing mean airway pressure by CPAP breathing reduced rCBF and rCBV and increased rMTT and rCVR in human volunteers.

An increase in mean airway pressure (i.e., by CPAP or PEEP) is commonly used to improve oxygenation in clinical routine by increasing pulmonary functional residual capacity. Transmission of increased mean airway pressure from the thoracoabdominal cavity to the CSF compartment has previously been shown to increase CSF pressure [Hormann et al., 1994]. Concomitant changes in CBF and CBV are assumable as the increased intrathoracic pressure hinders cerebral venous drainage via the jugular veins [Feldman et al., 1997].

In a transcranial Doppler sonography (TCD) study in anesthetized patients Werner et al. found an increased

TABLE II. Increased mean airway pressure (MPA = 12 cm H₂O) reduced rCBF and rCBV but increased rMTT and rCVR*

		Right Hemisphere					Left Hemisphere				
		MPA (0)		MPA (12)			MPA (0)		MPA (12)		
		Mean	SEM	Mean	SEM	<i>P</i>	Mean	SEM	Mean	SEM	<i>P</i>
WM	rCBF	94.70	0.66	67.08	0.48	*	93.03	0.68	62.94	0.47	*
	rCBV	7.59	0.06	6.31	0.05	*	7.37	0.05	6.00	0.05	*
	rMTT	5.15	0.04	6.13	0.05	*	5.07	0.03	6.17	0.05	*
	rCVR	1.16	0.01	1.57	0.01	*	1.19	0.01	1.67	0.01	*
GM_ST	rCBF	262.29	2.63	192.09	2.24	*	253.77	2.53	184.93	2.14	*
	rCBV	15.26	0.20	11.54	0.13	*	14.65	0.18	11.12	0.12	*
	rMTT	3.65	0.04	3.89	0.05	*	3.63	0.04	3.83	0.04	*
	rCVR	0.38	0.00	0.52	0.01	*	0.40	0.00	0.55	0.01	*
GM_TH	rCBF	235.71	3.71	163.84	3.20	*	250.71	3.67	170.40	2.86	*
	rCBV	14.58	0.26	11.35	0.20	*	14.98	0.30	12.41	0.20	*
	rMTT	3.88	0.05	4.49	0.08	*	3.70	0.05	4.68	0.07	*
	rCVR	0.44	0.01	0.63	0.01	*	0.41	0.01	0.60	0.01	*
GM_FR	rCBF	223.61	2.32	150.85	1.61	*	225.48	2.26	147.99	1.74	*
	rCBV	15.18	0.19	11.80	0.13	*	15.22	0.17	12.30	0.15	*
	rMTT	4.26	0.04	4.96	0.05	*	4.31	0.04	5.29	0.06	*
	rCVR	0.46	0.00	0.69	0.01	*	0.47	0.01	0.72	0.01	*
GM_PA	rCBF	246.29	2.35	170.21	1.78	*	234.12	2.48	149.24	1.70	*
	rCBV	16.81	0.20	13.25	0.15	*	15.46	0.18	12.37	0.15	*
	rMTT	4.31	0.04	4.92	0.05	*	4.24	0.04	5.23	0.05	*
	rCVR	0.43	0.00	0.63	0.01	*	0.46	0.01	0.71	0.01	*
GM_OC	rCBF	214.40	2.69	150.53	2.29	*	234.30	2.59	156.31	1.95	*
	rCBV	15.99	0.28	12.57	0.19	*	17.24	0.25	13.72	0.18	*
	rMTT	4.49	0.05	5.35	0.07	*	4.57	0.05	5.68	0.07	*
	rCVR	0.53	0.01	0.76	0.01	*	0.47	0.01	0.71	0.01	*

* Abbrev.: MPA(0), mean pressure airway 0 cm H₂O; MPA(12), mean pressure airway 12 cm H₂O; WM, white matter; GM_ST, striatal grey matter; GM_TH, thalamic grey matter; GM_FR, frontal grey matter; GM_PA, parietal grey matter; GM_OC, occipital grey matter; rCBF [mL · 100 mL⁻¹ · min⁻¹], rCBV [mL · 100 mL⁻¹], rMTT [s]; rCVR [mmHg · (mL · 100 mL⁻¹ · min⁻¹)⁻¹]. Values are given as mean ± SEM. P ≤ .05; n = 10.

mean airway pressure of 15 cm H₂O to reduce middle cerebral artery blood flow velocity (CBFV/MCA) [Werner et al., 1990], indicating reduced CBF. Results from animal studies, however, are inconsistent, showing either no effect of increased airway pressure on CBF [Toung et al., 1988] or a decrease in CBF when MAP decreased [Doblar et al., 1981].

In the present study increased mean airway pressure did not change MAP, but rCBF decreased in all white and grey matter regions studied. In contrast to the common concept that impaired cerebral venous outflow, e.g., from increased mean airway pressure, leads to cerebral congestion of blood in capillary and venous vessel areas [Feldman et al., 1997], rCBV was decreased as compared to baseline.

In this study, rCVR was calculated simply from the ratio of MAP to rCBF (see Methods). This simplification was justified as each volunteer served as his own

control and none of the volunteers showed clinical signs or MRI findings of intracranial pathology. In a recent study, Toung et al. [2000] showed cerebral venous pressure to not increase with positive end-expiratory pressure (PEEP) when the head was elevated but to linearly increase with increasing PEEP in the prone position. Thus, a small but systematic overestimation of rCVR during CPAP breathing in our supine-positioned volunteers can not be excluded totally. The observed increase in rCVR during CPAP is in good accordance with the decrease demonstrated in rCBV. However, rCBV had decreased significantly less than rCBF, because rMTT (see Methods) was increased.

From contrast-enhanced MRI perfusion measurements it is not possible to determine whether the changes found in cerebral hemodynamics during increased mean airway pressure are primarily caused by changes in arterial, capillary, or venous circulation. In

TABLE III. Increased mean airway pressure (MPA = 12 cm H₂O) increased the number of interhemispheric differences in rCBF, rCBV, rMTT and rCVR*

MPA (0 cm H ₂ O)	rCBF	rCBV	rMTT	rCVR
WM				
GM_ST		L < R		
GM_TH	L > R		L < R	L < R
GM_FR				
GM_PA	L < R	L < R		L > R
GM_OC	L > R	L > R		L < R
MPA (12 cm H ₂ O)	rCBF	rCBV	rMTT	rCVR
WM	L < R	L < R	L > R	L > R
GM_ST	L < R			L > R
GM_TH	L > R	L > R	L > R	L < R
GM_FR		L > R	L > R	
GM_PA	L < R	L < R	L > R	L > R
GM_OC	L > R	L > R	L > R	L < R

* Abbrev.: MPA, mean pressure airway; L, left hemispheric; R, right hemispheric; WM, white matter; GM_ST, striatal grey matter; GM_TH, thalamic grey matter; GM_FR, frontal grey matter; GM_PA, parietal grey matter; GM_OC, occipital grey matter. $P \leq .05$; $n = 10$.

a recent EPISTAR (echo-planar imaging and signal targeting with alternating radio frequency) perfusion MRI study performed in human volunteers, Schocke et al. [1999] showed that spontaneous CPAP breathing increases EPISTAR signal in white matter but not in

Figure 4.

Increased mean airway pressure (MPA = 12 cm H₂O) decreased regional cerebral blood volume (rCBV) bihemispherically. See Figure 3 for abbreviations.

Figure 5.

Increased mean airway pressure (MPA = 12 cm H₂O) increased regional mean transit time (rMTT) bihemispherically. See Figure 3 for abbreviations.

occipital or most of the other grey matter regions studied. Aside from the different choice of regions of interest (ROIs) for evaluation of rCBF and rCBV (e.g., size of ROIs, choice of slice in which the ROIs are to be outlined), method particularities of EPISTAR perfusion measurement must also be taken into consideration.

The EPISTAR signal depends on precapillary arterial rCBF and rCBV [Buxton et al., 1998]. If *only* rCBF or rCBV changes, the EPISTAR signal will change. If,

Figure 6.

Increased mean airway pressure (MPA = 12 cm H₂O) increased regional cerebrovascular resistance (rCVR) bihemispherically. See Figure 3 for abbreviations.

however, both rCBF and rCBV change, the EPSTAR signal can remain unchanged.

Therefore, it is conceivable that the present study's decrease in rCBF and rCBV during CPAP (12 cm H₂O) breathing is due to reduced rCBF and rCBV in arterial as well as in capillary and venous vessel areas.

The conceivable underlying mechanisms are vasoconstriction, vasocompression or a combination of both. Active vasoconstriction demands a properly developed tunica muscularis like in arterial vessels, which, however, is not developed in capillaries and only poorly developed in postcapillary venules. Therefore, vasoconstriction of precapillary arteries during CPAP breathing is well assumable. The extent, however, to which active venoconstriction, which exists in extracranial veins [Gaddis et al., 1986], plays a role in regulating cerebral perfusion (e.g., in the presence of elevated intracranial pressure), clearly awaits further investigation.

The second explanation for the observed decrease in rCBF and rCBV during increased mean airway pressure is passive vasocompression. In animal experiments, Doblar et al. [1981] found that brain interstitial fluid pressure is an important variable in determining CBF during increased mean airway pressure. In humans, CPAP breathing was found to increase CSF pressure [Hormann et al., 1994]. If such an increase in CSF pressure causes a corresponding rise in brain interstitial fluid pressure, vasocompression occurs in capillary and also to an unknown degree in venous and possibly also arterial vessel areas.

Of the above mentioned, passive vasocompression appears to be the prevailing mechanism in the capillary and venous vessel areas. Arterial vessels are significantly less compressible than venous vessels due to a more muscular wall [Berry et al., 1995]. Therefore, active vasoconstriction is more likely to occur in arterial vessel areas during CPAP breathing.

In accordance with others we found CBF and CBV control values to be higher than values reported from PET studies [Frackowiak et al., 1980; Lenzi et al., 1981; Leenders et al., 1990; Rempp et al., 1994]. In order to quantify absolute CBF and CBV values by use of contrast-enhanced MRI perfusion measurement, the concentration of the paramagnetic contrast agent in an arterial vessel, the arterial input function (AIF), needs to be determined. Any underestimation of AIF leads to an overestimation of CBF and CBV values. As AIF is taken in the region of the middle cerebral artery, which is a rather small vessel, underestimation of the AIF due to partial volume effects is possible. Moreover, the assumption of a linear [Rosen et al., 1990;

Ostergaard et al., 1996] instead of a nonlinear [Akudak et al., 1998; Edmister et al., 1997] relationship between blood concentration of paramagnetic contrast agent and the susceptibility contrast can cause the AIF to be underestimated. In the present study, part of the underestimation of AIF and hence overestimation of CBV and CBF was compensated for by using an improved AIF gamma variate fit [Ellinger et al., 1998].

A partial volume effect due to the rather poor spatial resolution of PET, however, could also be responsible for the 28% to 53% underestimation of CBF and CBV values in grey matter when using PET as previously reported by other authors [Muller-Gartner et al., 1992].

In a PET study, Perlmutter et al. [1987] reported regional asymmetries of CBF, CBV, and CMRO₂ in right-handed normal subjects. Similarly, in our right-handed, normocapnic volunteers interhemispheric differences in rCBF, rCBV but also rCVR and rMTT were found at baseline. These could reflect anatomical [Geschwind and Galaburda, 1985] and/or functional [Prohovnik et al., 1980; Deutsch et al., 1988] asymmetries. For example, increased attention or vigilance or a demanding mental activity causes an increase in regional asymmetries [Deutsch et al., 1987]. In this respect the increased number of interhemispheric differences in rCBF, rCBV, rMTT, and rCVR might well reflect a kind of task-induced change in cerebral function during CPAP breathing. Since in the present study CPAP breathing causes a general decrease in rCBF and rCBV, it is possible that not only changes in cerebral function but also regional differences in sensitivity to changes in brain interstitial fluid pressure play a role. These issues, however, require clarification in future research.

Reducing paCO₂ causes hypocapnic vasoconstriction, which has previously been shown to reduce global [van Rijen et al., 1989; Kraaier et al., 1991] and regional [Posse et al., 1997] CBF. In the present study, however, normocapnia was meticulously controlled by EtCO₂, which correlates well with paCO₂ [Young et al., 1991; Campbell et al., 1994; Bongard et al., 1994]. Therefore, it is unlikely that paCO₂-induced cerebral vasoconstriction influenced contrast-enhanced MRI perfusion measurements in the present study.

In conclusion, we show that an increase in mean airway pressure, as during spontaneous CPAP breathing at 12 cm H₂O, decreases rCBF and rCBV but increases rMTT and rCVR in human volunteers. Active vasoconstriction (e.g., arterial) and passive vasocompression (e.g., capillary and venous) due to increased brain interstitial fluid pressure must be

considered the underlying mechanism for the observed decrease in cerebral hemodynamics. Although our data were obtained from volunteers, the results of the present study should be taken into consideration when interpreting contrast-enhanced MRI perfusion measurements in patients with elevated mean airway pressure.

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