In Vivo CBF Autoregulation Studies Using Rheoencephalography

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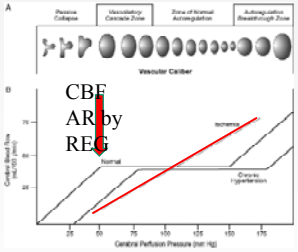
Abstract

Acute management of patients with traumatic brain/blast injury remains a challenge. To minimize secondary injury and improve outcome, it is critical to detect neurological deterioration early, when it is potentially reversible (Rubin et al, 2009). One potential monitoring method is cerebral electrical impedance (rheoencephalography, REG), because of its non-invasiveness and good time resolution. Here we compare the results of cerebral blood flow (CBF) manipulations comparing Doppler techniques with the electrical impedance technique. Our hypothesis was that REG would reflect CBF autoregulation. Animal experiments were performed using rats and pigs (with intracerebral electrodes) and monkeys (with surface electrodes). Challenges included CO_2 inhalation, carotid clamping, liposome infusion, hemorrhage, and positive end expiratory pressure (PEEP). Data were stored on a PC and evaluated off line. CBF autoregulation was also evaluated by a Matlab script.
These studies confirmed that REG reflects CBF autoregulation and can be used to the detect lower limit of CBF autoregulation.

Introduction

Changes in vascular caliber that can be associated with cerebral autoregulation failure. Altered intracranial autoregulation due to an intracranial lesion and/or edema results from vasodilatation in an effort to increase CBF. However, beyond the lower limit of autoregulation, vessels passively collapse, and ischemia results. Beyond the upper limit of autoregulation or the "breakthrough zone", increased intravascular volume and pressure results in vasogenic edema (Varon, 2007).

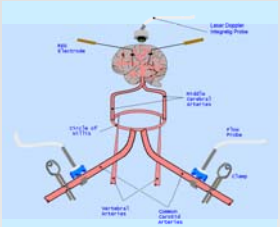


Summary of Experiments

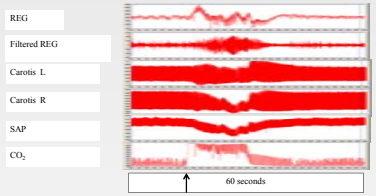
Challenge	Species	N/trial	Mesured modality			Correlation
			REG	Doppler	LDF	
CO2 inhalation	rat	13/89	+			
Aorta compression	pig	1/3	+		+	+
CO2 inhalation	rat	11/63	+	+	+	+
Carotid clamping	rat	5/13	+	+	+	+
Hemorrhage	rat	14/11/3	14	11	3	+
Liposome infusion	pig	24/57	+			
Hemorrhage, PEEP	pig	42/60	+	+		+
Hemorrhage	pig	13/92	+	+		+
Hemorrhage	monkey	8	+			
Hypotension	pig	17	+			

Methods - Rat

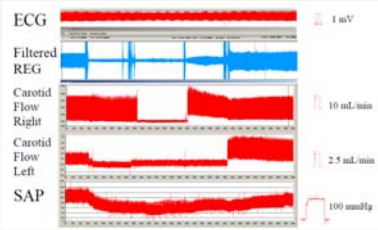
Electrode/Sensor Arrangement



Results - Rat



During CO_2 inhalation, increases in REG and LDF were significant, while carotid flow and systemic arterial pressure decreased. The transient increases in REG pulse amplitude (69 % ± 2.6) and LDF (78.1 %, 4.4) were highly significant ($p<0.001$).



•Effect of clamping of common carotid arteries. Following the first clip placement on the left carotid artery, the rheoencephalogram (REG) amplitude (filtered REG) decreased; the placement of the second clip right carotid artery had no further decrease. During the clamping

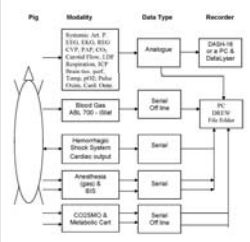
•period there was no pulse amplitude observed in either carotid trace. For better visibility the recording traces were blown up; the real flow calibration values appear on the right side. Amplification of left and right carotid flow differed. A few minutes after removal of one clip from

•the right carotid artery, REG amplitude moderately increased, and after removal of the second clip from the left carotid artery, the REG amplitude returned to slightly above the baseline level. Similarly, both carotids showed a slight hyperemic reaction. The baseline systemic arterial pressure (SAP) value was 135/80 mm Hg; during clamping, the minimal value was 80/40 mm Hg. The rat/trial ID was 5-23-02/11. REG was an intra-hemispherical left-side) derivation. The time window was 10 min; REG filter was 3–100 Hz. ECG: electrocardiogram.

Data Analysis: Calculation of Lower Limit of CBF Autoregulation

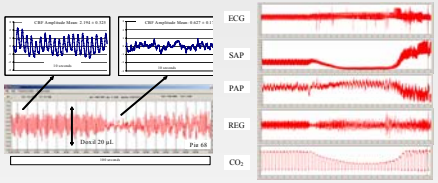
-Waveform data averaged in 10 second epochs
-Autoregulation plots examined (CPP vs. REG, CF, LDF, or CBF)
-Pearson correlation coefficient computed on 30 consecutive points (5 min) and updated every minute with a sliding window
For further details, see Czosnyka et al. Continuous assessment of the cerebral vasomotor reactivity in head injury. Neurosurgery. 1997 Jul;41(1):11-7.

Methods - Pigs



Block schematics of measuring and data collection. Dash-18 recorder collected analog signals. Drew recorder collected both analog and serial port data. Data from iSTAT and Metabolic cart were collected and stored off line and then added to the database.

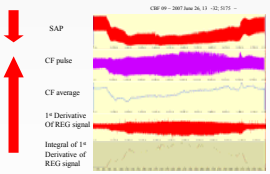
Results



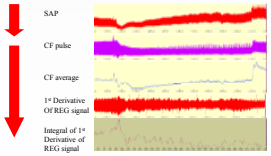
After the liposome injection, a transient decrease in REG pulse amplitude was observed. This result indicates the involvement of a cerebrovascular reaction during liposome/Doxil injection. (Bodo et al, 2005).

CBF AR Test: The Effect of 20 cm H_2O PEEP

Before hemorrhage Hemodynamic Status: BP 120/78; mean 92 CBF autoregulation present. SAP decrease elicited increase in CF and REG pulse amplitudes.

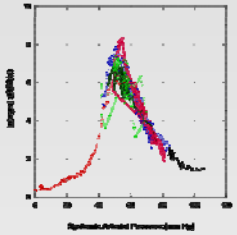


After hemorrhage (Blood loss of ~1.3 L with estimated SBV of 30%): Hemodynamic Status: BP 90/67; mean 75 CBF autoregulation impaired. SAP decrease elicited decrease in CF and REG pulse amplitudes



Results

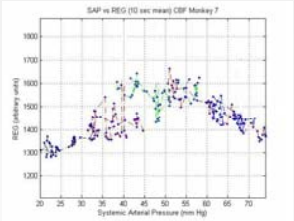
Relationship of REG to Systemic Arterial Pressure



The shape of this relationship strongly suggests that the REG signal is reflecting the cerebral vasodilation that occurs over the range of SAP from 90 to 55 mm Hg. The negative Pearson coefficient indicates the presence of autoregulation in this range; a positive Pearson coefficient below 55 mm Hg indicates the absence of autoregulation.

IMPACT: Brain injured patients are known to have compromised autoregulation, but currently there is no non-invasive way to assess the risk of implementing a hypotensive resuscitation strategy in the brain-injured patient. REG can identify the autoregulatory breakpoint for individual patients to determine their limit for permissive hypotension.

Relationship of REG to Systemic Arterial Pressure;
(Result from a monkey hemorrhage)



Relationship of SAP (10-sec means) to REG signals obtained from the scalp electrodes on a monkey. This demonstrates that with surface electrodes (non invasive), the slow wave oscillations of the REG signal are present (not filtered out by the skull).

Conclusion

These studies confirmed that:
-REG reflects CBF autoregulation
-With specialized algorithms, REG can be used to detect lower limit of CBF autoregulation.

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Disclaimer

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Research was conducted in compliance with the Animal Welfare Act and other federal statutes and regulations relating to animals and experiments involving animals and adheres to principles stated in the Guide for the Care and Use of Laboratory Animals, NRC Publication, 1996 edition.