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Comparison of cerebrovascular reactivity tests: a pilot human study

Michael Bodo[1,6], Richard Mahon[2], Alex Razumovsky[3], Efim Kouperberg[3], Michael Crimmins[1], Rocco Armonda[4], Martin Baruch[5]

1. *Department of Neurology, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Road, Bethesda, MD 20814 MD, USA*
2. *Naval Medical Research Center, Silver Spring, MD, USA*
3. *NeuroCare Services, Hunt Valley, MD, USA*
4. *Washington Hospital Center, Washington, DC, USA*
5. *Empirical Technologies Corporation, Charlottesville, VA, USA*
6. *E-mail any correspondence to: michaelbodo1947@gmail.com*

Abstract

In neurosurgery intensive care units, cerebrovascular reactivity tests for neuromonitoring are used to evaluate the status of cerebral blood flow autoregulation; lack of autoregulation indicates a poor patient outcome. The goal of neuromonitoring is to prevent secondary injuries following a primary central nervous system injury, when the brain is vulnerable to further compromise due to hypoxia, ischemia and disturbances in cerebral blood flow and intracranial pressure. Ideally, neuromonitoring would be noninvasive and continuous. This study compares cerebrovascular reactivity monitored by rheoencephalography, a noninvasive continuous monitoring modality, to cerebrovascular reactivity measured by currently used neuromonitoring modalities: transcranial Doppler, near infrared spectroscopy and laser Doppler flowmetry. Fourteen healthy volunteer subjects were measured. The tests used for comparison of cerebrovascular reactivity were breath-holding, hyperventilation, CO_2 inhalation, the Valsalva maneuver, and the Trendelenburg and reverse Trendelenburg positions. Data for all modalities measured were recorded by computers and processed off line. All measured modalities reflected cerebrovascular reactivity with variabilities. Breath-holding, CO_2 inhalation, and the Valsalva maneuver caused CO_2 increase and consequent brain vasodilatation; hyperventilation caused CO_2 decrease and brain vasoconstriction. The Trendelenburg and reverse Trendelenburg positions caused extracranial blood volume changes, which masked intracranial cerebrovascular reactivity. The hyperventilation test proved ineffective for measuring cerebrovascular reactivity with rheoencephalography due to respiratory artifacts. Some discrepancies among the various modalities tested were observed. Further validation studies are under preparation to test the applicability of rheoencephalography for noninvasive continuous brain monitoring, including enhanced computational methods, animal studies and clinical monitoring studies of humans.

Keywords: cerebrovascular reactivity, REG, TCD**,** NIRS, LDF, human

Introduction

Rheoencephalography

This study compared cerebrovascular reactivity monitored by rheoencephalography (REG), a noninvasive continuous monitoring modality, to cerebrovascular reactivity measured by currently used neuromonitoring modalities: transcranial Doppler, near infrared spectroscopy and laser Doppler flowmetry. Jenkner [1,2] first applied the term rheoencephalography to electrical impedance plethysmography, when applied to the head to measure continuous registration of cerebrovascular changes. The technique was originally developed to measure changes in peripheral circulation related to alterations in pulse volume. REG is based on the assumption that changes in cerebral circulation can be related to changes in electric impedance of the cranial tissues to high-frequency alternating current (20,000 cycles per second and higher)

applied by means of electrodes placed on the scalp. There have been a number of reports evaluating this method, and conflicting results have been reported [3].

Positive characteristics of REG are that it is non-invasive and is easy and inexpensive to administer continuously. However, before the availability of computerized data processing techniques, the usefulness of REG for neuromonitoring was limited since REG does not reflect absolute blood flow or provide direct diagnostic information; in addition, the REG signal may be contaminated by artifacts due to patient movement or biological causes, such as respiration.

Currently, available computerized data processing techniques make REG a potential method for neuro-monitoring by mitigating artifacts and extracting characteristics and information not visible in the raw REG signal [4].

This study reports results of a continuing investigation of the feasibility of using REG as a measurement modality of cerebral blood flow autoregulation (CBF AR). CBF AR is measured in clinical practice by cerebrovascular reactivity (CVR) tests. Our hypothesis was that during CBF AR tests, REG results will correlate with results of Near Infrared Spectroscopy (NIRS) [5-7] and transcranial Doppler (TCD) [8, 9], which measure middle cerebral artery blood flow. The purpose of measuring laser Doppler flow (LDF) in this study was to investigate the presence or absence of skin blood flow changes during CBF AR tests and to verify whether or not the REG signal is influenced by extracranial blood flow.

Materials and methods

Subjects and measurement modalities

Fourteen healthy volunteers were measured in two sessions (session 1, n=4; session 2, n=10) (Table 1). The tests used to induce CBF AR were breath-holding (BH), hyperventilation (HV), CO_2 inhalation (CO_2), Valsalva maneuver (VAL), Trendelenburg position (TREN), reverse Trendelenburg (R TREN) position. For all fourteen subjects, modalities recorded were fronto-temporal REG; near infrared spectroscopy (NIRS) on head and leg; electrocardiogram; respiratory volume and pressure; exhaled CO_2 level during respiratory tests; forehead skin blood flow by laser Doppler flow (LDF); and peripheral bio-impedance pulses. For ten of the subjects, middle cerebral artery blood flow velocity was measured simultaneously by TCD and fronto-mastoid REG.

Table 1. Epidemiology of test subjects; n=14; mean (upper numerical row) and SD values (lower numerical row). The differences between left and right systolic and diastolic values were not significant. *Body Mass Index. Protocols were approved by an Institutional Review Board.

				Left Arm		Right Arm		
Age	Weight	Height	BMI*	Systolic	Diastolic	Systolic	Diastolic	Heart Rate
year	kg	cm	kg/m^2	mmHg	mmHg	mmHg	mmHg	b/m
31.6	83.9	174.3	27.5	123.0	74.0	124.8	73.7	66.6
7.1	15.8	8.6	4.0	8.8	5.7	7.5	6.2	10.6

Devices used to measure cerebrovascular reactivity

The blood flow velocity of the middle cerebral artery was measured by Doppler-Box (CompuMedics Germany GmbH, Singen, Germany); a 2.5 MHz probe was placed in the Doppler-Box TCD headband. Regional tissue oxygen-ation was measured by NIRS (INVOS Cerebral Oximeter system, Somanetics Corporation, Troy, MI). REG was measured using two bipolar amplifiers, both with 125 kHz measuring frequency: REG1 was a brain monitor (Empirical Technologies Corporation, Charlottesville, VA); REG2 was Cerberus (QuintLab Bioelectronics, Ltd., Budapest, Hungary). Forehead skin blood flow was measured by LDF with an integrating probe and a Periflux System 4001 (Perimed AB, Sweden). Exhaled CO_2 (end-tidal CO_2) and respiratory volume and pressure data were generated by a respiratory profile monitor (CO_2SMO, Respironics Novametrix LLC, Wallingford, CT). For air pressure measurement during the Valsalva maneuver, a Model 505-P2 digital manometer (Testo, Flanders, NJ) was used. To study the effects of the Trendelenburg and reverse Trendelenburg positions, a tilting table was used.

Sensor placement and volunteer preparation

Sensor and electrode locations were as follow: NIRS1: right fronto-temporal; TCD: right temporal; LDF: left frontal; REG: left fronto-temporal and right fronto-temporo-mastoid; NIRS2: right ankle. The volunteer used a mouthpiece attached to the CO_2SMO sensor. The mouthpiece was modified to hold a thermal sensor connected to electronics (BAT-12, Physitemp and Transducer Pre-Amp, Kent Scientific, Torrington, CN) for generating analog waveform of respiration. A two-way non-rebreathing T-valve (Hans Rudolph Inc, Kansas City, MO) was connected to the mouthpiece. Ten to twenty percent CO_2 mixed with room air (21% O_2) was prepared using a gas mixer (Pegas 4000 mf, Columbus Instruments,

Columbus, OH) and stored in a breathing bag (Hudson RCI, Research Triangle Park, NC). For calibration, 5 % CO_2 was used (Scott Medical Products, Plumsteadville, PA). A three-way stopcock with a filled breathing bag was connected to the non-breathing T-valve (Hans Rudolph Inc, Kansas City, MO). A nose clip was used to block nasal breathing. Due to the limited hairless area on subjects' foreheads, it was necessary to place the REG electrodes under the TCD probe-holding frame (headband). The LDF probe holder was placed in a hole of the TCD probe-holding frame.

All recruited volunteers were required to give informed consent and to complete a verbal interview and written questionnaire to rule out existing disturbances in cerebrovascular autoregulation. Following blood pressure measurements on both arms, volunteers were instructed to lie in a supine position on the tilting table, which was initially positioned horizontally. For comfort, 13-cm diameter foam cylinder covered with a paper towel was placed under the neck, and skin sites for electrodes were cleaned with isopropyl alcohol. For control purposes, a 5-minute baseline recording was made for each volunteer before the first CBF challenge commenced.

Cerebrovascular reactivity tests

For each volunteer, the total continuous recording time was approximately 45 minutes for all tests. The sequence/time for tests were as follows: breath holding/30 seconds; hyperventilation/60 seconds; CO_2 inhalation/60 seconds; the Valsalva maneuver/20 seconds (pressure of 40 mmHg (=53.3 kPa) [10]. A 5-minute control recording was made before and after each test. For the Trendelenburg test (head down)/5minutes, the tilting table was adjusted to a 35 degree angle, measured by a circular retractor placed under the volunteer and fixed to the table; after 5 minutes, the table was returned to a horizontal position for the 5-minute control period, then adjusted to the reverse (head up) position (35 degree angle) for the 5-minute reverse Trendelenburg test, followed by a 5-minute control period.

Data recording

Analog waveforms were recorded as binary files by two Dash computers (Astro-Med Inc., West Warwick, RI), a Dash 18 (n=4; 200 Hz sampling rate) and Dash 32 HF (n=10; 250 Hz). TCD signals (waveform and mean values) were recorded with a Hewlett Packard laptop (n=10; ASCII file, 100 Hz sampling rate). CO_2SMO serial output was recorded into a binary file (Dell, Precision M4300, Round Rock, TX); waveform data for respiratory pressure volume, flow and end tidal CO_2 ($EtCO_2$) was exported as an ASCII file (n=14; Analysis Plus, Novametrix Medical Systems, Inc, Wallingford, CT) for later analysis (using Datalyser).

Data Processing

The Datalyser software program was used to inspect, measure and process data.

Measurements of increases and/or decreases in modality amplitude were obtained for comparison of each measurement modality (NIRS, REG, TCD, LDF) and test (breath holding; hyperventilation; CO_2 inhalation; the Valsalva maneuver; Trendelenburg; reverse Trendelenburg).

Prior to making a quantitative analysis to compare data for modalities and tests, the recordings were visually inspected and evaluated to ascertain physiological CBF reactions. To provide a qualitative comparison of each modality's reflection of CBF AR during each test, results were entered into a spreadsheet (Microsoft Excel, Redmond, WA), where assessment scores of successful and failed tests were recorded (Table 2). Artifact-contaminated data were not analyzed.

For quantitative comparisons of data, analog/digital (AD) conversion units (Y-axis) were measured and processed. For each test, a control value was obtained from the initial 5-minute control period before data were measured. Maximum and/or minimum values for the different tests were obtained from time windows during and/or immediately after each test.

Measurements were obtained for NIRS, REG, TCD and LDF. For NIRS and LDF, mean values were used; REG was characterized using the standard deviation value; TCD mean was calculated using a proprietary software program provided by the manufacturer [9]. All numbers were entered into an Excel spreadsheet; mean and standard deviation as well as CVR or vasomotor reactivity values were calculated for each respiratory test.

REG waveforms were smoothed (0.1s) and filtered (1 Hz Butterworth high-pass filter). The length of analyzed waveforms ranged from 4 to 30 seconds; the time periods analyzed were identical for both test and for control periods.

For processing CO_2 test data, CO_2SMO files were analyzed by obtaining readings for control, minimum (after hyperventilation) and maximum (after breath holding and CO_2 inhalation). Data were averaged for each test group.

Following initial data collection, CVR (defined as vasomotor reactivity) was calculated for each test; vasomotor reactivity is defined here as "the difference in velocity between the stimulation state and the control state, relative to the control state multiplied by 100" [9, 11]. For the comparison of TCD, NIRS and REG during breath holding, hyperventilation and CO_2 inhalation, CVR values were calculated according to normalization procedures used in clinical practice (CO_2 changes: percent CO_2/mmHg) [12].

To eliminate inter-individual differences for subjects in all tests, normalization against CO_2 levels (CVR) was used in calculating results for respiratory tests. For non-respiratory tests, results were calculated as a percentage of baseline values for each test. Software programs used for statistical analysis were the student t-test (Excel) and analysis of variance (ANOVA, Prism software, GraphPad, La Jolla, CA). Probability was considered significant at < 0.05; data are mean ± SD.

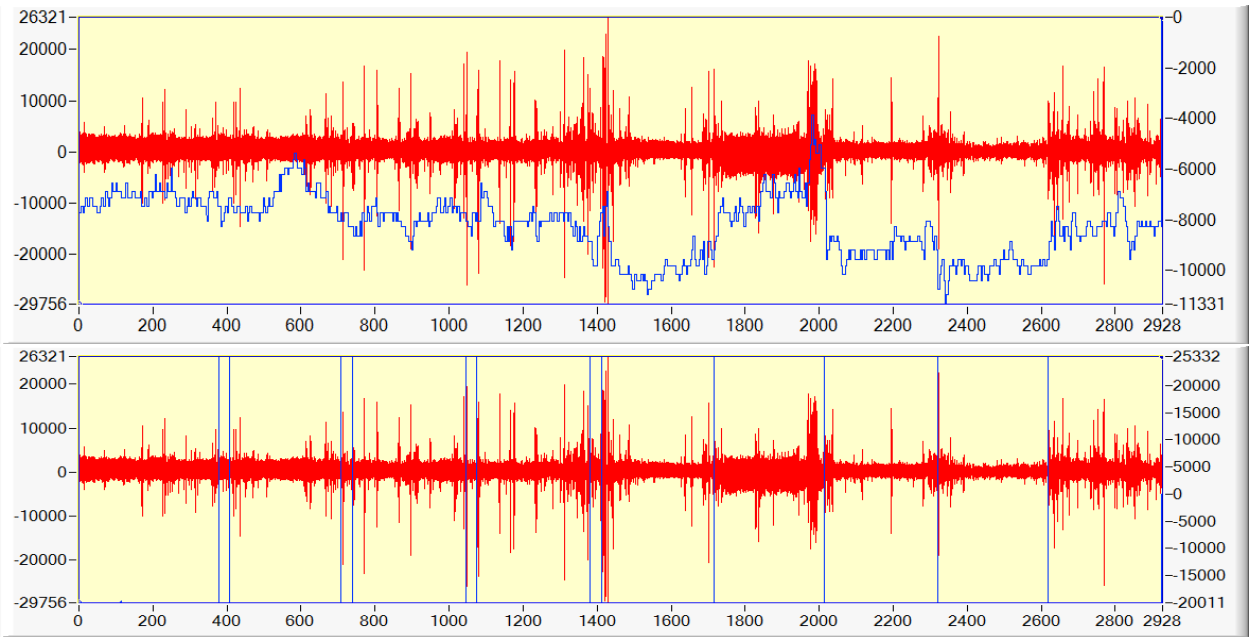

Fig. 1. Recording of a REG (red) and NIRS (blue) signals during sequence of tests (upper panel). Lower panel shows same REG signal and event markers indicating when a test started and ended (blue). Tests are as: breath holding, hyperventilation, CO_2 inhalation, Valsalva maneuver, Trendelenburg and Reverse Trendelenburg positions. Y-axis is in AD conversion units; X-axis is in seconds. Note the simultaneous amplitude increase of REG and NIRS signals during Trendelenburg position (1750-2000 s).

Results

All fourteen subjects completed the administered tests; none developed symptoms of cerebrovascular distress (nausea, headache, dizziness). Values for $EtCO_2$ were as follows: a) control, 41.8 ± 4.89 mmHg; b) after breath holding CO_2 increased: 48.7 ± 4.69 mmHg; c) after hyperventilation CO_2 decreased: 28.75 ± 5.38; d) during CO_2 inhalation its value increased: 111.68 ± 9.4 mmHg.

Breath-holding, CO_2 inhalation, and Valsalva maneuver increased CO_2 and caused brain vasodilatation. Hyperventilation decreased CO_2 and caused brain vasoconstriction. Trendelenburg position increased extracranial blood volume; reverse Trendelenburg position decreased extracranial blood volume. Both the Trendelenburg and reverse Trendelenburg positions masked intracranial CVR responses.

Table 2. Summary of tests and responses by modalities: BH (breath holding); HV (hyperventilation); CO_2 (CO_2 inhalation); VAL: Valsalva maneuver; TREN (Trendelenburg position); R TREN (reverse Trendelenburg position); N (number of measured subjects). In case of NIRS and TCD Trendelenburg measurement showed multyphasic change, not just increase or decrease in 7 (NIRS) and 10 cases (TCD). *Exceptions*: *LDF increased; **LDF decreased; NIRS and TCD showed multiphasic reactions for Trendelenburg and reverse Trandelenburg positions.

	BH increase	HV decrease	CO_2 increase	VAL increase	TREN increase	RTREN decrease	Total tests	Failed tests	Failed tests (%)	N
NIRS	11	13	12	11	13	12	78	6	7.7	13
TCD	9	9	8	9	3	0	60	22	36.7	10
REG	17	9	13	16	14	15	72	14	19.4	12
LDF	8	(7)*	7	11	(9**)	8	72	22	30.6	12

REG

Results for the 72 fronto-temporal REG tests analyzed for (N=12): pulse amplitude increased after breath holding (Fig.2-red), CO_2 inhalation, Valsalva maneuver and Trendelenburg position; pulse amplitude decreased after hyperventilation and reverse Trendelenburg position.

Fourteen REG tests (19.4 %) failed to produce a measurement of cerebrovascular reactivity. Fronto-mastoid REG derivation measurements were excluded from analysis because they contained more artifacts than fronto-temporal REG derivation measurements.

NIRS

Results for the 78 NIRS tests (N=13): increase in NIRS value was the typical reaction after breath holding (Fig. 2-blue), CO_2 inhalation, Valsalva maneuver and Trendelenburg position and decrease during hyperventilation and reverse Trendelenburg position. For seven subjects, Trendelenburg position the change was biphasic, not a simple increase).

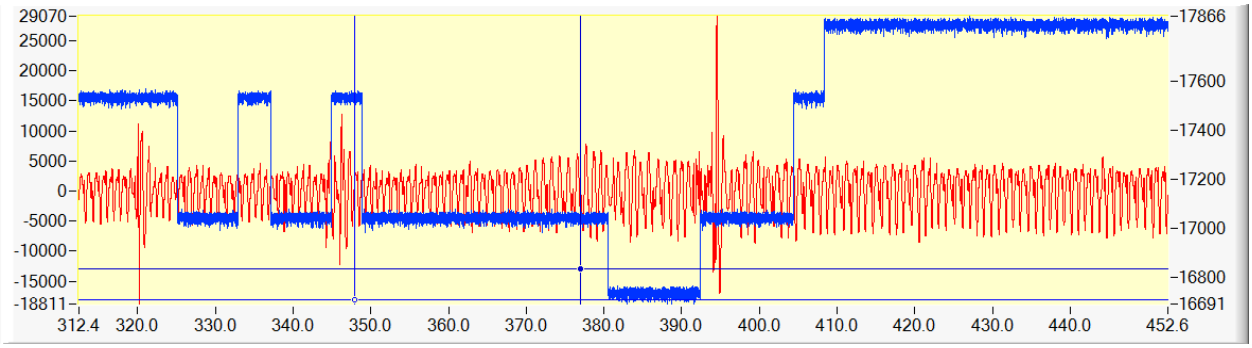

Fig. 2. *Breath holding*. REG (red) and NIRS (blue) signals during breath holding (see 350-380 seconds: breath holding is indicated by light blue vertical lines). REG and NIRS amplitude increases were simu1taneous: 20.2 % of baseline (after test). (Y-axis values are shown in AD conversion units; X-axis values are shown in seconds).

TCD

Results for the 60 TCD tests (N=10): increase in flow velocity was the typical reaction during breath holding, CO_2 inhalation, Valsalva maneuver; decrease in flow velocity was typical during hyperventilation and Trendelenburg position. In 38 tests (36.7%) the response did not follow the expected reaction. For all subjects, TCD change was biphasic during reverse Trendelenburg position.

LDF

Results for the 72 LDF tests (N=12): increase in flux (LDF unit) was the typical reaction during breath holding, hyperventilation, CO_2 inhalation and Valsalva maneuver; decrease in flux was observed during both Trendelenburg positions. In 22 of the 72 tests (30.6 %), no increase in flux was observed. LDF did not show CBF AR during respiration -based tests; however, flux decreased during Trendelenburg position (mean decrease 27.93 ± 23.56 %; N=10).

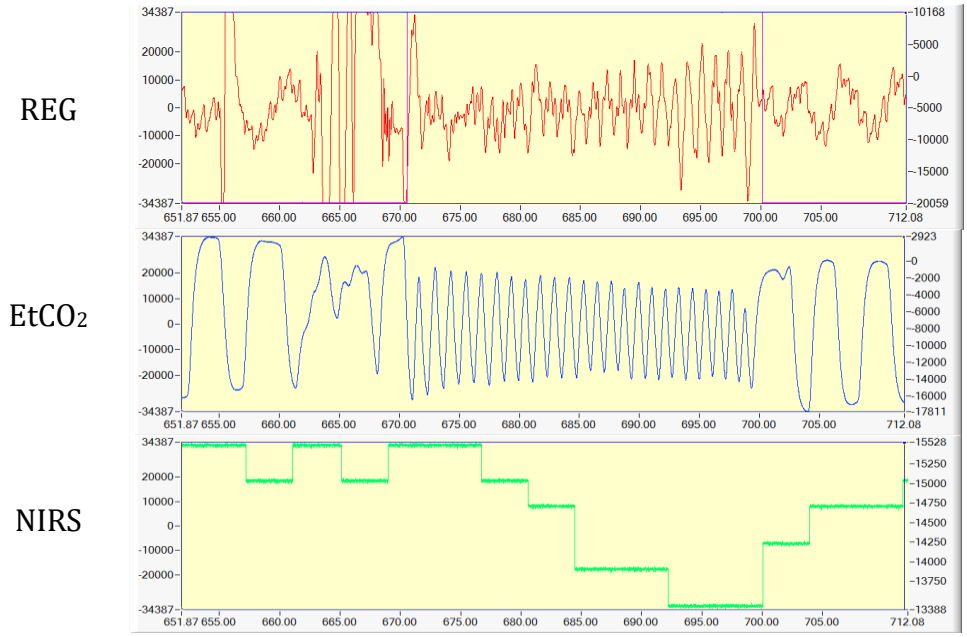

Fig. 3. *Hyperventilation.* REG signal after filtering during 30 sec hyperventilation (upper trace), $EtCO_2$ (middle trace), NIRS (lower trace). REG amplitude gradually increased during the test as NIRS synchronously decreased. (Y-axis values are shown in AD conversion units; X-axis values are shown in seconds).

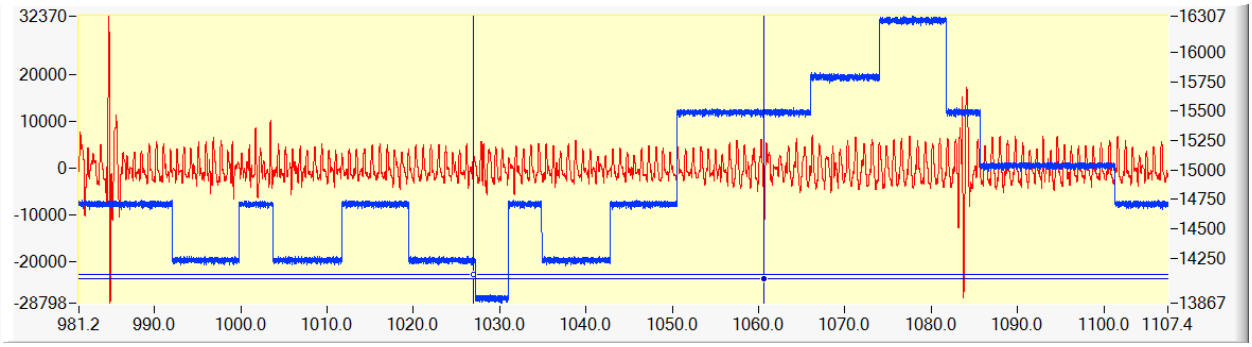

Fig. 4. *CO_2 inhalation*. REG signal (red) after filtering; NIRS (blue). Time of inhalation indicated by vertical lines (blue). REG amplitude increase was 179.23 % of baseline (before test), in identical time with NIRS. Y-axis is AD conversion units; X-axis is in seconds.

Test comparisons

All tests (REG, NIRS, TCD, LDF) reflected cerebrovascular reactivity (Fig. 5). Results varied by test and modality.

Both REG and NIRS showed higher SD values for most tests than TCD (Fig. 5). REG showed the influence of respiratory artifact more than the other modalities (Fig. 3). Examples of REG reflecting CVR are shown above (Fig. 2, Fig. 4).

Comparison of CVR (linear regression line calculation) for NIRS, TCD and REG during breath holding, hyperventilation and CO_2 inhalation yielded the following correlation coefficients: REG:0.7426; NIRS:0.8543; and TCD:0.9519. For results of a one-way ANOVA for the same data, see below (Table 3):

Table 3. Result of one-way analysis of variance of NIRS, TCD and REG during breath holding, hyperventilation and CO_2 inhalation.

P value:	0.2059		
P value summary:	ns		
Are means signif. different? (P < 0.05):	No		
Number of groups:	3		
F:	1.661		
R squared:	0.09406		
Bartlett's test for equal variances:			
Bartlett's statistic (corrected):	53.3		
P value:	P<0.0001		
P value summary:	***		
Do the variances differ signif. (P < 0.05):	Yes		
ANOVA Table:	SS	df	MS
Treatment (between columns):	653.8	2	326.9
Residual (within columns):	6297	32	196.8
Total:	6950	34	

Discussion

In neurosurgery intensive care units, cerebrovascular reactivity tests for neuromonitoring are used to evaluate the status of cerebral blood flow autoregulation (CBF AR); lack of autoregulation indicates a poor patient outcome. We have here described correlations among REG, TCD, NIRS and LDF during cerebrovascular reactions elicited by physiological CBF manipulations. Our REG results are consistent with published literature [13-15]. Data were not evaluated for failed tests (Table 2), which include those with no results or where data could not be evaluated due to artifacts, which occurred for all modalities (with variability; among the modalities, REG was the most sensitive to artifacts).

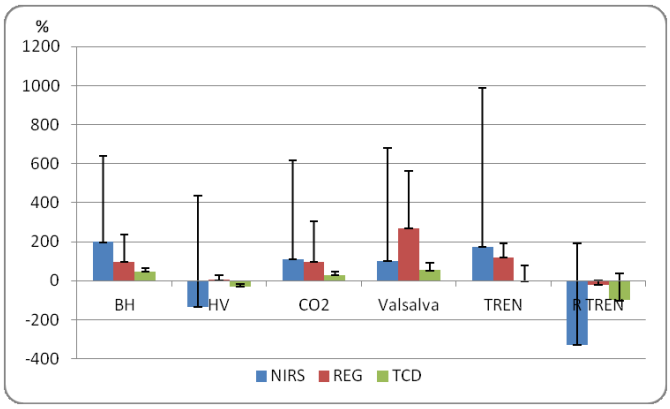

Fig. 5. NIRS, REG and TCD during tests. Data are as percent of baseline (mean + SD). Tests are as BH: breath holding; HV: hyperventilation; CO_2: CO_2 inhalation; Valsalva: Valsalva maneuver; TREN: Trendelenburg and R TREN: Reverse Trendelenburg positions.

REG

This pilot study has provided a comparison of REG measurements of cerebrovascular reactivity to measurements of current clinically used CVR modalities (NIRS, TCD). Historically, REG analysis has calculated pulse amplitude changes in the waveform, recorded on paper in chart form and analyzed visually. Contemporary REG analysis, accomplished by computerized data processing software, makes possible continuous CVR monitoring (REGx) [16].

Continuous computer generated results are more valuable for clinical CVR neuromonitoring than analysis of a single pulse amplitude change observed visually in the REG waveform. The goal of our future studies is to find

correlates in the REG signal to the currently used neuromonitoring methods compared in this study.

Presently it is not clear to what extent the observed artifacts, particularly for hyperventilation (Fig. 3), affect computerized REG data processing results; these results show that hyperventilation is not an adequate test for future REG studies.

Artifacts

REG. Artifacts were the primary measurement recording problem for both the REG signal and the other modalities measured. Artifacts caused by subjects' movements, such as speaking and eye-blinking, were the most frequent source of missing data in our study. Respiratory artifacts in the REG signal pulse wave were also observed, which were superimposed on the heart beat pulse wave, causing misleading readings and errors in averaged values for REG. For example, in some tests during hyperventilation, increases observed in REG pulse amplitude were due to the respiratory sub-harmonic (Fig. 3).

Due to the limited hairless area on subjects' foreheads, it was necessary to place the REG electrodes under the TCD probe-holding frame (headband). Artifacts in the REG signal were caused by adjustments to probe placement when the TCD signal was lost. Therefore, future comparisons of REG and TCD will require separate rather than simultaneous measurements of the two modalities.

The respiratory subharmonic interfered with the actual reading during hyperventilation even when there was no movement artifact. Often, the REG pulse wave was missing entirely, and only respiration was visible in the REG signal (Fig.3). Conveying instructions to the subject was sometimes problematic; often a subject would respond to the instructor, which caused movement artifacts in the REG signal. Frequently volunteers blinked their eyes, thereby causing artifacts in the REG signal. Inconsequential changes observed during Valsalva maneuver may have been caused by autonomic dysfunction, previously described by Castro [18].

TCD and NIRS

For the Trendelenburg / reverse Trendelenburg tests, TCD and NIRS values showed multiphase reactions, in contrast to monophase TCD and NIRS reactions for the other tests. During turning of the titling table, large artifacts in the signal occurred at the beginning and end of the tests. This multiphase reaction may reflect orthostatic intolerance, caused by complex interactions of central and peripheral cardiovascular control [18].

Impact of sensor placement

It is possible that fluctuations observed in the LDF and NIRS signals were caused by sensor placement. Both LDF and NIRS sensors were located on the forehead skin, where blood supply originates from ophthalmic artery (above the nose and eye) branches (supratrochlear - frontal, dorsal nasal, supraorbital); the ophthalmic artery branches, in turn, originate from the internal carotid artery.

During Trendelenburg position (Fig. 6), LDF reflected CBF change more clearly than REG. The consistent LDF flux decrease observed during Trendelenburg position may be explained by sensor placement. It has been shown that the organ of CBF AR is the arteriola, not an artery [19]. Since the LDF and TCD signals were collected on different computers, it was not possible to measure and compare the expected phase shift between data collected with LDF and TCD.

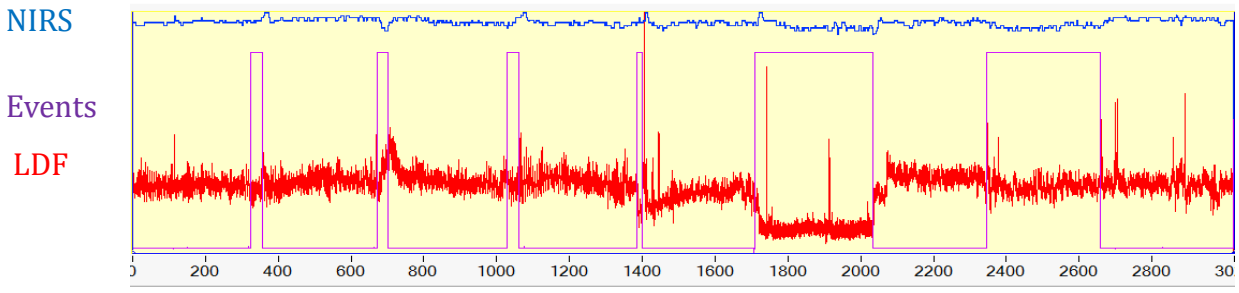

Fig. 6. Note the decrease of LDF flux signal during Trendelenburg position (1700-2050 sec). Also shown: LDF flux (red) and NIRS (blue) signals during all tests (purple). Y-axis is in AD conversion units; X-axis is in seconds.

REG: Medical application and military relevance

REG is a potential method for continuous monitoring of brain-injured patients. REG shows promise as a method for measuring cerebral blood flow autoregulation (CBF AR), both on the battlefield and en-route to the hospital when other measurements are not possible. Penetrating head injury accounts for a substantial percentage of injured military members unable to return to the battlefield. Fragments typically penetrate the calvarium through the face or underneath the lower border of the helmet; the resulting injury patterns are random and devastating. Following a brain injury, US Army

resuscitation doctrine [20] requires maintaining 90 mmHg mean arterial pressure; however, mean arterial pressure may fluctuate. Therefore, without continuous monitoring, secondary brain damage may occur. About 40% of the brain injury patients recently seen and treated at the Walter Reed National Military Medical Center suffer from traumatic vasospasm after brain injury [21]. Measuring vasospasm in the presence of metal fragments common in blast-injured patients using either Magnetic Resonance Imaging (MRI) or computed tomography angiography is prohibitive. REG offers the possibility of determining which patients are at risk for cerebral ischemia from vasospasm, which is associated with penetrating brain and blast injury, by monitoring the status of CBF AR [22] continuously, conveniently, and noninvasively.

REG: CBF autoregulation monitoring

Measuring brain electrical impedance is a potential technique for neuro-monitoring. In previous studies, we reported results of correlative studies indicating that REG has potential for use in neuro-monitoring [25]. A previous study documented that REG (REGx) and ICP (PRx) has high correlation in order to detect the lower limit of CBF autoregulation [4]. The fundamental relationships between arterial blood pressure (ABP), vessel tone, cerebral blood volume and intracranial pressure (ICP) form the basis for the pressure reactivity index (PRx) [17, 24]. PRx is analogous to other time domain autoregulation indices and is calculated as the continuous correlation between thirty consecutive time-averaged (10 s) ABP and ICP values. A positive index (positive correlation) implies impaired cerebral autoregulation, while a negative index (inverse correlation) implies intact autoregulation. Rheoencephalography as a monitoring modality has been discussed since the name 'REG' was initially used [3, 26], and the promise of REG has been demonstrated [4, 27].

Conclusion

Here we have presented initial results of pilot human study comparing CBF challenges in order to find an optimal CBF AR test for potential use on the battlefield, during transport of wounded warriors and for use in neurosurgery intensive care units (military and civilian). Some discrepancies among REG, NIRS, TCD and LDF methodologies were observed during these tests. Our future validation studies will include enhanced computational methods [4,17], further animal studies and clinical monitoring studies of humans. A human study using REGx calculation is currently being prepared.

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Disclaimer

The opinions expressed herein are those of the author(s), and are not necessarily representative of those of the Uniformed Services University of the Health Sciences (USUHS), the Department of Defense (DOD); or, the United States Army, Navy, or Air Force.

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