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Monitoring Cerebral Hemodynamics with Transcranial Doppler Ultrasound during Cognitive and Exercise Testing in Adults following Unilateral Stroke

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***Abstract*— An observational study was performed as a preliminary investigation into the use of transcranial Doppler ultrasound (TCD) for recording cerebral hemodynamic changes during multiple tasks. TCD is a method of measuring cerebral blood flow (CBF) using ultrasound transducers in contact with the surface of the head. Using the maximum flow envelope of the Doppler spectrum returning from the middle cerebral artery (MCA), standard clinical flow indices can be calculated and displayed in real time providing information concerning perturbations in CBF and their potential cause. These indices as well as flow velocity measurements have been recognized as useful in measuring changes in responses to various stimulus that can be used to indicate cardiovascular health. For this study, the pulsatility index (PI) and resistivity index (RI) were chosen since they indicate composite changes indicative of vasoconstriction and vasodilatation which are normal hemodynamic responses under appropriate conditions.**

A total of eleven participants were recruited to take part in this study. Nine of these individuals had no known disability (Controls); two had experienced unilateral cerebrovascular accidents (Strokes) in the ipsilateral MCA distribution. Maximum velocity envelopes of the spectral Doppler data were recorded using a fixation device designed to stabilize two ultrasound probes (2 MHz) to sample the bilateral MCAs CBF. These measures were performed separately while the subject performed four activities: 1) rest, 2) cognitive challenge, 3) cardiovascular exercise, and 4) simultaneous exercise and cognitive challenge. Cardiovascular parameters were calculated from the data by extracting maximum (Vs) and minimum flow velocities (Vd), PI, RI, and time signatures for each cardiac cycle. The data for all participants shows significant changes in cardiovascular parameters between states of rest and exercise, as well as slight trends across time. Although the data are preliminary, they show the capability of using Doppler spectral examination of the bilateral MCAs in individuals with physical limitation performing cardiovascular exercise. The novelty of examining a population using dynamic exercise who before could not perform such exercise offers the opportunity to study the impact of exercise on global cerebral recovery in unilateral stroke with significant physical impairment.

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***Index Terms*—CVA, stroke, multi-task, cerebral blood flow, ultrasonography, transcranial Doppler, rehabilitation**

I. Introduction

Transcranial Doppler ultrasound (TCD) is an ultrasound imaging modality used for examining multiple characteristics of CBF, notably within a basal cerebral artery (BCA). This method is nonintrusive, inexpensive, and relatively easy to perform. TCD has been used to examine changes in cerebrovascular function to determine vascular abnormalities such as attenuation of flow from increased intracranial pressure, vascular injury from vasospasm or vascular obstruction and detection of cerebral emboli arising from cardiac or carotid origin. The technique has proven vital in surveillance of patients with sickle cell disease at risk for cerebrovascular accident (CVA). This application has also proved useful in the intensive care unit for analyzing perturbations of CBF from a variety of conditions including cardiac arrest, asphyxia, intracranial hemorrhage, head trauma and brain death [1].

The Doppler frequency shift, and thus CBF velocity, changes in response to flow and vessel diameter. This signal envelope has several useful components used for CBF analysis. These include systolic velocity (Vs), diastolic velocity (Vd), mean velocity (Vm), pulsatility index (PI) and resistive index (RI) [1-3]. These components are routinely used to classify normal from abnormal flow patterns.

However, long-term monitoring of rehabilitation patients presents a challenge due to the complications of prolonged (> 30 s) monitoring while exercising or during a cognitive challenge (due to the need for steady manual manipulation of the transducer). Thus, one area that has not been systematically studied is the impact of functionally relevant exercise on the CBF of those recovering from a stroke. In

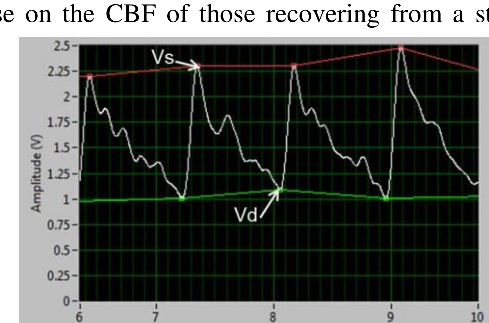

Fig. 1. Velocity scaled to voltage as a function of time for a sample four-second window envelope with maximum and minimum points for index calculation (Vs=55 cm/s, Vd= 22.5cm/s).

this study, we demonstrate a novel combination of a TCD stabilizer, modified exercise equipment for rehabilitating patients, and real-time tracking of CBF parameters to analyze unique data not previously achievable.

II. Methods

A. Data Collection

A TCD fixation device was designed to keep the transducers in place. Device development was crucial in order to ensure a consistent Doppler signal could be maintained over a period of at least 20 minutes without transducer movement (leading to loss or attenuation of signal) or discomfort to the study participant [4].

Experiments were performed at Madonna Rehabilitation Hospital. Exercise tasks were performed on the ICARE, a modified motorized elliptical trainer designed to enable individuals with and without physical disabilities to engage in sustained cardiovascular exercise that simulates a walking-like movement pattern [11-12].

Initially, the MCA location was identified through a manual freehand technique locating the vessel in relation to the scalp with each temporal window. The depth of insonation was chosen to be at least 1 cm above the interior carotid artery (ICA) bifurcation and without collateral interference from other vessels. Once MCA location was established, the fixation device was placed on the scalp and both MCA signals were reestablished. Stability of signal acquisition was assured by each subject by performing slow rotatory axial and lateral head movements for approximately 30 seconds. Insonation of the bilateral MCAs was performed for all cognitive and physical tests to maximize robustness of signal and ensure uniform recording. The MCA for each cerebral hemisphere was chosen for three reasons: 1) primary supply to 70% of each cerebral hemisphere encompassing the primary locomotive, speech and cognitive centers of the brain, 2) ease of identification during signal acquisition and 3) low angle of insonation relative to other BCAs within the circle of Willis [5].

Data containing the raw envelopes were recorded using an X2 Multidop system and 2 MHz transducers (Compumedics, DWL Singen, Germany). A LabView virtual instrument and NI-USB-6009 data acquisition system (National Instruments Corporation, Austin, TX) were connected to a personal computer in order to save the recorded envelopes. The tracing of the maximum Doppler spectrum is automatically performed by the X2 Multidop system and scaled from velocity to voltage corresponding to the pulse repetition frequency (PRF). The PRF was set to either 6 or 7 kHz depending on the scaling required to keep the signal from aliasing. The approximate scale factor of voltage to velocity in this study is 32.4 for 7 kHz and 24.4 for 6 kHz, found empirically. Signal envelope data were recorded at a sampling frequency of 500Hz.

Recordings were performed on nine individuals without known disabilities (Controls: 5 male, 4 female; 19 to 30 years of age) and two adult females greater than 6 months post unilateral left CVAs of the MCA with residual right hemiparesis (Strokes: 58 year old with hemorrhagic stroke; 55 year old with ischemic stroke; independent ambulators without assistive devices but velocity and duration reduced).

To evaluate stability of blood flow indices, Controls participated in 3 sessions each separated by 3-5 weeks. Measures recorded from the Stroke group were then compared to these normative values. Measures of blood pressure (BP), heart rate (HR), and oxygen saturation (O_2) were recorded to reduce the risk of adverse events during exercise.

B. Task Definition

Subjects performed four separate tasks while being monitored with TCD: 1) Resting, 2) Cognitive Challenge, 3) Exercise, and 4) Exercise plus Cognitive Challenge. The first task involved resting for two minutes in a controlled environment (room temperature, normal lighting, and no outside visual or auditory stimuli). The second task included an initial 30 seconds at rest, performing a cognitive-challenging task for 2 minutes (i.e., subject instructed to name as many words possible starting with a specific letter of moderate difficulty, excluding proper names or separate tense [9]), followed by 30 seconds of rest. After waiting a minimum of two minutes until the HR returned to resting condition, the third task was administered. The third task involved locomotor exercise on the ICARE elliptical trainer for a period of 2 minutes at a rated perceived exertion (RPE) of 13 on the 6 to 20 Borg Scale point. A 30 second rest period was performed before and after the exercise. After waiting a period of at least 2 minutes or until HR returned to the resting rate the final task was administered. The fourth task included 30 seconds of rest, followed by 30 seconds of ICARE training, and then (while still exercising on the ICARE) the participant performed the cognitive task for a duration of 2 minutes using a different letter of similar difficulty. Recording of the bilateral MCA signals was performed during the final test until HR returned to resting condition [6-8].

C. Data Analysis

Envelopes corresponding to the maximum velocity trace through each MCA were filtered with a 4^{th}-order Butterworth IIR lowpass filter (f_c = 10 Hz), then imported into Matlab, (MathWorks, Natick, MA) where an in-house algorithm was designed to automatically detect Vs and Vd values from beat to beat. The algorithm was designed to first pair Vs and Vd values belonging to the same systolic pulse, then calculate Vm, PI, and RI according to the pair. Fig. 1 displays a typical, resting maximum velocity envelope and characteristic velocities. Calculations are displayed in (1-3) [2].

$$PI = (Vs – Vd)/Vm \quad (1)$$

$$RI = (Vs – Vd)/Vs \quad (2)$$

$$Vm = (Vs+Vd)/2 \quad (3)$$

Due to the fact that Vs and Vd occur at non-uniform intervals, an interpolation filter (Matlab ‘interp1’) was used to linearly interpolate Vs and Vd according to the actual sampled frequency (500 Hz). Twenty-second epochs were extracted from the data according to the task using pre-

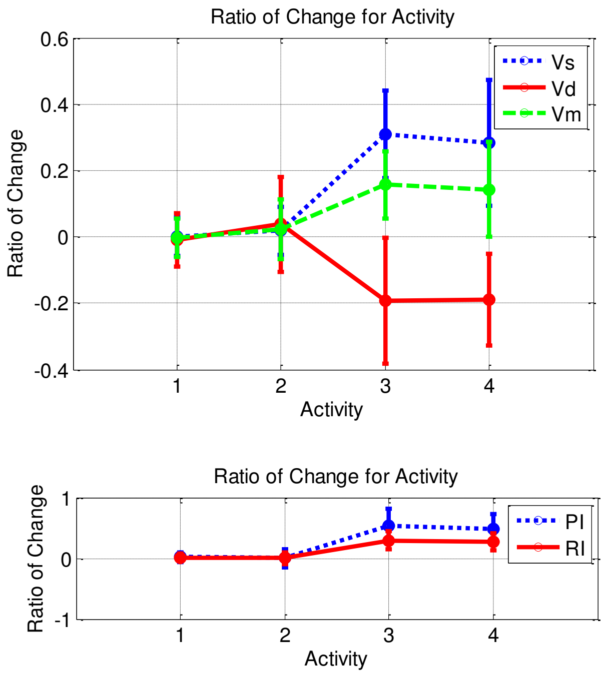

Fig. 2. Ratio of change values from resting to activity for Controls (Activity: 1-Resting; 2-Cognitive Challenge; 3-Exercise, 4-Exercise plus Cognitive Challenge).

recorded time intervals. The average value of Vs, Vd, Vm, PI, and RI were computed for each of these windows. Percent change calculations were performed between tasks. Each state change was analyzed along two separate 20 second windows belonging to subject state change within resting, resting to cognitive task, resting to exercise task, and resting to dual cognitive-physical task. These tasks and order were chosen to view changes in cerebral hemodynamics due to alterations in CBF and downstream vascular resistance that can be reliably identified through monitoring the flow velocity envelope and its analysis [9].

Cumulative data from the Control group's right and left MCA were averaged. The average and standard deviation measurements were reported on the pooled percent change from baseline. Data from MCA of the involved (ipsilateral) and uninvolved (contralateral) hemispheres of the two Stroke participants were analyzed separately to discern potential variations arising from the impact of the injury.

III. Results

A. *Unaffected Individuals (Controls)*

Ratios of change (fractional change) data for the Control group are displayed in Fig. 2. Two-sided t-tests revealed significant increase in all parameters when comparing the Resting vs. Exercise ($p< 0.01$), Resting vs. Exercise and Cognitive Challenge ($p<0.01$), Cognitive Challenge vs. Exercise ($p<0.01$), and Cognitive Challenge vs. Exercise plus Cognitive Challenge ($p<0.01$). No statistically significant differences were identified in the Control group between Resting vs. Cognitive Challenge and Exercise vs. Exercise plus Cognitive Challenge ($p>0.05$).

Table I displays the percent change within PI from Resting for each of the different tasks within the Control group during each of the three sessions. PI was chosen due to its representation of three characteristic variables within the signal (Vs, Vd, and Vm). Within two 20 second windows of Resting data there appears to be little to no change in the PI. A very small decrease in PI was observed when performing the Cognitive Challenge task. A near 50% increase in PI was seen when introducing the Exercise task. Similarly a 50% increase in average PI was seen when introducing the Exercise plus Cognitive task.

B. *CVA Participants*

Within the group of two MCA stroke participants, percent changes occur much differently from the unaffected individuals. These results are displayed in Fig. 3. Velocities decrease when tasks are introduced, particularly on the ipsilateral side. These velocity drops translate to a very slight increase in the PI and RI parameters. Vs, Vd, and Vm show a difference between the ipsilateral and contralateral regions.

IV. Discussion

Activity plays a major role in influencing blood flow to organs and tissues. Intact modulation of CBF is needed to ensure adequate perfusion and oxygenation regardless of body position, physical activity or cognitive task. In the Control group (subjects without known disability), cognitive tasks resulted in a slight decrease in PI and RI as a result of a slight but insignificant increase in Vs, Vm, and Vd. (Fig. 2). The findings of an increase in all cerebral blood flow velocities (CBFV) likely indicates an increase in CBF as a result of increased cerebral metabolism resulting from problem solving. The slight decrease in resistance indexes of PI and RI represents a reflex vascular relaxation to improve CBF within the metabolically more active cerebral territories involved in problem solving.

TABLE I. Average Percent Change Values of PI from Resting to Exercise of Each of the Test Sessions

Activity	**Test Sessions**		
	Session 1	***Session 2***	***Session3***
Resting-Resting	2.75	1.61	9.7
Resting-Cognitive	-3.06	-1.31	4.85
Resting-Exercise	52.40	51.50	54.39
Resting-Cognitive with Exercise	42.67	47.52	53.36

In the Control group, exercise raised Vs, Vm, and lowered Vd (Fig. 2). This pattern is a result of increased cardiac output and increased CBF needed to meet increased metabolic activity within the cerebral cortex engaged in controlling motor activity. The increased resistance indices witnessed during exercise most likely result from a reduction in arterial CO_2 levels which produces a reflex vasoconstriction in the cerebral vascular bed.

The cerebrovascular responses arising from cognitive challenge and exercise are considered normal physiologic responses and therefore can be used to assess the level of intact cerebrovascular regulation. Intact autoregulation is considered one of the fundamental physiologic functions of

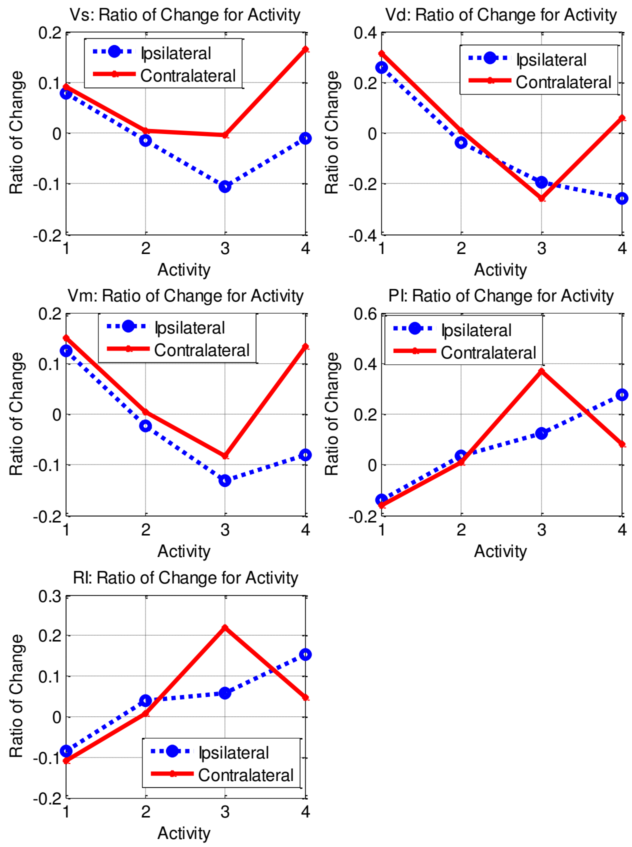

Fig. 3. Ratio of change values from Resting to activity for affected individuals (Activity: 1-Resting, 2-Cognitive Challenge, 3-Exercise, 4-Exercise plus Cognitive Challenge).

cerebral circulation. Its disruption is considered an indicator of poor neurologic outcome at least in the short term.

Conversely, in the participants affected by stroke, ratio changes did not follow the same pattern as in the Control group (Fig. 3). Within the Stroke group, activity brought on a negative percent change in Vs and Vd from baseline. This result possibly could indicate an inability to augment cardiac output or appropriate peripheral vasomotor response to exercise from the cumulative effects of lisinopril, amlodipine and propranolol used in one patient. Another possible factor could be that both participants were deconditioned to exercise as a result of the protracted period of recovery from their acute brain injury.

The differences between stroke affected cerebral hemisphere [ipsilateral] and unaffected hemisphere [contralateral] (Fig. 3) indicates that differences in cerebrovascular autoregulation differ not only by stimulus but also by magnitude. The small number of affected subjects precludes definitive interpretation of our preliminary data but does highlight the importance of monitoring CVA affected and normal hemispheric CBF simultaneously when determining the affect of various rehabilitative activities on cerebral autoregulation.

Further study is needed in this population to determine if subjects with unilateral stroke mount similar cerebrovascular responses as in healthy participants over time. This is especially true in comparing cerebral autoregulation in the intact cerebral hemisphere to the injured hemisphere to determine if there are substantive differences. Another area of study would determine if cerebral autoregulation can recover, or if rehabilitation measures influence neurologic outcome if this regulatory mechanism is not restored.

V. Conclusion

This study has proven the feasibility of monitoring CBF in individuals with and without disabilities over extended periods of time during exercise and cognitive challenge tasks. The ability to examine subjects with cerebral injury during tasks that are essential to independent, healthy living is expected to provide valuable insights into the design of therapeutic training interventions. TCD monitoring during task assessment may provide essential information regarding the appropriate types and intensities of rehabilitation critical to elicit not only optimal cognitive or physical function but also to normalize cerebrovascular autoregulation. The next natural step from this observational study is to expand preliminary understanding of the hemodynamics occurring during physical and cognitive activity to a larger population of stroke survivors. Currently, progress is being made in recording data from community dwelling stroke survivors as they undergo a structured physical rehabilitation program to view possible changes in CBF.

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