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# Concurrent Variations of Cerebral Blood Flow and Arterial Blood Pressure in Simulated Sleep Apnea

Raichel Alex, *Student Member,* Gauri Bhave, Mohammad A. Al-Abed, *Student Member,* Aditya Bashaboyina, Swathi Iyer, Donald E. Watenpaugh, Rong Zhang, and Khosrow Behbehani, *Senior Member, IEEE*

*Abstract*— **Obstructive Sleep Apnea (OSA) is one of the most common sleep disordered breathing which affects about 15 % of US adult population. OSA is considered to be an important risk factor for the development of cardiac dysfunction and stroke. In this paper, we present the initial results of our investigation of the relationship between arterial blood pressure and cerebral blood flow velocity in simulated apnea. Sixteen healthy subjects (9 male, 7 female) of 29±4.89 yrs age and body mass index of 24.07±4.84 kg/m$^2$ participated in the study. Our findings indicate that cerebral blood flow velocity variations has a relatively high correlation to changes in blood pressure during simulated apnea (r=0.74 ±0.06), suggesting that cerebral autoregulation may not compensate for the pressure changes during apnea.**

## I. Introduction

THE term Sleep apnea, derived from Greek word "apnea" which means "without breath", is characterized by shallow breaths or complete cessation of breathing for 10 seconds or more during sleep [1]. It is estimated that 15% of the U.S. adult population have sleep disordered breathing, approximately 18 million adults [2]. Obstructive sleep apnea (OSA) is the most common form of sleep disordered breathing and occurs when the airway collapses during sleep due to excessive muscle relaxation in the posterior oropharynx thereby obstructing the air flow to the lungs [1]. With reduced or zero ventilation, arterial oxygen concentration decreases and CO2 accumulates thus, signaling the brain to arouse the sleep apnea patients from sleep to resume breathing. Breathing will continue until the next episode of apnea. The duration of apnea episodes may last from few seconds to over a minute may recur as many as several hundred times during a single night of sleep [2]. Frequent drops in blood oxygen levels activate the sympathetic nervous system which in turn promotes release of the stress hormone adrenaline. Sympathetic nerve activity together with stress hormone causes constriction of peripheral blood vessels and places increased stress on the heart throughout night [3]. Over time, these responses lead to health complications including high blood pressure, stroke, cardiovascular diseases, and memory disorders [4], [5]. These physiological impacts increase the risk for automobile accidents, and poor performance in everyday activities due to excessive day time sleepiness [2].

Constriction of peripheral blood vessels by the sympathetic nervous system in response to hypoxia-hypercapnia conditions during apnea increases the blood pressure and makes it difficult for the heart to pump blood into smaller blood vessels [3]. These repetitive rises in nocturnal blood pressure may lead to long term hypertension and studies show that 45 % of sleep apnea patients without a previous history of hypertension develop high blood pressure within an approximate time period of 4 years [6], [7].

Due to oxygen desaturation during apnea episodes, brain and other vital organs are repeatedly deprived of oxygenated blood, which affects their function [8]. Under normal conditions, cerebral autoregulation mechanism tries to maintain a consistent supply of oxygen and blood flow to brain tissue despite the fluctuations in arterial pressure. However, increased oxidative stress due to hypoxemia-reoxygenation during apnea episodes, together with elevated arterial blood pressure can lead to the disruption of this autoregulation. As a result there will be a rise in both blood pressure and cerebral blood flow velocity during apnea episodes, followed by a rapid decrease in both during post hyperventilation period, resulting in oscillations of cerebral blood flow during the entire night [8]. There are various short term and long term effects of these fluctuations including chronic and pathophysiologically elevated cerebral blood flow. Further fluctuations may weaken the blood vessels which can predispose the apnea subjects to increased risk of cerebral ischemia and stroke.

This study describes the preliminary result of investigating concurrent changes in cerebral blood flow velocity and blood pressure variations during simulated apnea.

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R. Alex is a Ph.D. student with the Bioengineering Department, University of Texas at Arlington, Arlington, TX 76010 USA (phone: 801-897-8353; fax: 817-272-2251; e-mail: raichelmary.alex@ mavs.uta.edu).

G. Bhave is with University of Texas at Arlington, Arlington, TX 76010 USA (e-mail: gauri.bhave@gmail.com).

M. A. Al-Abed is Ph.D. student with Bioengineering Department, University of Texas at Arlington, Arlington, TX 76010 USA (e-mail: mohammad@uta.edu).

A. Bashaboyina is with Bioengineering Department, University of Texas at Arlington, Arlington, TX 76010 USA (e-mail: ab86work@gmail.com).

S. Iyer is with Bioengineering Department, University of Texas at Arlington, Arlington, TX 76010 (e-mail: swathi.iyer@gmail.com).

D. Watenpaugh is the Director of Sleep Consultants, Inc. Fortworth, TX 76104 USA (e-mail: dwatenpaugh@texaspulmonary.com).

R. Zhang is with Presbyterian Medical Center of Dallas, Dallas, TX 75231 USA (e-mail: zhangr@wpmail.phscare.org).

K. Behbehani is Professor and Chair of the Bioengineering Department, University of Texas at Arlington, Arlington, TX 76010 USA (e-mail: kb@uta.edu).

## II. Materials and Methods

### A. Subject Demographics

A healthy population of 16 volunteer subjects who did not had any known sleep apnea disorder or any other cardiac or respiratory disorder was recruited for this study. The mean age for this group was 29±4.89 years with an average BMI of 24.07±4.84 kg/m$^2$. These subjects were given complete instructions about the experiment and signed an Institutional Review Board informed consent. The subject demographics are as shown in Table I.

TABLE I
SUBJECT DEMOGRAPHICS

| Subjects | Age (years) | Height (cm) | Weight (kg) | BMI (kg/m$^2$) |
|---|---|---|---|---|
| Male (9) | 30.11±5.11 | 172±6.86 | 77.78±17.99 | 26.14±4.68 |
| Female (7) | 27.57±4.54 | 158±4.89 | 53.57±10.78 | 21.4±3.83 |

### B. Blood Pressure and Cerebral Blood Flow Measurements

This study monitored beat to beat blood pressure noninvasively using Nexfin HD monitor (BMEYE, Amsterdam, Netherlands). The Nexfin monitor utilizes the principle of Finapres volume clamp method of dynamic unloading of finger arteries [9], [10]. This is based on equation of transmural pressure ($P_t$), defined as the difference between intra arterial pressure ($P_a$) and external cuff pressure ($P_c$) and given as follows;

$$P_t = P_a - P_c \quad (1)$$

Hence at zero transmural pressure: $P_a = P_c$ .

Since the subjects in this study did not had a preference over the hand on which blood pressure measurement is done, left hand middle finger was used for all the subjects. An integrated heart reference system (HRS) is used to allow accurate heart level blood pressure measurement with free movement of hand irrespective of its vertical height with respect to the heart. HRS unit was provided by manufacturer of the blood pressure measurement system (BMEYE, Amsterdam, Netherlands).

The blood flow velocity in the Middle Cerebral Artery (MCA) is measured since its one of the major arteries supplying blood to the brain. The mean blood flow velocity in the MCA under normal conditions (in the supine posture) is approximately 55 cm/s with a standard deviation of about 12 cm/s. The velocity of blood flow through the MCA was measured using a Transcranial Doppler (TCD) (DWL, Compumedics, Singen, Germany) [11]. The principle of ultrasound Doppler for blood flow measurement is as shown in Fig 1.

The blood flow velocity can be calculated using the following equation:

$$f_d = [2 f_t V Cos(\theta)]/c \quad (2)$$

where c is the velocity of sound in tissue in cm/s and θ is angle of insonation (degrees) [12].

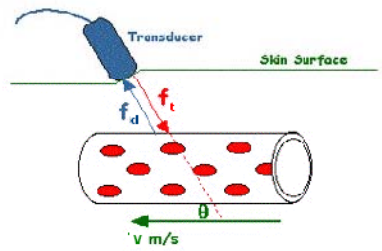



Fig. 1. Principle of Ultrasound Doppler. Here $f_d$ is Doppler shift (Hz) and $f_t$ is transmitted beam frequency (Hz). If a red blood cell is moving with a velocity V, with the beam to flow angle θ, the velocity can be calculated by measuring the frequency shift of the reflected wave.

The 2MHz transducer was placed on the temple of the subject and the ultrasonic beam was adjusted to insonate the root of the MCA. With the volunteer in a comfortable supine position ultrasonic gel was applied to the transducer and the temporal region of the volunteer's cranium, just above the eye. After the MCA signal was found, the transducer was secured by use of special headgear.

### C. Experimental Protocol

In this study, the physiological responses to apnea were elicited by a series of breath-hold maneuvers. The duration of breath hold was, as long as the subject could hold his/her breath. The experimental protocol consisted of a baseline of 60 s of natural breathing. Following this baseline breathing, the volunteer was asked to hold his/her breath as long as possible. A nose clip was place on the subject's nose to prevent accidental breathing during the maneuver. After the breath hold, the volunteer was allowed to breathe normally for 90 seconds before the next breath hold. This cycle of breath hold followed by normal breathing was repeated five times and these breath holds were named as BH1, BH2, BH3, BH4 and BH5 according to the order of occurrence.

### D. Data Analysis

The analog outputs from all the physiological monitors were sampled at 1 kHz and analyzed using Labview 9.0 (National Instruments, Austin Texas) and Matlab (Mathworks Inc. Natick, MA). A custom-designed graphical user interface (GUI) was developed and programmed in the MATLAB environment to visualize the data and clip it into separate breath hold and normal breathing segments. From the breath hold data, peaks and valleys of the waveforms were detected using custom made peak detection algorithm [13]. Once the peaks are detected, all the subsequent peaks are compared to the initial peak value and percentage rise of the peaks compared to the first peak is calculated as follows

$$\text{Percentage rise} = [(P(i) - P1)/P1] * 100 \quad (3)$$

where P1 is the first peak value at the starting of breath hold, P(i) are the subsequent peaks during the breath hold. Fig 2 illustrates the peak detection and delta calculation.

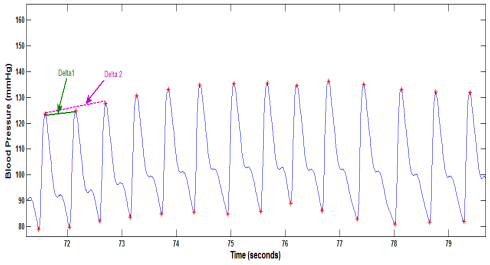


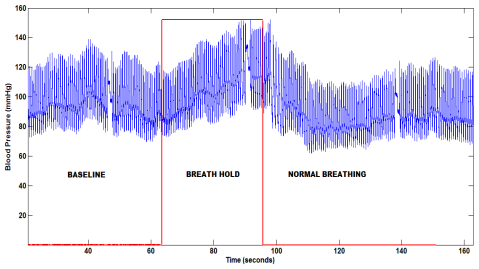

Fig. 2. Peak Detection and Delta Calculations. Delta 1 represents the difference between initial peak and the succeeding peak where as delta 2 is the difference between initial peak and the third peak.

The output of peak detection algorithm was visually inspected to correct any errors in detecting the peak values. The delta and percentage rise for cerebral blood flow velocity and Blood pressure were calculated for all the five breath holds and compared to each other.

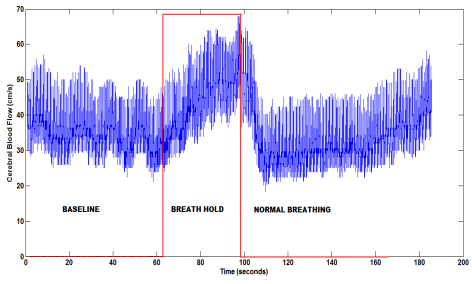
## III. Results

### A. Rise of Blood Pressure and Cerebral Blood flow

Simulated apnea episodes resulted in an elevation of both arterial blood pressure (BP) and cerebral blood flow velocity. The resulting increase along with their trend during normal breathing and baseline are as shown in Fig 3.




(a)




(b)

Fig. 3. Rise in Blood Pressure and Cerebral Blood flow Velocity. This illustration shows breath hold related elevation of (a) Blood Pressure, (b) Cerebral Blood Flow. The breath hold portion of the curve is marked by red rectangle.

### B. Arterial Blood Pressure-Cerebral Blood Flow Relation

Fig 4 shows an example of the relative rise in blood pressure (BP) and cerebral blood flow velocity (CBFV) during one breath hold. The percentage rise for both blood pressure and cerebral blood flow velocity and also Pearson product moment correlation coefficient (r) were calculated for all five breath holds of all subjects.

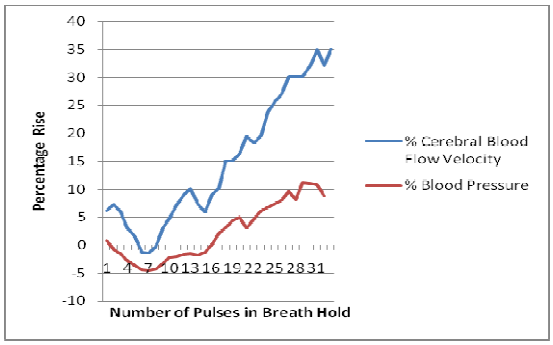



Fig. 4. Percentage Rise in Blood Pressure and Cerebral Blood flow Velocity. This figure shows that relative rise of CBFV is higher compared to BP.

Pearson coefficients for breath holds are grouped according to the breath hold order for all subjects and the average value is taken for each breath hold. Table II gives the result of average Pearson product moment correlation coefficient between BP and CBFV.

TABLE II
AVERAGE PEARSON PRODUCT MOMENT CORRELATION COEFFICIENT (R) ALONG WITH STANDARD DEVIATION FOR PERCENTAGE RISE IN BLOOD PRESSURE AND CEREBRAL BLOOD FLOW VELOCITY

| Breath Hold | R value |
|---|---|
| BH1 | 0.640±0.197 |
| BH2 | 0.762±0.192 |
| BH3 | 0.762±0.195 |
| BH4 | 0.765±0.134 |
| BH5 | 0.770±0.221 |

### C. Statistical Analysis

In order to test whether the order of breath holds has any effect on correlation between blood pressure and cerebral blood flow velocity, one way ANOVA followed by post hoc analysis is done on correlation coefficients obtained for the five different breath holds. Table III and Table IV summarizes the result of ANOVA and post hoc analysis respectively.

TABLE III
ANOVA STATISTICS FOR EFFECT OF DIFFERENT BREATH HOLDS ON CORRELATION

| Source of Variation | SS | df | MS | F | Prob>F |
|---|---|---|---|---|---|
| Between Groups | 0.1861 | 4 | 0.0465 | 1.27 | 0.2918 |
| Within Groups | 2.4603 | 67 | 0.0367 | | |
| Total | 2.6463 | 71 | | | |

SS = sum of squares; df = degree of freedom; MS =Mean Squares; F = F test; Prob>F = p value; $\alpha = 0.05$ is considered to be the significance level.

TABLE IV
POST HOC ANALYSIS FOR EFFECT OF DIFFERENT BREATH HOLDS ON CORRELATION

| Group 1 | Group 2 | C.I lower | C.I upper | Sig |
|---|---|---|---|---|
| BH1 | BH2 | -0.31760 | 0.07473 | NS |
| BH1 | BH3 | -0.32172 | 0.07755 | NS |
| BH1 | BH4 | -0.32005 | 0.07922 | NS |
| BH1 | BH5 | -0.33411 | 0.06516 | NS |
| BH2 | BH3 | -0.20029 | 0.19898 | NS |
| BH2 | BH4 | -0.19862 | 0.20065 | NS |
| BH2 | BH5 | -0.21268 | 0.18659 | NS |
| BH3 | BH4 | -0.20138 | 0.20472 | NS |
| BH3 | BH5 | -0.21544 | 0.19065 | NS |
| BH4 | BH5 | -0.21711 | 0.18898 | NS |

C.I lower=lower limit of 95% confidence interval; C.I upper=upper limit of 95% confidence interval; Sig= significance; NS= non significant.

## IV. Discussion

This study aimed to quantify the relationship between cerebral autoregulation and elevation in arterial blood pressure during simulated apnea episodes. In adults at rest 15% of the cardiac output, which is about 750 ml per minute is supplied to the brain. The brain requires about 50 to 54 ml of blood per 100 gm of tissue per minute which is closely regulated. Excessive blood flow can be dangerous, as it can increase intracranial pressure and damage brain tissue by compression.

As seen from Fig 3, there is a progressive rise in both blood pressure and cerebral blood flow velocity signal during the breath hold followed by rapid decrease after termination of breath hold. The percentage rise plot shown in Fig 4 shows that the rate of increase for cerebral blood flow velocity is higher compared to the rate of increase in arterial pressure. Hence from these results it appears that instead of maintaining constant blood flow velocity during blood pressure fluctuations, the cerebral blood flow velocity increases when pressure is increasing.

The correlation results from Table II, yielded r value of above 0.75 for most of the breath holds further confirming the parallel rise in both signals. These results indicate that during simulated apnea episodes cerebral autoregulation fails and constant brain blood flow may no longer be maintained. This frequent rise and drops in CBFV can predispose the sleep apnea subjects to cerebrovascular ischemia and stroke [8].

Further we analyzed the data for any dependence of this correlation on the order of breath holds. One-way ANOVA results and the post hoc analysis given in Table III and Table IV suggest that there is no significant difference in the correlation between BP and CBFV among different breath holds. Hence the order of breath holds does not have any effect on the BP- CBFV relation.

## V. Conclusion

We have investigated the relation between arterial blood pressure and cerebral blood flow velocity during simulated apnea episodes and our results indicate that cerebral autoregulation seems to be less effective during apnea episodes. These findings may ultimately provide a better understanding of the sleep apnea impact on the cerebral autoregulation and associated blood pressure variations.

## VI. Acknowledgment

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