The Internet Journal of Neurology
Volume 3 Number 2

Cerebral Blood Flow Velocity During A Short Period Of Carotid Baroreflex Stimulation In The Young And Middle-Aged Humans

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Citation

K Saeed, F Mehdi, N Houshang, A Mahmood. *Cerebral Blood Flow Velocity During A Short Period Of Carotid Baroreflex Stimulation In The Young And Middle-Aged Humans*. The Internet Journal of Neurology. 2004 Volume 3 Number 2.

Abstract

Objective: Cerebral blood flow velocity (CBFV) concomitant with the acute response and resetting of baroreflex has not yet been studied. The present study addresses this in the young and the middle-aged human beings.

Materials and Methods: Four groups of healthy volunteers were included into the study (13 members in each): young males (23.9±0.8 yrs), young females (24.2±0.7 yrs), middle-aged males (58±0.9 yrs) and middle-aged females (56.4±0.7 yrs). Transcranial Doppler ultrasonography and Eckberg's neck suction device were used for CBFV monitoring and carotid baroreceptors stimulation respectively. Pressure in the neck chamber was reduced immediately to -40 mmHg which lasted for 30 sec. CBFV and electrocardiograph were monitored before, during, and after the baroreceptors stimulation.

Results: In all the groups, baroreflex stimulation led to a significant increase in R-R intervals and was then followed by a gradual resetting. CBFV did not change during acute phase of the baroreflex stimulation, but it was reduced simultaneous to the resetting phase which reached to the significant levels in young females and middle-aged males ($p<0.05$).

Conclusions: Our findings support the existence of an effective local maintenance of CBFV during acute response of the carotid baroreflex in both young and middle-aged groups. However during the rapid resetting phase of the reflex it decreased in both age groups of the study.

THIS RESEARCH WAS DONE IN

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ABBREVIATIONS

CBFV: Cerebral Blood Flow Velocity BR: Baroreflex CA: Cerebral Autoregulation HR: Heart Rate BMI: Body Mass Index SE: Standard Error MCA: Middle Cerebral Artery TCD: Transcranial Doppler

UNITS OF MEASUREMENT

Height: cm Weight: kg Body Mass Index: kg/m^2 Heart Rate: beat per minute (bpm) Cerebral Blood Flow Velocity: cm/sec

INTRODUCTION

Cerebral autoregulation (CA) can be defined as the homeostatic mechanism that minimizes changes in cerebral blood flow in response to any change in cerebral perfusion pressure ([1]). Most researchers believe that cerebral blood flow (CBF) remains relatively constant over a wide range of perfusion pressure ([2,3]). But there are reports, which do not agree with the idea of constancy of CBF in the face of variable perfusion pressure ([4,5]). Furthermore cerebral blood flow velocity (CBFV) variability with normal aging is also controversial. While some studies have shown that in older subjects CBFV is fairly constant ([6,7]), others oppose such an idea ([8,9]).

However, the effect of baroreflex (BR) resetting on the CBFV has been overlooked. The acute response of baroreceptors stimulus occurs rapidly within 3 sec. This is immediately followed by resetting of its tone which is accomplished in 2 phases; short-term adaptation, which is completed within 30 sec and long-term adaptation, which needs hours to develop ([10, 11]). The present study aims to study the behavior of CBFV simultaneous with acute response and short term resetting of carotid baroreceptors. The effect of sex and age are also considered in this study.

SUBJECTS AND METHODS

The study population consisted of 52 healthy subjects. They were divided into four groups regarding to their age and sex each consisting of 13 volunteers representing young (20-30 yrs) males, young females, middle-aged (50-60 yrs) males and middle-aged females. They were nonsmoker, normotensive individuals and were on no medication. Also those suffering from a silent and significant carotid stenosis were excluded by using Doppler study.

In order to minimize the effects of relevant biological rhythms all subjects were tested at about 10 a.m. The local ethics committee approved the protocol of the study and subjects gave written consent to participate. General characteristics of the four groups are shown in table 1.

Figure 1

Table 1:Characteristics of the study population

Parameter	Young male	Young female	Middle-aged male	Middle-aged female
Age (yr)	23.9±0.8	24.2±0.7	58±0.9	56.4±0.7
Height (cm)	174±1.5	159±1.1	161.4±1.7	155.2±1.7
Weight (kg)	64.1±1.8	55±2.1	64.6±1.8	63.6±2.2
BMI (kg/m²)	21.2±0.74	21.6±0.74	24.8±0.55	26.3±0.67
HR (bpm)	74.9±2.7	73±3	68.1±2.2	79.3±1.8*

* Significantly different between two groups (young or old), P<0.05

HR: Heart Rate, BMI: Body Mass Index. All data are represented as mean±SE.

Eckberg's neck suction device ([12]) was used for stimulating the carotid baroreceptors and a standard surface electrocardiographic limb leads were attached for continuous monitoring. Cerebral blood flow velocity was measured using a transcranial Doppler (TCD) ultrasonography (Multidop-p, DWL, Germany) with a 2MHz probe. In order to avoid velocity variations due to any changes in probe angle, a special probe holder was used.

The study was conducted in a quiet, environmentally controlled laboratory with an ambient temperature of 20-25 C°. The subjects had a light breakfast 2-4 hours before the test and refrained from caffeinated beverages at least 12 hours prior to the study. They rested at least for 15 minutes in order to adapt and were asked to breathe ordinarily and not to talk during the test.

In each subject right middle cerebral artery (MCA) was identified by TCD using standard protocol ([13]). A probe holder was used to keep the probe in the same position and permit continuous blood flow velocity measurement. The MCA blood flow velocity was insonated at a depth of 50-55mm for all subjects. Limb leads of ECG device were also fixed and lead [illegible] was recorded during the entire test. The intensity of BR stimulation utilized in the study was –40 mmHg in the neck chamber and was applied at a 30-second. During the study the subjects were in the supine position with their heads slightly elevated.

The examination consisted of three stages: 1. Baseline stage (15 seconds). 2. Stimulation stage (30 seconds). 3. Post stimulation stage (30 seconds).

We analyzed data using the Minitab 12 software and nested analyze variance program. To evaluate the influence of age and sex on CA and CBFV, SPSS 10 software (general linear model or univariate program) was used. Student's t-test was applied for intra and inter group comparison. A p value of less than 0.05 was considered significant. All the data were expressed as mean ± standard error (SE).

RESULTS

The TCD apparatus gave the means of CBFV for every 3.5 sec period. Hence a similar mean data were derived for HR. Mean values of four 3.5 sec periods prior to carotid baroreceptors stimulation were considered as baseline and 3.5 sec periods during the stimulation were divided to eight 3.5 sec periods (1-8). The poststimulation 3.5 sec periods were eight too (9-16). Baseline HR was not significantly different between young groups but in older groups it was higher in females ($P<0.001$). Table 2 demonstrates CBFV concomitant to acute BR response (period 1), after its short term resetting (period 6) and postvagal tachycardia (period 11). Baseline CBFV was higher in females but this was significant only in young groups ($p<0.05$). Moreover, in older subjects (both males and females) CBFV was lower than that of young ones, reaching to significant level in females ($p<0.05$). As fig.1 shows all four groups had a sharp decline in heart rate with the induction of stimulation. This decline was greater in young female subjects compared to young males ($p<0.05$). In older subjects, the reverse was true ($p<0.05$). Then a partial retrieval of HR towards a higher values occurred. CBFV did not change significantly during acute phase of BR stimulation, but it was reduced at the resetting phase, which became significant at 5th and 6th periods in young females ($p<0.05$) and at 5th, 6th and 7th periods in middle-aged males ($p<0.05$).

Figure 2

Figure 1: Mean heart rate (HR) changes in young (A) and middle-aged (B) groups during baroreflex study. The arrows represent set in and cut off baroreflex stimulation. Time periods represent consequent 3.5 seconds.

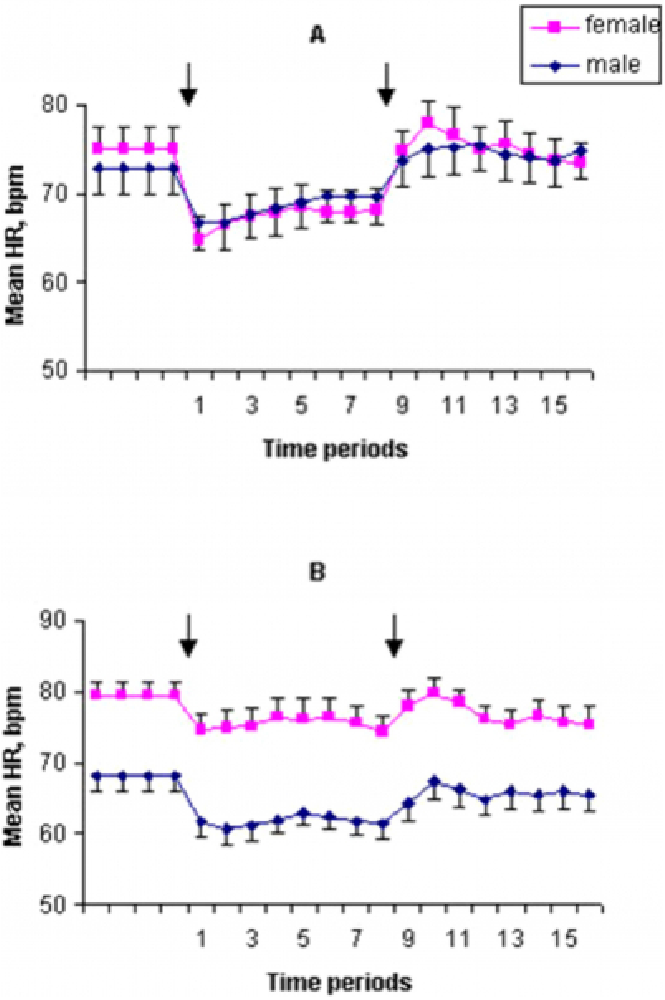


Figure 3

Table 2: Mean CBFV and HR at acute response (I), resetting of carotid baroreflex (II) and postvagal tachycardia (III).

Age	Sex	Parameter	Baseline	I	II	III
Young:	*Male*	CBFV□	55.4±0.8	54.8±2.6	53.8±2.5	58.3±3.6
		HR ◇	73±3	66.7±3.1*	69.8±3*	74.9±3.1
	Female	CBFV	60.1±0.9	59.4±2.6	56.3±2.5*	62.6±2.9
		HR	74.9±0.9	64.7±2.7*	68±2.5*	78±2.5*
Middle:	*Male*	CBFV	51.9±1	50.1±2.8	47.6±2.1*	50.2±2.3
		HR	68.1±0.7	61.6±2*	62.5±2*	68.3±2.7
	Female	CBFV	54±0.6	54.4±2.4	52.6±2.4	55.5±1.8*
		HR	79.3±0.6	74.6±2.2*	76.2±2.6*	79.7±2.1

□ **CBFV:** Cerebral Blood Flow Velocity measured as cm/sec, ◇ **HR:** Heart Rate, *significantly different from baseline, Values are mean ± SE.

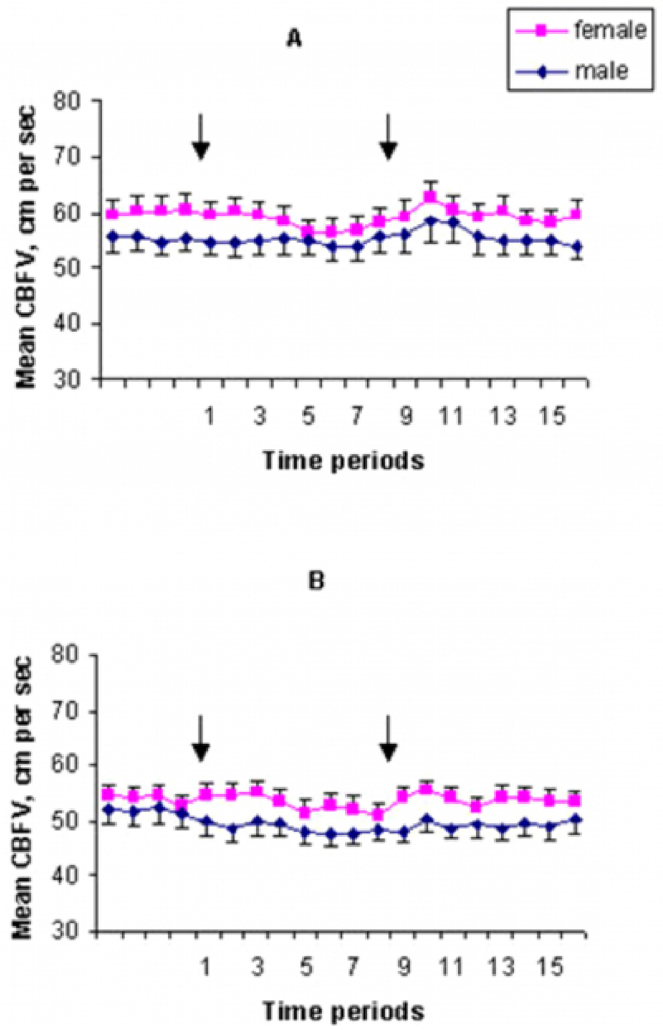
Following release of BR stimulation, all 4 groups showed an increase in CBFV, which was significant only in middle-aged females ($p<0.02$). This increase in CBFV was coincident with an increase in HR that was significant in young female group ($p<0.05$).

DISCUSSION

The present study is addressed any CBFV variability during a bout of carotid BR stimulation. A particular attention was focused on its possible alterations during BR adaptation. As given before (table 2 and fig 1 and 2), despite a dramatic fall in HR with onset of BR stimulation, no significant change occurred in CBFV in the four groups studied. But when short-term adaptation of BR started, reduction in CBFV occurred which were significant at fifth and sixth periods in the young females and at fifth, sixth and seventh periods in the middle-aged males.

Figure 4

Figure 2: Mean cerebral blood flow velocity (CBFV) changes in young (A) and middle-aged (B) groups during baroreflex study. The rest is similar to figure 1.



It is difficult to justify why CBFV is stable at the first stage of the stimulation when there is sharp decrease in HR. It looks strange that CBFV faces a reduction just when BR resetting led to a partial increase in HR. Apparently, following an acute change in systemic hemodynamic with a consequent CA via altering vascular resistance at the microcirculation level, when alterations in the systemic hemodynamic are reduced by BR resetting, in some way brain falls into an over reaction, and by creation of a higher resistance at its peripheral vessels results in such a discrepancy. This subject is reported for the first time so there seems to require more researches.

Meanwhile, although the Doppler technique measures blood velocity rather than absolute flow, these two quantities will change in parallel unless the diameter of the insonated vessel changes significantly, which has not been shown to occur (3,14). Regarding to the effective stabilization of CBFV at acute phase of intervention, our findings agree with the reports by Paulsen et al (2) and Aaslid et al (3), while Panerai et al (4) and Zhang et al (5) found a significant change in CBFV following concomitant systemic hemodynamic changes.

Moreover, the findings of others (8,9,15,16) and ours show that CBFV is higher in females which was statistically significant in young groups. This is attributed to the effect of estrogen (9,15,16). Krejza et al showed that this was not the case in women in their 60s (9), and could be restored by estrogen therapy (15). In our study older women were at just postmenopausal stage and we do not expect that estrogen level sharply reduced to its lowest level at primary stage of menopause (17).

Furthermore, as table 2 and figure 2 show mean CBFV was less in middle-aged groups compared to that of young groups. Krejza et al (9) and Naritomi et al (18) have attributed CBFV reduction with aging to an increase in cerebral blood flow resistance. While a recent study by Carey et al (19) suggested a concomitant increase in vessel diameter with normal aging and considered this being responsible for the reduced CBFV in aged persons.

In conclusion the present study postulates that coincident with an acute change in carotid BR tone, CBFV remains unchanged, but faces a partial decline at its short-term resetting period and then shows an incremental trend simultaneous to postvagal tachycardia. Furthermore, our findings confirm previous ones of a higher CBFV in females and in the younger individuals.

ACKNOWLEDGMENTS

We thank research Committee of Tabriz University of medical Sciences for their financial support. The authors would like to thank all staff members of physiology department and Doppler unit of Tabriz Imam Hospital for their kind cooperation. Our special thanks are due to those who volunteered and cheerfully took part in our study.

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