ANALYSIS OF MEAN BLOOD FLOW VELOCITIES IN POSTERIOR CEREBRAL ARTERIES BY TRANSCRANIAL DOPPLER DURING VISUAL STIMULATION

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SUMMARY – Changes of mean blood flow velocities (MBFV) in the posterior cerebral arteries (PCA) during visual stimulation were recorded in a group of 51 healthy, right-handed volunteers. There were 27 (52.9%) males and 24 (47.1%) females aged from 20 to 59 (mean age 36.98) years. Measurements were performed with a hand-held 2 MHz transcranial Doppler ('I'CD) probe through temporal window, while the subjects had their eyes open, closed, and when looking at white light. In half of the subjects, the right PCA was insonated first and then the left PCA, while in the other half a reverse procedure was used. Statistical analysis was performed using Wilcoxon's matched-pair signed-rank test. In the left PCA, MBFV was 41.2±8.6 cm/s (mean ± SD) with eyes open, 27.8±8.5 cm/s with eyes closed, and 42.3±9.1 cm/s while looking at white light. In the right PCA, MBFV was 41.7±8.9 cm/s with eyes open, 28.2±9.1 cm/s with eyes closed, and 42.4±8.8 cm/s while looking at white light. In the left PCA, differences between eyes open and closed, and between eyes open and while looking at white light were statistically significant ($p<0.001$, $z=-6.2146$, and $p<0.001$, $z=-3.4836$, respectively). In the right PCA, a statistically significant difference was found between eyes open and closed ($p<0.001$, $z=-6.2146$ and $p<0.001$, $z=-3.6928$), but not between eyes open and looking at white light ($p=0.03$, $z=-2.1693$). Study results demonstrated that straightforward visual stimulation had an effect on blood flow velocities in PCA and that it could be measured with TCD.

Key words: *Cerebrovascular circulation – physiology; Cerebrovascular disorders – ultrasonography; Blood flow velocity – physiology; Brain physiology*

Introduction

Primary visual fields of cerebral cortex are located in both occipital lobes around the calcarine sulcus in Brodman's area 17. Visual field is placed mainly on the medial aspect of the occipital lobe, but at the apex of the occipital lobe primary visual area partially extends into the lateral aspect of the occipital lobe. Around Brodman's area 17 there are Brodman's areas 18 and 19 functioning as associative visual areas that are called extracranial visual areas.

The brain is receiving arterial blood through the anterior (carotid) and posterior (vertebrobasilar) system. The vertebrobasilar system consists of the left and right vertebral arteries that fuse to form basilar artery. Basilar artery, after a short course divides into the right and left posterior cerebral arteries. Posterior cerebral artery

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(PCA), emerging at the basilar artery bifurcation, provides arterial blood supply for most parts of the occipital lobe. Primary and associative visual areas located in the occipital lobe also receive arterial blood supply by way of posterior cerebral arteries[1,2].

In 1982, Rune Aaslid[3] was the first to describe an original method that allowed visualization and measurement of blood flow velocities in the basal cerebral arteries. The method was named transcranial Doppler (TCD) and it has several advantages over other methods of cerebral blood flow visualization and measurement. Cranial bones create a barrier for intracranial ultrasound Doppler examination, because they weaken ultrasound waves. The problem of ultrasound weakening has been solved by use of low frequency (2 MHz) pulsed ultrasound and by placing the probe on the thinnest part of the temporal bone, right over the zygomatic arch (so-called temporal window). The reflected ultrasound waves have an acceptable signal to noise ratio.

TCD is a noninvasive, harmless, painless, and relatively inexpensive method. It provides data in real time and has optimal time resolution of the measurement. Measurement can be performed as long and as frequently as necessary. In recent years, TCD has been gaining ever more importance in the evaluation of cerebral hemodynamics, and it has many areas of diagnostic and research applications. TCD enables measurements of the effect of any mechanical manipulation or functional stimulation on intracranial circulation[4,5]. TCD has been used to measure blood velocities in basal cerebral arteries during functional stimulation of distinct brain regions (reading, writing, cognitive tasks, visual stimuli, etc.). Different functional tests and pharmaceutical substances have been used during TCD monitoring to assess the cerebral circulatory reserve (hypercapnia, hypoxia, acetazolamide, etc.)[6].

Systolic, diastolic and mean blood flow velocities are used to describe the flow in basal cerebral arteries. However, mean blood flow velocity (MBFV) has a greater physiological significance, since it least depends on cardiovascular factors such as cardiac frequency and contractility, peripheral resistance, and aortic elasticity. Also, MBFV has a better time correlation with perfusion than other values[7,8].

In this paper, measurements of MBFV in PCA during simple visual stimulation in healthy volunteers are presented.

Subjects and Methods

Measurements were performed in a group of 51 right-handed healthy volunteers with a hand-held 2 MHz probe using a Transscan 3D EME TCD device, at the Laboratory for Cerebrovascular Diagnostics, University Department of Neurology, Sestre milosrdnice University Hospital in Zagreb.

PCA was identified and insonated through temporal window using a standard technique[9], while subjects had their eyes wide open and closed, and MBFV in PCA was measured. After a resting phase of two minutes, the subjects watched a rectangular source of white light placed at a distance of one meter in front of them for one minute, and MBFV in PCA was measured. In half of the subjects, the measurements were first performed on the right side, then on the left side, while in the other half the measurements were first performed on the left side, then on the right side. So, each subject had MBFV measurements done in the right and left PCA with eyes wide open, eyes closed, and while looking at white light.

Statistical analysis was done using nonparametric Wilcoxon's matched-pair signed-rank test and analysis of variance with Bonferroni correction. Statistically significant differences were considered at p value less than

Table 1. Mean blood flow velocities in left posterior cerebral artery during visual stimulation

	Mean blood flow velocity mean±2SD (cm/s)	Statistical significance		
		%	Wilcoxon's matched-pair signed-rank test	Analysis of variance with Bonferroni correction
Eyes wide open	41.2±8.6	100.0		
Eyes closed	27.8±8.5	67.5 p<0.001	z=-6.2146 t=14.008,	p<0.001
White light	42.3±9.1	102.7	z=-3.4836 p<0.001	t=1.201, NS

NS, nonsignificant

Table 2. Mean blood flow velocities in right posterior cerebral artery during visual stimulation

	Mean blood flow velocity mean±2SD (cm/s)	%	Statistical significance Wilcoxon's matched-pair signed-rank test	Analysis of variance with Bonferroni correction
Eyes wide open	41.7±8,9	100.0		
Eyes closed	28.2±9.1	67.6	z=-6.2146 p<0.001	t=14.802, p<0.001
White light	42.4±8.8	101.7	z=-2.1693, NS	t=0.837, NS

NS, nonsignificant

0.01 (p<0.01). Results are presented as mean ± two standard deviations (SD).

Results

The study group consisted of 51 healthy, right-handed volunteers, 27 (52.9%) men and 24 (47.1%) women, aged 20-59, mean age 36.98 (SD 10.43) years. MBFV in the left PCA was 41.2±8.6 cm/s with the subjects' eyes wide open. Closing the eyes caused a drop of MBFV to 27.8±8.5 cm/s, i.e. to 67.5% of the MBFV with the eyes wide open. The difference was statistically significant at p<0.001 (z=-6.2146). While looking at white light, MBFV was 42.3±9.1 cm/s, i.e. 102.7% of the MBFV with the eyes wide open. In the left PCA, the increase in MBFV while looking at white light was approximately twelve times smaller than the decrease in MBFV while the subjects closed their eyes (2.7% to 32.5%) (Table 1).

MBFV in the right PCA was 41.7±8.9 cm/s while the subjects had their eyes wide open. Closing the eyes caused a drop of MBFV to 28.2±9.1 cm/s, i.e. to 67.6% of the MBFV with the eyes wide open. The difference was statistically significant at p<0.001 (z=-6.2146). While looking at white light, MBFV was 42.4±8.8 cm/s; i.e. 101.7% of the MBFV with the eyes wide open. The difference for white light was not statistically significant, p=0.03 (z=-2.1693). In the right PCA, the increase in MBFV while looking at white light was approximately nineteen times smaller (1.7% to 32.4%) than the decrease in MBFV with the eyes closed (Table 2).

There was no statistically significant difference in MBFV between the left and right PCA with the subjects' eyes wide open (p=0.28; z=-1.0867), closed (p=0.32; z=-0.9940), or while looking at white light (p=0.87; z=-0.1688) (Table 3).

Discussion

The application of visual stimuli (i.e. the light) is a practical method for different kinds of experimental research of the visual system. The light stimulus can be easily and precisely applied and controlled. Many authors recorded changes of blood flow velocities with TCD in the posterior cerebral arteries during visual stimulation[4,10-16]. Most of these studies report on a decrease in blood flow velocities with closing the eyes and an increase of flow velocities with opening the eyes as well as with various visual stimuli. However, the percentage of increase or decrease varies considerably among different authors. Some of them recorded smaller, and oth-

Table 3. Mean blood flow velocities in left and right posterior cerebral arteries (ACP) during visual stimulation (mean ± 2 standard deviations)

	Left ACP (cm/s)	Right ACP (cm/s)	Statistical significance	
			Wilcoxon's matched-pair signed-rank test	Analysis of variance with Bonferroni correction
Eyes wide open	41.2±8.5	41.7±8.9	z=-1.0867, NS	t=0.815, NS
Eyes closed	27.8±8.5	28.2±9.1	z=-0.9940, NS	t=0.0215, NS
White light	42.3±9.1	42.4±8.8	z=-0.1688, NS	t=0.450, NS

NS, nonsignificant

ers greater changes in blood flow velocities. These differences could be the result of different methods of visual stimulation used by various authors.

There are many mechanisms supposed to play a significant role in the autoregulation of the cerebral blood flow, however, cerebral blood flow is definitely increased by changes in the metabolic activity. Cerebral blood flow is directly or indirectly coupled with the metabolic activity of the brain (vasoneural coupling). In many instances, significant differences in the regional cerebral blood flow may exist when distinct parts of the brain have an increased metabolism[17,18].

Since the visual cortex in the occipital lobes receives blood supply almost exclusively from the posterior cerebral arteries[2], all changes in the arterial blood flow due to differences in the metabolism of the visual cortex neurons have their reflection in the arterial blood flow of the posterior cerebral arteries. So, changes in the blood flow of the posterior cerebral arteries could indirectly reflect changes in the metabolism of the visual cortex neurons. In the present study, MBFV was measured in the posterior cerebral arteries while the subjects were exposed to simple visual stimuli (eyes open and closed, and looking at white light). With closing the eyes, there was a significant decrease of MBFV in the right and left posterior cerebral arteries. On the other hand, while looking at white light, there was an increase in MBFV in both posterior cerebral arteries; in the left PCA, the increase was significant, while in the right PCA the increase did not reach statistical significance.

These changes in MBFV meet the concept of vasoneural coupling, i.e. the coupling of cerebral metabolism and brain blood flow. It is logical that with closing the eyes, the metabolism of visual cortex significantly decreases, because there are less visual stimuli conducted through visual paths and less visual information to process. On the other hand, while looking at white light, there are more visual stimuli and more visual information to process, thus enhancing the metabolism of visual cortex, resulting in the increase of MBFV recorded in the posterior cerebral arteries. However, the increase in MBFV while looking at white light was approximately twelve to nineteen times smaller than the decrease in MBFV with eyes closed. This could imply that most of the visual cortex neurons are metabolically active with the eyes open, and that additional stimulation with white light causes only a slight additional increase in the metabolism of the visual cortex neurons. However, additional studies are needed to confirm this presumption.

This study showed that TCD is an excellent method for measuring changes in the blood flow of basal cerebral arteries. Using TCD, changes in the brain activity in the area supplied by the posterior cerebral arteries can be measured indirectly, harmlessly, noninvasively, with high temporal resolution, and as frequently and as long as necessary.

References

1. SMITH CG, RICHARDSON WFG. The course and distribution of the arteries supplying the visual (striate) cortex. Am J Ophthalmol 1966;61:1391-6.
2. Van der ZWAN A, HILLEN B. Review of the variability of the territories of the major cerebral arteries. Stroke 1991;22:1078-84.
3. AASLID R, MARKWALDER TM, NORNES H. Non-invasive transcranial Doppler ultrasound recording of flow velocities in basal cerebral arteries. J Neurosurg 1982;57:769-74.
4. AASLID R. Visually evoked dynamic blood flow response of the human cerebral cortex. Stroke 1987;18:771-5.
5. AASLID R, LINDEGAARD KF. Cerebral hemodynamics. In: AASLID R, ed. Transcranial Doppler sonography. Vienna, New York: Springer-Verlag, 1986:60-85.
6. DEMARIN V, RUNDEK T. Acetazolamide test combined with transcranial Doppler (TCD): a simple, non-invasive test for the assessment of cerebral vasoreactivity in humans. Period Biol 1992;94:193-200.
7. KONTOS HA. Validity of cerebral arterial blood flow calculations from velocity measurements. Stroke 1989;20:1-3.
8. KIRKHAM FJ, PADAYACHEE TS, PARSONS S, SEARGEANT LS, HOUSE FR, GOSLING RG. Transcranial measurement of blood velocities in the basal cerebral arteries using pulsed doppler ultrasound: velocity as index of flow. Ultrasound Med Biol 1986;12:15-21.
9. ALEXANDROV AV, DEMARIN V. Insonation techniques and diagnostic criteria for transcranial doppler sonography. Acta Clin Croat 1999;38:97-108.
10. GOMEZ SM, GOMEZ CR, HALL IS. Transcranial doppler ultrasonographic assessment in intermittent light stimulation at different frequencies. Stroke 1990;21:1746-8.
11. KELLEY RE, CHANG JY, SCHEINMAN NJ, LEVIN BE, DUNCAIN RC, LEE SC. Transcranial doppler assessment of cerebral flow velocity during cognitive tasks. Stroke 1992;23:9-14.
12. SITZER M, DIEHL RR, HENNERICI M. Visually evoked cerebral blood flow responses – normal and pathological conditions. J Neuroimaging 1992;2:65-70.
13. STURZENEGGER M, NEWELL DW, AASLID R. Visually evoked blood flow response assessed by simultaneous two-channel transcranial doppler using flow velocity averaging. Stroke 1996;27:2256-61.
14. TRKANJEC Z, DEMARIN V. Transcranial doppler sonography during visual stimulation. Acta Clin Croat 1999;38:285-8.

15. LISAK M, TRKANJEC Z, MIKULA I, DEMARIN V. Mean blood flow velocities in posterior cerebral arteries during visual stimulation. Mt Sinai J Med 2005;72:346-50.
16. TRKANJEC Z, DEMARIN V. Hemispheric asymmetries in blood flow during color stimulation. J Neurol 2007;254: (in press).
17. DAFFERTSHOFER M, HENNERICI M. Cerebrovascular regulation and vasoneural coupling. J Clin Ultrasound 1995; 23:125-38.
18. SOKOLOFF L. Relationship among local functional activity, energy metabolism and blood flow in the central nervous system. Federation Proc 1981;40:2311-6.

Sažetak

ANALIZA SREDNJIH BRZINA KRVNOG PROTOKA U BAZALNIM MOŽDANIM ARTERIJAMA POMOĆU TRANSKRANIJSKOG DOPPLERA TIJEKOM VIDNE STIMULACIJE

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Promjene srednjih brzina krvnog protoka (MBFV) u stražnjim moždanim arterijama (PCA) bilježene su tijekom vidne stimulacije u skupini od 51 zdravog desnorukog dobrovoljca. Skupina se sastojala od 27 (52,9%) muških i 24 (47,1%) ženskih ispitanika u dobi od 20 do 59 (srednja dob 36,98) godina. Mjerenja su se izvodila pomoću ručne sonde od 2 MHz za transkranijski Doppler (TCD) kroz temporalni prozor, dok su ispitanici oči držali otvorenima, zatvorenima i dok su gledali u bijelo svjetlo. U polovice ispitanika najprije je ispitana desna PCA, a potom lijeva PCA, a u druge polovice primijenjen je obrnuti postupak. Statistička analiza je provedena pomoću Wilcoxonova parnog rank testa. U lijevoj PCA je MBFV bila 41,2±8,6 cm/s (srednja vrijednost ± SD) uz otvorene oči, 27,8±8,5 cm/s uza zatvorene oči i 42,3±9,1 cm/s dok su gledali u bijelo svjetlo. U desnoj PCA je MBFV bila 41,7±8,9 cm/s uz otvorene oči, 28,2±9,1 cm/s uza zatvorene oči i 42,4±8,8 cm/s dok su gledali u bijelo svjetlo. Razlike u MBFV između zatvorenih i otvorenih očiju, te između otvorenih očiju i gledanja u bijelo svjetlo bile su statistički značajne za lijevu PCA (p<0,001, z=-6,2146, odnosno p<0,001, z=-3,4836). U desnoj PCA je razlika u MBFV bila statistički značajna između otvorenih i zatvorenih očiju (p<0,001, z=-6,2146, odnosno p<0,001, z=-3,6928), ali ne između otvorenih očiju i gledanja u bijelo svjetlo (p=0,03, z=-2,1693). Rezultati su pokazali da izravna vidna stimulacija utječe na brzinu krvnog protoka u PCA te da se to može mjeriti pomoću TCD.

Ključne riječi: *Cerebrovaskularna cirkulacija – fiziologija; Cerebrovaskularne bolesti – ultrazvuk; Brzina krvnog protoka – fiziologija; Fiziologija mozga*