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Clinical Study

Hemispheric Asymmetry of Visual Cortical Response by Means of Functional Transcranial Doppler

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We assessed the visual evoked response and investigated side-to-side differences in mean blood flow velocities (MBFVs) by means of functional transcranial Doppler (fTCD) in 49 right-handed patients with severe internal carotid artery (ICA) stenosis and 30 healthy volunteers, simultaneously in both posterior cerebral arteries (PCAs) using 2 MHz probes, successively in the dark and during the white light stimulation. Statistically significant correlation ($P = 0.001$) was shown in healthy and in patients ($P < 0.05$) between MBFV in right PCA in physiological conditions and MBFV in right PCA during the white light stimulation and in the dark. The correlation between MBVF in right PCA and contralateral left PCA was not statistically significant ($P > 0.05$). The correlation between ipsilateral left PCA was significantly higher than the one with contralateral right PCA ($P < 0.05$). There is a clear trend towards the lateralisation of the visual evoked response in the right PCA.

1. Introduction

Functional transcranial Doppler (fTCD) studies indicated that simultaneous bilateral stimulation during a different visual tasks caused greater blood flow velocities in right hemisphere in healthy individuals, indicating that it may identify visual hemispheric dominance [1, 2]. Results of the studies testing the posterior cerebral circulation using visual stimuli in patients with severe carotid stenosis and consecutively compromised anterior cerebral circulation suggest the existence of an independent cerebral vascular reserve capacity of the posterior part of Willis circle [3–7]. Undoubtedly, collateral variations in circle of Willis have to be taken into consideration since they are highly variable [8]. In patients with carotid occlusive disease collateral flow from posterior to anterior circulation could be through the posterior communicating artery or via the leptomeningeal collaterals. In the first case, the blood flow in the vertebrobasilar artery system is shunted into the anterior cerebral circulation before the P2 segment branches leading to a decrease in the P2 flow velocities, and in the latter it is shunted through the P2 branch into the leptomeningeal collaterals leading to an increase resting blood flow velocity in the P2 [9, 10].

The aim of this study was to assess visual evoked response in PCA in patients with severe carotid stenosis and compromised anterior cerebral circulation, as the most powerful and fully noninvasive test of cerebral autoregulation, in vascular territory mostly supplied by posterior circulation, in order to investigate if flow through the circle of Willis might result in changes in the blood flow distribution in the PCA territory. Also, the aim was to investigate side-to-side differences of simultaneously measured PCAs blood flow velocities during white light stimulation in patients with severe carotid disease, in order to establish a possible functional hemispheric asymmetry of the visual cortex in patients.

2. Methodology

The study cohort consisted of 49 right-handed patients (mean age ± SD = 67 ± 8; 37 men), with no eye abnor-

Table 1: Mean blood flow velocities in posterior cerebral artery at baseline.

Mean blood flow velocities in posterior cerebral artery (cm/s ± 2SD) at baseline (eyes opened)				
		Patients ($n = 49$)	Healthy ($n = 30$)	P
PCA at baseline	right	29.08 ± 10.46	25.8 ± 7.32	0.14
	left	28.65 ± 9.58	25.93 ± 8.67	0.21

cm/s: centimeters in second.
n: number of patients/healthy subjects.
PCA: posterior cerebral artery.
SD: standard deviation.

Table 2: Mean blood flow velocities in posterior cerebral artery during the white light stimulation and in the dark in the group of healthy subjects.

Mean blood flow velocities in posterior cerebral artery (cm/s ± 2SD)			
		Light	Dark
Healthy ($n = 30$)	Right PCA	29.99 ± 9.5	20.12 ± 8.33
	Left PCA	30.56 ± 8.34	21.40 ± 7.32

cm/s: centimeters in second.
n: number of healthy subjects.
PCA: posterior cerebral artery.
SD: standard deviation.

malities, with high-grade (70–99%) symptomatic or asymptomatic ICA stenosis (20 right and 19 left ICAs) as measured by Doppler ultrasonography and 30 healthy volunteers (mean age ± SD = 67 ± 7; 22 men) with normal ICAs. The two groups were matched in age ($P = 0.91$) and sex ($P = 0.52$). For the comparison, in the group of healthy individuals, the proportion of the left and right ICA was matched to the proportion of left and right ICA in the group of patients with severe carotid stenosis.

Exclusion criteria were limited ultrasound temporal bone window, detectable stenosis or occlusion of any of the arteries of the Willis circle or vertebrobasilar circle by means of TCD, uncooperative patients (dementia, coma, etc.), heart disease (atrial fibrillation, myocardial infarction, patent foramen ovale, atrial septum aneurysm, and mitral valve prolapse), uncontrolled hypertension, diabetes mellitus, and migraine.

In all patients, the risk factors were under control for at least one year before the study was performed. None of the patients used vasoactive medications. Patients had abstained from alcohol, caffeinated beverages, and smoking, as well as certain drugs that may alter blood pressure or cause vasodilatation (nitrates, β-blocking agents, calcium channel blockers, anticoagulants, and vasodilatatory agents) for at least 24 hours prior to the study.

Carotid artery disease was assessed and defined using the carotid color Doppler flow imaging (CDFI) and power Doppler imaging (PDI) according to validated criteria [11]. The intracranial arteries were evaluated by TCD according to validated criteria [12]. Visual evoked response was obtained by means of TCD (MultiDop X4 DWL, Elektronische Systeme GmbH, Sipplingen) using a special application for evoked flow. It included transtemporal simultaneous insonation of P1 or proximal part of P2 segment if the P1 was not able to insonate, of both PCAs while obtaining the signal away from the probe at the depth of 60–70 mm using two 2 MHz probes mounted on an individually fitted head band. The test was performed while patient in a supine position, in a dark, quiet room, after an accommodation period of resting and closed eyes for 10 minutes. For the visual stimuli, a 100 W electric bulb was used, located 50 cm in front of the head of the examinee. After the accommodation period, mean blood flow velocities (MBFVs) in each PCA were measured, in a dark (closed eyes) and during a white light stimulation (opened eyes, looking at an electric bulb). The measurements were performed successively in the dark and during the white light stimulation, during three consecutive repetitive periods of 1 minute each. Mean values of MBFV during a one-minute period with and without visual stimuli were analyzed. Before the testing, all the subjects were introduced to the testing method and the testing measurements were performed before the study measurements in order to establish which subjects were suitable for the study.

Institutional Ethical Committee approved the study. All patients signed informed consent.

For statistical analyses, we used statistical program package Statistica for Windows, Kernel release (5.5) A (StatSoft, Inc. Tulsa, OK) (StatSoft, Inc. (2000); statistics for Windows (Computer program manual). Tulsa, OK: StatSoft, Inc.

We used paired Student t-test to compare quantitative variables between the two groups, t-test for dependent variables to compare values of repetitive measurements within the same group and linear regression analyses to analyze the correlation of quantitative variables.

From nonparametric statistics model, we used Pearson chi-square test to compare a distribution of qualitative characteristics of the group. Results with P-values of <0.05 were considered statistically significant.

3. Results

Regarding the symptomatic status, 9 of 49 patients were symptomatic, at least one year or more before the study was performed. Concerning the presence and functionality of the collateral cerebral circulation by TCD before testing for vasomotor reactivity, the patient's statuses were as follows: 5 patients had anterior collateral pathway, 17 patients had developed collateral flow through the ophthalmic arteries (2 of them were symptomatic), and 4 patients had developed both anterior collateral pathway and collateral pathway through the ophthalmic artery (2 of them were symptomatic). With regard to vascular risk factors, 30 patients had no vascular risk factors, 18 patients had arterial hypertension, 10 had cardiomyopathy, 4 had diabetes mellitus, 6 hypercholesterolaemia, 2 patients were cigarette smokers, and 1 patient was an alcohol abuser.

There was no difference at baseline between right PCAs ($P = 0.14$; Student t-test) and left PCAs ($P = 0.21$; Student t-test) between healthy and patients (Table 1).

Table 2 displays the difference in MBFV between dark and white light stimulation in the group of healthy subjects.

Table 3: Mean blood flow velocities in posterior cerebral artery during the white light stimulation and in the dark in the group of patients with severe carotid stenosis.

		Mean blood flow velocities in posterior cerebral artery (cm/s ± 2SD)	
		Light	Dark
Patients with severe carotid stenosis ($n = 49$)	Right PCA	29.88 ± 8.6	21.32 ± 7.08
	Left PCA	32.6 ± 11.49	21.40 ± 7.32

cm/s: centimeters in second.
n: number of patients.
PCA: posterior cerebral artery.
SD: standard deviation.

Table 4: Correlation between internal carotid artery stenosis and mean blood flow velocities in posterior cerebral artery.

		Mean blood flow velocities in posterior cerebral artery (cm/s)			
		Light		Dark	
Patients ($n = 49$)		Right PCA	Left PCA	Right PCA	Left PCA
Stenosis	Right ICA	0.1891, $P = 0.193$	0.0546, $P = 0.710$	0.2009, $P = 0.166$	0.1349, $P = 0.355$
	Reft ICA	−0.1092, $P = 0.455$	−0.008, $P = 0.955$	−0.072, $P = 0.622$	−0.0390, $P = 0.790$

cm/s: centimeters in second.
n: number of patients.
ICA: internal carotid artery.
PCA: posterior cerebral artery.

MBFV during the white light stimulation and in the dark in the group of patients with severe carotid stenosis are displayed in Table 3.

Linear regression analysis showed no statistically significant correlation between the degree of right ICA stenosis and MBFV either in any PCA in the dark and during a light stimulation (Table 4), but there was a trend of negative correlation between the degree of left ICA stenosis and MBFV both in contralateral PCA as well as in ipsilateral PCA, but with no statistical significance (Table 4).

In the same time, significant correlation ($P = 0.001$) of the measured parameters both during the white light stimulation and in the dark, regardless of the side of the measurement, was found in the group of healthy individuals (Table 5).

In the group of patients with severe carotid stenosis, correlation between MBFV in left and right PCA at baseline and MBFV in left and right PCA during the white light stimulation and in the dark showed statistically significant correlation (linear regression analyses; $P < 0.05$) between MBFV in right PCA at baseline and MBFV in right PCA during the white light stimulation and in the dark (Table 6). On the contrary, correlation between MBFV in right PCA at baseline and contralateral PCA either during the white light stimulation or in the dark was not statistically significant (linear regression analyses; $P > 0.05$) (Table 6). The results showed the higher flow response under various conditions in the right PCA compared to the left one.

Analyzing the correlation between MBFV in left PCA at baseline conditions, statistically significant correlation between MBFV in both ipsilateral and contralateral PCA, both during the white light stimulation and in the dark, was found, but the correlation with ipsilateral side was significantly higher than with contralateral side (linear regression analyses; $P < 0.05$) (Table 6).

Considering the small number of symptomatic patients, which is not suitable for statistical analyses, and the fact that they had symptoms at least one year or more before the study was performed, we did not find it suitable to separate the results by symptomatic status. Additionally, the number of symptomatic patients was too small to be suitable for separate analyses regarding the presence and functionality of the collateral cerebral circulation.

4. Discussion

We found no statistical difference in MBFV at baseline conditions between right and left PCAs between healthy subjects and patients. According to our results, a degree of ICA stenosis does not influence the MBFV in ipsilateral nor in contralateral PCA, showing that visual evoked response of the PCA remains similar both on the stenosed and the unstenosed side of ICAs in the case of more pronounced metabolic demands of the region and that the degree of ICA stenosis has no impact, or only exceptionally, on the collateralizing capacity of the PCAs. Those results that are in concordance with the results of the previous studies demonstrate an independent cerebral posterior circulation mechanism that compensates very successfully the anterior circulation insufficiency in severe carotid disease [3–7]. Concerning the correlation of the ICA stenosis, one of the limitations of our study was limited number of patients. Another limitation is that the ICA stenosis might serve as an indicator of vascular risk since it was shown that patients with increased risk factors have decreased hemodynamic response due to functional activation [13]. Our results show that our group of patients with severe carotid stenosis had the same response as healthy volunteers suggesting that carotid stenosis have no or only little impact on PCA flow velocities during various

Table 5: Correlation between mean blood flow velocities in physiological conditions and mean blood flow velocities during the white light stimulation and in the dark in healthy subjects.

Healthy ($n = 30$)					
		Light		Dark	
Mean blood flow velocities in posterior cerebral artery (cm/s)		Right	Left	Right	Left
Baseline(eyes opened)	Right	0.8812, $P = 0.001^*$	0.7035, $P = 0.001^*$	0.8459, $P = 0.001^*$	0.6690, $P = 0.001^*$
	Left	0.7556, $P = 0.001^*$	0.9235, $P = 0.001^*$	0.7553, $P = 0.001^*$	0.9450, $P = 0.001^*$

n: number of healthy subjects.
cm/s: centimeters in second.
*statistically significant.

Table 6: Correlation between mean blood flow velocities in physiological conditions and mean blood flow velocities during the white light stimulation and in the dark in severe carotid disease patients.

Pateints with severe carotid disease ($n = 49$)					
		Light		Dark	
Mean blood flow velocities in posterior cerebral artery (cm/s)		Right	Left	Right	Left
Baseline(eyes opened)	Right	0.7953, $P = 0.001^*$	0.2421, $P = 0.094$	0.7589, $P = 0.001^*$	0.2125, $P = 0.143$
	Left	0.4463, $P = 0.001^*$	0.6851, $P = 0.001^*$	0.3384, $p = 0.017^*$	0.6944, $P = 0.001^*$

n: number of patients.
cm/s: centimeters in second.
*statistically significant.

stimulation conditions suggesting an independent cerebral vascular reserve capacity of the posterior part of Willis circle.

Since the primary and associative visual areas located in the occipital lobes receive blood supply almost exclusively from the PCAs [14], every change in arterial blood flow due to differences in the metabolism of the visual cortex neurons is expected to have reflection on arterial blood flow in PCAs. Therefore, changes in blood flow in PCAs could indirectly reflect changes in metabolism of the visual cortex [15]. Although different authors used different methods and different kind of visual stimulation, making direct comparison quite difficult, previous fTCD studies have provided converging support for the view that visual stimulation might cause a greater activation of the visual cortex in right occipital lobe [16–22]. These studies on hemispheric asymmetry of the visual cortex were done on healthy subjects, raising questions about the potential impact of pathology on the research findings. In the present study, we, therefore, used fTCD to investigate hemispheric asymmetries of the visual cortex in patients with severe carotid stenosis and compromised anterior cerebral circulation, considering the importance of posterior collateral pathway via PCA. In the group of healthy subjects, we recorded statistically significant difference between MBFV in left and right PCA at baseline and MBFV in both PCAs during the white light stimulation and in the dark, regardless of the side of the measurement ($P = 0.001$). In the group of severe carotid disease patients, statistically significant correlation between MBFV in right PCA at baseline and MBFV in right PCA during the white light stimulation and in the dark was also found. On the contrary, correlation between MBVF in right PCA at baseline conditions and contralateral left PCA either during the white light stimulation or in the dark was not statistically significant. Moreover, analyzing the correlation between MBFV in left PCA at baseline, statistically significant correlation between MBFV in ipsilateral left PCA, as well as contralateral right PCA was found, both during the white light stimulation and in the dark, but the correlation between ipsilateral left side was significantly higher than the one with contralateral right side. Following our results, the correlation of MBFV with functional reserve capacity is more evident in the healthy subjects while the right-sided lateralization of the evoked responses more pronounced in the patients. Furthermore, the lateralization is less evident in the healthy subjects. The lower correlation coefficients in the group of patients with severe carotid stenosis could imply that carotid stenosis affects functional reserve capacity in the patients.

5. Conclusions

Considering the presented results obtained in our study, we can conclude that there is a clear trend towards the lateralization of the visual evoked response in the right PCA, being highly consistent with results of the previous studies and showing a general dominance of the right occipital lobe in the visual process. The right occipital lobe is more responsive to visual stimuli in terms of functional activation than the left one, indicated by a consistently higher blood

flow velocity response on the right. fTCD was able to assess hemispheric visual dominance not only in healthy individuals, but also in patients with severe carotid disease and thus compromised anterior cerebral circulation. Furthermore, velocity changes between sides as a measure of hemispheric perfusion lateralization could be an indicator of posterior collateral pathway. The demonstrated right-sided asymmetry in posterior cerebral circulation in patients with severe carotid disease could possibly be taken into consideration in further trials according to stroke risk or outcome.

References

[1] A. J. O. Whitehouse and D. V. M. Bishop, "Hemispheric division of function is the result of independent probabilistic biases," *Neuropsychologia*, vol. 47, no. 8-9, pp. 1938–1943, 2009.

[2] R. E. Kelley, J. Y. Chang, N. J. Scheinman, B. E. Levin, R. C. Duncan, and S. C. Lee, "Transcranial Doppler assessment of cerebral flow velocity during cognitive tasks," *Stroke*, vol. 23, no. 1, pp. 9–14, 1992.

[3] A. Y. Gur and N. M. Bornstein, "Cerebral vasomotor reactivity of the posterior circulation in patients with carotid occlusive disease," *European Journal of Neurology*, vol. 10, no. 1, pp. 75–78, 2003.

[4] M. Roje-Bedeković, M. Bosnar-Puretić, A. Lovrenčić-Huzjan, and V. Demarin, "Visual evoked response in patients with severe carotid disease—functional transcranial doppler study of posterior circulation," *Collegium Antropologicum*, vol. 33, no. 4, pp. 1353–1357, 2009.

[5] M. Roje-Bedeković, A. Lovrenčić-Huzjan, M. Bosnar-Puretić, and V. Demarin, "Prolonged mean reaction time in posterior cerebral artery during visual stimulation in patients with severe carotid stenosis," *Clinical Physiology and Functional Imaging*, vol. 31, no. 4, pp. 282–287, 2011.

[6] M. Roje-Bedeković, M. Bosnar-Puretić, A. Lovrenčić-Huzjan, and V. Demarin, "Cerebrovascular evoked response to repetitive visual stimulation in severe carotid disease–functional transcranial Doppler study," *Acta Clinica Croatica*, vol. 49, no. 3, pp. 267–274, 2010.

[7] A. Y. Gur and N. M. Bornstein, "Cerebral vasomotor reactivity of bilateral severe carotid stenosis: is stroke unavoidable?" *European Journal of Neurology*, vol. 13, no. 2, pp. 183–186, 2006.

[8] A. W. J. Hoksbergen, D. A. Legemate, D. T. Ubbink, and M. J. H. M. Jacobs, "Collateral variations in circle of willis in atherosclerotic population assessed by means of transcranial color-coded duplex ultrasonography," *Stroke*, vol. 31, no. 7, pp. 1656–1660, 2000.

[9] M. Kluytmans, J. van der Grond, K. J. van Everdingen, C. J. M. Klijn, L. J. Kappelle, and M. A. Viergever, "Cerebral hemodynamics in relation to patterns of collateral flow," *Stroke*, vol. 30, no. 7, pp. 1432–1439, 1999.

[10] J. Hendrikse, C. J. M. Klijn, A. C. van Huffelen, L. J. Kappelle, and J. van der Grond, "Diagnosing cerebral collateral flow patterns: accuracy of non-invasive testing," *Cerebrovascular Diseases*, vol. 25, no. 5, pp. 430–437, 2008.

[11] A. Lovrenčić-Huzjan, V. Vuković, and V. Demarin, "Neurosonology in stroke," *Acta Clinica Croatica*, vol. 45, no. 4, pp. 385–401, 2006.

[12] A. V. Alexandrov and V. Demarin, "Insonation techniques and diagnostic criteria for transcranial Doppler sonography," *Acta Clinica Croatica*, vol. 38, no. 2, pp. 97–108, 1999.

[13] M. L. Bots, A. Hofman, P. T. V. M. De Jong, and D. E. Grobbee, "Common carotid intima-media thickness as an indicator of atherosclerosis at other sites of the carotid artery: the Rotterdam Study," *Annals of Epidemiology*, vol. 6, no. 2, pp. 147–153, 1996.

[14] A. van der Zwan and B. Hillen, "Review of the variability of the territories of the major cerebral arteries," *Stroke*, vol. 22, no. 8, pp. 1078–1084, 1991.

[15] R. Aaslid, "Visually evoked dynamic blood flow response of the human cerebral circulation," *Stroke*, vol. 18, no. 4, pp. 771–775, 1987.

[16] M. Sturzenegger, D. W. Newell, and R. Aaslid, "Visually evoked blood flow response assessed by simultaneous two-channel transcranial Doppler using flow velocity averaging," *Stroke*, vol. 27, no. 12, pp. 2256–2261, 1996.

[17] P. C. Njemanze, C. R. Gomez, and S. Horenstein, "Cerebral lateralization and color perception: a transcranial Doppler study," *Cortex*, vol. 28, no. 1, pp. 69–75, 1992.

[18] G. Panczel, M. Daffertshofer, S. Ries, D. Spiegel, and M. Hennerici, "Age and stimulus dependency of visually evoked cerebral blood flow responses," *Stroke*, vol. 30, no. 3, pp. 619–623, 1999.

[19] Z. Trkanjec and V. Demarin, "Hemispheric asymmetries in blood flow during color stimulation," *Journal of Neurology*, vol. 254, no. 7, pp. 861–865, 2007.

[20] M. J. Kushner, A. Rosenquist, A. Alavi et al., "Cerebral metabolism and patterned visual stimulation: a positron emission tomography study of the human visual cortex," *Neurology*, vol. 38, no. 1, pp. 89–95, 1988.

[21] J. Klingelhöfer, G. Matzander, D. Sander, J. Schwarze, H. Boecker, and C. Bischoff, "Assessment of functional hemispheric asymmetry by bilateral simultaneous cerebral blood flow velocity monitoring," *Journal of Cerebral Blood Flow and Metabolism*, vol. 17, no. 5, pp. 577–585, 1997.

[22] M. Deppe, E. B. Ringelstein, and S. Knecht, "The investigation of functional brain lateralization by transcranial Doppler sonography," *NeuroImage*, vol. 21, no. 3, pp. 1124–1146, 2004.