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TCD study of hemodynamic changes in PCA response to photic stimulation

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Abstract: Objectives: During visual stimulation, the elevated metabolism rate will couple with increase of blood flow velocity(BFV) in posterior cerebral artery(PCA). This study with TCD was aimed to investigate whether the coupling might change according to the different vasoneuronal conditions. Methods: Ninety-nine volunteers including 24 hypertension(HT) patients and 2 patients suffering from both HT and diabetes mellitus (DM) were enrolled in this trial. BFV and pulse indexes(PI) in P2 segments of PCA on both sides were monitored during visual stimulation. Results: In all subjects, Mean BFV increased and PI went down in response to visual stimulation. The percentages of changes (ΔV and ΔP) of both mean BFV and PI were larger in young group(<55 years old) than in old one(≥ 55 years old). There was significant positive correlation between ΔV and ΔP. Multivariated regression analysis did not show HT and DM, but age related to $\Delta V(\Delta P)$. We did not find significant difference of $\Delta V(\Delta P)$ between left and right sides. Conclusions: Blood flow velocity in PCA P2 segment increased due to decreased cerebrovascular resistance during visual stimulation and the response weakened with aging of the patient.

Key words: Cerebral blood flow, Ultrasonography, Vasomotor reactivity, TCD(Transcranial Doppler)
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INTRODUCTION

Many imaging techniques, like PET, fMRI and SPECT, can demonstrate increases in regional cerebral blood flow (CBF) or metabolic rate during certain neuronal stimulation. But these techniques are always expensive and more time consuming and repeated measurements are difficult. TCD(Transcranial Doppler) is the perfect candidate for such detection. Although absolute blood flow velocity(BFV) cannot be used as an indicator of CBF, changes of BFV have been found to reliably correlate with changes in CBF as long as vessel diameter and perfusion territory remain constant(Newell et al., 1994). TCD detection of hemodynamic changes in posterior cerebral arteries(PCA) responding to photic stimulation is simple and may be used to evaluate the functional and parenchymal changes of the brain in certain patients.

METHODS

Subjects

Ninety-nine 17 to 82 years old volunteers (50 men, 49 women; mean ± SD age, 54.7 ± 13.9 years) were enrolled in this trial. They were all right-handed. Twenty-four cases suffered from hypertension (HT) and 2 cases suffered from both HT and diabetes mellitus (DM), but none had history of cerebrovascular or neurological disorders. No subject had been smoking on the test day before the study. All subjects had perfect temporal acoustic windows. Any suspected cerebral artery occlusive lesions were excluded.

Criteria for suspected cerebral artery stenosis (Liu et al., 2001): Intracranial: (1) V_s (systolic velocity) >140 cm/s or V_m (mean velocity) >80 cm/s, with prominent turbulence and murmur; (2) $V_s > 160$ cm/s or $V_m > 120$ cm/s, without prominent turbulence and murmur; (3) V_s: 140 – 160 cm/s or V_m: 80 – 120 cm/s, without prominent turbulence and murmur, but with asymmetric $V_m > 20\%$ between bilateral synonymous artery pair. Extracranial: $V_s > 120$ cm/s, with or without turbulence and murmur. Criteria for suspected cerebral artery occlusion: acoustic windows are good and all arteries (except suspected one) can be detected. Collateral circulation may be found.

TCD detection

We used a commercially available TCD unit (EME 2021, Germany) and undertook TCD detection by ourselves. Every volunteer lied quietly on a bed. All cerebral arteries were at first routinely detected. Then the PCAs were identified from the transtemporal approach according to standard criteria such as anatomic landmarks (insonation angle, depth of sample volume, and spatial relationship of the Doppler spectra to those of the MCA, anterior cerebral artery, and the bifurcation of the internal carotid artery), direction of flow, and compression and oscillation maneuvers of the common carotid artery and the vertebral arteries (Buedingen et al., 1992). It was also required to prove PCA insonation by a clear-cut BFV increase on both sides during "eyes open" as opposed to "eyes closed". We chose PCA P2 segments as aimed arteries. After optimal adjustment, two 2MHz probes were tightly fixed with the Marc 600 Spencer probe fixation system.

Photic stimulation

After probes were fixed, the subjects were asked to close eyes, breathe regularly and try to stay calm. We monitored mean BFV, pulse index (PI) and heart rate (HR) simultaneously. When HR became stable, we asked the subject to open eyes and stimulated the left eye continuously at a distance of 5 cm in front of it with flashlight often used by neurologists for physical examination. BFV increased suddenly, formed a sharp peak and afterward went down, while PI changed conversely. We stopped stimulation immediately after the peak. We took mean BFV and PI just before stimulation as the base and at the peak as the maximum. Percentages of mean BFV increase and PI decrease on both sides were calculated ($\Delta VL1$, $\Delta VR1$ and $\Delta PL1$, $\Delta PR1$). After that, we used the same procedure on the right eye and calculated $\Delta VL2$, $\Delta VR2$ and $\Delta PL2$, $\Delta PR2$. During each procedure, if HR fluctuated greatly, we would repeat the test until HR was maintained constant. At last, we averaged all corresponding percentages between the first and second stimulation to ΔVL($[\Delta VL1 + \Delta VL2]/2$), ($\Delta VR$($[\Delta VR1 + \Delta VR2]/2$) and ΔPL($[\Delta PL1 + \Delta PL2]/2$), ΔPR($[\Delta PR1 + \Delta PR2]/2$).

Statistical procedure

Statistical software package SPSS 9.0 was used. Difference of ΔV and ΔP between groups with different ages as well as between left and right sides were analyzed with independent and paired T tests; Relationship between ΔV and ΔP was evaluated with Pearson correlation test; In order to exclude interference of some certain factors on the relationship between ΔV (ΔP) and age, we took multivariated linear regression with ΔV(ΔP) as dependent and HT(negtive: 0, positive: 1), DM(negtive: 0, positive: 1), age, sex(male: 0, female: 1) as independent variables. Because the trend of PI could not be recorded at the beginning of the trial, 58 subjects' PI parameters were missed.

RESULTS

The difference between young and old groups in the responses of their BFV and PI changes to photic stimulation

Details are listed in the Table 1. During photic stimulation, BFV in all subjects increased while PI went down. When age of 55 was used as the out-off line, we found that the changes of mean BFV and PI were greater in the young group than in old one ($P < 0.05$).

Table 1 **Mean BFV and PI change with visual stimulation of young and old groups (%)**

	< 55 years old	≥55 years old	t value	P value
ΔV	43 ± 9($n = 44$)	35 ± 9($n = 55$)	4.46	0.000
ΔP	18 ± 6($n = 21$)	12 ± 5($n = 20$)	3.59	0.001

Correlation between BFV and PI changes

After we drew a scatter graph, we found that there might be positive linear correlation between ΔV and ΔP. Pearson correlation test showed $r^2 = 0.64$ and $P = 0.000$ ($n = 41$) between ΔV and ΔP.

Multivariated regression analysis between ΔV (ΔP) and its related influencing factors

Detailed results show in Table 2. Only the patients' age had negative standardized coefficients 0.42 and 0.78 with P values less than 0.05. Sex, HT and DM did not seem to influence changes of BFV and PI in PCA when patients were visually stimulated with continuous light.

Table 2 Multivariated regression analysis between ΔV (ΔP) and its related influencing factors

	Age	Sex	HT	DM
ΔV ($n = 99$)	-0.42^*	-0.08	-0.08	-0.03
ΔP ($n = 41$)	-0.78^*	-0.18	-0.16	0.21

*: $p < 0.000$

Difference of ΔV (ΔP) between left and right PCAs

In Table 3, We did not find any significant difference of ΔV (ΔP) between left and right side ($P > 0.05$). There might be no superiority of response on both sides of occipital lobes to continuous light stimulation.

Table 3 Difference of ΔV (ΔP) between left and right PCA (%)

	Left side	Right side	t value	P value
ΔV ($n = 99$)	39 ± 12	38 ± 11	0.92	0.36
ΔP ($n = 41$)	16 ± 9	14 ± 6	1.43	0.16

DISCUSSION

Local brain activity is always measured by means of CBF, because of the close relationship between neuronal activity and blood flow (vasoneuronal coupling). PCA supplies blood to the visual cortex mainly involved in processing visual tasks. CBF in P2 segment of PCA is more directly related to the territory than P1 segment since the latter may be influenced by the posterior communicating artery. Therefore, we took P2 segments as the target arteries.

Sturzenegger et al. (1996) reported velocity-averaging method in valuation of BFV response to neuronal tasks. Every stimulation trial was comprised several stimulus cycles (10 seconds of stimulus on plus 10 seconds of stimulus off, each cycle). The averaging algorithm calculated the arithmetic mean over all cycles for each sample time. This method saturated BFV fluctuation caused by a number of factors, such as respiratory (coughing, hyperventilation, Valsalva maneuver) and cardiovascular (blood pressure, heart rate) factors, changes in muscle activation, anxiety and excitement, pain and so on, other than selective activation. However, this method needs a specific program in the TCD system and this program is not popular in the machines commercially available, so we tried to find a simpler method for vasoneuronal coupling detection. As the same, we took the most popularly used flashlight as the photic stimulus, just because this method was the easiest for clinical application. We knew the intensity and complexity of the visual stimulation are related to the amplitude of BFV response.

In all individuals in the study, BFVs in P2 segments on both sides increased during visual stimulation. The increase of mean BFV corresponded to the decrease of cerebrovascular resistance due to arteriolar dilation, as evidenced by the highly significant linear correlation between ΔV and ΔP as shown in result 2. ΔV and ΔP response to photic stimulation were also significantly greater in < 55 years old patients than $\geqslant$ 55 years age patients which might be in accordance with the concept that the gain of the vasoneuronal coupling decreases with aging. Those results were similar with Niehaus's report (Niehaus et al., 2001). During aging, the structure of the arteriolar system changes, including hypertrophy and hyalinization of the tunica media; degeneration of the internal elastic lamina; intimal proliferation and atheroma formation, resulting in lumen reduction; loss of elasticity; and increased rigidity of the vessel wall (Ostrow et al., 1993). However, because TCD detection did not measure vasoreactivity but instead the complex vasoneuronal coupling, the decrease of ΔP with age might also result from age-related changes of the neuronal-metabolic or metabolic-vascular coupling, such as decrease in number of synaptic contacts consequent to loss and shrinkage of cortical neurons, which led to a reduced energy requirement of cortex in response to the same visual input as in young subjects (Terry et al., 1987). So knowledge about age-related changes in hemodynamic coupling is a prerequisite for differentiating disease-related or age-related changes in functional imaging studies of elderly patients. Vasoneuronal monitoring with TCD may also be used to evaluate brain regulatory dysfunction during pathological state. Becker et al. (1996) reported these patients with abolished visual stimulation-BFV response due to vasospasm in subarachnoid hemorrhage were more susceptible to delayed ischemia than those with reserved response ability. Urban et al. (1995) reported that photoreactive flow changes of the PCA represented a noninvasive and reliable measure of functional impairment due to occipital infarction. Diehl et al. (1998) reported that the increase of BFV in PCA in normal controls was higher than that in patients with focal epilepsy. However, our study did not show that the photoreactivity was significantly depressed in hypertension or diabetes mellitus patients; perhaps because those patients in our study suffered from not so severe HT and DM and less lesions were caused by these complications than aging.

PET studies suggested a general right hemispheric dominance for visual processing (Corbetta et al., 1990), while we did not observe significant left-right difference in the PCA pair, which was different from what Panczel et al. (1999) reported. It might be due to the difference of detection methods.

References

Becker, V.U., Hansen, H.C., Brewitt, U. and Thie, A., 1996. Visually evoked cerebral blood flow velocity changes in different states of brain dysfunction. *Stroke*, **27**(3): 446 – 449.

Buedingen, H.J. and Staudacher, T., 1992. Evaluation of vertebrobasilar disease. *In*: Newell DW, Aaslid R, eds. Transcranial Doppler. Raven Press Publishers, New York.

Corbetta, M., Miezin, F.M. and Petersen, S.E., 1990. Attentional modulation of neural processing of shape, color, and velocity in humans. *Science*, **248**(4962): 1556 – 1559.

Diehl, B., Stodieck, S.R., Diehl, R.R. and Ringelstein, E.B., 1998. The photic driving EEG response and photoreactive cerebral blood flow in the posterior cerebral artery in controls and in patients with epilepsy. *Electroencephalogr clin Neurophysiol*, **107**(1): 8 – 12.

Liu, Y., Huang, Y. and Wang, B., 2001. Intracranial artery occlusive diseasesin patients with hypertension and diabetes mellitus. *Zhonghua Yi Xue Za Zhi*, **81**(22): 1387 – 1389(in Chinese with English abstract).

Newell, D.W., Aaslid, R., Lam, A., Mayberg, T.S. and Winn, H.R., 1994. Comparison of flow and velocity during dynamic autoregulation testing in humans. *Stroke*, **25**(4): 793 – 797.

Niehaus, L., Lehmann, R., Roricht, S. and Meyer, B. U., 2001. Age-related reduction in visually evoked cerebral blood flow responses. *Neurobiology of Aging*, **22**(1): 35 – 38.

Ostrow, P.T. and Miller, L.L., 1993. Pathology of small artery disease. *In*: Advances in Neurology (Vol. 62:): Cerebral Small Artery Disease, Raven Press Publishers, New York, p.93 – 123.

Panczel, G., Daffertshofer, M., Ries, S., Spiegel, D. and Hennerici, M., 1999. Age and stimulation dependency of visually evoked cerebral blood flow responses. *Stroke*, **30**(3): 619 – 623.

Sturzenegger, M., Newell, D.W. and Aaslid, R., 1996. Visually evoked blood flow response assessed by simultaneous two-channel transcranial Doppler using flow velocity averaging. *Stroke*, **27**(12): 2256 – 2261.

Terry, R.D., De Teresa, R. and Hansen, L.A., 1987. Neocortical cell counts in normal human adult aging. *Ann Neurol*, **21**(6): 530 – 539.

Urban, P.P., Allardt, A., Tettenborn, B., Hopf, H.C., Pfennigsdorf, S. and Lieb, W., 1995. Photoreactive flow changes in the posterior cerebral artery in control subjects and patients with occipital lobe infarction. *Stroke*, **26**(10): 1817 – 1819.