TRANSCRANIAL DOPPLER MONITORING OF MIDDLE CEREBRAL ARTERY DURING VERBAL STIMULATION IN APHASIC PATIENTS

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SUMMARY – Hemodynamic changes can be noninvasively real-time monitored in stroke patients by means of transcranial Doppler sonography (TCD). The aim of this pilot study was to assess hemodynamic changes in both middle cerebral arteries (MCA) in aphasic stroke patients by means of TCD during verbal stimulation. Eight aphasic patients with stroke in the territory of the left MCA were tested by modified Boston Diagnostic Aphasia Examination (BDAE) within 3 days of stroke onset. Both MCA were monitored simultaneously by means of TCD with 2 MHz probes. Basic MCA mean blood flow velocity (MBFV) values were assessed and monitored during verbal stimulation. Verbal stimulation was performed with 30 photos of objects for daily usage, arranged by function. The same test was performed in 16 right-handed healthy controls. In stroke patients, the mean MBFV were 56 cm/s in the left MCA and 56 cm/s in the right MCA. A mean 30% increase was observed in the left MCA and 22% in the right MCA. In healthy controls, a mean 21.7% increase was observed in the left MCA and 18% in the right MCA. A trend toward higher percentage of MBFV increase was observed in the left MCA during verbal stimulations in aphasic patients as compared to control subjects.

Key words: *Ultrasonography, Doppler, transcranial; Aphasia – diagnosis; Middle cerebral artery; Speech therapy; Stroke; Cerebrovascular circulation*

Introduction

Language is one of the most complex and sophisticated brain functions. It is hierarchically organized through the many interconnected primary and secondary language brain areas activated according to the difficulty of the task[1]. Primary brain areas are localized in the dominant, usually left hemisphere, while secondary brain areas carry the compensatory role and are situated in the non-dominant hemisphere in right-handed individuals. The normal integrative function is carried out by collateral and transcallosal inhibition of secondary language areas. This pattern changes when the specialized and lateralized speech areas are damaged[1].

Aphasia is one of the most common early cognitive deficits after stroke and is present in 20%-38% of patients. Efficient recovery depends on repeated participation of patients in an early, active rehabilitation process that acts on brain plasticity and leads to functional reorganization and favorable recovery[2].

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Stroke patients with aphasia have problems in comprehension, repetition and production of meaningful speech as a result of stroke in the middle cerebral artery (MCA) of the dominant hemisphere[3].

Connection between neuronal activation and increased regional cerebral blood flow due to the increased metabolism of the cerebral cortex activated by external stimuli[4] was used in many different activation studies[5-11]. Although of lower resolution compared with other neuroimaging techniques like functional MRI and PET, functional transcranial Doppler sonography (fTCD) has an advantage of excellent temporal resolution and possibilities of follow-up[4,12]. Functional TCD showed high correlation with functional MRI in the hemisphere dominance testing[6].

The aim of this pilot study was to monitor blood flow changes in MCA by use of TCD during receptive and expressive verbal stimulation in aphasic stroke patients in the territory of the left MCA within three days of stroke onset.

Patients and Methods

We included eight right-handed patients with left MCA stroke and different degrees of aphasia within three days of stroke onset. Patient history was obtained and neurological status was assessed and graded according to the NIH stroke scale[13]. Routine neurosonologic investigation was performed to exclude craniocervical occlusive artery disease[14].

Assessment of speech and language abilities was achieved with subtests of speech comprehension and verbal expression of Boston Diagnostic Aphasia Examination (BDAE) translated into Croatian language and adjusted to clinical conditions[3]. Preservation of receptive and expressive speech was examined in eight patients (seven male and one female) in acute phase of stroke within the first three days of the disease. The same procedure was performed in 16 right-handed healthy control subjects.

The BDAE was modified to each patient individually, according to the patient condition and abilities. In the majority of cases, writing section was excluded from the test. The testing and verbal stimulation was performed by a speech therapist through a sequence of 30 color photos of items of daily use, classified according to their functions. Assessment of speech and language abilities was achieved with subtests of speech comprehension and verbal expression of BDAE translated in Croatian and adjusted to clinical conditions.

BDAE subtests applied in speech comprehension were: body orientation, left-right orientation, comprehension of simple and complex orders, and comprehension of symbolic situations.

Verbal expression was examined with the following subtests: speech automatisms, repetition of words and sentences, and naming.

Body orientation was assessed by showing the part of the body that the examiner named; left-right orientation by showing the named part of the body on the left or on the right side; comprehension of simple and complex orders by aligning from simple to complex; and comprehension of symbolic situations by answering with 'yes' or 'no', depending on whether the sentence was true or false.

Speech automatisms were assessed by counting the days of the week, the months in the year, from 1 to 21 and alphabet, repetition of words and sentences by repeating after the speech therapist, also possible articulating mistakes were allowed, and naming by naming the photo of items of everyday usage.

The test interpretation was primarily directed to determination into 'classical' anatomical typologies of aphasia after careful analysis of severity rating scale and assessment of speech characteristics and different patterns of speech performances.

Both MCA were examined and monitored simultaneously in baseline, resting condition and during testing. Maximal blood flow velocities (BFV) were calculated for each group separately in baseline condition and during testing. The relative increase from baseline to activation was calculated using the following equation: (BFV activation – BFV baseline)/BFV baseline *100. The percentage of MBFV increase was compared between the groups and performed by Student's t-test. Data were expressed as mean and SD.

Results

Patient demographic data and risk factors are shown in Table 1. Most of the stroke patients had preserved receptive speech that was manifested as minor impairment of the sensory component of the speech in five and moderate impairment in three patients.

Table 1. Demographic data and vascular risk factors in healthy controls and stroke patients

Demographic data	Control group	Stroke patients
Gender	3 males 13 females	7 males 1 female
Mean age (yrs)	38±13	47±19
Vascular risk factors		
Hypertension	3 (18.7%)	3 (37.5%)
Diabetes mellitus	1 (6.3%)	1 (12.5%)
Hyperlipidemia	5 (31.2%)	2 (25 %)
Atrial fibrillation	0 (0%)	1 (12.5%)
Craniocervical artery disease	0 (0%)	1 (12.5%)
Already on aspirin	0 (0%)	1 (12.5%)
Already on warfarin	0 (0%)	0 (0 %)
Previous stroke	0 (0%)	2 (25%)
Previous myocardial infarction	0 (0%)	0 (0%)
Previous carotid intervention	0 (0%)	0 (0 %)
Smoking	0 (0%)	4 (50 %)
Alcoholism	0 (0%)	2 (25 %)

Verbal communication was possible with very simple language forms (monosyllabic and bisyllabic expressions). Five patients had moderate impairment of the motor component of speech and three had severe impairment.

Data analysis revealed three patients to have severe motor aphasia, three moderately severe motor aphasia and two moderate sensorimotor aphasia.

Control group of healthy subjects solved the tasks 100% correctly.

Baseline (resting) MBFV in both MCA of patients and controls were expressed as mean and STDEV, as shown in Table 2. Lower MBFV were observed in stroke patients compared to controls, but no asymmetry of circulation was noticed.

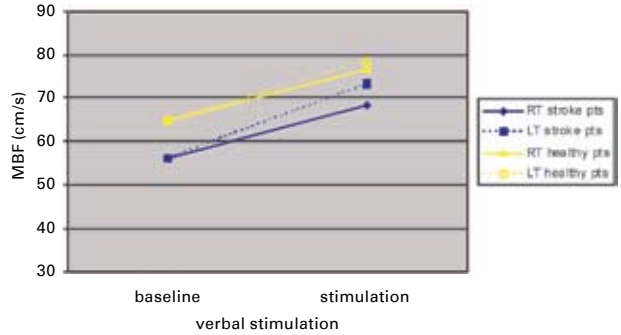

Fig. 1. Comparison of MBFV increase during verbal stimulation by Boston Diagnostic Aphasia Examination between stroke patients and healthy controls.

During verbal stimulation in stroke patients, a mean 30% increase was observed in the left MCA and 22% in the right MCA (Fig. 1). The difference between activation and baseline condition was statistically significant in the left MCA (P=0.004), and only a trend was observed for the right MCA (P=0.078), probably due to a low number of aphasic patients assessed. In healthy control group, a mean 21% increase was observed in the left MCA and 18% in the right MCA. The difference was statistically significant for both MCA (P<0.01). Intergroup comparison showed no statistically significant difference between the groups, although a trend toward higher percentage of MBFV increase was observed in the left MCA during verbal stimulations in aphasic patients compared to healthy controls.

Discussion

Our results showed lower baseline MBFV in both MCA in stroke patients compared to healthy controls. The MBFV increase in both MCA was noticed during verbal stimulation. Although there was no statistically

Table 2. Baseline mean blood flow velocity (MBFV) in both middle cerebral arteries (MCA) (mean ± STDEV)

	Mean blood flow velocity in the left MCA (cm/s)	Mean blood flow velocity in the right MCA (cm/s)
Healthy controls	64.6±10.6	64.6±7.8
Stroke patients	56.2±15	56±12

significant difference, a trend toward a higher increase in the left MCA in stroke patients was observed.

Based on fMRI and PET activation studies, Heiss described the following scheme: the processing of hearing words activates bilaterally the upper temporal gyrus[1]. Semantic attribution to a meaningful content is achieved in the left posterior temporal, temporoparietal, and anterior lower temporal cortical areas. For production of speech, the activity in the posterior upper temporal sulcus and in the left posterior lower temporal cortex is increased, and more further if words and sequences are repeated or read. The left posterior temporal cortex is activated by word fluency and also participates in lexical speech production. Planning of articulation activates the left anterior insula and frontal operculum. Phonologic word retrieval demands integration of the anterior insula/operculum and the posterior upper temporal sulcus or the left posterior temporal gyrus. Bilateral sensorimotor cortex is activated for the motor control of speech production and the hearing of the spoken response augments the activation in the upper temporal gyrus. Processing of written words activates the same areas, while reading activates only posterior fusiform and lingual gyrus, which also participates in picture naming[1].

The restoration of blood flow around the infarct, dynamic network remodeling, connecting and reconnecting of functionally disconnected brain areas[1] depend on the combination of the location and extent of the structural damage and demographic factors such as premorbid language representation, handedness, sex and education[15,16]. A variable amount of functional restoration of cognitive and motor abilities usually occurs spontaneously in the acute phase with reduction of edema and reperfusion of previously hypoxic tissue in the perilesional area. That perilesional tissue plays an important role in the chronic as well as in the acute stage after stroke onset, as the main site of neuroplasticity acting[1,2,16]. Neuroplasticity can be described as a neurological finding of synchronous firing of a group of neurons and repeated activation of their post-synaptic neuronal target leads to synaptic strengthening, whereas neurons that fire independently from others undergo synaptic weakening. This Hebbian mechanism suggests that massed practice and exploitation of residual neurological capacities can aid neurorehabilitation of patients with post-stroke aphasia[16]. In line with this, many randomized controlled trials of high-frequency regimen of speech-language treatment in the form of constraint-induced aphasia therapy took place recently, claiming for more efficacy and significant improvement in language performance compared to conventional treatment[16]. Improvements in verbal communication correlated with blood flow increases to specific regions of the left temporal lobe[5,6,16]. Metabolic disturbance in this area is related to outcome[17].

Our results with the increase in both and more pronounced in the left MCA indicated that the bare process of trying to solve a cognitive task represents a challenge for damaged brain and activates specific brain areas regardless of the task outcome[5]. It has been shown that when individuals read or hear action-related words, neuronal activity spreads from language to motor regions of the brain within tens of milliseconds[16]. The activation of primary and secondary language functionally interwoven areas[1] resulted in MBFV increase in both MCA, which is consistent with the latest fMRI study by Saur *et al*., who offered a new '3 phase model' of language reorganization, explaining the ongoing processes in the acute, 1 to 4 days after stroke onset, subacute (~2 weeks after stroke onset) and chronic (months after stroke onset) stage of post-stroke aphasia recovery[16].

In the acute stage, a weak activation of the left inferior frontal gyrus (IFG) was noticed[16]. In our study, the activation of the left IFG was also observed by recording increase of MBFV in the left MCA in stroke patients. The MCA is the main supply artery for the primary and secondary language areas. IFG determines the remaining language ability and has the key role in the acute stage of language recovery[1,16,18-23]. In the next subacute phase, there has been a strong compensatory 'up-regulation' of the whole language network with the activation peak in the right IFG (Broca homologue). Finally, in the chronic stage, months after stroke onset, activation was normalized through the re-shifting back to the left, dominant hemisphere again. This resulted in optimal and nearly full recovery[1]. These phases were not the target of our research.

Our pilot study results showed that fTCD could be a reliable assessment method of early phase changes of post stroke language reorganization, which showed activation of both hemispheres. Our study was limited

with a small number of aphasic patients, so further investigations with larger patient groups and longer follow up period are needed.

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Sažetak

PRAĆENJE SREDNJE MOŽDANE ARTERIJE TRANSKRANIJSKOM DOPLER SONOGRAFIJOM TIJEKOM STIMULACIJE GOVORA U AFATIČNIH BOLESNIKA

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Promjene moždane hemodinamike u srednjoj moždanoj arteriji (SMA) u bolesnika s moždanim udarom u irigacijskom području lijeve moždane arterije, te s posljedičnom afazijom mogu se neinvazivno pratiti pomoću funkcionalne transkranijske dopler sonografije (fTCD). Pritom se kao funkcionalni podražaj može koristiti stimulacija govora u obliku logopedskih vježbi. Da bismo procijenili aktivaciju SMA tijekom receptivne i ekspresivne verbalne stimulacije, ispitivanje afazije proveli smo modificiranim bostonskim dijagnostičkim testom u irigacijskom području lijeve SMA kod 8 bolesnika s moždanim udarom unutar 3 dana od nastanka ishemičnog moždanog udara. U obje smo SMA praćenje TCD-om proveli istodobno pomoću 2 ultrazvučne sonde frekvencija 2 MHz. Srednje brzine strujanja krvi (SBSK) u SMA procjenjivali smo i pratili prije i tijekom govorne stimulacije. Stimulaciju govorom proveo je logoped baterijom logopedskih vježbi, te zadacima imenovanja uz pomoć 30 fotografija predmeta svakodnevne uporabe grupiranih prema funkcijama. Isto ispitivanje je provedeno u 16 zdravih dešnjaka. Srednje brzine strujanja krvi bile su: 56 cm/s u lijevoj ACM, te 56 cm/s u desnoj SMA. U lijevoj je SMA tijekom stimulacije govora zabilježen srednji 30%-tni rast SBSK, a u desnoj SMA 22%-tni rast u odnosu na mirovanje. U zdravih kontrolnih osoba u lijevoj je SMA zabilježen porast SBSK od 21,7%, a u desnoj SMA od 18%. Uočen je trend rasta SBSK u lijevoj SMA tijekom stimulacije govora u afatičnih bolesnika u usporedbi sa zdravim kontrolnim osobama.

Ključne riječi: *Ultrasonografija, dopler, transkranijski; Afazija – dijagnostika; Arterija, cerebralna, medijalna; Govor, terapija; Moždani udar; Cerebrovaskularna cirkulacija*