CHANGES OF CEREBRAL HEMODYNAMICS DURING MUSIC PERCEPTION: A FUNCTIONAL TRANSCRANIAL DOPPLER STUDY

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SUMMARY – Studies have shown that the perception of musical information differs between musically educated and musically non-educated individuals. The aim of the study was to determine the time course and lateralization of changes in mean blood flow velocity (MBFV) in the middle cerebral artery (MCA) during auditory stimulation between musically educated and musically non-educated listeners as well as between sexes. Using transcranial Doppler (TCD), MBFV was assessed in 61 healthy right-handed subjects (18 musical educated and 43 musically non-educated). The ability to play an instrument was considered the minimum criterion for musical education. In both musically educated and non-educated groups, left MCA was activated earlier (p=0.013) and had higher MBFV (p=0.046). In the right MCA, habituation was obtained earlier in musically non-educated than in musically educated group (p=0.019). Female listeners had a shorter activation time of MBFV in the left MCA than in the right MCA (p=0.002), while in males no difference was found. Male listeners had a longer first activation time in the left MCA (p=0.003) and higher first maximal amplitude in the right MCA (p=0.038) than female listeners. Also, the time of activation of MBFV in the left MCA was longer in male than in female listeners (p=0.013). Study results suggest that music perception requires bilateral activation of cerebral hemispheres. The left hemisphere is firstly and predominantly activated regardless of musical education, whereas the right hemisphere is associative and is connected to the experience of music. Results from this study indicated sex differences in the perception. To confirm our preliminary results, further studies involving larger groups are needed.

Key words: *Auditory perception – physiology; Cerebrovascular circulation – physiology; Music; Ultrasonography – Doppler – transcranial*

Introduction

The correlation between music sounds and brain function is an exciting challenge in neuroscience. Music has well established psychological effects, including the induction and modification of cognitive states, moods and emotions. Brain activity, metabolism and blood flow have been found to be closely related, thus any changes in blood flow velocities (BFV) in large basal cerebral arteries are the reflection of changes in cognitive activity. An increase in cerebral BFV usually reflects an increase in cerebral metabolism due to activation in motor, sensory and cognitive tasks[1-3]. A relevant parameter for functional studies is the change in BFV that occurs when there is change from rest to the state of cognitive activity. For more than two decades transcranial Doppler

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(TCD) has been used in the assessment of cerebral hemodynamics, and in recent studies in the evaluation of mean BFV (MBFV) changes in relation to cognitive testing[4-9]. Apart from its noninvasiveness, the advantages of functional TCD (fTCD) are high temporal resolution and low cost as well as easy equipment transportation. The major drawback, however, is poor spatial resolution related to the large brain areas supplied by basal cerebral arteries.

Several studies have shown that the perception of musical information involves both cerebral hemispheres. Matteis *et al.* have described bilateral increase in cerebral BFV in non-musicians during the melody perception task and a significant increase in cerebral BFV in the right hemisphere during the melody recognition task[10]. Evers *et al.* have described the use of fTCD in the evaluation of cerebral hemodynamics when assessing music perception in musicians and non-musicians; they found a difference in hemisphere lateralization when musical stimuli were applied[11]. The aim of our study was to determine the time course and lateralization of MBFV in the middle cerebral artery (MCA) during auditory stimulation between male and female listeners as well as between musically educated and musically non-educated listeners.

Subjects and Methods

Subjects

We included 61 subjects (20 male and 41 female) in this study (Fig. 1). They were recruited from the hospital staff, students of the Department of Dental Medicine and patients with unspecific neurological symptoms from the University Department of Neurology, Sestre milosrdnice University Hospital in Zagreb. None of the subjects showed impairment of auditory acuity. The mean age of the subjects was 30.8±11.04 (range 17-73) years. All subjects were right-handed. Subjects were questioned about their musical experience. The ability to play an instrument was considered the minimum criterion for musical education. According to these criteria, 18 subjects (4 male and 14 female) had musical education. An informed consent was obtained from all subjects prior to their enrolment in the study.

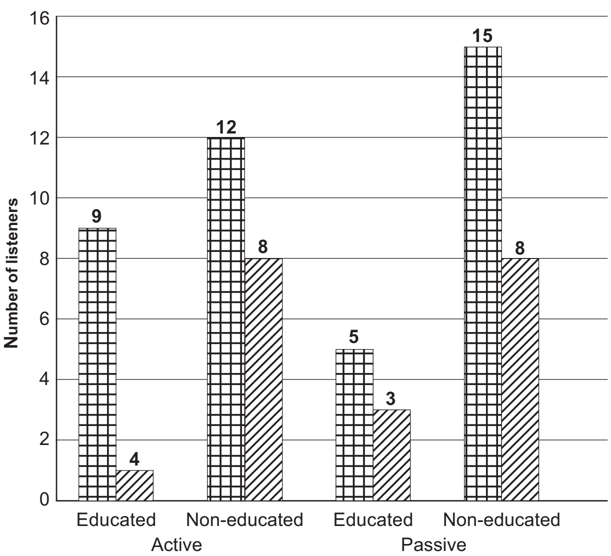

Fig. 1. Distribution of listeners.

Transcranial Doppler recording

Transcranial Doppler ultrasound was performed with a DWL MultiDop X4. One 2-MHz probe was attached to a headband and placed on the temporal bone window. The MCA was identified and insonated in all patients at a depth of 56 mm and only in one subject at a depth of 59 mm. The best signal with maximum velocity was obtained and recorded. Insonation and identification of the MCA were performed according to the previously established criteria[12].

Procedure

Subjects were examined supine in a dark room with a minimum of acoustic stimulation coming from the surroundings. After 10-min relaxation to allow blood pressure and heart rate to normalize, the subjects were instructed not to speak, move or chew during the examination. After they had laid down, the headband with the probe and the earphones were placed. The examination started with the left MCA, the probe was then switched to the right side. The subjects were first presented instrumental relaxing music (P.S. Voices by Vangelis). The musical piece consisted of harmonic sounds and no language or singing, and lasted for 2 min. The piece was unknown to the subjects prior to the examination and was presented as stereo with a commercially available portable CD player (First Austria) *via* earphones. The subjects could not hear any acoustic feedback of ultrasound signals. Half of the subjects were asked to relax throughout the presentation (passive group). The other half were asked to pay attention to the music that was presented. They were told that they would be asked about the presentation in detail (active group). Subjects were randomly allocated to subgroups. The active group consisted of 9 male and 21 female subjects, and passive group of 11 male and 20 female subjects. The baseline BFV registration without acoustic stimulation was performed for 2 min 20 s. It was followed by relaxing music. After the musical piece presentation, the MBFVs in the MCA were recorded for another 2 min and 20 s during which no sound was presented. For the first minute of each cycle (baseline, music, rest), the recording of MBFV was performed every 5 s, whereby relative BFV was calculated for these 5 s using the Fast Fourier transformation. After 1 min, the recording was performed every 20 s.

Data evaluation and statistics

MBFV was calculated for the first 2 min 20 s during the baseline measurement according to the formula:

$$MBFV = \Sigma\, BFV\,(t)/n,$$

where n is the number of cycles of 5 or 20 s. This value was defined as relative blood flow value (RBFV) = 0%. All values taken during the measurement were put in relation to that blood flow velocity using the formula:

$$RBFV = (BFV\,(t) - MBFV)/MBFV*100,$$

so that RBFV is expressed as change in percentage (Δ%).

Atypical curve was obtained and the indexes were measured (Fig. 2). Data were analyzed by non-parametric methods. Kolmogorov-Smirnoff test was applied to evaluate the amplitude and time of maximum RBFV and analyzed for gaussian distribution. Mann-Whitney test was used to reveal differences between the groups

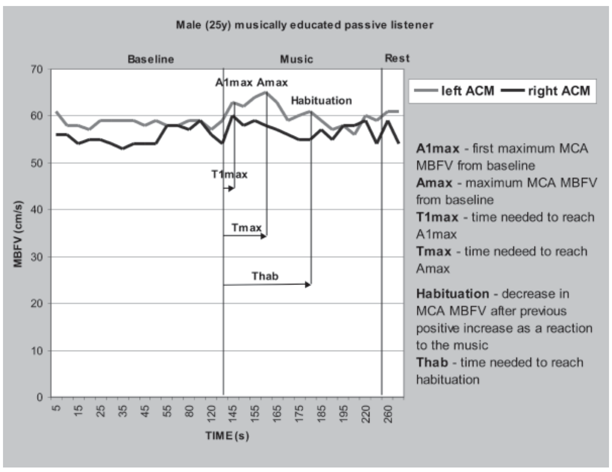

Fig. 2. Changes in middle cerebral artery (MCA) activation indexes in a male musically educated passive listener.

Table 1. Difference in middle cerebral artery (MCA) activation indexes between left and right brain hemisphere in all listeners

MCA	Δ Mean ± SD	p
A1maxLeft %	8.66±6.78	0.020*
A1maxRight %	5.98±6.99	
T1maxLeft (s)	8.69±5.32	0.113
T1maxRight (s)	7.29±3.60	
AmaxLeft %	11.55±5.60	0.046*
AmaxRight %	9.23±6.24	
TmaxLeft (s)	25.41±27.25	0.013*
TmaxRight (s)	38.20±33.91	
ThabLeft (s)	50.83±35.01	0.027
ThabRight (s)	45.68±29.69	

* statistically significant

and within the groups, to recognize differences between response to music and noise. The values of *p* were not corrected due to the descriptive character of the study. A p value of 0.05 or less was considered significant.

Results

In 61 right-handed individuals (41 female and 20 male) there were 18 musically educated and 43 musically non-educated listeners (Fig. 1). In all listeners the left MCA was activated earlier (p=0.013) and had higher MBFV (p=0.046). Also, habituation occurred earlier in the right MCA than in the left MCA (p=0.027). These results are shown in Table 1. Passive listeners, as shown in Table 2, reached first reaction (T1max) in the right

Table 2. Difference in middle cerebral artery (MCA) activation indexes between active and passive listeners

MCA	Active listeners	Passive listeners	p
A1maxLeft %	9.86	7.48	0.260
A1maxRight %	6.89	5.12	0.665
T1maxLeft (s)	8.50	8.87	0.943
T1maxRight (s)	8.17	6.45	0.025*
AmaxLeft %	12.87	10.27	0.106
AmaxRight %	9.65	8.83	0.708
TmaxLeft (s)	25.00	25.81	0.866
TmaxRight (s)	45.33	31.29	0.152
ThabLeft (s)	56.93	44.20	0.093
ThabRigh t(s)	48.44	43.40	0.930

* statistically significant

Table 3. Difference in middle cerebral artery (MCA) activation indexes between female and male listeners

MCA	Female listeners	Male listeners	p
A1maxLeft %	9.34	7.26	0.225
A1maxRight %	5.12	7.74	0.038*
T1maxLeft (s)	7.44	11.25	0.003*
T1maxRight (s)	7.32	7.25	0.963
AmaxLeft %	11.27	12.13	0.724
AmaxRight %	8.74	10.27	0.083
TmaxLeft (s)	21.95	32.50	0.013*
TmaxRight (s)	39.15	36.25	0.399
ThabLeft (s)	52.58	64.98	0.781
ThabRight (s)	48.05	39.73	0.559

* statistically significant

MCA faster than active listeners (p=0.025). Female listeners had shorter T1max and Tmax in the left MCA than male listeners (p=0.003, p=0.013), which is shown in Table 3. Also, as shown in Table 4, female listeners had higher A1max and Amax in the left than in the right hemisphere (p=0.003 and p=0.023). However, in male listeners right hemisphere was activated earlier (T1max right was shorter than T1max left) than the left hemisphere (p=0.026), as shown in Table 4. The difference between musically educated and musically non-educated listeners was found in habituation in the right MCA; musically educated listeners needed more time to reach habituation than the musically non-educated listeners (p=0.019). Musically educated passive listeners reached maximum MBFV in the right MCA and habituation in the left MCA faster than musically educated active listeners (p=0.032 and p=0.028). These results are presented in Tables 5 and 6.

Table 5. Difference in middle cerebral artery (MCA) activation indexes between musically educated and non-educated listeners

MCA	Musically educated listeners	Musically non educated listeners	p
A1maxLeft %	8.72	8.62	0.740
A1maxRight %	5.07	6.37	0.169
T1max Left (s)	7.78	9.07	0.365
T1max Right (s)	7.22	7.32	0.799
AmaxLeft %	7.86	11.42	0.580
AmaxRight %	9.25	9.23	0.527
TmaxLeft (s)	25.56	25.35	0.809
TmaxRight (s)	51.67	36.74	0.200
ThabLeft (s)	57.03	48.01	0.470
ThabRight (s)	58.87	38.34	0.019*

* statistically significant

Discussion

Our study showed that left MCA was activated firstly and predominantly in all listeners, which would indicate that music perception inevitably requires activation of the left cerebral hemisphere. This correlates with the PET study by Platel *et al.*, where they obtained the result pointing exclusively to the left hemispheric activation foci, particularly in the left cuneus/precuneus, in a task requiring detection of changes in pitch within 5- to 10-note melodies[13]. Several studies suggest a right hemisphere dominance for non-musicians and possible left hemispheric dominance for musicians, in the perception

Table 4. Difference in middle cerebral artery activation (MCA) indexes between left and right brain hemisphere in male and female listeners

MCA	Female listeners	p	Male listeners	p
A1maxLeft %	9.34	0.003*	7.26	0.765
A1maxRight %	5.12		7.74	
T1maxLeft (s)	7.44	0.932	11.25	0.026*
T1maxRight (s)	7.32		7.25	
AmaxLeft %	11.27	0.023*	12.13	0.794
AmaxRight %	8.74		10.27	
TmaxLeft (s)	21.95	0.002*	32.50	0.911
TmaxRight (s)	39.15		36.25	
ThabLeft (s)	52.58	0.581	46.98	0.139
ThabRight (s)	48.05		39.73	

* statistically significant

Table 6. Difference in middle cerebral artery (MCA) activation indexes between musically educated active and passive listeners

MCA	Musically educated listeners		p
	Active	Passive	
A1maxLeft %	9.58	7.66	0.374
A1maxRight %	4.55	5.72	0.859
T1maxLeft (s)	9.00	6.25	0.219
T1maxRight (s)	7.50	6.86	0.438
AmaxLeft %	13.08	10.32	0.534
AmaxRight %	9.78	8.59	0.286
TmaxLeft (s)	34.00	15.00	0.159
TmaxRight (s)	53.00	27.50	0.032*
ThabLeft (s)	77.59	33.55	0.028*
ThabRight (s)	66.91	49.68	0.298

* statistically significant

of music assessed by fTCD[10,14]. Non-musicians show a delayed, marked right hemisphere lateralization during harmony perception. Musicians, however, use an attentive mode of listening that is lateralized to the left hemisphere[11]. However, Artal *et al.* could not confirm the findings of Evers *et al.* related to melody perception, as they did not observe right hemisphere lateralization in melody perception of instrumental music[11,15]. Instead, they observed a bilateral increase of MBFV in both hemispheres.[15] Also, Marinoni *et al.* report that lateralization after musical stimuli depends not only on the level of musical competence of the subjects but also on the musical features of different musical tasks[16].

The results of our study showed that the difference between musically educated and musically non-educated listeners was in habituation in the right MCA, where musically educated listeners needed more time to reach habituation than musically non-educated listeners ($p=0.019$). This is consistent with the report by Matteis *et al.*, showing that, unlike perception task, recognition task was lateralized exclusively to the right side[10]. Lateralization differences between an active mode-recognition and passive mode of listening to musical stimuli were also found by Matteis *et al.* on fTCD in non-musicians. They describe a bilateral increase of cerebral MBFV in non-musicians during a melody perception task and a significant increase of MBFV in the right hemisphere during a melody recognition task[10]. In our study, passive listeners activated the right cerebral hemisphere a little bit faster than active listeners, suggesting that passive listening also requires activation of the right cerebral hemisphere. However, Vollmer-Haase *et al.* suggest that passive listening to the same music, when subjects do not expect any task to be performed, was associated with a symmetric BFV increase, pointing to a balanced activation of the left and right hemisphere[14].

The data acquired in our study showed that female listeners activated the left cerebral hemisphere faster than male listeners while listening to music, with a statistically much higher MBFV in the left than in the right MCA. However, male listeners activated the right cerebral hemisphere faster than the left one. This could possibly suggest that they listened to the music more passively than actively, unlike female listeners. On the contrary, Evers *et al.* obtained a significantly higher MBFV in the right hemisphere of female subjects when compared with male subjects. They also suggest that female non-musicians had the highest degree of lateralization to the right hemisphere during music perception regardless of the type of music stimuli[11].

The fact is that listening to music is influenced by many factors such as interest, education, learning, culture and personality, and we should be aware that not all possible influences could be completely eliminated[10]. In regard to other studies, our data showed that lateralization after musical stimuli depended not only on the level of musical competence but also on musical experience. The differences could probably be related to a different approach to music listening as well as emotional approach to music. Another influencing factor may be the sequence of MCA recording. Sequential unilateral insonation may be a confounding factor due to the effect of habituation and the potential loss of motivation. It has been reported that MBFV values in the MCA which were measured first tended to be higher than those measured from the subsequently examined side[5]. To avoid or reduce this potential confounding factor, we randomized all right and left MCA examinations. Therefore, simultaneous insonation technique would be the method of choice to analyze MBFV in future studies.

Music perception is a complex cognitive process involving different brain structures and is dependent on the type of music, musical experience, mode of listening, and sex. Our study suggests that music perception requires bilateral activation of cerebral hemispheres. The left hemisphere is firstly and predominately activated regardless of musical education or sex, whereas the right hemisphere is associative and is connected to the experience of music. Female listeners activate the left cerebral hemisphere faster with a higher MBFV.

However, male listeners as passive listeners activate the right cerebral hemisphere faster than the left one. Although some of our results are not consistent with previous findings, they still prove that fTCD is an appropriate method to evaluate cerebral lateralization of activation during complex cognitive processing; it is superior to other methods in detecting short duration changes of cerebral activation. To confirm our preliminary results, further studies involving larger groups are needed.

References

1. AASLID R. Visually evoked dynamic blood flow response of the human cerebral circulation. Stroke 1987;18:771-5.
2. DEMARIN V *et al.* Moždani krvotok – klinički pristup. Zagreb: Naprijed, 1994.
3. VINGERHOETS G, STROOBANT N. Between-task habituation in functional transcranial Doppler ultrasonography. Neuroreport 1999;10:3185-9.
4. DEMARIN V, RUNDEK T. Acetazolamide test combined with transcranial Doppler (TCD): a simple noninvasive test for the assessment of cerebral vasoreactivity in humans. Period Biol 1992;94:193-200.
5. DROSTE DW, HARDERS AG, RASTOGI E. A transcranial Doppler study of blood flow velocity in the middle cerebral arteries performed at rest and during mental activities. Stroke 1989; 20:1005-11.
6. MARTINIĆ-POPOVIĆ I. Transcranial Doppler measurement of middle cerebral artery blood flow velocity changes during mental activities. Acta Clin Croat 1998;37:81-6.
7. KNECHT S, DRAGER B, DEPPE M, BOBE L, LOHMANN H, FLOEL A. Handedness and hemispheric language dominance in healthy humans. Brain 2000;123:2512-8.
8. TRKANJEC Z, DEMARIN V. Transcranial Doppler sonography during visual stimulation. Acta Clin Croat 1999;38:285-9.
9. ZAVOREO I, DEMARIN V. Breath holding index in the evaluation of cerebral vasoreactivity. Act Clin Croat 2004;43:15-9.
10. MATTEIS M, SILVESTRINI M, TROISI E, CUPINI LM, CALTAGIRONE C. Transcranial Doppler assessment of cerebral flow velocity during perception and recognition of melodies. J Neurol Sci 1997;149:57-61.
11. EVERS S, DANNERT J, RODDING D, ROTTER G, RINGELSTEIN EB. The cerebral haemodynamics of music perception: a transcranial Doppler sonography study. Brain 1999;122:78-85.
12. ALEXANDROV AV, DEMARIN V. Insonation techniques and diagnostic criteria for transcranial Doppler sonography. Acta Clin Croat 1999;38:97-108.
13. PLATEL H, PRICE C, BARON JC, WISE R, LAMBERT J, FRACKOWIAK RS *et al*. The structural components of music perception: a functional anatomical study. Brain 1997;120:229-43.
14. VOLLMER-HAASE J, FINKE K, HARTJE E, BULLA-HELLWIG M. Hemispheric dominance in the processing of J.S. Bach fugues: a transcranial Doppler sonography (TCD) study with musicians. Neuropsychologia 1998;36:857-67.
15. ARTAL FJC, CABRERA CV, HORTAN TA. Lateralization of cerebral blood flow velocity changes during auditory stimulation: a functional transcranial Doppler study. Appl Neuropsychol 2004;11:167-74.
16. MARINONI M, GRASSI E, LATORRACA S, CARUSO A, SORBI S. Music and cerebral hemodynamics. J Clin Neurosci 2000;7:424-8

Sažetak

PROMJENE MOŽDANE HEMODINAMIKE ZA VRIJEME SLUŠANJA GLAZBE: FUNKCIONALNA TRANSKRANIJSKA DOPPLER STUDIJA

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Studije su pokazale da se percepcija glazbe razlikuje između glazbeno obrazovanih i glazbeno neobrazovanih osoba. Svrha studije je bila utvrditi vremenski slijed i lateralizaciju promjena u srednjoj vrijednosti strujanja krvi (SBSK) u arteriji cerebri mediji (ACM) kako između glazbeno obrazovanih i glazbeno neobrazovanih ispitanika, tako i između spolova za vrijeme slušne stimulacije. Kod 61 zdravog dešnjaka (18 glazbeno obrazovanih, 43 glazbeno neobrazovanih) pratila se SBSK pomoću transkranijskog Dopplera (TCD). Sposobnost sviranja instrumenta je bio minimalni kriterij glazbene izobrazbe. U objema skupinama glazbeno obrazovanih i glazbeno neobrazovanih ispitanika lijeva ACM se aktivirala ranije (p=0,013), a SBSK je bila viša u lijevoj ACM (p=0,046). Nije bilo razlike u habituaciji u lijevoj ACM između ovih dviju skupina. U desnoj ACM je kod glazbeno neobrazovanih došlo ranije do habituacije nego kod glazbeno obrazovanih (p=0,019). Kod žena je zabilježena brža aktivacija SBSK u lijevoj ACM nego u desnoj (p=0,002), dok kod muškaraca nije nađena razlika. Muški ispitanici su imali duže razdoblje prve aktivacije u lijevoj ACM (p=0,003) i višu amplitudu prve reakcije u desnoj ACM (p=0,038) nego ispitanice. Vrijeme reakcije SBSK u lijevoj ACM je također bilo duže u muških nego u ženskih ispitanika (p=0,013). Naši rezultati upućuju na to da je za percepciju glazbe potrebna aktivacija obiju hemisfera. Pretežito i prvenstveno se aktivira lijeva moždana hemisfera bez obzira na glazbenu izobrazbu, dok desna moždana hemisfera ima više asocijativnu funkciju i povezana je s glazbenim iskustvom. Kod muškaraca i žena su uz pomoć funkcionalnog TCD također zabilježene razlike u precepciji. Za potvrdu ovih preliminarnih rezultata našega istraživanja potrebno je proširiti istraživanje na veći broj ispitanika.

Ključne riječi: *Slušna percepcija – fiziologija; Cerebrovaskularna cirkulacija – fiziologija; Glazba; Ultrazvuk – Dopplerov – transkranijski*