



SOME ASPECTS OF BALANCE DISORDER IN PATIENTS WITH MULTIPLE SCLEROSIS

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ABSTRACT

The aim of this study was to analyze: frequency of balance disorder (vertigo and disequilibrium), frequency of abnormalities in auditory evoked potentials (AEP) and magnetic resonance imaging (MRI) changes of the brain in multiple sclerosis (MS) patients with balance disorder; relation of patient's disability status to balance disorder and relation of the changes in MRI of the brainstem to AEP abnormalities. It was analyzed 60 patients with relapsing-remitting form of MS. Two groups of patients were made consecutively under Expanded Disability Status Scale score (EDSS): A (EDSS $\leq 4,5$) and B (EDSS $\geq 5,0$). The study was retrospective-prospective. After the neurological exam AEP and MRI of the brain have been done. Balance disorder has been verified as initial symptom in 29 (48,4%) and out of them disequilibrium experienced 24 (83,4%) patients. During the relapses balance disorder experienced 48 (80%) patients and in 37 (77,1%) it was disequilibrium. Among them 33 (68,7%) were with lower EDSS ($\leq 4,5$) and 15 (31,3%) with higher EDSS score (≥ 5). There is no correlation between disability status and vertigo which means that vertigo is not more frequent in more disabled patients and vice-versa. The AEP were pathological in 57 (95%) patients. Of all 29 patients with vertigo AEP were pathological in 28 (96,5%) while in 31 patients without vertigo pathological AEP were in 29 (93,5%) but it is not statistical significant. The most frequent characteristic of AEP changes were prolonged inter-peak latency III-V waves (48 patients or 80%). The plaque in brainstem visualized by MRI was found in 41 (71,8%) of patients (38 or 92,6% of them had pathological AEP and in three patients AEP were normal). In group of patients with pathological AEP, 38 (66,6%) of them had plaque in brainstem. In other three patients with normal AEP it was visualized plaque in brainstem. In the group of 29 patients with balance disorder, 20 (68,9%) had plaque in brainstem as well as 21 (67,7%) out of 31 patients without balance disorder had plaque in the brainstem. This difference is not statistical significant. It is concluded that the vertigo (including disequilibrium) is relatively often (48,4%) initial symptom of MS. Vertigo is not more frequent in patients with higher EDSS score and vice-versa. Pathological AEP are frequent neurophysiologic finding in both (95%) patients with (96,5%) and without (93,5%) vertigo. The most often pathological characteristic of AEP are prolonged interpeak latency of III-V waves (78,5%), as well as abnormalities of V and than IV wave. MS plaques in brainstem visualized by MRI technique are frequent in both groups of patients with and without pathological finding of the AEP.

KEY WORDS: multiple sclerosis, balance disorder, auditory evoked potentials, MRI, EDSS

INTRODUCTION

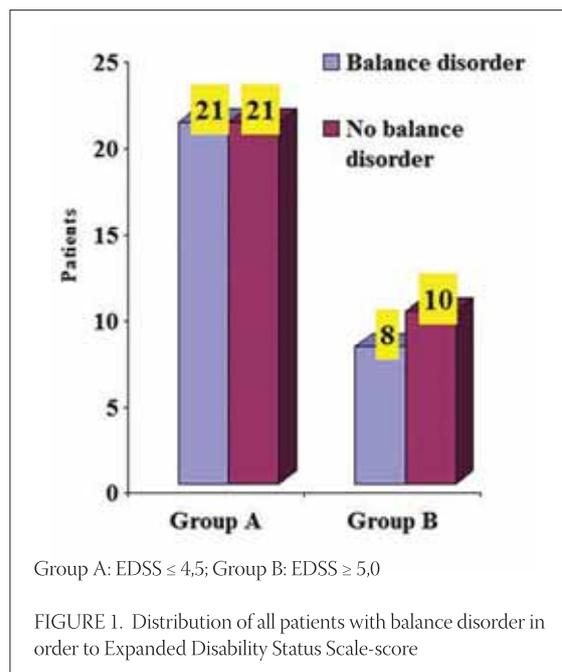
Multiple sclerosis (MS) is chronic, inflammatory immune disease of central nervous system characterized by destruction of myelin sheaths, axonal damage and oligodendrocytes degeneration in various parts of the brain and medulla. Among the most common symptoms (optic neuritis, ophthalmoplegia, paresis and paralysis, sensory disturbances, ataxia, bladder and bowel disorder), balance disorder (disequilibrium and vertigo) could be the symptom as well. Vertigo is not a disease. The term vertigo refers to the sensation of spinning or whirling that occurs as a result of a disturbance in balance (equilibrium). The sensation of movement is called subjective vertigo and the perception of movement in surrounding objects is called objective vertigo. Some other feelings of dizziness, lightheadedness, faintness, and unsteadiness are named: disequilibrium i.e. pseudovertigo (1). Therefore, for complete evaluation, diagnose and treatment it is very important to insist and realize what exactly term vertigo does mean for patients and how do they describe it.

PATIENTS AND METHODS

In retrospective – prospective study it was analyzed 60 patients with relapsing – remitting multiple sclerosis (RRMS). It was evaluated: the frequency of vertigo as initial symptom and during the course of disease; auditory evoked potentials (AEP); magnetic resonance imaging (MRI) of the brain; disability status and balance disorder. Disability status was defined by Expanded Disability Status Scale-score (EDSS) (2). Consecutively, the patients have been divided in two groups: A (EDSS \leq 4,5); B (EDSS \geq 5,0). MRI of the brain were focused on plaques in brainstem, cerebellum and both in brainstem/cerebellum. AEP exam have been done by standard protocol in Evoked potential laboratory, Department of neurology Tuzla. In the analysis, standard statistical tests have been used: mean value and standard deviation, T test, X²-test. Differences $p < 0,05$ were considered significant.

RESULTS

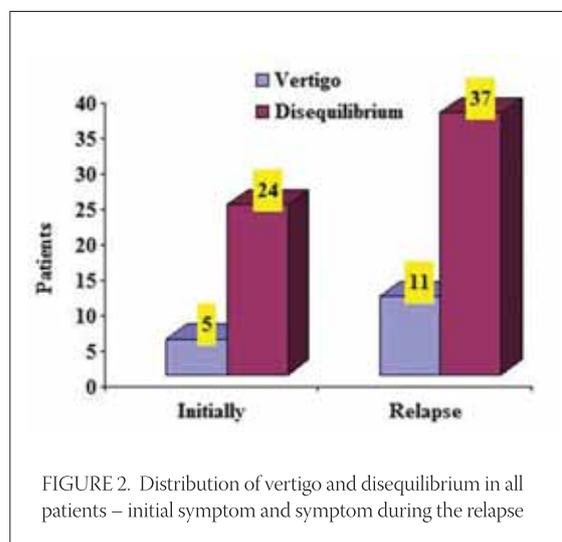
Of all patients it was 41 (68,3%) female and 19 (31,7%) male. Average age of all patients was $37,2 \pm 8,54$ (male: $36,7 \pm 8,55$, female: $37,6 \pm 8,06$). In group A (EDSS \leq 4,5) were 42 patients (70%) and in group B (EDSS \geq 5,0) 18 (30%). Average EDSS in group A was $3,45 \pm 0,82$, in group B was $6,1 \pm 1,1$. Balance disorder experienced 29 (48,4%) patients. Out of this 21 (50%) patients were in group

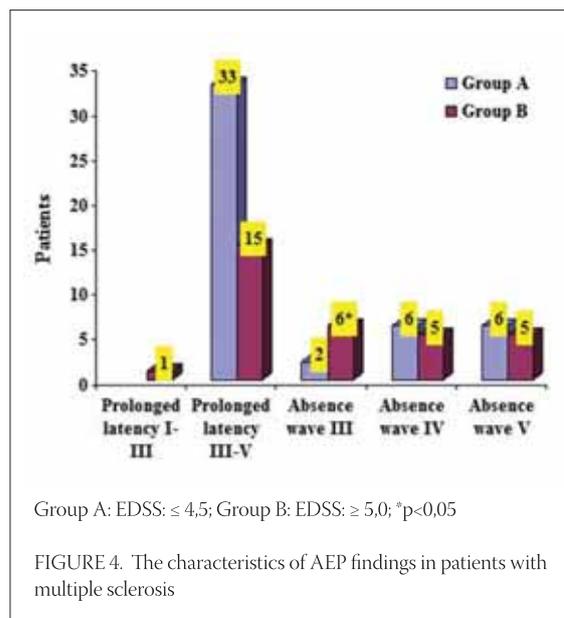
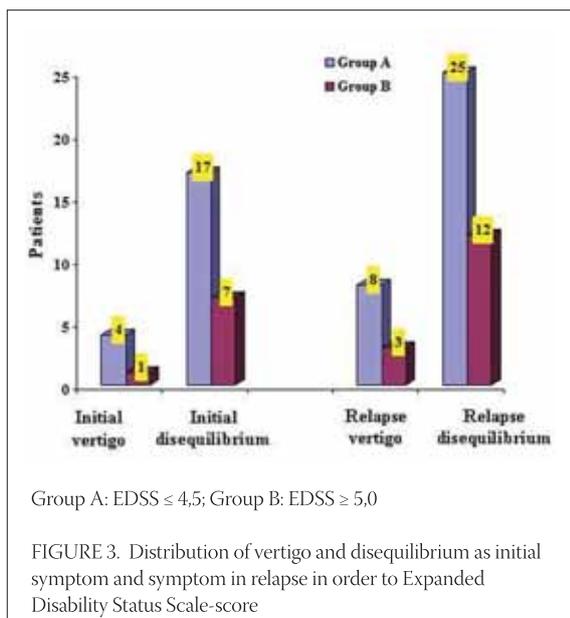


A (EDSS \leq 4,5), and 8 (44,5%) in group B (EDSS \geq 5,0) ($p > 0,05$) (Figure 1).

For all patients disequilibrium as initial and symptom during the relapse, was more frequent in both groups, but it was not significant neither as initial symptom (vertigo: $p = 0,9$; disequilibrium $p = 0,6$) nor during the relapse (vertigo: $p = 0,8$; disequilibrium: $p = 0,6$) in both separately analyzed groups (Figure 2).

Initially, vertigo was in 5 (8,3%) patients: group A 4 (9,5%), group B 1 (5,8%). Otherwise, disequilibrium as initial symptom was in 24 (40%) patients; group A 17 (40%), group B 7 (38,1%). During the relapse, out of 48 (80%) patients, vertigo had 11 (18,3%) patients: group A 8 (19%), group B 3 (16,7%); disequilibrium experienced 37 (61,7%) patients: group A 25 (59,5%), group B 12 (66,7%). In group A, as initial symptom, disequilibrium was more





frequent (17 or 42,4%) in order to vertigo (4 or 9,5%). It was the same in group B (disequilibrium 7 or 38%; vertigo 1 or 5,5%), but there was no statistical significance (Figure 3). AEPs was pathological in 57 (95%) patients: group A 39 (92,7%), group B 18 (100%). Twenty-eight patients (96,5%) out of 29 with balance disorder from both groups had pathological AEP; otherwise, 29 (93,5%) patients out of 31 with no balance disorder had same AEP finding. In group A (patients with no balance disorder) abnormal AEP was in 19 (90,5%) out of 21. In the same group (patients with balance disorder) it was abnormal in 20 patients (95,2%) (p=0,5). In group B 8 (44,4%) patients with balance disorder had pathological AEPs, as well as 10 (55,6%) patients with no balance disorder. No statistical significance (p=0,6) (Table 1). The characteristics of AEP findings are shown in Figure 4. The most fre-

quent AEP finding in group A was prolonged interpeak latency III-V waves, which was found in 33 (78,5%) patients. Same result was in group B as well (15 patients or 83,3%). There was no statistical significance (p=0,36). Absence of the wave III was registered in 2 (4,7%) patients of group A and 6 (33,3%) in group B what was significant (p=0,002). It was verified no significance in absence of waves IV and V in both groups. MRI of the brain and cervical spine has been done to all patients. In Figure 5 it was presented distribution of the plaques primarily being focused on plaques just in brainstem, than plaques just in cerebellum and both in brainstem and cerebellum. Patients with the plaques both in cerebellum and brainstem were separated group and were not included in group of patients with plaques just in cerebellum or just in brainstem. Most plaques have seen in brainstem.

AEP	Group A				Group B			
	Normal		Abnormal		Normal		Abnormal	
	N	%	N	%	N	%	N	%
Balance disorder	1	4,8	20	95,2	-	-	8	100,0
No balance disorder	2	9,5	19	90,5	-	-	10	100,0
Total	3	7,2	39	92,8	-	-	18	100,0

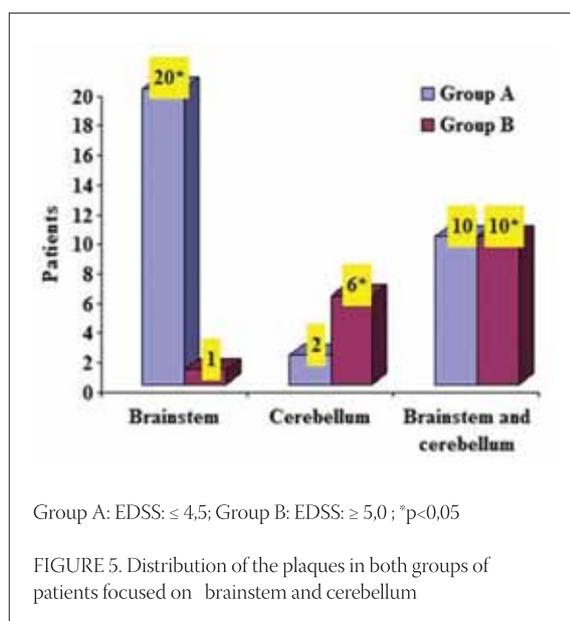
AEP – auditory evoked potentials
Group A: EDSS: ≤ 4,5; Group B: EDSS: ≥ 5,0

TABLE 1. Auditory evoked potentials in multiple sclerosis patients with and without balance disorder in both groups

Localization	Group A				Group B			
	BD		NBD		BD		NBD	
	N	%	N	%	N	%	N	%
BS	7	21,8	13	40,7	1	5,8	-	-
C	-	-	2	6,2	2	11,7	4	23,6
BSC	8*	25,0	2	6,2	4	23,5	6	35,4
Total	15	46,8	17	53,2	7	41,1	10	58,9

BS – Brainstem, C – Cerebellum, BSC – Brainstem and cerebellum, BD – balance disorder, NBD – no balance disorder; *p<0,05

TABLE 2. Distribution of patients in both groups in order to balance disorder and localization of the plaques



Found plaques in brainstem were in 20 (47,6%) patients of group A and 1 (5,5%) of group B what is significant for group A ($p=0,0013$). Plaque in cerebellum (group A) was in 2 patients (4,7%); in group B in 6 (33,3%) what is significant for group B ($p=0,0015$) as well as plaques in cerebellum/brainstem ($p=0,009$): 10 (55,5%) patients. Plaque in brainstem and/or cerebellum, of all analyzed patients ($N=60$), was in 49 (81,6%): 32 (65,3%) in group A 32 (65,3%) and 17 (34,7%) in group B. In group A, 15 (46,8%) out of 32 patients had balance disorder and in group B, 7 (41,1%) out of 17 patients experienced the same. In table 2 are presented patients in both groups A and B with balance disorder associated with plaques just in brainstem, cerebellum as well as in both brainstem/cerebellum. Plaque in group A had more patients with no balance disorder (13 or 40,7%), what is not significant. Otherwise, it is significant in patients' group A with balance disorder and registered plaques both in brainstem and cerebellum in order to patients in group B (25% or 8 patients) ($p<0,05$). In group B most frequent localization of the plaque both in brainstem and cerebellum is in patients with no balance disorder (6 or 35,4%), but it is not significant. Also, it was not significant verified plaques in brainstem or cerebellum with balance disorder in patients' group B. In group A pathological AEP finding

had 27 patients what is 90% of all patients in group A with verified plaques in brainstem. In the same group 14 (46,6%) patients experienced balance disorder and had plaques in brainstem as well as pathological AEP. Normal AEP finding had one patient and he had plaque in brainstem as well. Pathological AEP finding in patients with no balance disorder and plaques in brainstem had 13 (43,3%) patients. In group B pathological AEP finding had all patients with plaques in brainstem (11 patients). With balance disorder were 5 (45,4%) patients (Table 3). In group of all 60 patients, 57 (95%) had pathological AEPs finding, and 41 (68%) had plaque in brainstem.

DISCUSSION

Vertigo as diagnostic problem is big challenge for many doctors of various specialties. Experiences in balance disorders research pointed out that most usual was peripheral cause, so in such diseases like MS is, it is rare as the only sign of disease. Vertigo could be initial symptom of disease in approximately 5% of cases (3). Paty (4) also found that vertigo could be initial symptom and could be indicator for benign long term course of MS. Otherwise, Frohman et al. (5), published study that "real" vertigo could be verified in 20% of MS patients. According to this study, demyelination in vestibular nuclei generates vertigo in patients. During the course of disease majority of MS patients could have disequilibrium. Episodes of central (as opposed to peripheral) vertigo are not uncommon. The nystagmus accompanying central vertigo has a rapid onset, does not fatigue easily, and changes with direction of gaze. Vertigo usually is accompanied by other complaints that can be directly attributed to brainstem or cerebellar pathway involvement (eg., diplopia, dysarthria) (6). Alpini et al. (7) published that balance disorder due to changes in brainstem and cerebellum is common in MS patients although this disorder could be of peripheral origin, like positional paroxysmal benign vertigo. Also, in study done by Paty (4), more than 50% of MS patients have intermittent episodes of vertigo. Many years before definitive diagnose of MS, vertigo could be isolated symptom

Balance disorder	Group A				Group B			
	Plaque in brainstem (n=30)				Plaque in brainstem (n=11)			
	pathological AEPs		normal AEPs		pathological AEPs		normal AEPs	
	N	%	N	%	N	%	N	%
with	14	46,7	1	3,3	5	45,4	-	-
without	13	43,3	2	6,7	6	54,6	-	-
Total	27	90,0	3	10,0	11	100,0	-	-

AEPs: auditory evoked potentials

TABLE 3. Distribution of auditory evoked potentials findings and plaques in brainstem in both groups A and B in order to balance disorder

and this must not be avoided in patient's follow ups (8). Among 1153 MS patients, 25 could be clinically evaluated during one vertigo episode; 13 (52%) experienced benign paroxysmal vertigo, and 8 (32%) had relapse with lesions in brainstem (9). Rae-Grant et al. (10) in their study found that 5% of MS patients during relapses experienced disequilibrium. Results of this study are somewhat different than results in published analyses. Similar as in collected studies, vertigo as one kind of balance disorder and as initial symptom was not so often, although more frequent than results in these studies. In the current study, more often is disequilibrium during the relapse. Differences could be explained with possible new plaques during the relapse, primarily located in brainstem than in cerebellum as well. Also, it should not be avoided personal patients and their family's attitude to disease. In diagnostic protocols AEP finding is one of neurophysiologic methods and could be positive in 25-50% of patients even with no symptoms and could lead to diagnose of MS (11). With various approaches there have been done many AEP studies. Kitanoski et al. (12) analyzed AEP findings in 109 MS patients and 62% were abnormal. Otherwise, Bruner et al. (13) did not have any abnormal AEP finding although 15 patients out of 135 who had clear eighth cranial nerve affection. Robinson and Rudge (14) evaluated 227 patients with various

different neurological diseases (MS, Arnold – Chiari malformation, intracranial tumors, vascular lesions in brainstem) and found significant correlation between brainstem dysfunction and pathological AEP in MS patients. Japaridze et al. (15) in their analysis had abnormal AEP in 80% of patients with MS. According to one evaluation done in our EP lab., this percentage was 82,8% (16). In current study there are more pathological AEP than in collected articles. The explanation for this could be the fact that majority of patients had balance disorder during the relapses. Concerning the characteristics of pathological AEP, most frequent is prolonged inter-peak latency I-V waves as well as abnormalities and/or absence of the wave V. In group with more disabled patients most frequent is absence of the wave III. Analyzes Robinson (14) and Dabić-Jeftić (17) pointed out abnormalities in wave V but they did not do evaluation of AEP in order to disability status. With MRI done, definitive diagnose of MS become very reliable. Plaques could be visualized in any part of the brain and spinal cord, but most frequent in ventricular regions, supracalosal, and in 71% could be seen in brainstem (18). Grenmann et al. (19) concluded that balance disorder could be related to MRI finding. They have been focused on plaques verification in brainstem and cerebellum. The results we had in our study correlate with previously published results.

CONCLUSION

Vertigo was found in 48,4% of MS patients. As initial symptom disequilibrium is statistically more frequent (40%) than vertigo (8,3%). Changes in finding of auditory evoked potentials was found in 95% of MS patients, more in patients with vertigo (96,5%) than with no vertigo (93,5%). Concerning magnetic resonance imaging of the brain, demyelination (plaques) in brainstem was seen in 68% of MS patients, 30% in cerebellum, and both in cerebellum and brainstem in 33,3%. Vertigo experiences MS patients with various disability statuses. Patients with higher score do not have more prominent vertigo in order to patients with lower score of disability. In patients with higher score of disability, changes are in all region of brainstem what are different to patients with lower score. Mostly, changes in these patients are in upper parts of brainstem. There is no statistical significance in frequency of abnormal AEP and plaques in brainstem of MS patients. MS patients could have visualized by MRI of the brain plaque in brainstem as well as normal AEP and vice-versa.

REFERENCES

- (1) Adams D.R., Victor M. Dizziness and vertigo. In: Adams R.D., Victor M. (eds). Principles of neurology. McGraw-Hill, Inc. New York. 1993: 256-257.
- (2) Kurtzke J. Rating neurologic impairment in multiple sclerosis: An expanded disability status scale (EDSS). *Neurology*. 1983;33:1444-1452.
- (3) Maril K. 2001. Central vertigo. <http://www.emedicine.com/emerg/topic858.htm> [accessed 10.10.2007.]
- (4) Paty D., Ebers G. Vertigo. In: Reinhardt R.W., Wissler B.M. (eds). Multiple sclerosis. F.A. Davis Company, Philadelphia. 1997:164-165.
- (5) Frohman E.M., Zhang H., Dewey R.B., Hawker K.S., Racke M.K., Frohman T.C. Vertigo in MS: utility of positional and particle repositioning maneuvers. *Neurology*. 2000;55:1566-1569.
- (6) Dangond F. Multiple sclerosis. 2006. <http://www.emedicine.com/NEURO/topic228.htm> [accessed 01.11.2007.]
- (7) Alpini D., Caputo D., Pugnetti L., Giuliano D.A., Cesarini A. *Neurol. Sci.* 2001;22(8): 84-87.
- (8) Pagès M., Ondze B., Blard J.M. Benign multiple sclerosis with childhood onset. *Rev Neurol (Paris)*. 1994;150(2):155-156.
- (9) Frohman E.M., Kramer P.D., Dewey R.B., Kramer L., Frohman T.C. Benign paroxysmal positioning vertigo in multiple sclerosis: diagnosis, pathophysiology and therapeutic techniques. *Mult. Scler.* 2003;9(3):250-255.
- (10) Rae-Grant A.D., Eckert N.J., Bartz S., Reed J.F. Sensory symptoms of multiple sclerosis: a hidden reservoir of morbidity. *Mult. Scler.* 1999;5(3):179-183.
- (11) Chiappa K.H., Gladstone K.J., Young R.R. Brainstem auditory evoked responses: Studies of waveform variation among 50 normal human subjects. *Arch. Neurol.* 1979;36: 81-87.
- (12) Kitanoski B., Haralampiev K., Jovicic A., Ivanovic A., Ristic B. Auditory evoked brain stem potentials in the diagnosis of disseminated demyelinating processes of the central nervous system. *Vojnosanit. Pregl.* 1993;50:547-553.
- (13) Brünner M., Chilla R., Maurer K. Evoked response audiometry and vestibular examinations in patients with multiple sclerosis. *Laryngol. Rhinol. Otol. (Stuttg)*. 1977;56(1):80-87.
- (14) Robinson K., Rudge P. Abnormalities of the auditory evoked potentials in patients with multiple sclerosis. *Brain* 1977;100:19-40.
- (15) Japaridze G., Shakarishvili R., Kevanishvili Z. Auditory brainstem, middle-latency, and slow cortical responses in multiple sclerosis. *Acta Neurol. Scand.* 2002;106:47-53.
- (16) Raičević B., Sinanović O. Evocirani potencijali u dijagnostici multiple skleroze, Parkinsonove bolesti i vaskularnih lezija moždanog stabla. III Kongres medicinskih sestara i zdravstvenih tehničara Bosne i Hercegovine sa međunarodnim učešćem, Zenica, 9 – 11. oktobar 2003. Knjiga abstrakata: 218.
- (17) Dabić-Jeftić M., Mikula I. Slušni evocirani potencijali. In: Krznarić G. (ed.). Evocirani potencijali kore mozga. Školska knjiga Zagreb. 1994:53-68.
- (18) Morrisey S.P., Miller D.H., Kendall B.E. The significance of brain magnetic resonance imaging abnormalities at presentation with clinically isolated syndromes suggestive of multiple sclerosis. *Brain* 1993;116:135-146.
- (19) Grenmann R., Aantaa E., Katevuo K.V., Kormanen M., Panelius M. Otoneurological and ultra low field MRI findings in multiple sclerosis patients. *Acta Otolaryngol. (Stockh)*. 1988;449:77-83.