MOTOR PATHWAY ABNORMALITY IN MULTIPLE SCLEROSIS

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ABSTRACT

Background: Multiple Sclerosis (MS) is a chronic autoimmune demyelinating disease of the central nervous system. Motor symptoms represent one of the most frequent and disabling syndrome of MS. Transcranial magnetic stimulation is a technique used for the investigation of the cortico-spinal tract able to measure the modification at any level of motor pathway. The aim of the study was to determine the possible correlation of motor evoked potentials (MEP) abnormalities with clinical disability and the clinical diagnostic utility of transcranial magnetic stimulation.

Materials and methods: Fifty four patients with clinically definite multiple sclerosis and eighteen healthy volunteers were included in the study. Patients were divided in three subgroups according to the degree of pyramidal impairment calculated with Expanded Disability Status Scale. Transcranial magnetic stimulation (TMS) parameters were evaluated using single pulse TMS and a figure of eight coil. Parameters determined included: motor threshold, central motor conduction time (CMCT), latencies and amplitude of MEP at 120% of motor threshold.

Results: Patients with MS had significantly higher motor threshold, prolonged CMCT and reduced MEP amplitudes as compared to controls. Spinal cord latencies were similar in patients and controls.

Conclusion: Transcranial magnetic stimulation represents a useful tool able to measure motor parameters, to reveal the motor pathways involvement and bring useful information about the degree of pyramidal dysfunction. There was a significant correlation between abnormalities of MEP parameters and clinical disability. This technique allows evaluating the status of disease and could be a measure of treatment efficiency in multiple sclerosis.

Key words: multiple sclerosis, transcranial magnetic stimulation, pyramidal disability

INTRODUCTION

Multiple sclerosis (MS) is a chronic disease that usually begins in young adults and is characterized by multiple areas of central nervous system white matter inflammation, demyelination, and glial scarring (sclerosis) (1). Because no specific test for MS is available, diagnosis rests on the dissemination in space and time of lesions (demonstrated by MRI), clinical manifestations and laboratory tests (2). Because the natural history of MS can be favorably altered by treatment, the importance of early diagnosis has become more apparent (3).

Transcranial magnetic stimulation (TMS) is a relatively new technique that allows painless activation of cortical structures. TMS is primarily used for the investigation of the cortico-spinal tracts in various neurological diseases, being especially useful in the detection of sub-clinical dysfunction. The aim of the study was to determine the possible correlation of motor evoked potentials (MEP) abnormalities with clinical disability and the clinical diagnostic utility of transcranial magnetic stimulation.

MATERIALS AND METHODS

The present study was made on 72 subjects: 54 patients with clinically definite MS (according with McDonald's criteria) and 18 healthy controls. Patients were divided in three subgroups according to

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the degree of pyramidal impairment calculated with Expanded Disability Status Scale (EDSS):

- I – abnormal signs without disability (EDSS 1) – 13 patients;
- II – mild or moderate pyramidal disability (EDSS 2-3) – 31 patients;
- III – severe pyramidal disability (EDSS 4-5) – 10 patients.

Patients from group I showed exaggerated reflexes – 10 patients, sensory loss and/or pyramidal pathologic reflexes – 3 patients.

Patients from group II had right hemiparesis – 6 patients, left hemiparesis – 7 patients, lower limb monoparesis – 7 patients, mild spastic paraparesis – 7 patients, mild tetraparesis – 4 patients.

Patients from group III had spastic paraparesis – 2 patients, severe right hemiparesis – 1 patient, tetraparesis – 6 patients, and one patient had paraplegia and right brachial monoplegia.

TMS was applying over the motor cortex as single pulse with a figure of eight coil of 90 mm diameter of Magstim Rapid® (Magstim Co Ltd, Whitland, Dyfed, UK). The stimulator pulse was very brief (less than 200 microseconds) and the maximum generating magnetic field 1.2 Tesla. The center of the coil was positioned over the motor projection of the hand around 5 cm lateral and 1 cm anterior in relation with vertex. For people in which we did not obtain a motor response in the position the coil was moved 1-2 cm around that point in order to identify the motor hot spot. The muscle contraction was recorded with a Nihon-Kohden EMG device, bilaterally, from the abductor pollicis brevis (APB) on the upper limbs using surface silver/silver chloride electrodes.

The subjects were seated comfortable in an armchair and motor threshold (MT) was recorded in a relaxed target muscle. MT was taken as the minimum stimulus intensity (measured as a percentage of maximum stimulator output) needed to evoke a motor response >50 mV in three out of five consecutive trials. If no response was recorded even at maximum coil output (100%), the subjects were asked to contract target muscle and if still no response was recorded, then TM was considered as 101%. For motor evoked recorded the subjects keep the same relaxed position and the stimulus was applied over the motor hot spot at 120 % of MT. The magnetic stimulation of the spinal roots was done by placing the rim of the same coil over the seventh cervical vertebrae. The evaluated parameters were: MT; cortical latencies (CL) and spinal cord latencies (SL); amplitude (AM) of MEP at 120% of motor threshold; central motor conduction time (CMCT). CMCT was measured by subtracting the latency resulting from spinal stimulation from that on cortical stimulation.

Statistical analysis

Means and standard deviation were calculated for each parameter and each group. Statistical calculations were carried out with STATISTICA 6.0 (Statsoft Inc., USA). Student t-test was used to assess the relationships. All results were considered significant at the 5% level ($p < 0.05$).

RESULTS

Pyramidal symptoms appeared in results of affected cortico-spinal tracts (paresis or plegia, muscle tone modifications, exaggerated reflexes, pathologic reflexes or no abdominal reflexes) were observed at all patients included in the present study. MEP parameters obtained by TMS are shown in TABLE 1.

At patients with MS from the first group (EDSS – 1) there are not statistically significant modifications of MEP parameters (TABLE 2).

Patients with mild or moderate pyramidal disability (group – II) in comparison with healthy volunteers presented statistically significant modifications of MEP parameters: increase of cortical latencies, CMCT and decrease of MEP amplitude at 120% of MT (TABLE 3).

TABLE. 1 *MEP parameters at patients with MS and healthy volunteers*

MEP parameters	Healthy volunteers	Patients group I	Patients group II	Patients group III
Spinal cord latencies (ms)	12.3 ± 1.6	13.33 ± 1.18	13.14 ± 1.94	13.83 ± 1.92
Motor threshold %	57.85 ± 7.60	62.03 ± 10.58	66.83 ± 14.49	73.95 ± 19.48
Cortical latencies (ms)	20.6 ± 1.7	22.01 ± 2.43	23.6 ± 4.13	29.95 ± 6.57
CMCT (ms)	8.4 ± 0.7	8.68 ± 3.25	10.45 ± 4.17	16.12 ± 5.88
Amplitude of MEP at 120% of MT (mV)	2.5 ± 1.5	1.34 ± 1.2	1.38 ± 1.72	0.51 ± 0.45

TABLE 2. *MEP parameters at patients with MS from group I and healthy volunteers*

MEP parameters	Healthy volunteers	Patients group I	p
Spinal cord latencies (ms)	12.3 ± 1.6	13.33 ± 1.18	0.18
Motor threshold %	57.85 ± 7.60	62.03 ± 10.58	0.95
Cortical latencies (ms)	20.6 ± 1.7	22.01 ± 2.43	0.08
CMCT (ms)	8.4 ± 0.7	8.68 ± 3.25	0.15
Amplitude of MEP at 120% of MT (mV)	2.5 ± 1.5	1.34 ± 1.2	0.09

TABLE 3. *MEP parameters at patients with MS from group II and healthy volunteers*

MEP parameters	Healthy volunteers	Patients group II	p
Spinal cord latencies (ms)	12.3 ± 1.6	13.14 ± 1.94	0.14
Motor threshold %	57.85 ± 7.60	66.83 ± 14.49	0.89
Cortical latencies (ms)	20.6 ± 1.7	23.6 ± 4.13	0.05
CMCT (ms)	8.4 ± 0.7	10.45 ± 4.17	0.05
Amplitude of MEP at 120% of MT (mV)	2.5 ± 1.5	1.38 ± 1.72	0.04

TABLE 4. *MEP parameters at patients with MS from group III and healthy volunteers*

MEP parameters	Healthy volunteers	Patients group III	p
Spinal cord latencies (ms)	12.3 ± 1.6	13.83 ± 1.92	0.38
Motor threshold %	57.85 ± 7.60	73.95 ± 19.48	0.02
Cortical latencies (ms)	20.6 ± 1.7	29.95 ± 6.57	0.005
CMCT (ms)	8.4 ± 0.7	16.12 ± 5.88	0.004
Amplitude of MEP at 120% of MT (mV)	2.5 ± 1.5	0.51 ± 0.45	0.003

At patients from the third group with severe pyramidal disability were modified all MEP parameters except of the spinal cord latencies that had no statistically significance (TABLE 4).

DISCUSSION

Prolonged CMCT – essential parameter that shows nervous transmission of myelined axons – were found at all patients with mild, moderate or severe pyramidal disability (4).

Modifications of spinal cord latencies had no statistically significance which demonstrates that increase of cortical latencies is determined by increased CMCT and shows delay of neuronal transmission in the superior segment of cortico-spinal tract.

Demyelination and secondary of it degeneration of cortico-spinal tract fibers, conduct to desynchronized impulse and modification of all MEP parameters, facts that were shown in this study by correlations of pyramidal disability with degree of MEP parameters modifications.

It was shown that at patients with severe disability (EDSS 4-5) there is a significantly increased of CMCT, motor threshold and decreased amplitude of MEP at 120% of MT in comparison with patients with minor motor deficit.

Neuronal demyelination and/or neurodegenerative process is best shown by blocked neuronal conduction and cases of impossibility of MEP generations, even with facilitation and maximum output intensity of the stimulator (in our case 1.2 Tesla) (5-8). Such cases were registered at 5.55 % of MS patients. In one patient no MEP could be elicited at maximum stimulator output and in two patients the lack of MEP generation was present only unilateral. All three patients present a severe motor disability.

60% of patients with secondary progressive multiple sclerosis and severe pyramidal dysfunction

(EDSS 4-5) present significant modified MEP parameters. By contrast only 40% of patients with recurrent remissive form of MS present significant modification, of MEP parameters. It is important to notice that all these patients present a long history of illness (16.75 ± 8.5 years).

This study confirmed conclusions of other clinicians that found the correlation between clinical disability and MEP abnormalities (9-15).

CONCLUSIONS

1. The most important modified parameters of MEP were found at patients with severe pyramidal disability.
2. TMS may also detect sub-clinical lesions and CMCT abnormalities it seems to be the most sensitive parameter for motor disability.
3. There was significant correlation between CMCT, evolution of the disease, and with the degree of pyramidal signs.
4. TMS is an easy and reliable method to quantify pyramidal dysfunction in MS and monitoring the evolution of the disease and should be taken into account as a tool in monitoring motor disability in patients with MS.

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