THE USE OF TRANSCRANIAL MAGNETIC STIMULATION AND THERMOGRAPHY IN THE EXAMINATION OF PATIENTS WITH MULTIPLE SCLEROSIS

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Summary
The majority of patients with Multiple Sclerosis have motor dysfunction from the early onset of the disease. Both acute presentations and subsequent relapses of the disease contribute to the worsening of the motor deficits that can develop into quadriplegia. Quantification of the deficits is performed using EDSS scale (1, 7) which can quantify the gait deficits among other parameters.
Aim. The present study looked at the variability of both cortical and peripheral latencies on a group of RRMS patients at rest and after exercise on an ergonomic bicycle.
Material and methods. Furthermore the thermography investigation was performed by looking at the tissue located in posterior lodge of the calf back before and after exercise.
Results. The results found were that the shortening of the cortical latency after completion of physical activities was associated with a low temperature of the tissue.
Conclusions. Physical therapy improves at least transiently the motor cortex excitability as well as the velocities of the nervous impulse. Heat loss can be related to partial involvement of the motor units in the muscle contraction but also to the exaggerated losses by altering the sympathetic tone (10, 12).

Key words: Trans Magnetic Stimulation (TMS), Multiple Sclerosis (MS), Termography, Central Motor Conduction Time (CMCT), EDSS scale, Kurtzke scale

INTRODUCTION

Multiple sclerosis is a disease of young adults characterized by an association of impaired pyramidal, cerebellar, brain stem, visual, sensory, neuropsychological and bladder dysfunctions. Motor dysfunction is present in approximately 42% of patients (1), amplified along with evolution of the disease. Worsening can occur both as the consequence of the sequence of outbursts that adds new deficits but also in the primary progressive type. The deficits are quantified using EDSS scale, also known as the Kurtzke scale (1, 7). Paradoxically the patient identifies the upper limb motor deficits later, due to initial complaints of gait. The severity of motor dysfunction can be assessed by pyramidal functional system score (FS-P), which also influences the EDSS result (2, 8). Minor motor deficits correspond to FS grade 2, mild or moderate paraparesis, hemiparesis, monoparesis fall in FS grade 3. Tetraparesis, hemiparesis, paraparesis or monoplegia are rated with FS grade 4. Score 5 corresponds to the functional motor paraplegia, hemiplegia and tetraparesis. FS grade 6 is attributed to tetraplegia. There is a correlation between EDSS and motor functional system score. EDSS value is achieved by the maximum value of at least one FS parameter.

A patient who has a functional system score of 2 finds hard to walk the same distance in the usual time without having an obvious disability.

Demyelinating disease of the central motor neurons produces a disruption of nerve impulse transmission reflected in motor evoked potential (MEP) obtained with the use of transcranial magnetic stimulation (TMS) (3, 8, 11). Another ongoing hypothesis is linked to the fact that some motor units will not be involved in voluntary muscle contractions because of the central motor neurons' pathology. In turn, muscle contraction generates heat that is removed at least in part by the circulatory system and is subsequently modulated according to thermoregulatory mechanisms.

MATERIALS AND METHODS

A group of 12 patients with RRMS (relapsing/remitting multiple sclerosis) was studied: 4 men and 8 women aged between 20 and 48 years. MEP parameters obtained from the patients examined were compared with those measured in a group of 18 healthy volunteers aged between 20 and 50 years. Patients were examined using TMS (3, 8, 11) single pulse type in order to obtain central, cervical and lumbar latency values. The device

Table 1. Mean and Standard deviation of MEP parameters obtained in healthy volunteers and patients with MS – before exercise.

MEP Parameters	Volunteers	MS-Patients	p (student T test)
Cortical Latency upper limb (ms)	21.18 ± 1.08	24.18 ± 3.62	0.003
Cervical Latency (ms)	12.96 ± 1.22	12.12 ± 1.64	0.09
CMCT upper limb (ms)	8.35 ± 1.05	11.41 ± 3.6	0.006
Cortical Latency lower limb (ms)	27.5 ± 1.68	35.5 ± 10.96	0.006
Lumbar Latency (ms)	11.66 ± 1.93	12.67 ± 1.54	0.07
CMCT lower limb (ms)	15.83 ± 2.29	22.82 ± 10.19	0.008

Table 2. Mean and Standard deviation of MEP parameters obtained in healthy volunteers and patients with MS – after exercise.

Parameters MEP	Volunteers	MS-Patients
Cortical Latency upper limb (ms)	21.18 ± 1.08	22.85 ± 3.31
Cervical Latency (ms)	12.96 ± 1.22	11.35 ± 1.63
CMCT upper limb (ms)	8.35 ± 1.05	11.44 ± 3.58
Cortical Latency lower limb (ms)	27.5 ± 1.68	34.31 ± 11.57
Lumbar Latency (ms)	11.66 ± 1.93	12.52 ± 1.79
CMCT lower limb (ms)	15.83 ± 2.29	21.66 ± 10.74

Table 3. Thermal values recorded in healthy volunteers and patients with MS – before and after exercise.

Thermal values recorded (°C)	Volunteers	MS-Patients	p (student T test)
Before exercise	32.86 ± 0.54	32.01 ± 1.24	0.01
After 5 minutes exercise	33.25 ± 0.98	31.27 ± 1.25	0.002

used was a Magstim Rapid type capable of generating a magnetic field of 1.2 Tesla, produced in 2007 with an eight-shaped magnet of 7 cm in diameter. The magnet was placed both on the cortical projection of hand anatomy, but also with an angulation required to stimulate the medial cortex, a corresponding representation of the leg. For MEP registration, surface electrodes were used, placed in the first interosseous space for the adductor halucis longus muscle and the anterior tibial muscle. After recording the cortical latencies, stimulations were performed at the C7 root and L5 root with the same butterfly-shaped coil placed latero-dorsally, both on the right and on the left side. The same surface electrodes were used to record cervical and lumbar latency. Taking the difference between the central and peripheral latencies we have calculated separately the CMCT (4, 6, 9) for the upper and lower limb. This type of investigation was conducted before and after bicycle ergometer exercise performed for a total time of 5 minutes.

A thermal camera FLIR A320 type was used on the examined skin areas, with individual setting of heat emission and automatic correction of the reflected temperature, distance and relative humidity. The color code is blue, green, yellow, red and white, where blue color is the coldest and white, the warmest area. The thermal parameters of the posterior calf tissues were registered both before and after the exercise.

The control group (3) was composed of five healthy volunteers (2 men and 3 women) aged between 20 and 30 years, using the same investigation protocol as patients with MS. Statistical analysis of results was performed using STATISTICA 6.0 (StatSoft Inc.,USA) software package. Results are presented as mean values and standard deviation (M ± sd). Results were considered statistically significant at 5% ($p < 0.05$).

RESULTS

In patients with Multiple Sclerosis, recorded results were increased in all MEP parameters obtained with the use of transcranial magnetic stimulation (8). No significant changes were reported in peripheral cervical and lumbar latencies.

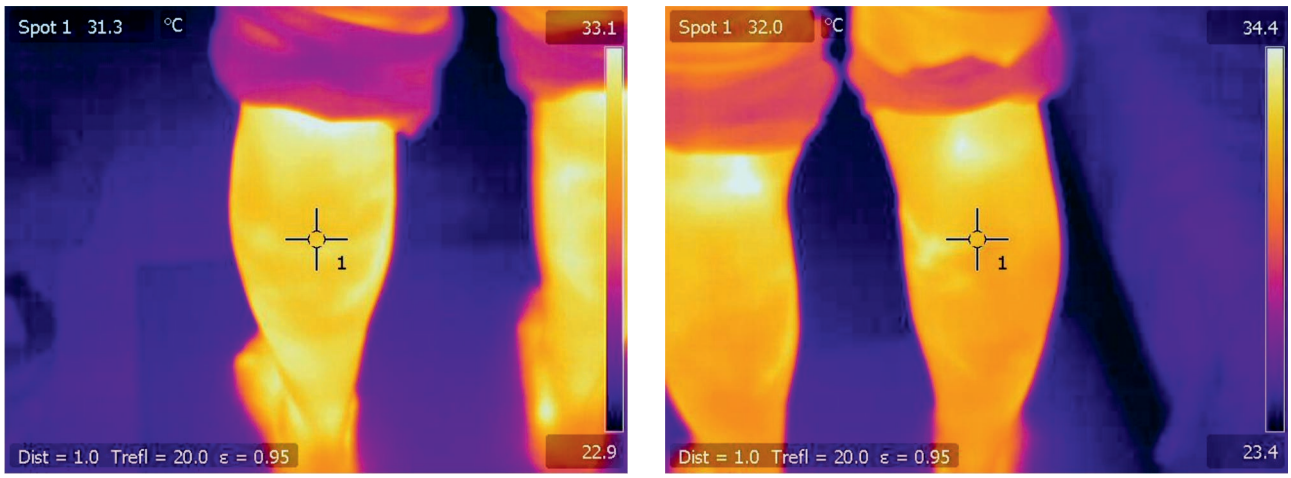
Statistically significant changes were noted in terms of both cortical latency and CMCT for the upper and lower limbs in MS patients compared to the healthy volunteers.

As expected, the largest changes in CMCT (4, 6, 9) were found by measuring the differences between cortical and the lumbar latencies.

After practicing the exercise bicycle ergometer for 5 minutes there were no statistically significant changes in MEP parameters both in healthy volunteers and patients with MS, although there were slight decreases in the initial lag time.

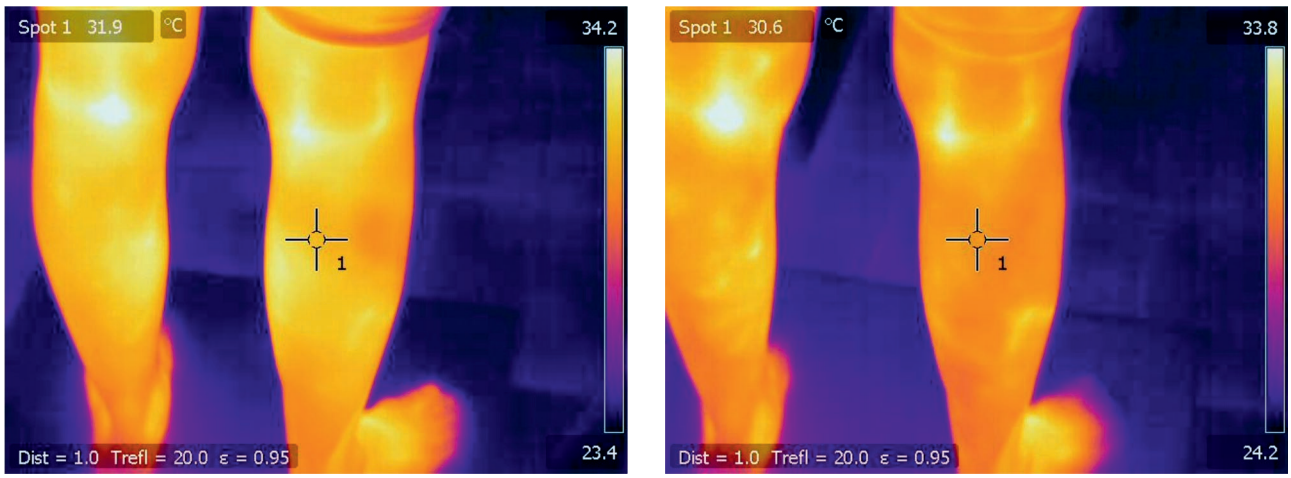
We recorded thermal values of the calf tissue before and after physical exercise in both volunteers and patients with MS. The data was processed, obtaining average values and their standard deviations (tab. 3).

a)



Volunteer (before effort) Volunteer (after effort)

b)



MS Patient (before effort) MS Patient (after effort)

Fig. 1 a, b.

Results revealed lower temperature values recorded in MS patients compared to healthy volunteers both before and after exercise. In order to obtain a statistically significant difference after exercise two factors were required: a temperature rise of leg's posterior tissue in healthy volunteers and, on the other hand, its temperature drop in patients with MS (fig.1a, b).

DISCUSSION

As expected CMCT (4, 6, 9) values increased with the qualification of patients to higher values of EDSS scale as a result of the demyelination and the degeneration reactions. This phenomenon was most obvious in lower limbs where medium or severe paraparesis or hemiplegia were the consequence of the involvement of the external component of the pyramidal tract in the repetitive and multileveled process of demyelination.

The axonal injury is present since the early stages of the disease, having dynamic character in the course of the disease due to existence of the re-myelination possibilities. Demyelination is not immediately followed by axonal transection which means that at least partial function is maintained. Axonal loss can be detected in apparently normal white matter, whereas morphological and structural investigations may not be sufficient to identify the function of the disturbing elements.

TMS (3, 8, 11)together with the use of evoked potential methodology, is one of the electrophysiological methods that substitute at least partially the use of complex imaging investigations. The ratio of motor axons that have lost their function is still imprecise and variably quantified.

Patman (1931) reported losses of about 50% of pyramidal tract axons following the research on 11 subjects. Other researchers (Greenfield & King) claim that the normal axons density is approaching 90%. In patients with SMSP the reduction of axons quantity may reach up to 61% of the total (p. 479). Axons with diameters smaller

than 3 mm are more affected than those with large diameters. MS lesions may affect gray matter or the cortex, including the medullar ventral horns. We felt that an extended CMCT (4, 6, 9) associated with a motor deficit type like paraparesis and hemiplegia or hemiparesis will be accompanied by a disruption of muscle contraction involved to some extent in the production of heat. The change of the cervical and lumbar peripheral latency was not statistically significant, demonstrating that the increase of CMCT is the main indicator of demyelination and degeneration and illustrates the slow transmission of nerve impulses through cortico-spinal tract. These changes are characteristic for the studied pathology as it is known that demyelinating lesions in MS particularly affect myelin in the central nervous system. The study by Jones et al. in 1991 focused on the evaluation of peripheral latencies in CMCT of the legs and found a high frequency of abnormalities detected at this level comparing to MEP parameters changes observed in the upper limbs. The most likely explanation of this phenomenon is the multitude of component fibers for lower limb pyramidal tract. These fibers are more vulnerable due to their length which increases the likelihood of demyelination at several topographic levels. Elongation of the lumbar peripheral latency objectified in this study in some subjects with MS and accompanied by clinical changes at this level, also demonstrates the involvement of junction between central and peripheral motor neuron.

Thermogenesis is a phenomenon influenced and modulated by the neuroendocrine system intervention. Muscles are involved in thermogenesis even when they change the tonus, by the influence of sympathetic nervous system, hypothalamus and catecholamines. The biggest heat producers are the skeletal muscle, liver, digestive tract and brain. The skin, subcutaneous tissue and fat layers prevent excess heat loss. The temperature is not constant over the whole body being lower on the skin than inside the body. There are regions "physiologically" warm like the forehead, palms, back and groin region. The "cold" regions cover the flanks, the inner arms surface and thighs with the knee being considered the cold pole. The back of the anatomical foot is "cold" and the scrotum has a temperature around 33.5°C. After repeated contractions, in the biceps muscle the temperature can reach 38°C. There are variations of the circadian temperature values with the minimum between 4 and 6 in the morning (36°C) and maximum 16-18 in the afternoon (37°C). Physical exercise produces an increase in temperature ranges in relation with the duration of the muscle contraction. Diet changes, stress, menstrual cycle and age may alter the body temperature. A number of conditions contribute to changes in thermal status of the organism, and multiple sclerosis is one of these factors. A large number of patients with MS tend to blame a phenomenon associated with a febrile infection, which means a low tolerance to high temperature compared to transient hyperthermia. This behavior suggests that demyelinating elements of the central nervous system are functional at temperatures slightly lower compared with healthy individuals. Patients with MS tend to express the development of this discomfort sensation and may be associated with the progression of the disease. Nervous system of patients with MS seems to be set to operate at lower temperatures compared to the healthy subjects. It is unlikely that changes are implicated by the sympathetic system which would increase the loss of heat to achieve the new level of comfort depending on the extent of existing deficits. High temperature favors easier passage through the blood/brain barrier by various metabolic components that could lead to decrease cell excitability in CNS. It is not ruled out that the reduction in the amount of heat produced by muscles occurs due to demyelination of central motor neurons so muscles do not contract normally any longer.

In these circumstances we expected thermal changes induced by MS by damage of central motor neuron. In MS, patients' body basal temperature in the lower limbs compared with the control group before exercise was lower and with a tendency for a temperature drop after the exercise in MS cases.

CONCLUSIONS

CMCT prolongation in MS patients is consistent with the motor functional scores which are improved by physical therapy, especially in patients with small degree of disability. In patients with MS, thermography values of calf muscles are lower than normal. Physical therapy causes higher heat losses in leg muscles with the possible involvement of sympathetic tonus. □

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