UNIVERSITY OF TURIN
DEPARTMENT OF CLINICAL AND BIOLOGICAL SCIENCES

PhD in Experimental Medicine and Therapy
Cycle XXIX

Effects of multilateral exercises on motor skills in people with multiple sclerosis: a longitudinal study

PhD CANDIDATE:
Luca Beratto

TUTORS:
Professor Massimiliano Gollin
Professor Maria Grazia Piancino

COORDINATOR:
Professor Giuseppe Saglio

ACCADEMIC YEARS
2014 – 2017
M-EDF/01

Index

1. Introduction

The central nervous system (CNS) is considered a communication net which analyzes the information coming from all the internal and peripheral receptors. The main CNS functions are sensory reception, the elaboration of information, and the human behavior. The brain send the useful signal for muscle coordination, which allows the interaction between organism and the environment. All the CNS activities depend on the connection between nervous cells and muscle fibers.

The nervous cell has four defined parts: the cell body or soma, dendrites, axons, and presynaptic terminal. The body cell contains two kinds of processes called axon and dendrites. The neurons have many dendrites, which are the system for the reception of information coming from other nervous cells.

The axon is the main communication system for neuron's signal, sending a short duration electrical signal in long-distance called action potential. The axons are covered of myelin, a lipidic sheath which increases the speed propagation of action potential. The sheath is interrupted at regular intervals by the nodes of Ranvier. Nervous conduction is defined as saltatory conduction because of the propagation of action potentials along myelinated axons from one node of Ranvier to the next node. Saltatory conduction provides an increase in the conduction velocity of action potentials.

The axon extremity is divided in many presynaptic terminals. These send information to dendrites and body cell of other neurons. The synapse allows the chemical or electrical signal to transmit to another neuron; presynaptic cell send the information and the postsynaptic receive it.

The brain neurons are classified in afferent neurons, motor neurons, and interneurons. Afferent neurons send data related to conscious perception and other information useful for motor coordination. Motor neurons send information to the muscle and glandular system; interneurons analyze the information and send them from one region of the brain to those in other regions.

The connecting interneurons or projection neurons send the information to wide distance brain regions and the local interneuron work out information within the same brain region.

Sensory axon is linked with both motor neurons that innervate the muscle which it comes from and the synergistic muscles. The motor coordination gives the opportunity to control and coordinate the movements of different muscles as one unit.

The spinal reflections supply to the nervous system different elementary schemes which may be activated by sensitive stimuli or by descending signal coming from the upper part of the brain and cerebral cortex. Most of the spinal reflections are made of complex spinal circuits.

In fact only few spinal reflections coordinate single muscles; other the spinal reflections coordinate the movements of muscle groups. Moreover the polysynaptic reflex pathway are characterized one or more interneurons between afferent (sensory) and efferent (motor) neurons.

Each muscle fiber is innervated by one single motor neuron. All muscle fibers innervated by one single motor neuron get contracted in response to an action potential which propagates throughout the motor neuron axon. The motor unit is the smallest functional unit of the muscle. It is consisted of one motor neuron and all the innervated muscle fibers, and it can be controlled by CNS.

The multiple sclerosis (MS) is considered a chronic degenerative and immune-mediated disease of the CNS and which brings a progressive loss of myelin. Inflammatory demyelinating disease affects different regions of the CNS and it causes lesions which altered the action potential saltatory conduction from the brain toward all other body parts and vice versa. Magnetic resonance imaging (MRI) measurements are able to define the disease and CNS areas affected by inflammatory demyelinating process. Clinical diagnosis of the MS are able to be valued trough time and space.

According to Gelfand[1] for an MS diagnosis it is necessary to observe two different inflammatory disease events separated one from the other for at least one month (dissemination in time).

Moreover, it is also necessary for the disease process to affect two different neuro-anatomic areas within the CNS. Clinically, MS is identified by "attacks" or "relapses" episode of CNS neurological dysfunctions.

MS symptoms shown by these episodes change considerably between patients and are determined by the affected neurological area. It is possible to identify four different MS types: Relapsing-Remitting MS (RRMS) in which relapses and attacks clearly defined followed by either complete or partial remission of symptoms with worsening between two episodes; Primary-Progressive MS (PPMS) in which it is possible to observe a slow worsening of the disability from the onset of symptoms, partial remission, and the absence of definite relapses; Secondary Progressive MS (SPMS) which begins as RRMS and it progresses to a slow worsening of symptoms with or without deficit improvement or remission; Progressive Relapsing MS (PRMS) is a progressive disease from onset with definite relapses with or without deficit decreasing and progressive degeneration between the attacks. Multiple sclerosis disease is characterized by different neurological symptoms related to CNS areas affected by neurodegenerative and demyelinating process.

In the last decades, many instruments have been developed to define clinical severity and functional deficits in multiple sclerosis[2]. The most common assessment scale evaluating used in MS is the Expanded Disability Status Scale (EDSS). The EDSS allows to assess the CNS functionality, to describe disease progression and to analyze therapeutic interventions effects. It consists of ordinal rating system ranging from 0 (normal neurological status) to 10 (death due to MS). Increments interval are set in 0.5 (when reaching EDSS 1). The lower values (< EDSS 6) identify neurological impairments, while the upper range of the scale (> EDSS 6) defines functional limitations and disability rate. Values of EDSS between 4 and 6 are dependent on walking abilities.

In MS patients, it is possible to observe acute and chronic symptoms. Pain can be directly correlated with the disease itself (related to optic neuritis) or as the development of secondary pain of MS chronic symptoms[3]. The most evident dysfunctions in MS patients are the alteration of the gait cycle and the postural control, the increase of weakness and fatigue, the cognitive system impairment and the depression. These alterations caused by MS reduce the ability to carry out activities of daily living with negative effects on the quality of life (QoL), increasing health costs due to the need for better resources.

One of the most debilitating consequences of MS is muscle spasticity, caused by the alteration of neuromuscular reciprocal inhibition that causes arrhythmic movements of the musculoskeletal system that involves walking, decreases strength and increases the risk of falls[4]. Larson et al.[5] showed significant differences between the right and the left lower limbs regarding strength and aerobic performance, which were not observed in the control group composed of healthy subjects. Daily activities, mainly walking, require a bilateral synchronization of movements. The differences between the limbs highlighted in this study underline the possibility of activating compensatory strategies in response to the lower limbs strength differences. The results of the study by Chung et al.[6] on a group of women with MS highlighted the asymmetries in the force of the knee extensor muscles and in the postural control with effects on fatigue, gait cycle and balance control.

Soyuer et al.[7] analyzed the balance control in relation to the MS type, underlining a more difficulty in the subjects affected by the primary and secondary progressive forms (PPMS and SPMS) compared to RRMS in postural control with consequent increase in the risk of falling.

Heat sensitivity in MS leads to the increase of the disease symptoms. Such sensitivity is observed when the patients are exposed in a warm environment or when they perform physical activity which causes an increase in body temperature. The presence of heat sensitivity has a negative effect on the ability to perform physical exercise and the motivation to maintain an active lifestyle by performing regular exercises[8].

Some studies have investigated the use of precooling techniques before physical exercise, observing a reduction in symptoms worsening[9] and a 35% capacity to prolong exercise[9]. However, most of the precooling methods are not very functional and hardly feasible.

Skjerbæk et al.[8] demonstrated that a resistance exercise program was well tolerated by most individuals with heat sensitivity with MS. The results support this type of exercise as an alternative to the use of cooling devices.

Changes in cognitive components and mood disorders, in particular the high percentage of depression in patients with different forms of MS, occur as a result of demyelination in the areas of the brain involved in emotions processing. Numerous studies underline the importance of physical exercise to maintain the functionality of the cognitive system.

Weuve et al.[11] studied the effect and relation between long term regular physical activity and cognitive function. Results highlighted that higher level of physical activity (walking) increase cognitive function and reduce cognitive deterioration in old women.

Smith et al.[12] pointed out that aerobic exercise increases the attention and the cognitive efficiency. Moreover, physically active persons have a better functional cognitive system in relation to the sedentary counterpart.

In MS patients, the reduction of cognitive function is mostly related to whole-brain atrophy[13] and atrophy within the frontal and temporal cortices[14,15].

The study of Kramer and Erickson[16] are significant because it showed that the variation of cortical brain structures correspond to an increase in cognitive functionality and physical activity.

Motl et al.[17] underlined the usefulness of physical activity on cognitive functioning such as in cognitive processing speed in MS patients. Present studies show how the physical activity increase cognitive functioning by improving brain cortical structure function and connectivity.

Furthermore, Fjeldstad and Pardo[18] showed that greater self-efficacy reduces negative effects of MS on physical and psychological components. The results of this study underlined the importance of self-efficacy to increase functionality and independence in daily activities and to management and the adaptation regarding the disease.

Fjeldstad and Pardo[18] underlined how high self-efficacy reduces the negative effects MS has on physical capacity and psychological elements. Results showed that greater self-efficacy increases independence in daily activity and functionality, and it decreases the amount of impact of MS on physical and psychological components.

Recent studies have given more attention to oxidative stress in MS pathogenesis[19]. The increase of reactive oxygen species (ROS) and the decrease of antioxidant agents elevate the oxidative stress level. Moreover, the inflammatory disease and demyelinating process, typical of MS, are elements that modify the oxidative stress level.

Saliva antioxidant test is non invasive, easy to use, and repeatable test to evaluate saliva markers in different diseases. Karlik et al.[20] observed similar results of oxidative stress level in MS patients through saliva and blood samples. These results validated the saliva antioxidant test usefulness to evaluate antioxidant agents level in MS.

Fatigue is defined as the lack of physical and mental energy. It has been described as typical symptom of MS patients and it has a negative effect on daily activities and working capacity[21]. The perceived fatigue is greater in MS patients[22] and it causes a reduced of maximal voluntary contraction[23]. Hameau et al.[23] shown a decrease of fatigue after a short and intensive combined rehabilitation program. Moreover, many studies pointed out the positive effects of physical exercise in MS fatigue[24,25].

In the past, physical activity was not suggested to avoid the increase of energy consumption with an adverse effect on perceived fatigue. Furthermore, physical exercise was considered negative cause of exacerbated symptoms and increase development of the disease.

Tallner et al.[26] analyzed the relationship between the level of sports activity and MS relapses. The results showed no significant effects of physical activity on MS course and that a high level of physical activity are not dangerous to MS patients. Gervasoni at al.[27] evaluated if induced fatigue would increase balance disorder, and consequently, risk of falling. Researchers observed an increase of fatigue after physical activity without signifcative reduction in balance performance.

Increase in strength plays a vita role with positive effects on gait cycle, body balance, reducing the risk of falling in daily activities of MS patients. Different types of training create specific neuromuscular adaptation. Strength, muscle power and, rate of force development (RFD) are not only caused by muscle structure alterations, but also as consequence of nervous system adaptation[28].

Taylor et al.[29] showed a maximal voluntary contraction (MVC) and resistance increase on upper and lower limbs in MS patients after a progressive resistance exercise (PRE). Moreover, there was an increase of speed and distance, a reduction of MS effects on daily activities during the 2-minutes walk test along gait cycle.

Souza-Teixeira et al.[30] studied the resistance training program effects on lower limbs and highlighted how a moderate training program could increase the strength, cross sectional area (CSA) of right and left thighs in MS patients. The lower limb CSA is a very important area during of daily living activities. Moreover, the CSA increased CSA can also be observed in MS patients.

Kjølhede et al.[31] analyzed the progressive resistance training (PRT) effects on the increase and maintenance of strength after a period of training. In the experimental group, there was an MVC increase in right and left knee extensors lasting after the follow-up maintenance training of 24 weeks. Moreover, an increase in functional walking was observed. Evaluations of neuromuscular adaptations including MVC, EMG signal and CSA showed a functional improvement in both lower limbs, but it was more significant in non dominat limb. The strength training effects with elastic band on old patients highlighted a strength increase on lower and upper limbs[32,33]. Similar results were observed with circuit training with elastic band in MS patients. De Souza Teixeira et al.[34] showed positive effects on lower limbs muscle power and functionality increase with elastic band training in MS patients. Strength and neuromuscular function are essential components of core stability. Core stability is the capacity to control the trunk position, the movement, and to coordinate upper and lower forces during functional activities[35].

MS patients showed a common difficulty in body balance and postural control, with reduced trunk stability during upper limb movements and reduced core functionality compared to healthy subjects[36]. The Pilates® Method is based on a specific and precise training of core stability, in which exercises for body muscles stimulation are offered.

Van der Linden et al.[37] supported the positive effects of Pilates and core training in postural control, flexibility, pain management and daily activities in a group of MS patients in wheelchair. Marandi et al.[38] observed significant increases in upper and lower limb strength, both dominant and non-dominant, in MS patients following a Pilates Exercise Protocol and water exercise. Other studies[36,39] showed positive effects in postural control, gait functionality and strength in MS patients after a Pilates® method exercise.

2. Aim of the study

Based on the evidence highlighted in the previous research on the positive effects of physical exercise in MS patients, the purpose of this study is to compare the effects of a combined exercises protocol using micro-weight, elastic bands and proprioceptive exercise with Pilates® method and, analyze their effects on: 1. flexibility; 2. lower limb strength; 3. handgrip strength; 4. spine morphology; 5. balance control; 6. gait cycle; 7. oxidative stress level in patients with multiple sclerosis.

3. Enrollment, study desing and methods

Eighteen patients affected by relapsing-remitting multiple sclerosis were enrolled in this study. They provided their formal approval for the participation in this study by signing a specific written informed consent form. Furthermore, the authors certify that all applicable institutional and governmental regulations concerning the ethical use of human participants were followed during the course of this research. All participants are member of the Italian Multiple Sclerosis Association (AISM). Exclusion criteria were identified for participants who had practiced the same physical activity proposed in the study in the previous twelve months. All subjects had to have a good health medical certificate for performing non-competitive physical activity and had not accused any acute episode in the six months previous to the beginning of the study. The trial did not foresee the use of drugs and the pharmacological treatment already underway before the start of the study was not changed and no dietary changes were required during the test and the study periods. The sample group were divided into two groups randomly: the first, neuromuscular multiple stimulation group (NMSG), consisting of 10 patients (8 female and 2 male, age 60±11 years, weight 67±20 kg, height 164±12 cm, Expanded Disability Status Scale, EDSS 5±2), performed the activity protocol using neuromuscular multiple stimulation exercises with micro-weight, elastic bands and unstable surfaces; The second, Pilates® group (PG), which includes 8 patients (7 female and 1 male, age 53±10 years, weight 60±5 kg, height 166±10 cm, EDSS 3±1), performed exercises using the Pilates® method.

Both NMS and Pilates® groups performed two weekly sessions of physical activity of 60 minutes for a period of 5 months. Each session began with a warm up to increase body temperature than joint mobility exercises and static stretching to increase flexibility.

The groups were evaluated three times during the 5 months, which is the total duration of the study: i) T0, after a month of learning the exercises proposed to exclude the learning effect and to identify the basal levels; ii) T1, two months after T0, to evaluate the effects of the first eight weeks of physical activity; iii) T2, two months later from T1, to evaluate the effects after sixteen weeks of training.

Evaluation tests were organized in the metabolic order from the least challenging to the most intense, in particular: 1) stabilometric and baropodometric test, 2) evaluation of the spine morphology, 3) gait analysis, 4) sit and reach, 5) hand grip, 6) sit to stand. The oxidative stress was measured before and after all tests in the first (T0) and in the last evaluation (T2). All functional evaluations were carried out at the Adapted Training and Performance Laboratory of the University of Turin.

3.1 Stabilometric and baropodometric test

Posturography has been described as a reliable tool to measure balance in upright position in people with multiple sclerosis[40]. The stabilometric and baropodometric test analyzes the pressure distribution, the contact surface and the pressure center oscillations. The evaluation of these parameters allows examining the characteristics of the foot pressure on the ground and the ability to control the balance in upright position. For the baropodometric analysis was used the P-Walk platform (BTS Bioengineering, Milan, Italy) consisting of a sensor mat (sensor dimensions 1cm x 1cm, sensor number 2304 and acquisition rate of 100Hz) capable of recording plantar pressures, the position of the center pressure (CoP) and to process the following variables:

CoP X and Y [mm]: average deviation of the patient oscillation on the sagittal and frontal plane;

Dev. St. CoP X and Y [mm]: standard deviation of the patient oscillation on the sagittal and frontal plane;

CoP Distance [mm]: the trajectory length of the center of pressure calculated as the sum of the single displacements of the CoP on the platform surface;

Body Barycenter Ellipse surface [mm2]: surface area calculated by trajectory of the CoP; Distance / Surface (LSF): ratio between the distance and the surface of the CoP used as the energy expenditure index for posture control;

Average Speed [mm/s]: CoP oscillation speed on the anterior-posterior and mid-lateral axes.

The subjects performed in a standing position with their arms along the hips and feet along the reference lines on the platform (Figure 1).

Figure 1 – Stabilometric and baropodometric platform used to analyze CoP parameters

Two tests lasted every 30 seconds, in two different experimental conditions, respectively with opened and closed eyes, with a recovery time of 3 minutes between trials.

3.2 Spine morphology with Spinal Mouse®

The evaluation of the spine morphology with the use of Spinal Mouse® (Idiag, Volketswil, Switzerland) is useful for analyzing the spine parameters related to the risk of falling[41,42].

The device consisting of 3 triaxial accelerometers for a reliable analysis of the morphology and range of motion (ROM) of the spine on the sagittal plane. Spinal Mouse® (Figure 2) is slid over spinous processes, identified by the operator with dermographic pencil, in the vertebrae between C7 and S1 with a sampling rate of 150Hz. The parameters processed after the data acquisition are: thoracic spine (ThSp) analysis from the first (ThSp1) to the last thoracic spinal vertebra (ThSp12); of the lumbar spine (LSp) from the first (LSp1) to the last lumbar vertebra (LSp5) and the whole spine inclination (Incl) from the first thoracic (ThSp1) to the first sacral vertebra (S1). All measurements were assessed only once with the following evaluation protocol: 1) test from the standing position with subjects looking toward the horizon, legs spread to the width of the shoulders with knees in the extension and arms along the sides; 2) maximum flexion test in which subjects reach the maximum bending forward of the bust while keeping the knees in extension; 3) maximum extension test keeping the lower limbs in extension, arms crossed on the chest, the subject reaches the maximum extension of the trunk.

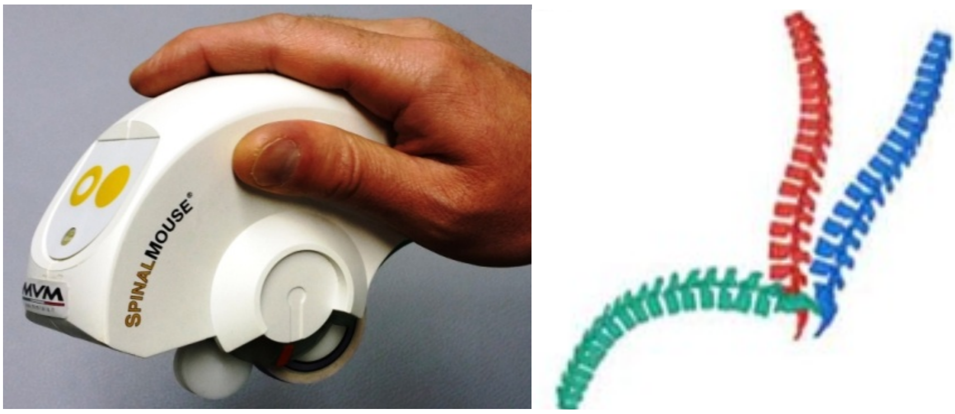

Figure 2 – Spinal Mouse® device use to analyze the spine morphology (left) and the graphic result of the test (right)

3.3 Gait cycle

Spatio-temporal gait parameters is measured using the G-Walk® sensor (BTS Bioengineering, Milan, Italy). The device with three accelerometers and a gyroscope is positioned at the height of the vertebral bodies between the L4-L5, thanks to an ergonomic customized belt that does not affect the performance of the movement during a walking test (Figure 3).

Figure 3 – G-Walk sensor used to evaluate the spatio-temporal parameters of the gait cycle

The subject in standing position walks a 10 meters straight line during which the following parameters are recorded:

Cadence (strides/min): Number of strides in a minute;

Speed (m/s): average velocity of walking;

Stride Length (m): average value of the distance between each heel strike and the next of the same foot;

Gait Cycle Duration (sec): average value of the time interval between two consecutive heel strikes of the same foot;

Left Step Duration (%): average value of the times between left heel strike and right heel strike. It is shown the value as percentage of gait cycle;

Right Step Duration (%): average value of the times between right heel strike and left heel strike. It is shown the value as percentage of gait cycle;

Left Stance Duration (%): duration of the left foot support phase as percentage of gait cycle;

Right Stance Duration (%): duration of the right foot support phase as percentage of gait cycle;

Left Swing Duration (%): duration of the left swing phase as percentage of gait cycle;

Right Swing Duration (%): duration of the right swing phase as percentage of gait cycle;

Double support duration (%): average value of percentage of the cycle duration in which both lower limbs are in support;

Single Support Duration (%): duration of the phase in which only one foot, right or left, is in stance position as a percentage of the gait cycle.

3.4 Flexibility

The sit and reach test was used to evaluate the flexibility of the muscles of posterior kinetic chain. To carry out the test, was built a metal and wood parallelepiped (height 30 cm, width 50 cm and depth 51 cm) on which an 80 cm-long metal binary was applied along centerline. On this, a movable carriage, is installed which supports a device (Bosch, Germany) for digital measurement (± 1 mm) with a laser beam that hits the plate at the end of the track to standardize the measurements. On the vertical plane in front of the subject there is the support of the feet.

Positioned at 30 cm from the start of the track, a wooden triangle with a downward angle is applied, whose sides form a 36 ° angle and are used to identify the correct positioning of the feet. The test is performed with the subject sitting with the lower limbs extended and without shoes. The operator supervised the correct starting position, which occurs with the overlapping hands on the movable trolley. The subject freely chooses the overlapping of the hands, which is kept in the same position in subsequent tests to reproduce the same experimental conditions. Subsequently, the subject is asked to bend their trunk progressively forward until reaching the maximum flexion without pain (Figure 4). To ensure that the test does not become a muscle stretching technique, the evaluation is performed only once.

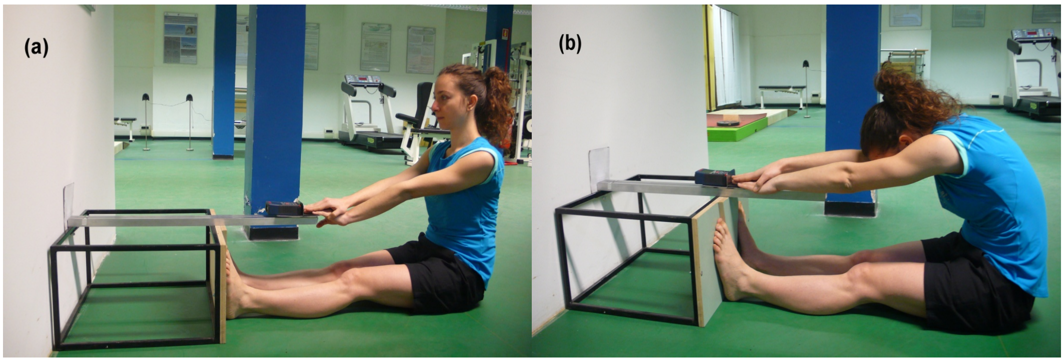

Figure 4 – Sit and reach test. Starting position (a) and final position (b)

3.5 Hand grip

Hand Grip (Baseline, White Plains, NY, USA, Figure 5) was used to evaluate the strength of hand flexors. The subject performs the sitting test, with the arm completely extended towards the ground and performed the maximum voluntary handgrip contraction for 3 ± 1 seconds. Three tests were performed for each limb with a 1 minute recovery and the best test was used for the analysis of the results.

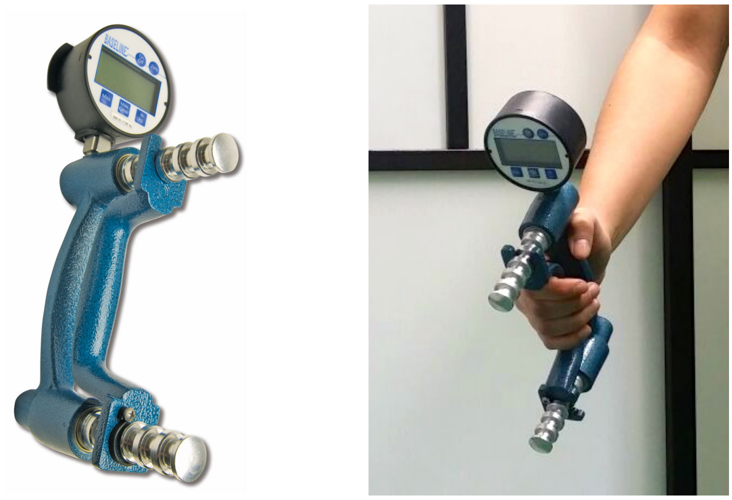

Figure 5 – Hand grip dynamometer to analyze hand grip strength

3.6 Lower limb strength

For the lower limb strength test was used a 43 cm high wooden and iron bench[43] on which a 1 cm rubber cushion was positioned to dampen the limbs basin support on the seat. The width (70 cm) and the length (1 m) of the bench have been adapted to the dimensions of the two bars of the Optojump (Microgate, Bolzano, Italy) positioned laterally and parallel to the seat, at a distance of 70 cm, one from the other. To ensure greater security for the persons, a backrest (height 33 cm) was placed at 40 cm from the front of the seat, two safety bars (height 1 m, length 1.30 m) were added laterally to the bench and an open able support positioned 1 m from the seat. The entire structure was fixed to the floor to prevent bench movement during the test. The test consists in the maximum number of times the subject sits and gets up in 30 seconds. The start occurred when the participant was in the upright position with the legs at the same distance apart as the shoulders. All subjects were previously instructed on the correct execution of the test to prevent the initial learning effect from affecting the test results and an operator checked the correctness of the movements (Figure 6).

Figure 6 – Sit to stand test with the Optojump device

3.7 Oxidative stress

The Saliva Antioxidant Test (SAT) is a non-invasive test for determining the level of antioxidants (AO) carried out using the WellLife system (H&D, Parma, Italy, Figure 7). The SAT test evaluates the ability of the saliva to reduce ferric ions (Fe^{3+}) to ferrous ions (Fe^{2+}) and the level in µmol/l of vitamin C, considered as an antioxidant agent, present in the saliva. The test involves taking a small amount of saliva from a cotton swab and this is inserted into a cuvette. Subsequently, the reagent liquid is added by the use of another transfer pipette. Finally, the cuvette is inserted into the WellLife system, which is a photometer that allows optical reading and vitamin C analysis in a saliva sample.

Figure 7 – WellLife test reader used to measure the saliva antioxidant level

3.8 Procedures

Table 1 shows the protocol for neuromuscular multiple stimulation exercises, serial number, repetitions and recovery time. The exercises have been divided into three groups and within each group there are exercises for the upper and lower body, proprioceptive and walking control exercises. NMS group was divided into three groups. All subjects performed the exercises at the same time in the order shown in Table 1 and at each training session they performed the exercises of all three groups.

Neuromuscular multiple stimulation exercise group 1

Exercise	Set and repetitions	Recovery	Muscles
Single Leg extension with ankle weight	2x10	30 seconds	Rectus Femoris
Hand grip	2x10	30 seconds	Hand Flexors, Fingers Flexors
Chest press with elastic band	2x10	30 seconds	Pectoralis Major, Triceps Brachii
Pulley with elastic band	2x10	30 seconds	Latissimus Dorsi, Biceps Brachii

Neuromuscular multiple stimulation exercise group 2

Exercise	Set and repetitions	Recovery	Muscles
Walking on balance disc	3x6 meters	30 seconds	Lower limbs
Step up on balance disc	2x10	30 seconds	Rectus Femoris, Hamstring, Gluteus
Single Leg curl ankle weight	2x10	30 seconds	Hamstring
Walking with ankle weight	6x10 meters	30 seconds	Lower limbs

Neuromuscular multiple stimulation exercise group 3

Exercise	Set and repetitions	Recovery	Muscles
Curl with wrist weight	2x10	30 seconds	Biceps Brachii
Push down with elastic band	2x10	30 seconds	Triceps Brachii
Isometric uprigth position on one balance disc	2x20 seconds	30 seconds	Rectus Femoris, Hamstring, Gluteus
Isometric uprigth position on two balance disc	2x20 seconds	30 seconds	Rectus Femoris, Hamstring, Gluteus
Squat with fitball	2x10	30 seconds	Rectus Femoris, Hamstring, Gluteus

Table 1 - Exercises utilized by neuromuscular multiple stimulation group divided in three groups and the related muscle groups trained.

The PG performed the Pilates® Exercise Program (Table 2) and two series of 10 repetitions were performed with 30 seconds of recovery for each exercise. Both activities were supervised by qualified trainer.

Exercise	**Set and repetitions**	**Recovery**	**Muscles**
Pelvis Rolling	2x10	30 seconds	Rectus Abdominis
Saw	2x10	30 seconds	Rectus Abdominis
Spine Twist	2x10	30 seconds	Lumbars, Latissimus dorsi, Transversus Abdominis
Spine Stretch	2x10	30 seconds	Lumbars, Latissimus Dorsi, Hamstring
Roll Down	2x10	30 seconds	Rectus Abdominis
Roll Up	2x10	30 seconds	Rectus Abdominis
Cat Stretch	2x10	30 seconds	Lumbars, Latissimus Dorsi
Plank with leg lift	2x10	30 seconds	Lumbars, Hamstring, Abdominals
Bridge	2x10	30 seconds	Hamstring, Lumbars, Glutes
Leg Changes	2x10	30 seconds	Rectus Femoris, Hamstring, Rectus Abdominis
Bicycle Kick	2x10	30 seconds	Hamstring, Rectus Femoris
Side Passè	2x10	30 seconds	Adductor Magnus, Rectus Femoris
Single Leg Stretch	2x10	30 seconds	Rectus Femoris, Rectus Abdominis
Rolling Like a Ball	2x10	30 seconds	Abdominals, Lumbars

Table 2 - Exercises utilized by Pilates group and the related muscle groups trained.

3.9 Statistical analysis

The data were described using the mean and standard deviation (±SD). Friedman's ANOVA and Dunn's post hoc were used to analyze the differences between evaluation sessions. The significance level p was set to <0.05 and the percentage difference was calculated by the following formula: % difference =((Fv-Iv)/Iv) x100 in which Iv corresponds to the initial value and Fv the final value. The non-parametric Wilcoxon test was used to analyze of the oxidative stress before and after the session test at T0, and to compare the measure at pre-test session between T0 and T2.

To estimate the relevance of the differences, the effect size (ES) was calculated and interpreted as following classification: 0.2 to <0.6, small; from 0.6 to <1.2, mean; from 1.2 to <2.0, great; from 2.0 to <4.0, very large; and ≥ 4.0, extremely large[44].

4. Results

All subjects completed a 16-week of physical activity. None of them reported episodes of disease exacerbation and all performed the three evaluation test sessions. No other adverse events were reported, and no falls occurred during the physical activities and during the evaluation tests.

The results show a statistically significant variation in the neuromuscular multiple stimulation group in:

1. sit to stand test (T0vsT2, $p<0.05$, +13%, Table 3, Figure 8);

2. grip strength test right hand (T0vsT1, $p<0.05$, +16%, Table 3, Figure 9a), left hand (T0vsT1, $p<0.01$, +20%, Table 3, Figure 9b).

Neuromuscolar multiple stimulation group results						
Parameters	**T0**	**T1**	**T2**	**Anova p value**	**Dunn's Post Hoc**	**Effect Size**
Sit and reach	21 (11)	23 (10)	23 (10)	0.06	ns	-
Sit to stand	10 (3)	11 (4)	12 (4)	0.007	T0 vs T2*	0.60
Right hand grip	22 (9)	25 (13)	23(13)	0.03	T0 vs T1*	0.29
Left hand grip	20 (9)	24 (11)	22 (11)	0.001	T0 vs T1**	0.43

Table 3 – Neuromuscular multiple stimulation group results of flexibility, lower limb strength and hand grip strength. Values are expressed as mean ± SD. * $p<0.05$, ** $p<0.01$ and *** $p<0.001$

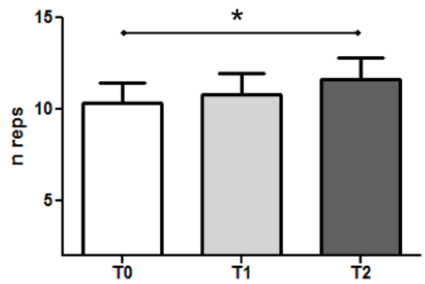

Figure 8 – Sit to stand test variation in NMS group

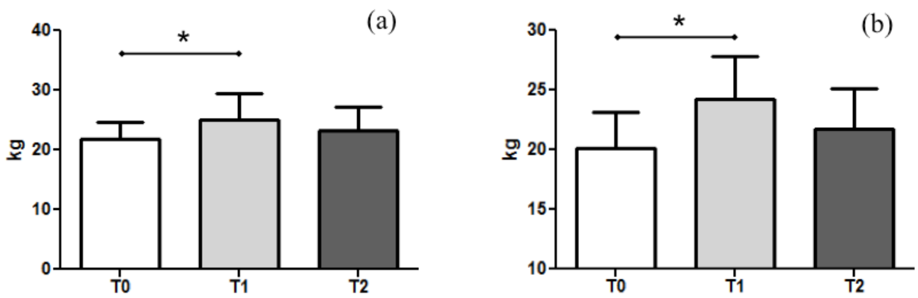

Figure 9 – Grip strength variations in right (a) and left hand (b) in NMS group

3. Spinal Mouse upright position Sac/hip (T0vsT1, p<0.05, -20%, Table 4, Figure 10a), Incl (T0vsT2, p<0.05, -67%, Table 4, Figure 10b);

Spinal Mouse® parameters in upright position in NMS group						
Parameters	**T0**	**T1**	**T2**	**Anova p value**	**Dunn's Post Hoc**	**Effect Size**
Sac / Hip	14 (6)	16 (7)	11 (7)	0.01	T0vsT1 *	0.32
ThSp	55 /11)	52 (8)	54 (9)	0.46	ns	-
LSp	30 (12)	30 (10)	28 (11)	0.46	ns	-
Inclination	3 (5)	2 (5)	1 (5)	0.03	T0vsT2 *	0.42
Spinal Mouse® parameters in flexion positionin NMS group						
Parameters	**T0**	**T1**	**T2**	**Anova p value**	**Dunn's Post Hoc**	**Effect Size**
Sac / Hip	75 (17)	79 (15)	77 (14)	0.07	ns	-
ThSp	60 (17)	59 (16)	57 (15)	0.18	ns	-
LSp	18 (10)	16 (10)	17 (11)	0.43	ns	-
Inclination	107 (13)	107 (13)	107 (12)	0.83	ns	-
Spinal Mouse® parameters in extension position in NMS group						
Parameters	**T0**	**T1**	**T2**	**Anova p value**	**Dunn's Post Hoc**	**Effect Size**
Sac / Hip	6 (8)	8 (14)	1 (14)	0.13	ns	-
ThSp	56 (13)	48 (13)	53 (13)	0.71	ns	-
LSp	34 (12)	35 (14)	32 (11)	0.83	ns	-
Inclination	11 (9)	12 (9)	15 (10)	0.6	ns	-

Table 4 – Neuromuscular multiple stimulation group results of Spinal Mouse® evaluation in upright, flexion and extension position. Values are expressed as mean ± SD. * p<0.05, ** p<0.01 and *** p<0.001

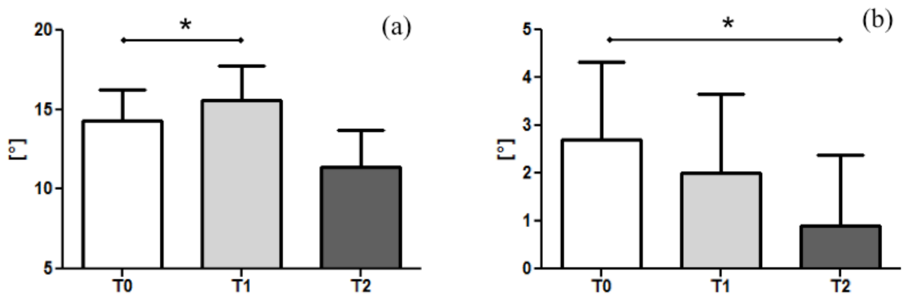

Figure 10 – Spinal Mouse® variations in upright position in Sac/hip (a) and Inclination (b) parameters in NMS group

4. baropodometric analysis (Table 5) CoP X (T0vsT1, $p<0.05$, -97%, Figure 11a), COP distance (T0vsT2, $p<0.05$, -32%, Figure 11b), Average speed (T0vsT2, $p<0.05$, -32%, Figure 11c), LSF (T0vsT1, $p<0.01$,-55%; T0vsT2, $p<0.05$, -53%, Figure 11d) in opened eyes condition;

Stabilometric and baropodometric test in opened eyes conditions in NMS group

Parameters	T0	T1	T2	Anova p value	Dunn's Post Hoc	Effect Size
CoP X	0.7 (0.4)	0.1 (0.8)	0.1 (0.6)	0.007	T0 vs T1 *	0.95
CoP Y	-1.7 (1.2)	-1.6 (1.2)	-1.5 (1.9)	0.61	ns	-
Dev. St. CoP X	1.4 (0.8)	2 (1.3)	1.6 (0.9)	0.60	ns	-
Dev. St. CoP Y	2.2 (0.7)	3.5 (2.4)	3.1 (1.2)	0.13	ns	-
CoP Distance	413 (53)	320 (184)	296 (141)	0.01	T0 vs T2 *	1.27
Ellipse Surface	69 (50)	181 (250)	122 (144)	0.43	ns	-
Distance / Surface	10 (8)	4 (3)	5 (4)	0.001	T0 vs T1 ** T0 vs T2 *	0.87 0.83
Average Speed	7 (1)	6 (3)	5 (2)	0.04	T0 vs T2 *	1.33

Stabilometric and baropodometric test in closed eyes conditions in NMS group

Parameters	T0	T1	T2	Anova p value	Dunn's Post Hoc	Effect Size
CoP X	0.7 (0.4)	0.2 (1.1)	0.2 (0.9)	0.22	ns	-
CoP Y	-1.6 (0.8)	-1.6 (1.2)	-1.0 (2.1)	0.18	ns	-
Dev. St. CoP X	2.1 (1.6)	3.1 (3.2)	2.7 (1.9)	0.08	ns	-
Dev. St. CoP Y	5.0 (3.6)	5.8 (3.1)	4.7 (3.3)	0.31	ns	-
CoP Distance	738 (344)	539 (279)	645 (508)	0.09	ns	-
Ellipse Surface	133 (171)	120 (164)	105 (104)	0.60	ns	-
Distance / Surface	9 (9)	3 (2)	5 (4)	0.09	ns	-
Average Speed	12 (6)	10 (6)	11 (8)	0.53	ns	-

Table 5 – Neuromuscular multiple stimulation group results of stabilometric and baropodometric evaluation in opened and closed eyes conditions. Values are expressed as mean ± SD. * $p<0.05$, ** $p<0.01$ and *** $p<0.001$

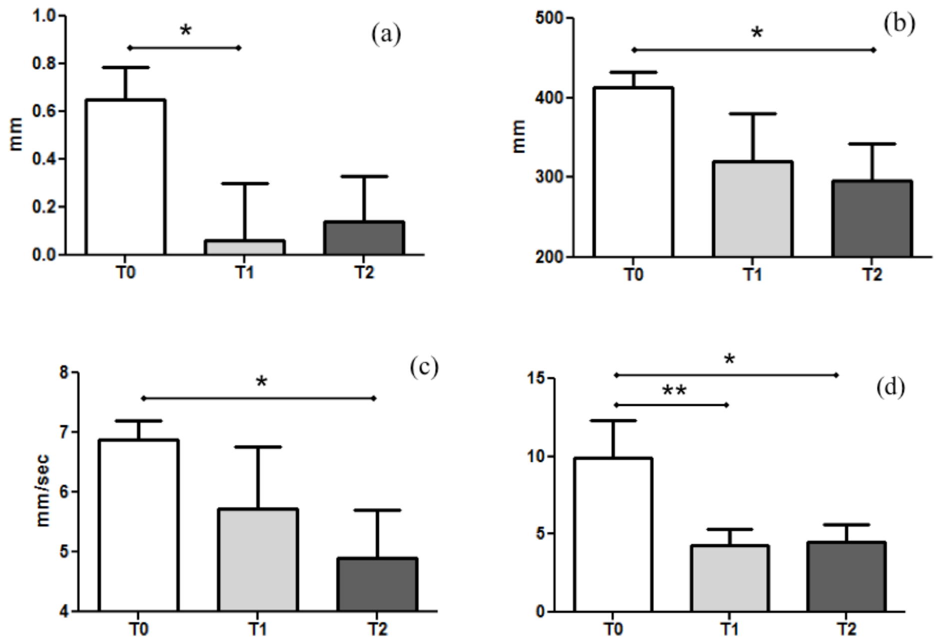

Figure 11 – Baropodometric variation in CoP X (a), CoP distance (b), average speed (c), LSF parameters (d) in NMS group

No significant variations were observed spatio-temporal gait analysis (Table 6).

Spatio-temporal Gait Parameters in NMS group						
Parameters	**T0**	**T1**	**T2**	**Anova p value**	**Dunn's Post Hoc**	**Effect Size**
Cadence (strides/min)	93 (17)	98 (21)	95 (18)	0.36	ns	-
Speed (m/s)	0.9 (0.3)	1.0 (0.4)	0.9 (0.3)	0.83	ns	-
Stride Lenght (m)	1.2 (0.3)	1.1 (0.3)	1.1 (0.2)	0.71	ns	-
Right Step Duration (sec)	1.3 (0.2)	1.2 (0.3)	1.3 (0.2)	0.43	ns	-
Left Step Duration (sec)	1.3 (0.3)	1.2 (0.3)	1.3 (0.3)	0.36	ns	-
Right Stance Duration (% of Gait Cycle)	68 (5)	67 (6)	66 (7)	0.83	ns	-
Left Stance Duration (% of Gait Cycle)	62 (4)	64 (6)	62 (5)	0.36	ns	-
Right Swing Duration (% of Gait Cycle)	32 (5)	33 (6)	33 (8)	0.60	ns	-
Left Swing Duration (% of Gait Cycle)	38 (4)	36 (6)	37 (6)	0.83	ns	-
Double Support Duration Right (% of Gait Cycle)	16 (6)	16 (5)	15 (5)	0.22	ns	-
Double Support Duration Left (% of Gait Cycle)	14 (3)	15 (5)	14 (5)	0.12	ns	-
Right Single Support Duration (% of Gait Cycle)	38 (4)	36 (5)	37 (6)	0.43	ns	-
Left Single Support Duration (% of Gait Cycle)	32 (5)	33 (6)	33 (8)	0.60	ns	-

Table 6 – Neuromuscular multiple stimulation group results of gait analysis. Values are expressed as mean ± SD.
* p<0.05, ** p<0.01 and *** p<0.001

In the Pilates® group protocol determined several improvements in:

1. sit and reach test (T0vsT2,p<0.05, +12%, Table 7, Figure 12);

Pilates® group results						
Parameters	**T0**	**T1**	**T2**	**Anova p value**	**Dunn's Post Hoc**	**Effect Size**
Sit and reach	26 (12)	28 (11)	29 (12)	0.001	T0 vs T2*	0.26
Sit to stand	14 (6)	15 (7)	14 (6)	0.79	ns	-
Right hand grip	24 (6)	26 (6)	24 (5)	0.04	ns	-
Left hand grip	22 (4)	24 (4)	22 (4)	0.04	ns	-

Table 7 – Pilates® group results of flexibility, lower limb strength and hand grip strength. Values are expressed as mean ± SD. * p<0.05, ** p<0.01 and *** p<0.001

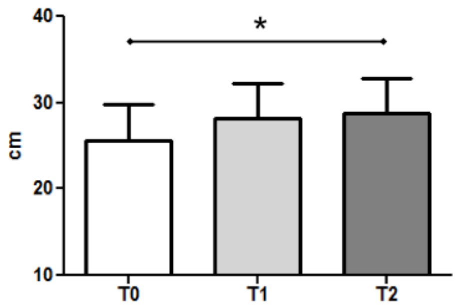

Figure 12 – Sit and reach test variation in Pilates® group

2. Spinal Mouse extension position Incl (T0vsT2, p<0.01, +34%, Table 8, Figure 13).

Parameters	T0	T1	T2	Anova p value	Dunn's Post Hoc	Effect Size
Spinal Mouse® parameters in upright position in Pilates® group						
Sac / Hip	16 (6)	15 (5)	14 (8)	0.79	ns	-
ThSp	49 (8)	50 (7)	52 (8)	0.06	ns	-
LSp	31 (8)	33 (8)	31 (13)	0.28	ns	-
Inclination	2 (4)	1 (4)	1 (4)	0.14	ns	-
Spinal Mouse® parameters in flexion position in Pilates® group						
Parameters	**T0**	**T1**	**T2**	**Anova p value**	**Dunn's Post Hoc**	**Effect Size**
Sac / Hip	74 (13)	77 (15)	78 (14)	0.28	ns	-
ThSp	63 (10)	65 (9)	69 (7)	0.14	ns	-
LSp	18 (10)	19 (9)	18(9)	0.79	ns	-
Inclination	106 (13)	110 (15)	112 (14)	0.04	ns	-
Spinal Mouse® parameters in extension position in Pilates® group						
Parameters	**T0**	**T1**	**T2**	**Anova p value**	**Dunn's Post Hoc**	**Effect Size**
Sac / Hip	5 (9)	1 (8)	4 (13)	0.03	ns	-
ThSp	52 (11)	54 (8)	53 (13)	0.96	ns	-
LSp	39 (9)	38 (9)	37 (10)	0.79	ns	-
Inclination	16 (8)	17 (12)	21 (11)	0.005	T0 vs T1 **	0.55

Table 8 – Pilates® group results of Spinal Mouse® evaluation in upright, flexion and extension position. Values are expressed as mean ± SD. * p<0.05, ** p<0.01 and *** p<0.001

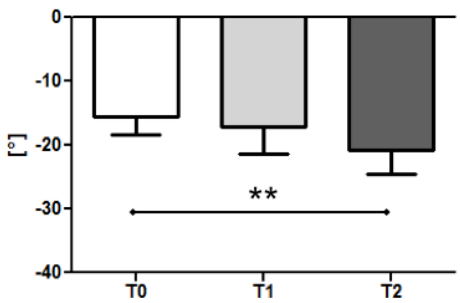

Figure 13 – Spinal Mouse® variation in extension position in Inclination parameter in Pilates® group

3. baropodometric analysis (Table 9) Standard Deviation CoP X (T0vsT2, p<0.01, -50%, Figure 14a), CoP distance (T0vsT2, p<0.05, -70%, Figure 14b), Average speed (T0vsT2, p<0.05, -70%, Figure 14c), Body Barycentre Ellipse surface (T0vsT2, p<0.05, -45%, Figure 14d);

Stabilometric and baropodometric test in opened eyes conditions in Pilates® group						
Parameters	**T0**	**T1**	**T2**	**Anova p value**	**Dunn's Post Hoc**	**Effect Size**
CoP X	0.4 (1.2)	-0.1 (1)	0.1 (1.1)	0.14	ns	-
CoP Y	-1.0 (1.4)	-0.8 (1.7)	-0.8 (1.1)	0.53	ns	-
Dev. St. CoP X	1.9 (1.7)	1.4 (1.3)	1.0 (0.6)	0.005	T0 vs T2 **	0.68
Dev. St. CoP Y	2.6 (0.9)	2.8 (1.5)	2.3 (1.3)	0.23	ns	-
CoP Distance	570 (702)	223 (92)	179 (48)	0.02	T0 vs T2 *	0.86
Ellipse Surface	104 (107)	110 (167)	59 (66)	0.04	T0 vs T2 *	0.52
Distance / Surface	11 (13)	7 (7)	11 (16)	0.23	ns	-
Average Speed	5 (1)	4 (2)	3 (1)	0.02	T0 vs T2 *	2.14

Stabilometric and baropodometric test in closed eyes conditions in Pilates® group						
Parameters	**T0**	**T1**	**T2**	**Anova p value**	**Dunn's Post Hoc**	**Effect Size**
CoP X	0.1 (1.1)	-0.1 (0.9)	0.1 (1.2)	0.23	ns	-
CoP Y	-1.0 (1.1)	-1.3 (1.5)	-0.9 (1.0)	0.53	ns	-
Dev. St. CoP X	1.9 (1.1)	1.3 (1.3)	1.3 (0.8)	0.23	ns	-
Dev. St. CoP Y	4.1 (2.0)	4.2 (2.3)	3.6 (2.5)	0.24	ns	-
CoP Distance	446 (113)	350 (206)	335 (159)	0.28	ns	-
Ellipse Surface	176 (125)	168 (236)	135 (188)	0.14	ns	-
Distance / Surface	8 (13)	9 (13)	8 (10)	0.79	ns	-
Average Speed	7 (2)	6 (3)	6 (3)	0.11	ns	-

Table 9 – Pilates® group results of stabilometric and baropodometric evaluation in opened and closed eyes conditions. Values are expressed as mean ± SD. * p<0.05, ** p<0.01 and *** p<0.001

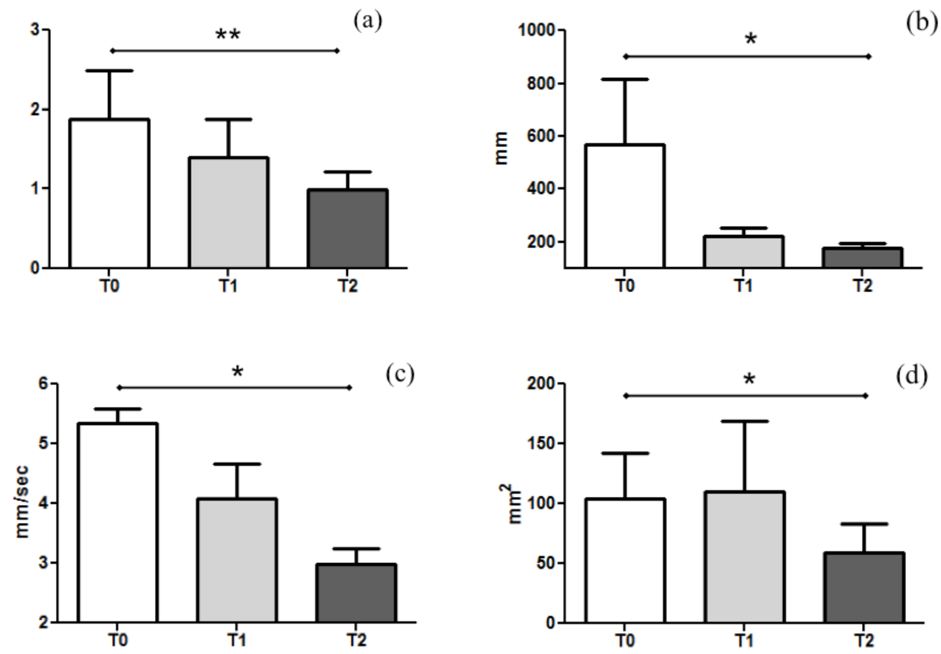

Figure 13 – Baropodometric variation in Dev. St. X (a), CoP distance (b), average speed (c), Ellipse surface (d) in Pilates® group

No significant variations were observed spatio-temporal gait analysis (Table 10).

Spatio-temporal Gait Parameters in Pilates® group						
Parameters	**T0**	**T1**	**T2**	**Anova p value**	**Dunn's Post Hoc**	**Effect Size**
Cadence (strides/min)	104 (15)	107 (16)	107 (17)	0.46	ns	-
Speed (m/s)	1.1 (0.2)	1.1 (0.3)	1.2 (0.3)	0.11	ns	-
Stride Lenght (m)	1.2 (0.2)	1.2 (0.3)	1.3 (0.2)	0.30	ns	-
Right Step Duration (sec)	1.2 (0.2)	1.2 (0.3)	1.1 (0.2)	0.23	ns	-
Left Step Duration (sec)	1.2 (0.2)	1.2 (0.2)	1.0 (0.2)	0.76	ns	-
Right Stance Duration (% of Gait Cycle)	62 (4)	65 (5)	63 (5)	0.75	ns	-
Left Stance Duration (% of Gait Cycle)	63 (6)	62 (5)	64 (7)	0.48	ns	-
Right Swing Duration (% of Gait Cycle)	37 (6)	38 (5)	36 (7)	0.46	ns	-
Left Swing Duration (% of Gait Cycle)	38 (4)	35 (5)	37 (5)	0.76	ns	-
Double Support Duration Right (% of Gait Cycle)	13 (4)	13 (4)	14 (3)	0.76	ns	-
Double Support Duration Left (% of Gait Cycle)	12 (2)	13 (3)	13 (4)	0.48	ns	-
Right Single Support Duration (% of Gait Cycle)	37 (5)	35 (5)	37 (4)	0.60	ns	-
Left Single Support Duration (% of Gait Cycle)	36 (6)	38 (6)	36 (7)	0.61	ns	-

Table 10 – Pilates® group results of gait analysis. Values are expressed as mean ± SD. * p<0.05, ** p<0.01 and *** p<0.001

No statistically significant acute (T0) and chronic (T0vsT2) variation were observed in saliva antioxidant test in both NMS and Pilates® group as showed in Table 11.

	Neuromuscular multiple stimulation group			**Pilates group**		
Parameters	**Pre Test T0**	**Pre Test T0**	**Wilcoxon test p value**	**Pre Test T0**	**Pre Test T0**	**Wilcoxon test p value**
Saliva Antioxidant Test	2226 (977)	2165 (1705)	0.18	1225 (382)	1190 (253)	0.64

	Neuromuscular multiple stimulation group			**Pilates group**		
Parameters	**Pre Test T0**	**Pre Test T2**	**Wilcoxon test p value**	**Pre Test T0**	**Pre Test T2**	**Wilcoxon test p value**
Saliva Antioxidant Test	2226 (977)	1602 (874)	0.79	1225 (382)	1922 (1513)	0.19

Table 11 – Neuromuscular multiple stimulation and Pilates® group results of saliva antioxidant test. Values are expressed as mean ± SD. * $p<0.05$, ** $p<0.01$ and *** $p<0.001$

5. Discussion

This study aims to analyze the effects of physical activities which includes exercises with micro-weight, elastic bands, and those exercises of proprioceptive control, compared with a protocol of exercises performed in accordance with the Pilates® method. As some patients had reported alteration of the symptoms related to the increase in body temperature during exercise, In the physical activity was not regular proposed to MS patients in the past[8,45]. Besides, exercise would not be recommended in order to reduce energy consumption and avoid increased fatigue. Recent scientific evidence[26] points out that there is no correlation between physical activity and the relapse of the disease. Gervasoni et al.[27] showed how exercise can increase the perception of fatigue but without significantly variation in postural control. Patients with high self-efficacy are more predisposed to collaboration and medical care acceptance and to perform physical activity[18]. The benefits of exercise to MS patients do not differ from healthy subjects regarding life quality improving and fatigue managment[18]. The continuous practice of physical activity increases autonomy in activities of daily living (ADL), improves the management of fatigue symptom[46] and reduces the loss of functionality of the cognitive system[17]. However, since multiple sclerosis is a chronic-degenerative autoimmune disease, rehabilitation and exercise protocols focus on maintaining residual capacities and improving quality of life[47].

In this study, the sit and reach test showed a statistically significant increase in the Pilates group between T0 and T2 (+ 12%), in agreement with Van der Linden et al.[37] and Ponzano et al. [48] on the usefulness of this type of activity to increase flexibility. The ability to lengthen the muscles allows to limit the stiffness and avoid a reduction in the range of movement, which occurs in MS, due to weakness and spasticity. In the NMS group there is a tendency to increase significantly the flexibility in the sit and reach test ($p = 0.06$, +11%), which supports the use of the exercises with micro-weight and elastic bands to mainten flexibility.

The difficulties in postural control and balance management, the reduction of trunk stability and the lower efficiency of the core stability are greater in those with MS patients rather than in healthy subjects as highlighted in Freeman et al.[36].

Postural control and stability were assessed with the descriptive centre of pressure (CoP) parameters measured with the use of a stabilometric and baropodometric platform. The results (opened eyes conditions) showed a statistically significant reduction in the NMS group in the Standard Deviation X parameter between T0 and T1 (-97%, ES=0.95) to indicate a reduction of the oscillations of the subjects on the frontal plane. The statistically significant reduction of the CoP distance parameters between T0 and T2 (-32%, ES=1.27) and average speed between T0 and T2 (-32%, ES = 1.33) are additional validation of the increase in postural control by a smaller distance of the CoP and a reduction in the oscillation speeds. Finally, the reduction in LSF parameter between T0 and T1 (-55%, ES=0.87) and between T0 and T2 (-53%, ES = 0.83) highlights the usefulness of the protocol of neuromuscular multiple stimulation exercises to reduce energy for posture control. In the Pilates group similar results are observed with statistically significant (opened eyes conditions) reductions in the Standard Deviation X parameters between T0 and T2 (-50%, ES=0.68), CoP distance between T0 and T2 (-70%, ES=0.86) and average speed between T0 and T2 (-70%, ES = 2.14). In the PG, it is also possible to observe a statistically significant reduction in the Ellipse Surface Body Barycenter between T0 and T2 (-45%, ES=0.52). The reduction in the length of CoP trajectory (CoP distance) and the sampled positions of the center of pressure (Ellipse surface) underlines the increase in the ability of the patients to control the posture in upright position. No significant variation in CoP parameters were observed in both Pilates and neuromuscular multiple stimulation groups in closed eyes conditions.

The positive effects of the exercises using the Pilates® method are reported in Freeman et al.[36] and Gulu-Gunduz et al.[39] in which the results show greater stability of the subjects after a protocol of exercises for the core stability. The results related to the balance control in our study are in agreement with the aforementioned studies. The effect size value of the average speed parameter in the PG supports the validity and effectiveness of the Pilates® method as a strategy for increasing stability in MS subjects. Moreover, the significant reduction of the LSF parameter, resulting from the relationship between the CoP distance and the surface area, highlights how the combined exercise proposed in NMS group increases the efficacy of postural control with less energy use and reducing the fatigue to keep the upright position.

None of the previous studies on the effects of the Pilates® method on the assessment of balance control[36,39] used the descriptive parameters of the CoP. The study of the reduction in the oscillations on the frontal plane[40], is an indicator of the decrease of the risk of falling. The results of our study, which show that both groups have increased frontal stability and reduced the speed of CoP movements, allow us to confirm the usefulness of both the proposed activities for reducing the risk of falling.

According to previous research, the percentage differences comparison supports the positive effects of the Pilates® method on balance control. However, the neuromuscular multiple stimulation activity showed an increase in balance control in the sagittal plane with a 97% reduction of CoP X parameter. Dev. St. CoP X parameter was reduced of 50% in GP. The Pilates® method is better to reduce the CoP distance parameter compared to repeated neuromuscular multiple stimulation. Indeed, we observed a reduction of 70% in the GP and 32% in the NMS group. The same situation was observed in the averaged swing speed , where the GP shows a reduction of 70% compared to 32% of the NMS group. Only in the GP the ellipse surface was significantly reduced with a decrease of 45%. The significant decrease of the distance surface ratio (LSF) was recorded in 55% (T0vsT1) and 53% (T0vsT2) respectively. This data validated the positive effects of multiple neuromuscular stimulation on postural control.

This result underline the positive effects of the exercises proposed in this study. Micro-weight, elastic band and unstable surfaces are able to reduce the amount of energy required for postural control in subjects with MS. Moreover, in according to previous research, the core stability exercise with Pilates® method decrease the swing number and their speed.

The increase in postural control is supported by the results observed in the evaluation of the rachis morphology with the use of Spinal Mouse®. In NMS group we observe a significant reduction of the Sac/hip parameter in the erect position between T0 and T1 (-20%, ES=0.32), which highlights a lower inclination of the sacrum on the sagittal plane. Furthemore, the reduction of the inclination (Incl) in the upright position between T0 and T2 (-67%, ES=0.42) demonstrates how the protocol of neuromuscular multiple stimulation exercises is useful for controlling the body inclination. Previous studies[41,42] underline how the increase in the inclination of the column is a determining factor for the risk of falling. The results of this study validate the positive effects observed in the NMS group on the reduction in predictive factors and the risk of falling. In the PG, it is possible to observe a significant increase between T0 and T2 (+ 34%, ES=0.55) in the mobility of the spine during the extension on the sagittal plane. Kasukawa et al.[42] showed how there is reduced mobility of the spine in subjects with a high risk of falling. The results of our study confirm the benefits of the Pilates® method for increasing joint mobility and preventing the risk of falling.

The reduction in strength and perceived fatigue are two factors, which diminish life quality and autonomy in activities of daily living[49]. In this study, the protocol of neuromuscular multiple stimulation exercises showed to be effective for improving the strength of the lower limbs as evidenced by the significant increase in the sit to stand test between T0 and T2 (+ 13%, ES=0.60). Moreover, in NMS group significant increases in the strength of the right hand were observed (T0 vs T1, + 16%, ES=0.29) and left (T0 vs T1, + 20%, ES=0.43) to confirm the positive effects of this activity. No variation was observed in the Pilates group, for which no specific exercises for hand flexors were proposed and no tools were used. The results observed in the NMS group highlight, after 16-week training, an increase in the strength of both the upper and lower limbs in subjects with SMRR. These results are in agreement with previous studies[29,31,34] which demonstrated the positive effects of training with the use of elastic bands and progressive resistance training on the increase of the functional capacity, on the reduction of the perception of the fatigue and on a lower negative impact of the disease on the daily life.

Walking is influenced by numerous factors such as strength of the lower limbs, body balance control and spasticity[3,5]. The evaluation of the spatio-temporal gait parameters did not show any statistically significant variation in both groups. This result shows that there has been no reduction in functionality in subjects with consequent negative effects on the gait cycle and underlines the validity of the proposed activities to contain the reduction of residual motor abilities. The same situation was observed in the oxidative stress evaluation with the use of saliva antioxidant test. There were no significant changes in the T0 evaluation before and after the test session and no difference in the comparison between T0 and T2. In the first case the results allow us to observe how the proposed functional assessment battery test does not have negative effects on MS patients. In the second case, there is no change in the level of antioxidants following the 16-week of physical activity. Not significant acute variation in oxidative stress were observed before and after the test session. The results allow us to highlight the non-invasiveness and the feasibility of the functional evaluation protocol proposed in subjects with multiple sclerosis.

A similar situation was observed in chronic analysis, before and after 16-weeks of physical activity. In both groups, not significant variations were observed in oxidative stress. These results indicate that both interventions did not increase oxidation processes and inflammatory conditions. The concentrations of oxidative stress markers in saliva are influenced by circadian rhythms and the presence of oral diseases. Factors such as food intake, the use of chewing gum and the control of antioxidant vitamins use have been reduced as much as possible[20]. However, the variability of the clinical status and the different pharmacological treatment of the subjects, which may have influenced the measurement of oxidative stress, are confounding factors. Despite the positive results observed, two limitations can be highlighted in this study. Firstly, the small number of subjects in the sample group did not give the possibility to analyze the results subdividing the subjects into subgroups according to the EDSS level. Secondly, the differences between the evolution of the disease and the variability of EDSS have reduced the homogeneity of the sample group may have influenced the observed minor differences between the groups.

6. Conclusions

The results of this study provide valid indicators of on the positive effects of physical activity in patients with RRMS. Firstly, neuromuscular multiple stimulation with the micro-weight and elastic bands has proved useful for increasing postural control and strength of the upper and lower limbs. Secondly, the Pilates® protocol contributed to the improvement flexibility and postural control. The practical consequences developed from this study allow us to hypothesize an increase in autonomy in activities of daily living with the practice of physical activity with the two different training methods studied.

Both physical activities improve functional capacity and reduce the risk of falling in subjects with RRMS. The increase in the a postural control analyzed with the CoP evaluation parameters supports and promotes the use of this type of evaluation with an objective test whose results give us indications on the risk of falling users. Also, strength training can be considered a valuable means of improving life quality in subjects with RRMS with mild to moderate EDSS levels, as it increases muscle strength and reduces physical fatigue. The results observed regarding the positive effects of both activities allow us to confirm the validity of the two different physical activity proposed for patients with RRMS. In the future, it might be interesting to study the effects of a combined protocol of motor activity with exercises in order to increase strength, postural control, along with the Pilates® method and proposed in the same training session.

7. References

1. Gelfand JM. Multiple sclerosis: diagnosis, differential diagnosis, and clinical presentation. Handb Clin Neurol. 2014;122:269-90
2. Meyer-Moock S, Feng YS, Maeurer M, Dippel FW, Kohlmann T. Systematic literature review and validity evaluation of the Expanded Disability Status Scale (EDSS) and the Multiple Sclerosis Functional Composite (MSFC) in patients with multiple sclerosis. BMC Neurol. 2014 Mar 25;14:58
3. Kerns RD, Kassirer M, Otis J. Pain in multiple sclerosis: a biopsychosocial perspective. J Rehabil Res Dev. 2002 Mar-Apr;39(2):225-32
4. Kasser SL, Jacobs JV, Foley JT, Cardinal BJ, Maddalozzo GF. A prospective evaluation of balance, gait, and strength to predict falling in women with multiple sclerosis. Arch Phys Med Rehabil. 2011 Nov;92(11):1840-6
5. Larson RD, McCully KK, Larson DJ, Pryor WM, White LJ. Bilateral differences in lower-limb performance in individuals with multiple sclerosis. J Rehabil Res Dev. 2013;50(2):215-22
6. Chung LH, Remelius JG, Van Emmerik RE, Kent-Braun JA. Leg power asymmetry and postural control in women with multiple sclerosis. Med Sci Sports Exerc. 2008 Oct;40(10):1717-24
7. Soyuer F, Mirza M, Erkorkmaz U. Balance performance in three forms of multiple sclerosis. Neurol Res. 2006 Jul;28(5):555-62
8. Skjerbæk AG, Møller AB, Jensen E, Vissing K, Sørensen H, Nybo L, Stenager E, Dalgas U.Heat sensitive persons with multiple sclerosis are more tolerant to resistance exercise than to endurance exercise. Mult Scler. 2013 Jun;19(7):932-40
9. White AT, Wilson TE, Davis SL, Petajan JH. Effect of precooling on physical performance in multiple sclerosis. Mult Scler. 2000 Jun;6(3):176-80
10. Grahn DA, Murray JV, Heller HC. Cooling via one hand improves physical performance in heat-sensitive individuals with multiple sclerosis: a preliminary study. BMC Neurol. 2008 May 12;8:14
11. Weuve J, Kang JH, Manson JE, Breteler MM, Ware JH, Grodstein F. Physical activity, including walking, and cognitive function in older women. JAMA. 2004 Sep 22;292(12):1454-61.
12. Smith PJ, Blumenthal JA, Hoffman BM, Cooper H, Strauman TA, Welsh-Bohmer K, Browndyke JN, Sherwood A. Aerobic exercise and neurocognitive performance: a meta-analytic review of randomized controlled trials. Psychosom Med. 2010 Apr;72(3):239-52

13. Benedict RH, Bruce JM, Dwyer MG, Abdelrahman N, Hussein S, Weinstock-Guttman B, Garg N, Munschauer F, Zivadinov R. Neocortical atrophy, third ventricular width, and cognitive dysfunction in multiple sclerosis. Arch Neurol. 2006 Sep;63(9):1301-6
14. Benedict RH. Integrating cognitive function screening and assessment into the routine care of multiple sclerosis patients. CNS Spectr. 2005 May;10(5):384-91
15. Calabrese M, Rinaldi F, Mattisi I, Grossi P, Favaretto A, Atzori M, Bernardi V, Barachino L, Romualdi C, Rinaldi L, Perini P, Gallo P. Widespread cortical thinning characterizes patients with MS with mild cognitive impairment. Neurology. 2010 Jan 26;74(4):321-8
16. Kramer AF, Erickson KI. Capitalizing on cortical plasticity: influence of physical activity on cognition and brain function. Trends Cogn Sci. 2007 Aug;11(8):342-8
17. Motl RW, Cadavid D, Sandroff BM, Pilutti LA, Pula JH, Benedict RH. Cognitive processing speed has minimal influence on the construct validity of Multiple Sclerosis Walking Scale-12 scores. J Neurol Sci. 2013 Dec 15;335(1-2):169-73
18. Fjeldstad C, Pardo G. Self-efficacy, Physical Activity and QOL in People with MS. J Neurol Neurophysiol 2014 (5):194
19. Van Horssen J, Witte ME, Schreibelt G, de Vries HE. Radical changes in multiple sclerosis pathogenesis. Biochim Biophys Acta. 2011 Feb;1812(2):141-50
20. Karlík M, Valkovič P, Hančinová V, Krížová L, Tóthová Ľ, Celec P. Markers of oxidative stress in plasma and saliva in patients with multiple sclerosis. Clin Biochem. 2015 Jan;48(1-2):24-8
21. Flensner G, Landtblom AM, Söderhamn O, Ek AC. Work capacity and health-related quality of life among individuals with multiple sclerosis reduced by fatigue: a cross-sectional study. BMC Public Health. 2013 Mar 15;13:224
22. Skurvydas A, Brazaitis M, Andrejeva J, Mickeviciene D, Streckis V. The effect of multiple sclerosis and gender on central and peripheral fatigue during 2-min MVC. Clin Neurophysiol. 2011 Apr;122(4):767-76
23. Hameau S, Bensmail D, Roche N, Zory R. Adaptations of fatigue and fatigability after a short intensive, combined rehabilitation program in patients with multiple sclerosis. J Rehabil Med. 2017 Oct 5
24. Andreasen AK, Stenager E, Dalgas U. The effect of exercise therapy on fatigue in multiple sclerosis. Mult Scler. 2011 Sep;17(9):1041-54
25. Motl RW, Pilutti LA. The benefits of exercise training in multiple sclerosis. Nat Rev Neurol. 2012 Sep;8(9):487-97

26. Tallner A, Waschbisch A, Wenny I, Schwab S, Hentschke C, Pfeifer K, Mäurer M. Multiple sclerosis relapses are not associated with exercise. Mult Scler. 2012 Feb;18(2):232-5
27. Gervasoni E, Cattaneo D, Montesano A, Jonsdottir J. Effects of fatigue on balance and mobility in subjects with multiple sclerosis: a brief report. ISRN Neurol. 2012; 2012: 316097
28. Aagaard P. Training-induced changes in neural function. Exerc Sport Sci Rev. 2003 Apr;31(2):61-7
29. Taylor NF, Dodd KJ, Prasad D, Denisenko S. Progressive resistance exercise for people with multiple sclerosis. Disabil Rehabil. 2006 Sep 30;28(18):1119-26
30. De Souza-Teixeira F, Costilla S, Ayán C, García-López D, González-Gallego J, de Paz JA. Effects of resistance training in multiple sclerosis. Int J Sports Med. 2009 Apr;30(4):245-50
31. Kjølhede T, Vissing K, de Place L, Pedersen BG, Ringgaard S, Stenager E, Petersen T, Dalgas U. Neuromuscular adaptations to long-term progressive resistance training translates to improved functional capacity for people with multiple sclerosis and is maintained at follow-up. Mult Scler. 2015 Apr;21(5):599-611
32. Dancewicz TM, Krebs DE, McGibbon CA. Lower-limb extensor power and lifting characteristics in disabled elders. J Rehabil Res Dev; 2003 Jul-Aug;40(4):337-47
33. Chen KM, Li CH, Chang YH, Huang HT, Cheng YY. An elastic band exercise program for older adults using wheelchairs in Taiwan nursing homes: A cluster randomized trial. Int J Nurs Stud. 2015 Jan;52(1):30-8
34. De Souza Teixeira F, Gonzalo RF, Murua JAH, Bresciani G, Gutierrez AJ, De Paz Fernandez JA. Elastic Band Training for Multiple Sclerosis Patients: a Pilot Study. Journal Of Physical Therapy Science, 2011, Vol.23(2):307-311
35. Silfies SP, Ebaugh D, Pontillo M, Butowicz CM. Critical review of the impact of core stability on upper extremity athletic injury and performance. Braz J Phys Ther. 2015 Sep-Oct;19(5):360-8
36. Freeman J, Fox E, Gear M, Hough A. Pilates based core stability training in ambulant individuals with multiple sclerosis: protocol for a multi-centre randomised controlled trial. BMC Neurol. 2012 Apr 5;12:19

37. Van der Linden ML, Bulley C, Geneen LJ, Hooper JE, Cowan P, Mercer TH. Pilates for people with multiple sclerosis who use a wheelchair: feasibility, efficacy and participant experiences. Disabil Rehabil. 2014;36(11):932-9
38. Marandi SM, Nejad VS, Shanazari Z, Zolaktaf V. A Comparison of 12 Weeks of Pilates and Aquatic Training on the Dynamic Balance of Women with Mulitple Sclerosis. Int J Prev Med. 2013 Apr; 4(Suppl 1): S110–S117
39. Guclu-Gunduz A, Citaker S, Irkec C, Nazliel B, Batur-Caglayan HZ. The effects of pilates on balance, mobility and strength in patients with multiple sclerosis. NeuroRehabilitation. 2014;34(2):337-42
40. Bellafiore M, Battaglia G, Bianco A, Paoli A, Farina F, Palma A. Improved postural control after dynamic balance training in older overweight women. Aging Clin Exp Res. 2011 Oct-Dec;23(5-6):378-85
41. Ishikawa Y, Miyakoshi N, Kasukawa Y, Hongo M, Shimada Y. Spinal curvature and postural balance in patients with osteoporosis. Osteoporos Int. 2009 Dec;20(12):2049-53
42. Kasukawa Y, Miyakoshi N, Hongo M, Ishikawa Y, Noguchi H, Kamo K, Sasaki H, Murata K, Shimada Y. Relationships between falls, spinal curvature, spinal mobility and back extensor strength in elderly people. J Bone Miner Metab. 2010;28(1):82-7
43. Lord SR, Murray SM, Chapman K, Munro B, Tiedemann A. Sit-to-stand performance depends on sensation, speed, balance, and psychological status in addition to strength in older people. J Gerontol A Biol Sci Med Sci. 2002 Aug;57(8):M539-43
44. Hopkins WG, Marshall SW, Batterham AM, Hanin J. Progressive statistics for studies in sports medicine and exercise science. Med Sci Sports Exerc. 2009 Jan;41(1):3-13
45. Dalgas U, Stenager E, Ingemann-Hansen T. Multiple sclerosis and physical exercise: recommendations for the application of resistance, endurance and combined training. Mult Scler. 2008 Jan;14(1):35-53. Epub 2007 Sep 19
46. Motl RW, Gosney JL. Effect of exercise training on quality of life in multiple sclerosis: a meta-analysis. Mult Scler. 2008 Jan;14(1):129-35
47. Octavia JR, Coninx K. Adaptive personalized training games for individual and collaborative rehabilitation of people with multiple sclerosis. Biomed Res Int. 2014; 2014: 345728
48. Ponzano M, Beratto L, Mazza C, Di Tommaso S, Abate Daga F, Allois R, Gollin M. Benefits of Static Stretching, Pliates® and Elastic Bands Resistance Training on Patients with Relapsing-Remitting Multiple Sclerosis: A Longitudinal Study. J Neurol Neurophysiol 2017, 8:4

49. Gutierrez GM, Chow JW, Tillman MD, McCoy SC, Castellano V, White LJ. Resistance training improves gait kinematics in persons with multiple sclerosis. Arch Phys Med Rehabil. 2005 Sep;86(9):1824-9

8. Appendix

Reliability of measurments of the spine in the frontal plane – article submitted to European Spine Journal

RELIABILITY OF MEASURMENTS OF THE SPINE IN THE FRONTAL PLANE

Piancino[1] MG, Alessandria[2] M, Beratto[2] L, Gollin[3] M

[1]Department of Surgical Sciences; Orthodontic Division, Dental School, University of Turin, Italy

[2]PhDc in Experimental Medicine and Therapy, University of Turin, Italy

[3] Department of Clinical and Biological Sciences; Motor Science Research Center, University School of Motor & Sport Sciences, University of Turin, Italy

Introduction

The evaluation of morphological parameters of the spine and its joint range, is of fundamental importance for the formulation of a correct diagnosis or for the recognition of the structural changes in a therapeutic path.

The assessment of the spinal curvature is generally made by radiographic investigations but the need to reduce stochastic damage, due to radiation exposure, forced health professionals to find reliability skin device to evaluate the progressions in treatment of spinal disorder.

The tests routinely used in the clinic for the evaluation of the spine, are reproducible if performed in the sagittal plane but the reproducibility decreases considerably in the frontal plane[1]. Several evaluation methods are used for the clinical evaluation as inclinometers[2,3], goniometers[4], movement analysis system with reflective markers[5], source of pulsed electromagnetic waves taken over by a sensor attached to the skin and potentiometers that allow a 3-dimensional motion survaillance[6]. The last one can present drawbacks related to the preparation of the skin for the apposition of sensor, shift of the skin from the underlying tissues during movement of the spine or the limited possibility to evaluate only one district of the spine (thoracic or lumbar)[7].

Regarding the functional evaluation, the most frequently used parameter to identify the functional efficiency of the spine are obtained from the ROM test (Range of Motion)[8,9,10] even if, the repeatability is still a controversial issue[11].

In this regard it is of clinical importance the validation of the measurements in the frontal plane. One of the tools used in clinical and rehabilitative field is the SpinalMouse®. Previous studies[7,12,13] have shown a good repeatability of the measurements on the sagittal plane. Ripani et al.[14] only have analyzed two parameters measured with the Spinal Mouse® (thoracic and lumbar spine) on the frontal plane in lateral flexion with measurements performed by 2 operators in 2 different days on 26 subjects. The ICC values resulted significant, between 0.879 and 0.995. The protocol of the Spinal Mouse® gives the data on the frontal plane also. These data have never been evaluated nor described in the scientific literature, probably due to the high variability and the difficulty of the study. The validation of the data in the frontal plane is of importance for the diagnosis and the therapeutical choice in the clinical practice.

The aim of this study was to verify the repeatability on the frontal plane of all values provided by the Spinal Mouse®, through the use of a dedicated tool to standardize the recording protocol.

Materials and methods

Sample group

Fifteen generally healthy subjects were recruited (12 males, 3 females; age 27±2 years, weight 73±7 kg, height 176±3 m, BMI: 23,4±2,2 kg/m^2). All subjects were free of symptoms of the spine in the two weeks before and during tests and none had dysmorphic features of the spine in the frontal and sagittal plane. The volunteers were informed about the aims and procedures of the study and signed as informed consent to participate.

Equipment

The measurements of the spine were performed with the use of the Spinal Mouse® (Idiag, Volkerswill, Switzerland), a device that allows a computer assisted analysis of the curves and the spinal mobility. It has a wireless communication system with the PC and an interface that allows the global assessment of the spine in the following parameters: length (mm), inclination (degrees), upright position compared to optimal vertical, right and left flexion on the frontal plane, forward flexion and extension (degrees). The parameters described, are provided for the dorsal, lumbar and sacral districts. The Spinal Mouse® has a sampling frequency of 150 Hz.

To standardize the recording protocol and to obtain reproducible data in the frontal plane with the Spinal Mouse®, a platform was built specifically as a reference for the patient during the flexion on the right and left sides to improve the reliability. This platform has a wooden base the size of 96x53 cm. To 35 cm from the long side of the front part of the platform, has been inserted a rail, which allows the sliding of two centimeter rods in aluminium height 84.5 cm and the housing of two sliding footrests, made of wood, the size of 14,5x40 cm (Fig. 1). On the footrests 4 diagonal lines were drawn with an open angle of 30° toward the forward[16].

Figure 1 - Specific instrument used to standardize the protocol test during recording acquisition with Spinal Mouse® in frontal plane

To evaluate the variability related to the skills of the operator two experienced operators were recruited, one right-handed and one left-handed, for the recording of the measurements. The spinous processes of the vertebrae from C7 to S2 were marked with the dermographic pencil on the patient's skin along the spine. Subsequently the subjects were asked to get on the footrests of the platform by placing the 2nd toe and the middle part of the heel on the reference line drawn on the platform. In this way, between the feet was formed an angle opened of 30° forward.

To standardize the width of the lower limbs, the subjects were asked to bring near their feet until the footrests were joined together; at this point the rods were positioned in contact with the trochanteric region of the subjects and the screw were tightening. After this operation the subjects were asked to open their feet and lower limbs until this reached the contact with the rods previously fixed. This position was maintained for all tests (Figure 2).

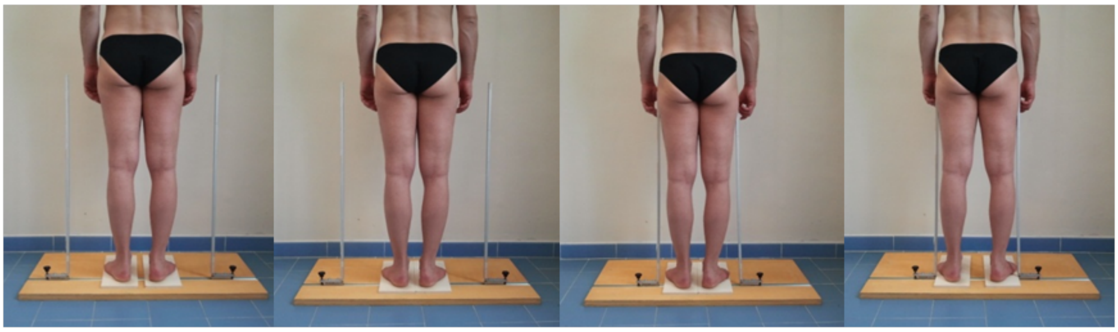

Figure 2 - Positioning sequence on the specific instrument for evaluation test

The first evaluation consisted in measuring the maximum lateral flexion of the trunk with. Then, the subjects were asked to slide the middle finger on the rods, at the maximum excursion. The operator measured the distance between the middle finger of the subjects and the platform and reported the measurement on an excel spreadsheet.

Measurement protocol

At this point we begin the execution of the test with the Spinal Mouse®. Each test were performed as follow:

1. without rods (F): the subjects performed lateral flexion of the trunk from a relaxed position with their arms by their sides and gaze at a point at eye level;
2. with rods and fixed lateral flexion (FXT): the subjects were asked to flex the trunk laterally up to touch with the middle finger the rigid plate held in place by the operator on the measurement previously reached;
3. with rods (FT): the subjects were asked to flex the trunk laterally up to maximum excursion.

Right-handed and left-handed operators performed each test consecutively. Each test (1. without rods; 2. with rods; 3. with rods) was repeated three times with 1 hour between trials in 3 different days. For each of the three tests, the operator carried out the measurements in upright position, right lateral flexion and left lateral flexion.

At the end of the tests the operator erased the signs on the spinous processes before the second operator resumed the same procedure with the same subject.

Statistical analysis

Data were expressed as mean and standard deviation. The intraclass correlation coefficient (ICC) was used to describe reliability. The ICC values regarding each measured parameter were computed for both the operators in the two experimental conditions. The ICC values were interpreted in accordance with the following criteria: values between 80% and 100% represent excellent reliability; values between 60% and 80% represent a good reliability and values lower than 60% represent a poor reliability[17].

Results

The results of 3 trials repeated 3 times in one week, with and without instrument of two operators, one right-handed ad one left-handed are presented in Tables 1 and 2.

The results showed a good reliability of right and left inclination, right and left lateral bending of the thorax spine recorded without instrument and an excellent reliability of the same parameters with instrument. The length of the tracing of right and left lateral bending and upright position was excellent with and without the instrument.

TEST RESULTS

	ICC				ICC		
	Without Instrument				With Instrument		
	Lateral bending Left	Uprigth position	Lateral bending right		Lateral bending Left	Uprigth position	Lateral bending right
Sac / Hip	38	37	54	**Sac / Hip**	51	22	47
ThSp	64 *	27	78 *	**ThSp**	80 **	33	81 **
LSp	46	26	77 *	**LSp**	54	21	70 *
Inclination	78 *	26	79 *	**Inclination**	85 **	34	83 **
Length	85 **	90 **	85 **	**Length**	88 **	90 **	86 **

Table 1 – ICC results right handed operator **excellent reliability, * good reliability

TEST RESULTS

	ICC				ICC		
	Without Instrument				With Instrument		
	Lateral bending Left	Uprigth position	Lateral bending right		Lateral bending Left	Uprigth position	Lateral bending right
Sac / Hip	49	34	24	**Sac / Hip**	44	26	20
ThSp	57	7	63 *	**ThSp**	64 *	9	68 *
LSp	46	32	59	**LSp**	46	28	55
Inclination	82 **	14	71 *	**Inclination**	83 **	24	82 **
Length	62 *	72 *	66 *	**Length**	65 *	70 *	75 *

Table 2 –ICC results left handed operator

Discussion

The aim of this study was to verify the reliability of all parameters measurable with the Spinal Mouse in the frontal plane with and without the use of an instrument to standardize and register the different phases of the assessment. Previous studies validated the Spinal Mouse recording in sagittal plane[7,13,14] but there are not studies evaluating all the parameters in the frontal plane by means of Spinal Mouse®[15]. The originality of this research lies in the utilization of an instrument to standardize the protocol of data acquisition.

The measurements were recorded 3 times in the same day and repeated in 3 different days by two different operators, one right-handed and one left-handed. The results highlighted the reliability of the measurements for the dorsal rachis parameters in the right and the left lateral bending (ThSp), the right and left inclination (Inc) and for the length of the tracings right, left and upright position.

The lumbar parameter (LSp) did not showed any reliability in all the conditions and the sacral parameter (Sac / Hip) showed a poor reliability.

The use of the specific instrument improved the ICC values regarding the parameters describe, optimizing the standardization of the protocol and allowing more reliable assessments. It is intriguing to underline the high level of reliability in the frontal plane exclusively for the lateral bending and not for the upright position.

This result could be due to the instability of the Spinal Mouse device during it sliding over the spinous processes. Moreover, it is difficult to standardize precisely the rachis posture in the upright position. The poor reliability of the sac/hip parameter could have been caused by the different anatomy of the sacrum with reference to the rest of the rachis and, hence, to the different type of movement obtained.

The high level of reliability during bending, despite the non-reliability in the upright position, is a very important data for the clinical evaluation of the postural and functional features of the rachis. Indeed, reliable results regarding the symmetry of lateral bending, based on trustworthy anatomic landmarks avoiding cutaneous landmarks, are important diagnostic data to evaluate rachis functionality. Asymmetry of lateral bending can be caused by muscular incoordination and asymmetrical function between sides. Validated instruments to provide functional information regarding rachis have never been describe in literature and are not available in the every day practice being the functional diagnosis based on subjective, non objectified evaluation.

Conclusions

The results of this study showed the reliability of the parameters in the frontal plane measured by means of Spinal Mouse, in particular with reference to lateral bending. The clinical meaning of this data refers to the diagnosis of symmetries and asymmetries concerning the functionality of the rachis assessed objectively by means of a standardized protocol.

References

1. Essendrop M, Maul I, Laubli T, Riihimaki H, Schibye B (2002) Measures of low back function: a review of reproducibility studies. Clin Biomech 17: 235–249
2. Mayer TG, Kondraske G, Beals SB, Gatchel RJ (1997) Spinal range of motion. Accuracy and sources of error with inclinometric measurement. Spine 22:1976–1984
3. Ng JK, Kippers V, Richardson CA, Parnianpour M (2001) Range of motion and lordosis of the lumbar spine: reliability of measurement and normative values. Spine 26:53–60
4. Portek I, Pearcy MJ, Reader GP, Mowat AG (1983) Correlation between radiographic and clinical measurement of lumbar spine movement. Br J Rheumatol 22:197–205
5. Chiou WK, Lee YH, Chen WJ, Lin YH (1996) A non invasive protocol for the determination of lumbar spine mobility. Clin Biomech 11:474–480
6. Mannion A, Troke M (1999) A comparison of two motion analysis devices used in the measurement of lumbar spinal mobility. Clin Biomech 14:612–619
7. Mannion AF, Knecht K, Balaban G, Dvorak J, Grob D (2004) A new skin-surface device for measuring the curvature and global and segmental ranges of motion of the spine: reliability of measurements and comparison with data reviewed from the literature. Eur Spine J. 13(2):122-36.
8. Miyakoshi N, Hongo M, Maekawa S, Ishikawa Y, Shimada Y, Okada K, Itoi E (2005) Factors related to spinal mobility in patients with postmenopausal osteoporosis. Osteoporos Int.;16(12):1871-4.
9. Goodsell M, Lee M, Latimer J (2000) Short-term effects of lumbar posteroanterior mobilization in individuals with low-back pain. J Manipulative Physiol Ther 23:332–342.

10. Hernandez-Reif M, Field T, Krasnegor J, Theakston H (2001) Lower back pain is reduced and range of motion increate after massage therapy. Int J Neurosci 106:131–145.
11. Mannion AF, Dvorak J, Müntener M, Grob D (2005) A prospective study of the interrelationship between subjective and objective measures of disability before and 2 months after lumbar decompression surgery for disc herniation. Eur Spine J;14(5):454-65
12. R. B. Post, V. J. M. Leferink (2004) Spinal mobility: sagittal range of motion measured with the SpinalMouse, a new non-invasive device. Arch Orthop Trauma Surg 124 : 187–192.
13. E. Kellis, g. Adamou, g. Tzilios, m. Emmanouilidou, Reliability of spinal range of motion in healthy boys using a skin-surface device, J Manipulative Physiol Ther. 2008 Oct;31(8):570-6
14. M. Ripani, A. Di Cesare, A. Giombini, L. Agnello, F. Fagnani, F. Pigozzi, Spinal curvature: comparison of frontal measurements with the Spinal Mouse and radiographic assessment, J Sports Med Phys Fitness 2008; 48: 488-94
15. Agostini V, Chiaramello E, Canavese L, Bredariol C, Knaflitz M (2013) Postural sway in volleyball players. Hum Mov Sci 32(3):445-56
16. Rainoldi A, Galardi G, Maderna L, Comi G, Lo Conte L, Merletti R (1999) Repeatability of surface EMG variables during voluntary isometric contractions of the biceps brachii muscle. J Electromyogr Kinesiol 9(2): 105-19