

**DIPARTIMENTO RIABILITAZIONE MALATTIA DI PARKINSON E DISTURBI DEL MOVIMENTO
RESPONSABILE: Dr Frazzitta Giuseppe**

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**To the local Scientific Committee and Institutional Review Board of the ‘Moriggia-Pelascini’
Hospital, Gravedona ed Uniti, Como.**

Proposed Study: effectiveness of an intensive, aerobic and multidisciplinary rehabilitation treatment and evaluation of the contribution of Lokomat® for the rehabilitation of patients suffering from Progressive Supranuclear Palsy.

Principal Investigator: Giuseppe Frazzitta, MD – Dipartimento di Neuroriabilitazione Malattia di Parkinson, Disturbi del Movimento e Gravi Cerebrolesioni, Ospedale Generale di Zona Moriggia-Pelascini, Gravedona ed Uniti - CO.

Introduction and rationale of the study

Progressive Supranuclear Palsy (PSP) (also known as *Steele-Richardson-Olszewski* Syndrome) is a neurodegenerative disorder first described in 1964. PSP shares different neuropathological and neurophysiological aspects in common with Parkinson’s Disease (PD) and some data provide insight into a common deficit in both pathologies. A biochemical alteration in the tau protein, resulting in neurodegeneration and gliosis in the basal ganglia, brainstem, prefrontal cortex and cerebellum, is the neuropathological hallmark of PSP. The principal clinical features of PSP are:

- Early postural instability with recurrent falls (principally backwards);
- Visual dysfunctions (vertical supranuclear gaze palsy);
- Neuropsychological deficits;

After about 3.9 years from onset of the disturbances, the clinical picture becomes particularly distinctive. To date, there are no effective medical or surgical treatments for this disease. Patients rapidly become disabled and death generally occurs after about 6-7 years from the onset of the disorder.

Literature data support the efficacy of *goal-based*, aerobic, intensive and multidisciplinary rehabilitation treatments for PD patients. Nevertheless, data about the effectiveness of these physical approaches in PSP patients are not consistent and basic questions remain to clarify. As a matter of fact, the severe gait and

balance disturbances, together with the high risk of falls, limit the design of specific rehabilitation protocols for PSP patients.

Gait is heavily impaired in PSP and causes imbalance: while walking the base of support is augmented, there is an important trunk retropulsion, posturo-kinetic instability and loss of the physiological postural reactive reflexes.

Given these premises, we hypothesize that the use of a robotic device such as Lokomat® could positively intervene on the typical gait and balance disturbances of PSP. Lokomat® is a driven-gait orthosis (gait robot) that allows gait by simulating physiological stride patterns and inducing a muscle coordination reflecting human walking. This robotic device is connected to a computer: the operator can set the gait parameters driven by the robotic orthosis (speed, stride length, range of motion of the knee and hips) on the basis of the clinical feature of each patient. Patients, in order to “actively” interact with the passive robot-driven movements, could use visual feedbacks provided by the computer. Therefore, it is arguable that Lokomat® could be a valid support for the rehabilitation of PSP patients. Anyhow it remains to be clarified the effectiveness of rehabilitative approaches designed for PD patients on subjects suffering from PSP.

The rehabilitative treatment known as MIRT (*Multidisciplinary Intensive Rehabilitation Treatment*) has been extensively described and its effectiveness on motor and functional parameters has been demonstrated in PD patients. MIRT aims at functional recovery and motor re-learning. It consists of a 4-week physical therapy in a hospital setting and entails four daily sessions for five days per week organized as follows:

- **From Monday to Friday** → ***First session (1 h/day):** it consists of a one-to-one session with physical therapist (front-to-front); **Second session (1 h/day):** it includes aerobic and repetitive activities to improve gait and balance using different devices (treadmill-plus with visual cues and auditory feedbacks, cycloergometer, crossover and posturographic platform with visual feedbacks); **Third sessions (1 h/day):** occupational therapy; **Fourth session (1 h/day):** speech therapy.*

Aims of the study

The aims of our study are:

- To evaluate whether an aerobic, intensive, goal-based and multidisciplinary rehabilitation treatment such as MIRT, previously conceived for PD, is effective for PSP patients;
- To evaluate, within MIRT, whether a robotic device, such as Lokomat®, is able to provide further benefits;

Materiali e Metodi

From January 2014 to December 2015, patients with a diagnosis of PSP, which will be hospitalized at the Department of Parkinson's Disease, Movement Disorders and Brain Injury Rehabilitation of the "Moriggia-Pelascini" Hospital (Gravedona ed Uniti, Italy), will be evaluated to be enrolled in the study.

Inclusion criteria:

- Diagnosis of PSP in accordance to the NINDS-SPSP International Criteria (*Litvan et al., 1996*);
- Ability to walk unassisted for at least 6 meters;
- Age 55-85;
- Stable dopaminergic drugs dosage in the month preceding the admission to the study;

Exclusion criteria:

- Any others significant neurological or orthopedic disorders;
- Osteoarthritis, osteoporosis, cutaneous lesions and/or other pressure wounds;
- Body weight exceeding 135 kg (the weight limit for the use of Lokomat®);
- Respiratory and cardiovascular diseases;

Written informed consent will be requested to participants before the beginning of the study.

Patients will be randomly assigned to two groups (each group was composed of 12 patients) using a computer-generated list:

MIRT Group

This group will undergo a 4-weeks MIRT exploiting the use of a treadmill plus (treadmill associated with visual cues and auditory feedbacks); *Treadmill-plus training* → 20-minutes training per day, 5 times a week for 4 weeks.

MIRT+Lokomat Group

This group will undergo a 4-weeks MIRT involving the use of Lokomat® for 5 days per week in spite of treadmill-plus; *Lokomat training* → 20-minutes training per day, 5 times a week for 4 weeks.

Outcome measures

Both groups will be evaluated at admission (T0) and discharge (T1) by neurologists and physiotherapists with expertise in movement disorders field, using the following outcome measures:

- Primary outcome measure → PSP rating Scale (PSPRS);
- Secondary outcome measures → a) Berg Balance Scale (BBS); b) Number of Falls (NoF); c) Six-Minutes Walking Test (6MWT);

Statistical Analysis

The normality of the distribution of all variables will be assessed by the Shapiro–Wilk test. For non-normally distributed variables, between- and within-group comparisons will be performed by the Mann-Whitney U test and Wilcoxon signed-rank test respectively. The unpaired and paired t-tests will be used for normally distributed variables. To assess whether, within our intensive and aerobic treatment, the use of Lokomat® in the MIRT-Lokomat protocol could lead to a better improvement as compared to MIRT, for each outcome variable we will compute the difference (discharge-admission) and then run the non parametric test on the treatment factor. All statistical tests are two-tailed and statistical significance are set at $p < 0.05$.

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Via Pelascini, 3 22015 **GRAVEDONA ED UNITI (CO)**

☎ (0344) 92.111 - TELEFAX (0344) 85.896

UFFICIO PRENOTAZIONI ☎ (0344) 92.401

ITALIA HOSPITAL S. p. A.

Capitale Sociale Euro 1.033.000,00 i.v. - Sede Legale: Corso Vittorio Emanuele II, 87 - 00186 ROMA

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