

## Preserved Brain Functional Plasticity After Upper Limb Task-Oriented Rehabilitation in Progressive Multiple Sclerosis

Giacomo Boffa<sup>1</sup>, Andrea Tacchino<sup>2</sup>, Elvira Sbragia<sup>1</sup>, Simona Schiavi<sup>1</sup>, Amgad Droby<sup>3</sup>, Nicolò Piaggio<sup>1</sup>, Giulia Bommarito<sup>1</sup>, Gaia Girardi<sup>2</sup>, Giovanni Luigi Mancardi<sup>1</sup>, Giampaolo Brichetto<sup>2</sup>, Matilde Inglese<sup>1,3</sup>

<sup>1</sup>Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genova and IRCCS AOU San Martino-IST, Genova, <sup>2</sup>Italian Multiple Sclerosis Foundation, Scientific Research Area, <sup>3</sup>Department of Neurology and Neuroscience, Icahn School of Medicine at Mount Sinai, New York

**Objective:** To investigate the effect of task-oriented upper limb (UL) rehabilitation in progressive multiple sclerosis (PMS) and to assess the MRI correlates of changes in motor performance.

**Background:** Despite clinical relevance of UL dysfunction, limited research has been dedicated to UL rehabilitation in PMS, leading to lack of evidence-based guidelines. It's therefore still unknown whether more disabled patients with advanced PMS could still benefit from motor rehabilitation.

**Design/Methods:** Thirty-five PMS patients were prospectively enrolled and randomized into 3 groups: active treatment group (ATG, n=13), passive treatment group (PTG, n=13) and control group (CG, n=9). At baseline and after training, patients underwent MRI scans and were evaluated with the action research arm test (ARAT), nine hole peg test (9-HPT), ABILHAND scale, modified fatigue impact scale (MFIS). Measures of motor finger performance were also obtained by engineered glove measuring.

**Results:** After rehabilitation, ATG improved in several UL motor tasks ( $0.02 \leq p \leq 0.03$ ) and showed increased ABILHAND scores compared to PTG ( $p < 0.01$ ). ATG showed increased functional connectivity of the sensorimotor and thalamic resting state networks compared to CG and PTG ( $p < 0.05$  cluster-wise-FDR-corrected). Correlations were found between motor improvement and thalamic, sensorimotor and basal ganglia networks ( $0.70 \leq r \leq 0.79$ ,  $0.008 \leq p \leq 0.04$ ). No structural MRI changes were detected as measured by DTI.

**Conclusions:** PMS patients could benefit from task-oriented UL rehabilitation, which seems to be more efficient than passive mobilization. Despite extensive brain damage, functional neuroplasticity seems to be preserved in PMS, thus providing a rationale for the use of rehabilitative treatments in late PMS.