



PROGETTO

Supervisore:

Maria A. Rocca

Titolo/Title:

Application of structural and functional MRI techniques to characterize the substrates of motor impairment and to investigate the mechanisms of different rehabilitative strategies in multiple sclerosis patients

Corso /PhD Course

Medicina Molecolare/*Molecular Medicine*

Curriculum:

Neuroscienze e Neurologia Sperimentale/*Neuroscience and Experimental Neurology*

Link alla pagina personale del sito web di Ateneo o del polo ospedaliero di riferimento:

<https://www.unisr.it/en/docenti/r/rocca-maria-assunta>

<https://research.hsr.it/en/institutes/institute-of-experimental-neurology/neuroimaging-of-CNS-white-matter/maria-assunta-rocca.html>

Descrizione del progetto (max 3.000 caratteri spazi inclusi)

Background/gap of knowledge

Multiple sclerosis (MS) is a chronic, inflammatory and neurodegenerative disease of the central nervous system (CNS),¹ commonly determining motor deficits and substantial clinical disability.²

Therapeutic strategies aim to reduce inflammatory activity, halt disease progression, and effectively manage MS clinical manifestations. Among them, physical rehabilitation plays an important role in improving patients' functional independence and quality of life (QoL).³⁻⁵ Innovative and tailored rehabilitative strategies, focusing on motor training for both upper and lower limbs, are emerging. They may be optimized to address clinical deficits at the individual patient level. Among them, action observation therapy (AOT) may improve impaired motor functions by modulating the mirror neuron system.^{6,7} Aerobic exercise may improve motor functions,^{8,9} but also cognitive performance,¹⁰ fatigue,¹¹ depressive symptoms and anxiety,¹² by promoting neuroplasticity and improving brain health.^{13,14}

However, the mechanisms underlying the beneficial effects of these rehabilitation approaches have not yet been clearly defined. Moreover, not all MS patients may benefit from these approaches, as individual response may vary due to heterogeneous subjects' characteristics.

Rationale and hypothesis

Thanks to the application of advanced magnetic resonance imaging (MRI) techniques that are sensitive and specific to MS-related pathological substrates, this project wishes to provide a comprehensive characterization of the MRI substrates of different motor outcomes in patients with MS to better understand the pathophysiological mechanisms underlying motor impairment. Moreover, the project aims to explore the structural and functional CNS modifications following different rehabilitation strategies to better understand the mechanisms underlying the beneficial effects of different rehabilitation approaches. Finally, we aim to identify reliable predictors of response to different rehabilitation strategies, to optimize treatment selection for each MS patient.

Objectives and specific aims

Specifically, the aims of this project are the following:

- to define structural and functional MRI substrates of cardiorespiratory fitness and of specific motor outcomes of upper and lower limbs in patients with MS;



- to evaluate the beneficial effects of different rehabilitation strategies, including aerobic training and AOT, on disability, QoL, fatigue and cognitive functions and to explore their possible structural and functional MRI correlates;
- to identify demographic, clinical and MRI characteristics associated with better response to different motor rehabilitation programs in patients with MS.

Expected outcomes

Advanced MRI tools will allow to identify potential MRI markers of motor outcomes useful for monitoring future rehabilitation protocols. The project will also identify MRI substrates associated to clinical improvement following various rehabilitative strategies, and predictors for treatment response.

Competenze che deve acquisire lo studente (Max 600 caratteri spazi inclusi):

Throughout the project, the student will develop the following skills:

- analysis and interpretation of clinical data in MS patients and healthy controls (HC);
- post-processing of volumetric, diffusion tensor and resting-state functional MRI data from MS patients and HC;
- analysis and interpretation of MRI data in MS patients and HC;
- defining correlations between clinical features and structural/functional MRI measures;
- presentation of works at National and International congresses;
- drafting of research reports and articles.

Bibliografia (max. 15)

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2. Browne P, Chandraratna D, Angood C, et al. Atlas of Multiple Sclerosis 2013: A growing global problem with widespread inequity. *Neurology* 2014; **83**(11): 1022-4.
3. Khan F, Amatya B. Rehabilitation in Multiple Sclerosis: A Systematic Review of Systematic Reviews. *Arch Phys Med Rehabil* 2017; **98**(2): 353-67.
4. Motl RW, Sandroff BM, Kwakkel G, et al. Exercise in patients with multiple sclerosis. *Lancet Neurol* 2017; **16**(10): 848-56.
5. Learmonth YC, Motl RW. Exercise Training for Multiple Sclerosis: A Narrative Review of History, Benefits, Safety, Guidelines, and Promotion. *Int J Environ Res Public Health* 2021; **18**(24).
6. Rizzolatti G, Craighero L. The mirror-neuron system. *Annu Rev Neurosci* 2004; **27**: 169-92.
7. Rocca MA, Tortorella P, Ceccarelli A, et al. The "mirror-neuron system" in MS: A 3 tesla fMRI study. *Neurology* 2008; **70**(4): 255-62.
8. Platta ME, Ensari I, Motl RW, Pilutti LA. Effect of Exercise Training on Fitness in Multiple Sclerosis: A Meta-Analysis. *Arch Phys Med Rehabil* 2016; **97**(9): 1564-72.
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10. Beier M, Bombardier CH, Hartoonian N, Motl RW, Kraft GH. Improved physical fitness correlates with improved cognition in multiple sclerosis. *Arch Phys Med Rehabil* 2014; **95**(7): 1328-34.
11. Hayes HA, Gappmaier E, LaStayo PC. Effects of high-intensity resistance training on strength, mobility, balance, and fatigue in individuals with multiple sclerosis: a randomized controlled trial. *J Neurol Phys Ther* 2011; **35**(1): 2-10.
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MO 20-5

rev. 00 del 29/11/2023

PO 20

Pag. 5 di 6

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14. Motl RW, Pilutti LA, Hubbard EA, Wetter NC, Sosnoff JJ, Sutton BP. Cardiorespiratory fitness and its association with thalamic, hippocampal, and basal ganglia volumes in multiple sclerosis. *Neuroimage Clin* 2015; **7**: 661-6.