PROJECT

Supervisor:	Rocca Maria Assunta
Title:	Features and substrates of cognitive dysfunction across inflammatory diseases of the central nervous system: comparative analyses in NMOSD, MOGAD and neuropsychiatric SLE
Curriculum:	Cognitive and Behavioural Sciences
Link to the personal page of the University or relevant hospital site website:	https://www.unisr.it/docenti/r/rocca-maria-assunta https://research.hsr.it/en/institutes/institute-of-experimental-neurology/neuroimaging-of-CNS-white-matter/maria-assunta-rocca.html

Description of the Project (max 3,000 characters including spaces)

Background/gap of knowledge

Cognitive dysfunction is increasingly recognized across inflammatory diseases of the central nervous system (CNS). In myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) and neuromyelitis optica spectrum disorder (NMOSD), deficits commonly involve processing speed and verbal fluency, with variable involvement of memory and executive function. Magnetic resonance imaging (MRI) studies have shown that cognitive deficits in MOGAD and NMOSD are associated with white matter (WM) microstructural abnormalities and deep gray matter (DGM) atrophy. In MOGAD, cognitive impairment was also reported to be related to resting-state (RS) functional connectivity (FC) alterations. In neuropsychiatric systemic lupus erythematosus (NPSLE), cognitive impairment has been linked to network-level functional abnormalities and diffusion-based WM alterations. A major knowledge gap remains in the comprehensive characterization of the cognitive profile of each disease, as well as in the systematic identification of their structural and functional MRI substrates and the delineation of shared versus disease-specific neural mechanisms across these inflammatory CNS disorders.

Rationale and hypothesis

MRI plays a crucial role in the diagnosis of CNS inflammatory diseases and in monitoring disease progression. The application of advanced MRI techniques contributes to identifying substrates associated with clinical manifestations, and a multimodal approach may clarify whether cognitive deficits are associated with shared neural substrates across disorders or reflect disease-specific patterns of structural damage and functional network abnormalities.

Objectives and specific aims

The aim of this project is to characterize and compare cognitive profiles across major inflammatory diseases of the CNS and to identify their structural and functional MRI substrates. The protective role of cognitive reserve will also be assessed. We will analyze clinical, structural, and functional MRI data from MOGAD, NMOSD, and NPSLE patients collected at our Unit. A cohort of healthy controls (HCs) and multiple sclerosis (MS) patients studied with the same MRI protocol will serve as comparison groups.

Specifically, in this project we will:

1) Characterize the clinical and cognitive profile across disease groups, compared with MS patients and HCs;

2) Evaluate structural substrates of cognitive dysfunction by analyzing lesion burden, regional atrophy, and diffusion-based WM microstructural damage across all groups;

3) Assess the functional substrates of cognitive dysfunction by investigating RS FC abnormalities within large-scale brain networks;

4) Perform cross-disease comparative analyses to quantify shared versus disease-specific MRI correlates of cognitive dysfunction.

Expected outcomes

We expect to characterize patterns of structural and functional alterations associated with cognitive impairment across inflammatory diseases of the CNS and to identify shared and disease-specific mechanisms.

Skills that the student should acquire (max. 600 characters including spaces):

- Collection of clinical data from patients with CNS inflammatory diseases;

- Interpretation of clinical, neuropsychological and MRI findings;

- Post-processing of structural and functional MRI data from patients with NMOSD, MOGAD, and NPSLE, as well as from MS patients and HCs;

- Identification of associations between clinical, neuropsychological and MRI measures in patients with NMOSD, MOGAD, and NPSLE;

- Presentation of findings at national and international congresses;

- Drafting of research reports and articles.

References (max. 15)

1. Sechi E, Cacciaguerra L, Chen JJ, et al. Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD): A review of clinical and MRI features, diagnosis, and management. Front Neurol. 2022; 13: 885218.

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longitudinal, multicentre study of 113 patients (CogniMOG-Study). Journal of Neurology, Neurosurgery & Psychiatry, 2025;96(3):296–305.

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5. Zhuo Z, Duan Y, Tian D, et al. Brain structural and functional alterations in MOG antibody disease. Multiple Sclerosis Journal, 2021;27(9):1350–1363.

6. Hümmert MW, Stern C, Paul F, et al. Cognition in patients with neuromyelitis optica spectrum disorders: A prospective multicentre study of 217 patients (CogniNMO-Study). Multiple Sclerosis, 2023;29(7):819–831.

7. Kim S-H, Park EY, Park B, et al. Multimodal magnetic resonance imaging in relation to cognitive impairment in neuromyelitis optica spectrum disorder. Scientific Reports, 2017;7:9180.

8. Oertel FC, Schließeit J, Brandt AU, et al. Cognitive impairment in neuromyelitis optica spectrum disorders: A review of clinical and neuroradiological features. Frontiers in Neurology, 2019;10:608.

9. Hanly JG, Robertson JW, Legge A, et al. Resting state functional connectivity in SLE patients and association with cognitive impairment and blood–brain barrier permeability. Rheumatology (Oxford), 2023;62(2):685–695.

10. Costallat BL, Ferreira DM, Lapa AT, et al. Brain diffusion tensor MRI in systemic lupus erythematosus: A systematic review. Autoimmunity Reviews, 2018;17:36–43.