

 <p>UniSR Università Vita-Salute San Raffaele</p>	<p>APPLICATION TO ACT AS SUPERVISOR AND RESEARCH PROJECT PROPOSAL</p>	<p>MO 20-5 ed. 02 of 16/01/2026 PO 20 Page 4 of 9</p>
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PROJECT

Supervisor: Paolo Preziosa

Title: Invisible symptoms across inflammatory diseases of the central nervous system: structural and functional brain substrates in NMOSD, MOGAD and neuropsychiatric SLE

Curriculum: Neurosciences and Experimental Neurology

Link to the personal page of the University or relevant hospital site website: <https://www.unisr.it/en/docenti/p/preziosa-paolo>
<https://research.hsr.it/en/institutes/institute-of-experimental-neurology/neuroimaging-of-CNS-white-matter/index.html>

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

Background/gap of knowledge

Across inflammatory diseases of the central nervous system (CNS), fatigue, neuropsychiatric manifestations, and sleep disturbances are common, clinically relevant, and often under-recognized symptoms. In neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), fatigue has been linked with gray matter (GM) and white matter (WM) atrophy, along with network-level functional abnormalities. In NMOSD, higher levels of inflammation were associated with depression and anxiety. In neuropsychiatric systemic lupus erythematosus (NPSLE), neuropsychiatric syndromes were frequently linked to structural GM alterations and functional abnormalities of large-scale brain networks. However, these invisible symptoms have not been systematically investigated across CNS inflammatory diseases within a unified framework. Their neural substrates remain incompletely characterized, and it is unclear whether these manifestations primarily reflect focal lesion burden, diffuse GM damage, WM microstructural abnormalities, or large-scale network dysfunction.

Rationale and hypothesis

Given the limited cross-disorder studies linking invisible symptoms to multimodal MRI markers, advanced structural and functional neuroimaging techniques may help explore their neural substrates in inflammatory diseases of the CNS. A multimodal approach might clarify whether invisible symptoms share a similar pathophysiological mechanism across diseases or reflect disease-specific patterns of structural damage and functional network alterations.

Objectives and specific aims

The objective of this project is to assess the association between invisible symptoms (fatigue, neuropsychiatric manifestations, and sleep disturbances) with functional, diffusion and structural MRI metrics and to compare them across major CNS inflammatory diseases. To this end, clinical measures will be integrated



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with MRI data from MOGAD, NMOSD and NPSLE patients collected at our Unit. Healthy controls (HCs) and multiple sclerosis (MS) patients examined with the same MRI protocol will be included as comparison groups.

Specifically, this project will:

- 1) Identify the structural and functional substrates of fatigue by assessing associations between fatigue severity and MRI measures of lesion burden, regional atrophy, WM microstructural damage, choroid plexus alterations and resting-state (RS) functional connectivity (FC) abnormalities;
- 2) Investigate the correlates of depression and anxiety by examining associations with structural damage and functional alterations within brain networks involved in emotional regulation;
- 3) Assess MRI correlates of sleep disturbances by analyzing structural and functional abnormalities within brain regions and networks involved in sleep regulation, including MRI markers of glymphatic system function;
- 5) Perform cross-disease comparisons to identify shared versus disease-specific mechanisms underlying the presence and severity of invisible symptoms.

Expected outcomes

We expect to delineate and compare the structural and functional correlates of fatigue, neuropsychiatric manifestations and sleep disturbances across inflammatory CNS diseases, improving our understanding of the mechanisms underlying these invisible symptoms.

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

- Collection of clinical data and self-reported measures of fatigue, neuropsychiatric manifestations, and sleep disturbances from patients with CNS inflammatory diseases;
- Interpretation of clinical 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, self-reported measures of fatigue, neuropsychiatric manifestations, and sleep disturbances, and MRI metrics 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. Loreface L, Carotenuto A, Fenu G, et al. Silent burden: recognising and managing invisible symptoms in neuromyelitis optica. *Journal of Neurology, Neurosurgery & Psychiatry*, 2025.
2. Liu J, Zhang X, Zhong Y, et al. The prevalence of depression, anxiety, and sleep disturbances in patients with neuromyelitis optica spectrum disorders: A



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systematic review and meta-analysis. *Multiple Sclerosis and Related Disorders*, 2023;79:105007.

3. Shi Z, Chen H, Lian Z, et al. Factors that impact health-related quality of life in neuromyelitis optica spectrum disorder: anxiety, disability, fatigue and depression. *Journal of Neuroimmunology*, 2016.

4. Yeo T, Dos Passos GR, Muhammed L, et al. Factors associated with fatigue in CNS inflammatory diseases with AQP4 and MOG antibodies. *Annals of Clinical and Translational Neurology*, 2020.

5. Tan YY, Saffari SE, Tye JSN, et al. The burden of psychiatric morbidity in multiple sclerosis, AQP4-antibody NMOSD and MOGAD before and after neurological diagnosis. *Multiple Sclerosis and Related Disorders*, 2024.

6. Yin R, et al. Association between depression and sleep quality in systemic lupus erythematosus: A meta-analysis. *Sleep and Breathing*, 2022.

7. Unterman A, Nolte JES, Boaz M, et al. Neuropsychiatric syndromes in systemic lupus erythematosus: A meta-analysis. *Arthritis & Rheumatism*, 2011.

8. Su L, Zhuo Z, Duan Y et al. Structural and Functional Characterization of Gray Matter Alterations in Female Patients With Neuropsychiatric Systemic Lupus. *Front. Neurosci*, 2022.

9. Camera V, Mariano R, Messina S, et al. Shared imaging markers of fatigue across multiple sclerosis, aquaporin-4 antibody neuromyelitis optica spectrum disorder and MOG antibody disease. *Brain Communications*, 2023.