

# Structural MRI predictors of cognition in Multiple Sclerosis: Evidence from a Multi-Site Cohort

G. MAGGI<sup>1,2</sup>, A. DE ROSA<sup>1,2</sup>, M. ALTIERI<sup>1,2</sup>, P. VALSASINA<sup>3</sup>, N. TEDONE<sup>3</sup>, P. PANTANO<sup>4,5</sup>, N. PETSAS<sup>6</sup>, N. DE STEFANO<sup>7</sup>, R. CORTESE<sup>7</sup>, M. BATTAGLINI<sup>7</sup>, L. LAVORGNA<sup>1</sup>, A. BISECCO<sup>1,2</sup>, A. D'AMBROSIO<sup>1,2</sup>, M. ROCCA<sup>3,8,9</sup>, M. FILIPPI<sup>3,8,9,10,11</sup>, A. GALLO<sup>1,2</sup>

- 1 First Division of Neurology and Neurophysiopathology, AOU Luigi Vanvitelli, Naples, Italy
- 2 Department of Advanced Medical and Surgical Sciences, University of Campania Luigi Vanvitelli, Naples, Italy
- 3 Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy
- 4 Department of Human Neuroscience, Sapienza University, Rome, Italy
- 5 IRCCS Neuromed, Pozzilli, Italy
- 6 School of Medical Statistics and Biometry, Dept of Public Health and Infectious Diseases, Sapienza University, Rome, Italy
- 7 Department of Medicine, Surgery and Neuroscience, University of Siena, Siena, Italy
- 8 Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
- 9 Vita-Salute San Raffaele University, Milan, Italy
- 10 Neurorehabilitation Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy
- 11 Neurophysiology Service, IRCCS San Raffaele Scientific Institute, Milan, Italy

**AOV:** Azienda Ospedaliera Universitaria Luigi Vanvitelli

**IRCCS** CENTRO sclerosi multipla NAPOLI

## OBJECTIVES

Cognitive impairment is a common feature of multiple sclerosis (MS) with a pooled prevalence of 32.5% (Wu et al. 2024), often associated with structural brain changes. Atrophy of cerebral cortex (CC) and deep GM (DGM) structures has been linked to cognitive decline in MS. However, large-scale, multi-site studies investigating these relationships remain limited. Therefore, we aim to investigate cross-sectional associations between CC/DGM measures and neuropsychological scores in a large, multi-site cohort of people with MS (pwMS).

## MATERIALS

Cross-sectional MRI, demographic, and clinical data from 1299 pwMS were retrieved from the Italian Neuroimaging Network Initiative (INNI) database. All participants completed the Brief Repeatable Battery of Neuropsychological Tests (BRB-N) evaluating verbal and visuospatial memory, information processing speed, attention and verbal fluency.

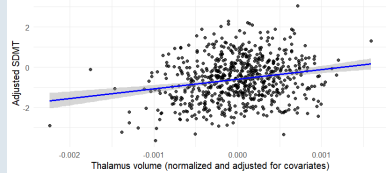
## METHODS

Subcortical volumes from 7 DGM structures and cortical thickness (CTh) from 34 regions were extracted using FreeSurfer. We investigated associations between MRI measures and neuropsychological scores using multiple linear regression models, while controlling for age, sex, education, disease duration, phenotype, site, and, for CTh measures, global CTh.

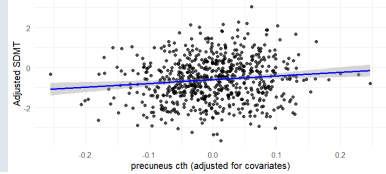
## RESULTS

Analysis of normalized DGM volumes revealed several significant positive associations with cognitive performance, with the strongest effect observed for thalamic volume on Symbol Digit Modalities Test (SDMT) scores (standardized  $\beta = 0.29$ ,  $p < 0.01$ , Bonf. corrected). Among CTh measures, we found a strong association between precuneus thickness and SDMT (standardized  $\beta = 0.35$ ,  $p < 0.01$ , Bonf. corrected).

Association between Thalamus and SDMT



Association between precuneus and SDMT



## DISCUSSION

Our findings revealed that thalamic volume and precuneus thickness were strongly linked to SDMT performance within a large multicenter MS cohort. Notably, the precuneus is a key structure of the most relevant cognitive cortical network (i.e. the Default Mode Network) (Utevsky et al. 2014), while the thalamus has been consistently associated to cognitive status in pwMS.

## CONCLUSIONS

SDMT represents the most reliable and sensitive proxy of the global cognitive status in pwMS (Kalb et al. 2018) and thus, MRI changes of thalamus and precuneus could be monitored to timely identify pwMS at higher risk of cognitive impairment.

## REFERENCES

- Wu W, Francis H, Lucien A, Wheeler TA, Gandy M. The Prevalence of Cognitive Impairment in Relapsing-Remitting Multiple Sclerosis: A Systematic Review and Meta-analysis. *Neuropsychol Rev*. Published online April 8, 2024. doi:10.1007/s11065-024-09640-8
- Utevsky AV, Smith DV, Huettel SA. Precuneus is a functional core of the default-mode network. *J Neurosci*. 2014;34(3):932-940. doi:10.1523/JNEUROSCI.4227-13.2014
- Kalb R, Beier M, Benedict RH, et al. Recommendations for cognitive screening and management in multiple sclerosis care. *Mult Scler*. 2018;24(13):1665-1680. doi:10.1177/1352458518803785

## ACKNOWLEDGEMENT

This work was funded by the European Union - Next Generation EU - NRRP M6C2 - Investment 2.1 Enhancement and strengthening of biomedical research in the NHS, PNRR-MAD-2022-12376530, Cup Master C43C22001290007



## DISCLOSURE

P. Pantano: travel (Novartis, Genzyme, Bracco); honoraria (Biogen).  
N. De Stefano: consulting/speaking/travel (Biogen-Idex, BMS, Celgene, Genzyme, Immunic, Merck, Novartis, Roche, Teva); advisory boards (Immunic, Merck, Novartis, Biogen-Idex, Roche, Sanofi).  
R. Cortese: honoraria/travel (Roche, Merck Serono, UCB, Sanofi-Genzyme, Alexion, Novartis, Janssen).  
A. Bisecco: consulting/honoraria (Biogen, Roche, Merck, Celgene, Sanofi Genzyme).  
M.A. Rocca: consulting/honoraria (AstraZeneca, Biogen, BMS, Bromatech, Celgene, Eli Lilly, Genzyme, Horizon, Janssen, Merck Serono, Novartis, Roche, Sanofi, Teva).  
M. Filippi: consulting/speaking/advisory (Alexion, Almirall, Bayer, Biogen, BMS, Celgene, Chiesi, Eli Lilly, Genzyme, Janssen, Merck, Neopharmaceut Genetili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, Teva).  
A. Gallo: consulting/speaking/travel (Biogen, Merck Serono, Mylan Italia, Novartis, Roche, Sanofi Genzyme, Teva).



24-28 Ottobre 2025  
Padova Congress

55° CONGRESSO  
SOCIETÀ ITALIANA  
DI NEUROLOGIA