

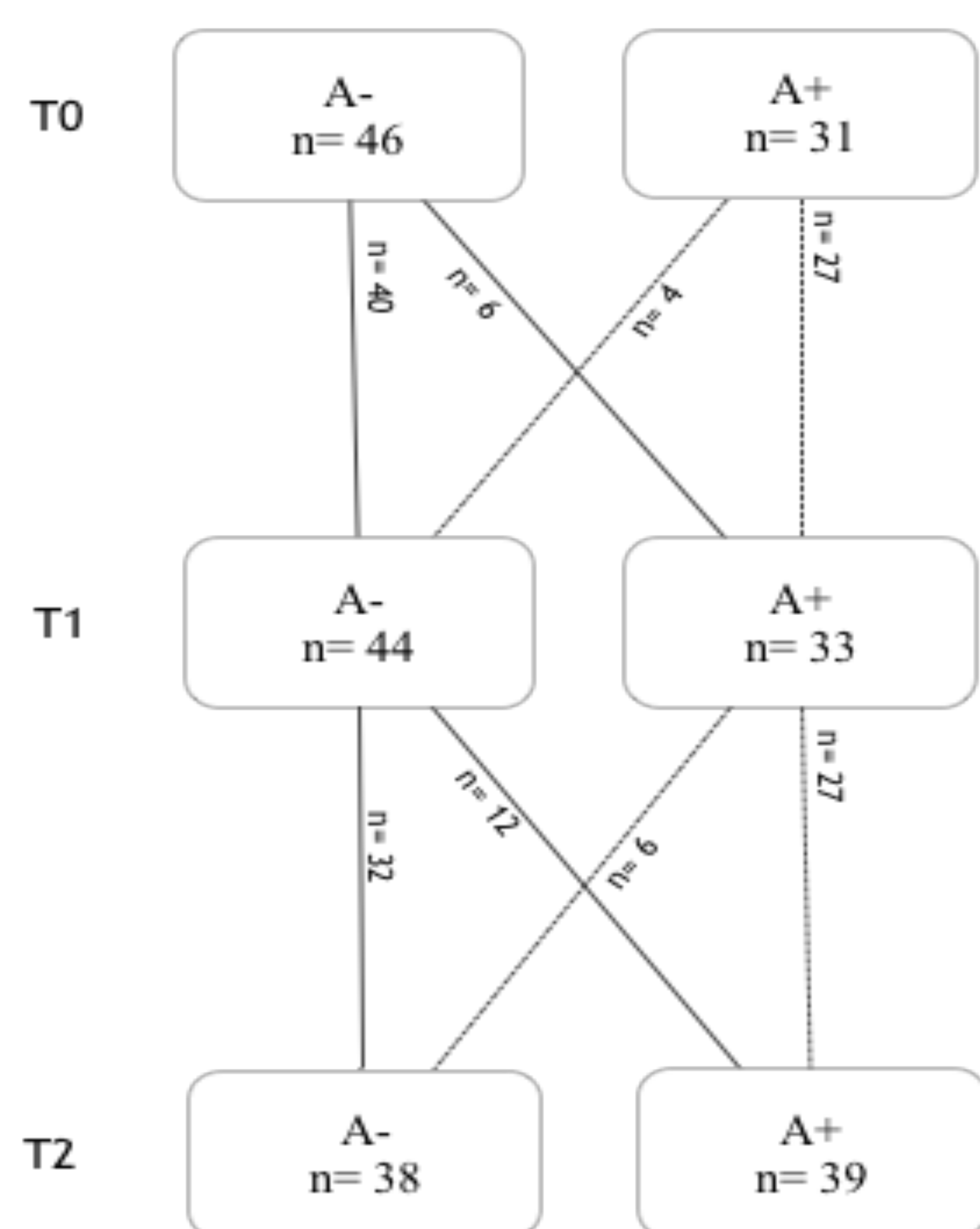
# APATHY AND COGNITIVE DYSFUNCTIONS IN MULTIPLE SCLEROSIS: A 4-YEAR FOLLOW-UP STUDY

Simona Raimo<sup>1</sup>, Luigi Trojano<sup>2</sup>, Mariachiara Gaita<sup>1</sup>, Florindo d'Onofrio<sup>3</sup>, Daniele Spitaleri<sup>3</sup>, Gabriella Santangelo<sup>2</sup>

1. Department of Medical and Surgical Sciences, University 'Magna Graecia' of Catanzaro, Catanzaro, Italy; 2. Department of Psychology, University of Campania 'Luigi Vanvitelli', Caserta, Italy; 3. Neurology Unit, 'San Giuseppe Moscati' Hospital, Avellino, Italy

**Objectives.** Cognitive dysfunctions are highly prevalent in people with Multiple Sclerosis<sup>1</sup> (MS), and negatively impact on occupational and social functioning<sup>2</sup>. Early detection and prediction of cognitive decline in people with MS remain a key challenge of the healthcare systems. In the present longitudinal study we applied recent statistical approach to model cognitive changes and to assess whether apathy could be a behavioural predictor of cognitive decline in people with MS.

**Methods.** We assessed 77 individuals with MS at three-time points (baseline, T0; 2-year follow-up, T1; 4-year follow-up, T2; Fig.1), by means of several clinical, behavioural, and cognitive measures. We applied a multivariate general linear model and a linear regression model to explore factors associated with cognitive change over time. We used a delta approach to measure cognitive decline during the follow-up period.



**Results.** Higher level of apathy at baseline predicted the progressive cognitive decline at follow-up, in particular of executive functioning (Beta=0.372;  $t=3.236$ ;  $p=0.002$ ; 95% CI=0.078 – 0.327; Fig.2); whereas higher level of depression at baseline predicted decline in visuospatial abilities (Beta=0.278;  $t=2.471$ ;  $p=0.016$ ; 95% CI=0.011 – 0.107). Interestingly, higher levels of education were significantly associated with a reduced rate of cognitive decline over time (Beta=-0.249;  $t=-2.153$ ;  $p=0.035$ ; 95% CI=-0.682 – -0.026), whereas age, age at onset, disease duration, and level of disability were not.

Moreover, participants with persistent apathy (diagnosis of apathy at T0, T1, and T2, A+A+A+) showed poorer inhibitory control ( $p<0.0001$ ) than participants who had never received diagnosis of apathy (A-A-A-), and worse global cognitive functioning ( $p=0.004$ ) and visuospatial planning ( $p=0.001$ ) than participants who remitted from apathy (A+A+A-).

Finally, global cognitive and executive functioning worsened during the 4-year follow-up in participants with persistent apathy (A+A+A+) and in those that developed apathy (A-A-A+;  $p\leq 0.038$ ).

**Conclusion.** Apathy represents an early marker of cognitive decline in MS. These findings have important clinical and prognostic implications, suggesting the need of an early detection of apathy and of an accurate differential diagnosis from depression in the clinical routine.

## References.

1. Grzegorski et al. *Reviews in the Neurosciences* 28, 845-860 (2017).
2. Raimo et al. *Neuropsychology* 31, 811-821 (2017).

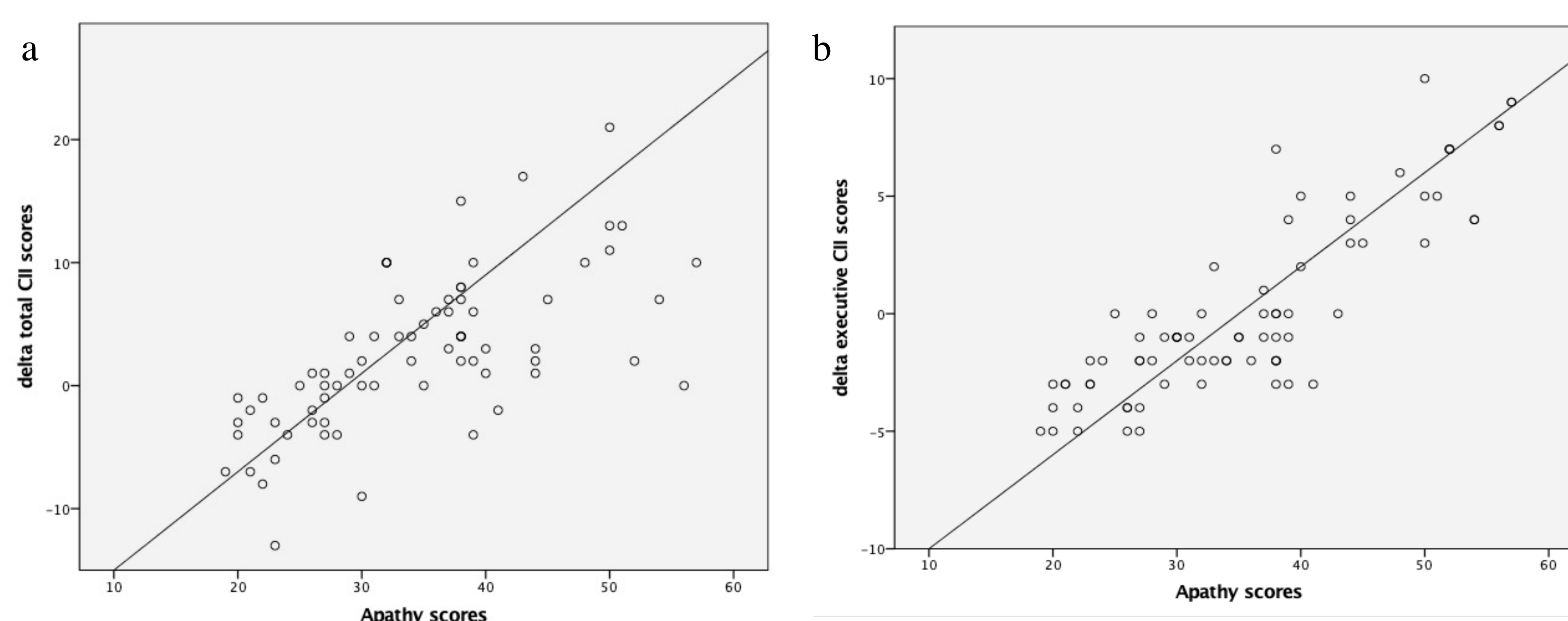


Fig 2. Scatter plots showing apathy scores at T0 versus delta total cognitive impairment index (CII) scores (a) and delta executive CII scores (b).