

## Relationship between white matter tract damage and executive functions in amyotrophic lateral sclerosis: a DT MRI tractography study

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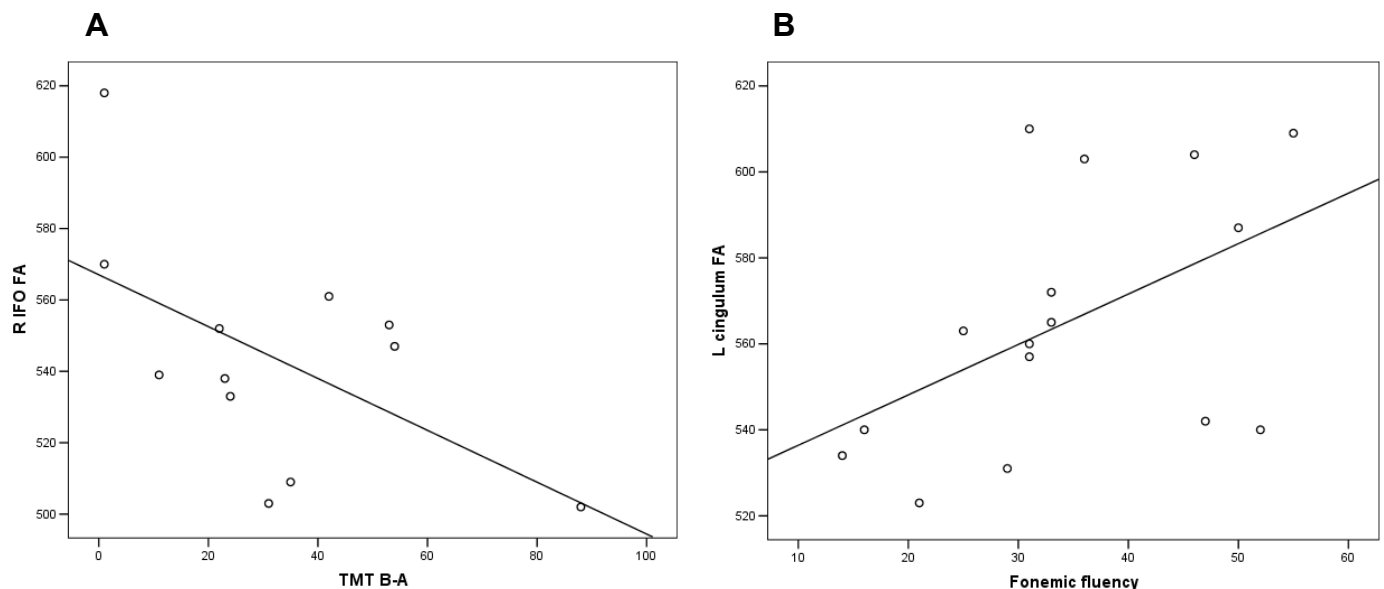
**Introduction.** Amyotrophic lateral sclerosis (ALS) has been associated with characteristic patterns of focal gray matter atrophy and degeneration of the corticospinal tracts (CST) [1]. A frontal dysexecutive syndrome may occur in ALS patients [2]. The anatomical correlates of such a syndrome have not been fully investigated yet.

**Objective.** To investigate the relationship between executive functioning and white matter (WM) tract damage in non-demented patients with ALS and mild disability.

**Methods.** DT MRI scans were obtained from 16 ALS patients with mild disability (ALS Functional Rating Scale score-revised [ALSFRS-r]  $\geq 20$ ). Patients with frontotemporal dementia were excluded. Executive functions were investigated using Trail Making (TMT) and/or Fluency tests. DT MRI tractography was used to assess the integrity of the major WM tracts [3]. Fractional anisotropy (FA) and mean diffusivity were obtained from each tract. The relationship between WM damage and executive functions was tested using regression analyses, corrected for subject's age and ALSFRS-r.

**Results.** Only two ALS patients scored at or below the 5<sup>th</sup> percentile on executive tests, compared to age- and education-matched norms. In ALS patients, TMT scores significantly correlated with the microstructural alterations of the corpus callosum, the major cortico-cortical association tracts (including inferior fronto-occipital, inferior longitudinal, and uncinate fasciculi), and the CST, bilaterally (**Figure A**). Performances on fluency were related to decreased FA of the left cingulum and right inferior longitudinal fasciculus in ALS patients (**Figure B**).

**Figure.** Scatterplots of the relationship between (A) the TMT B-A scores and the right inferior fronto-occipital (IFO) FA ( $r=0.36$ ,  $p=0.01$ ), and (B) the Fonic Fluency scores and the left cingulum FA ( $r=0.36$ ,  $p=0.01$ ) in ALS patients. Correlations were corrected for subject's age and ALSFRS-r.



**Conclusions.** The relationship between brain damage and executive performance in ALS patients with no cognitive impairment suggests that damage to WM tracts may precede the appearance of a frontal dysexecutive syndrome. DT MRI may have the potential to identify ALS patients at risk for cognitive impairment.

**References.** [1] Agosta et al., AJNR 2010 Epub ahead of print; [2] Strong et al., Amyotroph Lateral Scler. 2009;10:131-46; [3] Agosta et al., AJNR 2010 31:1457-61.