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] ≥ 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 5th 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 Fonemic 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.