CENTRO di RICERCA
SUN - FISM
di ALTI STUDI IN RISONANZA MAGNETICA
sulla sclerosi multipla e patologie similari

# Apathy is correlated with widespread DTI impairment in early stage of ALS

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## Background and objectives

There is increasing evidence that changes in behaviour may play a contributory role in disease progression of patients with lateral sclerosis (ALS). In particular, apathy is the most commonly reported behavioral change in both ALS and frontotemporal dementia. However, brain microstructural abnormalities underlying apathy are still not completely elucidated. In this regard, using a tract-based spatial statistics (TBSS) diffusion tensor imaging (DTI) approach, we aim to explore the potential association between brain microstructural damage and clinical scores of apathy in early stages of ALS.

## Methods

Seventeen consecutive ALS patients in King's clinical stages 1 or 2, and 15 age- and sex-matched healthy controls (HCs) underwent magnetic resonance imaging and neuropsychological examination, including assessment of long-term and short-term memory, executive and visuo-spatial functions, depression and apathy.

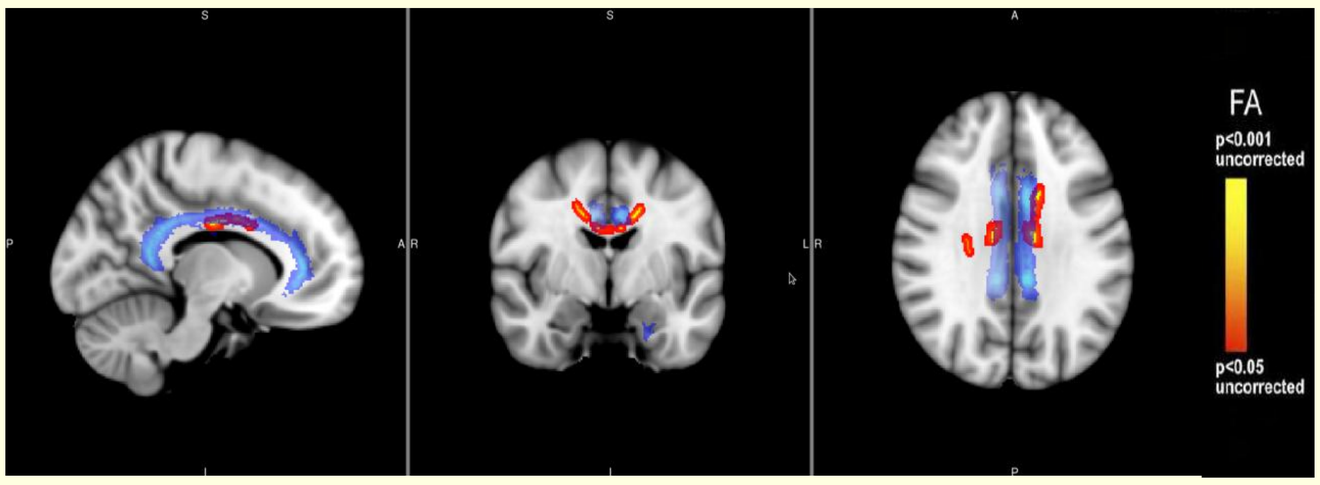
**Table 1** Detailed patients and controls characteristics.

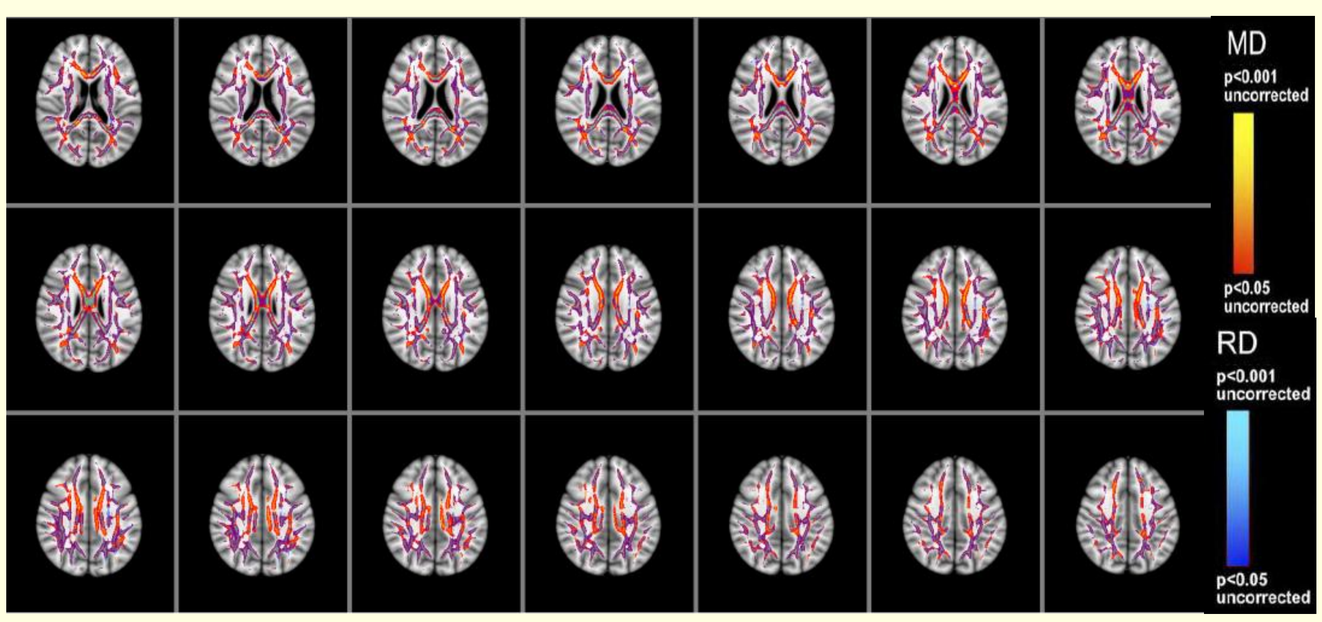
| Parameters | ALS patients mean (SD) (n = 17) | Controls mean (SD) (n = 15) |
|---|---|---|
| *Demographic and clinical measures* | | |
| Age | 57.88 (8.82) | 57.62 (10.54) |
| Education | 11.59 (4.58) | 11.46 (3.86) |
| Disease duration (months) | 17.82 (11.04) | - |
| ALSFRS-R score | 41.59 (3.83) | - |
| UMN score | 6 (4.61) | - |
| *Neuropsychological parameters* | | |
| ACE-R | 88.88 (8.20) | 94.92 (1.85) |
| Memory Prose Test | 11.9 (2.80) | 14.77 (1.84) |
| RCPM | 26.4 (5.37) | 31.15 (2.03) |
| Stroop test (errors) | .40 (.83) | .08 (.28) |
| Scrawls' test | 30.67 (1.18) | 30.23 (1.36) |
| Token Test | 34.13 (1.92) | 35.23 (1.01) |
| *Neurobehavioral variables* | | |
| AES (patient form, total score) | 26.94 (7.08) | 25.46 (5.06) |
| AES (caregiver form, total score) | 28 (8.26) | - |
| FrSBe (caregiver form, total score) | 74.31 (11.09) | - |
| BDI-II | 10.63 (6.12) | 8.62 (4.01) |

ACE-R = Addenbrooke's Cognitive Examination; ALSFRS-R = Amyotrophic Lateral Sclerosis Functional Rating Scale; AES = apathy evaluation scale; BDI-II = Beck Depression Inventory II; FrSBe = Frontal Systems Behaviour; RCPM = Raven's Coloured Progressive Matrices; UMN = Upper Motor Neuron

## Results

When compared to HCs, ALS patients exhibited a decrease of fractional (FA) measures ($p<.05$, corrected) in the corpus callosum and bilateral anterior cingulate cortices. Moreover, Apathy Evaluation Scale (AES) scores were significantly correlated with measures of mean (MD) and radial (RD) diffusivity ($p<.05$, corrected) in widespread white matter (WM) areas, including several associative fiber tracts in frontal, temporal and parietal lobes. From the neuropsychological point of view, between-groups comparisons did not show any significant difference of cognitive and behavioural performances.




## Discussion and conclusions

Our results point towards an early microstructural degeneration of brain areas biologically involved in behaviour regulation, such as anterior cingulum, although preceding the clinical appearance of neurobehavioural alterations in the ALS patients studied. However, the significant correlations described between clinical scores of apathy and DTI measures in several brain areas may suggest the involvement of a more widespread cerebral microstructural impairment in determining behavioural disturbances from early stages of ALS.

1. Tsujimoto M, Senda J, Ishihara T,Niimi Y, Kawai Y, Atsuta N, Watanabe H, Tanaka F, Naganawa S, Sobue G. Behavioral changes in early ALS correlate with voxel-based morphometry and diffusion tensor imaging. Journal of the Neurological Sciences 307 (2011) 34–40.
2. Woolley SC, Zhang Y, Schuff N, Weiner MW, Katz JS. Neuroanatomical correlates of apathy in ALS using 4 Tesla diffusion tensor MRI. Amyotroph Lateral Scler 2011 Jan;12(1):52-8.
3. Caga J, Turner MR, Hsieh S, Ahmed RM, Devenney E, Ramsey E, Zoing MC, Mioshi E, Kiernan MC. Apathy is associated with poor prognosis in amyotrophic lateral sclerosis. Eur J Neurol. 2016 May;23(5):891-7.