# TARDBP Ala382Thr mutation and C9orf72 expansion in Multiple Sclerosis: a possible role in brain atrophy

**L.Lorefice,[1]G. Fenu,[1] Murru MR,[1] Cabras F,[2] Sechi V,[2] Barracciu MA,[2] J.Frau,[1] GC. Coghe,[1] Cuccu S,[1] Tranquilli S,[1] E.Cocco,[1]MG.Marrosu [1]**

[1] Multiple Sclerosis Centre, ASL8-Binaghi Hospital, University of Cagliari, Italy

[2] Radiology Unit, Binaghi Hospital, ASL8- Cagliari, Italy

**Background.** Multiple sclerosis (MS) is a central nervous system disease that is specifically characterized by inflammatory demyelination and neurodegeneration [1]. Recently, the TARDBPAla382Thr mutation and the C9orf72 expansion were hypothesized to play a role in MS neurodegeneration [2].

**The aim of this study was to explore if these mutations play a role in enhancing brain atrophy in MS.**

## *Materials and Methods.*

The study included a group of MS patients that carried the TARDBP Ala382Thr mutation and the C9orf72 expansion and age-, sex-, disease course-, and EDSS-matched MS patients without the mutation. Recruited patients underwent brain MRI. Volumes of whole brain, white matter, and grey matter were estimated via SIENAX.

***Demographical data of MS mutated patients carrying mutation versus patients without mutation***

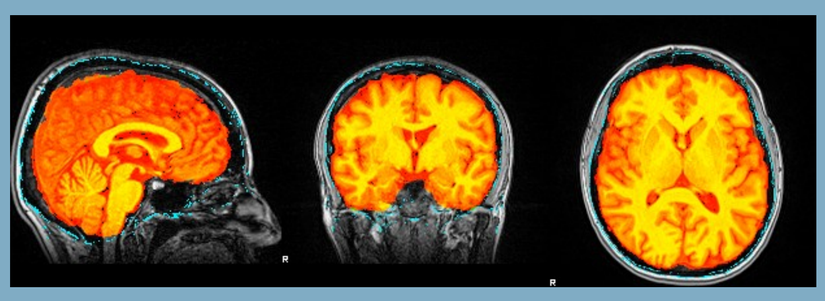
| | 18 MS patients carrying mutations* | 18 MS patients without mutations* |
|---|---|---|
| Female Gender [§] | 14 | 14 |
| Age (mean ± sd) [§] | 41.5 ± 11.8 | 41.6 ± 11.6 |
| Relapsing course[§] | 15 | 15 |
| EDSS score [§] | 2.8 ± 1.8 | 2.8 ± 1.8 |
| Disease Duration | 15.2 ± 9.2 | 13.8 ± 6.5 |

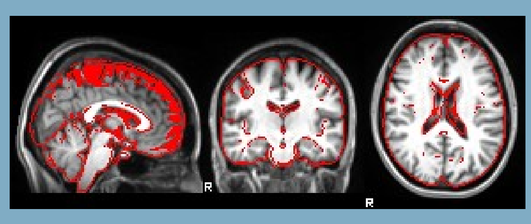
## RESULTS

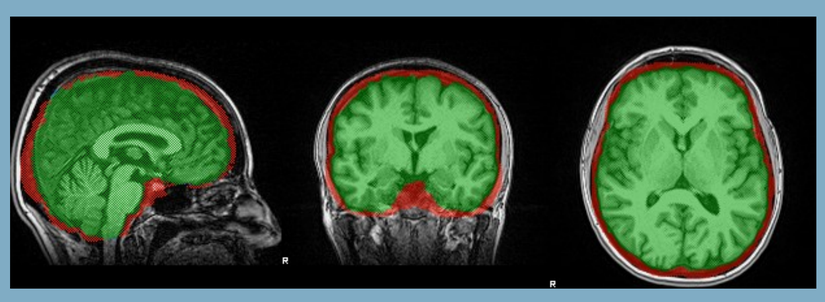
The MS sample comprised 18 patients without and 18 with the mutations. Fifteen patients reported the TARDBP Ala382Thr mutation and 3 the C9orf72 pathogenic expansion. The mean age at time of the brain MRI was 41.5 years (SD ± 11.8) and the mean EDSS score was 2.8 (SD ± 1.8). No differences in whole brain and grey matter volumes were reported between the two groups, but lower white matter volumes were found in the mutated group (p 0.03). A difference in white matter volumes was reported in an analysis limited to 15 patients with the TARDBP Ala382Thr mutation, compared to non-mutated patients (688.68 ml ± 36.55 vs 713.22 ml ± 27.34; p 0.04); no difference was reported between the C9orf72-mutated patients and controls.

| Volumes in ml | All mutated MS patients * | MS patients without mutations* | P value |
|---|---|---|---|
| GM[§] | 784,46 ± 56.14 | 804,12 ± 55.74 | 0.30 |
| WM[§§] | 687,81 ± 35 | 710,92 ± 26.62 | 0.03* |
| WB[§§§] | 1472,28 ± 77.97 | 1515,05 ± 66.84 | 0.08 |
| | MS patients carrying TDP mutation* | MS patients without mutations* | P value |
| GM[§] | 780,72 ± 55.48 | 807,38 ± 55.18 | 0.24 |
| WM[§§] | 688.68 ± 36.55 | 713,22 ± 27.34 | 0.04* |
| WB[§§§] | 1469.41 ± 79.49 | 1518,02 ± 65.04 | 0.07 |
| | MS patients carrying C9orf72 mutation* | MS patients without mutations* | P value |
| GM[§] | 803.16 ± 67.88 | 800.77 ± 76.79 | 0.9 |
| WM[§§] | 683.47 ± 32.03 | 699.44 ± 23.57 | 0.5 |
| WB[§§§] | 1486.64 ± 84.08 | 1500,21 ± 89.25 | 0.8 |

GM: gray matter; WM: white matter; WB: whole brain







## Conclusions.

Despite the fact that these mutations do not play a major role in MS pathogenesis, they may enhance brain atrophy, especially for white matter.

References.

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*No conflict of interest exists regarding the present study*