Increased serum TDP43 and anti-TDP43 auto-antibodies in ALS patients

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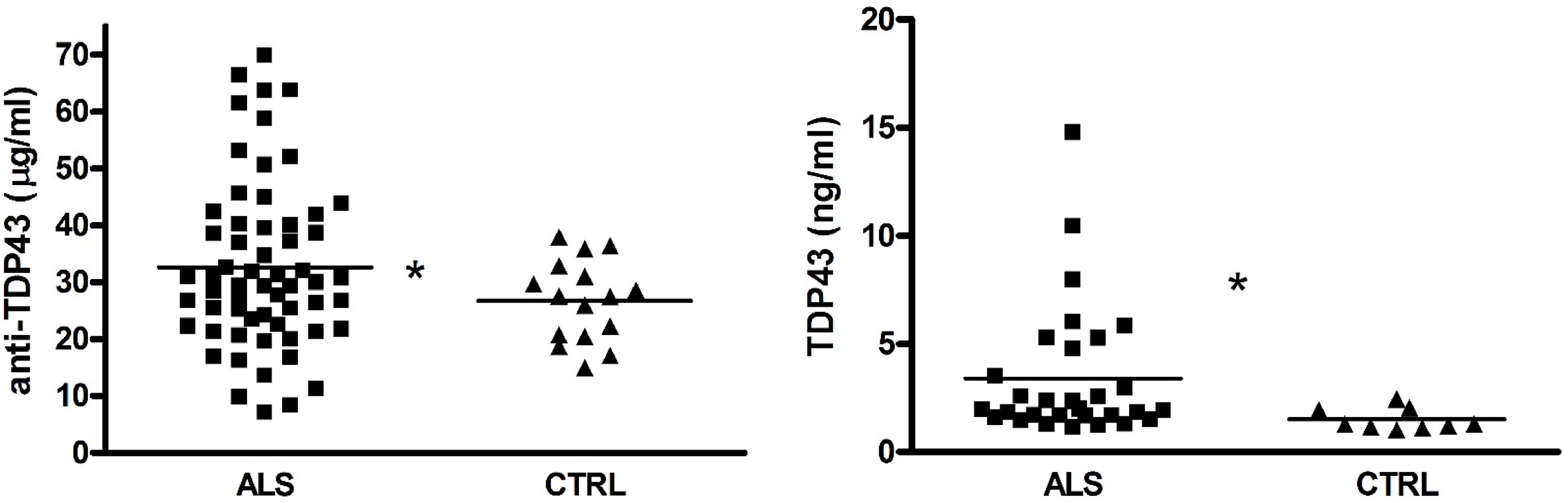
ALS patients express significant clinical heterogeneity that often hinders a correct diagnostic definition, a process that is still heavily relying on clinical bases. Therefore, there is a strong need for **peripheral markers** that could help in the diagnostic phase. ALS neuropathology is characterized by deposition of **TDP43, a protein involved in RNA metabolism**. Interestingly, this protein can be measured in **serum** were cognate **naturally occurring auto-antibodies (TDP43 NAb)** might be also present, albeit never documented before. If present, these NAb might potentially modify the peripheral and/or central TDP43 availability, and even its turnover, in a manner similar to that already proposed for the "amyloid peripheral sink" hypothesis.

Materials and Methods: In this exploratory study, serum TDP43 and TDP43 NAb were assessed by ELISA in 57 ALS outpatients (3 carrying TDP43 mutations) and 17 comparable healthy controls (CTRL).

Results: Serum TDP43 doubled in ALS patients with respect to CTRL ($p=0.003$); presence of TDP43 NAb was documented in serum samples, and a 22% increase was shown in ALS patients versus CTRL ($p<0.03$). The coefficient of variation for both markers was significantly wider in ALS patients when compared to CTRL. No correlation was found between the two proteins in either ALS patients or CTRL. TDP43 mutation carriers displayed values similar to those obtained for the other ALS patients.



Discussion: Serum TDP43 and TDP43 NAb are increased in ALS patients, albeit both fail to represent a state marker of the disease. The wider dispersions of values in ALS patients suggest that distinct pathogenic mechanisms might be operative in a subset of them.

Conclusions: Further studies are needed to clarify if these two proteins might represent suitable trait makers in ALS and to understand the specific role of TDP43 NAb.