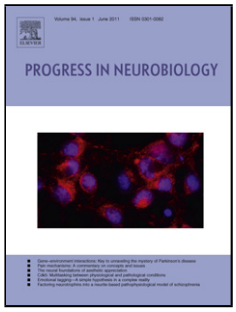

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TDP-43/FUS in Motor Neuron Disease: Complexity and Challenges

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Highlights

- Amyotrophic lateral sclerosis (ALS) is a group of motor neuron diseases involving a dozen distinct and overlapping protein inclusions.
- The complex neuropathology of RNA/DNA binding proteins TDP-43 and FUS in motor neuron disease is critically discussed.
- The loss of function due to nuclear clearance vs. gain of aggregating protein toxicity of TDP-43/FUS is comprehensively assessed.
- New avenues of research involving the role of genome damage and repair defects in FUS/TDP-43-associated ALS.
- Role of disease-linked TDP-43/FUS mutations in familial and sporadic ALS and other motor neuron diseases.
- Lessons learned from TDP-43/FUS animal models.
- Rationale and need for an overarching approach to unravel the fundamental mechanisms based intervention strategies.