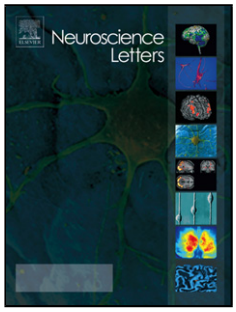


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**Oxidative stress and mitochondrial damage in the pathogenesis of ALS: new perspectives**

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**ABSTRACT**

This review attempts to reconcile the present dual view of the mechanisms operating in Amyotrophic Lateral Sclerosis (ALS). On one side, oxidative stress, mitochondrial damage and protein aggregation are considered as causative of the disease, as strongly supported by evidence obtained in models based on the expression of ALS-typical mutant SOD1. On the other hand, evidence from models expressing ALS-typical mutations in RNA-binding proteins such as FUS and TDP43 indicate that mRNA (dys)metabolism is a major pathway in this disease. A critical analysis of existing literature suggests that there may be more than one point of intersection.

**Abbreviations**: ALS, Amyotrophic Lateral Sclerosis; FTLD, Frontotemporal Lobar Degeneration; mPOS, Mitochondrial Precursor Over-accumulation Stress; ROS, Reactive Oxygen Species; UPRam, Unfolded Protein Response Activated by Mistargeting of proteins; UPRmt, Mitochondrial Unfolded Protein Response.

**Keywords:** ALS, SOD1, FUS/TLS, TDP43, oxidative stress, mitochondria, RNA metabolism, iron.