Investigating the Pathogenesis of Amyotrophic Lateral Sclerosis (ALS) Using Mutant Metal-Deficient SOD1 Protein

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Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disorder characterized by the progressive degeneration of motor neurons, leading to muscle weakness, paralysis, and ultimately respiratory failure. Despite extensive research, the precise cause of ALS remains unclear, though both genetic and environmental factors are believed to contribute to its onset and progression. Among the genetic mutations associated with ALS, mutations in the superoxide dismutase 1 (SOD1) gene are among the most studied. SOD1 is a critical enzyme involved in the detoxification of reactive oxygen species, and mutations in this gene are thought to contribute to ALS through mechanisms such as protein misfolding, oxidative stress, mitochondrial dysfunction, and neuroinflammation. In this study, Drosophila melanogaster was used as a model to investigate ALS through the expression of the mutant G85R SOD1 protein. Wild-type and mutant flies were treated with Ryanodine, Glutathione, Riluzole, and Edaravone, compounds known for their roles in calcium homeostasis, antioxidant activity, and neuroprotection. The effects of these treatments were evaluated through assays measuring motor function, neuronal survival, and mitochondrial health. Mutant flies exhibited ALS-like symptoms, including significantly impaired mitochondrial function, reduced motor neuron vitality in the central nervous system (CNS), and approximately 50% muscle strength reduction compared to wild-type controls. These findings support the conclusion that mutant SOD1 contributes to key ALS symptoms, providing insight into the pathogenesis of the disease. Further research is needed to explore the underlying mechanisms and potential therapeutic strategies for ALS.

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