Turkish Journal of Physiotherapy and Rehabilitation; 32(3)
ISSN 2651-4451 | e-ISSN 2651-446X

Key Molecular Mechanisms in the Pathogenesis of Amyotrophic Lateral Sclerosis (ALS).

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ABSTRACT

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder with a poor prognosis involving both upper motor neurons (UMN) and lower motor neurons (LMN). ALS is considered a multifactorial disease that involves multifactorial emergence of complex interrelation and mechanisms, therefore, therapeutics for ALS should be able to block or compensate for various aberrant pathological events. Growing evidence suggests that endoplasmic reticulum (ER) stress and the UPR pathway, autophagy and apoptosis may be implicated in the pathogenesis of ALS. This review focuses on the recent findings to elucidate potential molecular mechanisms for ALS. A comprehensive understanding of the pathogenesis of ALS may lead to the discovery of a breakthrough treatment strategy for this disease.

INTRODUCTION

Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, is a fatal progressive neurodegenerative disease without effective treatments. The disease is characterised by the loss of upper motor neurons in motor cortex and lower motor neurons in the brainstem and spinal cord, that results in progressive paralysis and death due to respiratory failure, within three years of onset of the first symptoms (1). It is also the most common adult-onset motor neuron disorder. The disease usually occurs between the 4th and the 6th decade of life and incidence of ALS diminishes rapidly after the age of 80 (2). Limb-onset ALS, is identified by the coexistence of upper motor neuron (UMN) and lower