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Riboflavin Responsive Mitochondrial Dysfunction in Neurodegenerative Diseases

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Abstract

Mitochondria are the repository for various metabolites involved in diverse energy-generating processes, like the TCA cycle, oxidative phosphorylation, and metabolism of amino acids, fatty acids, and nucleotides, which rely significantly on flavoenzymes, such as oxidases, reductases, and dehydrogenases. Flavoenzymes are functionally dependent on biologically active flavin adenine dinucleotide (FAD) or flavin mononucleotide (FMN), which are derived from the dietary component riboflavin, a water soluble vitamin. Riboflavin regulates the structure and function of flavoenzymes through its cofactors FMN and FAD and, thus, protects the cells from oxidative stress and apoptosis. Hence, it is not surprising that any disturbance in riboflavin metabolism and absorption of this vitamin may have consequences on cellular FAD and FMN levels, resulting in mitochondrial dysfunction by reduced energy levels, leading to riboflavin associated disorders, like cataracts, neurodegenerative and cardiovascular diseases, etc. Furthermore, mutations in either nuclear or mitochondrial DNA encoding for flavoenzymes and flavin transporters significantly contribute to the development of various neurological disorders. Moreover, recent studies have evidenced that riboflavin supplementation remarkably improved the clinical symptoms, as well as the biochemical abnormalities, in patients with neuronopathies, like Brown-Vialetto-Van-Laere syndrome (BVVLS) and Fazio-Londe disease. This review presents an updated outlook on the cellular and molecular mechanisms of neurodegenerative disorders in which riboflavin deficiency leads to dysfunction in mitochondrial energy metabolism, and also highlights the significance of riboflavin supplementation in aforementioned disease conditions. Thus, the outcome of this critical assessment may exemplify a new avenue to enhance the understanding of possible mechanisms in the progression of neurodegenerative diseases and may provide new rational approaches of disease surveillance and treatment.

Keywords: BVVLS; FAD; FMN; mitochondrial dysfunction; motor neuronopathy; riboflavin.

Figures

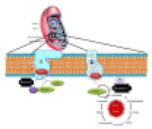

Figure 1 Riboflavin in mitochondrial pathways (RF-...

Figure 2 Riboflavin related mitochondrial dysfunction in...

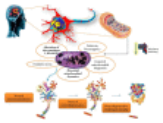

Figure 3 Riboflavin deficiency leading to mitochondrial...

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