The Role of Melanotropins in the Improvement of Cognitive Functions in Dementia-Related Disorders

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Current neurophysiological and neuropharmacological evidence suggests that melanotropins are one of the key regulators in a wide variety of physiological processes in the central nervous system (CNS). Fluctuations and decreased levels of the alpha-Melanocyte-stimulating hormone (alpha-MSH) in Dementia-Related Disorders, e.g., Alzheimer's disease, may underlie the physiological basis of these diseases. The aim of this research was to investigate the possible use of alpha-MSH in restoring cognitive abilities in affected individuals. Cognitive impairment was induced in Danio rerio using a novel yet inexpensive approach via a high-fat diet compared with a control diet. Groups that were diverse in terms of diet and cognitive functions were then treated with the synthetic analog of alpha-MSH: Melanotan II (MT-II). The peptide was dissolved in water, and the subjects were placed in the solutions. MT-II was used in the study since it is a cyclic molecule with increased stability and the ability to penetrate membranes; Melanocortin Receptors (MC3R and MC4R) are mostly expressed in the CNS and therefore need to be modulated by molecules with the ability to penetrate the blood-brain barrier (BBB). The cognitive state was measured by various methods, including the Y-Maze Test and the One-Trial Memory Test with a scoring method based on the Barnes Maze. Fish treated with a high-fat diet exhibited cognitive deficits in comparison to the group with a control diet; fish treated with MT-II exhibited a change in cognitive level depending on the diet used previously. Results are promising for further investigation and the potential development of the pro-cognitive drug. The non-invasive method of administering the compound by diffusion is also worth to be further developed.

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