Exploring Peptides for Neurological Health & Longevity

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Endogenous Peptides

Our bodies create peptides from genes that code for particular proteins or protein-coupled receptors, such as G-protein-coupled-receptors. These endogenous peptides range in length from two to 100 amino acids. Because peptides develop within a cell along with their relevant receptor, they tend to have high specificity for precise biochemical interactions. [1,2] Peptides are known to modulate innumerable downstream reactions via multiple mechanisms to have, among other properties, antioxidant, anti-inflammatory, antimicrobial, immunomodulatory, anticancer, antihypertensive, pain-modulating, and anti-lipidemic effects.[3,4] In fact, the peptidergic system is the largest ligand-receptor signaling complex within human beings, and fundamentally controls all cellular processes and functions. The body creates around 300,000 peptides, and the roles many of them play are still being determined.[5]

As well as occurring endogenously and being naturally present in certain foods, peptides have been synthesized for therapeutic purposes since the 1920s, beginning with insulin, and followed later by the synthesis of several peptide analogues including adrenocorticotropic hormone, growth-hormone releasing hormone, and cholecystokinin.[6] Currently, over 300 peptide drugs are FDA-approved and available on the market, including the glucagon-like peptide-1 agonists Ozempic and Victoza. Many more peptide drugs are undergoing development in preclinical and clinical trials.[7,8]

The Therapeutic Potential of Neuropeptides

The need for safe and effective therapies to promote cognitive health, and the growing interest in healthy longevity have brought the therapeutic promise of neuropeptides increasingly to the forefront of restorative medicine practice.[9] Neuropeptides are produced in the central nervous system and peripheral organs. Given that neuropeptide activity is crucial for neurological function and homeostasis, it is possible that dysfunction within the neuropeptide system could contribute to neurodegenerative conditions.[10,11]Levels of neuropeptides associated with cognitive function, including developing the neuronal circuitry that underlies learning and memory, have been found to be altered (increased or decreased) in the cerebral cortex of people with Alzheimer’s disease as well as in rodent models of Alzheimer’s disease.[12,13]

Oxidative and inflammatory damage also appear to be considerable factors in the pathology of many neurodegenerative conditions including Alzheimer’s disease and Parkinson’s disease. Consequently, there is great interest in the neuroprotective anti-inflammatory effects of peptides, which are capable of interacting with transcription factors to inhibit downstream signaling, transduction, and amplification of inflammatory and

oxidative cascades, thereby potentially preventing or reversing neurodegeneration.[14]

A tangible example of the positive impact of neuropeptides is seen with exercise. Certain neuropeptides, in particular neuropeptide Y, ghrelin, galanin, and vasoactive intestinal peptide are thought to mediate the beneficial effects that physical activity has been found to have on cognition.[15]In addition, two neuropeptides, epithalon and cerebrolysin, continue to be studied for their therapeutic promise in preventing and reversing brain damage.

Epithalon

Epithalon (aka epitalon) is a synthetic peptide consisting of alanine, glutamic acid, aspartic acid, and glycine. It is modelled on the endogenous peptide epithalamin, which modulates pineal gland function. Several studies indicate that epithalon crosses the blood-brain barrier. It may stimulate neurogenesis,[16]and increase levels of phosphor-CREB, a DNA-binding protein essential for learning and memory.[17]

Epithalon is also a powerful antioxidant that may promote healthy aging and longevity by supporting cellular health.[18] In experimental studies, it was shown to increase telomere length in human fetal fibroblasts.[19]It also allowed cells to proliferate beyond their Hayflick limit (the limit on normal somatic cell division as a result of the telomere shortening that occurs with each replication), which means that epithalon likely stimulates the production of telomerase to have senolytic activity.[20]Epithalon induced chromatin remodeling in cultured leukocytes, suggesting a possible epigenetic mechanism.[21,22] The actual epigenetic mechanism was further clarified in a later study of the effects of epithalon on human gingival mesenchymal stem cells, where it was found to support healthy neurogenic differentiation, gene expression, and protein synthesis.[23]

In pre-clinical trials, epithalon was shown to increase the lifespan of fruit flies,[24,25] and increase the lifespan and inhibit tumor growth in mice,[26] and rats.[27,28,29] In a mouse model of senescence, mice administered epithalon had lower levels of DNA damage than mice who were given melatonin.[30]

In a placebo-controlled trial of 70 adults aged around 65 who were experiencing accelerated aging as a result of cardiovascular disease, participants received 5 intramuscular injections of either 10 mg epithalamin or saline at three-day intervals, every six months for three years. Participants were followed for an additional nine years.[31] Over 12 years, the treatment group experienced a 28% decreased mortality rate and 2-fold lower rate of cardiovascular disease-specific mortality. Participants were then followed for an addition three years, making a total of 15 years, at which point researchers concluded that epithalamin treatment prevented age-associated decline in physical endurance, normalized the circadian rhythm production of melatonin, and normalized carbohydrate and lipid metabolism.[32] No serious adverse reactions were reported over this entire timespan.

Cerebrolysin

Cerebrolysin is a neuropeptide that mimics the activity of endogenous neurotrophic factors in the brain. Preclinical studies indicate that cerebrolysin is neuroprotective[33] and can facilitate recovery following acute ischemic stroke[34] and traumatic brain injury.[35]

It has also been found to be neuroprotective against neuronal death following epileptic seizures.[36]

Conclusion

Therapeutic neuropeptides hold tremendous promise for neurological health and healthy aging. Epithalon in particular appears to support neurological and cellular health through a number of mechanisms including promoting the production of telomerase, and recalibrating age-related circadian rhythm disruptions in melatonin

patterns. As age-associated markers of inflammation increase, levels of epithalamin and melatonin decrease, as does, therefore, our capacity for deep sleep, tissue repair, and cellular longevity. Epithalon may prove to be a robust piece of the puzzle in supporting anti-inflammatory and cell-longevity pathways.

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