ENHANCED MUSCARINIC RECEPTOR RESPONSES IN VITRO AFTER MULTI-NUTRIENT SUPPLEMENTATION

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Alzheimer’s disease (AD) is a progressive neurodegenerative disease and it’s clear that in addition to Abeta plaque and tangle formation, loss of dendritic spines and synaptic connections are a hallmark of AD. Previous work has demonstrated that nutrients such as DHA, EPA, UMP, choline, vitamins B6 and B12, folate, phospholipids (PLs), vitamin C and E, and selenium act synergistically in improving synapse formation. This specific combination of nutrients, combined in Fortasyn™Connect, was tested in a proof-of-concept clinical study that resulted in memory improvement in mild AD patients (Scheltens2010). In addition, activation of muscarinic receptors has been shown to stimulate non-amyloidogenic APP processing, possibly by facilitating synapse formation.

To investigate the effects of specific nutrient combinations on muscarinic receptor responses, we measured carbachol-induced changes in membrane potential using a FLIPR assay on PC12 cells. NGF differentiated cells were supplemented with combinations of DHA, EPA, UMP, choline, B-vits, PLs and vitamin C and E, and selenium. We also investigated binding properties and activation of muscarinic M1/M2 receptors in membranes prepared from CHO cells, stably transfected with human M1/M2 muscarinic receptor genes after nutrient supplementation.

Multi-nutrient supplementation improved muscarinic receptor response in PC12 cells. Combinations of nutrients displayed some changes in membrane potential but the complete formula showed maximum increase. Multi-nutrient supplementation of CHO cells increased muscarinic receptor density in plasma membranes and enhanced receptor-mediated G-protein activation.

The specific combination of nutrients in Fortasyn™Connect acts synergistically in enhancing muscarinic receptor responses, probably by facilitating receptor-mediated G-protein activation.

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