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POSTER ABSTRACT

Beta-Amyloid Peptide (1-42) Inhibits Transmitter Release via a NO-PKG Pathway Affecting Exocytosis

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Beta-Amyloid peptide (Aß) inhibits potassium-evoked acetylcholine (ACh) release in cultured ciliary ganglion(CG) neurons. These effects are calcium- and nitric oxide-dependent. Here we show that cGMP was able to mimic the inhibition of ACh release in a dose-dependent manner. In addition, 10 uM RP8pCPT-cGMP, a cyclic GMP-dependent protein kinase inhibitor (PKGI), coincubated with aggregated Aß in CG cell culture restored control levels of ACh release, while Aß alone completely inhibited evoked release. Identical experiments conducted using 1-5 uM A23184, a calcium-ionophore, to evoke release produced the same results, suggesting that Aß does not affect extracellular calcium influx. These results support a model in which a NO-PKG pathway mediates the effects of Aß on evoked neurotransmitter release. Total labeled ACh in Aß-treated and control cells were identical, suggesting that Aß does not decrease choline uptake or ACh synthesis. Supported by grants from The Dana Foundation and Grenolds Memorial Fund.