POSTER ABSTRACT

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

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Beta-Amyloid peptide (Aβ) 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 μM RP8pCPT-cGMP, a cyclic GMP-dependent protein kinase inhibitor (PKGI), coincubated with aggregated Aβ in CG cell culture restored control levels of ACh release, while Aβ alone completely inhibited evoked release. Identical experiments conducted using 1-5 μM A23184, a calcium-ionophore, to evoke release produced the same results, suggesting that Aβ does not affect extracellular calcium influx. These results support a model in which a NO-PKG pathway mediates the effects of Aβ on evoked neurotransmitter release. Total labeled ACh in Aβ-treated and control cells were identical, suggesting that Aβ does not decrease choline uptake or ACh synthesis. Supported by grants from The Dana Foundation and Grenolds Memorial Fund.