Butyrylcholinesterase interactions with amylin may protect pancreatic cells in metabolic syndrome

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Abstract:

The metabolic syndrome (MetS) is a risk factor for type 2 diabetes mellitus (T2DM). However, the mechanisms underlying the transition from MetS to T2DM are unknown. Our goal was to study the potential contribution of butyrylcholinesterase (BChE) to this process. We first determined the hydrolytic activity of BChE in serum from MetS, T2DM and healthy individuals. The ‘Kalow’ variant of BChE (BChE-K), which has been proposed to be a risk factor for T2DM, was genotyped in the last two groups. Our results show that in MetS patients serum BChE activity is elevated compared to T2DM patients and healthy controls (P < 0.001). The BChE-K genotype showed similar prevalence in T2DM and healthy individuals, excluding this genotype as a risk factor for T2DM. However, the activity differences remained unexplained. Previous results from our laboratory have shown BChE to attenuate the formation of beta-amyloid fibrils, and protect cultured neurons from their cytotoxicity. Therefore, we next studied the in vitro interactions between recombinant human butyrylcholinesterase and amylin by surface plasmon resonance, Thioflavine T fluorescence assay and cross-linking, and used cultured pancreatic beta cells to test protection by BChE from amylin cytotoxicity. We demonstrate that BChE interacts with amylin through its core domain and efficiently attenuates both amylin fibril and oligomer formation. Furthermore, application of BChE to cultured beta cells protects them from amylin cytotoxicity. Taken together, our results suggest that MetS-associated BChE increases could protect pancreatic beta-cells in vivo by decreasing the formation of toxic amylin oligomers.

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