Hyperglycemia- and neuropathy-induced changes in mitochondria within sensory nerves.

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Abstract

OBJECTIVE: This study focused on altered mitochondrial dynamics as a potential mechanism for diabetic peripheral neuropathy (DPN). We employed both an in vitro sensory neuron model and an in situ analysis of human intraepidermal nerve fibers (IENFs) from cutaneous biopsies to measure alterations in the size distribution of mitochondria as a result of hyperglycemia and diabetes, respectively. METHODS: Neurite- and nerve-specific mitochondrial signals within cultured rodent sensory neurons and human IENFs were measured by employing a three-dimensional visualization and quantification technique. Skin biopsies from distal thigh (DT) and distal leg (DL) were analyzed from three groups of patients; patients with diabetes and no DPN, patients with diabetes and confirmed DPN, and healthy controls. RESULTS: This analysis demonstrated an increase in mitochondria distributed within the neurites of cultured sensory neurons exposed to hyperglycemic conditions. Similar changes were observed within IENFs of the DT in DPN patients compared to controls. This change was represented by a significant shift in the size frequency distribution of mitochondria toward larger mitochondria volumes within DT nerves of DPN patients. There was a length-dependent difference in mitochondria within IENFs. Distal leg IENFs from control patients had a significant shift toward larger volumes of mitochondrial signal compared to DT IENFs. INTERPRETATION: The results of this study support the hypothesis that altered mitochondrial dynamics may contribute to DPN pathogenesis. Future studies will examine the potential mechanisms that are

responsible for mitochondrial changes within IENFs and its effect on DPN pathogenesis.

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