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Diabetes Mellitus Causes Early Ultrastructural Changes to the Nuclei and Mitochondria of Neurons and Astrocytes in Rats Subjected to a Brief Period of Cerebral Ischemia

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It has been previously demonstrated that hyperglycemia caused by glucose infusion or diabetes enhances neuronal damage induced by transient global or focal cerebral ischemia [1]. In addition to neurons, astrocytes may also be the target and damage to the astrocytes may in turn influence the neuronal survival [2]. The objective of the present study was to define the ultrastructural alterations of neurons and astrocytes in streptozotocin-induced diabetic rats subjected to a brief period of global ischemia.

Five minutes of global ischemia was induced in non-diabetic and diabetic rats. Brain samples were collected after 30 min, 6 h, 1, 3, and 7 days of recirculation as well as from sham-operated controls. Electron microscopy demonstrated homogenous neuronal nuclear chromatin, visible nuclei and intact nuclear membranes up to 1 d of recovery in both non-diabetic and diabetic rats. Mitochondrial morphology was normal up to 6 h of recovery, but disarray of mitochondrial cristae, mild lucency and swelling were observed in a few mitochondria after 1 d of recovery in non-diabetics. In contrast, diabetic rats showed disarray of mitochondrial cristae after 30 min and developed more severe swelling after 6 h and 1d of recovery. These findings are consistent with our previous published ultrastructural studies in rats subjected to an intermediate period of global ischemia [3]. No apoptotic bodies were observed in any of the sections examined. In astrocytes, the nuclear chromatin was homogenous, nuclei were visible, and nuclear membrane was intact up to 1 d of recovery in cortex. Mitochondrial morphology was normal up to 1 d of recovery in nondiabetic rats. Compare to nondiabetic rats, nuclear and mitochondrial morphological alterations were prominent in diabetic rats after 1 day of recovery. Nuclear shrinkage, chromatin condensation and void space were evident. Disarray of mitochondrial cristae, lucency, and swelling were observed in astrocytes after 1 d of recovery.

The results suggest that diabetic hyperglycemia causes damage to both neurons and astrocytes in early reperfusion phase. The damage to mitochondria in neurons and astrocytes may activate mitochondria-initiated cell death pathways results in DNA fragmentation and ischemic cell death.

References

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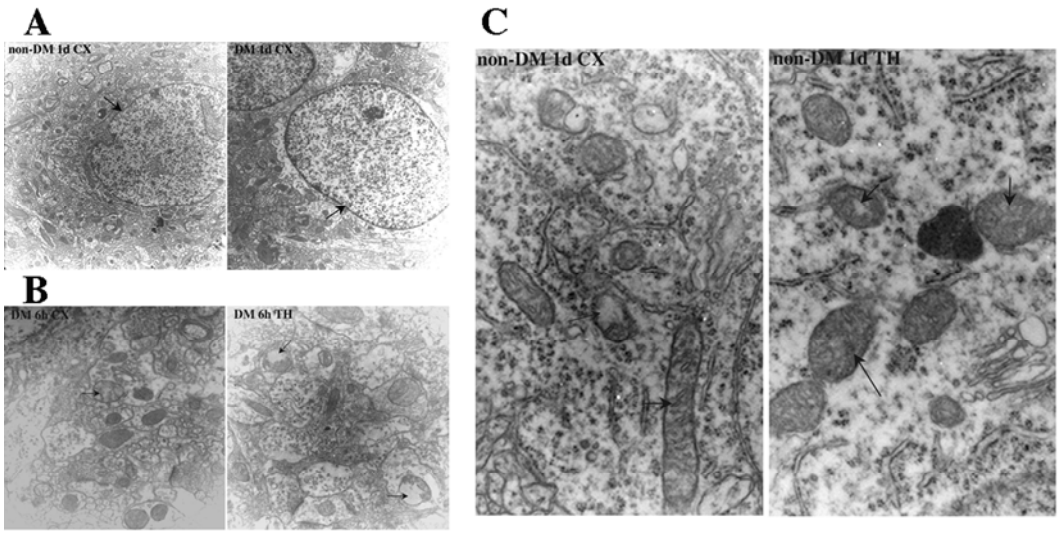

Figure 1. Electron micrographs of nuclei and mitochondria of neurons in the neocortex (CX) and thalamus (TH) in non-diabetic (non-DM) and diabetic (DM) rats subject to five minutes global ischemia. A, nuclear morphology in CX in both non-DM and DM rats after 1d recovery, magnification was 8,000X. Arrows denote nuclei. **B,** mitochondrial morphology in CX and TH in DM rats after 6 h recovery, magnification was 16,000X. **C,** mitochondrial morphology in CX and TH in non-DM rats after 1 d recovery, magnification was 10,000X. Arrows denote mitochondria with disarrayed cristae, mild lucency and swelling.

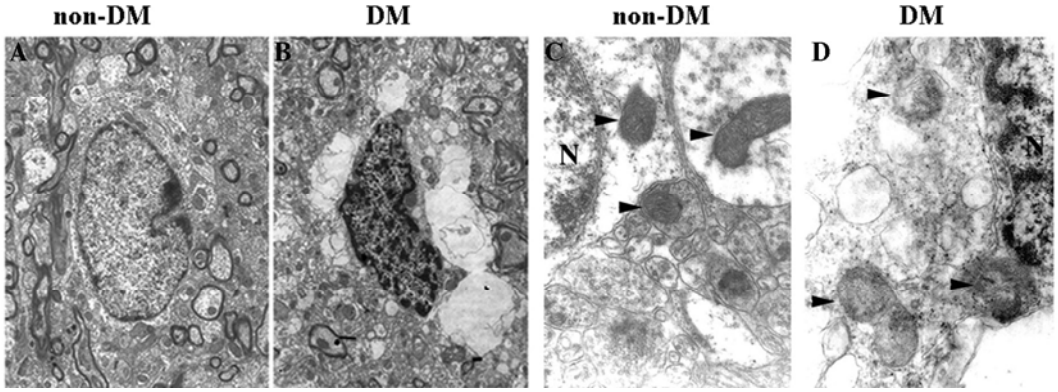

Figure 2. Electron micrographs of nuclei and mitochondria of astrocytes in non-diabetic (non-DM) and diabetic (DM) rats subject to five minutes global ischemia, followed 1 d of recirculation. Nuclear shrinkage, chromatin condensation and void space around the astrocytes are evident in diabetics (A) but not in non-diabetics (B). Magnification=2,000x. Mitochondrial lucency and swelling are observed in diabetic (C) but not in non-diabetic animals (D). Magnification=40,000X. Arrows denote mitochondria with disarrayed cristae, mild lucency and swelling.

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