

Mitochondria in Cell Death and Use of Alpha-Lipoic Acid for Neuroprotection

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Retinal ganglion cell axons within the globe are functionally specialised and are particularly enriched with mitochondria. Good evidence also exists to suggest that when these mitochondria are drastically impaired as might occur in retinal ischemia or glaucoma ganglion cell death occurs. Thus agents targeted specifically at enhancing ganglion cell mitochondrial energy production and/or scavenge free radicals (known to be generated by dysfunctional mitochondria) might therefore be useful to treat a disease like glaucoma. One such substance is possibly α -lipoic acid. This substance is tolerated when taken orally, diffuses readily into cells, serves as a co-factor to mitochondrial enzymes and is also a powerful antioxidant.

In this study rats were injected intraperitoneally with either vehicle or α -lipoic acid (100 mg/kg) once daily for 11 days. On the 3rd day, ischemia was delivered to the rat retina by raising the intraocular pressure above systolic blood pressure for 45 min. The electroretinogram was measured prior to ischemia and 5 days after reperfusion. Rats were killed 5 or 8 days after reperfusion and the retinas were processed for immunohistochemistry and for determination of mRNA levels by RT-PCR.

Ischemia-reperfusion caused a significant reduction of the a- and b-wave amplitudes of the electroretinogram, a decrease in nitric oxide synthase and Thy-1 immunoreactivities, a decrease of retinal ganglion cell-specific mRNAs and an increase in bFGF and CNTF mRNA levels.

The results show that α -lipoic acid provides protection to the retina and their ganglion cells from ischemia-reperfusion injuries. It is also known that α -lipoic acid blunts any loss of retinal neurons in culture caused by anoxia or light. The combined data therefore suggests that α -lipoic should be considered a candidate drug to treat glaucoma patients.