Lipoic acid in Alzheimer's disease – From basic therapeutic concepts to clinical trials

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Alzheimers disease (AD) is a progressive neurodegenerative disorder that destroys patient memory and cognition and the ability to carry out daily activities. Despite extensive research into the pathogenesis of AD, a neuroprotective treatment remains unavailable. LA has a variety of properties, which might be able to interfere with pathogenic principles of AD. For example, LA increases glucose uptake, chelates redox-active transition metals and scavenges reactive oxygen species (ROS. Since AD is characterized by chronic inflammation, reduction of pro-inflammatory cytokine expression and free radical production by interference with redox-active signalling by LA might be beneficial for AD patients. In a cell culture model of brain inflammation, we show that LA dose-dependently reduces LPS+IFN-gamma induced nitric oxide production in N-11 murine microglia, with the two enantiomers and the RS form being equally active. In an open clinical trial, 43 patients were given 600mg RS-LA for 48 months. Whereas LA did not show significant benefits in moderate and severe AD, cognitive scores in LA treated patients with early dementia (ADAScog<15) deteriorated significantly less than in the control group only treated with cholinesterase-inhibitors (ADAScog: 1.2 points/year vs. 2.6 points/year in untreated controls, MMSE: -0.6 points/year vs. -2 points/year in untreated controls). Despite the fact that this study was an open trial, our data suggest that LA acid might become a standard 'neuroprotective' therapy option for AD.