Abstract

Background
Energy deficiency and mitochondrial failure have been recognized as a prominent, early event in Alzheimer's disease (AD). Recently, we demonstrated that chronic exposure to amyloid-beta (Aβ) in human neuroblastoma cells over-expressing human wild-type amyloid precursor protein (APP) resulted in (i) activity changes of complexes III and IV of the oxidative phosphorylation system (OXPHOS) and in (ii) a drop of ATP levels which may finally instigate loss of synapses and neuronal cell death in AD. Therefore, the aim of the present study was to investigate whether standardized Ginkgo biloba extract LI 1370 (GBE) is able to rescue Aβ-induced defects in energy metabolism.

Methodology/Principal Findings
We used a high-resolution respiratory protocol to evaluate OXPHOS respiratory capacity under physiological condition in control (stably transfected with the empty vector) and APP cells after treatment with GBE. In addition, oxygen consumption of isolated mitochondria, activities of mitochondrial respiratory enzymes, ATP and reactive oxygen species (ROS) levels as well as mitochondrial membrane mass and mitochondrial DNA content were determined. We observed a general antioxidant effect of GBE leading to an increase of the coupling state of mitochondria as well as energy homeostasis and a reduction of ROS levels in control cells and in APP cells. GBE effect on OXPHOS was even preserved in mitochondria after isolation from treated cells. Moreover, these functional data were paralleled by an up-regulation of mitochondrial DNA. Improvement of the OXPHOS efficiency was stronger in APP cells than in control cells. In APP cells, the GBE-induced amelioration of oxygen consumption most likely arose from the modulation and respective normalization of the Aβ-induced disturbance in the activity of mitochondrial complexes III and IV restoring impaired ATP levels possibly through decreasing Aβ and oxidative stress level.

Conclusions/Significance
Although the underlying molecular mechanisms of the mode of action of GBE remain to be determined, our study clearly highlights the beneficial effect of GBE on the cellular OXPHOS performance and restoration of Aβ-induced mitochondrial dysfunction.

Figures

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