Amyloid-beta leads to impaired cellular respiration, energy production and mitochondrial electron chain complex activities in human neuroblastoma cells

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Evidence suggests that amyloid-beta (Abeta) protein is a key factor in the pathogenesis of Alzheimer's disease (AD) and it has been recently proposed that mitochondria are involved in the biochemical pathway by which Abeta can lead to neuronal dysfunction. Here we investigated the specific effects of Abeta on mitochondrial function under physiological conditions. Mitochondrial respiratory functions and energy metabolism were analyzed in control and in human wild-type amyloid precursor protein (APP) stably transfected human neuroblastoma cells (SH-SY5Y). Mitochondrial respiratory capacity of mitochondrial electron transport chain (ETC) in vital cells was measured with a high-resolution respirometry system (Oxygraph-2k). In addition, we determined the individual activities of mitochondrial complexes I-IV that compose ETC and ATP cellular levels. While the activities of complexes I and II did not change between cell types, complex IV activity was significantly reduced in APP cells. In contrast, activity of complex III was significantly enhanced in APP cells, as compensatory response in order to balance the defect of complex IV. However, this compensatory mechanism could not prevent the strong impairment of total respiration in vital APP cells. As a result, the respiratory control ratio (state3/state4) together with ATP production decreased in the APP cells in comparison with the control cells. Chronic exposure to soluble Abeta protein may result in an impairment of energy homeostasis due to a decreased respiratory capacity of mitochondrial electron transport chain which, in turn, may accelerate neurons demise.

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