Structure-function relationship of mitochondria in neuronal diseases

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The involvement of changes in mitochondrial functions and morphology in neuronal diseases receives growing attention. Diseases like Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease and temporal lobe epilepsy (TLE) are associated with alterations in neuronal mitochondrial functions and morphology. However, the underlying mechanisms are not well understood so far. One reason is probably the restricted access to live human brain tissue, limiting most of the studies to animal models. Due to the fast progressing stem cell research, nowadays, it is possible to investigate mechanisms involved in neuronal diseases in induced neurons obtained from patient's fibroblasts. In our study we will focus on alterations of mitochondrial functions and morphology of induced neurons derived from AD-, PD- and HD-specific fibroblasts.

Recently it was observed that the neuropeptide enkephaline (Enk) plays a crucial role in maintenance of mitochondrial respiration. Enk-KO (knockout) mice displayed less dynamic hippocampal mitochondrial respiration and increased seizure induced morphological changes compared to wild-type mice in the kainate model of TLE. Enk binds preferentially to the delta opioid receptors (DOR) known to elicit neuroprotective effects. It is thought that the neuroprotective effects of DOR activation are due to adaptations of mitochondrial respiration. In line with this, hypoxic preconditioning (HPC), which is known to decrease susceptibility to seizures, was suggested to act via DOR. We will investigate the effects of the Enk/DOR system on morphological and functional changes of mitochondria in HPC.