A (CoA), classified as Pantothenate Kinase Associated Neurodegeneration (PKAN), resulted in identification of the enzyme mitochondrial form, PANK 2, that was distinguished in regulatory properties from the cytosolic CoA synthesis from pantothenic acid (PA). Coenzyme biosynthesis in CNS structures is determined by PA uptake from circulating blood and biotransformation to intermediate products, such as 4′-phospho-PA (PPA) and 4′-phospho-pantetheine (PPN). For the mitochondrial neuronal compartment, the pathway remains to be open for CoA biosynthesis from pantetheine (PN), exactly, the oxidized form, pantethine (PT). The experiments with intraperitoneal injections of [^{3}H]-PA or [^{3}H]-PT at dose of 1.1 mCi/kg to albino Wistar rats showed active transport (uptake) of both forms of CoA precursors by the large hemispheres that reached a maximum by 180 min (PT treatment) and 12 h (PA administration). The PT treatment was accompanied by radionuclide accumulation predominantly in the postmitochondrial fraction in which HPLC identified PPA as the main form (other PA components, PN, PPN and low amounts of CoA). The predominant metabolite in perchlorate mitochondrial extracts was PPA and, probably, dephospho-CoA. The [^{3}H]-PA administration caused biotransformation of the radionuclide to CoA whose fraction reached 46% after 30 min and 72% after 12 h of the total radioactivity level in perchlorates, whereas the radionuclide was not deposited in the mitochondrial PPA and PPN fractions and the post-mitochondrial supernatant. The PT administration can be suggested to cause PPA accumulation while the PA treatment — to form CoA in the CNS, which reflects the peculiarities of their neuroprotective activity. A high level of uptake and biotransformation of CoA biosynthetic precursors was found in the hippocampus.

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8P.2 Analysis of mitochondrial DNA deletions in epileptic hippocampus

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Mitochondrial dysfunction is emerging as a key cause factor for therapy-resistant forms of severe epilepsy [1]. A broad variety of mitochondrial DNA mutations [2] is associated with mitochondrial respiratory chain failure, consequent mitochondrial dysfunction and different epileptic phenotypes. It is not yet clear whether dysfunction of mitochondrial oxidative phosphorylation has a causative role in temporal lobe epilepsy (TLE) with hippocampal sclerosis. In this study we compared amount of multiple deletions of the mtDNA in four different hippocampal subfields (CA1, CA3, AD and PH) in patients with TLE, by using a long range PCR technique. The samples were obtained after epilepsy surgery of 20–40 years old patients, belonging to two different TLE subgroups. The first group is represented by 21 TLE patients whom developed Ammon's horn sclerosis — the most common type of neuropathological damage in individuals with TLE, characterized by neuronal cell loss in the hippocampus. The second group includes 8 TLE patients, with identified brain lesion as primary cause of epilepsy. It is well known that these patients usually do not develop hippocampal degeneration. We found a significant difference in the mtDNA deletion amounts between the two groups of patients, in each of the four hippocampal subfields. Our findings demonstrate that, in difference to lesion TLE patients, mtDNA deletions are typical for patients with AHS, especially, in the CA3 region. Though, it is known that multiple deletions are accumulating with age, in this study we demonstrate that in AHS patients multiple deletions can be detected in early stage of life. We propose that mtDNA deletions might be relevant for seizure generation in AHS patients.

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8P.3 Abnormalities of mitochondrial physiology and phenotype in sensory neurons in diabetes

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Diabetic sensory neuropathy is a major complication of type 1 and 2 diabetes that leads to distal loss of nerve fibers. Impairments in mitochondrial function have been proposed to play a role in the etiology of the neurodegeneration. We tested the *hypothesis* that mitochondrial dysfunction in sensory neurons in type 1 diabetes is due to abnormal activity of the respiratory chain and an altered mitochondrial proteome. Rates of oxygen consumption in mitochondria from dorsal root ganglia (DRG) of age-matched control, 12–22 week streptozotocin (STZ)-induced type 1 diabetic rats and diabetic rats treated with insulin were measured by OROBOROS oxygraph. Rates of coupled respiration with pyruvate + malate (P + M; full respiratory chain) and with ascorbate + TMPD (Asc + TMPD; Complex IV) in lumbar DRG were unchanged after 12 weeks of diabetes. By 22 weeks of diabetes, respiration with P + M was significantly decreased by 31–44% and with Asc + TMPD by 29–39% compared to control. Attenuated mitochondrial respiratory activity of STZ-diabetic rats was significantly improved by insulin treatment that did not fully correct other indices of diabetes. Enzymatic activities of mitochondrial complexes I and IV and the Krebs cycle enzyme, citrate synthase, were decreased in mitochondria from DRG of 22 week STZ-diabetic rats compared to control. Quantitative proteomic analysis using $^{13}C_6$-Lys and $^{13}C_6$,$^{15}N_4$-Arg labeled mitochondria as isotope tagged internal standards indicated that proteins associated with oxidative phosphorylation and the citric acid cycle were significantly down-regulated. Western blotting of DRG samples confirmed the proteomic analysis results for a specific subset of proteins and revealed reduced activation of AMP kinase (AMPK) coupled with diminished expression of peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PGC-1α). In vitro confocal imaging studies with neurons from diabetic rats using TMRM+ in sub-quench mode showed mitochondria in axons to be depolarized and to exhibit an aberrant hyperpolarization in response to oligomycin. Mitochondrial dysfunction in sensory neurons in type 1 diabetes was associated with impaired rates of respiratory chain activity and modified adaption to hyperpolarization. The abnormal mitochondrial activity correlated with a down-regulation of an array of mitochondrial proteins that was associated with lowered activation status of the up-stream regulators of mitochondrial biogenesis, AMPK and PGC-1α.

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