corresponding to the distance between the lamellae which centers around 220 Å. At swelling of heart mitochondria (90 mOsm) the ordering sharply decreases and the interference peak becomes negligible. Hereby it was proved that under conditions of low-amplitude swelling of heart mitochondria the enzymes of respiration system and ATP-synthesis system function as supercomplex and these functional changes are accompanied by the changes of inner mitochondrial membrane ultrastructure.

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S2.P5

Adaptive reprogramming of brain mitochondrial biology during preconditioning prevents the sporadic Alzheimer's disease-like phenotype
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Brief episodes of sublethal hypoxia reprogram brain response to face subsequent lethal stimuli by triggering adaptive and pro-survival mechanisms — a phenomenon denominated by hypoxic preconditioning (HP). Notably, HP effectively prevents sporadic Alzheimer’s disease (sAD)-related pathological features including cognitive decline and cerebral hypometabolism in the sAD rat model induced by the intracerebroventricular administration of streptozotocin (STZ). However, a deeper knowledge on the protective molecular mechanisms underlying brain tolerance is still required. Given the importance of mitochondria in determining cell fate, the present study was devoted to monitor the structural and functional alterations of brain mitochondria in response to a well-established protocol of HP induced by the cyclic exposure to moderate hypoxia (2 h of 10% O\textsubscript{2}) with intervening 24 h reoxygenation periods, during 3 consecutive days. Several parameters related with mitochondrial bioenergetic function, biogenesis, and fusion and fission machinery were evaluated in the cortex and hippocampus of rats immediately, 6 and 24 h after the last hypoxic episode. HP induced a decrease in respiratory state 2 and an increase in ADP/O ratio in brain cortical and hippocampal mitochondria. Immediately after the last hypoxic episode, a significant increase in the protein levels of nuclear respiratory factor-1 (NRF-1), and mitochondrial transcription factor A (TFAM) was observed. 24 h after the last hypoxic episode, a shift in the mitochondrial fusion—fission balance towards fusion occurred, as evidenced by the significant increase in optic atrophy protein 1 (OPA1) protein levels and a decrease in dynamin-like protein 1 (DRP1) protein levels in the brain cortex, and the significant reduction in the fusion protein 1 levels in the hippocampus. Consistently, the electron microscopy analysis revealed HP generated mitochondria with an elongated phenotype. Overall, these results indicate that HP enhances mitochondrial bioenergetic function, probably due to a coordinated interplay between mitochondrial biogenesis and fusion/fission events, increasing brain tolerance. This work is supported by Alzheimer’s Association (NIRG-13-282387).
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S2.P6

Effects of ocean acidification and warming on the mitochondrial physiology of Atlantic cod
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The Atlantic cod (\textit{Gadus morhua}) is an economically important marine fish species exploited by both fishery and aquaculture, especially in the North Atlantic and Arctic oceans. Ongoing climate changes are happening faster in the high latitude oceans with a higher increase of temperature and a steeper decrease in water pH due to anthropogenic CO\textsubscript{2} than in the temperate regions threatening the existence of the Atlantic cod in the areas of its maximum exploitation. In this study, we investigated the mitochondrial physiology of two life-stages of cod under the sea water temperatures and pCO\textsubscript{2} conditions forecasted for the year 2100 in the North Atlantic (+5 °C, 1000 patm CO\textsubscript{2}). In embryos, the metabolism during development showed to be sensitive to rising temperatures with a general increase in respiratory activity until 9 °C (5 °C over the natural range) and a drop in activity at 12 °C mainly caused by a dramatic decrease in Complex I activity, which was not compensated by Complex II. In the adults, already well known for their metabolic plasticity, mitochondria from liver and heart are not affected by either increasing temperature or pCO\textsubscript{2}. However, in heart mitochondria of animals that were reared under warm hypercapnia (10 °C + C + 1000 patm CO\textsubscript{2}), we found OXPHOS to exploit already 100% of the ETS capacity. This suggests that a further increase in temperature or pCO\textsubscript{2} might lead to a mismatch in the ATP demand/production and consequently decrease heart performances. The different mitochondrial plasticities of the two life-stages reflect the sensitivity range at population level and thus can provide a more realistic reading frame of the potential survival of the North Atlantic cod population under climate change.

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S2.P7

Insulin induces cristae remodeling by decreasing complex I and increasing UCP1 expression in rat brown adipose tissue
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Brown adipose tissue (BAT) has an important role in maintaining energy balance throughout mitochondrial uncoupling e.g. thermogenesis. Insulin is one of the major hormones involved in BAT physiology, but its role is still controversial. Recent evidence pinpoints mitochondrial dysfunction in brown adipocyte as an underlying cause of decreased insulin sensitivity and thus disturbed bioenergetics. The mitochondrial function or dysfunction ensuring energy balance throughout mitochondrial uncoupling pathway was characterized by changes in inner membrane morphology and organization. Considering that cristae remodeling is pivotally involved in mitochondrial
bioenergetics and thermogenesis, the effects of insulin administration on complex I and UCP1 expression and cristae remodeling in BAT mitochondria were investigated in this study. Two months old Wistar rats were fed with standard pelleted food ad libitum. The rats were divided into three groups, each with six animals. The first two groups were treated with low (0.4 IU/kg) or high (4 IU/kg) dose of insulin i.p. (Novo Nordisk, Denmark), while the group treated with 0.9% saline solution served as control. The interscapular portion of BAT was used for Western blot and ultrastructural analysis. Western blot analyses were performed using primary antibodies against NDUFA9 and UCP1 (Abcam, UK). Samples for electron microscopy were routinely embedded in Araldite. Ultrathin sections were contrasted and examined on a Philips CM12 transmission electron microscope. Obtained electron micrographs were used for ultrastructural analysis of mitochondria and stereology (cristae volume density). Western blot analyses showed decrease of relative protein expression of NDUFA9 and increase of relative protein expression of UCP1 in treated groups. At ultrastructural level, changes in mitochondrial morphology can be observed. Namely, insulin induced extensive cristae remodeling in both treated groups, increasing cristae abundance e.g. cristae volume density. These results indicate that insulin can modify cristae structure in BAT mitochondria by decreasing complex I expression and increasing UCP1 expression and their incorporation. *This work is supported by grants #173054 and #173055 of MPNTR (Serbia); and by “Hubert Curien/Pavle Savic” Partnership — bilateral cooperation between Serbia and France.

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S2.P8

Effects of cell division activity, mitochondrial energy status and inhibition of mitochondrial fission on cell viability and distribution of native and mutant version of huntingtin in rat tissue culture model of Huntington's disease (PC12 cells)
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Huntington disease (HD) is an autosomal-dominant neurodegenerative disorder characterized by a selective loss of neurons, especially from the striatum and deep layers of cerebral cortex. It belongs to polyglutamine expansion diseases because it is caused by an increase in the number of glutamine codon (CAG) in exon 1 of the gene encoding the protein huntingtin (Htt). The number of the codon higher than 35 results in a mutated version of the protein (mHtt) that contains an abnormal stretch of over 35 glutamines at the N terminus. The clinical symptoms usually occur between 30 and 40 years of age. No therapeutic strategies capable of halting or delaying the disease progression have yet been proposed. Mitochondria play a vital role in HD pathogenesis. Available data indicate that mitochondrial defects initiate disease onset. Accordingly, two categories of phenomena are regarded to precede other HD symptoms, namely changes of mitochondrial energy status and changes of their fusion and fission. Therefore analysis of relationships between mitochondrial energy status and mitochondrial dynamics appears to be a logical step in elucidation of mitochondrial dysfunction in HD pathomechanism. We performed experiments on PC12 cells (derived from a pheochromocytoma of the rat adrenal medulla) with expression of exon 1 of huntingtin encoding gene containing 23 (Htt) or 74 (mHtt) repeats of glutamine codon, namely PC-12HD-Q23 and PC-12HD-Q74, respectively. Htt and mHtt expression was induced by doxycycline and monitored due to GFP labeling. PC12 cycling cells were differentiated into post-mitotic neuron-like cells upon treatment with the nerve growth factor (NGF). This enabled studies on cells differing in division activity and level of differentiation. We also applied media with different concentrations of glucose to affect mitochondrial energy status within intact cells as well as an inhibitor of Drp1, i.e. Mdivi-1 to estimate the impact of mitochondrial fission. The analysis of Htt and mHtt distribution and cell viability under the applied conditions was performed by confocal microscopy. Mitochondria were labeled due to transformation by pDsRed2-Mito Vector. The obtained results indicate that the presence of NGF and Mdivi-1 distinctly influences the levels of Htt and mHtt expression and distribution as well as the viability of PC12 cells. Therefore they contribute to the understanding of mitochondria role in HD etiology. The studies were supported by the grant: NCN 2011/01/B/NZ3/00359.

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S2.P9

Molecular motor protein kinesin-1 controls the localization of mitochondria and myofilbrils components
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Proper distribution of mitochondria in cells is important for cell functions. Here, we show that a molecular motor, kinesin-1 heavy chain Kif5b plays important roles in anterograde transport of mitochondria, alpha-sarcomeric actin, non-muscle myosin IIb, together with intermediate filament proteins' desmin and nestin in the elongating myotubes. Mice with Kif5b conditionally knocked out in myogenic cells showed aggregation of mitochondria, actin filaments and intermediate filament proteins in the differentiating skeletal muscle cells, which further affected myofilbril assembly and their linkage to the myotendinous junctions. The expression of Kif5b in mutant myotubes rescued the localization of mitochondria and the affected proteins.

Reference

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