Mice but not rats modulate liver mitochondrial machinery in chronic hypoxia

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Mitochondria are the ultimate users of oxygen in the process of energy production. This process has been suggested to be affected in environments with diminished O_2 availability (hypoxia) such as high-altitude habitats. Adjustments in mitochondria occur within the limits of plasticity of the electron transport chain (ETC). This feature represents a potential therapeutic target in high-altitude related conditions i.e. chronic mountain sickness. Previously we showed that lab mice and rats replicate well the ventilatory and hematological phenotype of people that properly or poorly acclimatize to high altitude correspondingly. Here we aimed to evaluate the mitochondrial metabolic adjustments in mice and rats along the acclimatization to hypoxia. Using liver tissue (most energy-consuming organ) from male-adult FVB mice and SD rats exposed to hypoxia (12% O_2, for 1, 7 or 21 days), we measured O_2 consumption rates (OCR) with mitochondrial complexes I, II, or I+II activated and after uncoupling (maximum activity) by high-resolution respirometry in the OROBOROS system. In mice, after one-day hypoxia the complex I-related OCR increased transiently (6%), while complex II-related OCR decreased. After 21 days of exposure, mice increased the maximum ETC activity by 43%. In rats, the only effect of hypoxia was an increased complex I-related OCR (67%) after 21 days-hypoxia. These results suggest that mice and rats modulate their liver mitochondrial machinery under chronic hypoxia in different ways. They also suggest more plastic liver-mitochondria in mice compared to rats. This might explain in part the ability of mice to better cope with hypoxia compared to rats.