Burtscher *et al.: Intrinsic Activity*, 2015; **3**(Suppl. 2):A2.13
http://www.intrinsicactivity.org/2015/3/S2/A2.13
published online: 9 September 2015

21st Scientific Symposium of the Austrian Pharmacological Society: Joint Meeting with the British Pharmacological Society and the Pharmacological Societies of Croatia, Serbia and Slovenia

Graz, 16–18 September 2015

MEETING ABSTRACT

A2.13

Oxidative phosphorylation in the healthy and in the epileptic mouse brain

Johannes BURTSCHER[1], Luca ZANGRANDI[1], Erich GNAIGER[2,3] and Christoph SCHWARZER[1,*]

[1]Department of Pharmacology, Innsbruck Medical University, Innsbruck, Austria; [2]Department of Visceral, Transplant and Thoracic Surgery, Innsbruck Medical University, Innsbruck, Austria; [3]Oroboros Instruments, Innsbruck, Austria

Background: Mitochondrial dysfunction appears to be a common factor in neurodegenerative diseases and epilepsy. Strikingly, neurodegenerative diseases show regional specificity in vulnerability and follow distinct patterns of neuronal loss. It is a challenge to understand how mitochondrial failure in particular brain regions contributes to specific pathological conditions.
Methods: High-resolution respirometry combined with specific pharmacological activation and inhibition protocols of elements of the respiratory system revealed significant differences of complex I- and II- (CI and CII)-linked oxidative phosphorylation (OXPHOS) capacity and coupling control between motor cortex, striatum, hippocampus and pons of naive mice.
Results: CI-linked respiration was highest in motor cortex. In contrast, CII-linked capacity was especially important in the striatum. Apparent excess capacities of the electron transfer system (ETS) over OXPHOS also differed between regions. In the kainic acid model of temporal lobe epilepsy in mice, we observed down-regulation of CI- and upregulation of CII-linked respiration in the injected dorsal hippocampus 3 weeks after treatment.
Discussion: In summary, respirometric OXPHOS analysis allows detailed analysis of mitochondrial function from small amounts of specific tissues (about 2 mg). It thus enables comparison of different brain tissues implicated in neurodegenerative diseases of the healthy mouse and disease models, while leaving enough material for further studies on the tissues. We propose that the presented differences may indicate risk factors for region-specific neuronal vulnerabilities. For example, a low apparent ETS excess capacity over OXPHOS capacity in the striatum together with the distinct pattern of respiratory control may contribute to the high vulnerability of striatal neurons in the presence of CII-inhibiting mutated huntingtin proteins.
Acknowledgements: Supported by the Austrian Science Fund (FWF), project W1206-B05.

*Corresponding author e-mail: *schwarzer.christoph@i-med.ac.at*