EPO10 e-Poster Oral
e-Poster Oral 10: Addictive Behaviours, Anxiety Disorders and Somatoform Disorders

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Abstract: 0463

Differential proteomics data integration reveals anxiety-associated molecular and cellular mechanisms in cingulate cortex synapses.

Introduction: The wide spectrum of neuropsychiatric conditions collectively known as "anxiety disorders" are highly comorbid with depression and are the most common psychiatric conditions encountered in the general population. Despite considerable advances in understanding symptomatology, the functional mechanisms of anxiety-related behaviour remain poorly understood.

Methods & Objectives: Using the CADI^{TM} platform, we carried out an analytical integration of quantitative differential proteomics data obtained from cingulate cortex (CC) synaptosomes of high and low-anxiety (HAB/LAB) mice to enable the detailed identification of the mechanisms that, at least in part, underlie the HAB phenotype.

Results: The synaptic environment in the CC of HAB animals is dominated by the stabilization and enlargement of existing excitatory dendritic spines, increased high-frequency stimulation of excitatory glutamatergic synapses, enhanced control over the modulation of synaptic strength and relatively weakened inhibitory GABAergic control together with increased spontaneous synaptic activity in non-glutamatergic network members. This is coupled with increased oxidative phosphorylation, enhanced fatty acid oxidation and ATP production in synaptic mitochondria. While ketone bodies appear to be the main energy source for ATP synthesis, glucose/lactate metabolism is mainly used to maintain NADH/$FADH_2$ homeostasis. The effects of increased oxidative and ionic stress appear simultaneously and synergistically controlled through at least seven different mechanisms without involving the glutathione-associated network.

Conclusions: In high-anxiety trait animals, cingulate cortex activity is characterized by low de novo synaptic spine generation, over-activation of excitatory networks, long-term potentiation (LTP) maintenance, significant neurotransmission imbalances and structural as well as metabolic adaptations to persistent mitochondrial Ca^{2+}loading and oxidative stress.

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