for 21 days. The motor coordination was then evaluated by the apomorphine-induced rotation test and immediately sacrificed to obtain blood and brain samples to evaluate the expression of Tyrosine Hydroxylase (TH) and Neuropeptide Y (NPY).

Results: It was observed that group E obtained a greater number of contralateral rotations versus group C (56.3 and 1.4, respectively). TH expression in the Black Substance (LN) area was significantly lower in group E than group C ($p < 0.05$). A greater expression of NPY was observed in areas such as LN, Lateral Hypothalamus (LH) and Ventral Tegmental Area (VTA) of group E.

Conclusion: NPY is a neuroactive peptide that could act as a compensatory system against Parkinson's disease in hypoxia conditions at the mesencephalon level.

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P22.47

Polymodal sensitivity of hTREK-1 channel to ischemia related factors

Sourajit Mukherjee[1], Sujit Sikdar[2,*]

[1] *Indian Institute of Science, Bangalore, India*
[2] *Molecular Biophysics Unit, Indian Institute of Science, Bangalore, India*

Brain ischemia is a condition where there is deprivation of glucose and oxygen. Recent study suggests that high local lactate concentrations along with increased TREK-1 activity provide neuroprotection during ischemic conditions. Hypoxia is hallmark condition of ischemia, where oxygen partial pressure decreases to 4 torr. Regulation of hTREK-1 by hypoxia has been studied previously which surprisingly showed resistance to hypoxia. Although these experiments were done in shorter hTREK-1 variant, a longer splice variant of hTREK-1 also exists which has extra 15 amino acids in the N-terminal region. Considering this difference and the possibility that oxygen can influence the activity of the channel by interacting with the extended N-terminal, we re-examined the sensitivity of the longer variant to hypoxia along with lactate. We used single-channel patch clamp technique on excised inside-out patches of long hTREK-1 channels expressed in HEK293 cells to assess the direct modulation of the channel activity by hypoxia. Analysis of single-channel data indicated an increase in the activity of long hTREK-1 channel during hypoxic conditions. Moreover, there was an additional increase in the presence of 20 mmol/L lactate in the hypoxic solution. To make recording conditions pathophysiological, TREK-1 activity was recorded in presence of low pH 6, hypoxia and 20 mM lactate. hTREK-1 activity showed an increase in this condition suggesting a neuroprotective role played by the channel. Sensitivity of N-terminus to hypoxia was confirmed further when the shorter variant showed a decrease in the activity in hypoxia. Moreover, since glutamate at 306th position responds to changes that arise due to hypoxia, E306A mutant showed that hypoxia alone can decrease the activity of the long hTREK-1. Our findings reveal increase in hTREK-1 activity in low oxygen, high lactate and low pH-conditions that typically accompany ischemic conditions and also that oxygen might interact with the channel at multiple sites.

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Role of adult hippocampal neurogenesis in the antidepressant effects of lactate

Pierre Magistretti[1], Anthony Carrard[2], Frederic Casse[3], Sophie Burlet-Godinot[2], Nicolas Toni[3], Jean-Luc Martin[2,*]

[1] *KAUST, Thuwal, Saudi Arabia*
[2] *Center for Psychiatric Neurosciences, Lausanne University Hospital, Lausanne, Switzerland*
[3] *University of Lausanne, Lausanne, Switzerland*

Astrocytes are key players in energy metabolism and glutamate transport. In particular, astrocytes respond to glutamate by increasing the rate of glucose utilization and the release of lactate (Magistretti and Allaman, 2018, *Nat Rev Neurosci.*). Growing evidence indicates that astrocytes are also involved in the pathophysiology and treatment of depression. For instance, SSRIs stimulate lactate release from cortical astrocytes. Recently, we showed that acute lactate administration increased lactate concentration in the hippocampus and reduced immobility in the forced swim test (Carrard et al., 2018, *Mol Psychiatry*). We further investigated the antidepressant-like effects of lactate in two animal models of depression that respond to chronic antidepressant treatment; the corticosterone model of depression and the open-space forced swim model of depression. We found that chronic administration of lactate reversed the corticosterone-induced anhedonia-like behavior and partially restored mobility in the open-space forced swim model of depression, in a manner similar to desipramine. The antidepressant effects of lactate are associated with changes in the expression of specific target genes of which Hes5 is involved in adult hippocampal neurogenesis. These findings led us to investigate the role of adult hippocampal neurogenesis in the antidepressant effects of lactate.

The involvement of hippocampal neurogenesis in the antidepressant effects of lactate was assessed in the corticosterone model of depression. We found that chronic peripheral injections of lactate counteracted the decreased neural progenitor proliferation and survival induced by chronic corticosterone treatment. In contrast, chronic administration of pyruvate did not produce antidepressant effects and did not prevent the inhibition of neural progenitor proliferation and survival induced by chronic corticosterone injections. Furthermore, depletion of adult hippocampal neurogenesis by administration of the antimitotic drug temozolomide suppressed the antidepressant-like effects of lactate in the chronic corticosterone paradigm. Collectively, these data emphasize the importance of adult hippocampal neurogenesis in the antidepressant effects of lactate.

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Autoantibodies to synapsin I in limbic encephalitis sequestrate cytosolic synapsin I and disrupt synaptic function

Anna Rocchi[*], Fabio Benfenati

Istituto Italiano di Tecnologia, Genova, Italy

Limbic encephalitis belongs to a group of neuropsychiatric disorders characterized by common core symptoms such as irritability, anxiety, depression, memory impairment and seizures that are associated with the presence of serum and cerebrospinal fluid autoantibodies. Autoantibodies against synaptic receptors,