Département de psychiatrie

Centre de Neurosciences Psychiatriques

CNP SEMINARS

ANNOUNCEMENT

Wednesday, September 2nd, 2020, 9:00 – 11:00 am

Neuron-glia metabolic coupling mediated by lactate: relevance for neuronal plasticity, memory and disease

Prof. Pierre J. Magistretti, MD, PhD

Division of Biological and Environmental Sciences and Engineering, KAUST, Thuwal, Saudi Arabia
Department of Psychiatry UNIL/CHUV, Switzerland
Brain Mind Institute, EPFL, Lausanne, Switzerland

A tight metabolic coupling between astrocytes and neurons is a key feature of brain energy metabolism (Magistretti and Allaman, Neuron, 2015). Over the years we have described two basic mechanisms of neurometabolic coupling. First the glycogenolytic effect of VIP and of noradrenaline indicating a regulation of brain homeostasis by neurotransmitters acting on astrocytes, as glycogen is exclusively localized in these cells. Second, the glutamate-stimulated aerobic glycolysis in astrocytes. Both the VIP-and noradrenaline-induced glycogenolysis and the glutamate-stimulated aerobic glycolysis result in the release of lactate from astrocytes as an energy substrate for neurons (Magistretti and Allaman, Neuron, 2015; Magistretti and Allaman, Nat Neurosci Rev, 2018).

We have subsequently shown that lactate is necessary not only as an energy substrate but also as a signaling molecule for long-term memory consolidation and for maintenance of LTP (Suzuki et al, Cell, 2011). At the molecular level we have found that L-lactate stimulates the expression of synaptic plasticity-related genes such as ***Arc***, ***Zif268*** and BDNF through a mechanism involving NMDA receptor activity and its downstream signaling cascade Erk1/2 (Yang et al, PNAS, 2014). A transcriptome analysis in cortical neurons has shown that the expression of a total of 20 genes is modulated by L-Lactate; of these, 16 involved in plasticity and neuroprotection are upregulated and 4 involved in cell death are downregulated (Margineanu et al. Front. Mol Neurosci, 2018). This set of results reveal a novel action of L-lactate as a signaling molecule in addition to its role as an energy substrate (Magistretti and Allaman, Nat Neurosci Rev, 2018).

These actions of L-Lactate are also relevant for animal models of neuropsychiatric disorders. Indeed we have shown that peripheral administration of lactate exerts antidepressant-like effects in three animal models of depression, Forced Swim test, Open Space Forced Swim Test and chronic corticosterone administration. These behavioral effects of L-Lactate administration are accompanied by changes in the expression of genes that have been involved in mood disorders (Carrard et al, Mol.Psy., 2016). Finally, we have shown that the transfer of L-Lactate from astrocytes to neurons plays a key role in an appetitive memory task involving the basolateral amygdala such as cocaine place preference in mice (Boury-Jamot et al. Mol Psy, 2016).

Invited by C.-B. Eap
Chin.Eap@chuv.ch

Auditoire Christian Muller - Bâtiment 17A - Rez - Salle 020
Hôpital Psychiatrique de Cery-Site de Cery, CH-1008 Prilly-Lausanne

Related publications

1) Vezzoli E, Calì C, De Roo M, Ponzoni L, Sogne E, Gagnon N, Francolini M, Braida D, Sala M, Muller D, Falqui A, Magistretti PJ. *Ultrastructural Evidence for a Role of Astrocytes and Glycogen-Derived Lactate in Learning-Dependent Synaptic Stabilization.* ***Cereb Cortex. 2019 Dec 6. pii: bhz226. doi: 10.1093/cercor/bhz226. [Epub ahead of print]***
2) Carrard A, Elsayed M, Margineanu M, Boury-Jamot B, Fragnière L, Meylan EM, Petit JM, Fiumelli H, Magistretti PJ*, Martin JL*. *Peripheral administration of lactate produces antidepressant-like effects.* ***Mol Psychiatry. 2016 Dec 6. doi: 10.1038/mp.2016.237.***
3) Magistretti PJ, Allaman I. *Lactate in the brain: from metabolic end-product to signalling molecule* ***, Nat Rev Neurosci. 2018 Apr;19(4):235-249. doi: 10.1038/nrn.2018.19***

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