

To beat or not to beat: a novel role for MCH in brain volume transmission.

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The cyclic peptide Melanin-Concentrating Hormone (MCH) is known to control a large number of brain functions in mammals such as food intake and metabolism, stress response, anxiety, sleep/wake cycle, memory and reward. Based on neuro-anatomical and electrophysiological studies these functions were attributed to neuronal circuits expressing MCHR1, the single MCH receptor in rodent. However, non-neuronal intercellular communication or “volume” transmission may also be involved. This was investigated in our lab^{1,2} as well as in a recently published article³ whose studies will be presented in this seminar. Collectively, these results demonstrated a dynamic control of MCH neurons on spontaneous cilia beat frequency of MCHR1 mRNA-expressing ependymal cells as well as on feeding behaviour through ventricular volume transmission. These novel mechanisms of action of a neuropeptide could contribute to maintain cerebro-spinal fluid homeostasis and long-term regulation of directed-behaviors.

First, we established that MCHR1 mRNA and proteins are expressed in the ependymal cells of the third ventricle epithelium and we mapped numerous MCH fibers in close vicinity to these cells. Second, developing new techniques to measure and analyze the ependymal cilia beat frequency (CBF) in acute mouse brain slice preparations, we showed that the CBF is modulated by MCH application, LHA stimulation or activation/inhibition of MCH-expressing neurons using in vitro optogenetics. These effects were blocked by a selective MCHR1 antagonist and absent in MCHR1-knockout (MCHR1-KO) mice. Third, using in vivo brain MRI, we demonstrated that the volume of both the lateral and third ventricles is increased in MCHR1-KO mice compared to their wild-type (WT) littermates. Finally, we performed in vivo measurements of CSF flow using fluorescent micro-beads in wild-type and MCHR1-KO mice.

1- Conductier G*, Brau F*, Viola A*, Langlet F, Ramkuma N, Dehouck B, Lemaire T, Chapot R, Lucas L, Rovère C, Maitre P, Hosseiny S, Petit-Paitel A, Adamantidis A, Lakaye B, Risold PY, Prévot V**, Meste O**, Nahon JL**§, Guyon A**§. Melanin-concentrating hormone regulates beat frequency of ependymal cilia and ventricular volume. **Nature Neurosci** (2013) **16**, 845-847, doi: 10.1038/nn.3401

2- Conductier G*, Martin AO*, Risold PY*, Jégo S, Lavoie R, Lafont C, Mollard P**, Adamantidis A**, Nahon JL**. Control of ventricular ciliary beating by the melanin concentrating hormone-expressing neurons of the lateral hypothalamus : a functional survey. **Front Endocrinol** (2013) **4** :182. doi: 10.3389/fendo.2013.00182

3- Noble EE, Hahn JD, Konanur VR et al. . Control of Feeding Behavior by Cerebral Ventricular Volume Transmission of Melanin-Concentrating Hormone. **Cell Metabolism** (2018) **28**, 55-68

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