

## DYNAMIC INTERACTION OF PONTINE CHOLINERGIC AND GABAERGIC NEURONS DURING REM SLEEP

*P.-H. Prouvot<sup>1</sup>, M. Tafti<sup>1</sup>, M. Bandarabadi<sup>1</sup>*

<sup>1</sup>Université de Lausanne, département des sciences biomédicales (DSB), Lausanne, Switzerland

**Background:** Cholinergic neurons of the laterodorsal tegmental (LDT) and pedunculopontine tegmental (PPT) nuclei are highly active during REM sleep, but their role in the regulation of REM sleep components and vigilance states transitions remain elusive. Here we aimed to investigate the dynamics of LDT/PPT cholinergic neurons and acetylcholine release in their two major targets of the sublaterodorsal tegmental nucleus (SLD) and centromedial thalamus (CMT) across vigilance states.

**Methods:** We used multisite monitoring of calcium activity and neurotransmitter release combined with EEG/EMG recordings in freely behaving mice. Using stereotaxic AAV injections containing calcium indicators (lox-GCaMP, lox-RCaMP, CamKII-GCaMP, and CamKII-RCaMP) and a genetically encoded acetylcholine sensor in ChAT-IRES-Cre, Vgat-Cre, and C57BL/6 mice, we monitored activity of LDT/PPT cholinergic, SLD GABAergic/glutamatergic, and ventral medulla GABAergic neurons, as well as acetylcholine release in the SLD and CMT across vigilance states.

**Results:** We found that LDT/PPT cholinergic neurons are highly active during both wake and REM sleep, but the release of acetylcholine in the SLD and CMT is restricted to REM sleep. We also found that activity of SLD glutamatergic cells is highly correlated with acetylcholine release in the SLD during REM sleep, and both signals showed interhemispheric synchronization. Additionally, we found a dynamic anticorrelation activity between GABAergic neurons of the ventral medulla and SLD during REM sleep.

**Conclusions:** The dorsal pons cholinergic nuclei are highly active during both wake and REM sleep with varying kinetics between the different nuclei. None of the cholinergic centers recorded showed clear activity prior to REM sleep, suggesting another role than direct NREM-REM transitions. An excitatory effect of acetylcholine on SLD glutamatergic neurons possibly controls SLD glutamatergic-GABAergic microcircuits to activate ventral medulla GABAergic neurons and induce muscle atonia during REM sleep.