during REM sleep under normal as well as pathological conditions, such as OSA.

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0073

OPTOGENETIC CONTROL OF SLEEP SLOW WAVES TO IMPROVE RECOVERY AFTER ISCHEMIC STROKE

Facchin L[1], Schöne C[1], Mensen A[2], Bandarabadi M[1], Schindler K[2], Adamantidis A[1], Bassetti C[1]

[1]Centre for Experimental Neurology, Inselspital University Hospital, Bern, SWITZERLAND, [2]Department for Clinical Research, Inselspital University Hospital, Bern, SWITZERLAND

Introduction: Experimental studies suggested a role for sleep in the reorganization of neuronal connectivity map and brain plasticity during stroke recovery. Here, we investigate the role of Slow Waves (SW) oscillations during sleep on brain plasticity following ischemic stroke using optogenetic tools and in vivo electrophysiology in mice.

Methods: Ischemic stroke was caused in wild type mice using middle cerebral artery occlusion (MCAO). SW-like oscillations were induced by optogenetic optical stimulations of ChR2- (activation) or ArchT (silencing)-expressing pyramidal neurons within the peri-lesional primary somatosensory forelimb (S1FL) cortex. Randomly distributed single light pulses were delivered for 2 h sessions from post-stroke day 5, and consecutively every day until post-stroke day 15. The effect of optogenetically evoked SW on motor outcomes was investigated with behavioural tests at post-stroke day 4, 7, 10 and 15.

Results: We showed that MCAO induced an increased amount of NREM sleep following ischemic stroke, where ipsilesional SW where longer in duration and wider in amplitude, compared to control animals. We first showed that optogenetic activation (ChR2) and silencing (ArchT) of pyramidal neurons in the per-lesional S1FL cortex successfully induced SW sleep-like responses in ipsilesional and contralesional electroencephalography (EEG) traces that were indistinguishable from spontaneous SW oscillations occurring during NREM sleep. Evoked and spontaneous SW were automatically detected and compared in amplitude, slope and duration. We next showed that chronic optogenetic induction of SW-like, predominantly during NREM sleep, significantly improved the recovery of fine motor movement as compared to control mice. Interestingly, SW post-stroke induction didn't affect the recovery of movement strength or symmetry.

Conclusion: Our results further confirmed the essential role of NREM sleep, and SW in particular, in brain plasticity following ischemic stroke. Importantly, we showed that optogenetically-induced SW-like oscillations, targeting the activity of pyramidal neurons within the peri-lesional cortex, significantly improved functional outcomes after stroke.

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0074

PHARMACOLOGIC AND OPTOGENETIC DISSECTION OF SLEEP HOMEOSTATIC CIRCUITS IN THE BASAL FOREBRAIN

Bouaouda H[1], Shukla C[1], McKenna JT[1], McNally JM[1], Winston S[1], Kalinchuk AV[1], Thankachan S[1], Strecker RE[1], Deisseroth K[2], Brown RE[1], Basheer R[1]

[1]VA Boston Healthcare System- Harvard Medical School, West Roxbury, MA, [2]Standford, Stanford University, CA

Introduction: Selective optogenetic stimulation of basal forebrain (BF) neuronal subtypes, Cholinergic (ChAT+), vesicular glutamate transporter2-expressing glutamatergic (vGluT2+) and parvalbumin-expressing GABAergic (PV+), causes arousal. However, it is unclear if they are equally effective in eliciting a homeostatic sleep response (HSR). The importance of interactions between these cell-types in the HSR has not previously been investigated. Thus, we used optogenetics and reverse microdialysis of pharmacological agents to investigate these questions.

Methods: C57BL/6 (WT) mice were sleep deprived (6h) with and without reverse microdialysis of cholinergic antagonists into BF. The amount of recovery sleep and delta activity (0.5–4.5Hz) were used as the markers of HSR. In ChAT-Cre, vGluT2-Cre, PV-Cre transgenic mice transduced with AAV-ChR2-EYFP in BF, we examined the effect of 6h laser (473nm) illuminations (5s/min, 10 Hz for ChAT+ and vGluT2+, 40Hz for PV+) on HSR, during the 2h poststimulation period and compared it with time matched sham stimulation (BL, TTLpulse without laser). In ChAT-Cre mice we performed optodialysis of cholinergic antagonists during 6h optical stimulation and examined the post stimulation HSR.

Results: In WT mice (n=4) microdialysis of cholinergic antagonists did not prevent HSR, as evaluated by an increase in sleep time (36%) and delta power (8.14%, $p<0.001$). Optogenetic stimulation of ChAT+ neurons (N=3), led to an increase in sleep (BL 52.6 ± 0.56 *vs* poststim 57 ± 2.88) and delta by 24% during the 2h poststimulation compared to BL, that was not blocked by cholinergic antagonist. In contrast, GABA/PV+ neuronal stimulation did not cause HSR. Optogenetic stimulation of vGluT2+ neurons in 1 mouse, showed a tendency towards HSR.

Conclusion: Preliminary results suggest that ChAT+ and vGluT2+, but not PV+ neurons, are involved in mediating HSR. Furthermore, local effects of acetylcholine on non-ChAT+ neurons are not required for HSR. These results, together with previous cholinergic lesion studies, suggest a model whereby direct or indirect excitation of ChAT+ neurons (via vGluT2+ neurons) is key to trigger HSR.

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0075

NITRERGIC NEURONS OF THE DORSAL RAPHE NUCLEUS ENCODE INFORMATION ABOUT STRESS DURATION

Nichols-Obande IS[1], Anderson S[1], Bush B[2], Gray C[2], Ehlen JC[2], Jones MI[3], Ananaba G[3], Okere CO[3], Brager A[4], Paul K[1]

[1]University of California- Los Angeles, Los Angeles, CA, [2]Morehouse School of Medicine, Atlanta, GA, [3]Clark Atlanta University, Atlanta, GA, [4]Walter Reed Army Institute of Research, Silver Spring, MD

Introduction: Nitrergic neurons of the dorsal raphe nucleus (DRN) are involved in the regulation of stress and sleep. Stress duration is an important variable to consider when discussing the response to stress because duration has been shown to have different effects on behavioral processes such as sleep. Duration of acute stress also affects intensity of HPA axis activation. Until now, the effects of acute stress duration on nitric oxide synthase activity have not been revealed.

Methods: Here NADPH-d was used as an index of NOS activity in rats that were restrained for either 1, 3, or 6 hours.

Results: These experiments revealed increased NOS activity through 6 hours of restraint in the caudal lateral wings and ventromedial sub-regions.

Conclusion: These data suggest that, NOS neurons may play a dynamic role in the response to stress duration. Future studies will determine the role of stress duration on sleep-wake states.

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