extrasynaptic GABA_A receptors and the local regulation of sleep
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GABA (γ-aminobutyric acid) is the main inhibitory transmitter in the mammalian brain. Recent studies emphasise the importance of extrasynaptic GABA_A receptors (i.e., GABA_A-Rs located outside the synapse) in controlling the excitability of local neuronal circuits. Extrasynaptic GABA_A-Rs mediate a persistent tonic inhibitory transmission and the majority contain the δ-subunit. This novel type of transmission plays a key-role in maintaining the excitability of the thalamo-cortical circuits that generate sleep slow waves. Interestingly, drugs enhancing tonic inhibitory transmission induce slow waves. Traditionally, the regulation of the alternation between sleep and waking was considered to be a global brain process, regulated by the interaction of the circadian clock and a homeostatic process keeping track of how long we have been awake and asleep. However, several studies demonstrated that sleep is also regulated in a local, use-dependent manner. Thus, brain regions that are most activated during wakefulness show more slow waves during subsequent sleep.

The aim of this project is to investigate the contribution of the δ-GABA_A-Rs-mediated tonic transmission to the local, use-dependent regulation of slow wave sleep. We use an established model of local sleep regulation (i.e., unilateral whisker stimulation inducing changes selectively in the corresponding somatosensory cortex) in a mouse model deficient in the GABA_A δ-subunit gene. We first investigate whether whisker stimulation during wakefulness alters the expression levels of δ-GABA_A-Rs and other components underlying tonic inhibitory transmission in the controlateral somatosensory cortex and thalamus. We will also assess whether these changes are reversed during subsequent sleep and whether they are correlated with changes in sleep slow waves in the electroencephalogram. In addition, to uncover whether tonic inhibitory transmission contributes to the control of sleep regulation by the circadian clock, we will use an established protocol to separate use-dependent and circadian contributions to sleep regulation.

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