

# Closed-loop acoustic stimulation during sleep to reduce cortical excitability and epileptic activity: study protocol

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**Introduction:** Slow-wave sleep plays role in decreasing cortical excitability and promotes synaptic downscaling. By enhancing slow-wave sleep, we hypothesize to promote synaptic downscaling and renormalization of neuronal activity in people with focal epilepsy.

**Methods:** We will: 1) deliver closed-loop acoustic stimulation (CLAS) in a preclinical model of focal epilepsy and measure its effects on cortical excitability, synaptic strength, and circuit activity; 2) deliver topographically targeted closed-loop acoustic stimulation (TT-CLAS) in people with focal epilepsy, and measure electric signatures of cortical excitability.

**Results:** In preclinical model, we expect to find reduced density and size of excitatory synapses, reduced excitatory-inhibitory synapse ratio, reduced cortical excitability, reduced frequency, duration, and spreading of epileptic activity, and reduced ratio of excitatory/inhibitory synaptic connectivity in animals subjected to CLAS relative to controls.

In humans, we expect to observe a local increase in NREM sleep slow-wave activity over the epileptic focus after TT-CLAS relative to a baseline night, and a decrease in the frequency, amplitude, and/or duration of epileptic activity during the following waking period.

**Conclusion:** This project will explore the enhancement of sleep through a non-invasive, non-pharmacological approach to ameliorate epileptic activity in people with epilepsy. We will elucidate the biological mechanisms underlying the beneficial effects of slow-wave sleep enhancement at the synaptic and circuit level. This study may pave the way for better understanding the impact of sleep on epileptic activity and identify new therapeutic strategies for people with uncontrolled focal seizures.

