

## **Abstract**

Non-pharmacological manipulations of sleep represent an important tool to study the function of sleep causally. Auditory stimulation, and closed-loop auditory stimulation (CLAS) in particular, represent an innovative, easy to apply, and effective method to alter sleep. This thesis introduced our original research in CLAS application (Study 1) and mechanisms of action (Study 2) in a chronic insomnia population for the first time. Study 1 assessed the feasibility and efficacy of CLAS for improving sleep quality and memory consolidation in chronic insomnia. This crossover, sham-controlled study involved 27 participants undergoing two nights of either CLAS or sham stimulation, monitored via polysomnography to measure sleep parameters, along with scales for assessing subjective sleep quality and a word-pair memory task for measuring overnight memory consolidation. Initial findings from 7 participants with sufficient amount of stimulations indicated that while CLAS significantly increased slow oscillation (SO) amplitude and power during slow-wave sleep, it did not alter sleep-dependent memory consolidation, overall sleep architecture, number of arousals, discrete sleep spindles, or subjective sleep quality. Additionally, Study 2 explored CLAS mechanisms with their effects on SOs on a subset of 9 participants from Study 1, comparing the phase-locked loop (PLL, PLL-XOR and PLL with an integral part) and fixed-step stimulus methods using our streamed sleep data. The fixed-step method proved more reliable and practical than the PLL methods. Importantly, we found significant phase synchronization of SOs, suggesting a possible mechanism of action of CLAS altering existing SOs rather than generating new ones. Despite its feasibility in insomnia patients, high variability in stimulation efficacy in our sample highlights the need for optimized and more tailored protocols to discover potential benefits of CLAS for sleep structure, memory consolidation, and subjective sleep quality in such clinical settings.