Closed-Loop Auditory Stimulation Technology to Enhance Sleep

White Paper

Tosoo AG

May 2025

Table of Contents

Executive Summary

Closed-loop auditory stimulation (CLAS) is an innovative, non-invasive technology that enhances the depth and quality of deep sleep by delivering precisely timed sounds that align with brain rhythms. Unlike pharmaceutical approaches, CLAS works in harmony with the brain's natural sleep structure, promoting deep sleep to support memory, recovery, cardiovascular function, and long-term brain health. Supported by a growing body of clinical and neuroscience research, Tosoo's CLAS headband allows this powerful method to be used safely and comfortably at home. This white paper outlines the science behind CLAS and highlights its transformative potential across a wide range of applications, from enhancing cognitive performance to supporting patients with neurodegenerative or neurological conditions.

Introduction

Good sleep is essential for our health, memory, and mental performance. In recent years, a novel technology known as closed-loop auditory stimulation (CLAS) has shown promising results in enhancing sleep quality by modulating brain activity. CLAS works by delivering brief auditory tones that are precisely timed with specific phases of brain waves during sleep. This stimulation can make sleep deeper and more restorative, leading to measurable benefits for both the brain and body.

The implementation of CLAS requires accurate monitoring of brain signals using electrodes, a device capable of interpreting this data in real time, as well as headphones to play the tones. To make this technology more accessible and user-friendly, our portable EEG headband provides a comfortable, all-in-one solution that integrates the electrodes, the recording device, and the audio delivery system. This way, individuals can benefit from CLAS independently in the comfort of their own homes.

CLAS has undergone numerous research studies and has shown strong potential to enhance the benefits of sleep in a safe, non-invasive manner. Unlike pharmaceutical sleep aids, CLAS does not disrupt the natural sleep structure. This white paper provides an overview of the scientific foundation of CLAS and highlights the key advantages of this technology for improving sleep and related brain functions, as well as potential clinical applications.

Our CLAS Technology

This section describes the protocol we use for closed-loop auditory stimulation (CLAS). In this established protocol, brief tones are played during deep non-rapid eye movement (non-REM) sleep, also known as slow-wave sleep. The term slow-wave sleep refers to the most typical brain waves occurring during this sleep stage, the so-called slow waves (see Fig. 1B). Slow waves are a hallmark of restorative sleep and are closely linked to sleep depth and recovery processes. The tones delivered during CLAS are precisely timed to a specific phase of these slow waves. Usually tones are played during the “up-phase” or peak of the ongoing slow waves (Fig. 1B, red dots). With our technology, it is, however, also possible to target other phases of slow waves during non-REM sleep, for example the “down-phase” (Fattinger et al., 2017; Leach et al., 2024).

The tones used in CLAS are typically short bursts of pink noise that sound like soft clicks, subtle enough not to wake the sleeper but adequate to influence brain activity. To determine when a person enters deep sleep, electrodes monitor brain signals, and the recording device utilizes real-time analysis to detect the optimal moment to play the sound. Figure 1 provides an overview of our standard CLAS protocol and shows the prototype of the Tosoo CLAS headband, which integrates brain signal detection and sound delivery into a single, user-friendly wearable device.

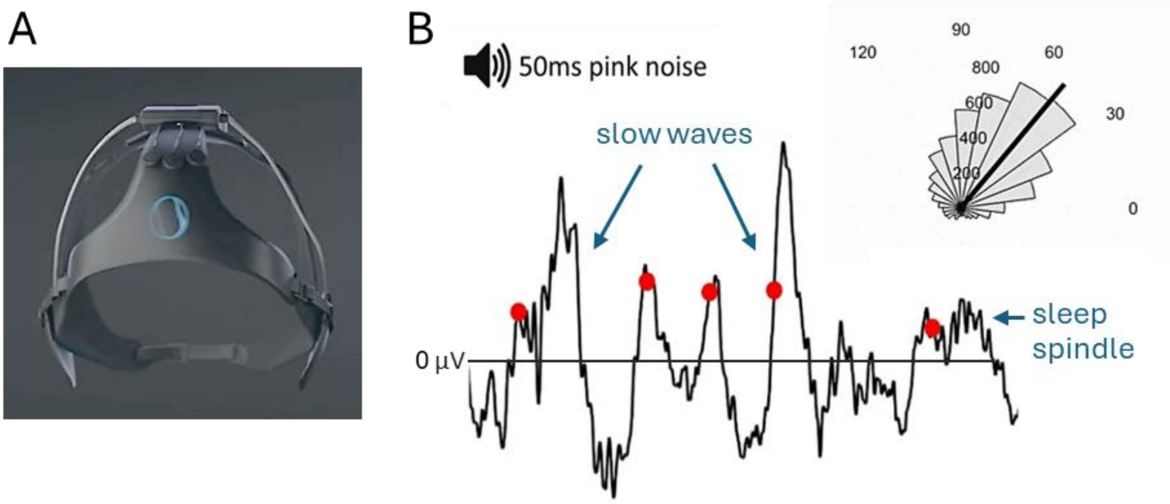

Figure 1. Schematic overview of our CLAS technology. A: Prototype of the Tosoo headband including detection electrodes, the recording device, and headphones. B: Example brain activity (EEG signal) typical for non-rapid eye movement (non-REM) sleep. Arrows indicate the typical EEG characteristics of this sleep stage including slow waves and sleep spindles. For auditory stimulation, a phase-locked loop is used to precisely target the rising phase (or up-phase) of sleep slow waves. Red dots illustrate the short (50 ms) tones of pink noise that are applied. The top-right corner shows the phase-precision of the Tosoo CLAS headband. Zero degrees corresponds to the zero-crossing and 90° to the positive peak. Illustration adapted from *Lustenberger et al., 2022* and *Huwiler et al., 2022*.

The first and primary part of this white paper provides scientific insights from studies utilizing established protocols of the CLAS technology, all of which target specific phases, usually the “up-phase”, of slow waves during non-REM sleep (as shown in Fig. 1). Alternative approaches, such as stimulation during rapid-eye movement (REM) sleep and wakefulness, will be discussed in the final section of this white paper.

Boosting Deep Sleep Brain Activity and Sleep Recovery

More than a decade ago, research by Ngo and colleagues (2013) demonstrated for the first time that playing auditory tones during the peak (up-phase) of ongoing slow waves in deep non-REM sleep can profoundly enhance these brain waves (Fig. 2A). Since then, numerous studies utilizing up-phase CLAS protocols have confirmed this effect (Kasties et al., 2024; Leach et al., 2024; Ong et al., 2018; Papalambros et al., 2017). Slow waves are typically quantified by analyzing slow-wave activity (SWA), which reflects their amplitude and serves as an indicator of sleep depth. The gradual decline of SWA across a night is considered a marker of the brain's recovery processes during sleep. A study by Krugliakova and colleagues (2022), which employed a previous version of our Tosoo CLAS headband in combination with a high-resolution electrode net, showed a widespread increase in SWA across the brain (Fig. 2B). Moreover, they demonstrated that CLAS accelerates the typical overnight decline in SWA and leads to improved attentional performance the next morning. These findings suggest that up-phase CLAS protocols deepen sleep in a way that enhances physiological sleep and thus sleep recovery.

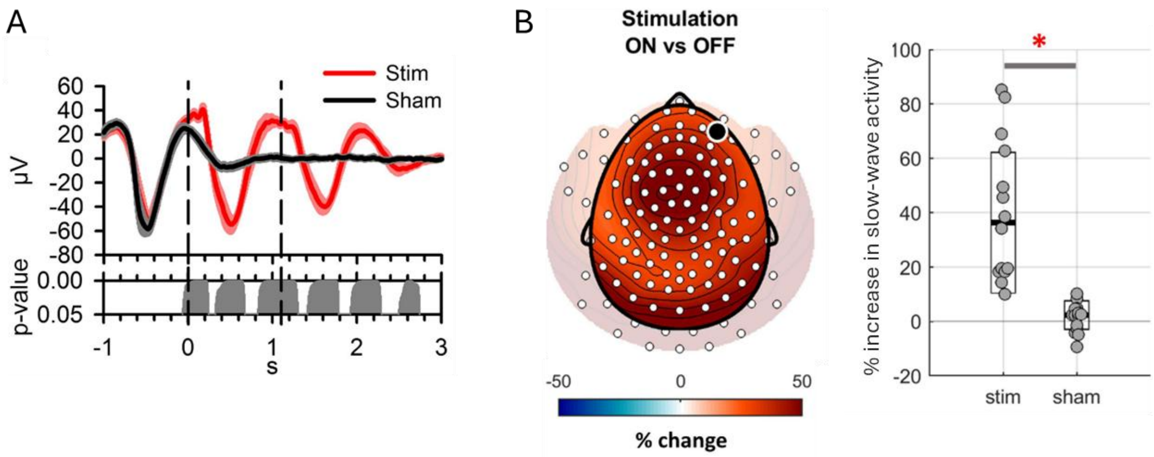

Figure 2. Boosting deep sleep brain activity using the CLAS technology. A: Averaged EEG signal (brain activity) from eleven participants time locked to the first auditory stimulus ($t = 0$ s). Each participant underwent one night with auditory stimulation (red line) and one sham night without stimulation (black). Bottom panel indicates significant differences between nights as grey shading. Figure adapted from *Ngo et al., 2013.* B: Comparison of slow-wave activity (EEG power in the slow-wave frequency range) between averaged six-second windows with stimulation (ON) and six-second windows without stimulation (OFF). The black dot indicates the target electrode represented on a model of the head. White dots indicate a significant change in slow-wave activity. The percentage change in slow-wave activity across all electrodes was significantly larger for the stim night as compared to sham night ($t_{13} = 5.07$, $p < 0.001$). Grey dots indicate individuals, the black line the median. Figure adapted from *Krugliakova et al., 2022.*

Improving Cognitive Function

Sleep plays a fundamental role in memory consolidation, the process by which newly acquired information is stabilized and transferred into long-term storage. Slow waves during non-REM sleep are associated with sleep-dependent memory consolidation. Another characteristic brain wave of non-REM sleep, sleep spindles (brief bursts of brain activity, see Fig. 1B), is also linked to the memory-supporting effect of sleep. Recent research suggests that the most crucial factor may not only be the occurrence of these oscillations individually but also their temporal coordination (Bergmann & Born, 2018). Interestingly, auditory stimulation has been shown to enhance not only slow waves but also sleep spindles and their temporal coordination (Krugliakova et al., 2020). It is therefore not surprising that a large body of research has demonstrated that using CLAS during non-REM sleep can enhance memory performance (Clark et al., 2024; Leminen et al., 2017; Ngo et al., 2013; Ong et al., 2016, 2018; Papalambros et al., 2017; Prehn-Kristensen et al., 2020). For instance, a recent study using our Tosoo CLAS headband found improved performance in a verbal memory task in participants subjected to a night of CLAS-enhanced sleep (Leach et al., 2024). This memory improvement was linked to the synchronization of sleep spindles to the up-phase of slow waves (Fig. 3). Boosting both slow waves and sleep spindles during non-REM sleep using our CLAS technology may thus directly enhance the brain's capacity for overnight memory consolidation.

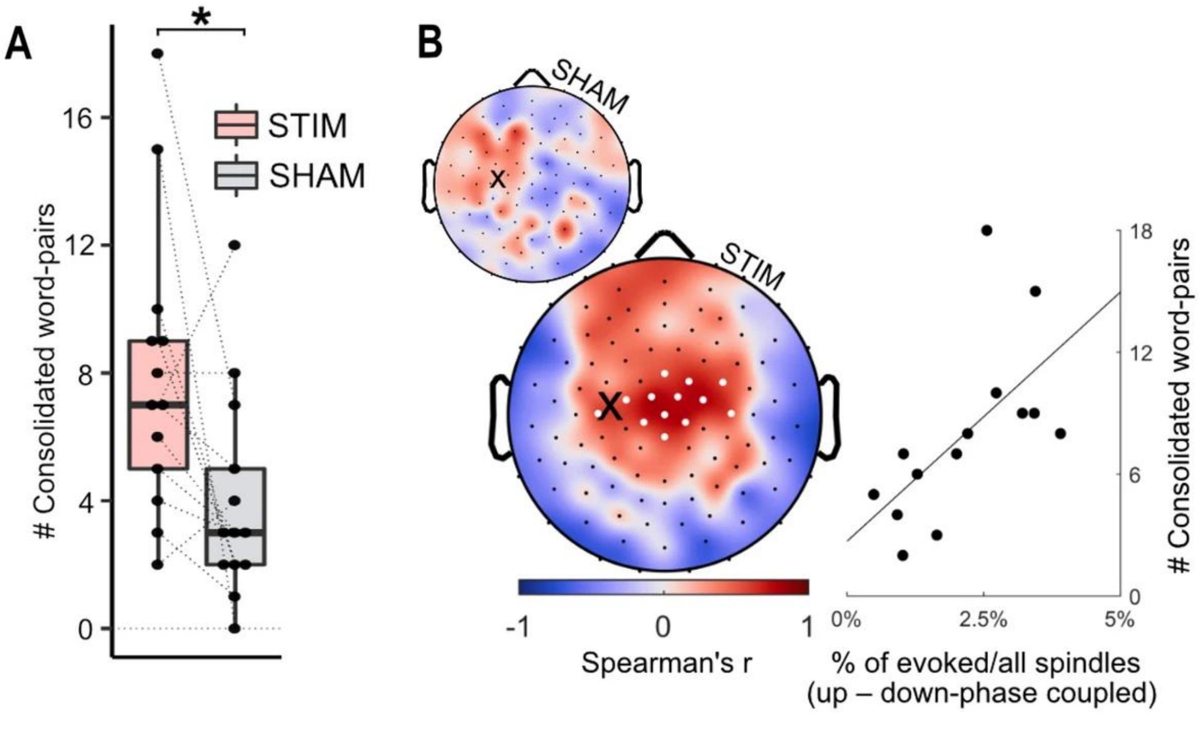

Figure 3. Improving memory consolidation using our CLAS technology. A. Memory improvement (morning–evening) in the word-pair memory task across a night with (STIM) and without (SHAM) auditory stimulation. Dots represent the performance of single participants. B. Correlation between the number of consolidated word pairs and the difference in the number of up- and down-phase coupled spindles relative to the total number of spindles detected during the entire night. White dots represent electrodes with significant correlations. The black cross indicates the target electrode. Figure adapted from *Leach et al., 2024*.

Strengthening Cardiovascular and Immune Health

Parasympathetic nervous system activity during sleep can be evaluated using heart rate variability (HRV), a key indicator of autonomic function. As illustrated in Figure 4A, Grimaldi and colleagues (2019) demonstrated that CLAS technology can increase HRV during sleep, suggesting a beneficial impact on the autonomic nervous system. Recent research by other research groups has supported these findings (Diep et al., 2022; Huwiler et al., 2022, 2023, 2024). Thus, strengthening the interaction between the brain and heart during sleep may hold significant potential for improving cardiovascular health.

Furthermore, auditory stimulation timed to the up-phase of sleep slow waves has been shown to enhance the hormonal environment typically associated with deep sleep, such as reducing cortisol levels and increasing aldosterone levels (Fig. 4B). These hormonal changes are known to support immune functions involving T and B cells. From a clinical perspective, this finding suggests potential applications for individuals with hormonal imbalances or immune system dysfunctions (Besedovsky et al., 2017).

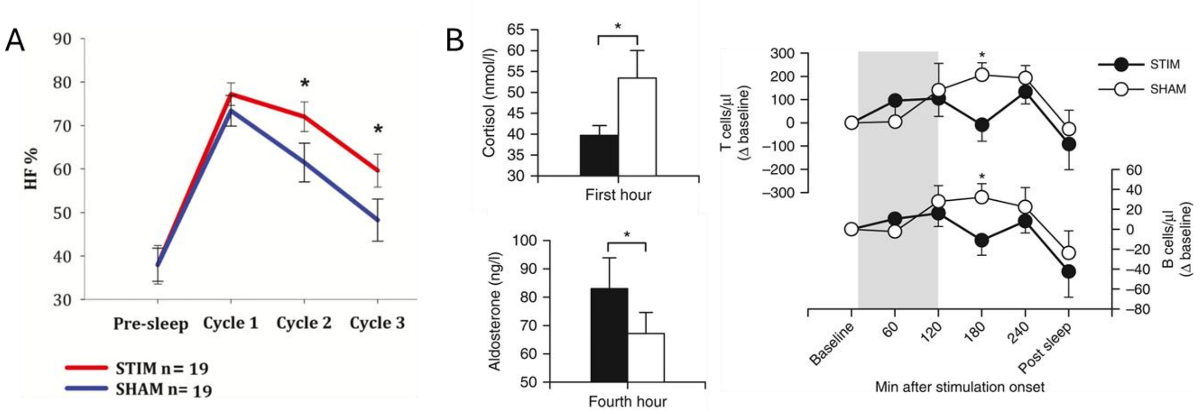

Figure 4. Improving cardiovascular health and immune function using the CLAS technology. A: Heart-rate variability high-frequency relative power (HF%) before sleep (Pre-sleep) and during slow-wave sleep in the first three sleep cycles. In the night with auditory simulation (STIM), HF% was significantly higher during sleep cycles 2 and 3 as compared to the night without stimulation (SHAM). Asterisks indicate significance (p <0.05, Wilcoxon signed-rank test with Bonferroni correction). Error bars represent standard error of the mean. Figure adapted from *Grimaldi et al., 2019*. B: Averaged cortisol levels, aldosterone levels, and circulating T and B cell numbers (difference from baseline) for the STIM (black) and SHAM (white) conditions (Wilcoxon tests, two-sided, $*p < 0.05$, $n = 9–14$). Gray area represents the 120-min stimulation period. Figure dapted from *Besedovsky et al., 2017*.

Clinical Applications: From Children to Elderly

Counteracting Neurodegeneration in Parkinson's and Alzheimer's Disease

Sleep disturbances are a common feature in aging and have been increasingly recognized as both a symptom and a contributing factor in several neurodegenerative conditions, including Alzheimer's and Parkinson's disease. Particularly impaired slow-wave sleep has been linked to the progression and severity of neurodegenerative symptoms. Enhancing slow-wave activity, therefore, represents a promising therapeutic target for mitigating neurodegeneration (Wafford, 2021).

Preclinical research using animal models has provided valuable insights into the potential of CLAS in this context. Recent findings by Dias and colleagues (2024) demonstrated that applying CLAS in a mouse model of Alzheimer's disease improved sleep quality by reducing brief awakenings (Fig. 5A). Their research also suggests a neuroprotective effect: CLAS appears to mitigate brain atrophy and reduce abnormal protein aggregation, hallmarks of neurodegenerative pathology.

Encouraging results have also emerged from studies in human participants. A previous version of our Tosoo headband has been successfully used in multiple investigations to enhance slow waves in aging populations at their homes (Huwiler et al., 2024; Lustenberger et al., 2022; Schreiner et al., 2025). Schreiner and colleagues (2025) investigated patients with Parkinson's disease. The stimulation boosted slow-wave activity by almost 30% and was associated with improved subjective daytime alertness after three nights of application (Fig. 5B). Research groups working with patients diagnosed with Alzheimer's disease have further reported similar slow-wave enhancement, underlining the potential of CLAS to counteract cognitive decline in clinical populations (Van den Bulcke et al., 2025).

Taken together, these findings highlight the wide-reaching potential of CLAS technology to address sleep-related dysfunction in aging and disease, offering a safe, non-invasive method to support both cognitive function and neurological recovery.

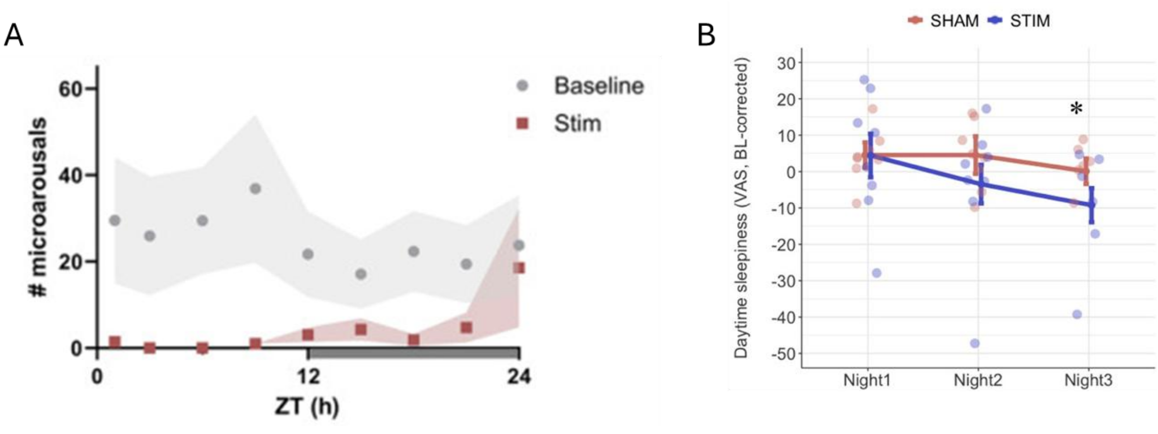

Figure 5. Effects of the CLAS technology in neurodegenerative disorders. A: Microarousal dynamics (i.e., brief awakenings) across 24 h in mice with a model of Alzheimer's disease. Microarousal dynamics were significantly reduced in the stimulation condition (Stim) in comparison with baseline dynamics (Baseline). Figure adapted from *Dias et al., 2024.* B: Subjective daytime sleepiness in patients with Parkinson's disease. Changes relative to baseline across the three intervention nights. Daytime sleepiness was significantly reduced after night 3 (p <0.05 resulting from RLMM analyses performed for each night separately). Figure adapted from *Schreiner et al., 2025.*

Supporting Recovery after Traumatic Brain Injury

Emerging research suggests that enhancing slow-wave activity shortly after a traumatic brain injury (TBI) may support recovery. In animal models, CLAS targeted to the up-phase of slow waves has been shown to boost slow waves and to reduce markers of brain damage, such as diffuse axonal injury (Fig. 6) and demyelination, while preserving cognitive function. These protective effects appear to be mediated by an enhanced microglia (the brain's immune cells) response during the acute phase of injury (Moreira et al., 2025). Importantly, the feasibility of applying CLAS has also been demonstrated in a highly sensitive clinical setting: a previous version of our headband was successfully used in children with severe TBI during their stay in a pediatric intensive care unit. This highlights the safety and adaptability of our technology, even under critical care conditions (Albrecht et al., 2022).

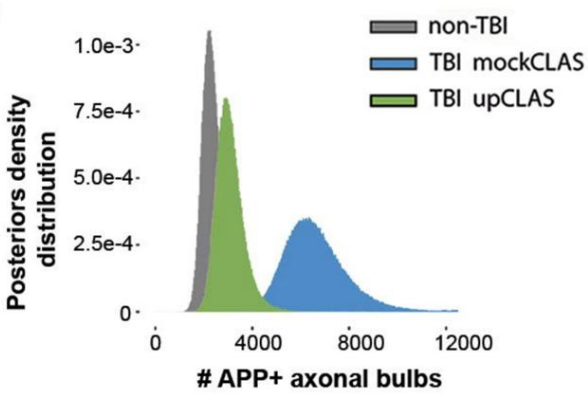

Figure 6. Reduction in axonal injury in traumatic brain injury (TBI) rats subjected to the CLAS technology. Histogram of the posterior density distributions for rats without TBI (non-TBI), TBI rats without stimulation (TBI mockCLAS) and TBI rats with up-phase stimulation (TBI upCLAS). The TBI mockCLAS group shows a clear difference to the other two groups (outside the 95% confidence interval) indicating that up-phase auditory stimulation normalized the APP+ axonal bulb estimate in TBI rats. Figure adapted from *Moreira et al., 2025*.

Reducing Abnormal Brain Activity in Epilepsy

Epileptic spikes during sleep (see Fig. 7), such as those seen in benign epilepsy with centrotemporal spikes (BECTS), are known to interfere with normal brain development and cognitive function in children. Recent studies suggest that CLAS is both feasible and well tolerated in pediatric patients with spike-wave activity during sleep (Fattinger et al., 2019). Early evidence indicates that CLAS may help reduce spike rates in BECTS (Klinzing et al., 2021), potentially by inducing a temporary refractory state in thalamocortical networks through precisely timed tones. These findings highlight the potential of our CLAS technology as a non-invasive approach to modulate pathological brain activity.

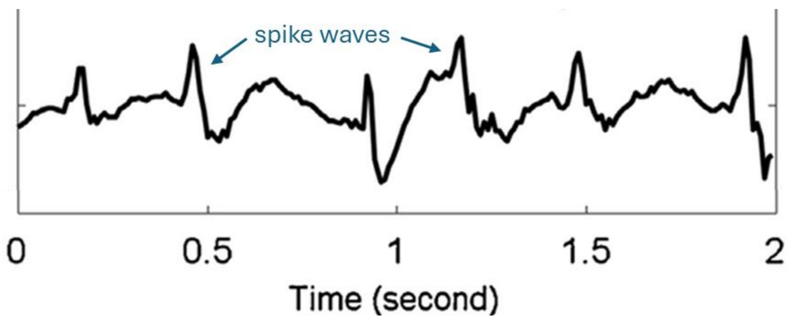

Figure 7. Example spike waves. Adapted from *Wang et al., 2017.*

Targeting Brain Oscillations during Wake and REM Sleep

While most research on CLAS has focused on deep non-REM sleep, recent investigations have begun to explore its application during other brain states such as relaxed wakefulness and rapid-eye movement (REM) sleep. These states are characterized by faster brain oscillations compared to non-REM sleep, predominantly in the alpha (around 10 Hz) and theta (around 7 Hz) frequency ranges. Figure 8 summarizes findings from Jaramillo and colleagues (2024), who were the first to investigate CLAS effects on alpha and theta activity during REM sleep. Their study showed that both alpha and theta rhythms during REM sleep can be enhanced. Furthermore, depending on the phase at which tones were played, these oscillations could either be slowed down or sped up. These findings are in line with a similar study by Hebron and colleagues (2024) illustrating that alpha rhythms during wakefulness can also be slowed down and sped up using the CLAS technology (Hebron et al., 2024).

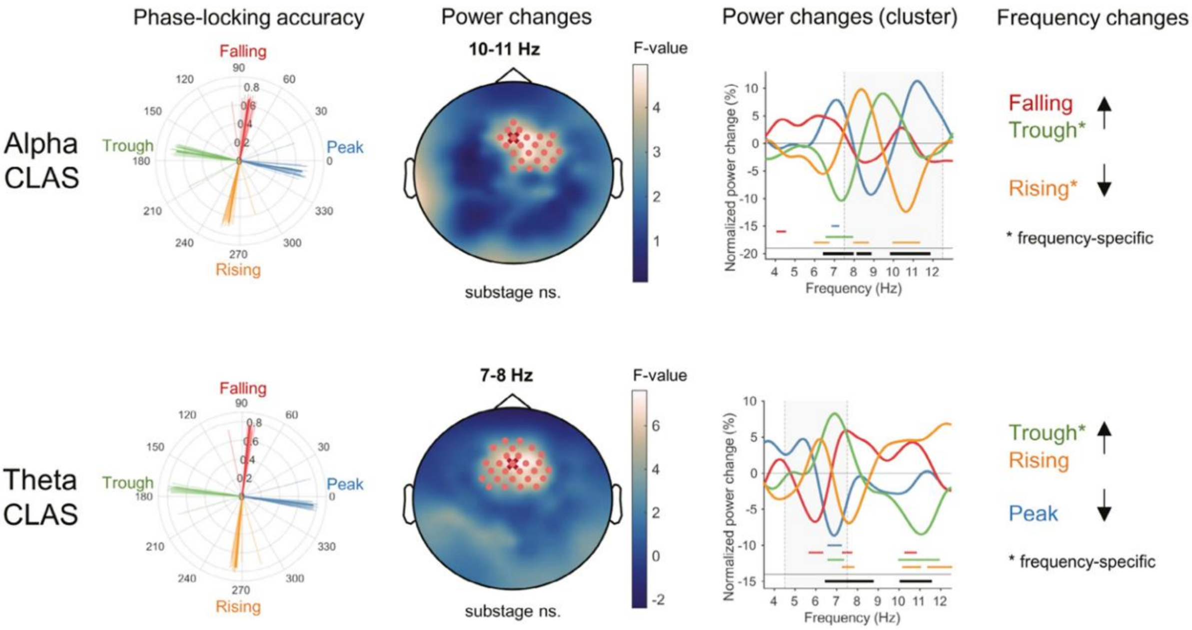

Figure 8. Modulation of alpha and theta oscillation during REM sleep using the CLAS technology. Auditory tones were locked to four different target phases of the ongoing oscillations. Power changes in alpha (10 – 11 Hz) and theta (7 – 8 Hz) activity are shown on a model of the head with significant electrodes shown as red dots. Plotting the normalized power change for each target phase separately shows the slowing-down and speeding-up of the ongoing oscillations. Figure adapted from *Jaramillo et al., 2024.*

Counteracting Age-Related Changes in Brain Activity

Aging is commonly associated with a slowing of alpha and theta oscillations, a change that has been linked to cognitive decline and dementia (Garcés et al., 2013; Jafari et al., 2020). The ability to modulate these rhythms, as demonstrated in recent CLAS studies targeting wakefulness and REM sleep, presents a promising avenue for counteracting age-related changes in brain activity. As described above, recent research has shown that alpha oscillations during wakefulness as well as both alpha and theta oscillations during REM sleep can be sped up using the CLAS technology (Hebron et al., 2024; Jaramillo et al., 2024), highlighting the *potential of CLAS as a non-invasive tool to preserve cognitive health in aging populations*.

Enhancing Emotional Well-Being

Beyond cognitive functions, REM sleep also plays a vital role in emotional processing. Theta activity during REM sleep has been associated with mood regulation and emotional memory consolidation (Hutchison & Rathore, 2015). This suggests that modulating REM oscillations via CLAS could support emotional well-being. By influencing brain rhythms linked to both cognition and mood, *CLAS opens up new therapeutic possibilities across a broad spectrum of mental health and neurodegenerative conditions*.

Facilitating Sleep Onset

When trying to fall asleep, the brain typically exhibits alpha oscillations, which are associated with a calm and restful mental state. Recent studies have demonstrated that slowing down these alpha rhythms through CLAS brings the brain's activity closer to early sleep patterns, thereby promoting sleep onset. Early evidence from studies using CLAS during wakefulness indeed show that alpha rhythms can be slowed down in real time and that sleep onset dynamics can be modulated (Bressler et al., 2024; Hebron et al., 2024). This positions our CLAS technology as *a promising non-pharmaceutical approach to supporting the transition into sleep*.

Conclusion

In conclusion, CLAS represents a groundbreaking, non-invasive technology that holds significant promise for enhancing sleep quality, cognitive functions, and overall well-being. Through its precise modulation of brain activity during sleep, CLAS has demonstrated potential benefits ranging from improved memory consolidation to enhanced cardiovascular health and even neuroprotection in clinical populations. As research continues to evolve, our CLAS technology offers an exciting avenue for both therapeutic applications and personalized sleep enhancement. At Tosoo, we are committed to making this scientific tool accessible to everyone, thereby providing sound sleep.

References

Albrecht, J. N., Jaramillo, V., Huber, R., Karlen, W., Baumann, C. R., & Brotschi, B. (2022). Technical feasibility of using auditory phase-targeted stimulation after pediatric severe traumatic brain injury in an intensive care setting. *BMC Pediatrics*, *22*(1). https://doi.org/10.1186/s12887-022-03667-7

Bergmann, T. O., & Born, J. (2018). Phase-Amplitude Coupling: A General Mechanism for Memory Processing and Synaptic Plasticity? *Neuron*, *97*(1), 10–13. https://doi.org/10.1016/J.NEURON.2017.12.023

Besedovsky, L., Ngo, H. V. V., Dimitrov, S., Gassenmaier, C., Lehmann, R., & Born, J. (2017). Auditory closed-loop stimulation of EEG slow oscillations strengthens sleep and signs of its immune-supportive function. *Nature Communications*, *8*(1). https://doi.org/10.1038/s41467-017-02170-3

Bressler, S., Neely, R., Yost, R. M., & Wang, D. (2024). A randomized controlled trial of alpha phase-locked auditory stimulation to treat symptoms of sleep onset insomnia. *Scientific Reports 2024 14:1*, *14*(1), 1–15. https://doi.org/10.1038/s41598-024-63385-1

Clark, V. P., Valverde, H. P., Briggs, M. S., Mullins, T., Ortiz, J., Pirrung, C. J. H., O'Keeffe, O. S., Hwang, M., Crowley, S., Šarlija, M., & Matsangas, P. (2024). Closed-loop auditory stimulation (CLAS) during sleep augments language and discovery learning. *Brain Sciences 2024, Vol. 14, Page 1138*, *14*(11), 1138. https://doi.org/10.3390/BRAINSCI14111138

Dias, I., Kollarik, S., Siegel, M., Baumann, C. R., Moreira, C. G., & Noain, D. (2024). Novel murine closed-loop auditory stimulation paradigm elicits macrostructural sleep benefits in neurodegeneration. *Journal of Sleep Research*, *34*(2), e14316. https://doi.org/10.1111/jsr.14316

Diep, C., Ftouni, S., Drummond, S. P. A., Garcia-Molina, G., & Anderson, C. (2022). Heart rate variability increases following automated acoustic slow wave sleep enhancement. *Journal of Sleep Research*, *31*(5). https://doi.org/10.1111/jsr.13545

Fattinger, S., de Beukelaar, T. T., Ruddy, K. L., Volk, C., Heyse, N. C., Herbst, J. A., Hahnloser, R. H. R., Wenderoth, N., & Huber, R. (2017). Deep sleep maintains learning efficiency of the human brain. *Nature Communications*, *8*(May), 1–39. https://doi.org/10.1038/ncomms15405

Fattinger, S., Heinzle, B. B., Ramantani, G., Abela, L., Schmitt, B., & Huber, R. (2019). Closed-loop acoustic stimulation during sleep in children with epilepsy: A hypothesis-driven novel approach to interact with spike-wave activity and pilot data assessing feasibility. *Frontiers in Human Neuroscience*, *13*, 454885. https://doi.org/10.3389/FNHUM.2019.00166/BIBTEX

Garcés, P., Vicente, R., Wibral, M., Pineda-Pardo, J. ángel, López, M. E., Aurtenetxe, S., Marcos, A., de Andrés, M. E., Yus, M., Sancho, M., Maestú, F., & Fernández, A. (2013). Brain-wide slowing of spontaneous alpha rhythms in mild cognitive impairment. *Frontiers in Aging Neuroscience*, *5*(DEC), 100. https://doi.org/10.3389/FNAGI.2013.00100

Grimaldi, D., Papalambros, N. A., Reid, K. J., Abbott, S. M., Malkani, R. G., Gendy, M., Iwanaszko, M., Braun, R. I., Sanchez, D. J., Paller, K. A., & Zee, P. C. (2019). Strengthening sleep-autonomic interaction via acoustic enhancement of slow oscillations. *Sleep*, *42*(5). https://doi.org/10.1093/sleep/zsz036

Hebron, H., Lugli, B., Dimitrova, R., Jaramillo, V., Yeh, L. R., Rhodes, E., Grossman, N., Dijk, D. J., & Violante, I. R. (2024). A closed-loop auditory stimulation approach selectively modulates alpha oscillations and sleep onset dynamics in humans. *PLOS Biology*, *22*(6), e3002651. https://doi.org/10.1371/JOURNAL.PBIO.3002651

Hutchison, I. C., & Rathore, S. (2015). The role of REM sleep theta activity in emotional memory. *Frontiers in Psychology*, *6*(OCT), 154468. https://doi.org/10.3389/FPSYG.2015.01439/XML/NLM

Huwiler, S., Carro Dominguez, M., Huwyler, S., Kiener, L., Stich, F. M., Sala, R., Aziri, F., Trippel, A., Schmied, C., Huber, R., Wenderoth, N., & Lustenberger, C. (2022). Effects of auditory sleep modulation approaches on brain oscillatory and cardiovascular dynamics. *Sleep*, *45*(9). https://doi.org/10.1093/sleep/zsac155

Huwiler, S., Carro-Domínguez, M., Stich, F. M., Sala, R., Aziri, F., Trippel, A., Ryf, T., Markendorf, S., Niederseer, D., Bohm, P., Stoll, G., Laubscher, L., Thevan, J., Spengler, C. M., Gawinecka, J., Osto, E., Huber, R., Wenderoth, N., Schmied, C., & Lustenberger, C. (2023). Auditory stimulation of sleep slow waves enhances left ventricular function in humans. *European Heart Journal*, *44*(40). https://doi.org/10.1093/eurheartj/ehad630

Huwiler, S., Ferster, M. L., Brogli, L., Huber, R., Karlen, W., & Lustenberger, C. (2024). Sleep and cardiac autonomic modulation in older adults: Insights from an at-home study with auditory deep sleep stimulation. *Journal of Sleep Research*, *34*(2), e14328. https://doi.org/10.1111/JSR.14328

Jafari, Z., Kolb, B. E., & Mohajerani, M. H. (2020). Neural oscillations and brain stimulation in Alzheimer's disease. *Progress in Neurobiology*, *194*, 101878. https://doi.org/10.1016/J.PNEUROBIO.2020.101878

Jaramillo, V., Hebron, H., Wong, S., Atzori, G., Bartsch, U., Dijk, D.-J., & Violante, I. R. (2024). Closed-loop auditory stimulation targeting alpha and theta oscillations during rapid eye movement sleep induces phase-dependent power and frequency changes. *Sleep*, *47*(12). https://doi.org/10.1093/SLEEP/ZSAE193

Kasties, V., Meier, N., Moser, N.-H., Sassenburg, R., Karlen, W., Ferster, M. L., Fattinger, S., Maric, A., & Huber, R. (2024). Longer interstimulus intervals enhance efficacy of automated phase-targeted auditory stimulation on procedural memory consolidation. *BioRxiv*, 2024.12.26.630252. https://doi.org/10.1101/2024.12.26.630252

Klinzing, J. G., Tashiro, L., Ruf, S., Wolff, M., Born, J., & Ngo, H. V. V. (2021). Auditory stimulation during sleep suppresses spike activity in benign epilepsy with centrotemporal spikes. *Cell Reports Medicine*, *2*(11), 100432. https://doi.org/10.1016/J.XCRM.2021.100432

Krugliakova, E., Skorucak, J., Sousouri, G., Leach, S., Snipes, S., Ferster, M. L., Da Poian, G., Karlen, W., & Huber, R. (2022). Boosting recovery during sleep by means of auditory stimulation. *Frontiers in Neuroscience*, *16*. https://doi.org/10.3389/fnins.2022.755958

Krugliakova, E., Volk, C., Jaramillo, V., Sousouri, G., & Huber, R. (2020). Changes in cross-frequency coupling following closed-loop auditory stimulation in non-rapid eye movement sleep. *Scientific Reports*, *10*. https://doi.org/10.1038/s41598-020-67392-w

Leach, S., Krugliakova, E., Sousouri, G., Snipes, S., Skorucak, J., Schühle, S., Müller, M., Ferster, M. L., Da Poian, G., Karlen, W., & Huber, R. (2024). Acoustically evoked K-complexes together with sleep spindles boost verbal declarative memory consolidation in healthy adults. *Scientific Reports*, *14*(1), 1–20. https://doi.org/10.1038/S41598-024-67701-7

Leminen, M. M., Virkkala, J., Saure, E., Paajanen, T., Zee, P. C., Santostasi, G., Hublin, C., Müller, K., Porkka-Heiskanen, T., Huotilainen, M., & Paunio, T. (2017). Enhanced memory consolidation via automatic sound stimulation during non-REM sleep. *Sleep*, *40*(3). https://doi.org/10.1093/sleep/zsx003

Lustenberger, C., Ferster, M. L., Huwiler, S., Brogli, L., Werth, E., Huber, R., & Karlen, W. (2022). Auditory deep sleep stimulation in older adults at home: a randomized crossover trial. *Communications Medicine*, *2*(1). https://doi.org/10.1038/s43856-022-00096-6

Moreira, C. G., Müllner, A., Gönel, M., Hofmann, P., Teixeira, F., Paolicelli, R. C., Dias, I., Nemirovsky, S. I., Baumann, C. R., & Noain, D. (2025). Sound-enhanced sleep depth reduces traumatic brain injury damage and sequelae and supports microglial response. *BioRxiv*, 2025.01.21.634054. https://doi.org/10.1101/2025.01.21.634054

Ngo, H. V, Martinetz, T., Born, J., & Molle, M. (2013). Auditory closed-loop stimulation of the sleep slow oscillation enhances memory. *Neuron*, *78*(3), 545–553. https://doi.org/10.1016/j.neuron.2013.03.006

Ong, J. L., Lo, J. C., Chee, N. I., Santostasi, G., Paller, K. A., Zee, P. C., & Chee, M. W. (2016). Effects of phase-locked acoustic stimulation during a nap on EEG spectra and declarative memory consolidation. *Sleep Med*, *20*, 88–97. https://doi.org/10.1016/j.sleep.2015.10.016

Ong, J. L., Patanaik, A., Chee, N. I. Y. N., Lee, X. K., Poh, J. H., & Chee, M. W. L. (2018). Auditory stimulation of sleep slow oscillations modulates subsequent memory encoding through altered hippocampal function. *Sleep*, *41*(5). https://doi.org/10.1093/sleep/zsy031

Papalambros, N. A., Santostasi, G., Malkani, R. G., Braun, R., Weintraub, S., Paller, K. A., & Zee, P. C. (2017). Acoustic enhancement of sleep slow oscillations and concomitant memory improvement in older adults. *Front Hum Neurosci*, *11*, 109. https://doi.org/10.3389/fnhum.2017.00109

Prehn-Kristensen, A., Ngo, H. V. V., Lentfer, L., Berghäuser, J., Brandes, L., Schulze, L., Göder, R., Mölle, M., & Baving, L. (2020). Acoustic closed-loop stimulation during sleep improves consolidation of reward-related memory information in healthy children but not in children with attention-deficit hyperactivity disorder. *Sleep*, *43*(8), 1–13. https://doi.org/10.1093/SLEEP/ZSAA017

Schreiner, S. J., Horlacher, J., Fattinger, S., Renerts, K., Brogli, L., Kämpf, L., Scandella, M., Poryazova, R., Valko, P. O., Ferster, L., Sassenburg, R., Jaramillo, V., Poian, G. Da, Lustenberger, C., Karlen, W., Huber, R., Baumann, C. R., & Maric, A. (2025). Auditory enhancement of sleep slow waves in people with Parkinson's disease: A proof-of-concept study. *MedRxiv*. https://doi.org/10.1101/2025.01.30.25320306

Van den Bulcke, L., Davidoff, H., Heremans, E., Potts, Y., Vansteelandt, K., De Vos, M., Christiaens, D., Emsell, L., Jacobson, L. H., Hoyer, D., Buyse, B., Vandenbulcke, M., Testelmans, D., & Van Den Bossche, M. (2025). Acoustic stimulation to improve slow-wave sleep in Alzheimer's disease: A multiple night at-home intervention. *The American Journal of Geriatric Psychiatry*, *33*(1), 73–84. https://doi.org/10.1016/J.JAGP.2024.07.002

Wafford, K. A. (2021). Aberrant waste disposal in neurodegeneration: why improved sleep could be the solution. *Cerebral Circulation - Cognition and Behavior*, *2*, 100025. https://doi.org/10.1016/J.CCCB.2021.100025

Wang, L., Long, X., Arends, J. B. A. M., & Aarts, R. M. (2017). EEG analysis of seizure patterns using visibility graphs for detection of generalized seizures. *Journal of Neuroscience Methods*, *290*, 85–94. https://doi.org/10.1016/J.JNEUMETH.2017.07.013