Researchers find new origin of deep brain waves

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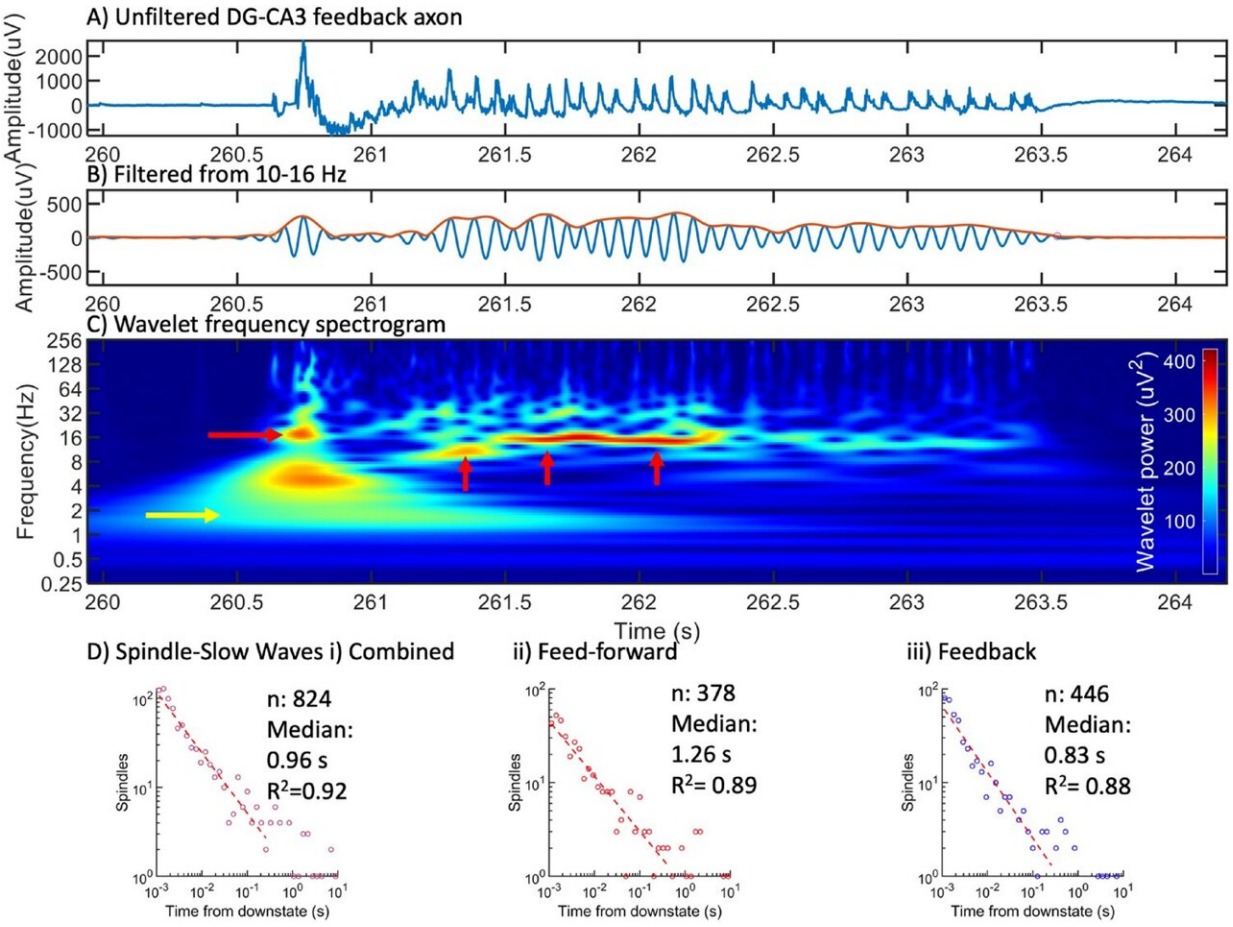

Spindle frequencies embedded in the spike train. (A) Raw data of single axon from CA3 feedback to DG (F12-G12) channels, array ECDGCA3CA1 19908 160518 160610 d22). (B) Same data filtered from 10 to 16 Hz and a Hilbert-

transformed envelope to reveal several spindle events. (C) Continuous wavelet transform to show wave power and relative timing at different frequencies. Red arrows point to spindle events. Yellow arrow points to slow wave near 1.5 Hz. (D) Log–log distribution of spindle events relative to slow waves for all subregions, (i) feed forward and feedback in all subregions combined, (ii) feed forward spindles, (iii) feedback spindles. Best fit linear models are overlayed. Credit: *Scientific Reports* (2024). DOI: 10.1038/s41598-024-58002-0

University of California, Irvine biomedical engineering researchers have uncovered a previously unknown source of two key brain waves crucial for deep sleep: slow waves and sleep spindles. Traditionally believed to originate from one brain circuit linking the thalamus and cortex, the team's findings, published in *Scientific Reports*, suggest that the axons in memory centers of the hippocampus play a role.

For decades, slow waves and sleep spindles have been identified as essential elements of deep sleep, measured through electroencephalography recordings on the scalp. However, the UC Irvine-led team revealed a novel source of these brain waves within the hippocampus and were able to measure them in single axons.

The study demonstrates that slow waves and sleep spindles can originate from axons within the hippocampus's cornu ammonis 3 region. These oscillations in voltage occur independently of neuronal spiking activity, challenging existing theories about the generation of these brain waves.

"Our research sheds light on a previously unrecognized aspect of deep sleep brain activity," said lead author Mengke Wang, former UC Irvine undergraduate student in biomedical engineering who is now a graduate student at Johns Hopkins University (Wang conducted the study while at

UC Irvine). "We've discovered that the hippocampus, typically associated with memory formation, plays a crucial role in generating slow waves and sleep spindles, offering new insights into how these brain waves support memory processing during sleep."

The team utilized innovative techniques—including in vitro reconstructions of hippocampal subregions and microfluidic tunnels for single axon communication—to observe spontaneous spindle waves in isolated hippocampal neurons. These findings suggest that spindle oscillations originate from active ion channels within axons, rather than through volume conduction as previously thought.

"The discovery of spindle oscillations in single hippocampal axons opens new avenues for understanding the mechanisms underlying memory consolidation during sleep," said co-author Gregory Brewer, adjunct professor of biomedical engineering. "These findings have significant implications for sleep research, potentially paving the way for new approaches to treating sleep-related disorders."

Brewer's other research affiliations include the Institute for Memory Impairment and Neurological Disorders and the Center for Neurobiology of Learning and Memory.

By uncovering the hippocampus's role in generating slow waves and sleep spindles, this research expands our understanding of the brain's activity during deep sleep and its impact on memory processing. The findings offer a promising foundation for future studies exploring the therapeutic potential of targeting hippocampal activity to improve sleep quality and cognitive function.

Joining Brewer and Wang in this study were William Tang, professor emeritus of biomedical engineering; Bryce Mander, associate professor of psychiatry & human behavior; and Samuel Lassers, graduate student

researcher in biomedical engineering.

More information: Mengke Wang et al, Spindle oscillations in communicating axons within a reconstituted hippocampal formation are strongest in CA3 without thalamus, *Scientific Reports* (2024). DOI: 10.1038/s41598-024-58002-0

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