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Waves of CSF Flow Into the Brain During Sleep

— Findings may have implications for Alzheimer's and dementia

by Judy George, Senior Staff Writer, MedPage Today
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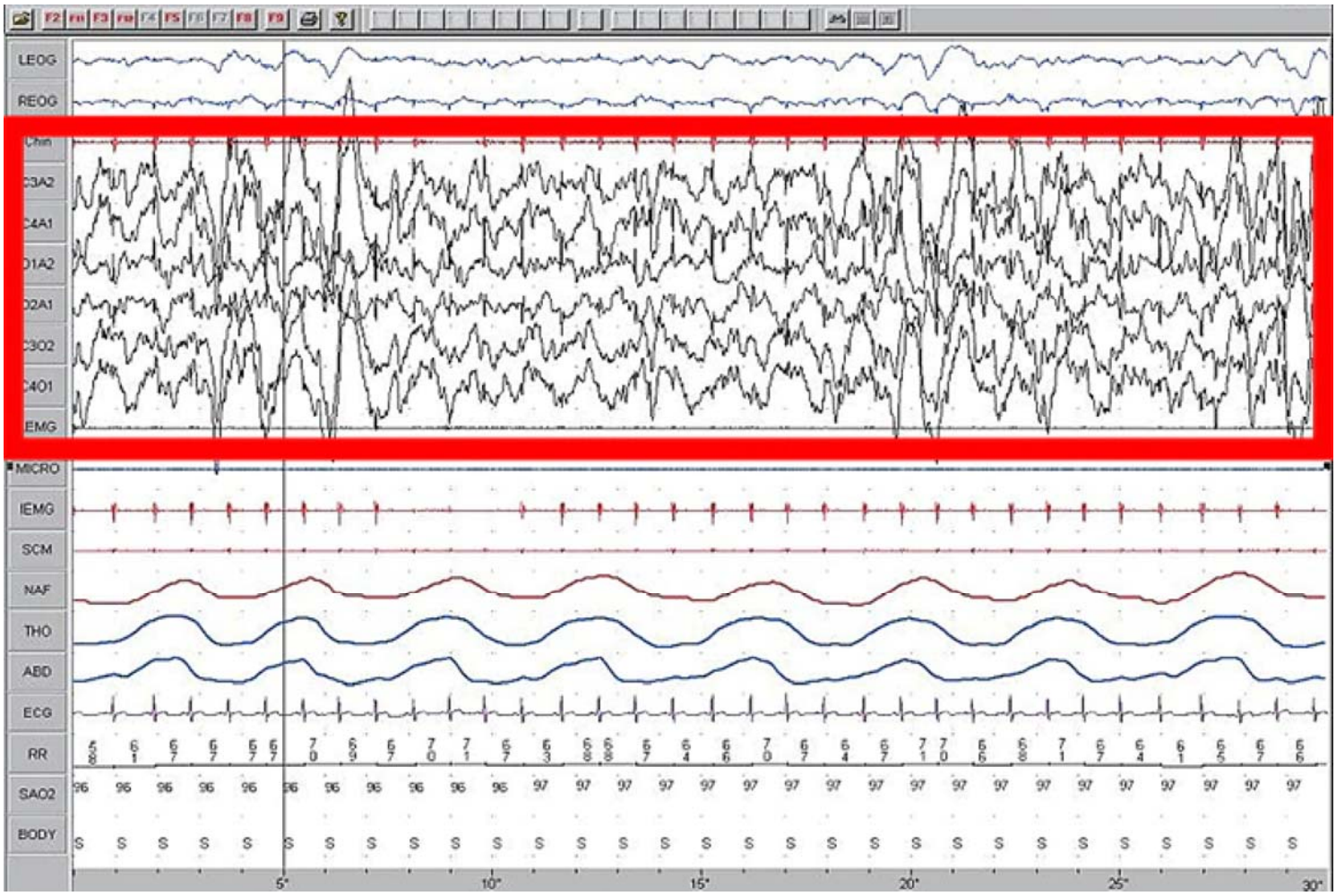
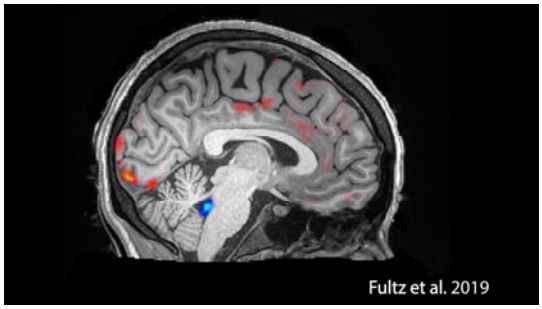


The brain's cerebrospinal fluid (CSF) pulses during deep sleep and this appears to be tied to brain wave activity and blood flow, an exploratory study showed.

Large oscillations of CSF inflow to the brain appeared about every 20 seconds and were tightly coupled to functional magnetic resonance imaging (fMRI) signals of blood flow and electroencephalogram (EEG) slow waves, reported Laura Lewis, PhD, of the Boston University College of Engineering, and co-authors, who described this activity for the first time in *Science*.

"We've known for a while that there are these electrical waves of activity in the neurons," Lewis said in a statement. "But before now, we didn't realize that there are actually waves in the CSF, too."

"It's such a dramatic effect," she added. "Now we can just glance at one brain region and immediately have a read-out of the brain state someone's in."



During sleep, the brain shows large-scale waves: waves of blood oxygenation (red), followed by waves of cerebrospinal fluid (blue). Copyright Laura Lewis, Boston University.

The findings may have implications for neurodegenerative diseases, including Alzheimer's disease and dementia. Recent studies have shown that tau and amyloid beta levels were tied to sleep and that slow wave activity during non-REM sleep was inversely related to Alzheimer's pathology.

"Disturbances of slow wave sleep commonly accompany aging, major depressive disorders, and dementia," noted Soren Grubb, PhD, and Martin Lauritzen, MD, both of the University of Copenhagen in Denmark, in an accompanying editorial.

"It will be interesting to assess whether the CSF dynamics linked to slow wave sleep can be used as a biomarker for disease states and whether strategies that restore slow wave sleep can rescue brain function in neurodegeneration," Grubb and Lauritzen wrote.

In their study, Lewis and colleagues simultaneously measured blood oxygen level–dependent (BOLD) fMRI dynamics, EEG, and CSF flow simultaneously in 13 young people during sleep. They acquired fMRI data at fast rates to detect fluid inflow: fresh fluid arriving at the edge of the imaging volume has high signal intensity because it has not yet experienced radiofrequency pulses, the team noted.

EEG, BOLD, and CSF signals displayed a specific timing sequence during slow wave sleep, with neural rhythms preceding BOLD signals and CSF waves. "The neural change always seems to happen first, and then it's followed by a flow of blood out of the head, and then a wave of CSF into the head," Lewis said. It's not clear how the waves are related to each other, but one explanation may be that when neurons shut off, they don't require as much oxygen, so blood leaves and CSF quickly flows in to maintain pressure in the brain, she noted. "But that's just one possibility," she said.

The results address a key question in sleep neurophysiology about CSF and waste clearance, the researchers noted. "Neurovascular coupling has been proposed to contribute to clearance, but why it would cause higher clearance rates during sleep was not known," they wrote. "Our study suggests slow neural and hemodynamic oscillations as a possible contributor to this process, in concert with other physiological factors."

Studies in animals could test for causal relationships, the team suggested. And because the people studied in this research were ages 23 to 33 years, the researchers plan to recruit older adults next to see how aging might affect blood and CSF flow during sleep.

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Several members of the research team are inventors on a provisional patent cover sheet.

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