First evidence of replay during sleep in the human motor cortex, which governs voluntary movement

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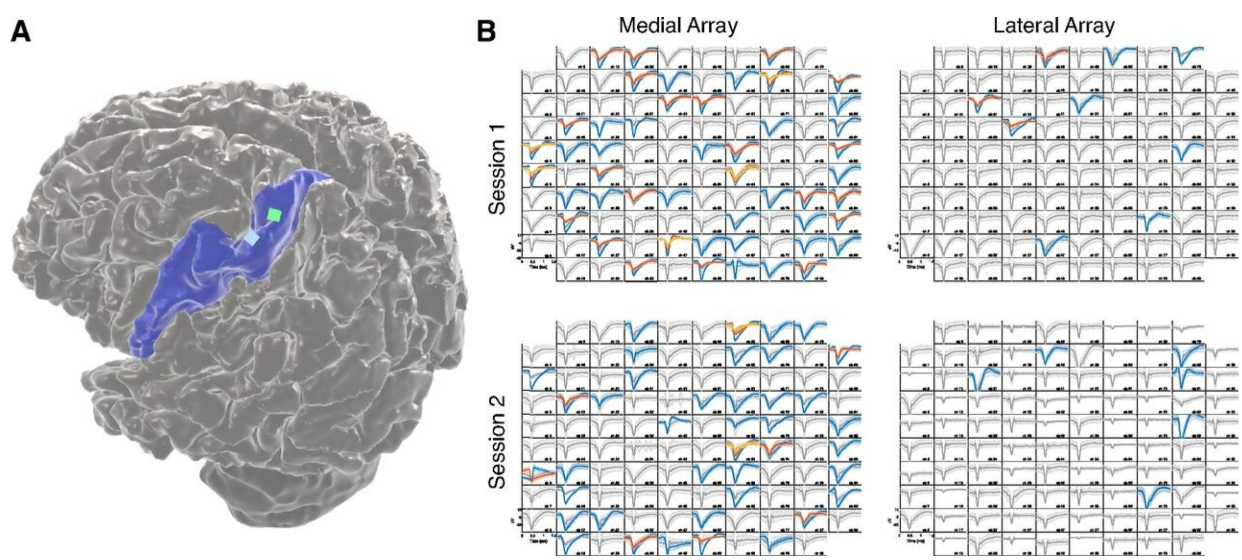

Neural signals for this study were acquired from two microelectrode arrays chronically implanted in left precentral gyrus. A, A three-dimensional reconstruction of the research participants' brain. Blue represents left precentral gyrus. Green and blue squares represent the precise location of the two Utah arrays. B, Spike sorting reveals single-unit and multiunit activity on each array (medial array on the left, lateral array on the right) during the first (top) and second (bottom) recording session. All amplitude plots demonstrate mean ± SD of activity for each threshold crossing event, with color representing event type based on automated sorting algorithm (Vargas-Irwin and Donoghue, 2007). Gray amplitude plots represent multiunit activity. Blue, orange, and yellow amplitude plots represent isolated single-unit activity. There were 78 and 51 single units isolated from the medial array and 12 and 6 single units isolated from the lateral array from Sessions 1 and 2, respectively. The smaller number of single units recorded from the lateral array comports with the finding that activity on the lateral array is typically sparser and less closely associated with task performance. Credit: *The Journal of Neuroscience* (2022). DOI: 10.1523/JNEUROSCI.2074-21.2022

Why do we sleep? Scientists have debated this question for millennia, but a new study by researchers at Massachusetts General Hospital (MGH), conducted in collaboration with colleagues at Brown University, the Department of Veterans Affairs, and several other institutions, adds new clues for solving this mystery. Their findings, published in the *Journal of Neuroscience*, may help explain how humans form memories and learn, and could eventually aid the development of assistive tools for people affected by neurologic disease or injury.

Scientists studying laboratory animals long ago discovered a phenomenon known as "replay" that occurs during sleep, explains neurologist Daniel Rubin, MD, Ph.D., of the MGH Center for Neurotechnology and Neurorecovery, the lead author of the study. Replay is theorized to be a strategy the brain uses to remember new information. If a mouse is trained to find its way through a maze, monitoring devices can show that a specific pattern of brain cells, or neurons, will light up as it traverses the correct route. "Then, later on while the animal is sleeping, you can see that those neurons will fire again in that same order," says Rubin. Scientists believe that this replay of neuronal firing during sleep is how the brain practices newly learned information, which allows a memory to be consolidated—that is, converted from a short-term memory to a long-term one.

However, replay has only been convincingly shown in lab animals. "There's been an open question in the neuroscience community: To what extent is this model for how we learn things true in humans? And is it true for different kinds of learning?" asks neurologist Sydney S. Cash, MD, Ph.D., co-director of the Center for Neurotechnology and Neurorecovery at MGH and co-senior author of the study. Importantly, says Cash, understanding whether replay occurs with the learning of motor skills could help guide the development of new therapies and tools for people with neurologic diseases and injuries.

To study whether replay occurs in the human motor cortex—the brain region that governs movement—Rubin, Cash, and their colleagues enlisted a 36-year-old man with tetraplegia (also called quadriplegia), meaning he is unable to move his upper and lower limbs, in his case due to a spinal cord injury. The man, identified in the study as T11, is a participant in a clinical trial of a brain-computer interface device that allows him to use a computer cursor and keyboard on a screen. The investigational device is being developed by the BrainGate consortium, a collaborative effort involving clinicians, neuroscientists, and engineers at several institutions with the goal of creating technologies to restore communication, mobility, and independence for people with neurologic disease, injury, or limb loss. The consortium is directed by Leigh R. Hochberg, MD, Ph.D., of MGH, Brown University, and the Department of Veterans Affairs.

In the study, T11 was asked to perform a memory task similar to the electronic game Simon, in which a player observes a pattern of flashing colored lights, then has to recall and reproduce that sequence. He controlled the cursor on the computer screen simply by thinking about the movement of his own hand. Sensors implanted in T11's motor cortex measured patterns of neuronal firing, which reflected his intended hand movement, allowing him to move the cursor around on the screen and click it at his desired locations. These brain signals were recorded and wirelessly transmitted to a computer.

That night, while T11 slept at home, activity in his motor cortex was recorded and wirelessly transmitted to a computer. "What we found was pretty incredible," says Rubin. "He was basically playing the game overnight in his sleep." On several occasions, says Rubin, T11's patterns of neuronal firing during sleep exactly matched patterns that occurred while he performed the memory-matching game earlier that day.

"This is the most direct evidence of replay from motor cortex that's ever been seen during sleep in humans," says Rubin. Most of the replay detected in the study occurred during slow-wave sleep, a phase of deep slumber. Interestingly, replay was much less likely to be detected while T11 was in REM sleep, the phase most commonly associated with dreaming. Rubin and Cash see this work as a foundation for learning more about replay and its role in learning and memory in humans.

"Our hope is that we can leverage this information to help build better brain-computer interfaces and come up with paradigms that help people learn more quickly and efficiently in order to regain control after an injury," says Cash, noting the significance of moving this line of inquiry from animals to human subjects. "This kind of research benefits enormously from the close interaction we have with our participants," he adds, with gratitude to T11 and other participants in the BrainGate clinical trial.

Hochberg concurs. "Our incredible BrainGate participants provide not only helpful feedback toward the creation of a system to restore communication and mobility, but they also give us the rare opportunity to advance fundamental human neuroscience—to understand how the human brain works at the level of circuits of individual neurons," he says, "and to use that information to build next-generation restorative neurotechnologies."

More information: Daniel B. Rubin et al, Learned Motor Patterns Are

Replayed in Human Motor Cortex during Sleep, *The Journal of Neuroscience* (2022). [DOI: 10.1523/JNEUROSCI.2074-21.2022](https://doi.org/10.1523/JNEUROSCI.2074-21.2022)

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