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New research reveals competition between brain hemispheres during sleep

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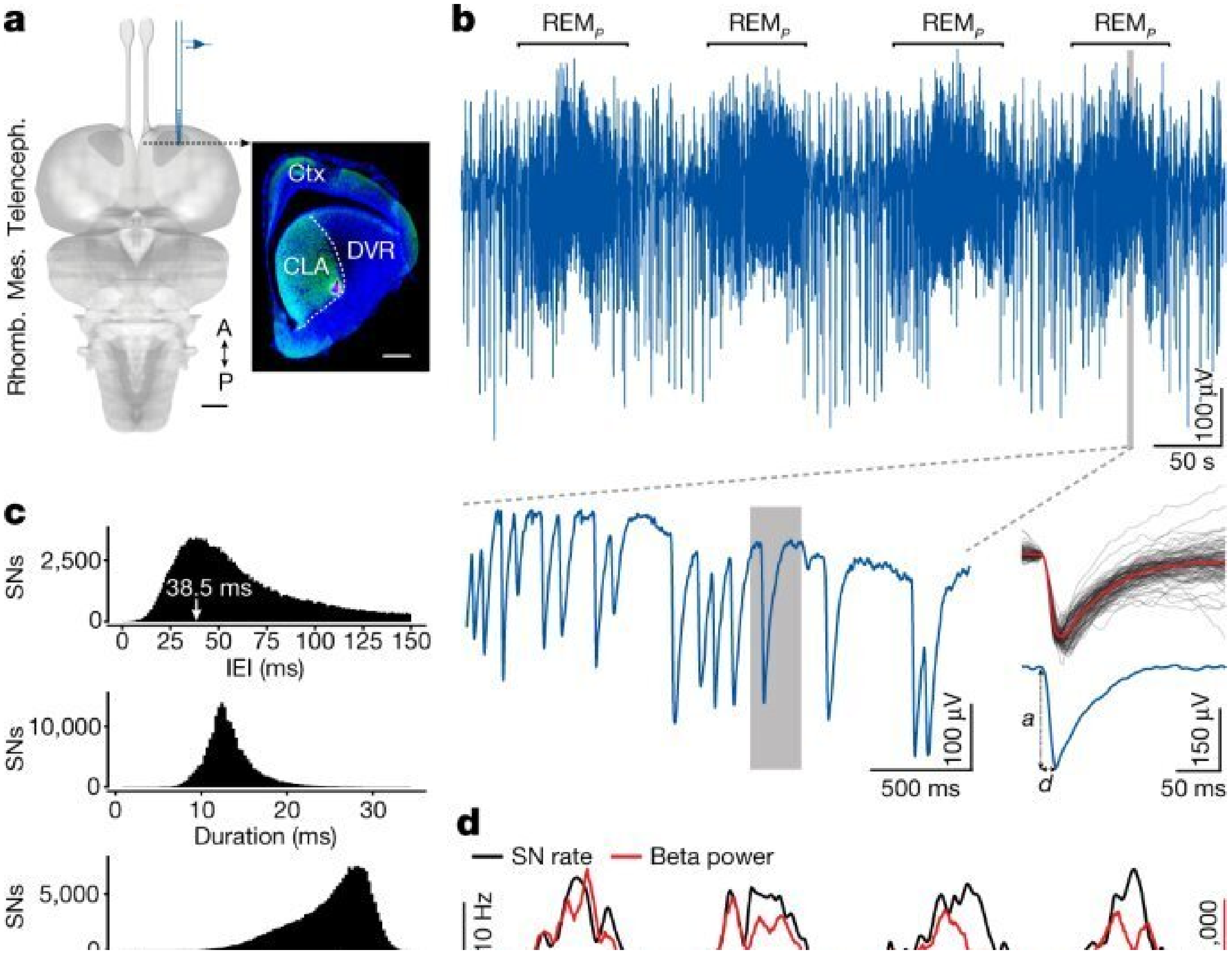

REM_P activity is characterized by sharp negative field-potential events.a, Dorsal view of the Pogona brain (Mes., mesencephalon; Rhomb., rhombencephalon; Telenceph., telencephalon; A, anterior; P, posterior), with recording site (CLA, claustrum). Inset, coronal section showing the claustrum (within dashed line; green fluorescence, hippocalcin) and the electrode tip position in red (DiI fluorescence). Ctx, cortex. Scale bars, 1 mm (left); 500 μm (right). b, Top, LFP recording from site in a, during around 8 min of sleep. Epochs between REM_P episodes correspond to SW sleep, characterized by sharp-wave ripples. Bottom left, expanded trace within shaded window at top (fourth REM_P episode). Note the single sharp negative extracellular potential (SN), expanded on the right. Bottom right, blue: trace shaded on the left (a, amplitude and d, duration of falling phase; see c); gray: 100 superimposed SNs and their average (red). c, Statistics of IEI, duration (as in b) and amplitude across 190,578 SNs. IEI distribution truncated at 150 ms. d, Instantaneous rate of SN production superimposed on power in beta band (same epoch as in b). e, Extracellular SN potentials correspond to the production of phasic and synchronized firing in claustrum units. Left, SN and four sorted single units. Right, Histograms, distributions of spike times in the four units, relative to the time of peak |dV/dt| of the SNs (red line) (n = 100,632 events). Probability of these units producing at least one spike: 14–43%; probability of these units producing more than one spike: 0.3–3%. The small dip preceding the firing peak is likely to reflect the effects of down states that usually surround SNs, combined with those of the SN interval distribution during REM_P. Calibration bars represent 500 spikes. Credit: *Nature* (2023). DOI: 10.1038/s41586-023-05827-w

Human beings are bilaterally symmetrical. As such, our brains are made of two halves called hemispheres, which communicate with each other using specialized fiber tracts running across the midline. While each hemisphere tends to deal with the senses (vision, hearing, touch) and motor control of the opposite side of the body, we are generally not aware of this partitioning of function, thanks to constant inter-hemispheric communication. In humans, the two hemispheres are also specialized for certain functions: language areas, for example, are typically in the left hemisphere.

Most animals (birds, reptiles, amphibians, fish, insects, mollusks, etc.) are, like humans, bilaterally symmetrical, and possess bilaterally symmetrical brains. Studying sleep in a reptile, the Australian dragon

Pogona vitticeps, Lorenz Fenk, Luis Riquelme and Gilles Laurent of the Max Planck Institute for Brain Research in Frankfurt, Germany report in *Nature* that during one phase of sleep, the two halves of the Pogona brain compete with one another such that one side imposes its activity on the other, until the dominant hemisphere switches over to the other side, alternating back and forth throughout the night.

Lorenz Fenk explains, "Sleep in Pogona is divided into two states, similar to those described in mammals, including humans: a phase of so-called slow-wave sleep, where the electroencephalogram shows low-frequency waves—hence the name—and a second phase, called REM (for Rapid Eye Movement) or paradoxical sleep, where the EEG resembles that recorded during the awake state (hence 'paradoxical') and the eyes tend to make jerky movements under the eye lids (hence REM) while the body is otherwise paralyzed."

In humans, sleep starts with a long slow-wave phase (for about 60 minutes) followed by 5-10 minutes of REM, and this alternating cycle starts over again, 5-7 times per night. As the night progresses, the fraction of REM sleep increases at each sleep cycle. In Pogona, the sleep cycle is much shorter (less than 2 minutes) and the two sleep states are equal in duration (45-60 seconds each) throughout the night. A dragon undergoes 250-350 such sleep cycles each night, alternating regularly between its versions of slow-wave and REM sleep.

By recording neuronal activity simultaneously from the same area (called the claustrum) on the two sides of the Pogona brain, the scientists discovered that each side operates independently of the other during the slow-wave phase of sleep. To their surprise, however, the two sides became precisely synchronized during REM, but with a very short delay of 20 milliseconds (a millisecond is a thousandth of a second) between the left and right brains. More surprising still, they found that the side leading the other by 20ms switched on average once per sleep cycle between left and right sides.

By comparing the intensity of the signals recorded in left and right claustrum during REM, they observed also that the side with the stronger activity was typically the one leading. This—together with other evidence presented in their paper—suggested that the two sides of the brain compete with one another during REM sleep, but not during slow-wave sleep, and that when competing, the stronger side imposes its activity on the other. This form of competition is called winner-takes-all.

Interestingly, although the left and right sides take the leading role about equal times throughout the night (about half of the sleep cycles each), the switch between sides does not occur exactly with each sleep cycle. In addition, the switching between sides became less frequent in the last hours of the night, with one side dominating the other over many sleep cycles, before relinquishing dominance to the other one, again for many successive cycles.

"This indicates the existence and interplay of several sleep-control circuits, each with different time scales, and a systematic evolution of some of these time scales throughout the night; this suggests that whatever functions sleep plays in these animals, different mechanisms might be at play early and late in the night, with different consequences," says Laurent.

In an effort to understand how the two sides of the brain interact and compete with one another during REM sleep, the scientists discovered that this competition was not due to direct interactions between left and right claustra, but rather to circuits found further back in the brain, at the junction between the midbrain and the hindbrain. These so-called isthmic circuits are found in all vertebrates, including mammals and humans, and have been particularly well studied in birds. There, they have been shown to be important for certain forms of visual attention in awake birds (owls and pigeons). By lesioning a component of these isthmic circuits on one side only of the Pogona brain, Fenk and colleagues were able to cancel the regular switching of side dominance, causing the intact side to dominate the other throughout the night (and the successive ones).

While the circuit components implicated in this study (claustrum, midbrain and isthmus) exist in mammals including humans, it is not known yet whether similar competitive interactions occur during REM sleep in humans as well. The mechanisms and functions of sleep are complex and still poorly understood in any animal. These new results in a reptile add a new level of complexity to the important questions of sleep dynamics and functions.

More information: Lorenz A. Fenk et al, Interhemispheric competition during sleep, *Nature* (2023). DOI: 10.1038/s41586-023-05827-w

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