Individualized fingerprints from sleep brainwaves provide a powerful new tool for understanding disease

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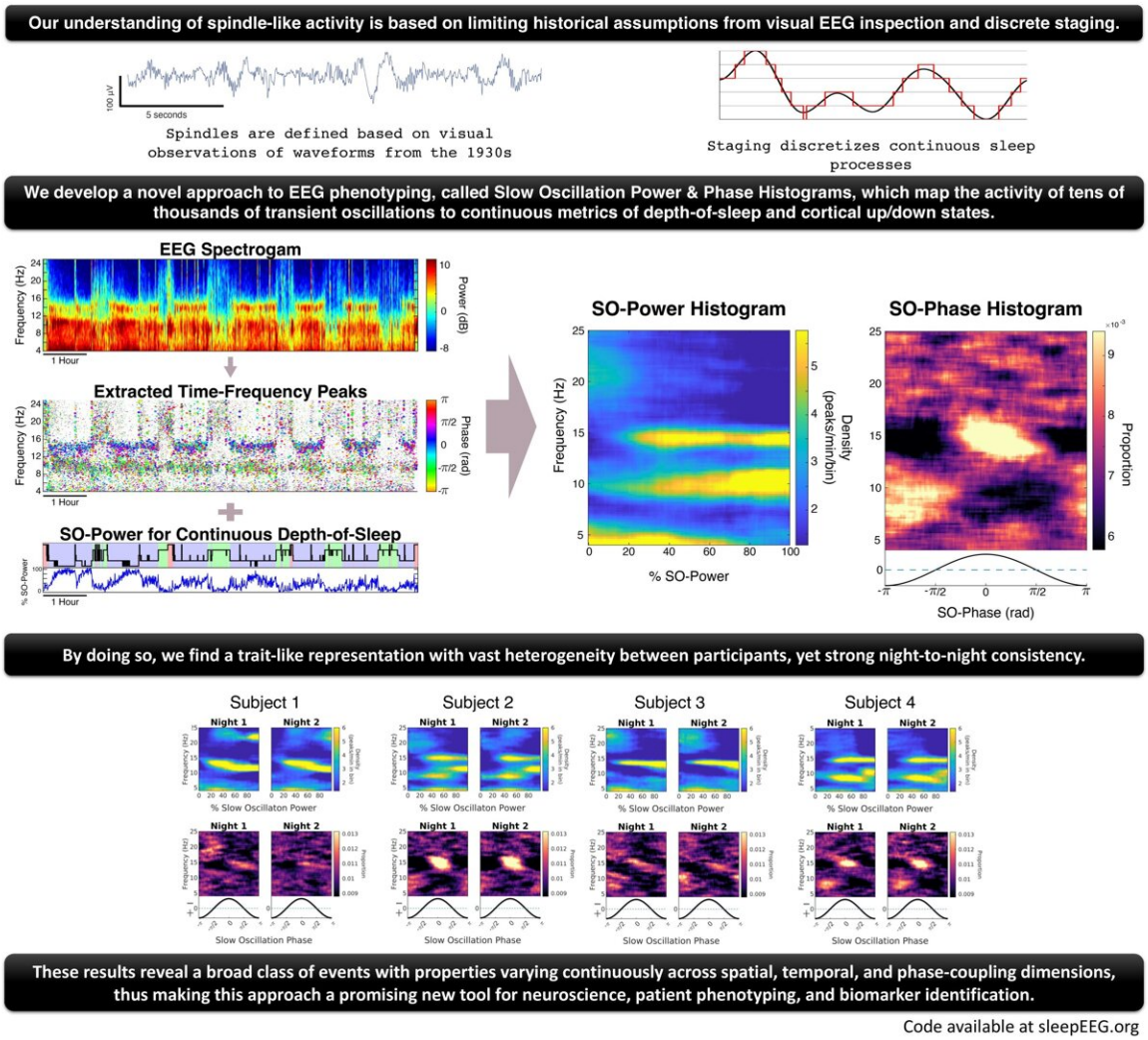

Graphical abstract. Credit: *Sleep* (2022). DOI: 10.1093/sleep/zsac223

A team led by researchers from Brigham and Women's Hospital, a founding member of the Mass General Brigham healthcare system, in close collaboration with investigators at Mass General Hospital and Beth Israel Deaconess Medical Center has developed a powerful computational tool for understanding brain health and disease, providing an enhanced way of characterizing the activity of the brain during sleep.

The researchers devised a new method that extracts tens of thousands of electrical events from the brainwaves of a sleeping person. Information from these waveforms is then used to create a picture of brain activity that seems to act like a fingerprint—unique for each person and consistent from one night to the next. They then used their approach to identify new potential biomarkers in the brain activity of people with schizophrenia. Their findings are published in the journal, *Sleep*.

Postdoctoral fellow, Patrick Stokes, Ph.D., was the first author on the study and the senior author was Michael Prerau, Ph.D., associate neuroscientist and the director of the Neurophysiological Signal Processing Core in the Division of Sleep and Circadian Disorders at the Brigham.

"This work expands the way we can look at brain activity during sleep," said Prerau. "By moving beyond traditional notions that break up the complex continuum of sleep into specific categories and waveform classes, we can reveal new types of signals and dynamics that may be important for understanding brain health and disease."

Scientists typically study brain activity during sleep using the electroencephalogram, or EEG, which measures brainwaves at the scalp. Starting in the mid 1930s, the sleep EEG was first studied by looking at the traces of brainwaves drawn on a paper tape by a machine. Many

important features of sleep are still based on what people almost a century ago could most easily observe in the complex waveform traces.

Even the latest machine learning and signal processing algorithms for detecting sleep waveforms are judged against their ability to recreate human observation. In this study, the researchers asked: What can we learn if we expand our notion of sleep brainwaves beyond what was historically easy to identify by eye?

One particularly important set of sleep brainwave events are called sleep spindles. These spindles are short oscillation waveforms, usually lasting less than 1-2 seconds, that are linked to our ability to convert short-term memories to long-term memories. Changes in spindle activity have been linked with numerous disorders such as schizophrenia, autism, and Alzheimer's disease, as well as with natural aging.

In this study, rather than looking for spindle activity according to the historical definition, the team developed a new approach to automatically extract tens of thousands of short spindle-like waveform events from the EEG data throughout the entire night. Next, instead of looking at the waveforms in terms of fixed sleep stages (i.e., Wake, REM, and non-REM stages 1-3) as standard sleep studies do, they characterized the full continuum of gradual changes that occur in the brain during sleep.

Using all these data, the team created graphical representations called slow oscillation power and phase histograms, which provide a powerful visualization of the activity of all the waveforms as a function of continuous sleep depth and synchronized activity in the cortex. "This further demonstrates the richness of the information that traditional, manual scoring leaves on the table," said co-author Shaun Purcell, Ph.D., of the Department of Psychiatry at the Brigham.

When the team looked at a group of healthy participants, each with two nights of sleep recordings, the patterns observed appeared to be almost like fingerprints—highly specific to each person with strong consistency across nights. These results suggest new ways in which brain activity differs from person to person, even within groups of healthy people selected as control groups.

The researchers then compared the activity between the healthy subjects and a population of people with schizophrenia, a disorder that reduces spindle activity. Using their approach, the team not only saw the known differences in participants with schizophrenia, but also found differences in other spindle-like waveforms occurring at other frequencies in the brain. This suggests new potential EEG biomarkers of schizophrenia that could be useful in better understanding the mechanisms of the disorder and in the development of targeted treatments.

"This approach is really exciting," said co-author Dara Manoach, Ph.D., of the Department of Psychiatry at Massachusetts General Hospital. "We look forward to seeing how we can enhance our understanding, not only of schizophrenia, but also of other neurodevelopmental disorders characterized by differences in sleep, such as autism and pediatric epilepsy."

"We are just starting to understand the scope of neurodiversity that exists within the general population," said Prerau. "If we can more accurately characterize the individual differences observed in both neurological health and disease, we can work towards improved diagnostics and treatments."

More information: Patrick A Stokes et al, Transient Oscillation Dynamics During Sleep Provide a Robust Basis for Electroencephalographic Phenotyping and Biomarker Identification,

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