Can a ‘Fingerprint’ of Your Brain Help Predict Disorders?

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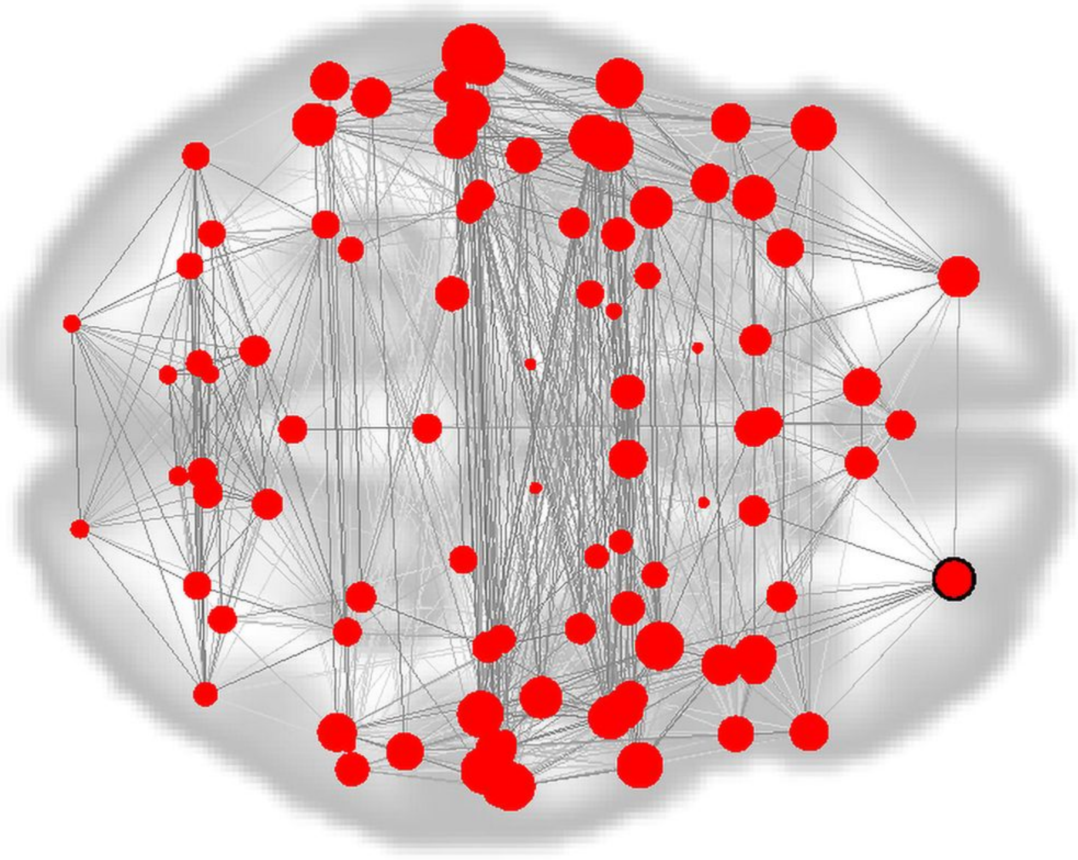

SCIENCE

Using new medical imaging techniques, researchers are working to identify early signs of developmental disorders and mental illness

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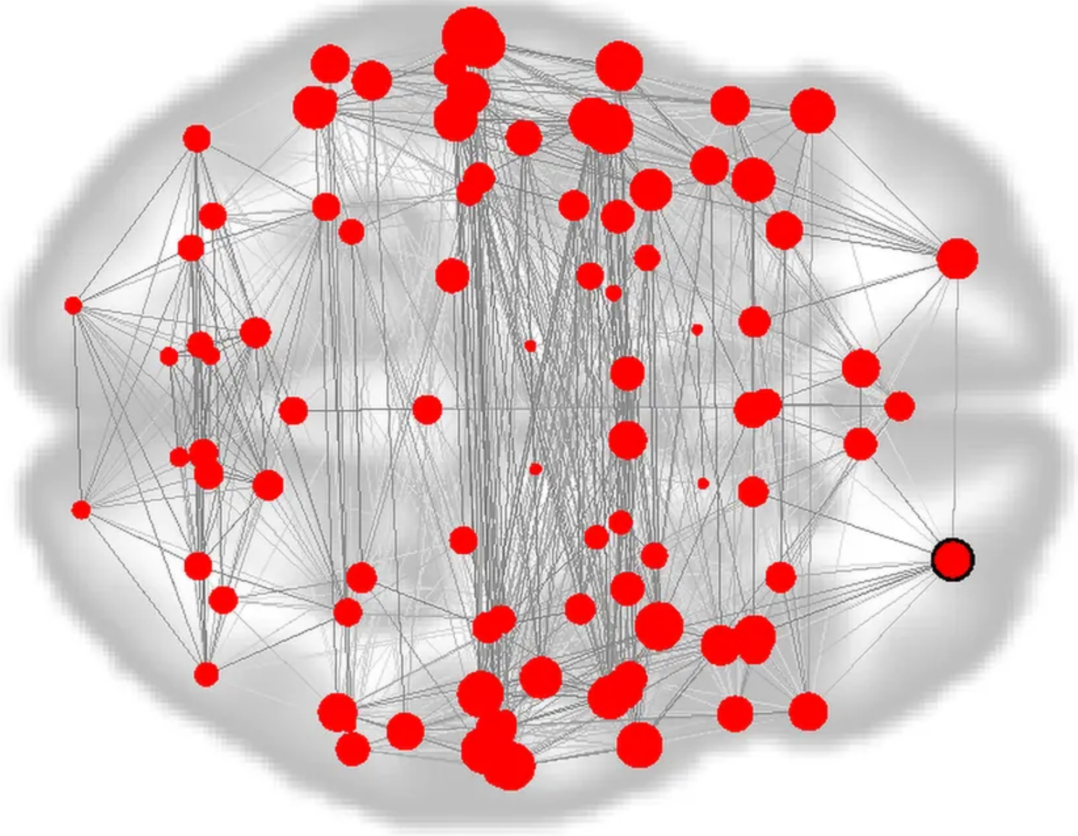
March 24, 2023



This functional connectivity map, a kind of “fingerprint” of the brain, displays how different regions interact with each other in 12-year-olds. The map was constructed from resting-state MRIs, where participants were lying down and not completing a task. Larger red circles denote brain “nodes” with more connections. Abdalla Mohamed

When she gets ready for bed, Ava Manning doesn’t bother wearing an eye mask or earplugs, but she takes five minutes to strap on her electroencephalography (EEG) headband. The accessory is made of plush foam and adorned with six electrodes that press comfortably against her temples, allowing Manning to peacefully sleep while the device monitors, analyzes and acts on her brain waves overnight.

Although EEG headbands have been available to consumers since the early 2010s, researchers are now using these devices to track the sleeping brain’s activity outside of traditional university labs. By producing accurate readings of someone’s sleep patterns at home and wirelessly transmitting the data to researchers, the headbands offer promising insight into disorders associated with disruptions in sleep, like post-traumatic stress disorder and autism spectrum disorder (ASD).

Manning, who was diagnosed with autism when she was 9, received an EEG headband as a participant in a study on ASD-related sleep disorders. She recalls a long history of sleep problems. “I learned how to ride a bike before I learned how to sleep,” she jokes. Now 21 years old, Manning has bouts of intermittent insomnia, a condition many clinicians consider a side effect of ASD.

Manning uses the EEG headband to track her sleeping brain's "fingerprint"—the pattern of thousands of electrical signals firing across her 180 brain regions. When the fingerprint shows slow waves in brain activity, which correspond with deep sleep, the headband emits a 50-millisecond burst of soft noise. The sound synchronizes Manning's brain regions, enhances its slow waves and sustains her smooth sleeping pattern. "For the first time since I was 9, I can sleep through the night," she says.

Modern, non-invasive neuroimaging techniques, like the EEG that Manning employs, have revealed our brain's fingerprint-like qualities. Another method is functional connectome mapping, which tracks blood-flow changes as different brain regions communicate with one another. When someone performs an action, even while sleeping, their brain regions synchronize and create a picture of neural activity that is individualized, incredibly detailed and unchanging from night to night, much like the impression of a thumb. These neural imprints are strong markers of individual identity but may also broaden our understanding of mental conditions for patients like Manning.

Like many developmental disorders, ASD lacks clear-cut measurements or diagnostic tests. Instead, clinicians rely on behavioral tests and questionnaires, which are inherently subjective. Manning recalls years of being misdiagnosed: "My parents were told I had ADHD, learning disabilities, you name it." In contrast, brain fingerprints, despite being unique to each person, share similar characteristics that allow them to be categorized and classified. From these groupings, researchers can better pinpoint objective biological markers—telltale indicators of a medical condition's presence and potentially its severity.

In this way, brain fingerprinting promises to carve a path toward more individualized diagnosis and treatment. Scientists are already using those two primary techniques—EEGS and functional connectome mapping—to trace our brain's distinctive patterns and identify biological markers of mental health problems. Some researchers have even combined machine learning techniques and brain fingerprinting to successfully predict an individual's risk of mental distress. But more studies are needed before clinicians can use these tools to accurately diagnose mental illness on a wide scale. With further honing, brain fingerprints could lead to earlier diagnoses, targeted therapies and greater insight into the origins of certain neurological disorders.

Sleep abnormalities and illness

Allan Rechtschaffen, the father of modern sleep research, often referred to sleep as a highly individual experience that served a universal biological function. "If sleep does not serve an absolutely vital function, then it is the biggest mistake the evolutionary process has ever made," he once said.

Indeed, in the last several decades, scientists have demonstrated that sleep is a critical player in brain function and necessary for memory consolidation, immunity and mood regulation. Now, researchers like Dara S. Manoach, a neuropsychologist in the Department of Psychiatry at Harvard Medical School, are using brain fingerprints to flip conventional understandings of the relationship between sleep and some cognitive disorders.

Diseases like ASD, schizophrenia and Alzheimer's have long been associated with deficits in sleep spindles, brief bursts of brain activity that are involved in memory consolidation. Sleep abnormalities are often seen as a consequence of these disorders' natural progression. But in 2014, Manoach found that low sleep spindle activity is present early in the course of schizophrenia, meaning poor sleep likely contributes to the illness rather than being a mere side effect.

Manoach has a similar hypothesis for ASD, noting that many patients experience sleep issues long before their diagnoses. Her lab is exploring this theory with sleep headbands, which can be easily shipped to and used by study participants. Like EEG readings taken in a sleep lab, the headbands track the brain's electrical activity, but they bypass the cumbersome setup and often stress-inducing clinical setting of traditional sleep studies. "It can be hard for patients to come into the lab, and even harder for them to fall asleep in the unfamiliar environment," Manoach says.

Additionally, while sleep studies typically require a trained technician to read, record and analyze data, the headband's built-in artificial intelligence can automatically analyze brain activity. From there, these devices can detect whether a patient is in a deep sleep stage or experiencing a sleep disturbance, and act accordingly. The ultimate output that goes back to the lab is a full recording of a participant's brain-wave activity, head movement and heart rate, tracked over multiple nights.

Manoach, whose research with the headbands is in its pilot stages, points to several studies that have demonstrated the efficacy and safety of these technologies. She adds that large sample sizes are needed to increase reproducibility in ASD research. "These devices are one way to democratize sleep studies and expand the literature on autism," Manoach says.

Using EEGs to understand the sleeping brain

Beyond making research more accessible, some scientists are creating an entirely new picture of the sleeping brain. Since the 1930s, EEGs have been the first-line method for recording the sleeping brain's electrical activity. In its earliest renditions, the EEG used crude ink to scrawl a patient's brain waves on paper tape. Scientists would then examine the readout of wavy lines to manually find patterns and abnormalities in the oscillations. For instance, Alfred L. Loomis, a Wall Street tycoon and pioneer of the early EEG, used this system to track and classify brain rhythms of the cerebral cortex during sleep. In 1935, Loomis noted that different people had significant variation in sleeping brain-wave patterns, a precursor to modern brain fingerprinting observations. (Loomis also lamented the inefficiency of paper tape EEGs, stating that “examination of the one-half mile of tape necessary for an eight-hour run was too time-consuming.”)

Modern EEG recordings, including the ones produced by sleep headbands, are still depicted as wavy lines that correspond to tiny voltage fluctuations in brain activity. The strategy for analyzing these recordings has only marginally changed: Subjective identification, wherein a scientist locates bursts of oscillating brain waves with a frequency range of 11 to 16 hertz, remains the gold standard for detecting sleep spindles.

Even the most current machine learning algorithms for sleep spindle detection are based on human observation, says Michael Prerau, a neuroscientist at Harvard Medical School’s Brigham and Women’s Hospital. But human observation of the “wiggly wave forms” associated with sleep spindles isn’t a perfect science: Researchers are biased toward high-amplitude, eye-catching brain waves, even though less visible brain waves may be equally important for cognitive function. So, Prerau wondered, what if scientists expanded their analysis of sleep brain waves beyond what is easily identifiable by eye?

“The way we look at a problem can deeply influence the way we think about the system that we study,” Prerau says. “If you’re only looking at color, a fire truck and a strawberry are the same thing.”

Rather than zooming in on brain waves that were easily visible to the human eye due to larger wiggles, Prerau and his team developed a new technique that automatically extracts tens of thousands of spindle-like wave patterns—including slight ones—from an entire night of EEG data. The researchers also departed from the traditional approach of examining brain waves in segregated sleep stages—like rapid eye movement (REM) and non-REM sleep—and instead analyzed wave patterns as part of a full continuum of gradual changes that occur during sleep. Their findings, published in the journal *Sleep* last September, revealed the sleeping brain’s “fingerprint”: Brain-wave pictures were highly heterogeneous between participants but uniform across nights for each person.

These results have two major clinical implications. First, the “fingerprint” findings highlight the immense neurodiversity of human brains. “Just because someone hasn’t seen a brain like yours doesn’t mean that there’s something wrong with your brain,” Prerau says. He is hopeful that his team’s technique can be used to redefine how patients are categorized in clinical neuroscience studies. Rather than rely solely on race, sex and other demographic characteristics, researchers could group patients by patterns in their brain fingerprints. The fingerprints would be a more direct reflection of differences in brain structure and activity, helping researchers identify the effect of a drug or other therapy across diverse brain anatomies.

Prerau and his team also compared brain fingerprints from healthy subjects and patients with schizophrenia, finding new biomarkers for the disease at EEG frequencies that traditional methods have glossed over. Manoach, a co-author of the *Sleep* study, explains that these findings reinforce how sleep abnormalities may contribute to the progression of schizophrenia in adults.

“If you’ve ever played the piano, you’ve probably had that experience of hitting a brick wall. You just can’t get any better that day. But after a night of sleep, you try again and you make improvements,” Manoach says. However, schizophrenia hinders the neural connections that typically enhance implicit muscle memory during sleep. Because of this, Manoach explains, a patient with schizophrenia may continue hitting the brick wall, getting stuck on the same set of notes as the day before. Researchers could use new biomarkers from patients’ brain fingerprints to more precisely locate where the sleep circuit for motor skill learning is disrupted, an important step toward developing targeted treatments and antipsychotic drugs.

Using fMRI scans to check for illness in adolescents

The second technique for fingerprint analysis involves awake, and much younger, brains. With half of all mental disorders emerging by the mid-teens, the adolescent brain is a crucial target for early diagnosis and intervention. “Adolescence kick-starts and sculpts the brain’s individual uniqueness, but it’s also a period of extreme vulnerability. It’s a double-edged sword,” says Dan Hermens, a cognitive psychophysiologist at the University of the Sunshine Coast, in Australia, and the director of the Longitudinal Adolescent Brain Study.

Hermens and his Longitudinal Adolescent Brain Study team are using functional magnetic resonance imaging (fMRI) to map adolescents’ functional connectomes, the wiring diagram for the brain’s neural networks. The team uses those functional connectomes to identify predictive markers of mental distress in young people. The researchers administered fMRI scans when study participants were lying down and in resting state. This technique is analogous to mechanics listening to an engine idling before it’s taken for a drive. The resting functional connectomes allowed the team to visualize patterns associated with crucial brain activity.

In a study published in *NeuroImage* last September, Hermens’ team found that unique brain fingerprints are already present in 12-year-olds—albeit with a few notable similarities across fingerprint patterns. For one, adolescents have similar maps of the cingulo-opercular network, which is involved in controlling goal-directed behavior and the ability to withstand negative influences. This lack of originality suggests that the network has not reached maturation, which Hermens and his team say offers a biological explanation of increased vulnerability to stress in young people. The researchers also examined multiple fMRI scans from the same participants captured four months apart. At each point, they used a psychological distress scale to measure participants’ emotional status. They found that adolescents whose cingulo-opercular networks fluctuated more and were less distinct from their peers' at the first measurement reported a greater severity in anxiety and depressive symptoms in the subsequent measurement.

Researchers at the Longitudinal Adolescent Brain Study administer an MRI scan that will be used to create a functional connectivity map. The project has taken over 650 brain scans from 150 participants ranging from 12 to 17 years old. Dan Hermens

For Hermens, the key is to recognize brain fingerprinting as a "supplement, not substitute" for traditional methods of diagnosis. His vision includes widespread screening programs for brain fingerprints, so clinicians can track changes in a patient's brain activity in real time and identify mental health risks before they become embedded. Where he lives in Australia, for instance, residents over 50 are mailed a free urine test to screen for colon cancer. "What if we could implement a similar brain fingerprint screening for young people?" Hermens asks.

The future of brain fingerprinting

Each technique for brain fingerprinting boasts certain advantages. While fMRIs offer greater structural and functional detail, the EEG provides quicker and more accessible insights about brain function. Currently, companies like Dreem and Muse are partnering with health care researchers to capitalize on the EEG's consumer-friendly technology. These devices promise to be scalable for widespread at-home treatment. In April 2022, researchers from ETH Zurich reported that they had delivered auditory stimulation via sleep headbands to adults between 60 to 80 years old, successfully enhancing deep sleep brain activity. Importantly, however, participants responded to the stimuli in variable ways, underscoring that EEG headbands aren't a panacea for sleep problems. Researchers also caution against using these devices for unsupervised treatment or self-diagnosis of sleep disorders.

“This is a medical device, not just a wellness consumer product,” says Walter Karlen, a biomedical engineer who developed the technology used in the ETH Zurich study. “Use of the device must be medically indicated and supervised by a doctor.”

The fMRI brain fingerprinting model may be a powerful tool in advancing clinical diagnosis. Scientists at Stanford University integrated fMRI brain fingerprints and artificial intelligence algorithms to successfully predict the severity of autism symptoms in individual patients. They suggest that brain fingerprinting can be used to assess the brains of children as young as 6 months old, so therapies for autism can be introduced in early childhood when they are most effective. Although these fMRI-based algorithms boast remarkable advocacy at this early stage of development, further honing is necessary to get clinically reliable results. A March 2022 paper published in *Nature* argued that tens of thousands of brain scans are needed to identify reproducible links between brain structure and mental health phenotypes. (The Stanford study used a sample of 1,100 participants.)

While Hermens acknowledges that big-data studies are a crucial next step, he also emphasizes that brain fingerprinting shouldn't be mischaracterized as a unilateral diagnostic tool. “These fingerprints are a complement to other measures of mental health. They're important because they demonstrate that mental health treatment needs to be personalized,” he says. “Brain uniqueness would only be part of the predictive algorithms of the future.”

Brain fingerprinting continues to advance as scientists adapt their methods to create more detailed pictures of the brain's one-of-a-kind code to our identity. While the techniques evolve, the ultimate goal of brain fingerprinting remains constant.

“Our hope is we can intervene early and alleviate a person's mental health burden,” Prerau says.

“The dream is early detection and prevention,” Hermens agrees.

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Lucy Tu studies sociology and the history of science at Harvard University. Her work has appeared in the *Guardian*, *Discover* magazine, the *Lancet* and the *New England Journal of Medicine*.

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