Scientists use new MRI technology to create time-lapse images as the living brain responds to experiences

April 11 2022, by Michael Haederle

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Magnetic resonance imaging (MRI) has transformed the field of neuroscience over the past 40 years, enabling scientists to create clear snapshots of living brain structures and even detect functional changes associated with certain activities.

Unlike X-rays or CT scans, MRI does not rely on beams of radiation. Instead, powerful magnetic fields and radio waves are used to temporarily align the hydrogen atoms in the body's water molecules, meaning it can create a clear picture of soft tissues, like the brain.

But a newer technology developed by UNM neuroscientist Elaine Bearer, MD, Ph.D., and collaborators at California Institute of Technology and the University of Southern California takes MRI one step further.

In a paper published in the journal *NMR in Biomedicine*, they report on the use of manganese, a trace mineral found throughout the body, as a contrast agent with MRI that enables a "time-lapse" series of images revealing the brain's response to specific experiences.

"This report emphasizes the power of manganese-based contrast to study dynamic transitions throughout the brain," said Bearer, a professor in the UNM Department of Pathology. "The brain is not a static thing. This MRI technique images the slow consequences of an experience over time. It's enabling us to peer more deeply into the amazing complexity of thinking and feeling."

In manganese-enhanced MRI (MEMRI), small amounts of manganese enter neurons via the same cellular pathway as calcium, which plays a key role in brain signaling. As manganese ions move through the neuron they highlight the cell's activities, highlighting the projections via which it communicates with adjacent neurons.

"This exciting emergent methodology captures the brain's function during normal behavior, which otherwise cannot be known at this scale," said Taylor Uselman, a Ph.D. student in Bearer's lab who co-authored the paper. Christopher Medina, MD, a UNM School of Medicine graduate, was also a co-author.

"Our publication also provides critical insight into safety considerations for the use of the contrast agent," Uselman said. "We give a number of examples of how MEMRI reveals the development of the hearing system, as well as Down syndrome, Alzheimer's disease and anxiety disorders."

Standard MRI scans have great diagnostic value for detecting tumors or vascular abnormalities in the brain, and they can reveal that changes in certain brain structures are associated with specific behaviors, such as meditation or learning a second language. But they don't show what the brain is actually doing, Bearer says.

"The MR that we standardly do for human diagnosis is just an image of your anatomy," she says. Neuroscientists also use a technique called functional MRI that measures cerebral blood flow, based on the idea that highly active regions of the brain use more oxygen.

However, the blood-oxygen-level-dependent (BOLD) signal is weaker, requiring computational analysis, and it mixes both vascular and neural activity, Bearer said. "With BOLD, what you're detecting is a proxy for neural activity."

Bearer and partners Harry Gray at Caltech and Russell Jacobs at USC have been exploring the potential of MEMRI technology for some time. In 2020, together with Uselman and post-doctoral fellow Daniel Barto, they reported on the use of MEMRI to demonstrate how exposure to a frightening stimulus evolves into chronic anxiety.

"The major things that made it possible to learn from this technology was the computational analysis I did with my students at UNM," Bearer said. "This review is going to be a go-to reference for all investigators, especially when using this emergent technology."

More information: Taylor W. Uselman et al, Longitudinal manganese-enhanced magnetic resonance imaging of neural projections and activity, *NMR in Biomedicine* (2022). DOI: 10.1002/nbm.4675

Provided by University of New Mexico