

## **Neuroscientists prove ultrasound can be tweaked to stimulate different sensations**

Eurekaalert!

A century after the world's first ultrasonic detection device – invented in response to the sinking of the Titanic – Virginia Tech Carilion Research Institute scientists have provided the first neurophysiological evidence for something that researchers have long suspected: ultrasound applied to the periphery, such as the fingertips, can stimulate different sensory pathways leading to the brain.

And that's just the tip of the iceberg. The discovery carries implications for diagnosing and treating neuropathy, which affects millions of people around the world.

"Ideally, neurologists should be able to tailor treatments to the specific sensations their patients are feeling," said William "Jamie" Tyler, an assistant professor at the Virginia Tech Carilion Research Institute, who led the study published this week in PLOS ONE. "Unfortunately, even with today's technologies, it's difficult to stimulate certain types of sensations without evoking others. Pulsed ultrasound allows us to selectively activate functional subsets of nerve fibers so we can study what happens when you stimulate, for example, only the peripheral fibers and central nervous system pathways that convey the sensation of fast, sharp pain or only those that convey the sensation of slow, dull, throbbing pain."

An estimated 20 million people in the United States alone suffer from neuropathy, a collection of nervous system disorders that may cause pain, numbness, and sensations of burning, itching, and tingling. One of the most common causes of neuropathy is Type 2 diabetes. Autoimmune disorders, such as lupus and Guillain-Barré syndrome; traumatic nerve injury; genetic abnormalities; movement disorders; and infectious diseases such as HIV/AIDS, Lyme disease, and leprosy can also trigger neuropathy.

"Neuropathy involves both motor nerves that control how muscles move and sensory nerves that receive sensations such as heat, pain, and touch," Tyler said. "So clinicians may use, for example, small resonator devices to vibrate the skin or lasers to heat the surface of the skin. But we wanted to develop a method that could activate superficial and deep mechanical receptors, thermal receptors, and even combinations of both. So we used pulsed ultrasound."

In the 1970s, a group of Soviet scientists made observations that ultrasound could stimulate distinct neural pathways, but their evidence was only anecdotal, with subjects merely describing sensations of heat, pain, or vibration. In the current study, the researchers used functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) to provide physiological proof of those early observations.

Study participants rested their index fingers on ultrasound transducers while having their brain activity monitored with fMRI and EEG. The scientists found that they could stimulate specific somatosensory pathways just by tweaking the ultrasound waveforms.

Tyler believes the finding has important implications for pain diagnosis.

"Current methods of diagnosing and characterizing pain can sometimes seem archaic," Tyler said. "To measure pain through mechanical stimulation, for example, physicians might touch the skin with nylon monofilaments known as von Frey hairs, or they'll stroke the skin with a paintbrush. For thermal sensory testing, patients may even plunge their hands into ice water until the pain becomes too great. We're hoping to provide physicians with more precise diagnostic tools."

Better diagnostics will lead to better therapeutics, said neuroscientist Michael Friedlander, executive director of the Virginia Tech Carilion Research Institute.

"By combining pulsed ultrasound with the technologies to record brain activity, Jamie Tyler and his colleagues are taking this to a whole new level of diagnostics," Friedlander said. "And the diagnostics will ultimately drive the therapeutics. This research is a great example of how new technologies can be adapted for real-world, patient-centered diagnoses and treatments."

Tyler noted the discovery could lead to other applications.

"Ultrasound transducers could be fashioned into flexible, flat insoles to provide sensory stimulation to people who have lost sensation in their feet, including the elderly, who are at such risk of falling," he said. "Surgical instruments could provide tactile feedback to surgeons in training. And I can imagine countless applications for consumer electronics. Users already rely on two-way somatosensory communication with their devices, and peripheral stimulation using ultrasound could add new dimensionalities to this communication."

Researchers will now investigate which ultrasound parameters stimulate which types of nerve fibers or receptors. Tyler also hopes to study people with Type 2 diabetes who have not yet developed neuropathy, with the ultimate goal of providing clues to treating or even preventing the pain associated with the condition.

This research may get a boost from a discovery that surprised Tyler during the PLOS ONE study.

"One thing we didn't expect is that some brain scans showed activation of pain pathways, yet the volunteers reported feeling no discomfort," Tyler said. "That's an intriguing finding. Though we don't yet know its full implications, being able to activate classic pain pathways without inducing perceptual pain can help us understand how the brain processes pain."

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