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Targeting the Brain with Sound Waves

Ultrasound might provide a new, noninvasive way to control brain activity.

By Emily Singer

Ultrasound waves, currently used in medicine for prenatal scans and other diagnostic purposes, could one day be used as a noninvasive way to control brain activity. Over the past two years, scientists have begun experimenting with low-frequency, low-intensity ultrasound that can penetrate the skull and activate or silence brain cells. Researchers hope that the technology could provide an alternative to more-invasive techniques, such as deep-brain stimulation (DBS) and vagus nerve stimulation, which are used to treat a growing number of neurological disorders. "Once people have found out what they can do with DBS and vagus nerve stimulation, we think we can unplug those devices and control activity from outside the body," says William (Jamie) Tyler, a neuroscientist at Arizona State University, in Tempe. Tyler has started a company called SynSonix to commercialize the technology.

Devices designed to treat brain disorders have grown in popularity in recent years. DBS, which is used to treat Parkinson's disease, dystonia, and obsessive-compulsive disorder, delivers an electrical jolt to the brain via an implanted electrode. Because of its invasive nature, however, DBS is only used for severe cases that are untreatable with medication. A less invasive technique is transcranial magnetic stimulation (TMS), in which an electric coil placed over the head generates a magnetic field that passes through the skull and excites neurons in the brain below. TMS is used to treat clinical depression, but it can only target the more superficial parts of the brain. "With ultrasound, we have a much better spatial focus than [with] DBS," says Tyler. "And unlike TMS, we can get anywhere in the brain." Ultrasound--consisting of sound waves with a frequency above 20 kilohertz--has been used for decades in medicine to image muscle, organs, and fetuses. In the past five years, better tools for focusing ultrasound energy have enabled its use as an ablation tool: surgeons can now use high-intensity, high-frequency ultrasound (HIFU) to essentially burn away uterine fibroids. HIFU is also in clinical testing for treating brain tumors, breast tumors, and prostate cancer.

These same tools are now allowing scientists to apply ultrasound to control the brain, an idea that has actually been around for decades. Better ultrasound transducers, which generate the acoustic waves, enable more-precise focusing of ultrasound energy. And magnetic resonance imaging (MRI) used in conjunction with ultrasound allows surgeons to target specific areas of the body more precisely. "The ability to marry focused ultrasound with MR [magnetic resonance] guidance is exceedingly powerful," says Neal Kassell, a neurosurgeon at the University of Virginia, in Charlottesville, and chairman of the Focused Ultrasound Surgery Foundation, a nonprofit based in Charlottesville that was founded to develop new applications for focused ultrasound. One of the challenges in using ultrasound to target the brain is figuring out how to get the sound waves through the skull in a controlled manner. Typically, ultrasound operates in the megahertz to gigahertz range--frequencies that are fine for passing through soft tissue but would liquefy bone.

(As bone absorbs the energy of the acoustic wave, it heats up.) Researchers at Brigham and Women's Hospital, in Boston, havefound that an ultrasound frequency of less than one megahertz can do the trick, but with a trade-off: the lower the frequency, the more difficult it is to focus the energy on a particular point in the brain.

In the past year, however, scientists have had some success in solving this trade-off. Detailed images of the skull generated via CT scan and MRI can help scientists calculate the best way to focus the sound waves, says Seung-Schik Yoo, a neuroscientist at Brigham and Women's and Harvard Medical School. In as yet unpublished work, Yoo and his colleagues have demonstrated that low-frequency, low-intensity ultrasound can successfully suppress visual activity in rabbits' brains, as well as selectively trigger activity in the motor cortex. "We are also looking at the ability to modulate hormones or neurotransmitters, which may have application for psychiatric disorders, obesity, and addiction," says Yoo.

In a paper published last year in the journal PLoS ONE, Tyler demonstrated that low-frequency, low-intensity ultrasound can activate channels that sit in the membrane of nerve cells in a slice of brain tissue, triggering the cells to send an electrical message through the neural circuit. He has since been able to use ultrasound to stimulate the motor cortex and trigger movement in live mice. This work has not yet been published. Researchers hope to co-opt instruments developed for HIFU for this new application. Several instrument companies have developed phased arrays of ultrasound transducers, which allow precise targeting of ultrasound energy, and which are currently being tested for removal of brain tumors. "Depending on individual anatomy of the skull, you can program the ultrasound equipment to fire individual elements to deliver a well-characterized beam, in terms of location and size, that can be tailor-made to each patient," says Yoo.

Because focused ultrasound is already used extensively, researchers are optimistic that it will not face any major hurdles in moving toward clinical testing. "For neurologists and neurosurgeons, it's a well-established technique," says Tyler. "The safety margins are well known." Adds Kassell, "I think it will actually be easier to get approval [than it was for HIFU] because the pressure of the focused ultrasound is less pressure than the brain gets from transcranial Doppler, a diagnostic device used to look at vessels in the head after stroke and hemorrhage." Kassell says that the foundation is most interested in using low-intensity, low-frequency ultrasound for surgical planning. In epilepsy patients, surgeons could use the technology to temporarily silence a piece of brain tissue thought to be responsible for triggering seizures, thus confirming the correct localization, and then use HIFU to ablate that piece of tissue.

Tyler is most interested in using focused ultrasound for treating Parkinson's disease. "Since it's not invasive, we might be able to treat patients much earlier in progression," he says. "Right now, people who get DBS are the worst-case patients." While initial devices would likely resemble a smaller version of MRI machines, treating Parkinson's patients would require a wearable or implantable device capable of delivering continual stimulation. Tyler's team is working on flexible ultrasound transducers that could be implanted on top of the skull or formulated into a cap. It's not yet clear how ultrasound triggers electrical activity in neurons, but some believe that it is through thermal energy generated by sound waves. Tyler, however, says he has evidence that the neurons are activated through mechanical energy. Previous research has indeed shown that the neuron channels that control electrical activity in the brain can be activated with mechanical pressure. "What we think is happening is some kind of microcavitational effect, such as radiation or sheer strain, which affect the channels that control neural activity," he says.

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