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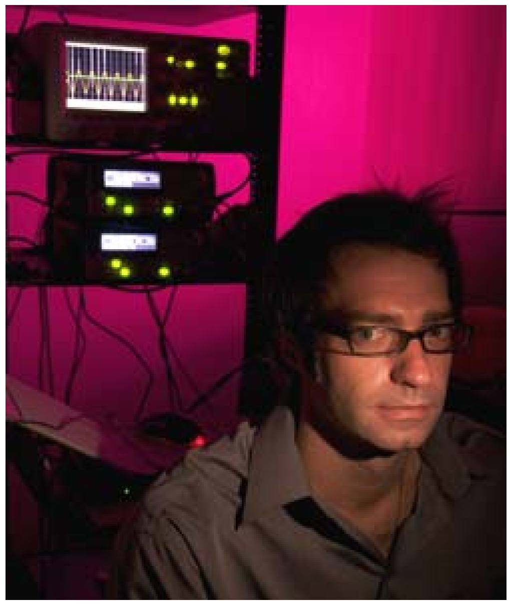
Good vibrations...sound brain health



by Margaret Coulombe

> *"...And the sound that abounds and Resounds and rebounds off the ceiling*
> *You gotta have it, baby You can't do without..."* – Rage Against the Machine

Great discoveries—how are they made? Sometimes, you have to "kick out the jams" anc take risks. Other times it's relentless patience and methodical testing. Of course, sometimes a mere accident holds the key.

William (Jamie) Tyler says that his "Aha" moment occurred in graduate school during ai aural overload of the bands "Dr. Dre" and "Rage Against the Machine." His revolutionar discovery is that ultrasound can be harnessed to remotely stimulate brain circuits.

"I often played really loud music while conducting experiments designed to monitor cir activity in brain slices," says Tyler, a synaptic physiologist in the School of Life Science Arizona State University. "I told my mentor that I believed some of the neurons I was studying responded to pressure fluctuations induced by the sound waves. It was a possil I kept thinking about."

Nine years later, Tyler has a doctorate, postdoctoral fellowship, and assistant professor under his belt. But he still had cogitations around the potential for sympathetic syncop betwixt neurons and sound waves. Those cogitations led Tyler to position a stereo subwoofer beneath a neurophysiological recording apparatus bearing brain neurons and "crank up the beat." The neurons indeed responded to the vibrations. The results sent down a research path toward the use of ultrasound.

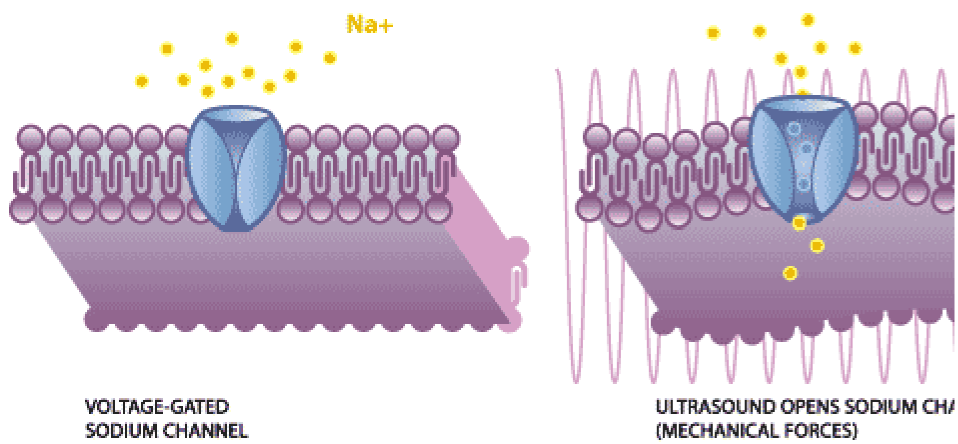
Was it just an audiophile's wild leap of imagination that spurred him on? Not exactly.

Ultrasound is sound beyond the range of human hearing. It has been harnessed for lots o applications in our daily lives. For example, physicians use ultrasound in fetal and other diagnostic medical imaging, ultrasonic cleaning, physiotherapy, or for the surgical remo of diseased tissue. There are many non-medical uses as well. Ultrasound is used in pharmaceutical manufacturing, food processing, nondestructive materials testing, sonar communications, oceanography, and acoustic mapping.

"Studies of ultrasound and its interactions with biological tissues have a rich history dati back to the late 1920s," Tyler points out. "For more than half a century research groups have demonstrated that ultrasound can produce changes in excitable tissues, such as ne and/or muscle. It can even influence brain activity. However, detailed studies at the cellular level to explain how ultrasound may interact with neurons have been lacking."

Tyler and his colleagues use fluorescent probes to monitor neural circuit activity in brair slices. They have uncovered some mechanisms by which ultrasound, pulsed at low intensities, influenced the activity of neurons.

The ASU researchers found that when they remotely delivered low-intensity, low-freque ultrasound, neurons in the brain reacted immediately. Ultrasound caused the release of docked vesicles (neurotransmitter release) from synapses in the neurons. Tyler says that ultrasound increases the activity of voltage-gated sodium and calcium channels in a man sufficient to trigger action potentials.



The discovery of how ultrasound can directly stimulate neuronal activity in brain tissue Tyler and his partners new insight. They quickly recognized the power and potential suc remote approach could provide. It meant that the noninvasive modulation of the activit neural circuits in the intact brain is possible.

"Many of the stimulation methods now used by neuroscientists require direct contact wi nervous tissue," Tyler explains. "The work must be done through the surgical implantati of stimulating electrodes in the brain or the introduction of proteins from outside the body."

More than 2 billion cases of human nervous system disorders exist worldwide. As a result scientists and engineers have accelerated the search for new neurostimulation methods controlling nervous system activity. Several treatment approaches show great promise.

For example, Deep Brain Stimulation (DBS) and Vagal Nerve Stimulation (VNS) are effect in the management of psychiatric disorders such as depression, bipolar disorders, post-traumatic stress disorder, and drug addition. They also are used as treatment of neurological diseases such as Parkinson's disease, Alzheimer's disease, Tourette Syndron epilepsy, tinnitus, recovery of cognitive and motor function following stroke, and chroni pain.

However, these treatments pose risks to patients because they still require the surgical implantation of stimulating electrodes. And the new techniques are often only available patients presenting the worst of prognoses.

Remote use of ultrasound as a preferred treatment would seem like a no-brainer. But Ty faced one more, very large stumbling block to its development as a noninvasive treatme the skull. The skull can weaken acoustic power and scatter the focus of sound waves. Th could be generally considered a good thing, even if simply a byproduct of building a stro brain case for protection. Imagine if all the sounds people heard (and those that humans can't) were also bombarding their senses, literally?

Tyler and his team discovered that tinkering with acoustic frequencies of the ultrasound allowed them to easily penetrate bone in focused ways. They also could do the work at power levels capable of stimulating brain circuit activity without damaging delicate brai tissue. Tyler's findings were further bolstered by studies released from several other research groups. Those findings showed that high-intensity, low-frequency ultrasound ca be used to focally remove very small regions of brain tissue without affecting surroundin regions.

"It's an electrifying time right now, with exciting surprises. So far, we have a good grasp how ultrasound, at power levels lower than those typically used in routine diagnostic medical imaging procedures, can produce an increase in the activity of neurons—even in intact brains," Tyler says. "We figure out something new almost every day."

What about the potential for using these new methods to remotely control brain activity Tyler says the technique opens new doors in uses that range from medical treatments to video gaming.

"The prospects are exhilarating," Tyler says. "The improved patient access that low-intensity, low-frequency ultrasound confers over surgical intervention or gene-therapy means that literally millions of people might be helped through use of ultrasonic neuromodulation."

The ASU scientist also believes that other possibilities exist as well. There may be a time the future that this technology could, for example, even make it possible to create artif memories. The results would be something along the lines of Arnold Schwarzenegger's character in "Total Recall."

"Imagine taking a vacation without actually going anywhere?" Tyler jokes. "Seriously though, while it's too early to understand the full impact of this technology, it's this kin speculation that's brought us this far."

Tyler and his colleagues are now carefully characterizing the influence of ultrasound on intact brain circuit. They are pursuing translational neuroscience research. The goal is to take low-intensity ultrasound from the laboratory bench into pre-clinical trials.

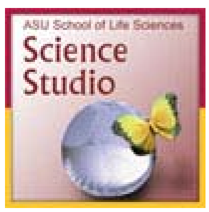
The ASU researcher has filed a patent on some specific aspects of the technology. Along with other partners, he is launching SynSonix, a startup medical device company geared toward further development and marketing of ultrasonic neuromodulation technology ar equipment.

It's been a risky journey with a steep learning curve involving lessons in patent law, business and marketing. These are areas that aren't typically part of a neuroscientist's training. Tyler says that translating basic research into clinical research is similar to mountaineering, one of his favorite hobbies. Both require a lot of patience, determinati and a focused strategy. He keeps listening, learning, and moving forward.

"There was a time when I thought that making a novel discovery in the lab was the hard part. I've found that's only where it begins," Tyler says. "The real challenge, effort, tim and money come into play when transforming that discovery into a medical treatment."

He adds, "When I was at Harvard [University], we would have intellectually engaging discussions to come up with 200 reasons why something should not work. All the pieces came together at ASU. Here, we could simply try something because we believed it was possible—despite hundreds of reasons why it shouldn't be."

Because of Tyler's risk taking, "healing what ails you" may some day—as the Beach Boys sing—simply be a matter of "good vibrations."



Listen to a Science Studio podcast with Jamie Tyler.

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