CHEN TIANQIAO & CHRISSY INSTITUTE

SOUNDMIND

Is Background Noise the Key to Beating Alzheimer's?

The SoundMind project is pioneering a new approach to treating neurodegenerative diseases.

Alexander Khalil's father, a prominent scholar of Eastern Orthodox theology at San Diego State University, dedicated his career to the life of the mind. That made it all the crueler when, at the age of 87, he suddenly began to show symptoms of dementia.

"It was a big shock," recalls Khalil, a cognitive scientist, ethnomusicologist, and senior lecturer at University College Cork. "Of course, as a scientist, the first thing I did was to start reading everything I could about neurodegenerative diseases."

Khalil disappeared into his laboratory, emerging months later with a set of headphones rigged to serve as his father's hearing aid—while also unobtrusively generating noise at a 40-hertz frequency. "I'd learned there was evidence that sounds of this frequency could reduce the symptoms of Alzheimer's, at least in animal studies," Khalil explains. A team at MIT, for instance, found that mice exposed to 40-hertz vibrations show lower levels o f the disease's hallmark proteins and amyloid plaques, along with decreased neuron death and improved learning and memory.

Khalil's father wore the headphones almost continuously during his waking hours until he passed away some years later. "Did wearing these headphones help my father? Scientifically, there's no way to know—he's just one person, and dementia is an idiosyncratic disease," Khalil says. "But subjectively, it did seem to slow his symptoms."

Almost a decade later, Khalil is now lead researcher with the SoundMind project, a groundbreaking international research initiative exploring the use of augmented audio reality (AAR) to potentially slow or even reverse the progress of Alzheimer's. "The basic idea is that the sounds we hear change the way our brain operates," he explains. "By digitally manipulating the auditory landscape, we can rewire the brain in ways that are profoundly important for the treatment of diseases like Alzheimer's."

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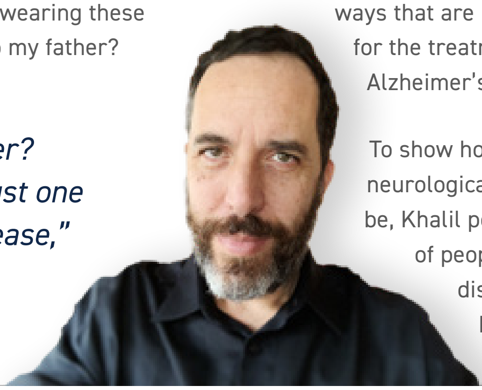

To show how powerful the neurological impact of sound can be, Khalil points to the example of people with Parkinson's disease, who often have an awkward,

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shuffling gait. When patients listen to music, however, their symptoms often evaporate, leaving them able to walk normally. "It's an example of neuromodulation, which is when the brain's electrical rhythms synchronize with an outside stimulus," Khalil explains. "Essentially, we're using the brain's natural tendency to coordinate with external stimuli to guide it into more beneficial patterns of activity."

Researchers around the world are exploring using neuromodulation to treat conditions including anxiety, chronic pain, epilepsy, and depression. Such efforts are often held back, though, by their use of intrusive or distracting stimuli—including loud clicking noises, physical vibrations, flashing lights, or even electromagnetic stimulation—to influence the brain's rhythms. That forces researchers to use short, intense bursts of stimulation to create the desired neuromodulation effect, significantly limiting the method's real-world utility.

To sidestep that problem, Khalil developed an AAR algorithm that encodes the required frequencies into background noise, enabling far less obtrusive interventions. "You might be listening to a conversation, and not notice that I've subtly retuned the hum of your AC unit, or the sound of a passing bus, to match the target frequency," he explains. "You can achieve neuromodulation with far fewer annoying distractions—and that means

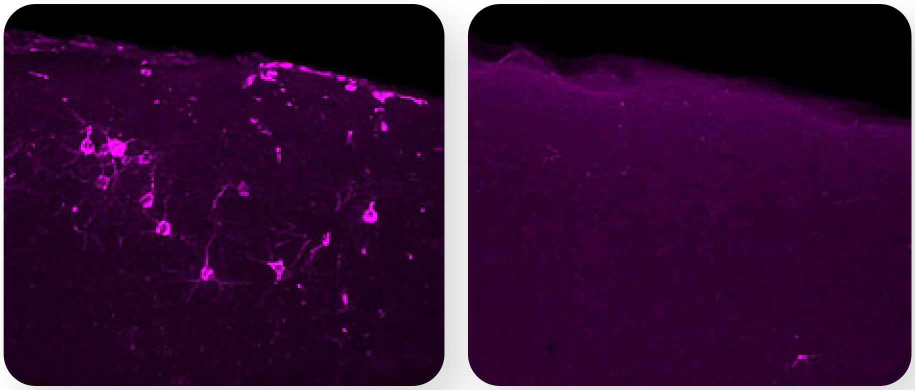

Image: Tsai Lab/ The Picower Institute we can deliver continuous low-level stimulation, potentially yielding a stronger and more continuous impact."

Khalil had originally begun working on neuromodulation to try to help his father—but that changed when a team from the Tianqiao & Chrissy Chen Institute reached out. "They'd heard about my work and realized that it had much broader potential, and told me they wanted to support its development," Khalil explains. "Normally, as a researcher you have to keep knocking on doors to try to find support, but the Chens were extraordinarily proactive. If it hadn't been for their help and encouragement, this research would be gathering dust in a filing cabinet somewhere."

Instead, with TCCI's support, Khalil partnered with Gráinne McLoughlin, a neuroscientist with the Institute of Psychiatry, Psychology, and Neuroscience at King's College London, to launch SoundMind. "We'd met more than a decade before while doing our postdocs at the Institute for Neural Computation at University of California, San Diego," Khalil explains. "King's is known for cutting-edge research into dementia, and Gráinne brought the expertise we needed to really hit the ground running."

Together, Khalil and McLoughlin set out to develop and test wearable technologies that could subtly alter background noise to provide continuous neuromodulation for Alzheimer's patients. Part of the appeal of that approach, McLoughlin explains, is that most current Alzheimer's research focuses on more invasive and risky treatments. "Sensory stimulation appears entirely safe—it engages the brain in a way that closely resembles its natural way of interacting with the world around us," she says.

McLoughlin's team at King's has already found that Khalil's AAR algorithms can successfully induce neuromodulation in healthy populations; now, they are testing the process in patients with mild cognitive impairment. "Cognitive impairment is associated with hearing loss, along with overall brain dysfunction, so we need to clearly demonstrate that this technology can induce neuromodulation in these populations," McLoughlin explains. "Our initial findings are extremely promising—we're seeing a very large effect size using our methods, which tells us it's definitely worth moving forward with clinical trials."

Next year, the team hopes to start testing in patients with early-stage Alzheimer's, and to validate the benefits of continuous neuromodulation in real-world contexts. "That's the Holy Grail," Khalil says. "We want to do cognitive tests and take baseline neurophysiological measurements, then have Alzheimer's patients use our devices for a year and come back so we can see what's changed."

If all goes well, the SoundMind team envisions adding their neuromodulation technologies to hearing aids or other devices already used by patients,

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or even making their AAR algorithm available on consumer smartphones using off-the-shelf headphones. "If we find that this helps slow the onset of Alzheimer's, then this could become a routine preventative treatment for people as they start to enter late middle age," McLoughlin says.

Future versions of the technology could even be combined with wearable EEG devices to provide customized neuromodulation based on changes in an individual's brain activity, or could provide varying kinds of neuromodulation to treat a wider range of conditions. "We see this as fitting into an ecosystem of wearable technologies that could help aging populations to stay healthy and live independently," Khalil explains.

There's still a long way to go, but Khalil and McLoughlin say that with the Chen Institute's backing, they're poised to open an important new front in the war against neurodegenerative diseases. "It's still very early days, but we believe that auditory neuromodulation could become a highly effective treatment for Alzheimer's disease," McLoughlin says. "Will it completely reverse it? We don't know that yet. But this clearly has the potential to make a profound difference for Alzheimer's patients."

About SoundMind The SoundMind project aims to develop therapeutic and assistive uses of Augmented Audio Reality (AAR) for people with Alzheimer's Disease. SoundMind, a collaboration between King's College London and University College Cork, is funded by the Tianqiao and Chrissy Chen Institute and is led by Dr Alexander Khalil, Department of Music, University College Cork and Dr Grainne McLoughlin, Social Genetic Developmental Psychiatry (SGDP) Centre, Institute of Psychiatry Psychology and Neuroscience (IoPPN).

About the Tianqiao and Chrissy Chen Institute The Tianqiao and Chrissy Chen Institute (TCCI®) was created in 2016 by Tianqiao Chen and his wife Chrissy Luo, the founders of Shanda Group, with a US $1 billion commitment to help advance brain science. The organization's vision is to improve the human experience by understanding how our brains perceive, learn, and interact with the world.

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