EMILY MULLIN SCIENCE MAR 6, 2024 10:35 AM

A New Headset Aims to Treat Alzheimer’s With Light and Sound

An experimental device developed by Cognito Therapeutics seeks to slow cognitive decline in Alzheimer’s patients using light and sound.

PHOTOGRAPH: COGNITO THERAPEUTICS

SAVE

New drugs for Alzheimer's are finally coming onto the market after decades of failed attempts to slow its devastating progression. But startup Cognito Therapeutics is taking a drug-free approach to treating the memory-robbing disease. The Cambridge, Massachusetts–based company is developing a headset to combat cognitive decline.

In results from a Phase II trial published March 6 in the journal *Frontiers in Neurology*, the company showed that its novel treatment is safe and reported early hints that it may also have benefits for Alzheimer's patients.

"I think it's extremely promising," says Murali Doraiswamy, a professor of psychiatry and geriatrics at Duke University and an Alzheimer's expert who isn't involved with Cognito. "It's preliminary, so there's a lot of reason for cautious optimism. But if it works, it would be totally different from anything else we have in the field."

Cognito's headset, dubbed Spectris, delivers flashing lights and sounds through a pair of connected glasses and headphones to stimulate gamma waves in the brain. Different types of brain waves have different paces, or frequencies. Gamma waves are fast-frequency brain waves associated with thinking skills and memory, and people with Alzheimer's are known to have fewer of these fast brain waves.

The Spectris device produces light and sound at 40 hertz, or 40 flashes and sounds per second, to activate the brain's visual and auditory pathways, which then generates these gamma waves. "Our brains make gamma waves normally, so this is activating a capacity that's already there," says Ralph Kern, Cognito's chief medical officer. (Gamma waves naturally oscillate at around 30 to 100 hertz in the brain.)

Brain waves are the result of thousands of neurons making connections and communicating through electric signals. In Alzheimer's, connections among these networks break down. Cognito thinks its device could slow the cognitive decline that comes with the disease by strengthening and synchronizing these connections.

The Spectris device delivers light and sound to stimulate gamma waves in the brain. PHOTOGRAPH: COGNITO THERAPEUTICS

The company's study included 74 participants with mild to moderate Alzheimer's who received either the Cognito stimulation or a sham device that acted as a

placebo. Subjects were asked to use the headset for an hour every day for six months.

Compared with the placebo group, those who got the Cognito stimulation showed a 77 percent slowing in functional decline as measured by a scale that assesses how well Alzheimer's patients are able to carry out daily activities, such as eating, dressing, and getting around.

The treatment group also showed a 76 percent slowing in cognitive difficulties compared with placebo, as measured by a test that evaluates orientation, memory, and attention, as well as verbal and written ability.

Interestingly, the treatment arm also had a 69 percent reduction in brain atrophy, or shrinkage, as measured by MRI, compared with the sham group. In Alzheimer's, as connections among networks of neurons break down, parts of the brain can start to shrink.

"By doing it one hour a day, we produced these lasting biological changes," Kern says. He likens wearing the device once a day to getting regular physical exercise—the brain is being trained, in a way. The downside is people must stay stationary while wearing the device and can't fall asleep. In Cognito's study, 85 percent of participants were able to use the device consistently.

Cognito's approach is based on research by MIT neuroscientist Li-Huei Tsai, who cofounded the company with another MIT professor, Ed Boyden. Previously, they found that stimulating mice with light and sound at 40 hertz made them perform better on memory tasks and also reduced levels of amyloid—a protein that builds up and forms plaques in the brains of people with Alzheimer's disease. A new paper in the journal *Nature* by Tsai, Boyden, and their colleagues explains that it may do this by activating a waste-disposal mechanism in the mice's brains.

The accumulation of amyloid has long been the leading theory to explain Alzheimer's. But in Cognito's trial, researchers did not find a reduction in amyloid plaques in participants' brain scans. However, the Cognito trial used a type of brain imaging called positron emission tomography, or PET, which detects dense amyloid plaques. In the MIT team's new study, Tsai and her colleagues found that stimulation seems to clear a more diffuse type of amyloid that spreads throughout the brain and

is not detected by PET scans. She says it's possible that the stimulation in the Cognito trial had an effect on this type of amyloid, but the company's current study wasn't designed to measure that.

Christopher Weber, director of global science initiatives at the Chicago-based Alzheimer's Association, is encouraged by the safety of the Cognito device, but says the size of the study was too small to properly test efficacy.

"Research in this area is still in its early stages, and more studies with larger, diverse cohorts are needed to fully understand the relationship between gamma wave activity and Alzheimer's, specifically whether restoring or enhancing gamma wave activity could have therapeutic benefits," Weber says.
Cognito is now beginning a Phase III trial of more than 500 participants that will wear the device daily for 12 months. Kern sees potential for Cognito's headset to be a standalone therapy or used alongside new Alzheimer's drugs that target amyloid and which modestly slow the worsening of the disease. These include the antibody treatment from Biogen and Eisai, called Leqembi, which won full FDA approval last summer, and a similar therapy, Eli Lilly's donanemab, which is poised to get FDA approval soon.

These antibodies are given intravenously in an outpatient setting, and while they offer hope to Alzheimer's patients, they are not without risk. Notably, they can cause temporary swelling or bleeding in the brain.

In its paper, Cognito highlighted that its treatment did not cause these adverse events or other serious side effects. Some trial participants did report headache, dizziness, or ringing in the ear after wearing the device, but the effects were not long lasting.

Doraiswamy is encouraged. "We need safe treatments. We need treatments that can be administered at home, and we need treatments that are really complementary to what we already have. This meets all of those criteria," he says. "All we need is a consistent positive signal in the big trial."

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