Flickering lights may illuminate a path to Alzheimer’s treatment

In a study published Dec. 7 in the journal Nature, neuroscientists discovered that flickering lights at a precise frequency may help to fight off Alzheimer’s. (Dec. 7, 2016)

New research demonstrates that, in mice whose brains are under attack by Alzheimer’s dementia, exposure to lights that flicker at a precise frequency can right the brain’s faulty signaling and energize its immune cells to fight off the disease.

Light therapy for Alzheimer’s is miles from being ready to treat patients — even those with the earliest signs of the disease. But the new research has already prompted creation of a start-up company — Cognito Therapeutics Inc. — to approach the Food and Drug Administration about clinical trials, and to explore ways to deliver precisely calibrated flickers of light to human research subjects.
Even if the new research does not yield a treatment for Alzheimer’s, it is expected to deepen understanding of a key player in the disease — the brain’s dedicated immune system — and point to ways it can be used to fight the disease. In 2016, 5.4 million Americans are believed to have Alzheimer’s, which causes progressive loss of memory and cognitive function.

In a study published Wednesday in the journal Nature, neuroscientists demonstrated that microglia — immune cells that are a key part of the brain’s cleanup crew — can be activated by inducing rhythmic electrical impulses in the brain called gamma oscillations.

In the region of the brain that processes sight, at least, researchers at the Massachusetts Institute of Technology showed they could induce cells to fire in synchronous gamma oscillation without so much as a needle stick: When they set mice in a box illuminated by LED lights flickering precisely at 40 Hz, the neurons of each animal’s visual cortex began humming along at the same frequency.

The effect was dramatic in mice bred to develop the sticky brain plaques and tangles that are a hallmark of Alzheimer’s disease in humans. After only an hour in front of the lights, the scientists found reduced levels of amyloid protein in the visual cortices of the animals. They
detected a noticeable uptick in the size and activity of microglia, suggesting that these immune cells were vacuuming up more amyloid protein and stepping up their trash-disposal efforts.

Noting that this effect lasted less than a full day, the scientists then gave some of the mice a week of daily sessions in the flickering light. Compared to mice who did not get the weeklong light therapy, those that did had 67% fewer amyloid plaques — the clumps of amyloid protein that appear to gum up the function of a brain in the grips of Alzheimer’s. And the plaques that they had were, on average, 64% smaller.

In mice, these effects were limited to the visual cortex. In humans with Alzheimer’s, that’s not one of the brain regions that gets gummed up early or significantly by amyloid plaques. But the authors of the new research held out hope that the light therapy might induce gamma oscillations, or their immune-boosting effect, more broadly in human brains, or that some change in delivery of the light might extend its effects to brain regions, such as the hippocampus, that are profoundly affected by Alzheimer’s.

It’s not hard to induce gamma oscillations naturally: Our neurons achieve such synchrony when we are learning, paying attention or engaging our short-term memory. But getting populations of neurons to fire in such resonance is hard even for the healthy to sustain for very long, and with the onset of many brain diseases, it becomes harder.

The new findings are a welcome victory for an approach to treating Alzheimer’s disease that has fallen on hard times. Just two weeks ago, Eli Lilly & Co. researchers acknowledged disappointing clinical trial results for solanezumab, an experimental therapy that also aimed to prevent or slow Alzheimer’s by blocking the formation of amyloid plaques.

Some scientists have grown discouraged with treatment efforts that focus on such “biomarkers” of the disease in the brain. Others, including the authors of the new paper, suggest instead that scientists aren’t using such therapies early enough, or that they just haven’t found the best way to prevent the protein clumping and the cascade of cell death that follows.
“I think we have something very fundamentally different” from previous attempts to develop an anti-amyloid treatment for Alzheimer’s disease, said Li-Huei Tsai, a senior author of the new paper.

The light therapy “doesn’t involve any chemicals or small molecules that have to be delivered directly into your body,” said Tsai, who directs MIT’s Picower Institute for Learning and Memory. While its effects still must be tested in humans, she said that inducing gamma waves with flickering light gets around some of the problems that have doomed so many experimental Alzheimer’s medications. Among those problems have been unintended drug effects and the inability of some drugs to reach the brain from the bloodstream.

“We just directly recruit other neurons and other cell types in the brain to sort of enable the brain’s inner ability to repair itself,” Tsai said. She described the flickering light that kick-starts the process as “very low intensity, very ambient, very soft light.”

“You can hardly see the flicker itself, actually,” she added.

The researchers focused on gamma oscillations in the brain partly because these synchronized brain rhythms are severely reduced in the hippocampus and other regions acutely affected by Alzheimer’s. To establish that increasing gamma oscillations would energize microglial cells in structures such as the hippocampus, the team first used optogenetics, a technique in which lights implanted into the brain are used to turn specially tagged brain cells off and on.

That technique essentially established the link between gamma oscillations and activation of the brain’s immune cells. But the researchers reasoned that optogenetics would ultimately be too intrusive to use in a human treatment. So they began exploring ways to energize those special cells in less invasive ways.

Gamma oscillation and immune system activity also appear to be reduced in other neuropsychiatric conditions, including autism, Parkinson’s disease and schizophrenia. Tsai said her lab and others have begun collaborating to explore the possible benefits of light therapy for those diseases as well.
Keith Fargo, director of scientific programs and outreach at the Alzheimer’s Assn., cautioned that it’s not time yet for those worried about Alzheimer’s to go looking for LED lights that emit electromagnetic radiation in the gamma range. The value of the new research, he said, lies mostly in what it reveals about the role of the immune system in Alzheimer’s disease.

“It’s more like a proof of concept that you can, in various ways, improve brain synchronicity and stimulate the immune system,” said Fargo, who was not involved in the new research. “What’s important here is that you can harness the immune system, whether with a drug or a noninterventional method like this,” to fight Alzheimer’s, he added.

“We’re not all going to go out and get 40-hertz light bulbs for our brains,” he said.

Senior study coauthor Edward S. Boyden, a pioneer in optogenetics, echoed that caution and the hope is that the new research will generate broader insights into the brain’s electrical oscillations and its self-repair mechanisms.

“There may be other ways to engage these circuits,” said Boyden, a professor of bioengineering and brain and cognitive sciences at MIT. “There may be a universal circuit motif that can be found in many regions.”

[Medical EXPOSE](http://www.medicalexpose.com/)

[IMUNE](https://www.imune.org/)

Evidence Based Natural Energetic Medicine Education