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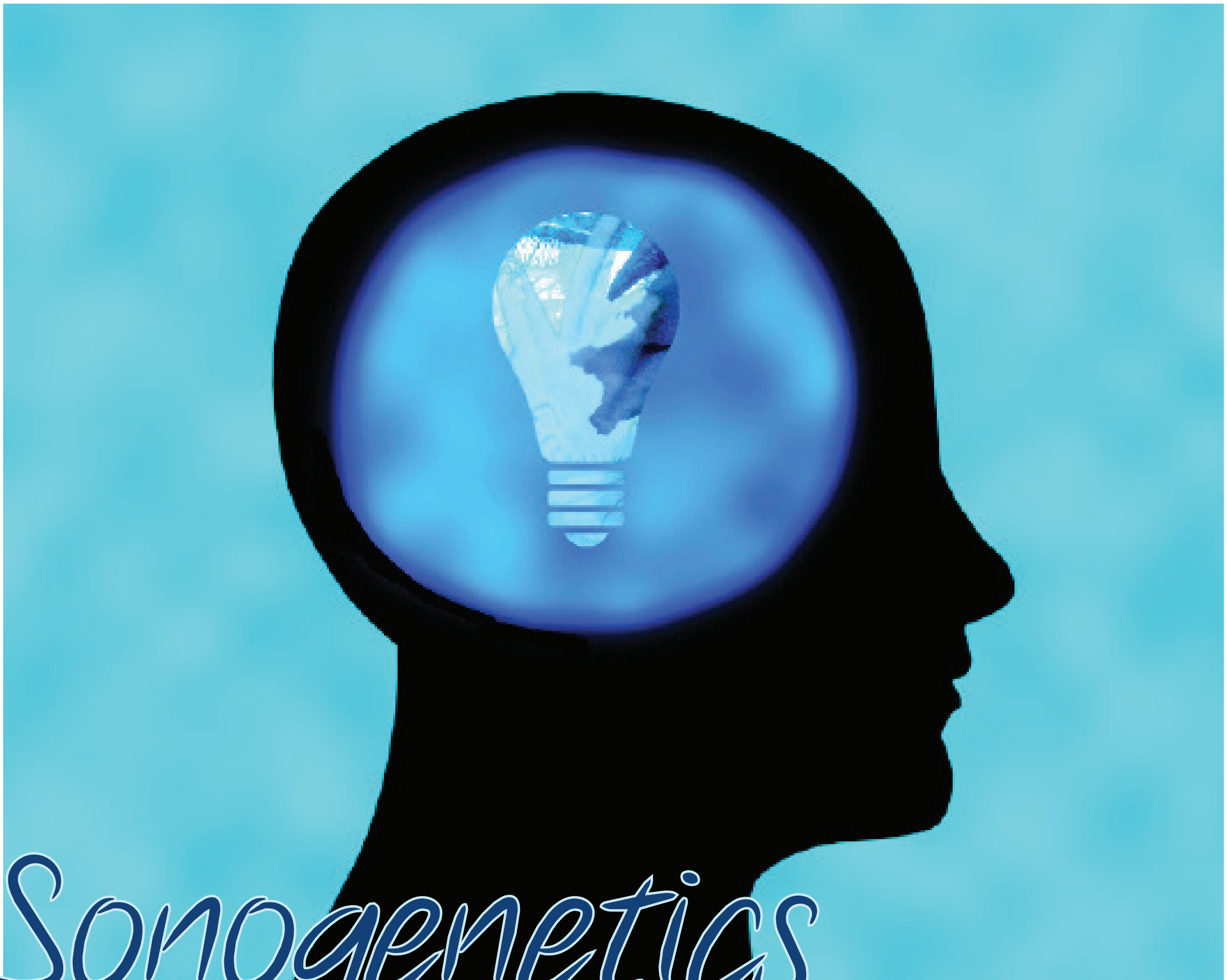

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The human brain contains billions of neurons, which are brain cells that form intricate and complex connections with each other. Neurons use these connections to send electrical signals to each other, and this signaling forms a dense network of all brain activity. These neural networks allow the formation of behavior, thought, emotion, motor skills, and everything else controlled by the brain.

In modern neuroscientific research, one of the most profound recent developments has been the rise of optogenetics, a technique that gives researchers unprecedented control over neural networks. Put simply, optogenetics is a technique that gives researchers an on/off switch for whichever neurons they choose. The technique works by inserting certain light-sensitive proteins, which act as the on/off switch, into neurons. Light can then be shone on the brain and used to 'turn on' the specifically modified neurons in any desired region [1]. With optogenetics, researchers can directly switch on and off individual neurons in living organisms. For example, researchers in one experiment were able to modify neurons that activate the muscles of a rat, and could then control its movement with a fiber optic cable that shone light on the modified neurons in the brain. The technique is so revolutionary that in 2010, Nature Methods awarded it "Method of the Year" across all fields of science [2], and Science called it one of the "Breakthroughs of the Decade" [3]. Dr. Karl Deisseroth, one of the creators of optogenetics, estimates that there are now more than a thousand laboratories utilizing the technique, up from just his own in 2009 [4].

Despite all of the benefits that optogenetics seems to have for modern research, there are some inherent limitations. In order to activate modified light-sensitive neurons in the brains of live mice, for example, experiments often require that a small fiber-optic wire be inserted into the specific part of the brain being targeted, which can potentially disrupt normal brain functions. In all forms of optogenetics, researchers must invasively insert a physical conduit for light to travel through and reach the brain areas being targeted [5].

Neuroscientists have long dreamed about the ability to one day have these tools to precisely target and control individual neurons within the brain. Even Francis Crick, the co-discoverer of DNA's structure, claimed in 1979 that a tool like optogenetics would one day be necessary to fully understand how the brain works [6]. More recently, numerous attempts have been made by researchers to discover techniques of manipulating neurons in the living brain without having to cut through the skull and insert objects into the brain. Two of the most prominent current methods of noninvasively manipulating neurons aretranscranial direct-current stimulation and transcranial magnetic stimulation [8,7]. These techniques both involve electrically stimulating the brain externally by either placing electrodes on the scalp, or by running magnetic currents through the brain via an apparatus that is held a few inches away from the head. Although both techniques have measurable effects on the brain, they can only target general brain areas, and neither technique can target individual neurons like optogenetics can.

However, Dr. Sreekanth Chalasani and his team at the Salk Institute in San Diego seem to be on the cusp of making this fabled technique of noninvasive stimulation of neurons a reality. In a recent report published in Nature Communications, Dr. Sreekanth Chalasani and his team outline how they were able to modify the neurons of the C. elegans species of Nematodes so that they would be sensitive to ultrasound. By adding genes that create pressure sensitive ion channels to a targeted neuron that controls movement, researchers were then able to activate the neuron using external pulses of low-energy ultrasound, which allowed the researchers to control the movement of the worm. They call this technique ‘sonogenetics,’ and it promises to give researchers the same control over neurons that optogenetics does, without having to insert anything like optic fiber wires into the brain [9].

Soon, Dr. Chalasani hopes to soon perform a similar experiment on mice to see if sonogenetics can be used on their brains as well. If his experiments with mice prove successful, then sonogenetics could likely become a technique one day used to manipulate neurons in the brains of humans. Dr. Chalasani believes that “it may be possible to make human neurons temporarily susceptible to the ultrasound signal in a clinical setting for certain neurological treatments” [10].If it proves viable, this ability to target and control specific neurons in the brain using only ultrasound could lead to massive developments in the treatment of many different neurological disorders.

Sonogenetics could also potentially become a viable treatment for those with certain mental disorders. Targeted optogenetic stimulation within certain areas of mice brains has already been proven to reverse their symptoms of depression [11]. Also, the fact that vagus-nerve stimulation, a precursor to optogenetics where measured bursts of electricity are sent to ‘turn on’ general groups of neurons through an implant in a nerve within the neck, has seen recent clinical success in treating epilepsy and depression suggests that targeted stimulation of neurons in specific brain regions could be the key to treating many of these neurological disorders [2].

While this paper is promising, sonogenetics is by no means a perfect technique yet. There is still much research to be done on its effectiveness, and researchers will need to overcome a host of potential hurdles. In Dr. Chalasani’s experiment, gas-filled microbubbles were inserted into the nematodes in order to amplify the low-pressure ultrasound to a level that could activate their modified neurons. These microbubbles can only remain active for about sixty minutes, which could place temporal constraints any potential sonogenetic treatments in humans [1]. Also, for practical noninvasive use in humans, the ultrasound waves will need to be powerful enough to pass through the skull and layers of brain tissue, while still being weak enough to avoid damaging tissue. Ultrasound is also known to heat the tissue it passes through slightly, which could create unintended complications within the brain as certain regions like the hypothalamus are known to contain temperature-sensitive neurons [12,13]. However, even in the face of these challenges, Dr. Chalasani and his team seem poised to make the dream of noninvasive targeted neuron manipulation our reality.

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