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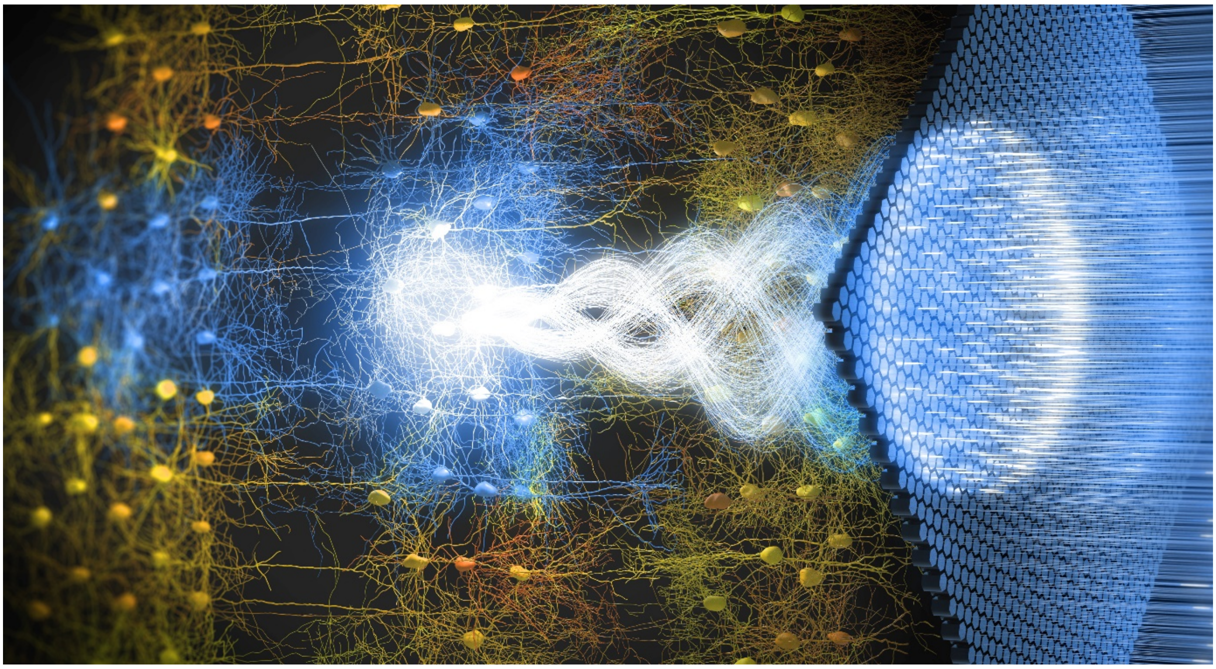
Press information

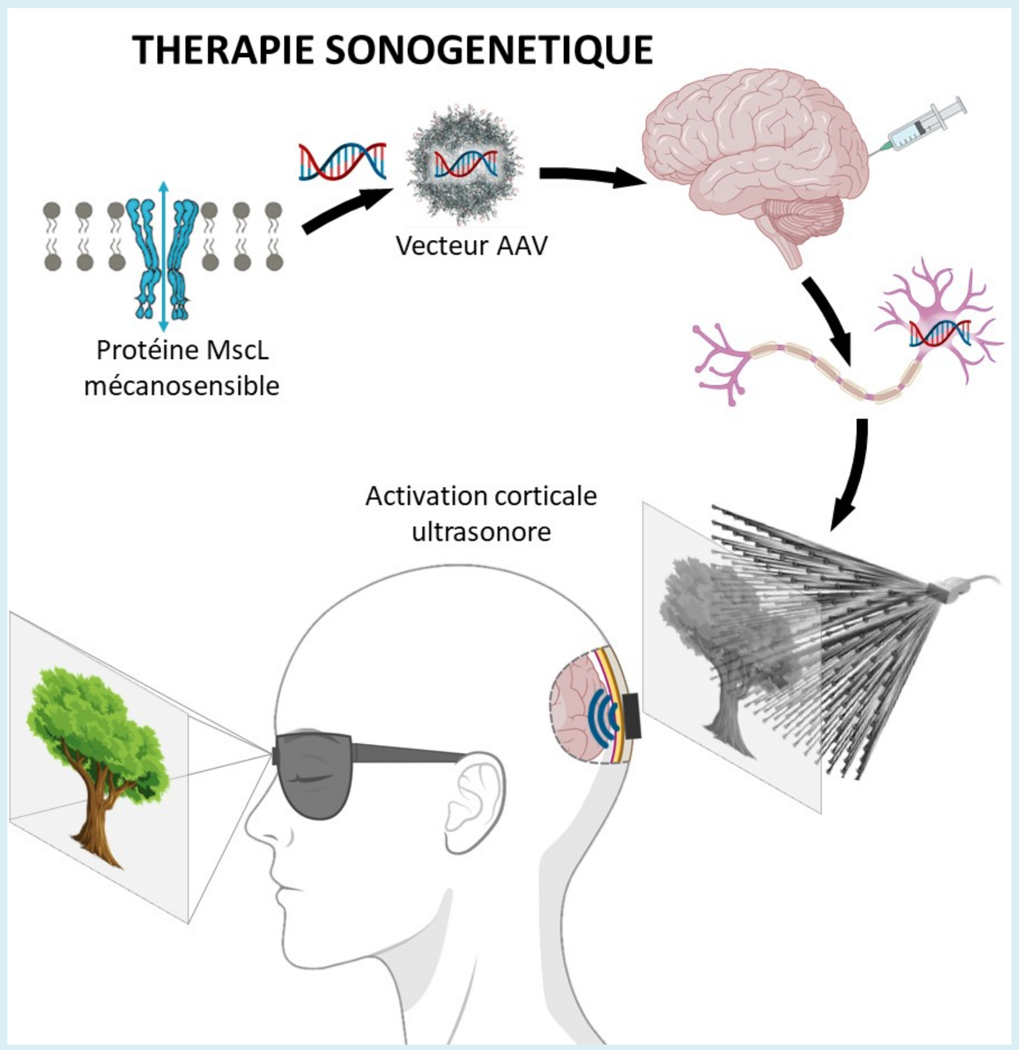
Restoring Vision Through a New Brain-Machine Interface: Sonogenetic Therapy



Sonogenetic therapy consists of genetically modifying certain neurons in order to activate them remotely by ultrasound. © Alexandre Dizeux/Physics for Medicine Paris

Restore vision using a combination of ultrasound and genetics? This is the goal of an international team led by Inserm research directors Mickael Tanter and Serge Picaud from Paris' Physics for Medicine unit (ESPCI Paris/PSL Université/Inserm/CNRS) and Vision Institute (Sorbonne Université/Inserm/CNRS), respectively, in partnership with the Institute of Molecular and Clinical Ophthalmology in Basel. In a new study, they provide proof of concept of this so-called "sonogenetic" therapy in animals. This consists of genetically modifying certain neurons in order to activate them remotely by ultrasound. The results show that when used on rodent neurons sonogenetics can induce a behavioral response associated with light perception. This discovery makes it possible to envisage, in the longer term, an application in blind people with optic nerve atrophy. The study has been published in *Nature Nanotechnology*.

Sonogenetic therapy consists of genetically modifying certain neurons in order to activate them remotely by ultrasound. This technology had previously been tested in culture and the first in vivo tests did not enable the researchers to become aware of its therapeutic potential linked to its very high spatiotemporal resolution. The genetic modification in question consists of introducing the genetic code of a mechanosensitive ion channel into the cells. The neurons that express this channel can then be remotely activated by low-intensity ultrasound applied to the surface of the brain without the need for contact (*see diagram below*).



THERAPIE SONOGENETIQUE	SONOGENETIC THERAPY
Protéine MscL mécanosensible	Mechanosensitive MscL protein
Vecteur AAV	AAV vector
Activation corticale ultrasonore	Ultrasound cortical activation

Ultrasound waves can access tissue deep down, such as in the visual cortex – even from the surface of the dura mater[1] that surrounds the brain – and target very specific areas. It is these waves that form the basis for high-resolution brain imaging or ultrasound technologies. In this case, they enable highly selective activation, because only those neurons carrying the mechanosensitive channel and targeted by the ultrasound beam are stimulated.

In a recent study, a team of researchers led by Inserm research directors Mickael Tanter and Serge Picaud tested the efficacy of this sonogenetic therapy in animals. The aim of this research is to provide a solution to restore vision to patients having lost the connection between their eyes and brain due to conditions such as glaucoma, diabetic retinopathy, or hereditary or dietary optic neuropathies.

Their findings show that sonogenetic stimulation of the visual cortex induces a behavioral response associated with light perception. The animal learns an associative behavior in which it seeks to drink as soon as it perceives light. Ultrasound stimulation of its visual cortex induces the same reflex, but only if the neurons in the cortex express the mechanosensitive channel. The animal's behavior suggests that sonogenetic stimulation of its cortex induced the light perception at the origin of the behavioral reflex.

The study showed that therapy works on different types of neurons, whether in the retina or visual cortex of the rodents, thereby demonstrating the universal nature of this approach.

[1] Outermost layer of the meninges that protect the brain

By converting the images of our environment into the form of a coded ultrasound wave to directly stimulate the visual cortex – at rates of several tens of images per second – sonogenetic therapy appears to offer genuine hope for restoring vision to patients who have lost optic nerve function.

More generally, this sonogenetic stimulation approach offers innovative technology for interrogating brain function. Unlike current neuron stimulators or prostheses, its "non-contact" and selective cell type functioning represents a major innovation in relation to electrode devices.

"This sonogenetic therapy to ultimately restore the vision of blind people illustrates the power of a multidisciplinary project and a beautiful human adventure between a retinal biologist like Serge Picaud, and myself, a wave physicist for medicine," declares Tanter, Inserm research director at the Physics for Medicine unit in Paris (ESPCI Paris/PSL Université/Inserm/CNRS).

"The development of a clinical trial of sonogenetic therapy still has many steps to go through to validate its efficacy and safety. If the results are confirmed, this therapy could succeed in restoring patients' vision in a stable and safe manner," concludes Picaud, Inserm research director and director of the Vision Institute (Sorbonne Université/Inserm/CNRS).

References

Ectopic expression of a mechanosensitive channel confers spatiotemporal resolution to ultrasound stimulations of neurons for visual restoration

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