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Researchers report that gene therapy awakens the brain despite blindness from birth

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Researchers at the University of Pennsylvania have demonstrated that gene therapy used to restore retinal activity to the blind also restores function to the brain's visual center, a critical component of seeing.

The multi-institutional study led by Geoffrey K. Aguirre, assistant professor of neurology in Penn's School of Medicine, shows that gene therapy can improve retinal, visual-pathway and visual-cortex responses in animals born blind and has the potential to do the same in humans.

"The retina of the eye captures light, but the brain is where vision is experienced," Aguirre said. "The traditional view is that blindness in infancy permanently alters the structure and function of the brain, leaving it unable to process visual information if sight is restored. We've now challenged that view."

The results support the potential for human benefit from retinal therapies aimed at restoring vision to those with genetic retinal disease.

Researchers used functional MRI to measure brain activity in blind dogs born with a mutation in gene RPE65, an essential molecule in the retinoid-visual cycle. The same mutation causes a blindness in humans called Leber congenital amaurosis, or LCA. It is the first human eye-retinal disorder slated for gene therapy.

Gene therapy, performed by introducing a working copy of RPE65 into the retina, restored eye function in canines. Yet, it was previously unclear if the brain could “receive” the restored sight.

The team found that gene therapy to the eye dramatically increased responses to light within the visual cortex of the canine brain. The recovery of visual brain function occurred in a canine that had been blind for the first four years of its life, and recovery was found to persist in another dog for at least two-and-a-half years after therapy, suggesting a level of permanence to the treatment.

Penn scientists then studied the structure and function of the visual brain of human patients with the same form of blindness. Young adults with blindness from RPE65 mutation had intact visual brain pathways with nearly normal structure. The Penn team also found that, while the visual cortex of these patients with LCA did not respond to dim lights, the brain’s reaction to brighter lights was comparable to that of individuals with normal sight.

"It seems these patients have the necessary brain pathways ready to go if their eyes start working again,” Aguirre said.

The results of the current study are critical to these human clinical trials, led at Penn’s Scheie Eye Institute by Samuel G. Jacobson, professor of ophthalmology, and Artur V. Cideciyan, research associate professor of ophthalmology.

“Existence of functional potential both in the eye and brain are prerequisites for successful gene therapy in all forms of LCA,” Cideciyan said. “In the RPE65 form of the disease, we now have evidence for both, and treatment at the retinal level has the hope of recovery of useful vision in patients.”

Source: University of Pennsylvania