

NEUROBIOLOGY

Childhood Recovered

"Lazy eye" studies show how adult brains can be rewired back to youth **BY GARY STIX**

The pirate look is a time-honored way to fix children's "lazy eye": the patch over the good eye forces the weak one to work, thereby preventing its deterioration. Playing video games helps, too. The neural cells corresponding to both eyes then learn to fire in synchrony so that the brain wires itself for the stereo vision required for depth perception. Left untreated past a critical age, lazy eye, or amblyopia, can result in permanently impaired vision. New studies are now showing that this condition, which affects up to 5 percent of the population, could be repaired even past the critical phase.

What is more, amblyopia may provide insights into brain plasticity that could help treat a variety of other disorders related to faulty wiring, including schizophrenia, epilepsy, autism, anxiety and addiction. These ailments "are not neurodegenerative diseases that destroy part of the neural circuitry," notes Takao Hensch, a Harvard Medical School researcher. So if the defective circuits "could be stimulated in the right way, the brain could develop normally."

The recent findings have their roots in work from 10 years ago. Then, Hensch led a team that discovered the specific visual circuitry that induces a "critical period" during early life in which the two eyes must work together to establish the connections in the cortex underlying proper visual acuity. So-called parvalbumin basket cells release the neurotransmitter GABA, which puts the brakes on cell activity. But GABA and compounds that behave like it—the drug Valium, for one—can also trigger the critical phase. It is paradoxical that neurochemicals that turn cells off play a role in initiating a key developmental stage.

Hensch's discovery, along with the recognition of the important part played by the proteins and sugars that form a

matrix surrounding parvalbumin cells, has resulted in a set of recent experiments that demonstrate ways to reinstate the critical period in adult animals—and perhaps to map a path toward treatments. In 2006 a group led by Lamberto Maffei, a neurobiologist at the University of Pisa in Italy, injected an enzyme called chondroitinase into the visual cortex of adult rats with amblyopia to dissolve the extracellular matrix and restore the critical period. After patching a rat's good eye, the researchers witnessed the recovery of normal vision: cortical circuitry for both the left and right eyes were nudged into firing together, just as they are during the early phase of childhood development.

More recently, Hensch's team reported in *Cell* last summer on a protein that has the same effect as Valium in the developing visual cortex. Called Otx2, it has a role in the embryonic development of the head and becomes prominent again after birth, serving as the starting gun for the critical period. The protein actually travels from the retina to the visual cortex at the rear of the brain, perhaps because the visual cortex needs to wait for a signal from the eyes that it is ready to undergo maturation.

Hensch also presented work at the Society for Neuroscience annual meeting in November on adult mice with amblyopia that were genetically engineered to lack a recep-

SCIENCE FACULTY NYU Abu Dhabi

New York University (NYU) is establishing a new comprehensive liberal arts campus in Abu Dhabi, the capital of the United Arab Emirates. New York University Abu Dhabi (NYUAD), a partner campus of New York University New York (NYUNY), will consist of a highly selective liberal arts college (Arts, Humanities, Social Sciences, Sciences and Engineering), distinctive graduate programs, and a world-class Institute for advanced research, scholarship, and creative work. NYUNY and NYUAD will be integrally connected, together forming the foundation of a unique global network university, actively linked as well to NYU's study and research sites on five continents.

The Division of Science, Engineering, Technology and Mathematics at NYUAD is now recruiting faculty of exceptional quality in teaching and in professional accomplishment. The Division is specifically looking for professors of Biology, Chemistry, Computer Science, Neuroscience, Mathematics and Physics. Recruited faculty will start by teaching an innovative, three-semester foundational core, called the Science Foundations series. The Science Foundations series is especially designed to integrate basic concepts from mathematics, physics, chemistry, biology, computer science, and neuroscience and is required for all science majors at NYUAD. Science instruction at NYUAD will start in AY2010; however, applicants could start at NYUNY in September, 2009. Modern science laboratories will be constructed and become available for faculty research within a start-up phase spread over several subsequent years. Faculty may spend time at NYU in New York and at its other global campuses. The terms of employment are competitive compared to U.S. benchmarks and include housing and educational subsidies for children.

The review of applications will begin in January 2009 and will continue until the positions are filled. To apply for this position, please send ONE document only (pdf or word) via email to: nyuad.science@nyu.edu. This document should contain a cover letter (please address the letter to NYUAD Science Search Committee), a curriculum vitae, statements of teaching experience and research interests, contact information for references and representative publications. Electronic submissions are preferred, but you may also send a hard copy to: NYUAD Science Search Committee, New York University, 70 Washington Square South, Rm. 1242, New York, NY 10012. Information concerning the faculty, programs and facilities of NYU Abu Dhabi, can be obtained at: <http://nyuad.nyu.edu>



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NEWS SCAN



OPTICAL WORKOUT: Patching a child's good eye during a "critical period" may rewire the brain to restore visual acuity in the impaired eye.

tor on neurons for Nogo, a growth-inhibiting protein that originates in the myelin insulation around the neural wires called axons. In the experiment, suturing shut one of the two healthy eyes during the critical period induced amblyopia and its attendant decrease in visual acuity. When the sutures were removed, however, the mice that did not have the molecular brake of the Nogo receptor spontaneously regained their vision.

"This work is inspirational for me," remarks Dennis Levi, a neuroscientist at the University of California, Berkeley. "The future will be some kind of molecular intervention for amblyopia."

Such a future may not be far off. In fact, oral compounds may already exist on the pharmaceutical shelves. Last year Maffei's group found that the antidepressant Prozac can restore plasticity in the adult visual system of rats.

The ability to revert neural cells back

to their younger, plastic state could potentially be a treatment breakthrough. But fully restoring the brain's original sponge-like quality would nonetheless give clinicians pause. Turning the brain into malleable mush at the age of 30 would not be the best solution—some scientists think that an excess of plasticity, in fact, may lie at the root of conditions such as schizophrenia.

Some investigators are already exploring how far they can bring back plasticity and mend patients through environmental cues alone. In his own work, Levi found that after thousands of sessions in video game–like exercises—"kilo trials" as he calls these mini clinical trials—adult amblyopia patients achieved substantial improvements in visual acuity. Levi is already doing research with actual video games. Grand Theft Auto IV or Medal of Honor may retrain the brain in ways its developers never imagined.

Perils of a Badly Wired Brain

The research showing that neural systems can be forced back to an earlier, more pliable state may extend beyond treatments for "lazy eye." Schizophrenia may emerge from faulty signals transmitted during the critical developmental period, causing an excess of plasticity throughout life. Autistic children may suffer a surfeit of overexcited connections, another offshoot of errors in wiring that occur during this early-childhood window. Biochemicals similar to those in the visual system may be activated by auditory, olfactory and tactile signals. Adjusting their levels up or down in the central nervous system could conceivably treat a variety of disorders.

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