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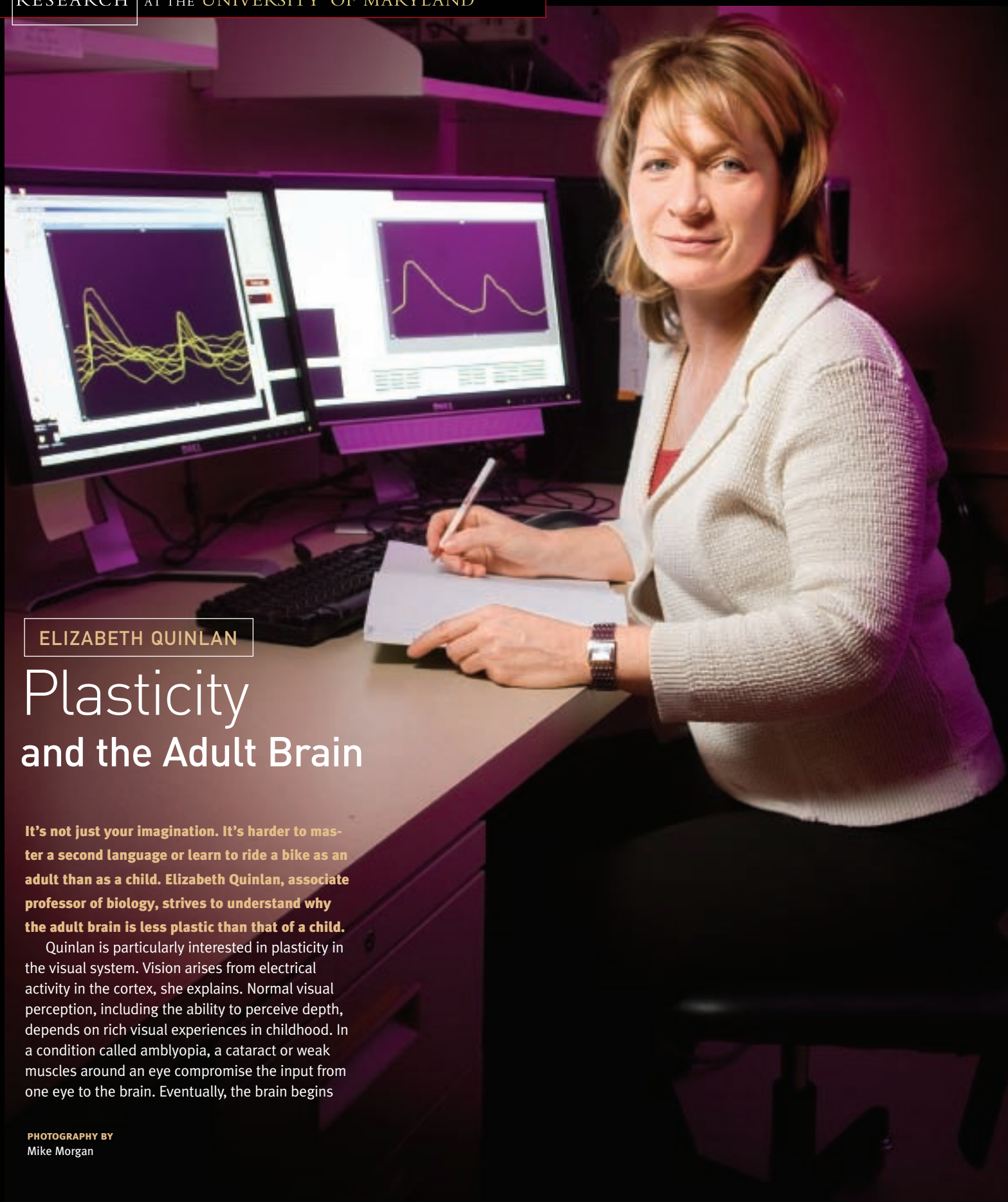


ELIZABETH QUINLAN

Plasticity
and the Adult Brain

It's not just your imagination. It's harder to master a second language or learn to ride a bike as an adult than as a child. Elizabeth Quinlan, associate professor of biology, strives to understand why the adult brain is less plastic than that of a child.

Quinlan is particularly interested in plasticity in the visual system. Vision arises from electrical activity in the cortex, she explains. Normal visual perception, including the ability to perceive depth, depends on rich visual experiences in childhood. In a condition called amblyopia, a cataract or weak muscles around an eye compromise the input from one eye to the brain. Eventually, the brain begins

PHOTOGRAPHY BY
Mike Morgan

Neuroplasticity and Vision

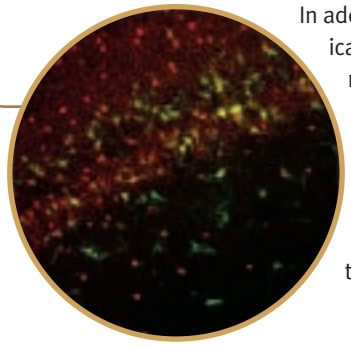
to ignore signals from the weak eye, resulting in "cortical blindness" in that eye and the loss of depth perception. Removing the cataract and patching the stronger eye can help children recover full vision, but such remedies don't cure cortical blindness in adults.

Researchers can mimic amblyopia in rodents. If one eye is patched from birth to adulthood, the animal becomes cortically blind in the patched eye. Visual discrimination tasks show that animals cannot see from the eye. Physiological tests confirm that the chronically deprived eye does not drive electrical activity in the visual cortex.

In thinking about how to promote the recovery of vision, Quinlan was inspired by stories of people who have had remarkable recoveries after strokes. Maybe, Quinlan reasoned, normal, ongoing activity in the adult brain constrains its plasticity. She hypothesized that removing input into the visual system could remove this constraint and restore a symmetry to the connections between each of the two eyes and the brain. Quinlan and her research team tested this hypothesis by putting animals in the dark to see if complete visual deprivation would promote restoration of vision in adult animals with amblyopia.

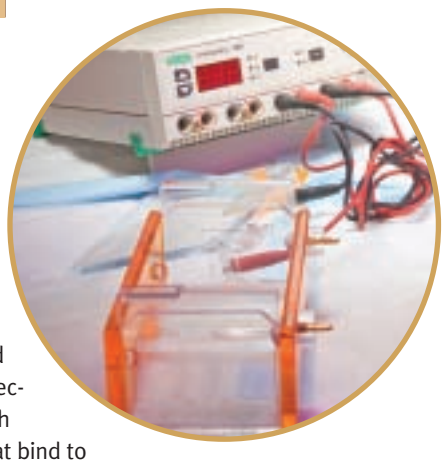
The researchers put rodents that had been rendered blind in one eye by long-term patching of that eye into a dark room for 10 days. Within days of being returned to normal light, behavioral and physiologic tests showed that the animals could see from the previously blind eye. Quinlan had cured cortical blindness in the animals.

"We're interested in understanding the molecular cascade that starts with putting animals in the dark and ends with recovery of vision," Quinlan says. Her team is testing molecules that could promote the recovery of vision.



In addition to potentially pointing to medical treatments for amblyopia, these mechanistic studies are helping to tease out the key differences between juvenile and adult brains.

Quinlan believes that visual deprivation decreases the driving force on inhibitory synaptic connections in the visual cortex and that reducing the inhibitory signals is necessary to enhance plasticity and promote recovery of function in a "blind" eye. Whole-scale removal of cortical inhibition with drugs would induce a seizure. A medical treatment for amblyopia would have to remove inhibitions selectively. Quinlan and her research team are testing molecules that bind to cannabinoid receptors located on inhibitory neurons. Quinlan hypothesizes that drugs that bind to these receptors may promote plasticity by limiting the activity at a subset of inhibitory synapses.



"There is a wealth of data on the molecular changes that occur from early stages of development to late stages of development in the cortex," Quinlan notes. For every molecule that her group has investigated, the composition or distribution in an adult that has undergone visual deprivation by being placed in the dark looks more like the juvenile brain than the usual adult one. Her group has also looked at gene expression patterns following visual deprivation and found that a surprisingly small set of molecules appear to be affected. These tests could point to targets for future drugs to promote plasticity.

Quinlan is very much interested in applying her findings to helping treat human amblyopia. Working with an optometrist who uses exercises to promote visual recovery, she plans to combine visual deprivation with behavioral therapy to promote recovery of function. Instead of putting adults in the dark, she will fit them with special glasses that block input to the "binocular" neurons in the brain that are stimulated by both eyes. Patients would still be able to use their peripheral vision while undergoing treatment.

For human treatment, Quinlan predicts that a combination of low levels of a drug combined with behavioral treatments, like light deprivation, will have the best chance of curing cortical blindness, and she is working on both strategies—the behavioral and the molecular—to promote plasticity in the adult brain. *—Karin Jegalian*

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Impact Profile is a supplement to *Impact*, a research digest from the University of Maryland. To learn more about research at Maryland, go to www.umresearch.umd.edu.

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