Eye-Tuned

April 30, 2014

Three years ago, the Singapore Eye Research Institute launched a photographic art exhibition called “Eyes That Tell Stories.” The project features detailed macro images of eyes from famous subjects including a well-known chef, an Olympic swimmer, and a filmmaker. With all their tiny ridges, bumps, and crevices in clear view, the pictures resemble aerial views of dormant volcanoes rather than close-up photos of a human organ.

Designed to raise awareness about the prevention and treatment of eye disorders, the project emphasizes how our peepers can reveal health risks that may lie dormant and otherwise undetectable for years.

But the human eye has become more than a window into such medical problems as thyroid disease and hepatitis. It is inspiring a host of cutting-edge studies on brain abnormalities and behavioral conditions. Experts in cognition, epidemiology, ophthalmology, and neuroscience are collaborating to explore the potential of our eyes to identify our risk for mood disorders, learning disabilities, or cognitive impediments. The research largely remains preliminary, but it holds the promise of providing new ways to diagnose impending problems involving the brain.

Some of the research is simply focused on the link between vision impairment and learning disabilities. Several studies, for example, have found a significantly elevated incidence of ADHD in children with such ophthalmological problems as exotropia, an outward turning of the eye that can impede vision; convergence insufficiency, a common eye muscle coordination problem that is linked to learning difficulties; and color perception.

Some of the earliest research treated the eyes as the proverbial windows to the soul, striving to connect eye patterns to personality traits. But over time, scientists have achieved significant advances in understanding what the eyes can tell us — about cognition, mood, and human health.

The Iris and the Pupil

In the 1960s, Raymond Cattell reported differences in cognitive styles between people with blue and brown eyes. Since then, several other studies have drawn connections between eye color and physiological or behavioral traits. But few scientists have been able to replicate those findings, in part because the eye color effect appears to fade over the course of childhood.

But a few years ago, researchers at Örebro University in Sweden looked beyond eye color to find personality variables, focusing on other features of the iris. Psychological scientist Mats Larsson and colleagues administered a standard personality test to 428 volunteers and also took photos of their eyes. They found that a low number of squiggly lines, known as crypts, radiating out from the pupil was associated with tender-mindedness, warmth, trust, and positive emotions. Distinct furrows (circular lines around the edge of the iris) were connected to impulsiveness and neuroticism.

Larsson suggested that these traits in the iris could reflect genetic influences on personality development. He pointed to previous research linking a mutation in a gene called PAX6, which controls the development of the iris in an embryo, to impulsiveness and poor social skills.

The pupil has also been an endless focus of research for behavioral scientists. Nobel laureate and APS William James Fellow Daniel Kahneman showed that pupil size increases in proportion to the difficulty of the task being performed. In his best-selling book, *Thinking Fast and Slow*, he described being able to determine when people gave up on a multiplication problem in an experiment simply by watching their pupils contract.

The pupil expands in response to stimuli that generate intense emotions, a fact that had led scientists to look at pupil size as a potential biomarker for mood instability. Researchers at the University of Pittsburgh have conducted studies showing that adults with depressive disorders show increased and sustained pupil dilation when exposed to emotion-laden words. But they interestingly found the opposite effect with children and adolescents.

Led by Jennifer S. Silk, associate professor of psychiatry and psychology at Pitt, the study involved 63 children ages 8 to 17. Twenty of them had major depressive disorder, and another 21 had at least one relative with a history of depression (meaning they were considered high risk for becoming depressed themselves). The rest showed a low risk for depressive disorder.

The researchers tested the response that each child had to a series of emotional words — some negative, others positive, and yet others neutral. As they looked at each word, an infrared camera snapped a digital image of their eyes every 16 milliseconds.

Children showed greater pupil dilations when seeing negative words compared to neutral or positive words. But to the researchers' surprise, participants with major depression, as well as those deemed at high risk for depression, showed *diminished* pupil dilation when exposed to the negative words. And the greater the severity of the depressive symptoms, the more blunted the dilation when seeing negative words.

The same differences did not occur when the children were exposed to positive and neutral words.

In a second phase of the study, Silk and her colleagues gave each child a cell phone and called them 12

times over the course of 4 days. In those phone calls, the researchers asked the children about their feelings and social interactions. The children who had decreased pupil dilation in the lab also reported the most negative emotions and the least positive emotions among the participants.

Silk and her colleagues concluded that the lower pupil dilation may reflect problems in regulating emotions. That notion is consistent with clinical studies that showed children who devote fewer cognitive resources to processing negative emotions "shut down" emotionally when facing too much arousal. And this could have harmful long-term effects.

"By blunting, avoiding, or overregulating negative emotions, the depressed child would lose the opportunity to develop and practice more adaptive skills for tolerating and regulating negative emotions, potentially leading to greater difficulty managing emotion as an adult," the researchers write in a report on the study in *American Journal of Psychiatry*.

The Retina

More recently, studies involving the predictive aspects of the eyes have looked beneath the surface and into the retina, which contains cells that react to light and signal the brain to interpret visual stimuli. And here, those studies are revealing possible harbingers of not only mood disorders, but also actual cognitive decline.

At the Albert Ludwigs University of Freiburg in Germany, for example, researchers attached electrodes near participants' eyes to record electrical retinal responses as study participants viewed a series of checkerboard patterns with varying degrees of black-and-white contrast. The participants who had been diagnosed with clinical depression were significantly less able to see differences in black and white contrasts on the checkerboards. In fact, the participants who were the most depressed showed the lowest electrical recordings of retinal activity.

In addition to being a possible depression indicator, the retina is the source of an increasing exploration of impaired brain functioning. A recent study at Duke University led by psychological scientists Idan Shalev and APS Fellow Terrie E. Moffitt* found that the width of blood vessels in the retina may indicate brain health years before the onset of dementia and other deficits.

Shalev and his team used digital retinal imaging, a relatively new and noninvasive method, to gain a window into vascular conditions in the brain by looking at the small blood vessels of the retina. Retinal blood vessels share similar size, structure, and function with blood vessels in the brain and can provide a way of examining brain health in humans.

The researchers examined data from participants taking part in the Dunedin Multidisciplinary Health and Development Study, a longitudinal investigation of health and behavior in over 1,000 people born between April 1972 and March 1973 in Dunedin, New Zealand.

Having wider retinal venules was linked with lower IQ scores at age 38, even after the researchers accounted for various health, lifestyle, and environmental risk factors that might have played a role. And even more surprisingly, the data revealed that people who had wider venules at age 38 also had lower IQ in childhood.

The findings, reported in June 2013 in *Psychological Science*, suggest that the processes linking vascular health and cognitive functioning begin much earlier than previously assumed — years before the onset of dementia and other age-related declines in brain functioning.

“Digital retinal imaging is a tool that is being used today mainly by eye doctors to study diseases of the eye,” said Shalev, now an assistant professor of biobehavioral health at Pennsylvania State University. “But our initial findings indicate that it may be a useful investigative tool for psychological scientists who want to study the link between intelligence and health across the lifespan.”

The study didn’t address the specific mechanisms that drive the relationship between retinal vessels and cognitive functioning, but the researchers surmised that it may have to do with oxygen supply to the brain.

“Increasing knowledge about retinal vessels may enable scientists to develop better diagnosis and treatments to increase the levels of oxygen into the brain and by that, to prevent age-related worsening of cognitive abilities,” they concluded.

More recently, Shalev, Moffitt, and others joined then-Duke clinical psychology researcher Madeline Meier (now an assistant professor in Arizona State University’s psychology department) in using the data from the Dunedin study to show a heightened prevalence of schizophrenia among the participants with wider venules. Those individuals also showed a higher rate of psychosis symptoms in childhood.

Tracking Eye Movements

While eye physiology offers new insights on cognition and behavior, eye movement and fixation have become methods for studying developmental abnormalities.

In 2008, British psychology researchers Deborah Riby and Peter Hancock used eye-tracking methodology to examine both the social withdrawal associated with autism and the hyper-sociability associated with Williams syndrome.

The researchers asked child participants with autism or Williams syndrome to view color photographs of social situations ranging from family meals to weddings. They then used a special eye tracker to monitor each child’s gaze and fixation patterns. The results showed that participants with either condition exhibited atypical eye movements. People with autism spent less time looking at faces in the photographs, while children with Williams syndrome spent significantly *more* time focusing on faces, particularly eyes. This added new insights into the atypical social attention patterns associated, in contrasting ways, with each of the developmental conditions.

More recently, integrative research has raised the possibility that autism can be diagnosed much earlier than previously thought. The neural developmental disorder isn’t typically diagnosed until after age 2, when the first delays in social behavior and language appear. But scientists at the Marcus Autism Center in Atlanta found evidence for the disorder within the first 6 months of life.

Biomedical scientist Warren Jones and psychological scientist Ami Klin used eye-tracking equipment to measure eye movements in babies who watched video scenes of an adult caregiver. The researchers

divided the infants into two groups based on their risk for developing an autism spectrum disorder. Babies who had an older sibling already diagnosed with autism were put in a high-risk group, while the others were dubbed low risk. Jones and Klin tracked the children for 3 years, calculating the percentage of time each child fixated on the caregiver's eyes, mouth, and body, as well as other areas in the images.

By age 3, nearly all the children in the high-risk group had been diagnosed with autism spectrum disorder. The researchers then looked at the eye-tracking data to investigate which factors differed between children who received an autism diagnosis and those who did not. They discovered that the children diagnosed with autism showed a steady drop in eye fixation beginning as early as 2 months of age and continuing through the course of the study. By 2 years of age, the children later diagnosed with autism focused on the caregiver's eyes only about half as long as did those without autism. What's more, infants who showed the fastest decline in eye fixation over time were those who later showed the highest levels of developmental disability.

The results challenged a long-held notion that children with autism innately lack social engagement skills, including eye contact. While eye fixation declines in children on the spectrum, it isn't completely absent during infancy.

Implications

Scientists are quick to point out that results of these studies are largely preliminary and will need plenty of replication. But the potential implications the research holds for medical and psychological care are enormous. Could tracking eye movements lead to early diagnosis and interventions for autism and other developmental disorders? Could a depressive episode be identified and dealt with simply by looking at the patient's pupils?

Some of the most exciting outcomes could come from retinal imaging, which is quick and noninvasive, thus representing a potentially simple way to identify people at risk for psychiatric diseases. Diagnosticians may someday be able to use digital retinal imaging to identify juveniles at risk for developing psychosis or adults at risk for dementia.

Disorders of the mind are like stealthy predators, lying still for years and then jutting forth without warning. But integrative research on the eyes could pull those dangers out of hiding, giving us time to react to and even subdue the problems before they surprise us. œ

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