



## Studies Probe Autism Anatomy, Genetics

Bridget M. Kuehn

WASHINGTON, DC—Advanced imaging technologies and techniques that allow scientists to efficiently comb through the genome for rare gene variants are helping researchers better understand autism and identify its genetic basis, according to new research findings.

Many scientists believe that autism, a disorder defined by a spectrum of social, behavioral, and cognitive deficits, is the result of abnormal brain development caused in part by genes. But identifying the precise genetic and physiological basis of the disorder has proved difficult.

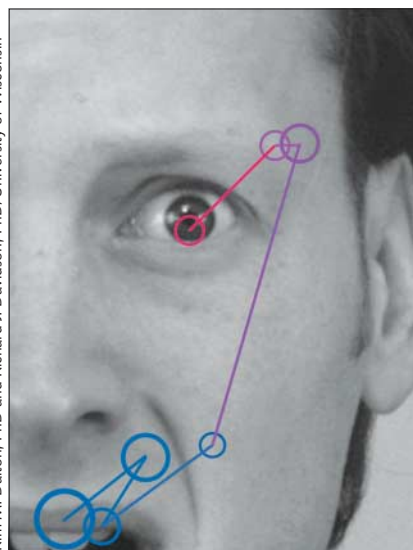
Two studies presented here at the annual meeting of the Society for Neuroscience in November identified structural abnormalities in certain regions of the brain in unaffected relatives of individuals with autism. Another study linked rare variants of a gene that codes for a serotonin transporter protein to the disorder in some families, providing further evidence that faulty serotonin processing may be involved in the disorder.

Beyond aiding scientists hoping to better understand and treat autism, these studies may provide insights into normal brain function. “We’re going to understand the brain more through understanding autism,” said Daniel H. Geschwind, MD, PhD, director of the Center for Autism Research and Treatment at the University of California at Los Angeles.

### FAMILY CONNECTIONS

In the first study, a multi-institution team of researchers from Colorado compared magnetic resonance imaging (MRI) scans of the brains of 40 par-

ents of autistic children with scans of 40 age- and sex-matched controls (individuals with no personal or family history of autism). The MRI scans revealed that some brain abnormalities associated with autism were found in parents of autistic children but not in controls. These include abnormalities



Using an automated system to track eye movements, scientists discovered that autistic individuals and their nonautistic siblings appear to spend less time looking at a person's eyes than do control subjects.

ents of autistic children with scans of 40 age- and sex-matched controls (individuals with no personal or family history of autism). The MRI scans revealed that some brain abnormalities associated with autism were found in parents of autistic children but not in controls. These include abnormalities in the cerebellum (a region involved in speech, learning, emotions, and attention) and the basal ganglia (which play a role in compulsive or rigid repetitive behavior). Some of these brain regions were smaller than normal and others were larger than normal in the parents of autistic individuals.

Eric Peterson, PhD, of the University of Colorado Health Sciences Center in Denver, who presented the findings, said they may indicate that these anomalies are inherited. But he cau-

tioned that the group's findings must be replicated and further studies are needed to determine whether the abnormalities identified in parents of autistic children have any behavioral consequences for them.

One previous imaging study of the brains of parents of individuals with autism also discovered brain abnormalities associated with the disorder (Rojas et al. *Am J Psychiatry*. 2004;161:2038-2044). This study, also conducted by University of Colorado scientists, compared the MRIs of 17 parents of children with autism, 15 adults with autism, and 17 age-matched controls with no personal or family history of the disorder. It found larger hippocampal volumes in individuals with autism and in parents of autistic individuals than in controls, which might suggest a genetic basis for such a difference. Another recent imaging study of 38 parents of individuals with autism (19 couples) and 40 matched controls (20 couples) found no significant differences in overall brain volumes between these two groups, but did not compare individual regions (Palmen et al. *Psychol Med*. 2005;35:1411-1420).

In a second small study, researchers from the laboratory of Richard J. Davidson, PhD, of the University of Wisconsin, in Madison, used MRI, functional MRI, and eye-tracking technologies to study 9 brothers of individuals with autism, 9 age- and IQ-matched nonautistic controls, and 9 age-matched boys with autism spectrum disorders. They found that the nonautistic brothers of individuals with autism displayed the same avoidance of eye contact that is characteristic of individuals with autism. In addition, amygdala size was similar in both



nonautistic brothers and their autistic siblings but smaller than in controls.

Although the findings need to be replicated in a larger population, they suggest that eye contact avoidance may be a useful trait for researchers to use “to tease out the heritable versus environmental contributions in autism,” said Brendon M. Nacewicz, a doctoral student and the first author of the study. He also noted that because the brothers of the autistic individuals are behaviorally normal, they may be able to compensate for their behavioral or neurological differences in a way that their autistic brothers cannot.

**GENETIC CLUES**

Since the 1960s, scientists have suspected that abnormalities in the seroto-

nin system may be involved in autism, according to James S. Sutcliffe, PhD, an assistant professor at the Vanderbilt Kennedy Center for Research on Human Development in Nashville, Tenn. Some studies have found that treatment with selective serotonin reuptake inhibitors reduces some of the symptoms of autism in some autistic patients, but responses to such treatments vary from patient to patient (Moore et al. *Ann Pharmacother.* 2004;38:1515-1519).

Research findings presented by Sutcliffe support a role in a subset of individuals with autism for variations in a gene encoding serotonin transporter protein. By analyzing DNA samples from 120 families that include individuals with autism, Sutcliffe and colleagues identified 19 variants of this

gene in families that included autistic males but not autistic females (Sutcliffe et al. *Am J Hum Genet.* 2005;77:265-279). Previous studies have also identified a sex-biased linkage between autism and chromosome 17, where these variants are located.

Four of the 19 variants had mutations in the protein-coding region of the gene, and families with these variants were significantly more likely to include autistic individuals who exhibit severe rigid or repetitive behaviors. The research suggests that a variety of rare serotonin transporter gene variants may increase the risk of autism.

“[The research] reinforces that serotonin is important in autism and it may be important in treatment,” Sutcliffe said. □

# Aspirin, “Super Aspirin” Use in Women for Cardioprevention Probed

Mike Mitka

**Dallas**—Scientists continue to discover benefits of aspirin use for women in preventing or reducing risk of cardiovascular disease and stroke. But are clinicians and patients getting the news?

Findings presented at the American Heart Association’s Scientific Sessions held here in November highlighted contradictions that continue to surround aspirin use by women.

Current research holds that aspirin works for risk reduction in women with established cardiovascular disease but may not reduce risk for women without established disease. Much of this knowledge has emerged from subset analysis of major trials primarily involving men, or from more recently published trials focusing specifically on women. Indeed, the most definitive findings on primary prevention came just earlier this year with publication of the Women’s Health Study, which showed that low-dose aspirin (100 mg on alternate days) lowered stroke risk

but had no effect on risk of myocardial infarction or death from cardiovascular causes, although subgroup analyses showed it did reduce risk for



**New research findings suggest that a daily regimen of low-dose aspirin may be associated with reduced risk of all-cause and cardiovascular mortality in older women.**

major cardiovascular events and myocardial infarction in women older than 65 years (Ridker PM et al. *N Engl J Med.* 2005;352:1293-1304).

But such clear evidence does not translate directly into practice or perception, argued Raymond J. Gibbons, MD, president-elect of the American Heart Association. Gibbons said that the results from the Women’s Health Study have been turned into a shorthand message believed by the public that aspirin does not work to reduce cardiovascular disease risk in women.

“I’ve had a number of women under the age of 65 with known coronary disease ask now whether they should still be taking aspirin,” said Gibbons, who is also a professor of medicine at the Mayo Clinic in Rochester, Minn. “Clearly they should be.”

**ASPIRIN UNDERUSED**

Bolstering Gibbons’ comments were results reported by Jeffrey S. Berger, MD, a cardiology fellow at Duke University Medical Center in Durham, NC. Berger and colleagues presented a longitudinal multicenter cohort study analyzing 8928 postmenopausal women with stable cardiovascular disease who participated in