Abnormal Mirror Neurons May Impair Social Skills

BY BRUCE K. DIXON
Chicago Bureau

CHICAGO — The impaired social interaction and communication characteristic of autistic children is the result of abnormally functioning mirror neurons in the brain, judging from the findings of a novel imaging study.

A controlled study of 25 children revealed those with autism have increased gray matter in several areas of the parietal lobes, Manzar Ashtari, Ph.D., said at the annual meeting of the Radiological Society of North America.

"What we found was that the larger the brain matter, the more restrictive the child's interest and the more stereotypical his or her behavior, indicating the increased gray matter in autistic children is abnormal," said Dr. Ashtari, senior neuroscientist at Children's Hospital of Philadelphia. "This suggests that the inability of autistic children to relate to people and life situations in an ordinary way may result from an abnormally functioning mirror neuron system," she said.

Mirror neurons are brain cells that are active both when an individual is performing an action and experiencing an emotion or sensation, and when that individual witnesses the same actions, emotions, and sensations in others, Dr. Ashtari explained. "Mirror neurons were first discovered in the macaque monkey, and there is a similar system in the human brain," she said, adding that the mirror neuron system is part of the motor system and plays an essential role in controlling our own actions. The "broken mirror" theory of autism, which was first proposed about a decade ago, argues that dysfunction of the mirror neuron system is a root cause of social disability in autism.

The study led by Dr. Ashtari was conducted at the Fay J. Lindner Center for Autism, North Shore–Long Island Jewish Health System, Bethpage, N.Y., and involved 13 boys diagnosed with high-functioning autism or Asperger syndrome who had IQs greater than 70, and 12 healthy controls. The subjects, average age 11 years, underwent diffusion tensor imaging (DTI), a technique that tracks the movement of water molecules in the brain.

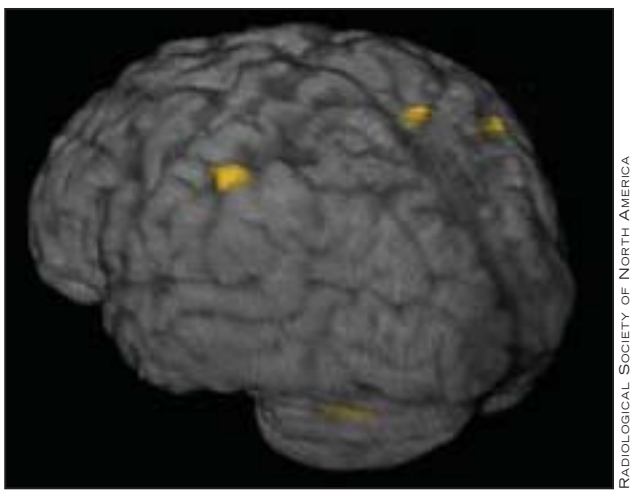
Although DTI traditionally is used to study the brain's white matter and fiber content, Dr. Ashtari's team applied it to the assessment of gray matter by employing apparent diffusion coefficient based morphometry, which highlights brain regions with changes in gray matter volume.

In addition to the gray matter abnormalities linked to the mirror neuron system, the investigators reported that the amount of gray matter in the left parietal area correlated with higher IQs in the control group but not in the autistic children. While this finding was interesting, said Dr. Ashtari, the difference did not reach statistical significance. "However, this does suggest that the gray matter in children with autism is dysfunctional."

Dr. Antonia Hamilton doubts the "broken mirror" theory. "I am skeptical of the mirror neuron–autism link, and the Ashtari study does nothing to change my mind," she said in an interview. In her own study, Dr. Hamilton reported that children with autism do not suffer general imitation impairment or a global mirror neuron system deficit (Neuropsychologia 2007;45:1859-68).

"Mirror neurons are active any time you perform an action with your own hand. When you pick up a cup of coffee, or see another person picking up a cup of coffee, the same neurons are involved," said Dr. Hamilton, a lecturer at the School of Psychology, University of Nottingham (England). "My experiment found that autistic children do fine when it comes to these practical, goal-oriented actions; however, they do not do well with social actions that involve imitation, such as smiling or waving at another person," she explained.

Dr. Hamilton studied 25 children with an independent clinical diagnosis of autism or autism spectrum disorder (ASD). The group had a mean age of 8 years and a mean verbal mental age of just over 4 years and were compared with 29 controls. Children were tested in their ability to copy the experimenter's hand movement to a target location on a table top, using mirror imitation. The investigators found no evidence for differences in performance between the ASD group and the matched controls. Both showed the typical pattern of hand errors on contralateral trials. "We can conclude that typical and autistic children have the same tendency to imitate the goal of another person's action," the scientists said, noting the concurrency of their results with previous studies.



RADIOLOGICAL SOCIETY OF NORTH AMERICA

Yellow areas highlight clusters of increased gray matter in the right and left parietal cortex as seen on DTI.

In a second experiment, 23 children with ASD and 31 controls completed a grasp imitation and motor planning task. "Motor planning is known to rely on the frontoparietal circuit which makes up the mirror neuron system, so the [autistic mirror neuron dysfunction, or] AMND predicts poor performance in autism spectrum disorder, which was not found," they wrote.

In another experiment, the children with autism showed no impairment in gesture recognition, and in fact performed better than did the matched controls. The authors concluded that their data are not compatible with the hypothesis of an action representation deficit or mirror neuron deficit in children with autism spectrum disorder.

"The broken-mirror-in-autism idea is a very appealing hypothesis which has received a lot of press in the last few years, despite the fact that there [is a scarcity of] hard data to support it," Dr. Hamilton said in an interview.

"Also, none of the studies of imitation in autism—which claim to support the mirror neuron idea—have really shown that the problem is in the mirror neurons themselves, rather than some other social process which controls the mirror neurons," she added. ■

Abnormal Brain Growth Starts Early in Autism, Then Slows

BY BETSY BATES
Los Angeles Bureau

STANFORD, CALIF. — Increasing evidence suggests that children with autism have a normal head circumference at birth, but that many develop macroencephaly in childhood, Dr. Antonio Y. Hardan said at a recent pediatric update sponsored by Stanford (Calif.) University.

Distinguishing features within the brain are evident in utero, with abnormal neuronal migration and a decrease in the size of the cerebellum seen in the first trimester.

Both findings have important implications for research into the causes, and one day perhaps the prevention, of autism.

The first suggestion of abnormal head circumference in children with autism appeared in 1943, with Dr. Leo Kanner's groundbreaking description of 11 children with what would come to be known as autistic features. He noted that five had "relatively large heads," and one had "markedly prominent" occipital and frontal regions.

Since the advent of modern neuroimaging techniques, nine studies have found increased brain size in individuals with autism, but four studies have had negative findings, said Dr. Hardan, director of the autism and developmental disabilities clinic at Stanford's Lucile Packard Children's Hospital. Recent work in Dr. Hardan's laboratory and other centers may explain this discrepancy.

One of the negative studies measured only brain area, not total volume, and two included mostly adults.

It has now become clear that changes occur over time.

Head circumference at birth is no different in children who go on to exhibit autism than in normal children, but during childhood, the total brain volume of autistic children is significantly larger than their age-matched peers. In adulthood, the brain size of individuals with autism appears to normalize or even atrophy slightly, but the head circumference in about 20%-30% of individuals with autism will remain larger than normal.

"The brain can shrink, but the cranial box cannot," Dr. Hardan noted.

A study at the University of Pittsburgh found that despite differences in early childhood, by age 12, brain volumes among children with autism were the same as in normally developing children, when controlled for height (Neurology 2002;59:175-83).

Research from the University of California, San Diego, found that patterns of brain growth were irregular in very young children with autism, with 2- and 3-year-olds possessing 39% more cerebellar white matter, 18% more cerebral white matter, and 12% more cerebral cortical gray matter than their peers, but with differences dissipating as the children grew older (Neurology 2001;57:245-54). Abnormally accelerated growth of some regions of the brain gave way over time to abnormally slowed brain growth.

Dr. Hardan's group has found that among children aged 8-12 with autism, compared with healthy controls, increases in gray matter volume and total brain size may be explained by marked increases in total sulcal and gyral thicknesses in the cerebrum and temporal and parietal lobes, but not in the frontal and occipital lobes.

Cortical thickness, striking in young children, also decreases over time, he said.

Importantly, cortical thickness abnormalities in autism can be distinguished from those in children with attention-deficit/hyperactivity disorder, which are thinner at baseline than in normal children and continue to decrease over time.

The specific patterns of cortical thickness abnormalities may offer important new clues as to the underlying defects in neural circuitry that may explain behavioral and social deficits in children with autism, he explained.

Dr. Hardan also underscored the importance of functional MRI imaging for children with autism, which is another new avenue of research into the neurobiology of autism.

Rather than looking at the brain itself, this approach studies cortical activation within the brain as children with autism are shown images of faces or objects. Unlike in normal children, the fusiform gyrus is activated when children with autism look at objects, not faces.

Related research has tracked the visual focus of very young children and demonstrated that those with autism focus on the chin or cheek of a human face, rather than the eyes, as is the case for normal subjects shown still images or movies. The same pattern has now been seen in how toddlers at high risk of developing autism focus on their mothers' faces, he said.

The technique might be used to intervene early with children at risk for autism, and also can be used to objectively measure improvement when medications or behavioral interventions are employed. ■