Inside the Autistic Brain

Scientists are getting down to gray matters concerning a tragic developmental disorder

By BRUCE BOWER

Childhood autism was first described in 1943, and since then it has been acknowledged as a devastating, lifelong disorder. Yet it is only in the last couple of years that researchers have uncovered clues to what distinguishes an autistic's brain from that of a normally developing person.

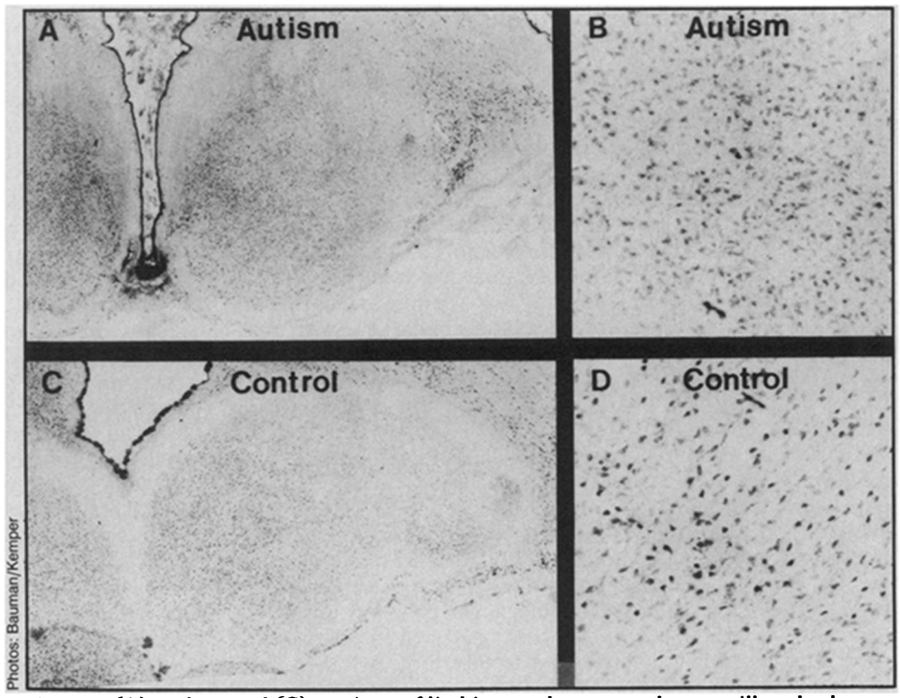
Some of the findings stem from a 10-year effort to obtain the brains of deceased autistics, conducted jointly by scientists at the University of California at Los Angeles and autism researchers affiliated with the National Society for Children and Adults With Autism in Washington, D.C. "This is the first systematic study of autistics' brains," says psychiatrist and project director Edward R. Ritvo of UCLA.

Studies of microscopic slices taken from throughout autistics' brains are also being conducted by neurologist Margaret Bauman of Massachusetts General Hospital in Boston and Thomas L. Kemper of Boston City Hospital.

The two research teams have noticed an intriguing abnormality in the brains of the small group of autistics they have examined: The cerebellum, a portion of the brain involved with muscle coordination and the regulation of incoming sensations, contains fewer neurons known as Purkinje cells. There are also preliminary indications that growth in parts of the limbic system, which oversees emotion and memory, is arrested while autistics are still in the womb.

The aim of the brain autopsy projects is to unravel the anatomy of a disorder that stunts critical aspects of development. Autistic youngsters look normal, but they never connect with the outside world mentally or socially, even as their bodies reach adulthood. Hallmarks of autism include few or no language and thinking skills, repetitive behavior such as rocking and abnormal responses to sensations, people, events and objects. In some cases, an autistic child will bang his head (the majority of children with this disorder are male) against a wall or attempt to hurt himself in other ways.

The cause — or causes — of autism remain unknown. As with other perplexing behavior and development problems, speculation and debate have revolved around the relative influence of "nature versus nurture." In the past decade, however, a consensus has emerged that autism results from biological and inborn factors (SN: 3/7/81, p. 154). Investigators have noted that many autistic children have seizures or unusual electrical activity on the brain surface. There are also isolated reports of abnormal brain-stem electrical responses, rapid eye movement sleep patterns and brain metabolism.



Autistic (A) and control (C) sections of limbic area known as the mamillary body. Magnifications in B and D show that autistic neurons are packed together more closely.

But autopsy studies of autistics' brains are rare and findings have been inconclusive. Obtaining the brain of a deceased autistic person for scientific study is no easy task; autistics have a normal life span, surviving relatives are often unaware of the few autopsy research efforts and the disorder is uncommon, affecting an estimated 5 of 10,000 persons. Until recently, the few brain autopsies that had been reported were conducted without the benefit of standard diagnostic guidelines for autism, which were established in 1980.

Now, in the July AMERICAN JOURNAL OF PSYCHIATRY, Ritvo and his co-workers present data from the first four autistic brains they obtained from subjects whose clinical records satisfied the new diagnostic criteria. They compared these brains with the brains of three controls who had been healthy at the time of death and one with brain damage due to an overdose of an anticonvulsant drug.

Autistic subjects ranged in age from 10 to 22 years old at death; comparison subjects were 3 to 13 years old. In two cases, autistics' deaths were accidental; another was a suicide and one was of undetermined cause.

Autistics' brains, say the researchers, displayed irregularities in the butterfly-shaped cerebellum, which is located at the back of the head below the cerebral hemi-

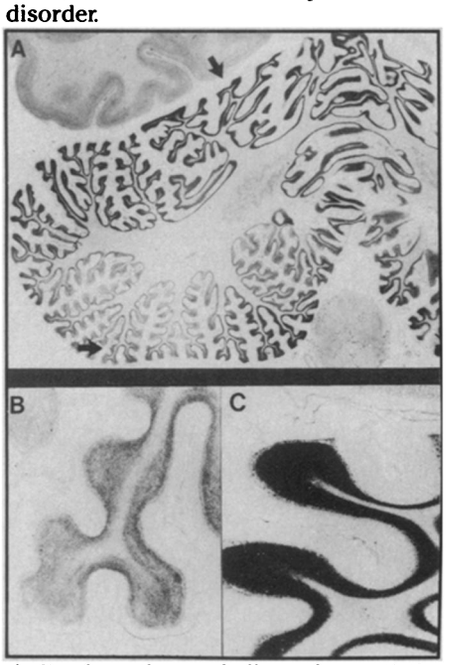
spheres. Random slices of the cerebellum were examined under the microscope and revealed significantly fewer Purkinje cells among autistics. These picturesque neurons, with elaborate branches of dendrites and long axons, extend from the cerebellum to inhibit the action of other brain cells.

Groups of Purkinje cells apparently release specific neurotransmitters that depress the firing of target neurons. The UCLA investigators did not identify the chemical messengers associated with the Purkinje cells they counted. Brain studies would need to be conducted almost immediately after death in order to track neurotransmitter activity, says Ritvo. So far, this has not been possible.

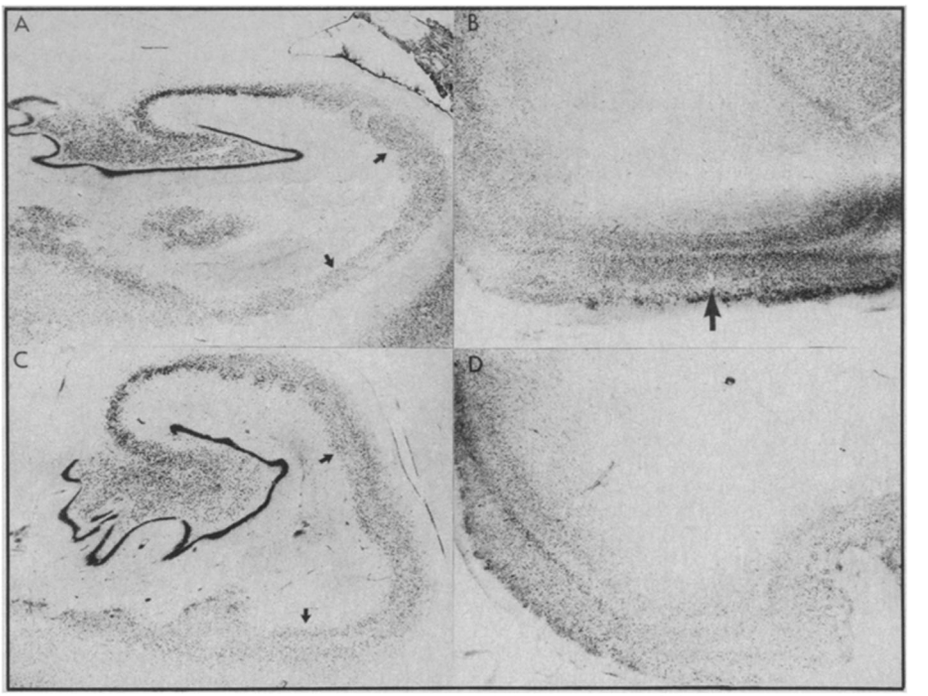
He suspects, however, that the neurotransmitter serotonin is an important player in some cases of autism. A multicenter study headed by Ritvo and reported in the April PSYCHOPHARMACOLOGY BULLETIN charted marked behavior improvements in about one-third of a large sample of autistic children treated with fenfluramine, a medication that lowers serotonin levels and has been used as a weight-control drug by adults (SN: 7/24/82, p. 54).

Ritvo adds that since the cerebellum regulates incoming sensations, its cellular quirks may account for sensory defects experienced by many autistics, such as insensitivity to pain or oversensitivity to sounds and textures.

"At this point," he says, "we don't know if we have the dog or the tail." Purkinje cells embedded in the cerebellum may cause autistic symptoms or, explains Ritvo, reflect a more widespread brain disorder.



A slice from the cerebellum of an autistic brain (A) reveals regions of atrophy (lower arrow) and intact areas (upper arrow). Magnification of an atrophied area (B) contrasts with an enlarged view of an unaffected area (C).



Sections from the hippocampus of an autistic (A) and control (C) brain show increased cell-packing density in the autistic section (see arrows). The entorhinal cortex of the autistic brain (B) contains a clear zone, indicated by the arrow, that is absent in the same area of the control brain (D).

Adds Mass General's Bauman, "We're very surprised at how devastated the cerebellum is in the two autistic brains we've studied. But a heck of a lot more than Purkinje cells are involved."

She and Kemper examined microscopic slices from throughout an autistic brain and a comparison brain, which they discuss in the June 1985 NEUROLOGY, and from the cerebellum of a second autistic brain. Bauman described the latter case, which is still under study, at a meeting of the American Academy of Neurology earlier this year.

Although both brains showed cerebellar damage, "the major role [in autism] may be played by the limbic system," says Bauman. There are preliminary reports, she adds, of cell pathways that connect limbic areas with the cerebellum.

Her initial study, in which the brain of a 29-year-old male autistic was compared with that of an age- and sex-matched control, uncovered marked abnormalities in the autistic's limbic structures, which are located deep within the brain's hemispheres and importantly influence emotions and behaviors. Cells were smaller and more closely packed together in several interrelated limbic regions, including the hippocampus, subiculum and entorhinal cortex.

There are several indications that changes in the autistic brain occurred before birth, notes Bauman. In a normal brain, neurons begin to push away from each other after birth as their cell bodies sprout more and longer dendrites, and glial cells – the "glue" that holds brain cells together – proliferate. This maturing process was cut short in the autistic subject. Furthermore, the autistic brain showed a clear zone between two cell layers in the entorhinal cortex, a characteristic that normally appears during the second trimester of fetal life and disappears by age 15 months. Finally, on the brain stem, an olive-shaped mass of cells that is anatomically connected to the Purkinje cells remained intact in the autistic brain; damage to the cerebellum after birth typically destroys these "olivary" neurons.

"I have no idea what causes these brain defects in a developing fetus," says Bauman. But it is significant, she explains, that the hippocampus and related parts of the brain are critical regulators of memory. Defects in storing and retrieving memories have been little studied among autistics and may, suggests Bauman, underlie difficulties in social interaction, language and learning.

Although the anatomic clues are tantalizing, both research teams acknowledge the need for a larger sample of autistic brains.

And even with larger autopsy studies, the ways in which the brain's billions of neurons work under the best of circumstances will remain, in many ways, a mystery. The cerebellum is a good example. "To be honest, we really don't know what the cerebellum does," says anatomist Arnold B. Scheibel of UCLA, a co-worker of Ritvo's who plans to study brain stem and hippocampal sections from the autistic brains. "But the horizons are rapidly becoming larger for what it is capable of doing." □