Anti-convulsant drugs: new research findings

Anticonvulsant drugs do not increase the incidence of behavior disorders, mental illness or personality disorders among mentally retarded individuals with epilepsy, according to Scottish researchers S. Deb and D. Hunter. In fact, they say, one seizure medication, carbamazepine (commonly known by its brand name Tegretol), "seems to have some protective effect against aggressive behavior" in these individuals.

Deb and Hunter studied 150 adult epileptic mentally retarded individuals and a control group of retarded individuals without epilepsy. Most of the subjects with epilepsy were receiving a single anticonvulsant.

Comparing the epileptic group to the non-epileptic group, Deb and Hunter found that "the epileptic group who received monopharmacy [a single medication] and particularly carbamazepine monopharmacy showed significantly less aggressive behavior compared to those who did not sustain epilepsy." The researchers say their findings "suggest that the new generation of anticonvulsants including carbamazepine has less effect on the mental state of individuals with epilepsy" than older drugs such as phenobarbital, which were linked to increased rates of psychopathology.

The researchers did find, however, that among the group taking carbamazepine, "personality disorder...was found to be more prevalent in the group in whom the serum level of carbamazepine was in excess of the local laboratory reference range."

New view about febrile seizures

A new study by Anne T. Berg and colleagues found that there is little value in prescribing long-term anticonvulsant drugs after a child suffers a febrile (fever-related) seizure—even if the child comes from a "high-risk" family with a history of epilepsy or developmental disorders.

Researchers have known for some time that the risk of developing epilepsy following a febrile seizure is slight. In an editorial accompanying Berg's report in the *New England Journal of Medicine*, John Freeman notes that "febrile seizures do not increase the risk of death, injury, mental retardation, or cerebral palsy . . . the only medical consequences of an initial febrile seizure are a greater chance of having further febrile seizures and a slight risk of later epilepsy (2% by seven years of age)."

Berg found that children of "at risk" families had no higher risk of recurrence of febrile seizures than other children. And while children with developmental disabilities have a high risk of developing epilepsy, Berg found no evidence that treating a first febrile seizure in these children was of any benefit.

Berg et al. did find that the strongest predictors of recurrence of febrile seizures were a shorter duration of fever prior to the seizure, and a lower temperature at the time the seizure occurred. Children whose first seizure occurred before they were 18 months old, and those with family histories of febrile seizures, were more likely to have recurrences.

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"The effect of anticonvulsant medication on the psychopathology of adults with a mental handicap and epilepsy," S. Deb and D. Hunter; *Human Psychopharmacology*, Vol. 7, 1992, pp. 129-134. Address: S. Deb, Dept. of Mental Health, University of Aberdeen, Woodlands Hospital, Cults, Aberdeen AB1 9PR, Scotland.

—and—

"A prospective study of recurrent febrile seizures," Anne T. Berg et al., *New England Journal of Medicine*, October 15, 1992. Address not given.

Fragile X/autism link questioned

Fragile X, a constriction on the X chromosome, is the most common form of inherited mental retardation in males—but is it associated with autism as well? Two new studies offer differing views on this controversial issue.

Fisch: link "unlikely"

Gene Fisch, who recently analyzed 19 studies of autistic males and 21 studies of mentally retarded males, reports that "epidemiological analyses fail to uncover any relative risk of autism associated with fragile X over and above that which is already associated with mental retardation." In other words, fragile X is linked with mental retardation—a common symptom of autism—but not with autism itself.

A 1991 study by Cohen et al. had suggested that fragile X and autism are related because the number of reported cases of the two disorders co-occurring was higher than would be predicted if they were independent. Stewart Einfeld and Wayne Hall say, however, that "such a relationship simply means that the fragile X syndrome is one of a long list that causes brain impairment with mental retardation, e.g., PKU, tuberous sclerosis, congenital rubella."

The researchers say that "the important issue is whether fragile X syndrome has any special predilection to cause autism," a question they say can only be answered by comparing the rate of autism among fragile X and non-fragile X individuals with mental retardation. Several such studies, they say, "have failed to find any association between autism and fragile X syndrome."

Reiss and Freund: autistic behaviors more common in Fragile X

Allan Reiss and Lisa Freund, on the other hand, compared retarded children with and without fragile X, and found that "fragile X males show increased dysfunction in peer social play, nonverbal communication (e.g., gaze aversion, gesturing), verbal communication...and repetitive motor behaviors (e.g., handflapping, rocking)." Fragile X children also were more likely to be oversensitive to sound, and to mouth or smell objects, than the control subjects.

The researchers say their study "supports the contention that fragile X males manifest a specific subset of behaviors from the autistic spectrum."

The continuing debate over a fragile X/autism link, they say, may be due to differing ideas about what constitutes autism. "If one believes that the core manifestations of autism must involve abnormalities in attachment behavior to caregivers or resistance to environmental change, few boys with fragile X will satisfy these criteria when evaluated," they say. "If one believes that...verbal and non-verbal communication abnormalities...are the cornerstone of the autistic syndrome, then many children with fragile X syndrome will be considered autistic."

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"Is autism associated with the Fragile X syndrome?," Gene S. Fisch; "Behavioral phenotype of Fragile X syndrome: DSM-III-R autistic behavior in male children," Allan L. Reiss and Lisa Freund; and "Behavior phenotype of the Fragile X syndrome" (editorial comment), Stewart Einfeld and Wayne Hall; all in *American Journal of Medical Genetics*, No. 43, 1992.

Brainstem defects

(continued)

Editor's note: When I began my research in the late 1950s into possible brain mechanisms underlying autism, it seemed to me the trail led to subcortical structures, especially to the brainstem, and, within the brainstem, to the brainstem reticular formation (BSRF). My book, *Infantile Autism: The Syndrome and its Implications for a Neural Theory of Behavior* (1964), explains why I believed the BSRF was important, and what functions I believed the BSRF performed. Needless to say, I find the research reported here especially interesting and gratifying.

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"Reduced brainstem size in children with autism," Toshiaki Hashimoto, Masanobu Tayama, Masahito Miyazaki, Noriko Sakurama, Tsutomu Yoshimoto, Kazuyoshi Murakawa, and Yasuhiro Kuroda; *Brain & Development*, Vol. 14, No. 2, 1992, pp. 94-97. Address: Toshiaki Hashimoto, Department of Pediatrics, University of Tokushima School of Medicine, Kuramoto-cho 3-18-15, Tokushima 770, Japan.

-and-

"Central conduction time in childhood autism," R. J. McClelland, D. G. Eyre, D. Watson, G. J. Calvert and Eileen Sherrard; *British Journal of Psychiatry*, 1992, 160, pp. 659-663. Address: R. J. McClelland, Department of Mental Health, The Whitla Medical Building, Queen's University, 97 Lisbum Road, Belfast BT9 7BL.

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