

## More interest in autism/seizure link

As interest in Landau-Kleffner syndrome continues to mount (see page 1), researchers are reporting cases of autism that appear to be linked to other forms of seizures. ARRI recently received two such reports, one from Switzerland and one from Sweden.

### Reversible autism due to seizures?

Swiss researcher Thierry Deonna and colleagues recently reported on a 28-month-old boy referred to their clinic for "severe fluctuating reversible behavioral regression of autistic type," which they believe was directly due to the boy's seizure disorder.

Although the child's parents were not aware that he was having seizures, Deonna et al. say, "an EEG showed very frequent generalized polyspike and spike-wave discharges followed by brief flattening, both during waking and sleep state on a disorganized slow wave background." The re-

searchers also observed seizures, consisting of head and shoulder spasms and sometimes laughter. Treatment with the anticonvulsant drug clonazepam, the researchers report, resulted in "immediate cessation of seizures and a marked rapid improvement in behavior, communication and language with disappearance of the autistic behavior."

Deonna et al. have followed the child up to the age of four, and report that he regressed on one other occasion—at which time an EEG again revealed abnormal activity. His medication was changed to carbamazepine, and they report that "he has had no new regression since then and he progresses in all domains without major behavioral problems."

The researchers report that they have seen one other child whose autistic

continued on page 7

## Surgery for LKS

(continued from page 1)

side of the brain. Two of the three surgical patients considered to be "failures" had seizures occurring independently in both brain hemispheres. (The other patient was found to have chronic encephalitis.) In addition, the physicians say, surgery candidates should have relatively intact non-linguistic cognitive capacities.

The researchers add that the surgery should be performed only on patients who have had no effective speech for at least two years. "We insisted upon this long duration of disease," they say, "because some cases have been reported in whom spontaneous remission has occurred within weeks or a few months of onset. If such rapid recovery does not occur, however, the ultimate prognosis appears quite dismal with respect to effective command of language."

The operation performed by Morrell et al. consists of severing substantial numbers of horizontal connections between neurons in the affected area. The technique is based on research showing that normal functioning of the cerebral cortex depends primarily on vertical connections between neurons, while abnormal discharges occur only when there are substantial horizontal connections between neurons. Morrell has compared the operation, which leaves brain functions virtually unimpaired, to "digging fire lanes" to stop a forest fire.

### What causes LKS?

One peculiar feature of LKS is that the seizures LKS victims suffer are relatively benign in and of themselves, and are easily controlled with drugs. Yet these seizures appear to be at the root of the children's severe symptoms, and when the seizures are stopped, either through surgical intervention or steroid treatment, other symptoms frequently disappear. In their new paper, Morrell et al. suggest an explanation for this mystery.

LKS, the researchers say, "develops during the period of life when the basic functional circuitry of speech is in process of establishment, i.e. 1-8 years of age." During this time, the brain initially "overwires" itself, establishing many more connections between cells than are normal for an adult brain. Later, the excess cell connections are "pruned."

Morrell et al. suggest that one effect of the seemingly benign seizures that occur in LKS is to disrupt this pruning process, and "thereby to perpetuate and sustain synaptic arrangements that are functionally inappropriate." Eventually, they say, these connections become permanent, and thus the cessation of seizures—which generally occurs during adolescence in LKS patients—does not reverse other symptoms because "the genetically determined 'window' for network establishment has ended."

"Landau-Kleffner syndrome: treatment with subpial intracortical transection," Frank Morrell et al.; *Brain*, 118, 1995, pp. 1529-1546. Address: Frank Morrell, Rush-Presbyterian-St. Luke's Medical Center, 1653 W. Congress Parkway, Chicago, IL 60612.

## CHAT passes large-scale U.K. test

The most effective treatment currently available for autism is early educational intervention, beginning as soon as possible after a child's diagnosis. Unfortunately, intervention rarely begins before the age of three, because few autistic children are diagnosed before they reach preschool age.

English researchers say, however, that a diagnostic test called the CHAT (Checklist for Autism in Toddlers) may offer physicians a means of diagnosing autism in infancy, so that educational programs can be started months or even years before most symptoms become obvious. The test, first developed and tested in 1992 (see ARRI 7/1), recently underwent a large-scale evaluation, and appears to have passed with flying colors.

Simon Baron-Cohen and colleagues, who developed the CHAT, recently obtained data

—"Gaze monitoring," or turning to look in the same direction as an adult is looking.

—pretend play.

In the current study, twelve children tested by doctors or health care workers consistently failed all three of these items. The researchers later examined these children extensively, and concluded that ten of them were autistic. "When the 10 children with autism were reassessed at 3.5 years of age," the researchers say, "their diagnosis remained the same." Furthermore, Baron-Cohen et al. note, "the two cases in the autism risk group who did not receive a diagnosis of autism nevertheless received a diagnosis of developmental delay. Thus, the false positive rate for detection of autism [using the CHAT] is 16.6%, but even these cases are not normal."

Twenty-two additional children failed the CHAT's "protodeclarative pointing" and/or "pretend play" questions, but passed the "gaze monitoring" section. None of these children received a diagnosis of autism, but 15 were diagnosed as having language delays.

The researchers conclude that "consistent failure of the three key items from the CHAT at 18 months of age carries an 83.3% risk of autism, and this pattern of risk indicator is specific to autism when compared to other forms of developmental delay." They add, "We stress that the CHAT should not be used as a diagnostic instrument, but it can alert the primary health professional to the need for an expert... referral."

Baron-Cohen et al. say the next step in testing the CHAT will be to determine the rate of "false negatives"—that is, the number of autistic children missed by the test.

"Psychological markers in the detection of autism in infancy in a large population," Simon Baron-Cohen, Antony Cox, Gillian Baird, John Swettenham, Natasha Nightingale, Kate Morgan, Auriol Drew and Tony Charman; *British Journal of Psychiatry*, 1996, 168, pp. 158-163. Address: S. Baron-Cohen, Univ. of Cambridge, Dept. of Exp. Psychology, Downing Street, Cambridge CB2, 3EB, U.K.

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on 16,000 children in southeast England who were screened for autism at the age of 18 months by physicians or health care workers using the test. Earlier research had suggested that children who failed three items on the CHAT were at high risk of being autistic. The items include:

—"Protodeclarative pointing," or pointing at an object in order to direct another person's attention to it—not to obtain the item, but simply to share an interest in it.