Biomedical update:

Drugs and the elderly with autism

Elderly people with autism often receive drugs to control their behavior problems—but M. G. Aman warns physicians to use extra caution when giving drugs to older developmentally disabled patients.

Aman notes that:

1. Elderly individuals' capacity to metabolize drugs and eliminate them from the body is reduced, which can cause toxicity at lower doses than in younger people. "In most but not all cases," Aman says, the effect of aging is "a more potent or longer lasting response to psychotropic drugs."

2. The elderly are at greater risk for developing tardive dyskinesia (involuntary muscle movements caused by chronic exposure to antipsychotic drugs). One study by Toenniessen et al., Aman says, revealed that "the probability of developing tardive dyskinesia in the elderly who receive neuroleptic drugs is approximately 50%, and, furthermore, that within this group tardive dyskinesia is likely to occur within two years."

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"Considerations in the use of psychotropic drugs in elderly mentally retarded persons," M. G. Aman; *Journal of Mental Deficiency Research*, 1990, 34, pp. 1-10. Address: Michael G. Aman, The Nisonger Center, Ohio State University, 1581 Dodd Drive, Columbus, OH 43210-1205.

Autism and attention

Eric Courchesne and colleagues are conducting brainwave studies in an attempt to zero in on the specific attention deficits that may underlie autistic individuals' unique behavior and learning problems.

In a recent study, the researchers found that autistic subjects did well at tasks requiring *sustained* attention (such as pushing a button when an unusual colored slide or tone was detected, while ignoring other stimuli). But when asked to switch attention back and forth between visual stimuli (colored slides) and auditory stimuli (tones), the researchers say, "the autistic subjects had many false alarms and misses within several seconds following a cue to shift attention."

During the tests, the researchers measured participants' *event-related potentials* (ERPs)—patterns of brainwaves that occur in response to stimulation such as lights or sounds. When people in the control group shifted their attention, a normal brainwave response (called the "P700") appeared. In autistic participants—even those with the best performance on the attention-shifting test—this brainwave, seen primarily over the parietal area of the brain, was much smaller than in the non-disabled controls.

In another study by Courchesne et al., the researchers asked subjects to attend selectively to either a rare tone or a rare color. They say the ERP readings obtained during this study were "remarkable": autistic participants completely lacked certain brainwave patterns normally seen in the frontal cortex of the brain during periods of selective attention, and another attention-related brainwave, the P3b, was greatly diminished. Since even the autistic subjects who performed as well as normal controls lacked the brainwave patterns thought to be necessary for such attention, the researchers say that autistic individuals may be using a totally different selective-attention mechanism than non-disabled people use.

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Shifting attention abnormalities in autism: ERP and performance evidence," E. Courchesne, N. A. Akshoomoff, and K. T. Ciesielski; pres. to the Int. Neuropsychol. Soc. meeting, Orlando, FL, Feb. 14-17, 1990; and "Effects of focused selective attention tasks on event-related potentials in autistic and normal individuals," K. T. Ciesielski, E. Courchesne, and R. Elmasian; *Electroenceph. and Clin. Neurophys.*, 1990, 75: 207-220. Address: Eric Courchesne, Neuropsychology Research Lab., Children's Hospital Research Center, 8001 Frost Street, San Diego, CA 92123.

Fingerprints offer clues

Fingerprints are one of the many physical clues studied by researchers investigating the causes of autism.

Dermatoglyphics is the study of the patterns of ridges on the fingers, palms, toes and soles of the feet. Abnormal patterns (such as the well-known 'simian creases' on the palms of children with Down syndrome) can indicate the presence of genetic defects, and help determine the roles that genes and environment play in causing disorders.

In Spain, M I. Arrieta and colleagues compared the finger and palm patterns of 60 autistic Basque children without known genetic defects to those of non-disabled controls of the same ethnic background.

The researchers found significant differences between the palms of autistic and non-disabled girls, although fingerprints were comparable. The reverse was true for autistic boys, whose fingerprints were significantly different from those of controls, but whose palm patterns were close to normal. (Autistic children of both sexes had more abnormal palm creases than controls.)

While the traits the researchers studied appear to have a strong genetic basis, it is possible that prenatal environment has an effect as well; for instance, they note, the differences between autistic boys and girls are interesting because palm and finger patterns do not appear to be sex-linked genetic traits.

Arrieta et al. say their findings "do not contradict the hypothesis that genetic factors may be important" in autism; but they add that no consistent pattern was seen in autistic subjects, adding weight to the prevailing idea that autism may have various causes.

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"Dermatoglyphic analysis of autistic Basque children," M. I. Arrieta, B. Martinez, B. Criado, A. Simón, L. Salazar, and C. M. Lostao; *Am. J. of Med. Genetics*, 35, pp. 1-9, 1990. Address: Maria Isabel Arrieta, Universidad del Pais Vasco, Facultad de Ciencias, Dpto. De Biologia Animal y Genetica, Apdo. 644-48080 Bilbao, Spain.

Fenfluramine, B6: brainwave tests indicate different effects

About 45% of autistic children improve when given high doses of vitamin B6 and magnesium, while about 30% improve when given the drug fenfluramine. French researchers J. Martineau et al. report, however, that the mechanisms of the two treatments appear to be different.

Martineau and colleagues measured brainwave readings of six children who benefitted from B6/magnesium and six who benefitted from fenfluramine. They found evidence that B6/magnesium treatment helps improve autistic children's impaired ability to form associations between visual and auditory (or auditory and tactile) stimuli.

While improvement on B6/magnesium was "global," they say, "improvement . . . was particularly evident for behaviors which can be grouped together under the functional term "association"—inappropriate/ritualistic treatment of inanimate objects, no attempt to control bowel or bladder function, and disordered eating behavior. Other improvements can occur in the larger associative process of relating to other people."

Fenfluramine, they say, appears to help normalize attentional mechanisms; this, they say, "can be related to data showing that fenfluramine produces an improvement in attention and a reduction in motility disorders, anxiety and mood disturbances."

The fenfluramine responders and B6 responders had significantly different brainwave patterns before treatment, indicating that the two treatments may benefit different subgroups of autistic children.

Neurotoxic effects of fenfluramine noted

Meanwhile, a new study by researchers at Johns Hopkins Medical School adds to previous cautions about fenfluramine's possible harm to brain cells.

Derek and Mark Molliver found that the axons of rat brain cells which synthesize and use the brain chemical serotonin were "swollen and fragmented" 36 hours after injection of fenfluramine; this, they say, "is indicative of axonal degeneration, and provides . . . evidence for a neurotoxic effect of . . . fenfluramine upon 5-HT axon terminals."

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"Electrophysiological effects of fenfluramine or combined vitamin B6 and magnesium on children with autistic behavior," J. Martineau, C. Barthelemy, S. Roux, B. Garreau, and G. Lelord; *Developmental Medicine and Child Neurology*, 1989, 31, 728-736. Address: J. Martineau, INSERM U 316, CHU Bretonneau, F-37044 Tours Cedex, France.

—and—

"Anatom. evidence for a neurotoxic effect of (+/-) fenfluramine upon serotonergic projections in the rat," Derek C. and Mark E. Molliver; *Brain Research*, 511, 1990, pp. 165-168. Address: M. E. Molliver, Department of Neuroscience, The Johns Hopkins University, School of Medicine, 725 N. Wolfe Street, Baltimore, MD 21205.