

Biomedical Update:

Can Pepcid reduce autistic symptoms?

It seems like a bizarre idea: using an over-the-counter heartburn medication to reduce autistic symptoms. But pediatrician L. A. Linday suggests that it might be a safe and effective alternative to existing drugs.

Although no researchers have studied the use of Pepcid for autism, Linday notes that several studies have found that Pepcid reduces "negative" symptoms (including "flat" affect, poor eye contact, social withdrawal, and impoverished speech) in schizophrenic patients. (The drug does not appear to affect "positive" symptoms, such as hallucinations and delusions.) Among the studies:

—R. Kaminsky et al. reported on one patient with a 15-year history of schizophrenia who improved dramatically when placed on Pepcid for an ulcer. When the ulcer treatment was discontinued, the man's negative symptoms returned. Reinstatement of Pepcid again led to a decrease in symptoms.

—In a subsequent study, Kaminsky tested Pepcid on three schizophrenic adults and reported that all showed significant decreases in negative symptoms.

—L. K. Oyewumi et al. reported that 7 of 12 treatment-resistant psychotic patients improved markedly when their medications were augmented with Pepcid.

—R. Rosse et al. reported that Pepcid added to a treatment-resistant schizophrenic patient's other medication led to significant clinical improvement.

Dosages of Pepcid in these studies, which all involved adults, ranged from 40 to 100 mg per day. Noting that children metabolize drugs more quickly than adults, Linday suggests that high doses might be necessary in children. Although Pepcid is not approved for use by children, Linday notes that it appears to be much safer than standard psychotropic drugs; in clinical trials, she says, subjects taking the drug reported no more side effects than subjects taking a placebo.

Linday believes that Pepcid may have the same effects on autistic individuals as on schizophrenics. She notes that "an analogy can be drawn between the deficit (or negative) symptoms of schizophrenia and the social deficit symptoms of autism, such as poor eye contact and social withdrawal." Furthermore, she notes, the cerebellar defects reported in autistic individuals are also seen in adults with schizophrenia, and many drugs that ameliorate some symptoms of autism (for instance, haloperidol and risperidone) also are effective in treating schizophrenics.

Pepcid, generally used to treat digestive disorders and ulcers, works by blocking histamine-2 receptors.

Linday says "there is substantial evidence that histamine serves as a neurotransmitter and neuromodulator in the brain," and primarily inhibits activity. Thus, she says, there is "[a] theoretical basis for postulating that overactivity of H2 receptors could contribute to the deficit symptoms of schizophrenia" as well as autism.

Editor's note: We are interested in hearing from parents or physicians who try this treatment on autistic patients.

"Oral famotidine: a potential treatment for children with autism," L. A. Linday, *Medical Hypotheses*, Vol. 48, 1997, pp. 381-386. Address: Linda A. Linday, 340 West 55th Street, Suite 9A, New York, NY 10019.

Study points to peptides

Autism is considered a brain disorder, but could it also be—at least in part—an intestinal disorder? Much evidence suggests that autistic symptoms can result when certain peptides (protein fragments), particularly from milk and from grains containing gluten, escape the digestive tract without being broken down properly. These peptides, which have opium-like brain-altering properties, may then reach the brain and cause behavioral disturbances.

Recently, P. D'Eufemia and colleagues published research strongly supporting this concept. D'Eufemia et al. tested 21 autistic children with no known intestinal disorders, comparing them to 40 healthy, age-matched children. None of the subjects were taking drugs that affect intestinal function.

"An altered intestinal permeability was found in 9 of the 21 autistic patients," D'Eufemia et al. say, "but in none of the 40 controls." They conclude that "an altered intestinal permeability could represent a possible mechanism for the increased passage through the gut mucosa of peptides derived from foods with subsequent behavioral abnormalities."

"Abnormal intestinal permeability in children with autism," P. D'Eufemia, M. Celli, R. Finocchiaro, L. Pacifico, L. Viozzi, M. Zaccagnini, E. Cardi, and O. Giardini; *Acta Paediatrica*, 85, 1996, pp. 1076-1079. Address: P. D'Eufemia, Institute of Pediatrics, "La Sapienza" Univ. of Rome, Viale Regina Elena, 324, I-00161 Rome, Italy.

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Autism, epilepsy: early evaluation is critical

In children with epilepsy, B. G. Neville et al. state in a new report, "autistic regression should prompt urgent investigation if drug treatment is not effective."

Neville et al. report on two cases in which surgery partially ameliorated social and language regression in children with epilepsy:

—One child, who had seizures starting at two weeks of age, had a temporal lobe tumor. Surgery, when the child was 12 months old, eliminated the seizures and also led to improvement in autistic symptoms.

—Another child developed epilepsy at age three and became aphasic at age five, regressing socially and "manifesting a very severe behavior disorder." After surgery (a multiple subpial transection), the researchers say, the boy "exhibited a significant improvement in communication, social functioning, and behavior."

The researchers say both children exhibited subclinical temporal lobe seizures, and the second child showed symptoms consistent with Landau-Kleffner syndrome (LKS) (see ARRI 10/2, 9/4, 9/2). LKS, once considered extremely rare, is increasingly being diagnosed and surgically treated in children with autistic symptoms. Symptoms include:

- normal development and age-appropriate speech for the child's first 3 to 7 years.
- loss of receptive language, followed by loss of expressive speech (aphasia).
- "telegraphic" speech with few verbs.
- remissions followed by deterioration.
- autistic symptoms including "flat" voice, rituals, hyperactivity, and aggression.

LKS is diagnosed using a specialized sleep EEG. Children with the disorder exhibit a bilateral spike-wave disturbance, focused in the posterior temporal regions of the brain and almost continuous during some stages of sleep. Seizures are often subclinical, and detectable only through this type of EEG.

Frank Morrell and colleagues, who pioneered surgery for LKS (see ARRI 10/2, 5/1), also stress the need for early intervention, noting that the disorder develops at the time speech circuitry is being established in the brain. The seizures associated with LKS, they say, may permanently disrupt this circuitry if the disorder is not corrected early enough.

"Surgical treatment of severe autistic regression in childhood epilepsy," B. G. Neville, W. F. Harkness, J. H. Cross, H. C. Cass, V. C. Burch, J. A. Lees, and D. C. Taylor; *Pediatric Neurology*, Vol. 16, No. 2, Feb. 1997, pp. 137-140. Address: B. G. Neville, Neurosciences Unit, Institute of Child Health, London, U.K.