Secretin's role in amygdala, cerebellum revealed

(continued from page 1)

istering the hormone to rats influenced the function of the amygdala. Using levels of c-Fos protein as a marker of amygdala activation, the researchers found that protein expression increased significantly in the central amygdala and slightly in another area after secretin treatment. Activation of neurons in the amygdala, they say, "may facilitate improvement and development of social behavior in autistic individuals."

Researcher Walter Herlihy says, "Our Phase 2 clinical trial established that secretin can improve the social deficits in young children with autism. Our finding that secretin activates the amygdala in animals may provide a neurobiological mechanism for the action of secretin."

Repligen, which manufactures synthetic human secretin, is participating in brain-imaging experiments to investigate whether secretin injections activate the amygdala in human subjects.

Is secretin a neuropeptide?

In related research, Billy K.C. Chow and colleagues report data from rat studies showing that both secretin and secretin receptors (which recognize and utilize secretin) are active in the cerebellum.

The researchers say secretin appears to modulate the activity of GABA, a neurotransmitter, in the cerebellum. "These novel actions of secretin, which are distinct from those on the endocrine system, strongly support the hypothesis that secretin serves as a neuropeptide in the rat brain," the researchers say.

Chow et al. theorize that Purkinje cells in the cerebellum release secretin to stabilize

continued on page 6

Amantadine study: only modest effects detected

The drug amantadine hydrochloride (Symmetrel) may have modest beneficial effects on the hyperactivity and inappropriate speech of autistic children, according to a double-blind, placebo-controlled study by Bryan King and colleagues.

Amantadine is an anti-viral drug often prescribed for the treatment or prevention of flu. In addition, the drug is used to treat Parkinson's disease, and is being tested as a treatment for depression, hyperactivity, and other psychiatric disorders.

King and colleagues administered amantadine to 19 children between the ages of 5 and 19, giving a placebo to 20 matched controls. Treatment lasted for four weeks, with subjects receiving 2.5 mg/kg per day for the first week, and 5 mg/kg per day (in two doses) during the remainder of the study.

The researchers say that parent ratings failed to show a significant effect of amantadine, although 47 percent of children were rated as responders compared to 37 percent on the placebo. Clinical ratings by the researchers showed statistically significant improvement in inappropriate speech and hyperactive behavior. Children taking the drug did not experience more side effects than those on the placebo in this study, although amantadine side effects reported by other researchers include hallucinations, insomnia, tremors, confusion, poor concentration, depression, and orthostatic hypotension (a significant drop in blood pressure upon standing).

King et al. suggest that amantadine's effects may be due to its effects on the NMDA subclass of glutamatergic receptors. "Areas of the brain found to exhibit cellular abnormalities associated with autism," they note, "show a high degree of NMDA binding sites." The drug also affects dopamine function in the brain.

An earlier study by a different group of researchers suggested that amantadine may sometimes influence behavioral symptoms through its anti-viral effects. Several years ago, Liv Bode and colleagues reported findings linking some cases of depression to Borna virus (see ARRI 10/3). Testing amantadine's effects on 30 depressed subjects with identified Borna infections, the researchers detected a "significant antidepressive response" in 19 of them. Responders also showed significant reductions in their infections.

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Double-blind, placebo-controlled study of amantadine hydrochloride in the treatment of children with autistic disorder," Bryan H. King, Mark Wright, Benjamin L. Handen, Linmarie Sikich, Andrew W. Zimmerman, William McMahon, Erin Cantwell, Pablo A. Davanzo, Colin T. Dourish, Elisabeth M. Dykens, Stephen R. Hooper, Catherine A. Jaselskis, Bennett L. Levanthal, Jennifer Levitt, Catherine Lord, Martin J. Lubetsky, Scott M. Myers, Sally Ozonoff, Bhavik G. Shah, Michael Snape, Elisa W. Shernoff, Kwanna Williamson, and Edwin H. Cook, Jr., *Journal of the American Academy of Child and Adolescent Psychiatry*, Vol. 40, 2001, 658-65. Address: Bryan King, Department of Psychiatry, Dartmouth-Hitchcock Medical Center, One Medical Center Drive, Lebanon, NH 03756-0001.

—and—

"Amantadine revisited: an open trial of amantadinesulfate treatment in chronically depressed patients with Borna disease virus infection," R. Ferszt, K. P. Kuhl, L. Bode, E. W. Severus, B. Winzer, A. Berghofer, G. Beelitz, B. Brodhun, B. Muller-Oerlinghausen, and H. Ludwig, *Pharmacopsychiatry*, Vol. 32, No. 4, July 1999, 142-7. Address: R. Ferszt, Dept. of Gerontopsychiatry, Freie Universitat Berlin, Germany.

New study supports link between autism, intestinal disorders

A Harvard researcher's new findings support the research of Andrew Wakefield, the physician who first reported the presence of chronic intestinal tract inflammation in many autistic children (see ARRI 12/1, 1998). Wakefield was recently removed from his position at Royal Free and University College Medical School, after linking the digestive system abnormalities that he detected in many autistic children to MMR vaccinations (see related article on page 1 of this issue).

Timothy Buie says biopsy results showed the presence of abnormalities including esophagitis, gastritis, and entercolitis, as well as lymphoid nodular hyperplasia in 15 of 89 autistic children studied.

The study also revealed that many of the children suffered from deficiencies of lactase (needed to break down the lactose in milk) and sucrase (needed to digest table sugar), a finding that may explain why many autistic children improve dramatically on diets that eliminate these foods. In addition, the researchers found that the children had low disaccharide/glucoamylase enzyme levels, supporting findings that digestive enzyme supplements benefit many autistic children.

Buie concludes, "These children are ill, in distress and pain, and not just mentally, neurologically dysfunctional."

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Buie's research was reported at the Oasis 2001 Conference for Autism, Portland Oregon, November 2001. Dr. Buie and Dr. Wakefield will speak at the May 2 DAN! Conference.

SCHOOLS AND SERVICES LIST

The Autism Research Institute maintains a list of schools and services for autistic individuals. If your facility should be included on our list, and you believe it may not be, please send a self-addressed, stamped envelope to receive our referral list questionnaire.

ARI also maintains a list of physicians who are interested in the DAN! approach to diagnosis and treatment, and who use drugs only as a last resort. If you are a physician who wishes to be considered for that list, send a self-addressed, stamped envelope with a request for our "Doctor Referral List Questionnaire."