Secretin activates amygdala, affects glutamate and GABA levels in hippocampus

One new study reports that a "tremendous" increase in activity occurs in a brain region called the amygdala in response to intravenous infusions of the hormone secretin, while another study in turn adds to evidence linking damage or dysfunction of the amygdala to autism—and a third shows that secretin alters amino acid concentrations in the hippocampus

Staci Gruber and colleagues injected 12 normal adult males with secretin or a placebo, and then showed them images of happy, fearful, and neutral faces. The researchers say MRI scans conducted during the experiment revealed that secretin "alters amygdala responsiveness to affective stimuli," and also activates the prefrontal cortex, fusiform gyrus, and cerebellum. (Defects of the cerebellum are a common finding in autism, and lack of normal activation of the fusiform gyrus is linked to the inability of autistic individuals to process facial features normally.)

The MRI findings of Gruber and colleagues validate early findings reported in 2002 by Deborah Yurgelun-Todd et al., who discovered that secretin is a neuroactive peptide in humans, and increases activity in the amygdala. At that time, Walter Herlihy, CEO of Repligen, the firm that holds the relevant patent rights, stated, "These studies show that secretin is active in a part of the human brain involved in social interaction and potentiates its activity during a social task known to be difficult for people with autism."

The finding that secretin activates the amygdala is particularly interesting in light of new research by Philip Shaw and colleagues, linking early amygdala damage to difficulties in "theory of mind"—that is, the ability to understand that other people have thoughts and feelings. Impaired theory of mind is considered to be a key element underlying autistic social difficulties.

Shaw et al. compared subjects who had suffered early amygdala lesions to those who suffered similar damage in adulthood, comparing both groups to controls on 'theory of mind' tasks. The adult subjects with amygdala damage showed no deficits, while those whose damage occurred in childhood—and especially those with seizures—showed deficits that "encompassed the understanding of both the beliefs and emotional states of others." This was true whether subjects had right- or left-sided amygdala damage.

Additional evidence of amygdala abnormalities in autism comes from a study by C. M. Schumann and colleagues, who recently reported that in autistic children, both right and left amygdala volumes are abnormally large—a finding not seen in autistic adolescents. Noting that the amygdala normally increases in size between childhood and late adolescence, the researchers say, their findings "indicate an abnormal program of early amygdala development in autism."

In another recent study, A. Kuntz and colleagues found that following secretin injections, rats show a considerable increase in extracellular glutamate and gamma-aminobutyric acid (GABA) levels. Noting that

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Major health groups cite antipsychotic dangers

Four major health organizations have issued a consensus statement cautioning doctors that newer antipsychotic drugs put users at significant risk for diabetes and related metabolic disorders, and urging physicians to carefully assess and monitor patients taking these drugs.

The American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, and North American Association for the Study of Obesity singled out two of these drugs in particular, saying, "Despite limitations in study design, the data consistently show an increased risk for diabetes in patients treated with clozapine (Clozaril) or olanzapine (Zyprexa) compared with patients not receiving treatment with first-generation antipsychotics or other second-generation antipsychotics." They noted, however, that there also is some evidence implicating risperidone (Risperdal) and quetiapine (Seroquel) as contributors to diabetes. Two newer antipsychotic drugs, ziprasidone (Geodon) and aripiprazole (Abilify), were not linked to metabolic problems, although the panel noted that the drugs are too new for sufficient epidemiological data to be available.

The panel concluded that "the data consistently show an increased risk for diabetes in patients treated with clozapine (Clozaril) or olanzapine (Zyprexa) compared with patients not receiving treatment with first-generation antipsychotics or other second-generation antipsychotics."

The consensus statement also urges doctors to educate patients about the symptoms of diabetic ketoacidosis, a potentially deadly condition that can be caused by the use of newer atypical antipsychotics. These symptoms include confusion, rapid breathing, dehydration, excessive water drinking, excessive urination, nausea, vomiting, and weight loss.

While the panel came to its conclusions after hearing presentations from 14 experts as well as representatives from pharmaceutical companies and the FDA, and after reviewing the medical literature pertaining to antipsychotics and metabolic disorders, the consensus report was challenged by Eli Lilly, the makers of Zyprexa, who called the panel's conclusions "controversial."

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"Consensus development conference on antipsychotic drugs and obesity and diabetes," Consensus Statement, February 2004, available at http://care.diabetesjournals.org.

—and—

"Antipsychotics' diabetes risk prompts call for better assessment," Jim Rosack, *Psychiatric News*, Vol. 39, No. 5, March 5, 2004.

SCHOOLS AND SERVICES: 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.

Risperdal causes rapid weight gain in autistic children, teens

A new study confirms prior reports that large weight gains are common in autistic children and adolescents treated with risperidone (Risperdal).

A. Martin and colleagues measured the weight of 63 autistic children and teens during six months of risperidone therapy, also measuring levels of serum leptin (a hormone that affects metabolism and hunger) after the first two months to see if leptin level changes predicted weight gain.

The researchers say subjects gained an average of 5.6 kilograms (12.3 pounds) during the study. Changes in leptin levels did not predict which subjects would gain large amounts of weight.

UPDATE: The manufacturer of Risperdal, Janssen Pharmaceutica Products, has just sent a letter to physicians admitting that it has minimized the safety risks of the drug (including strokes, diabetes, and other potentially fatal complications) and made misleading claims about its effectiveness.

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"Weight and leptin changes among risperidone-treated youth with autism: 6-month prospective data," A. Martin, L. Scahill et al., *American Journal of Psychiatry*, Vol. 161, No. 6, June 1, 2004, 1125-7. Address not listed.