Biomedical Update:

Risperidone reduces Tourette's symptoms

ARRI recently reported on a small study showing that risperidone, a drug commonly used to treat schizophrenia, may reduce the symptoms of pervasive developmental disorder (ARRI 8/4). Now researchers report that the drug may also be useful in treating Tourette's syndrome (a condition sometimes associated with autism) and other tic disorders, in cases where other drugs fail.

Paul Lombroso and colleagues studied the effects of risperidone on seven children (five boys and two girls). Five of the children had Tourette's, and two had chronic motor tic disorders. Three of the children were also diagnosed as having obsessive-compulsive disorder (OCD). All of the subjects had tics which had not responded to other drugs commonly used to treat tic disorders.

The researchers report that after 11 weeks of risperidone treatment, "all subjects showed improvement in tic severity ranging from 18% to 66%." One of the three subjects with a dual diagnosis of Tourette's and OCD also showed a significant reduction in obsessive-compulsive symptoms.

In addition, the researchers note, few side effects were noted. Four subjects complained of temporary tiredness, one experienced visual sensitivity to sunlight, and all gained weight, but the only significant side effects (muscle stiffness and dystonia) occurred in two children also taking the drug paroxetine. "Given that both of these medications are metabolized by the same degradation pathway in the liver," the researchers say, "the effective dose of risperidone may have been elevated" in these children.

Lombroso et al. caution that their study did not use controls and was not "blind"—that is, researchers, subjects, and subjects' parents were aware that the children were taking the drug. They also note that several subjects were taking other medications, and that beneficial effects might have been caused by the interaction of these drugs with risperidone. They add, however, that their data are consistent with those of a 1994 study by C. van der Linden et al., who found that the frequency and severity of tics decreased markedly in 9 of 11 adults treated with risperidone.

Lombroso et al. note that risperidone appears to have fewer dangerous side effects than Haldol and other neuroleptic drugs used to treat tic disorders. In addition, risperidone reduced symptoms in some subjects for whom clonidine—a drug sometimes used for Tourette's because of its relative safety—was not effective. The researchers suggest increasing the dosage of risperidone gradually, to reduce the chance of adverse effects.

While a number of studies suggest that risperidone is safer than many other psychotropic drugs, subjects in these studies have reported side effects including menstrual irregularities, breast enlargement in males, heart palpitations, constipation, fatigue, low blood pressure, and mild dizziness. Weight gain, such as that experienced by Lombroso et al.'s subjects, also appears to be common. At high doses, the drug can cause muscle stiffness and body shakes, but these symptoms are less common than with Haldol. To ARRI's knowledge, the drug is not approved for general use with children.

Editor's Note: we have heard very little about this drug from parents, but we have received one anecdotal report from a father whose son experienced severe side effects.

—

"Risperidone treatment of children and adolescents with chronic tic disorders: a preliminary report," Paul J. Lombroso, Lawrence Scahill, Robert A. King, Kimberly A. Lynch, Phillip B. Chappell, Bradley S. Peterson, Christopher J. McDougle, and James F. Leckman; *Journal of the Am. Academy of Child and Adolescent Psychiatry*, Vol. 34, No. 9, Sept. 1995, pp. 1147-1152.

Debate escalates over desipramine

The controversy over the use of the drug desipramine continues to grow, with one physician calling for an end to its use for children.

Desipramine has been used to treat children with autism, obsessive-compulsive disorder, hyperactivity, and other brain disorders. However, reports of sudden death in children taking the drug have led to a reexamination of its benefits and risks. ARRI 9/3 summarized an article by Yona Amitai et al., calling on doctors to reduce dosages of the drug, and ARRI 8/4 noted warnings by Mark Riddle et al. about the drug's danger to patients with family histories of cardiac disorders. But New Zealand psychiatrist John Werry has now gone further, saying that "...pharmacological and toxicological data, pragmatic and ethical considerations suggest that desipramine should no longer be used clinically in children" except in carefully monitored research studies.

Werry notes that desipramine has been shown to be two to four times more toxic than other tricyclic antidepressants such as imipramine, and says that "there are equally effective, less opprobrious alternatives" such as fluoxetine and monoamine oxidase A inhibitors.

"Desipramine merely ameliorates to a variable, though valuable, degree," he concludes. "It does not cure any of the disorders in children for which it is prescribed. It is most unlikely that its action could ever be described as truly life-saving. This makes the threat to life that it poses unacceptable."

—

"Resolved: cardiac arrythmias make desipramine an unacceptable choice in children," John Werry, *Journal of the American Academy of Child and Adolescent Psychiatry*, Vol. 34, No. 9, September 1995, pp. 1239-1241.

Is contraceptive drug neurotoxic?

Many parents of autistic and other developmentally disabled girls have opted, when their daughters reach puberty or adulthood, to have them receive Norplant contraceptive implants. Norplant, which is implanted under the skin of the arm, releases synthetic progesterone over a five-year span—meaning that an autistic girl or woman can be protected from unwanted pregnancy for years without the need for daily birth control pills.

This convenience, however, may be outweighed by the problems Norplant can cause. A number of studies indicate that the drug can cause side effects including abnormally heavy menstrual bleeding, migraine headaches, and nausea. Now neurologist Alan R. Hirsh reports that the drug may also be neurotoxic—that is, harmful to brain cells.

Hirsh carefully examined five young nondisabled women who developed neurological symptoms, including headaches, dizziness, depression, and lack of emotional control, after receiving Norplant implants. In a presentation to the International Neurotoxicology Conference in November, Hirsh reported that cognitive and electrophysiological tests performed on the women uncovered brain and nerve abnormalities he believes are traceable to the implants. Hirsh plans a larger study to determine the validity of his findings.

—

"Neurotoxicity of contraceptive implant," *Science News*, Vol. 148, November 11, 1995.

Simple test aids in search for "autism genes"

Researchers Susan Santangelo and Susan Folstein are using a simple questionnaire called the Friendship Interview to help trace the genetic roots of autism.

Santangelo and Folstein administered the 13-question test, which measures the quality of subjects' friendships, to the parents of 90 autistic children, and to parents of 40 children with Down syndrome. (The parents of children with Down syndrome were selected to control for the effects of having disabled children.) The researchers report that parents of autistic children were nearly four times as likely to have abnormal scores on the Interview as the parents of children with Down syndrome.

Santangelo and Folstein say the interview will aid geneticists in their search for genes linked to autism, by identifying parents who have mild symptoms of the disorder themselves.

—

"Tracking autism genes," *Science*, Vol. 270, November 24, 1995, p. 1305.