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Prozac: early results encouraging, but is it safe?

Approved by the FDA in 1987, fluoxetine (better known by the brand name Prozac) appears to be very effective in treating depression. According to several reports, however, the drug has a "down" side: it has been tentatively linked to suicidal urges and aggression in individuals who exhibited only minor depressive symptoms before Prozac treatment. (In addition, ARI has received reports from parents who have found it extremely difficult to wean their autistic children from Prozac.)

While the debate over Prozac's safety continues (see ARRI 4/3), physicians are cautiously prescribing the drug not only for patients with depression, but also for autistic patients with depressive symptoms or extreme ritualistic and compulsive behaviors. Researchers also are testing the drug's usefulness for Tourette's syndrome.

In a recent issue of the *American Journal of Psychiatry*, Richard Todd reports that three of four autistic individuals he treated with Prozac improved markedly. While none of Todd's patients had symptoms of depression, he notes, all had "pronounced preseverative or ritualistic behaviors."

One autistic girl treated by Todd, a 13-year-old with a normal IQ, had spent several hours each evening arranging and sniffing objects. After six weeks of treatment with 20 mg per day of Prozac, he reports, "the rituals were completely eliminated."

Todd also treated an 11-year-old autistic boy with a normal IQ who insisted on listening to his local baseball team's games but had violent tantrums whenever the team lost. After two weeks on 20 mg/day of Prozac, Todd says, the boy was able to listen to the games without having tantrums, "although the team wasn't any better." However, his stereotyped behaviors did not lessen.

A third patient treated with Prozac (also with 20 mg/day) was a 19-year-old with borderline retardation, whose aggression, insistence upon routines, and hand-flapping and head-swaying were reduced by half after four weeks on the drug and have remained at low levels for 14 months. A fourth patient did not respond to fluoxetine, and the drug was discontinued.

Todd comments that the improvements seen in autistic individuals taking Prozac may be related to the drug's effects on the levels of serotonin, a neurotransmitter, in the brain. (Approximately one third of all autistic individuals appear to have elevated serotonin levels.) However, Prozac's effect on serotonin levels worries some physicians, among them psychiatrist Peter Breggin. Breggin noted recently in *Insight* that by flooding brain synapses with serotonin, Prozac lowers the brain's own production of the substance, leading to abnormally low levels that could trigger violent behavior.

Caution recommended

A "cautious approach" to Prozac is also urged by Mohammad Ghaziuddin and colleagues in the *Journal of the American Academy of Child and Adolescent Psychiatry*. Ghaziuddin et al., reporting mixed results with four autistic teenagers and adults they have treated with Prozac, say that "fluoxetine seems to be most useful when a clear-cut superimposed depressive illness is present," and particularly when there is a family history of depression.

While the drug significantly reduces depressive symptoms in many autistic individuals, Ghaziuddin and colleagues say that "compulsive rituals and other non-specific behaviors such as stereotypies [inappropriate repetitive behaviors such as spinning or hand-flapping] do not seem to respond well" — a finding which differs from Todd's.

Ghaziuddin et al. found that two of their patients became agitated and nervous while taking the drug, although one became more relaxed when her dosage was lowered. They note that physicians must carefully monitor behavioral side effects in autistic patients, because the suicidal thoughts and other behavioral changes which may occur in people taking Prozac could be difficult to detect in autistic individuals with significant communication impairments.

Mehlinger et al: "moderately successful response"

Renee Mehlinger and colleagues report in the same journal on a 26-year-old autistic woman whose severe rituals, tantrums, perseveration, aggression and lack of bladder control had jeopardized her placement in a

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SPECIAL FEATURE ISSUE: News about drugs for autism

New evidence points to opioids

Does a natural opioid "high" cause autism? That theory, originated by researcher Jaak Panksepp and others in the 1970s, has gained new support following recent studies by Paul Shattock of England and Karl Reichelt of Norway. ***(See related article on page 2 on the opioid-blocking drug naltrexone.)***

Shattock: test results abnormal

Shattock and colleagues measured the levels of peptides in the urine of three groups: non-disabled, autistic, and developmentally disabled but non-autistic individuals. (Peptides are fragments of proteins; some of these fragments are opioids, substances which exert opium-like effects on brain cells.)

The possible link between these opioids and autism has been studied for more than a decade, since researchers observed that numerous symptoms of autism — including insensitivity to pain, irritability, aloofness, and stereotyped behaviors — also occur in opium addicts, as well as in the offspring of animals whose mothers are given opium-like drugs during pregnancy. Studies by Panksepp and others have also shown that animals given small doses of opiates have less desire for companionship and physical contact, higher pain thresholds, and learning problems.

Abnormal peaks seen

Shattock's data showed that "somewhere in the region of 80% of our subjects with autism gave . . . distinctly abnormal patterns" of peptides in an area he refers to as the "critical zone where biologically active peptides [such as opioids] appear." When the peaks and valleys of peptide levels were measured, autistic individuals showed a pattern different from non-disabled controls. Individuals with other disabilities, such as Down syndrome and Fragile X, also showed abnormal urinary peptide patterns, but these were different from autistic individuals' pattern.

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