Naltrexone: researchers voice optimism, offer advice

Naltrexone—a drug that blocks brain cells' uptake of natural opium-like substances—is a promising treatment for autistic withdrawal, self-injury, and other symptoms (see ARRI 6/1 and earlier issues). As pioneers in the use of naltrexone to treat autistic individuals, Jaak Panksepp and colleagues have gained important insights into the drug's effects — insights they shared at a recent conference.

It is common, the researchers note, for children beginning naltrexone treatment to appear tired or acutely distressed. "The emotional distress, seen in a minority of children, starts about half an hour following medication and continues for only a short time (about 2 hours), but this 'weepiness' typically wanes during chronic treatment," they say.

The researchers believe this distress is a positive, not a negative, sign. They suggest that it is a result of the autistic child experiencing his first feelings of social need, and say parents should view this period as a "window of opportunity" during which "the child may be especially capable of viewing the social world as a source of emotional support."

Saying that it is vital to combine drug treatment with intensive playful, friendly social stimulation, Panksepp et al. encourage parents to "provide clear indications of a positive and sustaining environment which the child can subsequently utilize as a secure base for broadening social initiatives and interactions." They note that "under naltrexone, we...commonly see more creative object play by autistic children, and parallel play often changes to social-interactive play." The researchers add that except for this brief period of negative emotions, children taking naltrexone appear to be more cheerful than usual.

Maintenance dosage suggested; latest study very positive

Panksepp et al. have found that the dose of naltrexone needed for maximum control of self-injurious behavior tends to be high (about 1.5 mg/kg), while lower doses (about .5 mg/kg) appear to have a greater effect on social behaviors. They speculate that different receptors on brain cells may be affected by the differing dosages.

The researchers say that "low doses of naltrexone that yield pro-social tendencies can be given quite infrequently (about every other day)," as a maintenance medication. "To the best of our knowledge," they say, "it may have to be given on a constant schedule indefinitely."

A recent study by Panksepp and colleagues indicated that naltrexone's effect is most obvious on social behaviors, including interaction, happiness, smiling, eye contact, and attempts to communicate. They add, however, that "there are also substantial increments in attention and interest in the world, reductions in stereotypies and activity levels, and a general increase in curiosity and interest which tends to feed into more creative play."

Panksepp et al. have detected physiological changes in naltrexone-treated subjects that parallel the children's behavioral changes. Levels of peptides that were abnormally elevated before treatment began are normalized by naltrexone administration, an effect seen at all dosages of the drug.

"Our data [have] already suggested that responders exhibit elevations of various plasma neuropeptides and biogenic amines, and that responders typically exhibit the strongest normalization of these parameters,"

The distress evidenced by children starting naltrexone treatment, Panksepp says, may signify that they are experiencing their first feelings of social need.

they note. They cite the surprising finding of Scifo et al. that normalization of plasma endorphin and natural killer cell activities during naltrexone treatment can occur regardless of whether initial levels are abnormally high or abnormally low.

It is important, the researchers say, to use "the most sensitive behavioral measures available" when judging the effects of naltrexone treatment, because parental diaries and videotaping may reveal significant improvements not detected by standard tests. The results of one recent study (Leboyer et al., 1991) initially appeared lackluster, they note, until careful data analysis showed that the most severely affected children exhibited significant improvement. "While there was a robust difference in symptom severity between high and low symptom groups prior to treatment," they note, "the difference between groups was eliminated completely during naltrexone (primarily because of a reduction of symptoms in the high-symptom group), and the differences reappeared during placebo and post-experimental periods."

Looking to the future

Combining autism treatments, such as naltrexone and B6/magnesium therapy, is an approach that may yield exciting results, Panksepp and colleagues say. They note that laboratory tests on animals provide "a hint" that naltrexone and dimethylglycine (DMG) may work synergistically to promote social interaction. In one study on an autistic child, DMG appeared to enhance naltrexone effectiveness at first, but later seemed to reduce the drug's benefit.

Another combination worth investigating, the researchers say, is naltrexone and Haldol; naltrexone might lower the risk of tardive dyskinesia (involuntary muscle movements caused by neuroleptic drugs), they speculate, while Haldol might minimize the emotional reactions some children experience while taking naltrexone. (See p. 7 article re vitamin E and tardive dyskinesia.)

Other drugs that hold promise in the treatment of autism, Panksepp et al. say, include eltoprazine, which appears to reduce aggression and enhance social behavior; and buspirone, which (like eltoprazine) blocks serotonin receptors in the brain. The researchers are particularly excited about eltoprazine, which has shown positive results in animal tests, and recommend that "this drug be high on the list of potential new therapeutic agents in the treatment of autism."

The researchers also recommend research regarding the hormone melatonin, which may be secreted in abnormally high or low amounts by autistic children. In addition to melatonin's possible effectiveness as an autism treatment, they say, measurements of melatonin and opioid rhythms may help identify infants with autism.

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"Naltrexone and other potential new pharmacological treatments of autism," Jaak Panksepp, Patrick Lensing, Marion Leboyer, and Manuel P. Bouvard; presentation to the OASI Institute, 1991; also, *Brain Dysfunction*, in press. Address: Jaak Panksepp, Department of Psychology, Bowling Green State University, Bowling Green, Ohio 43403.

Auditory Training

(continued from page 1)

is now a considerable body of clinical experience available, consisting of first-hand observations of a number of children who have been through auditory training, as well as telephone conversations and letters from many parents whose children have had auditory training. I must say that I am really very pleasantly surprised at how consistently positive, and often very enthusiastic, these preliminary reports have been. My optimism is shared by others who have had similar experience with children who have undergone auditory training.

Based on what I know thus far, I have little doubt that the experimental studies of auditory training now underway, and soon to get underway, will indeed show that auditory training is a valid method for improving the status of many (certainly not all) autistic children."

A preprint of the report of the first study is available from the Autism Research Institute (send $1.00 and a self-addressed, stamped envelope). ARRI has available the above report and all of our other publications to date on auditory training, including a list of practitioners in the U.S. and Canada who provide AIT, for $4.00 (no self-addressed envelope).

Another development: Annabel and Peter Stehli have founded the Georgiana Foundation to provide professional training to those who wish to become AIT practitioners. Dr. Berard has already trained two groups. The third session with Dr. Berard will begin July 14th. For information contact the Georgiana Foundation at P.O. Box 2607, Westport, CT 06880, phone 203-454-1221.