Biomedical Update:

B6 beneficial for TD

A new study adds to evidence showing that vitamin B6 is a highly beneficial treatment for tardive dyskinesia, a common neurological disorder caused by psychotropic drugs.

C. Miodownik and colleagues administered vitamin B6 (up to 400 mg per day) to 15 patients with schizophrenia or schizoaffective disorder, in a double-blind, placebo-controlled crossover study. They say that while the behavioral symptoms of the patients were unaffected, "there was significant improvement in tardive dyskinesia and parkinsonian symptoms."

These findings are similar to those of a previous study by the same researchers, who reported in 2002 that vitamin B6 (900-1200 mg daily) eliminated drug-induced tremors in four of five patients taking lithium.

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"Vitamin B6 add-on therapy in treatment of schizophrenic patients with psychotic symptoms and movement disorders," C. Miodownik, H. Cohen, M. Kotler, and V. Lerner, *Harefuah*, Vol. 142, No. 8-9, September 2003, 592-6. Address: C. Miodownik, Ministry of Health, Mental Health Center, Faculty of Health Sciences, Ben Gurion University of the Negev, Beer Sheba, Israel.

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"Lithium-induced tremor treated with vitamin B6: a preliminary case series," C. Miodownik, E. Witztum, and V. Lerner, *International Journal of Psychiatry in Medicine*, Vol. 32, No. 1, 2002, 103-8. See address above.

New autoimmunity clues

The identification of casomorphin peptides in the urine of many autistic individuals, coupled with suspected problems with adenosine metabolism, has led researchers to the hypothesis that the protein dipeptidylpeptidase IV (DPPIV) (also denoted as CD26 and adenosine deaminase binding protein) is somehow inhibited in many cases of autism. The beneficial effect of digestive enzymes containing DPPIV analogs also points to this possibility, as does the depression of CD26 expression on lymphocytes in milk (casein) allergy cases.

In further support of an autism/DPPIV connection, new immunologic research by Dr. Vojdani and colleagues reveals that certain substances bind to the CD26 protein on lymphocytes, often resulting in an autoimmune response. The tested substances include dietary peptides from casein and gliadin, ethyl mercury, and streptokinase, an enzyme protein produced by streptococci, that is capable of producing antigenic reactions in some humans.

The researchers tested their theory by measuring antibodies against CD26, CD69 (a protein produced by activated lymphocytes), streptokinase, gliadin and casein peptides, and ethyl mercury in autistic children. They found that a significant percentage of the children developed antibodies to the dietary peptides and toxins concomitant with the appearance of autoantibodies to CD26 and CD69. Additional analysis showed that streptokinase, casein and gliadin peptides, and ethyl mercury bind to CD26 and CD69, leading Vojdani and colleagues to conclude that "bacterial antigens (streptokinase), dietary peptides (from gliadin, casein) and Thimerosal (contains ethyl mercury) in individuals with predisposing HLA molecules bind to CD26 and CD69 and induce antibodies against these molecules."

The researchers say their study "is apparently the first to demonstrate that dietary peptides, bacterial toxins and xenobiotics bind to lymphocyte receptors and/or tissue enzymes, resulting in autoimmune reactions in children with autism."

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"Infections, toxic chemicals and dietary peptides binding to lymphocyte receptors and tissue enzymes are major instigators of autoimmunity in autism," A. Vojdani, J. B. Pangborn, E. Vojdani, and E. L. Cooper, *International Journal of Immunopathology and Pharmacology*, Vol. 16, No. 3, September-December 2003, 189-99. Address: Aristo Vojdani, Immunosciences Lab., Inc., 8693 Wilshire Blvd., Suite 200, Beverly Hills, CA 90211, immunsci@ix.netcom.com.

Perfect pitch and autism

One skill seen in many autistic individuals is perfect pitch—the ability to identify a musical note by name, or to sing a specific note perfectly on key. A recent study suggests that this talent may offer insights into genetic influences on autism.

Employing interviews and tests used to detect subclinical autism, W. A. Brown et al. evaluated 13 non-autistic musicians with perfect pitch, comparing them to musicians without this ability. The researchers report that nearly half of the musicians with perfect pitch were socially eccentric, compared to only 15 percent of controls. The musicians with perfect pitch also scored higher on tests of block design than on other performance IQ subtests, a pattern common in autism spectrum disorders. The researchers suggest that the gene or genes involved in perfect pitch may be among those contributing to autism.

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"Autism-related language, personality, and cognition in people with absolute pitch: results of a preliminary study," W. A. Brown, K. Cammuso, H. Sachs, B. Winklosky, J. Mullane, R. Bernier, S. Svenson, D. Arin, B. Rosen-Sheidley, and S. E. Folstein, *Journal of Autism and Developmental Disorders*, Vol. 33, No. 2, 2003, 163-7. Address: W. A. Brown, Department of Psychiatry, Brown Medical School, Providence, Rhode Island 02905.

Cannabinoids: effective treatment for epilepsy?

Two new studies indicate that the centuries-old tradition of using marijuana to treat epileptic seizures is grounded in fact.

Giovanni Marsicano et al. recently reported that natural cannabinoids produced by the body, and similar to those in marijuana, protected mice against experimentally induced seizures. When the researchers genetically engineered mice to lack cannabinoid receptors, the animals exhibited a high rate of seizure activity. "Our research," says study coauthor Beat Lutz, "shows that the cannabinoids act as a brake on the brain.... When the brain's nerve cells begin to fire too much, then there is a huge production of innate cannabinoids which calms everything down."

Related findings were reported at the same time by Robert De Lorenzo et al., who injected epileptic rats with different combinations of six drugs—a marijuana extract; two synthetic drugs containing the active ingredients of marijuana; the anticonvulsants Phenobarbital and phenytoin (Dilantin); and a drug that blocks the CB1 receptor that is activated by cannabinoids in the brain. They report that the marijuana extract and the two synthetic marijuana drugs completely stopped the rats' seizures, while phenobarbital and phenytoin were only partially effective. Injection of the drug that blocked the effects of cannabinoids led to a marked increase in both the duration and the frequency of seizures, and in some cases caused life-threatening, non-stop seizures.

Both groups say their findings could lead to new treatments for seizures, which currently cannot be controlled in a third of epileptic patients. Marsicano et al. caution against use of marijuana itself, however, noting that the brain's natural cannabinoids are active only when they are needed and that flooding the brain with cannabis may be ineffective or even make seizure disorders worse.

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"CB1 cannabinoid receptors and on-demand defense against excitotoxicity," G. Marsicano, S. Goodenough, K. Monory, H. Hermann, M. Eder, A. Cannich, S. C. Azad, M. G. Cascio, S. O. Gutierrez, M. van der Stelt, M. L. Lopez-Rodriguez, E. Casanova, G. Schutz, W. Zieglgansberger, V. Di Marzo, C. Behl, and B. Lutz, *Science*, Vol. 302, No. 5642, Oct. 3, 2003, 84-8. Address: Beat Lutz, Max-Planck-Institute of Psychiatry, Kraepelinstr. 2-10, D-80804, Munich, Germany, lutz@mpipsykl.mpg.de.

—and—

"Marijuana hope for epileptics," Steve Connor, *New Zealand Herald*, October 6, 2003.

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"Marijuana and its receptor protein in brain control epilepsy," news release, Virginia Commonwealth University, September 30, 2003.