Biomedical Update:

B6 stops tremors induced by lithium

Lithium, used to treat symptoms of bipolar disorder in some autistic individuals, can cause debilitating hand tremors. While doctors generally administer potentially dangerous drugs such as Inderal in an attempt to control this side effect, a recent Israeli study indicates that vitamin B6 can safely reduce or even eliminate lithium-induced tremors.

In an open-label trial, C. Miodownik and colleagues administered vitamin B6 (900 to 1200 mg/day) to five patients suffering from lithium-induced tremors. The researchers report that four of the five subjects showed "an impressive improvement," with their tremors eventually disappearing completely over the course of the four-week trial. No adverse effects were seen.

Miodownik et al. say their results are not surprising in light of research showing that vitamin B6 can effectively treat a variety of drug-induced movement disorders including tardive dyskinesia and parkinsonism.

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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. Address: C. Miodownik, Be'er-Sheva Mental Health Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Be'er-Sheva, Israel.

More evidence of link between fragile X, Parkinson's symptoms

In 2001, Randi Hagerman and colleagues reported seeing a surprising number of cases of Parkinson's disease in the grandfathers of children with fragile X syndrome, a genetic disorder that frequently causes autistic-like symptoms (see ARRI 15/3). A new post-mortem study of elderly male fragile X pre-mutation carriers with Parkinson's symptoms, conducted by the same group, adds weight to the theory that these men suffer from a unique neurological disorder.

Fragile X occurs when a mutation in the FMR1 gene silences the instructions to make a protein called FMRP. The mutation involves a DNA repetition, with affected individuals having more than 200 repeats and carriers (including the men identified by Hagerman et al. as having Parkinson's-like symptoms) having 50 to 200. Carriers do not have fragile X syndrome, but many exhibit mild cognitive or emotional problems.

C. M. Greco, Hagerman, and colleagues studied the brains of four men with the fragile X pre-mutation, all of whom had suffered from symptoms resembling Parkinson's. They report that in all four cases, abnormal intranuclear inclusion bodies (formations inside the nuclei of brain cells) were present. Inclusion bodies were most common in the hippocampus. Other abnormalities included a marked "dropout" of Purkinje cells in the cerebellum, gliosis (an abnormal proliferation of cells called astroglia, associated with damage), and axonal swelling (a sign of Purkinje cell deterioration).

The researchers conclude, "The presence of inclusions in the brains of all four fragile X carriers with the neurological findings provides further support for a unique clinical entity associated with pre-mutation FMR1."

The pre-mutation-carrying grandfathers of fragile X children originally identified by Hagerman et al. were in their fifties and sixties. The researchers say they do not yet know the prevalence of Parkinson's-like symptoms among pre-mutation carriers.

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"Neuronal intranuclear inclusions in a new cerebellar tremor ataxia syndrome among fragile X carriers," C. M. Greco, R. J. Hagerman, F. Tassone, A. E. Chudley, M. R. Del Bigio, S. Jacquemont, M. Leehey, and P. J. Hagerman, *Brain*, Vol. 125, Part 8, August 2002, 1760-71. Address: C. M. Greco, Department of Pathology, University of California, Davis, School of Medicine, Davis, CA 95616.

Omega 3 spread cuts seizure severity

A ketogenic (high-fat, low-carbohydrate, low-protein) diet is often used successfully to control epilepsy in children. A recent study indicates, moreover, that even supplementing a typical diet with certain fatty acids can significantly benefit individuals with epilepsy.

S. Schlanger and colleagues added a special nutritional spread, containing 65 percent omega-3 polyunsaturated fatty acids (PUFAs) to the diets of five epileptic patients taking anticonvulsant drugs. Patients used the spread at breakfast every day for six months.

"In all of them," the researchers say, "a marked reduction in both frequency and strength of the epileptic seizures was recorded." They conclude, "Incorporation of [a] dietary supplement containing omega-3 PUFAs may be beneficial in suppression of some cases of epileptic seizures."

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"Diet enriched with omega-3 fatty acids alleviates convulsion symptoms in epilepsy patients," S. Schlanger, M. Shinitzky, and D. Yam, *Epilepsia*, Vol. 43, No. 1, 2002, 103-4. Address: S. Schlanger, The Kalanit Institute for the Retarded Child, Rishon LeZion, Israel.

Thiamine benefits autistic children; may work by removing heavy metals

Treatment with a form of thiamine (vitamin B1) can reduce symptoms of autism and aid in removing heavy metals from the body, according to a new pilot study.

Derrick Lonsdale and colleagues treated ten autistic children twice daily for two months with rectal suppositories containing 50 mg of thiamine tetrahydrofurfuryl disulfide (TTFD). Urine samples from the participants were analyzed at the beginning of the study, after 30 days, and after 60 days, and the children's behavior was measured using the Autism Treatment Evaluation Checklist (ATEC).

At the outset of the study, three of the children were shown to be deficient in thiamine. Six of the children also had unusually high concentrations of arsenic, a toxic metal, in their urine.

The researchers report that eight of the ten children showed significant improvement after two months of treatment. In the children with elevated arsenic levels, they say, the levels increased after 30 days of treatment with TTFD and decreased after 60 days, indicating that the treatment was removing the toxin from the children's bodies. The researchers also detected sporadic increases in mercury, cadmium, lead, and nickel in the children's urine samples.

Lonsdale and colleagues say their findings add to evidence linking autism to an impaired ability to eliminate toxic heavy metals from the body. Their findings are consistent with those of William Walsh, who has reported that more than 90 percent of the autistic children he has tested showed evidence of an inborn error involving metallothionein proteins, which play a critical role in detoxifying heavy metals.

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"Treatment of autism spectrum children with thiamine tetrahydrofurfuryl disulfide: A pilot study," D. Lonsdale, R. J. Shamberger, and T. Audhya, *Neuroendocrinology Letters*, Vol. 23, No. 4, August 2002, 303-8. Address: D. Lonsdale, Preventive Medicine Group, 24700 Center Ridge Road, Westlake, OH 44145.