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ATTENTION DEFICIT AND COMORBID DISORDERS

SEARCH FOR A CHEMICAL MARKER FOR ADHD

B-phenylethylamine (PEA), 3-methoxy-4-hydroxyphenyl glycol (MHPG), homovanillic acid (HVA), and 5-hydroxy-indolacetic acid (5-HIAA) were measured in 24 hour urine specimens from 37 children with attention deficit hyperactivity disorder (ADHD), and concentrations were compared to those from 21 age-matched controls without neurologic disease, and 12 children with autistic disorder, in a study at Kurume University School of Medicine, Kurume City, and other centers in Japan. All subjects received a low-amine diet for 72 hours before and during the 24-hour urine collection period. Mean PEA levels were significantly lower in children with ADHD (21.7 +/- 20.5 mcg/gm creatinine; $p<0.05$) than in controls (46.61 +/- 46.55 mcg/gm creatinine). Mean urinary levels of MHPG, HVA, and 5-HIAA in ADHD children were not significantly different from controls, with or without autistic disorder.

In 22 of the children with ADHD (18 responders and 4 nonresponders) who were treated with methylphenidate (MPH), PEA urine levels were significantly increased after treatment only in MPH responders ($p<0.05$). Urinary levels of MHPG, HVA, and 5-HIAA were not significantly changed after MPH therapy. The severity of ADHD showed no correlation with levels of PEA. (Kusaga A, Yamashita Y, Koeda T et al. Increased urine phenylethylamine after methylphenidate treatment in children with ADHD. Ann Neurol September 2002;52:371-374). (Respond: Dr T. Matsuishi, Department of Pediatrics and Child Health, Kurume University School of Medicine, Kurume City, Japan).

COMMENT. A reliable chemical marker for ADHD and for MPH responders would provide a practical advantage in diagnosis and treatment, and a much superior guide to the subjective and controversial AAP DSM criteria for ADHD. Low mean levels of phenylethylamine (PEA) in the urine of children with ADHD and an increase in PEA associated with a beneficial response to treatment with MPH are findings that may explain a possible neurochemical mechanism for ADHD. However, the PEA levels are not sufficiently consistent to use as a diagnostic tool for ADHD; PEA levels are not correlated with ADHD severity, and

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the variation in urinary PEA levels among individual patients is large.

The above report confirms previous findings of decreased urinary levels of PEA in children with ADHD (Zametkin AJ et al. 1984; Baker GB et al. 1991). An abnormality in the absorption or transportation of phenylalanine is suggested as one explanation for the decreased PEA excretion, but symptoms of ADHD are not improved by treatment with phenylalanine (Zametkin AJ et al. 1987). Monoamines including HVA and 5-HIAA have been linked to ADHD in some studies, but the present report does not support an association. Further investigations are warranted.

TRIAL OF DIVALPROEX FOR BIPOLAR DISORDER

The safety and effectiveness of divalproex sodium (Depakapote®) in the treatment of 40 children and adolescents, aged 7 to 19 years, with a primary diagnosis of bipolar disorder were evaluated by open-label study (2-8 weeks) at the University of Texas, Galveston; University of Pennsylvania, Philadelphia; SUNY Stonybrook, NY; Massachusetts General Hospital, Boston; and University of Texas, San Antonio. Six subjects (15%) had comorbid ADHD that required stimulant therapy in addition, and 23 (58%) had a comorbid psychiatric diagnosis that was treated with concurrent medications, including lithium, haloperidol, or lorazepam. A greater than 50% improvement was obtained in 22 subjects (61%) as measured by the Mania Rating Scale (MRS). Mean scores of all efficacy measures showed significant improvements ($p<.001$) from baseline, including the MRS, Manic Syndrome Scale, Behavior and Ideation Scale, Psychiatric Rating Scale, and Hamilton Rating Scale. At the completion of the study, the mean divalproex dose was 17.5 mg/kg per day, and the mean serum valproate level was 83.4 mcg/ml. Twenty seven subjects (68%) reported one or more adverse events, the most common including headache (7), nausea (7), vomiting (6), diarrhea (4), and somnolence (4). Twenty four subjects discontinued treatment because of lack of efficacy (6), drug intolerance (6), noncompliance (6), and other reasons (6). None required drug withdrawal because of abnormal laboratory values. A planned double-blind, placebo-controlled study to follow the open-label period was abandoned because of insufficient number of patients. (Wagner KD, Weller EB, Carlson GA et al. An open-label trial of divalproex in children and adolescents with bipolar disorder. J Am Acad Child Adolesc Psychiatry October 2002;41:1224-1230). (Reprints: Dr Wagner, Department of Psychiatry and Behavioral Sciences, University of Texas Medical Branch, 301 University Blvd, Galveston, TX 77555).

COMMENT. The authors conclude that the results provide support for the safety and effectiveness of divalproex in the treatment of bipolar disorder in children and adolescents. However, failure to complete the study period in more than 50% of patients is not a favorable recommendation.

Tha comorbidity of ADHD in children with bipolar disorder is a frequent occurrence, with estimates up to 94% (Wozniak et al. 1995). Treatment often requires a combination of stimulant medications and antidepressants.

NEUROMUSCULAR DISORDERS

TICK PARALYSIS

Six children aged 3.3 to 5.5 years (5 girls and 1 boy), of 26 admitted with acute muscle weakness to the University of Mississippi Medical Center, Jackson, over a 5 year period (1992-97), were diagnosed with tick paralysis. The initial