had increased metabolism, and those with lower D2 measures had decreased metabolism. MPH, like cocaine, binds to the dopamine transporter, but their effects on metabolism are not identical. The cocaine craving induced by MPH in cocaine abusers is not associated with an MPH addiction. In fact, if substance abuse becomes a problem in adolescence, it is independent of ADHD and does not involve addiction to MPH (Biederman J et al, 1997, in Millichap JG. Attention Deficit Hyperactivity and Learning Disorders. PNB Publ, 1998;pp129-130)

The right striato-orbitofrontal regions are thought to be involved in the neuroanatomic and biochemical basis for ADHD. A deficiency in brain dopamine and norepinephrine may explain a loss of inhibition and excessive activity levels in children with ADHD. MPH, by increasing dopamine activity in the right frontal lobe, may normalize motor activity while preserving and heightening the degree of alertness.

PRENATAL PCB AND DIOXIN AND COGNITIVE DYSFUNCTION

The effects of environmental exposure to polychlorinated biphenyls (PCB) and dioxins on cognitive abilities in Dutch children at 42 months of age were assessed at the Sophia Children's Hospital, Rotterdam, The Netherlands. Maternal plasma and breast milk concentrations were compared with scores of cognitive function. Maternal plasma total PCB concentrations were associated with lower cognitive functioning, and the effect was related to the degree of prenatal in utero exposure. Lactational and current childhood exposure to PCBs and dioxins were not related to 42-month cognitive performance. (Patandin S, Lanting CI, Mulder PGH, et al. Effects of environmental exposure to polychlorinated biphenyls and dioxins on cognitive abilities in Dutch children at 42 months of age. J Pediatr Jan 1999;134:33-41). (Reprints: Svati Patandin MD, Department of Pediatrics, Division of Neonatology, SP 3435, Sophia Children's Hospital, PO Box 2060, 3000 CB Rotterdam, The Netherlands).

COMMENT. The developing fetal brain is particularly sensitive to environmental toxins. Prenatal in utero exposure to PCBs causes impaired cognitive performance in children, whereas lactational and childhood exposure may not have adverse effects on learning. These results are in agreement with previous Chinese poisoning and Michigan fish exposure studies. Although deficits are often small, the implications of low-level PCB exposure may be compared to that of lead exposure. Furthermore, the effects on intellectual performance are long-lasting, and ADHD is a potential complication. (Progress in Pediatric Neurology III, PNB Publ, 1997;pp226-8).

ANTIEPILEPTIC DRUGS

TOPIRAMATE AND OTHER AED EFFECTS ON COGNITION

The acute and steady-state cognitive effects of three new antiepileptic drugs (AED), gabapentin, lamotrigine, and topiramate, were studied in healthy young adults at the University of Alabama Epilepsy Center, Birmingham, AL. Compared with baseline tests of attention and memory, topiramate (TPM) caused statistically significant declines on measures of attention and word fluency at acute doses, whereas gabapentin (GBP) and lamotrigine (LTG) had minimal effects on performance. Only topiramate subjects had persistent neurocognitive impairments when tested after 2 and 4 weeks of drug administration. The TPM group's verbal fluency rate dropped an average of 50% per subject, and the visual attention task showed a threefold increase in rate of errors. The adverse effects of

TPM were not explained by sedation. Mead blood levels by the 4-week test period were within clinical therapeutic ranges: TPM (11 mcg/mL); LTG (8.1); and GBP (9.6). (Martin R, Kuzniecky R, Ho S et al. Cognitive effects of topiramate, gabapentin, and lamotrigine in healthy young adults. Neurology Jan 1999;52:321-327). (Reprints: Dr Roy C Martin, UAB Epilepsy Center, Department of Neurology, University of Alabama at Birmingham, 312 CIRC, 1719 6th Avenue South, Birmingham, AL 35294).

COMMENT. The adverse effects on cognitive functioning caused by topiramate in healthy young adults have also been observed in patients treated for epilepsy. The potential long-term effects beyond one month were not addressed. Early-onset side effects may subside and may be less evident when the drug is introduced more slowly.

RENAL TUBULAR DYSFUNCTION WITH VALPROATE AND CBZ

Renal tubular function in epileptic children receiving antiepileptic drugs was evaluated by measurement of lysosomal enzymes at Istanbul University, Turkey. N-acetyl-B-glucosaminidase and B-galactosidase were determined before and 8 months after administration of valproate in 14 children, and carbamazepine in 17, and also in 25 healthy untreated controls. Increased enzyme activities were found in patients treated with AEDs, and valproate-treated patients were affected more frequently than the carbamazepine group (50% cf 18%, respectively). (Yuksel A, Cengiz M, Seven M, Cengiz S, Cenani A. N-acetyl-B-glucosaminidase and B-galactosidase activity in children receiving antiepileptic drugs. Pediatr Neurol Jan 1999;20:24-26). (Respond: Dr Adnan Yuksel, Akdeniz Caddesi No 85 Ki, Fatih, Istanbul, Turkey).

COMMENT. Children treated with AEDs and especially valproate in large doses for extended periods may develop renal tubular dysfunction. In addition to tests of liver function, valproate-treated patients should receive urinary function tests in certain circumstances.

Valproate-induced hyponatremia is reported in an adult with Henoch-Schonlein nephritis who was treated with 2000 mg/day of VPA for idiopathic epilepsy. Water loading tests at different dosages of sodium valproate showed reduced water excretion that was dose-dependent. Inappropriate secretion of antidiuretic hormone was the proposed mechanism. (Branten AJW, Wetzels JFM, Weber AM, Koene RAP. Ann Neurol February 1999;43:265-267). Having regard to the renal tubular dysfunction reported above, renal insufficiency may be an alternative explanation.

CARBAMAZEPINE AND METHYLPHENIDATE LEVELS IN ADHD

A carbamazepine (CBZ)-induced lowering of methylphenidate (MPH) serum levels in a 13-year-old female treated for ADHD and aggressive behavior, is reported from the Eastern Pennsylvania Psychiatric Institute, Philadelphia. ADHD symptoms that had responded to MPH became worse when CBZ was introduced and the dose increased to 800 mg/day (serum level 8.9 mcg/mL). Peak morning serum levels of MPH and ritalinic acid were 5.3 ng/mL on 20 mg MPH 3 times a day (standard range of MPH level is 5-20 ng/mL). After 6 weeks on CBZ, the MPH levels decreased to 4.2, and later to 2.4, when the dose of CBZ was increased to 1000 mg/day. ADHD symptoms worsened despite an increase in MPH dose to 35 mg 3x daily. The beneficial effects of MPH were regained only at doses of 60 mg 3x daily. (Schaller JL, Behar D. Carbamazepine and methylphenidate in ADHD. J Am Acad