

ATTENTION DEFICIT AND BEHAVIOR DISORDERS

NEONATAL CEREBRAL ISCHEMIA: A RISK FACTOR FOR ADHD

The effect of low neonatal cerebral blood flow (CBF) on dopaminergic neurotransmission was studied in 6 genetically susceptible high-risk, preterm neonates followed with attention deficit hyperactivity disorder (ADHD) at Aarhus University Hospital, Denmark, and tested at 12-14 years of age. The authors hypothesized that cerebral ischemia at birth might contribute to deficient dopaminergic neurotransmission, which is considered to be the basis for ADHD. Dopamine receptor binding in the striatum was examined with positron emission tomography (PET), and inattention and impulsiveness were measured by continuous reaction times (RT) and RT variability determined by a computerized test of variables (TOVA). In 6 adolescents (12-14 years of age; 5 boys) with CBF measurements at preterm birth and a subsequent diagnosis of ADHD, high striatal dopamine receptor availability ('empty receptors') was correlated with increased RT and RT variability, findings that supported a dopaminergic role in ADHD symptomatology. The link demonstrated between high dopamine receptor availability with low neonatal CBF supports the hypothesis of cerebral ischemia as a risk factor for ADHD. (Lou HC, Rosa P, Pryds O et al. ADHD: increased dopamine receptor availability linked to attention deficit and low neonatal cerebral blood flow. *Dev Med Child Neurol* 2004;46:179-183). (Respond: Dr Hans C Lou, Centre of Functionally Integrative Neuroscience and PET Centre, Aarhus University Hospital, DK-8000 Aarhus, Denmark).

COMMENT. These results support the long held theory that some cases of ADHD may be a consequence of prematurity and low cerebral blood flow (CBF) with perinatal hypoxic-ischemic encephalopathy. The low neonatal CBF predisposes to dopamine depletion in the prefrontal-striatal-limbic system that, in genetically susceptible individuals, leads to ADHD. The beneficial effect of methylphenidate is further convincing evidence that dopaminergic systems are implicated in the pathogenesis of ADHD.

CONCERTA cf RITALIN EFFECTS ON DRIVING PERFORMANCE

The effects of different methylphenidate (MPH) delivery profiles on driving performance of 6 male ADHD adolescents, aged 16 to 19 years, were evaluated by a randomized, crossover, single-blind study comparing controlled-release (OROS) MPH (Concerta) given q.d. to immediate-release MPH (Ritalin) in equal doses t.i.d. in a study at the University of Virginia, Charlottesville, VA. A computer-quantified Impaired Driving Score (IDS) was used to measure driving performance tested on a driving simulator at 2 PM, 5 PM, 8 PM, and 11 PM after treatments had been maintained for 7 days. In participants receiving MPH t.i.d. the IDS worsened in the evening (8 PM) compared to those on OROS MPH q.d. ($p=.01$). Performance was significantly better overall when on once daily Concerta compared to MPH given t.i.d. ($p=.004$). (Cox DJ, Merkel RL, Penberthy JK et al. Impact of methylphenidate delivery profiles on driving performance of adolescents with attention-deficit/hyperactivity disorder: a pilot study. *J Am Acad Child Adolesc Psychiatry* March

2004;43:269-275). (Respond: Dr Daniel J Cox, Box 800-223, University of Virginia Health System, Charlottesville, VA 22908).

COMMENT. Adolescent drivers with ADHD when treated with Concerta q.d. demonstrated less variability and performed significantly better throughout the day than when treated with immediate release MPH t.i.d. During the MPH t.i.d. treatment regimen driving performance deteriorated significantly by 8 PM., a time when adolescents are likely to be driving. Concerta-treated adolescents were less likely to brake inappropriately on the open road, their driving was less erratic, and they were less likely to run stop signals. The participants unblinded self-appraisals correlated significantly with the objective measures of driving performance on the simulator. ADHD is not only a school-based disorder, impacting behavior and learning, but also predisposes to accidental injuries related to bicycles and motor vehicles. Treatment benefits with the various formulations of MPH, amphetamines, and Strattera should consider the impact on risk of serious accidents in addition to school performance.

Extended release methylphenidate (MPH) formulations in ADHD. Once-daily doses of Metadate CD (MCD) and Concerta (CON) produced statistically different effects on measures of behavior and performance in children with ADHD as measured in a laboratory school setting (The Comacs Study) (Swanson JM, Wigal SB, Wigal T et al. **Pediatrics** March 2004;113:e206-e216). The formulation with the highest expected plasma MPH concentration had the most benefits at any point in time. MCD was superior in the morning, MCD and CON were equivalent in efficacy during the afternoon, and CON was superior in the early evening.

NEOPLASTIC DISORDERS

SYSTEMIC LYMPHOMA MIMICKING ADEM

The case of a 10-year-old immunocompetent male who initially presented with fatigue and ataxia following a viral illness, and MRI findings compatible with acute disseminated encephalomyelitis (ADEM), and who later was diagnosed with systemic lymphoma is reported from Children's Memorial Hospital, Chicago, Illinois. Brain MRI showed white matter signal abnormalities in frontal and parietal lobes, the right temporal lobe, and in the basal ganglia, cerebral peduncles, and left brachium pontis. CSF contained 7 white cells/mcL, protein 28 mg/dL, glucose 68 mg/dL, and negative cytology. Ataxia and fatigue improved following treatment with a 5-day course of methylprednisolone 20 mg/kg/day, and the MRI showed resolution of the lesions. An acute exacerbation of the fatigue and ataxia occurring within 1 month was unresponsive to IV immunoglobulin, and the patient was referred for a second opinion. Examination revealed a horizontal nystagmus, and left hemiplegia, left axillary lymphadenopathy, and halo nevi on the back. The white blood cell count was 2.5×10^3 /mcL, serum lactate dehydrogenase 944 IU/L, and serum neopterin 58 (normal <10 nmol/L). CSF showed 12 wbc/mcL, protein 196 mg/dL, and glucose 66 mg/dL. MRI revealed new areas of abnormal signal in the right caudate head, basal ganglia, and internal capsule. T-cell lymphoma was diagnosed by supraclavicular lymph node biopsy, and confirmed by stereotaxic biopsy of the right caudate. Chemotherapy