

## HEADACHE DISORDERS

### TOPIRAMATE AND COGNITIVE FUNCTION IN MIGRAINE

Researchers at the Johnson & Johnson Pharmaceutical Research & Development, New Jersey and Belgium, and University of California, Los Angeles, CA used the Cambridge Neuropsychological Test Automated Battery (CANTAB) and cognitive adverse events to evaluate neurocognitive effects of topiramate 100 mg/day vs placebo in 70 migraine patients aged 12 through 17 years. The CANTAB includes measures of object recognition, spatial memory span, paired associates learning, reaction time, sustained attention, and word fluency. Subjects responded to visually presented stimuli on a touch-sensitive screen. Slight statistically significant score increases in 3 CANTAB measures, indicating slowing of reaction time and processing, were associated with topiramate during double-blind treatment lasting 16 weeks. The most common adverse events included anorexia, insomnia, fatigue, and dizziness. Learning, memory, and executive function were unchanged. The tolerability profile of topiramate, including cognitive adverse events, appeared to be acceptable. (Pandina GJ, Ness S, Polverejan E, et al. Cognitive effects of topiramate in migraine patients aged 12 through 17 years. **Pediatr Neurol** 2010;42:187-195). (Respond: Dr Pandina, Clinical Leader, Psychiatry, Johnson & Johnson Pharmaceutical Research & Development, 1125 Trenton-Harbourton Road, Titusville, NJ 08560. E-mail: [gpandina@its.jnj.com](mailto:gpandina@its.jnj.com)).

COMMENT. An open-label study of the effectiveness of topiramate in 97 children with migraine found that the most common side effects were cognitive (12.5%), weight loss (5.6%), and paresthesia (2.8%) (Hershey AD et al. **Headache** 2002;42:810-818). A randomized, double-blind, placebo-controlled trial of topiramate in 162 children (age, 6-15 years) with migraine found 6.5% discontinued treatment because of side effects (URI infection, anorexia, weight decrease, gastroenteritis, paresthesia, and somnolence (Pearlman WP et al. **Headache** 2005;45:1304-1312). A review of 5 published reports of topiramate and migraine found the frequency of side effects varied considerably among studies, the most frequent being weight loss, anorexia, abdominal pain, difficulties in concentrating, sedation and paresthesia. It was concluded that the disability caused by the migraine should be assessed before initiating prophylactic treatment with potential side effects (Ferraro D et al. **J Headache Pain** 2008;9:147-150).

## DEMYELINATING DISEASE

### CSF ABNORMALITIES IN EARLIER- AND LATER-ONSET PEDIATRIC MULTIPLE SCLEROSIS COMPARED

CSF cellular and immunoglobulin G (IgG) profiles in 40 earlier-onset (<11 years) and 67 later-onset (>11 and <18 years) pediatric MS patients were compared in a multicenter US study. Earlier-onset patients had a mean age of 7.2 +/- 2.7 years (60% female), and later-age patients 15.1 +/- 1.7 years (63% female). CSF white blood cell counts were higher in earlier-onset patients (median= 9 mm3 vs 6mm3 (p=0.15) but had a

lower proportion of lymphocytes (70% vs 93%,  $p=0.0085$ ) and a higher proportion of neutrophils ( $p=0.033$ ). An elevated IgG index occurred in fewer earlier-onset disease patients than in the later-onset group (35% vs 68%,  $p=0.031$ ). An activation of the innate rather than the adaptive immune system in the earlier stages of MS is suggested or an immature immune response. (Chabas D, Ness J, Belman A, et al, for the US Network of Pediatric MS Centers of Excellence. **Neurology** Feb 2, 2010;74(5):399-405). (Reprints: Dr Dorothy Chabas, UCSF Regional Pediatric MS Center, 350 Parnasus Avenue, Suite 908, San Francisco, CA 84117). E-mail: [dchabas@gmail.com](mailto:dchabas@gmail.com)).

COMMENT. The CSF profile in pediatric MS is dependent on age of onset, and the age-related variations are important in diagnosis. Pohl D et al (**Neurology** 2004;63:1966-7) reported the CSF characteristics of 136 childhood-onset (<16 years) cases of MS. CSF pleocytosis occurred in 66%, and oligoclonal IgG in 92%.

## ACUTE DISSEMINATED ENCEPHALOMYELITIS AND MULTIPLE SCLEROSIS COMPARED

Clinical characteristics at presentation and follow-up of a cohort of 13 cases (age range 5-67, median 43 years) of *perivenous* demyelination were compared with a cohort of 91 cases (age range 10-69, median 39 years) of *confluent* demyelination (76 [84%] cases of confirmed multiple sclerosis) in a study at the Mayo Clinic, Rochester, MN. Clinical criteria for ADEM were applied to both groups to assess their ability to distinguish ADEM from MS, as determined pathologically. Only two patients with perivenous demyelination were pediatric (aged 5 and 17 years). All but one patient with perivenous demyelination had a monophasic course, whereas two of three with both perivenous and confluent demyelination had a relapsing course. The perivenous cohort was more likely than the confluent demyelination cohort to present with encephalopathy, depressed consciousness, headache, meningismus, CSF pleocytosis or multifocal enhancing MRI lesions. Pathological studies showed a distinct pattern of cortical microglial activation and aggregation without associated cortical demyelination in six perivenous demyelination patients, all of whom had encephalopathy. This cortical pathology was not found in the confluent demyelination cohort. Clinical criteria were 80% sensitive and 91% specific for pathologically defined ADEM. Perivenous demyelination has a meningoencephalopathic presentation and a monophasic course. The co-occurrence of perivenous and confluent demyelination in some patients suggests an overlap between ADEM and MS and misclassification. (Young NP, Weinschenker BG, Parisi JE, et al. Perivenous demyelination: association with clinically defined acute disseminated encephalomyelitis and comparison with pathologically confirmed multiple sclerosis. **Brain** Feb 2010;133:333-348). (Respond: Claudia F Luchinetti MD, Department of Neurology, Mayo Clinic College of Medicine, 200 1<sup>st</sup> Street SW, Rochester, MN 55905. E-mail: [luchinetti.claudia@mayo.edu](mailto:luchinetti.claudia@mayo.edu)).

COMMENT. Lassmann H (**Brain** Feb 2010;133:317-318) comments that the study shows the clinical criteria for the differentiation of ADEM and MS are imperfect, with considerable overlap in clinical presentation. Pathological confirmation of the clinical diagnosis of ADEM may help to refine ADEM clinical criteria.