

neurocognitive impairment. Patient 1, a 13-year-old girl developed a severe headache during a volleyball game and on neurologic examination she had global aphasia, right-sided weakness, and ataxia. The initial MRI was normal, but the initial EEG revealed generalized slowing, 1-2 Hz, in the left hemisphere. Follow-up MRI 9 days after onset of signs revealed increased T2 signal involving the left hemisphere, with mild mass effect and midline shift. Her mother and brother had frequent migraine episodes accompanied by confusion, aphasia and hemiplegia. Treatment included verapamil, valproic acid, methylprednisolone, and IV immunoglobulin. The diagnosis of familial hemiplegic migraine was supported by CACNA1A gene mutations. She was maintained without further migraine episodes while taking verapamil as prophylactic. MRI and EEG repeated at 4 months follow-up were normal, but she had attention and memory problems in school. Two male patients, ages 8 and 15 years, with similar histories to that of case 1 had EEGs that revealed slowing in one hemisphere, 1-2 Hz, consistent with the MRI finding of unilateral cerebral edema. Mutation was located on ATP1A2 gene in case 2, and gene mutation was lacking in case 3; minor head trauma may have precipitated this patient's migraine attack. Neuropsychological evaluation and/or school reports at follow-up revealed cognitive impairment, memory and attention problems in all 3 patients. (Asghar SJ, Milesi-Halle A, Kaushik C, Glasier C, Sharp GB. Variable manifestations of familial hemiplegic migraine associated with reversible cerebral edema in children. **Pediatr Neurol** 2012 Sep;47(3):201-4). (Respond: Dr Asghar, Section of Pediatric Neurology, University of Arkansas Children's Hospital, Little Rock, AR 72202. E-mail: asgharsheilaj@uams.edu).

COMMENT. Genetic heterogeneity and persistent cognitive impairment are illustrated by these case reports of variable manifestations of familial hemiplegic migraine. EEG slowing was consistent with the temporary cerebral edema as a feature of FHM. A triad of prolonged hemiplegic migraine, cerebellar ataxia, and epileptic seizures is linked to CACNA1A gene mutations and may be complicated by status epilepticus. (Zangaladze A et al. **Epilepsy Behav** 2010 Feb;17(2):293-5). This report recommends that patients with prolonged hemiplegic migraine attacks and confusion be tested with continuous EEG to rule out electrographic status.

Sporadic hemiplegic migraine presenting as acute encephalopathy. A 10-year-old boy with psychomotor delay and cerebellar vermis atrophy developed right hemiplegia with vomiting, loss of consciousness, convulsions, and fever. EEG showed delta activity over the left hemisphere, and MRI revealed swelling of the left temporo-occipital cortex. Interleukin-6 was elevated in the CSF. Acute symptoms resolved after 3 weeks and recurred 7 months later with migraine attacks. A de novo mutation in the CACNA1A gene was identified. Family history was negative for migraine. Both familial and sporadic hemiplegic migraines are genetically heterogeneous, the majority caused by CACNA1A mutations. (Ohmura K, et al. **Brain Dev** 2012 Sep;34(8):691-5).

SEX DIFFERENCES IN BRAIN OF MIGRAINEURS

Researchers at Children's Hospital Boston and other Harvard Medical School centers studied alterations in brain structure in male and female age-matched interictal

(migraine free) migraineurs and controls, using high-field MRI. Female migraineurs had thicker posterior insula and precuneus cortices and functional differences in response to noxious stimuli compared with male migraineurs and healthy controls of both sexes. Female migraineurs show greater activation in brain regions involved in emotional processing: amygdala, parahippocampus, basal ganglia and posterior cingulate cortex. (Maleki N, Linnman C, Brawn J, Burstein R, Becerra L, Borsook D. Her versus his migraine: multiple sex differences in brain function and structure. **Brain** 2012 Aug;135(Pt 8):2546-59). (Respond: Nasim Maleki PhD, Department of Anesthesia, Children's Hospital Boston, Harvard Medical School, Boston, MA 02115. E-mail: nasim.maleki@childrens.harvard.edu).

COMMENT. These findings may be important in therapy of migraine and development of specific drugs for female migraineurs, targeting stress related disorders. *Papez' circuit*, a major pathway of the limbic system that controls emotion, is involved in female migraine. The initial description of the pathway by Papez is as follows: hippocampal formation, fornix, mammillary bodies, mammillothalamic tract, anterior thalamic nucleus, internal capsule, cingulate gyrus, parahippocampal gyrus, entorhinal cortex, hippocampus. The prefrontal cortex and amygdala were included later in a larger loop or "circuit of emotion." (Eggers AE. Redrawing Papez' circuit: a theory about how acute stress becomes chronic and causes disease. **Med Hypotheses** 2007;69(4):852-7).

Therapeutic strategies in migraine patients with mood and anxiety disorders list amitriptyline, flunarizine, pregabalin, valproate, topiramate, and lamotrigine (for migraine with aura). (Finocchi C, et al. **Neurol Sci** 2010 Jun;31 Suppl 1:S95-8).

SEIZURE DISORDERS

OUTCOME OF THERAPIES IN REFRACTORY CONVULSIVE STATUS EPILEPTICUS

Researchers at Queen Square, London, review the long-term outcome of therapies in refractory convulsive status epilepticus. Of 596 patients reported (51% of the total of 1168). 201 (35%) died, 79 (13%) had severe neurological deficit, 80 (13%) mild neurological deficit, 22 (4%) with undefined deficit, and 208 (35%) recovered to baseline. The quality of reported outcome data is generally poor, and only broad recommendations for optimal therapy are possible. General anesthesia remains the backbone of therapy, and immediate control is achieved in two-thirds of cases. Agents analyzed include thiopental/pentobarbital, midazolam, propofol, and ketamine, each having advantages and disadvantages. Children are least likely to be treated with propofol because of risk of propofol infusion syndrome, with myocardial failure and high mortality on prolonged infusion. Ketamine is a second-line drug with potential neurotoxic effects. First-line anesthesia therapy should be used with intensive care support and treatment of the underlying cause. Second-line therapies include hypothermia, magnesium and pyridoxine infusions, immunological therapy, ketogenic diet, and neurosurgery. Antiepileptic drug therapy should be used concurrently with anesthesia but outcome data are sparse. Choice of drug regimens include polytherapy with 2 antiepileptic drugs, high-dose, avoid frequent switching, drugs with low interaction