(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

potential, predictable kinetics, drugs without renal or hepatic toxicity, and avoidance of GABAergic AEDs. (Shorvon S, Ferlisi M. The outcome of therapies in refractory and super-refractory convulsive status epilepticus and recommendations for therapy. **Brain** 2012 Aug;135(Pt 8):2314-28). (Respond: Dr Simon Shorvon, UCL Institute of Neurology, Queen Square, London WC1N 3BG, UK. E-mail: s.shorvon@ucl.ac.uk).

COMMENT. The authors comment that the most striking conclusion of their review of literature was the poor quality of outcome data. Only broad recommendations were possible from the analysis of reports. Refractory status epilepticus is heterogeneous and prognosis depends on factors other than treatment, such as age and etiology. General anesthesia is generally effective, and the rate of withdrawal seizures is lower than often quoted. Propofol infusion syndrome is a rare but frequently fatal complication caused by impaired fatty acid oxidation. The hallmarks are metabolic acidosis, lipemia, rhabdomyolysis and myocardial failure. A 10-year-old boy with status epilepticus treated with propofol developed fatal propofol infusion syndrome when a ketogenic diet was initiated. (Baumeister FA, et al. **Neuropediatrics** 2004 Aug;35(4):250-2).

LONG-TERM OUTCOME IN JUVENILE MYOCLONIC EPILEPSY

Researchers at University of Greifswald, Germany; and Cleveland Clinic, OH, studied the long-term seizure outcome in patients with juvenile myoclonic epilepsy (JME) and identified factors predictive of seizure remission. Of 31 patients followed for at least 25 years (mean 39.1 years), 21 (67.7%) were seizure-free, and 6 (28.6%) had AEDs discontinued. Significant predictors for a poor long-term seizure outcome included occurrence of generalized tonic-clonic seizures (GTCS) preceded by bilateral myoclonic seizures ($p=0.03$), long duration of drug refractory epilepsy ($p=0.022$), and AED polytherapy ($p=0.023$). Complete remission of GTCS with AED significantly increases the chance for complete seizure freedom ($p=0.012$). Photoparoxysmal responses significantly increase risk of seizure recurrence after AED discontinuation ($p=0.05$). Long-term seizure freedom in two thirds of patients and validation of outcome predictors should permit clinicians to provide patients with a more favorable potential response to treatment. (Geithner J, Schneider F, Wang Z, et al. Predictors for long-term seizure outcome in juvenile myoclonic epilepsy: 25-63 years of follow-up. **Epilepsia** 2012 Aug;53(8):1379-86). (Respond: Dr Felix Schneider, Department of Neurology, Epilepsy Center, University of Greifswald, Sauerbruchstrasse, 17489 Greifswald, Germany. E-mail: felix.schneider@uni-greifswald.de).

COMMENT. A previous long-term study of JME in 24 patients, 25.8 years after seizure onset, found that 11 (48%) had discontinued treatment and 6 (25%) were seizure-free without AEDs for 5-23 years. (Camfield CS, Camfield PR. **Neurology** 2009 Sep 29;73(13):1041-5). Contrary to current opinion, these reports show that continuation of AED therapy in JME is not required in all patients, and predictive factors for long-term management and outcome are now available.