1. Daily DHA injections raise seizure thresholds and blood but not brain free DHA levels in rats—Marc-Olivier Trépanier, Ameer Y. Taha, Richard P. Bazinet, W.M. Burnham (Departments of Nutrition and Pharmacology, University of Toronto, Canada)

**Background:** Docosahexaenoic acid (DHA) is an omega-3 polyunsaturated fatty acid (n–3 PUFA), which has previously shown to have anticonvulsant activity rats. The purpose of the present experiment was: (1) to confirm that sub-chronic DHA raises thresholds in the maximal pentylenetetrazole (PTZ) model, and (2) to determine whether that increase is correlated with an increase in serum and brain DHA.

**Methods:** Animals received daily i.p. injections of 50 mg/kg of DHA, 50 mg/kg DHA ethyl ester (DHA EE) or volume-matched vehicle for 14 days. On day 15, one group of animals was seizure tested in the maximal PTZ model, while another group provided blood and brain samples. Brain samples were obtained after the animals were euthanized via head-focused microwave fixation. Lipid analyses were performed on both blood and brain. Since the DHA and DHA EE groups did not differ significantly, they were combined for statistical analyses.

**Results:** In the maximal PTZ model, DHA significantly increased seizure latency by approximately 3 fold, as compared to vehicle-injected controls. This increase in seizure latency was associated with an increase in serum unesterified DHA levels. Total brain DHA and brain unesterified DHA, however, were not significantly different between treatment and control groups.

2. Photoparoxysmal response in patients with migraine and epilepsy—Umang Modi a,b, Paul Hwang a,c (a North York General Hospital EEG Lab, Canada, b University Of Toronto EEG Research Program, Canada, c Ontario Brain Institute-EpLink, Toronto, ON, Canada)

**Objectives:** 5% of patients with epilepsy and migraines are photosensitive and liable to visually induce seizures. The similarity between intermittent photic stimulation (IPS) that provokes seizures and those provokes minimal discomfort and a headache suggests that the precipitants share a common neural mechanism.

**Material and methods:** With 10–20 system of electrode placement and Stellate-Harmonie EEG recording system for at least 20 min in bipolar montage with inclusion of ear reference and often sub temporal electrodes. Activation procedures include, eye opening–closing and hyperventilation, for 3–5 min; in early part of recording and IPS near end of recording at a stroboscope distance is 0.5 m from eyes and frequency runs from 1 Hz to 30 Hz every 10 s in incremental fashion.

**Results:** Photoparoxysmal responses (PPR) are abnormal electrographic responses to photic stimulation marked by diffuse paroxysmal discharge occasional minor twitching of fingers or eye balls or clonic movements of the part of body. If it presents with generalized tonic clonic discharge, it is called photoconvulsive response. IPS induces spikes, spike-waves or sometimes intermittent slow waves, bilaterally synchronous, outlasting the end of IPS. It is hypothesized that membrane depolarization of some of the neurons to light stimuli, especially over the posterior head region contribute to photosensitivity.

EEG lab, at NYGH, prevalence of migraine in epileptic population has been assessed at 8.3%, and EEG findings of PPR occurs in 1% of individuals aged 6–18 with seizures where as less than 1% in epileptic patients aged >18. The prevalence figure for migraine is assumed to be 5–10%; where as epilepsy is considered to be 0.5–1%. Prevalence of migraine in epileptic population has been assessed at 8–15%, and prevalence of epilepsy in migrainous population at 1–17%. Lifetime prevalence of 1 in 10,000 in the general population, as low as 2%, of the epilepsy population. PPR is present in 1.3–1.4% of healthy individuals aged 6–18.

**Discussion:** It’s been reported by Ernst and Quesnay that apomorphine, a dopamine receptor agonist, stops clinical and EEG findings of PPR without significantly reduction of spontaneous spike and wave activity. These signify different pathogenic mechanism in origin of spontaneous and evoked generalized epilepsy. It has been shown in cats that decreased endogenous release of dopamine and noradrenaline enhance pre-existing state of cortical excitability. Paroxysmal abnormalities including PPR found increased frequency with migraine and homozygous autosomal recessive inheritance.

PPR sometimes outlasted the stimulus, and self-limited PPR probably have greater significance and are highly correlated with epilepsy. The PPR extending beyond the stimulus carries no increased risk of seizures. Photosensitive epilepsy has a good prognosis for seizure control that is independent of the persistence or disappearance of Photosensitivity. Encephalography has been much dispute in the study of migraine and epilepsy especially when both present as vice-versa triggers. An apparent increase in abnormalities, most of the times nonspecific and used as lateral relationship between migraine and epilepsy in presence of PPR, particularly in children.
Table 1

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</table>

* At least one (past or present) EEG documentation of epileptogenic activity.

Table 1

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Valproate reduces spontaneous generalized spikes and waves but not photoparoxysmal reactions in patients with idiopathic generalized epilepsies. Epilepsia. 2011; 52(7):1297–302 (ISSN: 1528-1167) Muhle H; Ettle E; Boor R; Stephani U; Sinitchkin M Department of Neuropediatrics, University Medical Center.


Although the proband only had nocturnal GTCS, she had four nocturnal generalized tonic-clonic seizures (GTCS), all occurred around 5–6 am, the first one at age 19 years. Diphenylhydantoin was prescribed and later replaced by carbamazepine CR. She has been seizure free since adequate compliance with treatment. Her first EEG performed at 19 years showed an excess of slow waves at 2–4 Hz over both posterior head regions without epileptic activity. Her second EEG at 22 years showed spikes and slow spike waves alternating over both temporal regions, mostly during drowsiness, and increased during hyperventilation. During intermittent photic stimulation, a photomyoclonic response appeared.

4. Familial generalized seizures due to LGI1 mutation: Importance of family history for genetic testing—Dina Amrom, Eva Andermann, Frederick Andermann (Montreal Neurological Hospital and Institute and the Departments of Neurology & Neurosurgery, Human Genetics and Pediatrics, McGill University, Montreal, Quebec, Canada)

Background: It is well known that patients with temporal lobe epilepsy may present with generalized seizures, and the temporal localization depends on further investigation.

We present a family with five individuals in three generations where the clinical pattern consisted largely of generalized seizures, but who were then shown to have epilepsy due to an LGI1 mutation. We wish to discuss the clinical and EEG findings in these patients, and to compare these with families with autosomal dominant partial epilepsy with auditory features (ADPEAF) or familial lateral temporal lobe epilepsy (FTLTE) reported in the literature.

Family report: The proband is a 46-year-old female college graduate who had normal development and no history of head trauma, central nervous system infection or febrile seizures. She had four nocturnal generalized tonic-clonic seizures (GTCS), all occurred around 5–6 am, the first one at age 19 years. Diphenylhydantoin was prescribed and later replaced by carbamazepine CR. She has been seizure free since adequate compliance with treatment. Her first EEG performed at 19 years showed an excess of slow waves at 2–4 Hz over both posterior head regions without epileptic activity. Her second EEG at 22 years showed spikes and slow spike waves alternating over both temporal regions, mostly during drowsiness, and increased during hyperventilation. During intermittent photic stimulation, a photomyoclonic response appeared.

Her 40-year-old sister had her first GTCS at 12 years which was generalized from the onset. All but one of her subsequent attacks occurred during sleep. Before the only seizure that occurred while awake, she felt numbness of her whole body and heard a whooshing sound suggestive of neocortical temporal lobe involvement.

The third sister is 52 years old; she had her first GTCS at 19 years. A year prior to this, she had transient symptoms of a tingling sensation associated with a whooshing noise. She later had other generalized attacks preceded by this aura. A diagnosis of neocortical or lateral temporal lobe epilepsy, possibly ADPEAF or FTLTE, was suggested.

Although the proband only had nocturnal GTCS, LGI1 sequencing was performed on the basis of the family history. A c.611delC mutation leading to a frameshift and premature termination of the protein was identified.
Discussion: Generalized nocturnal and diurnal seizures associated with interictal generalized spike-wave activity occurring in a family with ADPEAF is unusual. They may represent secondarily generalized seizures or primary generalized seizures or both. In addition, photosensitivity in the proband is unusual as well. Among the reported patients with LGII mutation, there are several who have had GTCs and interictal generalized spike-wave and/or polyspike-wave discharges [Ottman et al., 2004].

This family further illustrates that patients with ADPEAF or FLLTE may present with generalized seizures and generalized spike and wave epileptic discharges. Intensive monitoring and attention to aura with auditory features should lead to accurate diagnosis of this genetically determined epileptic syndrome.

This report points to the importance of detailed family history to help orient the diagnosis by genetic testing.

is not well understood, and only limited information is available about post-stroke seizures in aging/aged animals. In particular, early-onset seizures that occur within 24 h post stroke remain to be examined in aging/aged animals. We thus attempted to model the early-onset seizures in aging mice.

Methods: C57 black mice of 16–20 month-old were used. Unilateral hemispheric ischemia was induced by hypoxia-ischemia or middle cerebral artery occlusion (MCAO) models. The animals were under intensive behavioral monitoring and intracranial EEG recordings to detect post-ischemic seizures and then were euthanized for histological assessments of brain injury. Exposure of mouse brain slices to hypoxia-hypoglycemia episodes were used as in vitro model of brain ischemia, and regional population activities were examined via extracellular recordings.

Results: Vigorous convulsive seizures were observed within 24 h following the hypoxia-ischemia or MCAO episode. These seizures were associated with EEG discharges in the brainstem regions but not in the hippocampal and neocortical areas. Development of these convulsive seizures correlated closely with extensive brain injury and poorer overall outcomes. In addition, non-convulsive seizures, characterized by hippocampal and cortical EEG discharges in the absence of convulsions, were observed following the MCAO episode and prior to the convulsive seizures. When examined in brain slices, seizure-like discharges were observed from the hippocampal CA3 area but not from the brainstem or neocortical area.

Conclusions: The early-onset seizures result from severe cerebral ischemia and brain injury. Generation of the convulsive seizures may involve deeper sub-cortical structures particularly the brainstem, and the non-convulsive EEG discharges may originate from the hippocampus. Our data may help understanding genesis of post-stroke seizures in the aging/aged population.


8. Genetic basis of Mabry's syndrome—Miles D. Thompson, Tony Roscioli, Paul A. Hwang, Peter N. Robinson, Danielle M. Andrade, Peter Krawitz (Department of Pharmacology, University of Toronto, Canada, University of New South Wales, School of Women's and Children's Health, Canada, Pediatric Neurology, North York General Hospital, Division of Neurology, Toronto Western Hospital, Canada, Charité Universitätsmedizin Berlin, Institute of Medical Genetics and Human Genetics, Canada)

We review the discovery of two genes disrupted in Mabry syndrome (hyperphosphatasia with developmental disability; OMIM#239300): a syndrome notable for characteristic facial dysmorphology (hypertelorism, a broad nasal bridge and a tented mouth); subtle hand bone abnormalities (variable shortening of middle and distal phalanges) and nerve abnormalities (plaques disrupting Schwann cells) and persistently elevated serum alkaline phosphatase (ALP). In approximately two thirds of cases, the biochemical abnormalities present in Mabry syndrome result from disruption of the phosphoinositol glycan (GPI) anchor as a result of mutations in the phosphoglycan-inositol biosynthesis type V (PIGV) and type O (PIGO) genes. The remaining one third of cases have no known mutation in the GPI anchor pathway. These idiopathic cases are reported to accumulate lysosomal storage material that has been putatively identified as a glycolipid material. As twenty genes are integral to GPI anchor synthesis, we hypothesize that idiopathic cases of Mabry syndrome may result from disruptions in other genes encoding GPI anchor biosynthesis enzymes. We are using exome sequencing and candidate gene approaches to identify the gene(s) responsible for idiopathic Mabry syndrome. This work will assist in elucidating the inborn errors of metabolism that underlie the seizures associated with Mabry syndrome.