

MRI-documented lesions included mesial temporal sclerosis, focal cortical dysplasia, periventricular nodular heterotopia, tuberous sclerosis complex, polymicrogyria, and cortical atrophy. Seizure-onset patterns (n=7) identified across the 53 seizures sampled were as follows: low-voltage fast activity (43%); low-frequency high-amplitude periodic spikes (21%); sharp activity at  $<13\text{Hz}$  (15%); spike and wave activity (9%); burst of high amplitude polyspikes (6%); burst suppression (4%); and delta brush (4%). Periodic spikes were only observed with mesial temporal sclerosis, and delta brush was exclusive to focal cortical dysplasia. Otherwise, each pattern occurred across several pathologies. Compared to other patterns, low voltage fast activity was associated with a larger seizure-onset zone ( $P=0.04$ ). Four patterns (sharp activity, low voltage fast, spike and wave, and periodic spikes) were also found in regions of seizure spread. Each of the 7 patterns was accompanied by a significant increase in high-frequency oscillations at seizure-onset. In periodic spikes and spike and wave activity, ripple and fast ripple densities continued to increase after seizure-onset. (Perucca P, Dubeau F, Gotman J. Intracranial electroencephalographic seizure-onset patterns: effect of underlying pathology. **Brain** 2014 Jan;137(Pt 1):183-96).

**COMMENTARY.** The authors conclude that (1) biologically distinct epileptogenic lesions share intracranial electroencephalographic seizure-onset patterns, suggesting that different pathological substrates can affect similarly networks or mechanisms underlying seizure generation; (2) certain pathologies are associated with EEG signatures at seizure-onset, eg. periodic spikes may reflect mechanisms specific to mesial temporal sclerosis; (3) some seizure-onset patterns (eg periodic spikes) are found in regions of spread and may not always define the epileptogenic zone; and (4) high-frequency oscillations increase at seizure-onset, independently of the pattern. Delta brush, previously described as the EEG signature of the premature infant [1], and with ANMDA encephalitis [2], the association of delta brush with epilepsy and focal cortical dysplasia appears to be a novel finding.

**References.**

1. Milh M, et al. *Cereb Cortex.* 2007 Jul;17(7):1582-94.
2. Kirkpatrick MP, et al. *Epilepsy Behav.* 2011 Feb;20(2):392-4.

## **METABOLIC DISORDERS**

### **FOLINIC ACID RESPONSIVE EPILEPSY IN OHTAHARA SYNDROME**

Investigators at Queen Mary Hospital, Hong Kong, report a case of Ohtahara syndrome with transient folinic acid responsiveness but without evidence of antitoxin dysfunction in a girl later found to have a known STXBP1 mutation. At day 3 of life she had a cluster of epileptic spasms lasting less than 2 min. Ultrasound showed grade 1 intraventricular hemorrhage, but MRI was normal. EEG showed electrographic seizures from both frontal and anterior temporal regions without clinical seizures, unresponsive to 100mg iv pyridoxine. Seizures were controlled with phenobarbital. At day 70, the infant presented with clusters of flexion or extension epileptic spasms with generalized

myoclonic seizures not related to sleep. EEG showed burst suppression pattern, refractory to medication and typical of Ohtahara syndrome. Seizures were unresponsive to pyridoxal phosphate and AEDs. Finally, folinic acid 5 mg/kg per day was added with dramatic response. The child was seizure-free in 1 day, and the EEG showing only generalized slowing had no burst-suppression pattern 4 days later. She was seizure-free for 6 months but relapsed at 10 months of age during a febrile illness. Seizures were finally controlled with sodium valproate and clobazam, but she had severe global developmental delay. Mutation analysis of the ALDH7A1 (antiquitin) gene was negative. Mutation screening revealed a missense mutation in exon 16 of the STXBP1 gene. Analysis of parental DNA confirmed the mutation as de novo. (Tso WWY, Kwong AKY, Fung CW, Wong VCN. Folinic acid responsive epilepsy in Ohtahara syndrome caused by STXBP1 mutation. **Pediatr Neurol** 2014 Feb;50(2):177-80).

COMMENTARY. In addition to Ohtahara syndrome, STXBP1 mutations are associated with West syndrome, and learning disabilities. For Ohtahara syndrome caused by STXBP1 mutations, a trial of folinic acid is indicated. Folinic acid responsive seizures are identical to pyridoxine-dependent epilepsy, and both are caused by a-AASA dehydrogenase deficiency with mutations in the ALDH7A1 (antiquitin) gene [1]. Two patients with neonatal epileptic encephalopathy are reported whose CSF showed the marker of folinic acid-responsive seizures, but who responded to pyridoxine [1]. Treatment with both pyridoxine and folinic acid is recommended for infants with alpha-AASA dehydrogenase deficiency. The Hong Kong patient's seizures caused by mutations in the STXBP1 gene showed transient folinic acid responsiveness and no response to pyridoxine.

#### References.

1. Gallagher RC, et al. *Ann Neurol*. 2009 May;65(5):550-6.

## EARLY NEUROIMAGING IN MOLYBDENUM COFACTOR DEFICIENCY

Investigators at Wakayama Medical University, Japan, report the neuroimaging features soon after birth in 2 siblings with molybdenum cofactor deficiency (MoCoD) type A. Seizures occurred soon after birth. Brain ultrasound revealed subcortical multicystic lesions in the frontal white matter, and brain MRI at 4-24 hours after birth showed restricted diffusion on diffusion-weighted images, with severe atrophy of the entire cortex within 1 month. The corpus callosum was absent or underdeveloped in both infants. (Higuchi R, Sugimoto T, Tamura A, et al. Early features in neuroimaging of two siblings with molybdenum cofactor deficiency. **Pediatrics** 2014 Jan;133(1):e267-71).

COMMENTARY. MoCo is a coenzyme common to sulfite oxidase, xanthine dehydrogenase and aldehyde oxidase. Encephalopathy in MoCoD may result from isolated sulfite oxidase deficiency. MoCoD presents with intractable seizures in the neonatal period and MRI findings are similar to those of hypoxic ischemic encephalopathy (HIE). Since MoCoD progresses rapidly after birth, early diagnosis suspected by MRI findings can be confirmed with low plasma uric acid, positive sulfite