

ADHD-hyperactive-Impulsive subtype (ADHD-C) comorbidity, when compared to non-ADHD/epilepsy patients. Methylphenidate with AEDs may be beneficial in treatment of ADHD and AED refractory epilepsy [2][3].

References.

1. Gross-Tsur V, et al. *J Pediatr*. 1997 Apr;130(4):670-4.
2. Fosi T, et al. *Epilepsia*. 2013 Dec;54(12):2071-81.
3. Millichap JG. *Pediatr Neurol Briefs*. 2014 Feb;28(2):10-11.

TOBACCO SMOKE, NICOTINE AND EPILEPSY

Investigators at University of South Florida, Tampa, FL, review the literature on the differences between tobacco smoke and nicotine, and their roles in causing or protecting against seizures in animal studies and in humans with epilepsy. In addition to nicotine, tobacco smoke contains many harmful constituents, including carbon monoxide, associated with increasing levels of carboxyhemoglobin (CO-Hb) in the blood, a potential cause of seizures. The level of CO-Hb in non-smokers is 1-2%, in heavy smokers 5-6%, while in patients with seizures it can be as high as 10%. Other chemicals in tobacco smoke that can trigger seizures include ammonia, lead, hexane, toluene, cresol, arsenic, and acetone. Some constituents of tobacco smoke, such as carbon dioxide, have anticonvulsant effects. Even nicotine is reported to control seizures in patients with autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE), the first partial epilepsy syndrome in humans caused by a single gene mutation in the nicotinic acetylcholine receptor (nAChR) gene subunits. For people with a past history of smoking, there is no association between epilepsy risk and the number of cigarettes smoked daily. The etiologies of seizures in chronic smokers are numerous, and include noncompliance with taking AEDs, and multisystem disorders such as COPD. Seizure risks are higher in acute secondhand smokers, chronic active smokers, and babies whose mothers smoke. Tobacco smoking agents can be inactive, proconvulsant, or in some cases, anticonvulsant. (Rong L, Frontera AT Jr, Benbadis SR. Tobacco smoking, epilepsy, and seizures. *Epilepsy Behav* 2014 Feb;31:210-8).

COMMENTARY. The use of a nicotine patch, gum or inhaler in the treatment of drug refractory ADNFLE is of interest, but the risk of nicotine addiction may be a contraindication. The efficacy and safety of nicotine as an anticonvulsant for severe pharmacoresistant frontal lobe epilepsy requires further study [1][2][3].

References.

1. Brodtkorb E, Picard F. *Epilepsy Behav*. 2006 Nov;9(3):515-20.
2. Willoughby JO, et al. *Epilepsia*. 2003 Sep;44(9):1238-40.
3. Zerem A, et al. *Epilepsia*. 2013 Jan;54(1):e13-5.

INTRACRANIAL EEG SEIZURE-ONSET PATTERNS

Investigators at Montreal Neurological Institute and Hospital, Canada, studied intracranial electroencephalographic seizure-onset patterns associated with different epileptogenic lesions, and defined high-frequency oscillation correlates of each pattern.

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