

COMMENTARY. **Association of FCD with dysembryoplastic neuroepithelial tumor (DNT).** DNT is a glioneuronal tumor, increasingly recognized as a cause of intractable partial epilepsy in children. Located in the supratentorial cortex, especially the temporal lobe, DNT occurs in three histologic subtypes (simple, complex, and nonspecific). Complex and nonspecific forms are frequently associated with FCD. Based on a series of 78 patients, aged 3-54 years, seen at Sainte-Anne Hospital and other centers in Paris, France, 73% of DNTs were located in the temporal lobe. Histologic subtypes differentiated by MRI were Type 1 (cystic/polycystic-like, complex or simple forms), and Type 2 (nodular-like) and Type 3 (dysplastic-like) nonspecific forms. The epileptogenic zone varied according to MRI subtype: surgical resection could be restricted to the tumor in type 1 and was more extensive in other MRI subtypes, especially in type 3 MRI. Early surgical excision is important in control of DNT-associated epilepsy [1].

References.

1. Chassoux F, Dumas-Duport C. *Epilepsia*. 2013 Dec;54 Suppl 9:129-34.

ATTENTION DEFICIT DISORDERS

METHYLPHENIDATE IN ADHD AND REFRACTORY EPILEPSY

Investigators from Great Ormond Street Hospital, and Institute of Child Health, London, UK, reviewed the case notes of all patients treated with methylphenidate (MPH) for ADHD at an epilepsy center between 1998 and 2005. All patients were taking AED treatment for at least 6 months at time of starting MPH. Of 18 patients identified with refractory epilepsies (14 generalized, 4 focal) and ADHD, 13 were male and 5 female, median age 11.5 years (range 6-18 years). ADHD symptoms improved in 61% of patients following behavioral management and daily MPH 0.3-1 mg/kg/day. Treatment was discontinued because of adverse effects in 3 (18%) patients (dysphoria in 2, anxiety in 1). Seizure control showed no statistical impairment caused by use of MPH; one patient showed an increase in seizure frequency after initiating MPH, and seizure frequency remained elevated after discontinuation of MPH. (Fosi T, Lax-Pericall MT, Scott RC, Neville BG, Aylett SE. Methylphenidate treatment of attention deficit hyperactivity disorder in young people with learning disability and difficult-to-treat epilepsy: Evidence of clinical benefit. *Epilepsia* 2013 Dec;54(12):2071-81).

COMMENTARY. MPH may be beneficial in treatment of ADHD and AED refractory epilepsy, without significant impairment of seizure control. Despite benefits of MPH in the majority of comorbid epilepsy/ADHD patients, an exacerbation of seizures occurring in the occasional patient requires caution and moderation in introduction of MPH and continuation of AED therapy in optimal dosage. Of 20 epilepsy/ADHD patients whose seizures were controlled by AEDs, none had attacks while taking MPH [1]. MPH is generally safe in children with comorbid epilepsy/ADHD whose seizures are controlled with AEDs. In contrast, children with ADHD and subclinical epileptiform EEG not treated with AED are at increased risk of seizures with introduction of MPH. The incidence of seizures following MPH was 16.7% in children with ADHD and centro-temporal (rolandic) spikes compared to 0.6% in ADHD patients with normal EEGs [2].

References.

1. Gross-Tsur, et al. *J Pediatr.* 1997 Apr;130(4):670-4.
2. Hemmer SA, et al. *Pediatr Neurol.* 2001 Feb;24(2):99-102.

RISK FACTORS BY GENDER FOR CHILDREN WITH ADHD

Investigators at University of Western Australia conducted a population-based, case-control study of maternal, pregnancy, and newborn risk factors by gender for children prescribed stimulant medication for treatment of ADHD. Mothers of children with ADHD were significantly more likely to be younger, be single, have smoked in pregnancy, have labor induced, and experience threatened preterm labor, preeclampsia, urinary tract infection in pregnancy, or early term delivery irrespective of the gender of the child, compared with the control group. A possible protective effect of oxytocin augmentation is noted in girls. Factors not identified as risk factors included low birth weight, postterm pregnancy, small for gestational age infant, fetal distress, and low Apgar scores. (Silva D, Colvin L, et al. Environmental risk factors by gender associated with attention-deficit/hyperactivity disorder. ***Pediatrics*** 2014 Jan;133(1):e14-22).

COMMENTARY. Evidence of environmental mediators in ADHD is demonstrated in twin studies, affected twins having greater exposure to certain risk factors [1]. A familial, genetic factor in an estimated 80% of cases may involve the dopamine receptor and transporter genes, but gene-environment interaction is increasingly recognized as a mechanism in the etiology of ADHD [2][3]. Environmental factors may occur prenatally, in the perinatal period, or postnatally [4]. Of all the environmental factors implicated, maternal smoking and nicotine exposure attract the most attention in the literature, but in practice, maternal cigarette smoking is almost invariably denied [4].

References.

1. Lehn H, et al. *J Am Acad Child Adolesc Psychiatry.* 2007 Jan;46(1):83-91.
2. Thapar A, et al. *Br J Psychiatry.* 2007 Jan;190:1-3.
3. Ficks CA, Waldman ID. *Curr Psychiatry Rep.* 2009 Oct;11(5):387-92.
4. Millichap JG. *Pediatrics.* 2008 Feb;121(2):e358-65.

NEUROMUSCULAR DISORDERS

AXONAL NEUROPATHY, MICROCEPHALY AND VRK1 MUTATIONS

Investigators from Baylor College of Medicine, Texas Children's Hospital, Houston, TX; Kennedy Krieger Institute, Baltimore, MD; and University of Minnesota, MN, report 3 patients from 2 unrelated families with a complex neuropathy phenotype characterized by axonal sensorimotor neuropathy, severe nonprogressive microcephaly and cerebral dysgenesis. Compound heterozygous alleles responsible for the clinical phenotype were identified by whole-genome and whole-exome sequencing in 2 affected siblings from 1 family and a homozygous nonsense variant in the third unrelated patient