

Investigators at the John Radcliffe Hospital, University of Oxford, UK, provide a review with updates of new mutations of known CMS causative genes and treatment strategies. The use of salbutamol and ephedrine alone or combined with physostigmine or 3,4-DAP is reported to benefit various CMS subtypes [2].

Of 51 patients attending the myasthenia clinic at the Massachusetts General Hospital, Boston, in 1958–1960, 35 were the juvenile type, 10 the transient neonatal type, and 6 a congenital myasthenia syndrome, under-recognized as a separate phenotype at that time [3].

#### References.

1. Parr JR, et al. Arch Dis Child. 2014 Jun;99(6):539-42.
2. Cruz PM, et al. Curr Opin Neurol. 2014 Oct;27(5):566-75.
3. Millichap JG, Dodge PR. Neurology. 1960 Nov;10:1007-14.

## SEIZURE DISORDERS

### **MOTOR CO-ACTIVATION OF JUVENILE MYOCLONIC EPILEPSY IN SIBLINGS**

Investigators at UCL Institute of Neurology, Queen Square, London, UK, used functional magnetic resonance imaging to study the effect of cognitive effort during a working memory task as a trigger of myoclonic jerks in 15 unaffected siblings (10 female; age range 18-65 years, median 40 yrs) of 11 patients with juvenile myoclonic epilepsy (6 female; age range 22-54 yrs, median 35). fMRI activations were compared with 20 age- and gender-matched healthy control subjects.

Unaffected siblings showed abnormal primary motor cortex and supplementary motor area co-activation with increasing cognitive load, as well as increased task-related functional connectivity between motor and prefrontal cognitive networks, with a similar pattern to that in patients with JME ( $P < 0.001$ ). This finding in unaffected siblings suggests a mechanism for impairment of frontal lobe functions in both patients and siblings, independent of effects of medication or seizure, an endophenotype of JME. (Wandschneider B, Centeno M, Vollmar C, et al. Motor co-activation in siblings of patients with juvenile myoclonic epilepsy: an imaging endophenotype? **Brain** 2014 Sep;137(Pt 9):2469-79).

COMMENTARY. The abnormal frontal lobe function demonstrated by fMRI in adults with JME and their siblings is also demonstrated in children.

**Neurodevelopment in new-onset juvenile myoclonic epilepsy.** Investigators at Irvine University, CA, studied the maturation of cognitive and brain development in 19 children with new-onset JME in the first 2 years after diagnosis and 57 healthy controls. Abnormal patterns of brain development affecting frontoparietotemporal regions, as assessed by MRI, were evident in children with JME and included attenuation of age-related decline in cortical volume, thickness, and surface area. Children with JME have abnormal structural brain development and impaired cognitive development early in the course of the epilepsy [1].

#### References.

1. Lin JJ, et al. *Ann Neurol*. 2014 Aug 1. [Epub ahead of print].

## NEUROMETABOLIC CAUSES OF INFANTILE SPASMS

Investigators at King Abdulaziz Medical City, Riyadh, Saudi Arabia, studied the prevalence of hereditary neurometabolic causes of infantile spasms in 80 cases presenting over a 15-year period. Of 10 patients (12.5%) diagnosed with metabolic causes, 2 had a Leigh-like disorder, and 1 patient had each of the following diagnoses: ethylmalonic aciduria, nonketotic hyperglycinemia, hyperinsulinemic hypoglycemia, leukodystrophy, short-chain acyl-coenzyme A dehydrogenase deficiency, molybdenum cofactor deficiency, primary carnitine deficiency, and neonatal hypoglycemia due to panhypopituitarism. Most of the patients were born of consanguineous parents, and the hereditary group had a strong history of other family members affected. The typical hypsarrhythmia pattern in the EEG was more common in the hereditary metabolic group ( $P=0.003$ ), and this group had a poor response to therapy ( $P=0.04$ ). Metabolic disorders are a relatively common cause of infantile spasms in this subpopulation of Saudi patients. Early diagnosis with metabolic and genetic testing is important in selection of specific treatments and facilitating family counseling. (Alrifai MT, AlShaya MA, Abdulaban A, Alfadhel M. Hereditary neurometabolic causes of infantile spasms in 80 children presenting to a tertiary care center. *Pediatr Neurol* 2014 Sep;51(3):390-7).

COMMENTARY. In patients suspected of having a hereditary metabolic cause for infantile spasms, the authors recommend a more liberal application of advanced diagnostic techniques, such as whole exome sequencing, muscle biopsy for mitochondria biochemical and genetic studies, and newer neuroimaging techniques such as 3 Tesla MRI and PET scanning [1]. More extensive genetic testing is justified in higher risk populations where high consanguinity rates are prevalent. A review of etiology of infantile spasms in the United Kingdom where consanguinity is rare finds the common causes are hypoxic-ischemic encephalopathy (10%), chromosomal anomalies (8%), malformation (8%), perinatal stroke (8%), and tuberous sclerosis complex (7%) [2][3].

#### References.

1. Alrifai MT, et al. *Pediatr Neurol*. 2014 Sep;51(3):390-7.
2. Pavone P, et al. *Brain Dev*. 2014 Oct;36(9):739-751.
3. Osborne JP, et al. *Epilepsia*. 2010 Oct;51(10):2168-74.

## DEVELOPMENTAL DISORDERS

### AAP GENETICS DIAGNOSTIC APPROACH TO INTELLECTUAL DISABILITY OR GLOBAL DEVELOPMENTAL DELAY

The American Academy of Pediatrics Committee on Genetics present a recommended clinical genetics diagnostic approach to the evaluation of intellectual disability or global developmental delays. The report addresses the advances in diagnosis and treatment of children with intellectual disabilities since the original AAP report in