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# Abstracts

Articles appearing in the August 2019 issue

## Congenital myopathies in the adult neuromuscular clinic: Diagnostic challenges and pitfalls

**Objective** To investigate the spectrum of undiagnosed congenital myopathies (CMs) in adults presenting to our neuromuscular clinic and to identify the pitfalls responsible for diagnostic delays.

**Methods** We conducted a retrospective review of patients diagnosed with CM in adulthood in our neuromuscular clinic between 2008 and 2018. Patients with an established diagnosis of CM before age 18 years were excluded.

**Results** We identified 26 patients with adult-onset CM and 18 patients with pediatric-onset CM who were only diagnosed in adulthood. Among patients with adult onset, the median age at onset was 47 years, and the causative genes were *RYR1* (11 families), *MYH7* (3 families), and *ACTA1* (2 families), and *SELENON*, *MYH2*, *DNM2*, and *CACNA1S* (1 family each). Of 33 patients who underwent muscle biopsy, only 18 demonstrated histologic abnormalities characteristic of CM. Before their diagnosis of CM, 23 patients had received other diagnoses, most commonly non-neurologic disorders. The main causes of diagnostic delays were mildness of the symptoms delaying neurologic evaluation and attribution of the symptoms to coexisting comorbidities, particularly among pediatric-onset patients.

**Conclusions** CMs in adulthood represent a diagnostic challenge, as they may lack the clinical and myopathologic features classically associated with CM. Our findings underscore the need for a revision of the terminology and current classification of these disorders.

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## Human *GABRG2* generalized epilepsy: Increased somatosensory and striatothalamic connectivity

**Objective** To map fMRI connectivity within and between the somatosensory cortex, putamen, and ventral thalamus in individuals from a family with a GABAergic deficit segregating with febrile seizures and genetic generalized epilepsy.

**Methods** We studied 5 adults from a family with early-onset absence epilepsy or febrile seizures and a $GABA_A$ receptor subunit γ2 pathogenic variant (*GABRG2[R43Q]*) vs 5 age-matched controls. We infer differences between participants with the *GABRG2* pathogenic variant and controls in resting-state fMRI connectivity within and between the somatosensory cortex, putamen, and ventral thalamus.

**Results** We observed increased fMRI connectivity within the somatosensory cortex and between the putamen and ventral thalamus in all individuals with the *GABRG2* pathogenic variant compared with controls. Post hoc analysis showed less pronounced changes in fMRI connectivity within and between the primary visual cortex and precuneus.

**Conclusions** Although our sample size was small, this preliminary study suggests that individuals with a *GABRG2* pathogenic variant, raising risk of febrile seizures and generalized epilepsy, display underlying increased functional connectivity both within the somatosensory cortex and in striatothalamic networks. This human network model aligns with rodent research and should be further validated in larger cohorts, including other individuals with generalized epilepsy with and without known GABA pathogenic variants.

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## Most-Read Articles

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**_KCNQ2_ encephalopathy: Features, mutational hot spots, and ezogabine treatment of 11 patients**

J.J. Millichap, K.L. Park, T. Tsuchida, et al. 2016;2:e96. doi.org/10.1212/NXG.0000000000000096

***CHCHD10* variant p.(Gly66Val) causes axonal Charcot-Marie-Tooth disease**

M. Auranen, E. Ylikallio, M. Shcherbii, et al. 2015;1:e1. doi.org/10.1212/NXG.0000000000000003

**The Clinical Outcome Study for dysferlinopathy: An international multicenter study**

E. Harris, C.L. Bladen, A. Mayhew, et al. 2016;2:e89. doi.org/10.1212/NXG.0000000000000089

**Mendelian randomization shows a causal effect of low vitamin D on multiple sclerosis risk**

B. Rhead, M. Bäärnhielm, M. Gianfrancesco, et al. 2016;2:e97. doi.org/10.1212/NXG.0000000000000097

**A novel *DYNC1H1* mutation causing spinal muscular atrophy with lower extremity predominance**

Q. Niu, X. Wang, M. Shi, Q. Jin. 2015;1:e20. doi.org/10.1212/NXG.0000000000000017

**Redefining the phenotype of ALSP and AARS2 mutation–related leukodystrophy**

R. Lakshmanan, M.E. Adams, D.S. Lynch, et al. 2017;3:e135. doi.org/10.1212/NXG.0000000000000135

 