WHAT'S HAPPENING IN Neurology® Genetics

Neurology.org/NG

Abstracts

Articles appearing in the October 2020 issue

D-DEMØ, a distinct phenotype caused by *ATP1A3* mutations

Objective To describe a phenotype caused by *ATP1A3* mutations, which manifests as dystonia, dysmorphism of the face, encephalopathy with developmental delay, brain MRI abnormalities always including cerebellar hypoplasia, no hemiplegia (Ø) (D-DEMØ), and neonatal onset.

Methods Review and analysis of clinical and genetic data.

Results Patients shared the above traits and had whole-exome sequencing that showed de novo variants of the *ATP1A3* gene, predicted to be disease causing and occurring in regions of the protein critical for pump function. Patient 1 (c.1079C>G, p.Thr360Arg), an 8-year-old girl, presented on day 1 of life with episodic dystonia, complex partial seizures, and facial dysmorphism. MRI of the brain revealed cerebellar hypoplasia. Patient 2 (c.420G>T, p.Gln140His), an 18-year-old man, presented on day 1 of life with hypotonia, tremor, and facial dysmorphism. He later developed dystonia. MRI of the brain revealed cerebellar hypoplasia and, later, further cerebellar volume loss (atrophy). Patient 3 (c.974G>A, Gly325Asp), a 13-year-old girl, presented on day 1 of life with tremor, episodic dystonia, and facial dysmorphism. MRI of the brain showed severe cerebellar hypoplasia. Patient 4 (c.971A>G, p.Glu324Gly), a 14-year-old boy, presented on day 1 of life with tremor, hypotonia, dystonia, nystagmus, facial dysmorphism, and later seizures. MRI of the brain revealed moderate cerebellar hypoplasia.

Conclusions Conclusions D-DEMØ represents an *ATP1A3*-related phenotype, the observation of which should trigger investigation for *ATP1A3* mutations. Our findings, and the presence of multiple distinct *ATP1A3*-related phenotypes, support the possibility that there are differences in the underlying mechanisms.

NPub.org/NG/9521a

Variant repeats within the *DMPK* CTG expansion protect function in myotonic dystrophy type 1

Objective We tested the hypothesis that variant repeat interruptions (RIs) within the *DMPK* CTG repeat tract lead to milder symptoms compared with pure repeats (PRs) in myotonic dystrophy type 1 (DM1).

Methods We evaluated motor, neurocognitive, and behavioral outcomes in a group of 6 participants with DM1 with RI compared with a case-matched sample of 12 participants with DM1 with PR and a case-matched sample of 12 unaffected healthy comparison participants (UA).

Results In every measure, the RI participants were intermediate between UA and PR participants. For muscle strength, the RI group was significantly less impaired than the PR group. For measures of Full Scale IQ, depression, and sleepiness, all 3 groups were significantly different from each other with UA > RI > PR in order of impairment. The RI group was different from unaffected, but not significantly different from PR (UA > RI = PR) in apathy and working memory. Finally, in finger tapping and processing speed, RI did not differ from UA comparisons, but PR had significantly lower scores than the UA comparisons (UA = RI > PR).

Conclusions Our results support the notion that patients affected by DM1 with RI demonstrate a milder phenotype with the same pattern of deficits as those with PR indicating a similar disease process.

NPub.org/NG/9521b

Most-Read Articles

As of September 28, 2020

Homozygous deletion in *MICU1* presenting with fatigue and lethargy in childhood

D. Lewis-Smith, K. J. Kamer, H. Griffin, et al. 2016;2e59. doi.org/10.1212/NXG.0000000000000059

***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

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

***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

