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Abstracts

Articles appearing in the October 2019 issue

Epidemiology of DYT1 dystonia: Estimating prevalence via genetic ascertainment

Objective To estimate the prevalence of TOR1A sequence variants associated with DYT1 dystonia.

Methods We determined the frequency of the common trinucleotide deletion that causes DYT1 in the Genome Aggregation Database and the Penn Medicine Biobank, totaling exomes from over 135,000 individuals. We also evaluated the prevalence of other possible pathogenic variants in this gene and asked whether the D216H polymorphism is linked to a higher diagnostic rate for dystonia independent of the DYT1-causing mutation.

Results The estimated range of prevalence of the most common pathogenic variant that causes DYT1 is ~17.6–26.1 carriers per 100,000 individuals. Based on the different data sets used, we predict that there are between 54,366 and 80,891 mutation carriers in the United States, which, due to the reduced penetrance of this variant, would translate into 16,475–24,513 DYT1 patients.

Conclusions Our data provide a prevalence estimate of the most common DYT1 mutation in the general population. This information is specifically important for those with interest in the development of precision therapeutics for dystonia.

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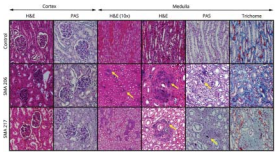
Impaired kidney structure and function in spinal muscular atrophy



Objective To determine changes in serum profiles and kidney tissues from patients with spinal muscular atrophy (SMA) type 1 compared with age- and sex-matched controls.

Methods In this cohort study, we investigated renal structure and function in infants and children with SMA type 1 in comparison with age- and sex-matched controls.

Results Patients with SMA had alterations in serum creatinine, cystatin C, sodium, glucose, and calcium concentrations, granular casts and crystals in urine, and nephrocalcinosis and fibrosis. Nephrotoxicity and polycystic kidney disease PCR arrays revealed multiple differentially expressed genes, and immunoblot analysis showed decreased calcium-sensing receptors and calbindin and increased insulin-like growth factor–binding proteins in kidneys from patients with SMA.

Conclusions These findings demonstrate that patients with SMA type 1, in the absence of disease-modifying therapies, frequently manifest impaired renal function as a primary or secondary consequence of their disease. This study provides new insights into systemic contributions to SMA disease pathogenesis and the need to identify coadjuvant therapies.

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

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

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H Mitsumoto, PL Nagy, C Jennings, et al. 2015;1:e3. doi.org/10.1212/01.NXG.0000464294.88607