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Abstracts

Articles appearing in the June 2020 issue

Phenotypic variability in chorea-acanthocytosis associated with novel *VPS13A* mutations

Objective To perform a comprehensive characterization of a cohort of patients with choreaacanthocytosis (ChAc) in Sweden.

Methods Clinical assessments, targeted genetic studies, neuroimaging with MRI, [^{18}F]-fluorodeoxyglucose (FDG) PET, and dopamine transporter with ^{123}I FP-CIT (DaTscan) SPECT. One patient underwent magnetic resonance spectroscopy (MRS).

Results Four patients living in Sweden but with different ethnical backgrounds were included. Their clinical features were variable. Biallelic *VPS13A* mutations were confirmed in all patients, including 3 novel mutations. All tested patients had either low or absent chorein levels. One patient had progressive caudate atrophy. Investigation using FDG-PET revealed severe bilateral striatal hypometabolism, and DaTscan SPECT displayed presynaptic dopaminergic deficiency in 3 patients. MRS demonstrated reduced N-acetylaspartate/creatine (Cr) ratio and mild elevation of both choline/Cr and combined glutamate and glutamine/Cr in the striatum in 1 case. One patient died during sleep, and another was treated with deep brain stimulation, which transiently attenuated feeding dystonia but not his gait disorder or chorea.

Conclusions Larger longitudinal neuroimaging studies with different modalities, particularly MRS, are needed to determine their potential role as biomarkers for ChAc.

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Genotyping single nucleotide polymorphisms for allele-selective therapy in Huntington disease

Background The huntingtin gene (*HTT*) pathogenic cytosine-adenine-guanine (CAG) repeat expansion responsible for Huntington disease (HD) is phased with single nucleotide polymorphisms (SNPs), providing targets for allele-selective treatments.

Objective This prospective observational study defined the frequency at which rs362307 (SNP1) or rs362331 (SNP2) was found on the same allele with pathogenic CAG expansions.

Methods Across 7 US sites, 202 individuals with HD provided blood samples that were processed centrally to determine the number and size of CAG repeats, presence and heterozygosity of SNPs, and whether SNPs were present on the mutant *HTT* allele using long-read sequencing and phasing.

Results Heterozygosity of SNP1 and/or SNP2 was identified in 146 (72%) individuals. The 2 polymorphisms were associated only with the m*HTT* allele in 61% (95% high density interval: 55%, 67%) of individuals.

Conclusions These results are consistent with previous reports and demonstrate the feasibility of genotyping, phasing, and targeting of *HTT* SNPs for personalized treatment of HD.

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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

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

The Alzheimer's Disease Sequencing Project: Study design and sample selection

G.W. Beecham, J.C. Bis, E.R. Martin, et al. 2017;3:e194. doi.org/10.1212/NXG.0000000000000194

