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Abstracts

Articles appearing in the December 2018 issue

Anti-inflammatory effects of dietary vitamin D_3 in patients with multiple sclerosis

Objective To assess the effects of dietary vitamin D_3 on proinflammatory (interleukin [IL]-17A and IL-6) and anti-inflammatory (IL-10) cytokines.

Methods Our study was conducted on 75 participants who were divided into 3 groups: multiple sclerosis participants (MSPs, n = 25), first-degree relative participants (FDRPs, n = 25), and healthy participants (HPs, n = 25). All groups received 50,000 IU vitamin D_3/wk for 8 weeks. Serum 25-(OH) vitamin D_3 levels and messenger RNA (mRNA) expression levels of ILs were determined using electrochemiluminescence assay and real-time PCR, respectively.

Results Vitamin D_3 affected the levels of IL-17A, IL-10, and IL-6 among the 3 groups ($p < 0.001$ for all). Levels of IL-17A (MSPs: fold change [FC] = 5.9, $p = 0.014$; FDRPs: FC = 5.2, $p = 0.006$; HPs: FC = 4.2, $p = 0.012$) and IL-6 (MSPs: FC = 5.6, $p = 0.003$; FDRPs: FC = 5.5, $p = 0.002$; HPs: FC = 5.1, $p < 0.001$) were downregulated after vitamin D_3 treatment. In addition, levels of IL-10 (MSPs: FC = 6.2, $p = 0.005$; FDRPs: FC = 4.6, $p < 0.001$; HPs: FC = 5.2, $p < 0.001$) were upregulated after 8 weeks.

Conclusions Although supplementation with vitamin D_3 reduced the mRNA expression levels of IL-17A and IL-6, it increased the mRNA expression level of IL-10 in all groups. However, these effects were more considerable in the MSP group than in the other groups. Of interest, in a deficiency state of serum vitamin D_3, IL-17A expression had a positive feedback effect on the expression of IL-6. Conversely, in the sufficient state, IL-10 expression had a negative feedback effect on the expression of IL-17A and IL-6.

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Novel genotype-phenotype and MRI correlations in a large cohort of patients with *SPG7* mutations

Objective To clinically, genetically, and radiologically characterize a large cohort of *SPG7* patients.

Methods We used data from next-generation sequencing panels for ataxias and hereditary spastic paraplegia to identify a characteristic phenotype that helped direct genetic testing for variations in *SPG7*. We analyzed MRI. We reviewed all published *SPG7* mutations for correlations.

Results We identified 42 cases with biallelic *SPG7* mutations, including 7 novel mutations, including a large multi-exon deletion, representing one of the largest cohorts described so far. We identified a characteristic phenotype comprising cerebellar ataxia with prominent cerebellar dysarthria, mild lower limb spasticity, and a waddling gait, predominantly from a cohort of idiopathic ataxia. We report a rare brain MRI finding of dentate nucleus hyperintensity on T2 sequences with *SPG7* mutations. We confirm that the c.1529C>T allele is frequently present in patients with long-standing British ancestry. Based on the findings of the present study and existing literature, we confirm that patients with homozygous mutations involving the M41 peptidase domain of *SPG7* have a younger age at onset compared to individuals with mutations elsewhere in the gene (14 years difference, $p < 0.034$), whereas c.1529C>T compound heterozygous mutations are associated with a younger age at onset compared to homozygous cases (5.4 years difference, $p < 0.022$).

Conclusions Mutant *SPG7* is common in sporadic ataxia. In patients with British ancestry, c.1529C>T allele represents the most frequent mutation. *SPG7* mutations can be clinically predicted by the characteristic hybrid spastic–ataxic phenotype described above, along with T2 hyperintensity of the dentate nucleus on MRI.

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

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

KCNQ2 encephalopathy: Features, mutational hot spots, and ezogabine treatment of 11 patients

J.J. Millichap, K.L. Park, T. Tsuchida, B. Ben-Zeev, et al. 2016;2:ex. doi.org/10.1212/NXG.0000000000000096

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

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