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Abstracts

Articles appearing in the December 2019 issue

Yield of comparative genomic hybridization microarray in pediatric neurology practice

Objective The present study investigated the diagnostic yield of array comparative genomic hybridization (aCGH) in a large cohort of children with diverse neurologic disorders as seen in child neurology practice to test whether pathogenic copy number variants (CNVs) were more likely to be detected in specific neurologic phenotypes.

Methods A retrospective cross-sectional analysis was performed on 555 children in whom a genetic etiology was suspected and who underwent whole-genome aCGH testing between 2006 and 2012. Neurologic phenotyping was performed using hospital medical records. An assessment of pathogenicity was made for each CNV, based on recent developments in the literature.

Results Forty-seven patients were found to carry a pathogenic CNV, giving an overall diagnostic yield of 8.59%. Certain phenotypes predicted for the presence of a pathogenic CNV, including developmental delay (odds ratio [OR] 3.69 [1.30–10.51]), cortical visual impairment (OR 2.73 [1.18–6.28]), dysmorphism (OR 2.75 [1.38–5.50]), and microcephaly (OR 2.16 [1.01–4.61]). The combination of developmental delay/intellectual disability with dysmorphism and abnormal head circumference was also predictive for a pathogenic CNV (OR 2.86 [1.02–8.00]). For every additional clinical feature, there was an increased likelihood of detecting a pathogenic CNV (OR 1.18 [1.01–1.38]).

Conclusions The use of aCGH led to a pathogenic finding in 8.59% of patients. The results support the use of aCGH as a first-tier investigation in children with diverse neurologic disorders, although whole-genome sequencing may replace aCGH as the detection method in the future. In particular, the yield was increased in children with developmental delay, dysmorphism, cortical visual impairment, and microcephaly.

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Migraine polygenic risk score associates with efficacy of migraine-specific drugs

Objective To assess whether the polygenic risk score (PRS) for migraine is associated with acute and/or prophylactic migraine treatment response.

Methods We interviewed 2,219 unrelated patients at the Danish Headache Center using a semistructured interview to diagnose migraine and assess acute and prophylactic drug response. All patients were genotyped. A PRS was calculated with the linkage disequilibrium pred algorithm using summary statistics from the most recent migraine genome-wide association study comprising ~375,000 cases and controls. The PRS was scaled to a unit corresponding to a twofold increase in migraine risk, using 929 unrelated Danish controls as reference. The association of the PRS with treatment response was assessed by logistic regression, and the predictive power of the model by area under the curve using a case-control design with treatment response as outcome.

Results A twofold increase in migraine risk associates with positive response to migraine-specific acute treatment (odds ratio [OR] = 1.25 [95% confidence interval (CI) = 1.05–1.49]). The association between migraine risk and migraine-specific acute treatment was replicated in an independent cohort consisting of 5,616 triptan users with prescription history (OR = 3.20 [95% CI = 1.26–8.14]). No association was found for acute treatment with non–migraine-specific weak analgesics and prophylactic treatment response.

Conclusions The migraine PRS can significantly identify subgroups of patients with a higher-than-average likelihood of a positive response to triptans, which provides a first step toward genetics-based precision medicine in migraine.

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