Novel *MECP2* mutations in Czech patients with Rett syndrome

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Background: Rett syndrome (RTT) is a progressive X-linked dominant neurodevelopmental disorder primarily caused by *de novo* mutations in the methyl-CpG binding protein 2 gene (*MECP2*). MeCP2 is a multifunctional protein involved in transcription regulation, chromatin architecture, and other biologically relevant phenomena. We report an update on mutation analysis of the *MECP2* gene in Czech patients with Rett syndrome and intellectual disability with Rett-like features and describe 3 novel pathogenic mutations.

Subjects and Methods: The *MECP2* gene was analyzed in 350 patients using high-resolution melting analysis and Sanger sequencing. Large deletions and duplications were analyzed by multiplex ligation-dependent probe amplification (MRC-Holland).

Observations: Pathogenic mutations were identified in 76 patients (75 girls, 1 boy): 55 had classic RTT, 8 had atypical RTT, 11 had intellectual disability with Rett features or possible Rett syndrome, 1 had autism, and 1 boy had *MECP2* duplication syndrome. We identified 3 novel mutations: c.155_1189del1035;909_932inv;insC, c.573delC, and c.1163_1200del38. A boy with *MECP2*-duplication syndrome inherited the mutation from his asymptomatic mother. The duplication involved genes *MECP2*, *SLC6A8*, *IRAK1*, *IDH3G*, and *L1CAM*.

Conclusions: We confirmed high frequency of *MECP2* mutations in classic RTT (80%) and identified 3 novel pathogenic mutations. Confirmation of molecular defect enabled genetic counseling in affected families.

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