The most recurrent monogenic disorders that overlap with the phenotype of Rett syndrome

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Rett syndrome (RTT) is an early-onset neurodevelopmental disorder that is caused by mutations in the MECP2 gene; however, defects in other genes (CDKL5 and FOXG1) can lead to presentations that resemble classic RTT, although they are not completely identical. Here, we attempted to identify other monogenic disorders that share features of RTT. A total of 437 patients with a clinical diagnosis of RTT-like were studied; in 242 patients, a custom panel with 17 genes related to an RTT-like phenotype was run via a HaloPlex-Target-Enrichment-System. In the remaining 195 patients, a commercial TruSight-One-Sequencing-Panel was analysed. A total of 40 patients with clinical features of RTT had variants which affect gene function in six genes associated with other monogenic disorders. Twelve patients had variants in STXBP1, nine in TCF4, six in SCN2A, five in

KCNQ2, four in MEF2C and four in SYNGAP1. Genetic studies using next generation sequencing (NGS) allowed us to study a larger number of genes associated with RTT-like simultaneously, providing a genetic diagnosis for a wider group of patients. These new findings provide the clinician with more information and clues that could help in the prevention of future symptoms or in pharmacologic therapy.