Cystic center and calculated the total costs of these patients’ diagnostic trajectory in order to evaluate early WES implementation. Materials and Methods: We compared 17 patients’ trio-WES yield with the retrospective costs of diagnostic procedures by comprehensively examining patient records and collecting resource use information for each patient, beginning with patient admission and concluding with WES initiation. We calculated cost savings using scenario analyses to evaluate the costs replaced by WES when used as a first diagnostic tool. Results: WES resulted in diagnostically useful outcomes in 29.4% of patients. The entire traditional diagnostic trajectory average cost was $15,490 per patient, substantially higher than the $3,972 trio-WES cost. WES resulted in average cost savings of $5,547 for genetic and metabolic investigations in diagnosed patients and $1,727 for genetic investigations in undiagnosed patients. Conclusion: The increased causal variant detection yield by WES and the relatively high costs of the entire traditional diagnostic trajectory suggest that early implementation of WES is a relevant and cost-efficient option in patient diagnostics. This information is crucial for centers considering implementation of WES and serves as input for future value-based research into diagnostics.

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Eight further individuals with intellectual disability and epilepsy carrying biallelic CNTP2 aberrations allow delineation of the mutational and phenotypic spectrum.
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Introduction: Heterozygous copy number variants (CNVs) or sequence variants in the contactin-associated protein 2 gene CNTP2 have been discussed as risk factors for a wide spectrum of neurodevelopmental and neuropsychiatric disorders. Biallelic aberrations in this gene are causative for an autosomal-recessive disorder with epilepsy, severe intellectual disability (ID) and cortical dysplasia (CDFS), however, due to the limited number of reported individuals, the full mutational and clinical spectrum has still to be characterized.

Methods and Results: Targeted sequencing, chromosomal microarray analysis or multi gene panel sequencing identified homozygous mutations, compound heterozygous CNVs or compound heterozygous CNVs and mutations in eight individuals from six unrelated families. All mutations were inherited from healthy, heterozygous parent and are predicted to be deleterious for protein function. Epilepsy occurred in all patients with onset in the first three and a half years of life. Further common aspects were severe ID (7/8), regression of speech development (5/8), and behavioural anomalies (7/8). Interestingly, cognitive impairment in one of two affected brothers was comparatively mild with good speech and simple writing abilities. Cortical dysplasia that was previously reported in CDFS, was not present in MRIs of six individuals and only suspected in one.

Conclusion: By identifying novel homozygous or compound heterozygous, deleterious CNVs and mutations in CNTP2 in eight individuals from six independent families with moderate to severe ID, early onset epilepsy and behavioural anomalies, we considerably broaden the mutational and clinical spectrum associated with biallelic aberrations in CNTP2.