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Extended Abstract
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Go for the Cause: Significant Genomic Rearrangements in Cryptogenic Cerebral Palsy

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Aims: To determine the prevalence and characteristics of copy number variations (CNVs) and other genetic abnormalities in children with cerebral palsy (CP) of unknown etiology, comprising approximately 20% of the CP population.

Methods: Fifty-two participants (age 10.5±7.8 years; Gross Motor Function Classification System scale 2.8±1.3) with non-progressive pyramidal and/or extrapyramidal signs since infancy and no identified etiology were enrolled. Individuals with evidence of acquired causes were excluded. Participants underwent neurologic and clinical genetic examinations before the genomic testing. Chromosomal microarray analysis to detect CNVs was performed using the Affymetrix platform. CNVs identified were classified as pathogenic, likely pathogenic, likely benign, or benign. Only pathogenic and likely pathogenic CNVs were defined as clinically significant. Children with , likely benign, or benign were tested for other genetic abnormalities using Exome.

Results: Thirty-nine CNVs were found in 25 of 52 participants (48%). Sixteen participants (31%) had clinically significant CNVs: 10 pathogenic and 6 likely pathogenic, of which 7 were not previously associated with motor disability. Nine participants had likely benign CNVs. Clinically significant

CNVs were more frequently de novo (12/16; $p<0.001$) including in 5 of 8 individuals who had a first- or second-degree relative with a major neurologic disorder. Dysmorphic features and non-motor comorbidities were more prevalent in individuals with clinically significant CNVs ($p< 0.05$ for both). Exome was performed for 20 participants with some initial results.

Conclusion: CNVs, most frequently de novo, are common in individuals with cryptogenic CP. pathogenic genetic mutations were detected by Exome testing . We recommend CNV and Exome testing in individuals with CP of unknown etiology.

Keywords—Cerebral Palsy, copy number variations, cryptogenic, etiology.

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