ADDENDUM

Disruption of *Contactin 4* (*CNTN4*) Results in Developmental Delay and Other Features of 3p Deletion Syndrome

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In our 2004 paper, we described a patient who carried a balanced translocation disrupting *CNTN4*; this patient had features of 3p deletion syndrome and also presented with significant language delay and impairment in social functioning, consistent with an Autism Spectrum Disorder (ASD) diagnosis. In a more recent paper, Bakkaloglu et al.,[1] we justified resequencing of Contactin Associated Protein 2 (*CNTNAP2*) in individuals with ASD based on four lines of evidence: (1) our finding of a de novo balanced chromosomal rearrangement transecting *CNTNAP2* in a patient with mental retardation (MR) and social disability;[1] (2) prior identification of rare homozygous mutations in this transcript in patients with intractable epilepsy and autism;[2] (3) the expression pattern of the transcript and our demonstration of the protein product in the synaptic plasma membrane fraction of rat forebrain lysates;[1] and (4) our previous identification, reported in Fernandez et al., of a de novo rearrangement disrupting *CNTN4* in a patient with MR and ASD.[3] It has been brought to our attention that in this original paper we did not include a full description of the patient's autism assessment, which was conducted at the time of presentation and supervised by one of the authors (A.K.).[3]

Results of that evaluation, which included the Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observation Schedule-Generic (ADOS-G), as well as assessment of cognitive and adaptive functioning, revealed the following. On the ADI-R algorithm, the patient's scores were Social 25 (cut-off 10), Verbal 13 (cut-off 8), and Repetitive Behaviors 3 (cut-off 3), meeting criteria for an ASD diagnosis. Indeed, based on the Autism Genetics Resource Exchange (AGRE) diagnostic algorithm, used to categorize the subjects resequenced in our recent paper,[1] the patient meets criteria for a diagnosis of autism (http://agre.org/agrecatalog/algorithm.cfm). The patient also completed a standardized evaluation with the ADOS-G, resulting in scores of 4 in reciprocal social interaction (cut-off for Pervasive Developmental Disorder Not Otherwise Specified [PDD-NOS] = 4) and 2 in communication (PDD-NOS cut-off = 2), with a total score of 6, falling one point below the threshold for PDD-NOS. Based on the entirety of the available data and direct exam, the expert consensus from two experienced clinicians, generally considered the gold standard in the field, was an ASD diagnosis of PDD-NOS, although this was not stated explicitly in our paper.[3]

Subsequent to publication of Bakkaloglu et al.,[1] a manuscript has been published demonstrating copy number variations interrupting *CNTN4* in patients with autism, further supporting a possible role for Contactin and associated molecules in ASD.[4] We appreciate the opportunity to clarify the record.

References

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