2p16.3 (NRXN1) Deletions

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Deletions at 2p16.3 involving exons of NRXN1 are associated with susceptibility for autism and schizophrenia, and similar deletions have been identified in individuals with developmental delay and dysmorphic features. We have identified 34 probands with exonic NRXN1 deletions following referral for clinical microarray-based comparative genomic hybridization. To more firmly establish the full phenotypic spectrum associated with exonic NRXN1 deletions, we report the clinical features of 27 individuals with NRXN1 deletions, who represent 23 of these 34 families. The frequency of exonic NRXN1 deletions among our postnatally diagnosed patients (0.11%) is significantly higher than the frequency among reported controls (0.02%; P = 6.08 × 10(-7)), supporting a role for these deletions in the development of abnormal phenotypes. Generally, most individuals with NRXN1 exonic deletions have developmental delay (particularly speech), abnormal behaviors, and mild dysmorphic features. In our cohort, autism spectrum disorders were diagnosed in 43% (10/23), and 16% (4/25) had epilepsy. The presence of NRXN1 deletions in normal parents and siblings suggests reduced penetrance and/or variable expressivity, which may be influenced by genetic, environmental, and/or stochastic factors. The pathogenicity of these deletions may also be affected by the location of the deletion within the gene. Counseling should appropriately represent this spectrum of possibilities when discussing recurrence risks or expectations for a child found to have a deletion in NRXN1.