A Case of Autism Associated with Partial Tetrasomy 15

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We report a male individual with partial tetrasomy 15 and severe mental retardation, who met ICD-10 criteria for autism. The relevance of this to the etiology of autism is discussed.

INTRODUCTION

Investigations of groups of subjects with idiopathic autism all point to some neurobiological basis for the disorder. Recent twin and family studies indicate that idiopathic autism is largely determined by genetic factors with heritability estimated at 91-93% (Bailey et al., in press; Bolton et al., 1994). Known medical disorders are found in about 10% to 15% of cases and this rate is probably higher amongst the more profoundly handicapped autistic individuals (Rutter, Bailey, Bolton, & Le Couteur, 1994). The medical conditions reported represent a diverse set of genetic, infectious, and metabolic conditions (Bolton & Rutter, 1990), and for the most part it is uncertain what role they play in etiology. Clearly, an understanding of the ways these conditions produce autism could be helpful in identifying the processes involved in the causation of idiopathic autism. Extra material from chromosome 15 represents one of the more recent chromosomal abnormalities reported in association with autism (Gillberg et al., 1991). An extra marker

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chromosome involving chromosome 15 was first described by Parker and Alfi (1972), following the development of cytogenetic procedures for identifying the origin of the extra derived chromosomal material, and since then over 50 cases have been described. The risk of abnormality appears to be related to increased parental age (Connor & Gilmore, 1984). The nature of the chromosomal abnormality varies from case to case and the associated clinical features show some correspondence to the type of genetic abnormality (Robinson et al., 1993a). Thus, inv(dup)15(pter→q11;q11→pter) is sometimes found in normal individuals and seems not to confer any risk for developmental abnormalities. On occasions, this type of abnormality has been reported in patients with Prader-Willi (PWS) or Angelman syndrome (AS) (Maraschio, Cuoco, Gimelli, Zuffardi, & Tiepolo, 1988), and in these instances the clinical syndrome appears to be due to the occurrence of uniparental disomy, rather than the inv(dup)15 (Robinson et al., 1993b). Abnormalities that involve inversion and duplication of more of the long arm of chromosome 15, extending into the PWS and AS critical region [for example, inv(dup)15(pter→q14;q14→pter)] are usually associated with a range of developmental and physical abnormalities. It has been suggested that the clinical picture may vary according to gene dosage, the length of the region involved and the parental origin of the chromosomal material (Robinson et al., 1993a), but detailed karyotype-phenotype studies of large series have only just begun (Clayton-Smith, Webb, Cheng, Pembrey, & Malcolm, 1993) so no firm conclusions are possible. In the reports of inv(dup)15 extending beyond q11 published to date, pregnancy and delivery are usually described as normal, but developmental abnormalities are often noted in early infancy. Motor milestones are frequently delayed and hypotonia is common. Mental retardation is universal and tends to be severe or profound. Gross physical anomalies are uncommon, but many children have seizures, growth retardation, and a range of facial anomalies (abnormal ears, strabismus, antimongoloid stand, high arched palate, and epicanthic folds—see Table I (Gilmore, Boyd, McClure, Batstone, & O’Connor, 1984).

In previous case reports a range of behavioral disorders have been noted in association with the genetic abnormality, most notably hyperactivity and aggression (e.g., Wisniewski, Hassold, Heffelfinger, & Higgins, 1979). More recently, Gillberg et al. (1991) have reported six cases of marker chromosome 15 who exhibited features of autism. They showed typical impairments of social interaction, with gaze avoidance and failure to seek comfort or develop social play. Only two of the six had speech and in these cases it was characterized by pronoun reversal and echolalia. In the nonverbal cases there was a failure to use gesture. Four of the cases showed stereotypies and were distressed by environmental change. All but one case met DSM-III-R criteria for autistic disorder.