An analysis of the parental age effect for inv dup (15)

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SUMMARY Parental ages and birth order were analysed in 16 sporadic cases of inv dup (15) using the method of Smith.1 A significant maternal age effect was apparent (d_m = 5.989, SE 1.86; d_r = 2.02, SE 2.496; d_b = -0.138, SE 0.46).

Inv dup (15) is a clinically important cause of mental retardation with few or no dysmorphic features.2 The parental origin of the extra chromosomal material is not known but several authors have commented on the increased parental ages.3 We decided to analyse this parental age effect since a major contribution from one parent would be an important clue to the likely origin of the extra chromosome.

Methods and results

A survey of published reports on inv dup (15) revealed 16 cases which included maternal age, paternal age, birth order, and normal parental karyotypes. These data are presented in table 1, which also includes the year of birth and country of origin of each patient and a numerical reference.

The choice of control data presents a problem in view of the diverse countries of origin of these patients. Data from England and Wales were chosen as complete figures for average paternal age, maternal age, and birth order, and correlations of these three variables are available (table 2). The year 1973 was chosen as this was the median year of birth of the patients.

Mean maternal age, paternal age, and birth order were all raised in comparison with these control data. Analysis by the method of Smith1 revealed a direct maternal age effect (d_m) of 5.989 (2 SE 3.72), a direct paternal age effect (d_r) of 2.02 (2 SE 4.992), and a direct birth order effect (d_b) of -0.138 (2 SE 0.4222). The direct maternal age effect exceeds thrice its standard error and thus is highly statistically significant. Neither the direct paternal age effect nor the direct birth order effect exceed twice their standard errors.

Discussion

Older mothers tend to be married to older fathers and tend to have more children than younger mothers. Thus an analysis of raised parental ages needs to determine the relative contribution of these three components: paternal age, maternal age, and birth order. Analysis by the method of Smith1 uses multiple linear regression to provide values for the direct effect of each of these variables. It also

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provides a standard error for each and if any of the direct estimates exceeds twice their standard error then they are statistically significant. In the present study a significant direct effect was apparent only for maternal age.

In all such studies the choice of appropriate control data is important as parental ages and birth order are liable to change with time in various ethnic groups. Generally data are used for the mean or median year of birth of the patients. This was possible in the present study, but the choice of ethnic group was more difficult since the patients had diverse countries of origin. Control data from England and Wales were chosen as these were both complete and readily available. With this limitation, the presence of such a strong direct maternal age effect suggests, as in trisomy 21, that the mother is the usual source of the extra chromosome in inv dup (15). This proposition could be studied further by the use of restriction fragment length polymorphisms in the involved region of chromosome 15.

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References


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