Possible Linkage between X_g and the Locus for a Gene causing Mental Retardation with or without Hydrocephalus

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Summary. The X_g groups of a kindred in which an X-borne gene evidently caused mental retardation with or without hydrocephalus suggest that the locus for this gene may be linked to X_g .

Hereditary hydrocephalus (Bickers and Adams, 1949) is now known, at least in some families, to be an X-borne condition (Edwards, 1961).

A few families with the X-borne type of hydrocephalus have been tested for the X_g blood groups but with no hint of linkage between their two loci (Edwards, 1968; Jabbour, 1968).

In a kindred recently reported by Fried (1972) a single X-borne gene has apparently caused mental retardation sometimes with and sometimes without hydrocephalus. The X_g groups of the family (Fig. 1) pose a difficult exercise in scoring for linkage.

The deceased maternal grandparents, I.1 and I.2, of the propositus could have had one of three arrangements of X_g genotypes.

1. $X_g^a X_g^a \times X_g$. From the groups of the family this is the most likely guess and the linkage information would then be:

Generation II, no score

Generation III, 9 non-recombinants:1 recombinant

for which the lod scores for the various recombination fractions would be:

0.00	0.05	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45
$-\infty$	1.511	1.596	1.547	1.438	1.283	1.092	0.871	0.614	0.323

and very suggestive of linkage with a most likely recombination fraction of 0.11.

2. $X_g^a X_g \times X_g^a$. This we calculate to be about 15 times less likely than arrangement 1, but cannot be disregarded. The linkage information would now become:

Generation II, z_1 6:0

Generation III, 1 non-recombinant:8 recombinants

and the evidence, though notably conflicting between the two generations, would, in the sum, be strongly against linkage.

3. $X_g^a X_g \times X_g$. This is the least likely arrangement, for the probability of finding all eight daughters and sons in generation II to be $X_g(a+)$ would be only 1 in 256. However, the score (excluding II.2 who may or may not be a carrier) would be:

Generation II, z_1 6:1

Generation III, 9 non-recombinants:1 recombinant

and again very suggestive of linkage.

Professor G. R. Fraser and Professor J. H. Edwards kindly gave a great deal of thought to presenting all the possible arrangements in this family to the assessment of the computer: the outcome (Fig. 2) was in favour of linkage between the disease locus and X_g with a maximum likelihood of 20.2 at a recombination fraction of 0.11.

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FIG. 1. The Xg groups of the family.

FIG. 2. Relative probabilities of linkage for various values of the recombination fraction between the locus for this form of mental retardation and Xg. (With acknowledgment to Professor G. R. Fraser and Professor J. H. Edwards.)

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