LETTERS TO THE EDITOR

Genes for intelligence on the X chromosome

Some 20 years ago Robert Lehrke, a psychologist from Minnesota working in a state hospital for the mentally retarded, suggested that genes that determine the major intellectual traits are carried on the X chromosome.[1 2] At that time Lehrke was severely criticised on the grounds that his hypothesis was inherently improbable,[3] and that the evidence was meagre and could be interpreted in other ways.[4 5] Since then more medical evidence has accumulated to support two of the steps in Lehrke's argument.

(1) *"The well documented excess of males among the mentally retarded (25–50%)"*. Two further studies[6 7] have shown that this male excess results from mutations on the X chromosome, using as evidence the excess of affected brothers over affected sisters and calculating this as a gene frequency for X linked forms of mental retardation.

(2) *"A review of families published at that time with mental retardation showing an X linked pattern of inheritance—which only numbered 5, together with 5 new families that he had identified"*. In the former group three were shown later to have the fragile X syndrome and this we now know is very common. A further two had specific features, one spasticity and the other obesity, and in the remainder, as best as can be judged, the clinical description fell into the non-specific group. As we can see in this issue, this is the most common form. There are now three separate gene localisations, *MRX1, MRX2,* and *MRX3,* and it seems likely that more loci will be defined in the future. His suggestion, therefore, that X linkage may be important, is being cemented by fact.

Lehrke's two other arguments were the lesser variability and reduced extremes of intelligence in the female when compared with the male, which he suggested resulted from the averaging out of the effects at different alleles through Lyonisation. He also noted that mental retardation was transmitted more often from mother to child than from father to child.

If there are genes which directly determine intellectual traits, then one would expect that mutations of such genes would produce phenotypes showing only effects on intelligence, perhaps with secondary effects on behaviour and personality. If so, there should also be no somatic changes, no recognisable metabolic abnormalities, no other neurological signs, and no progression with age, although the effects of the mutations would be less obvious in infancy than in childhood when intellectual thought becomes evident. This is the clinical picture of non-specific mental retardation. Clinical descriptions of autosomal dominant and recessive forms of non-specific mental retardation are rare, ill defined, and found mainly in older publications. The X linked forms are common and are now being mapped on the X chromosome. We would like to reawaken Lehrke's hypothesis and suggest that the mutations that we are now locating associated with non-specific mental retardation are those that have determined the higher intelligence of homo sapiens.

Why should intelligence be coded primarily on the X chromosome? Although, as Ohno[8] and others have stressed, genes on the X chromosome have been conserved throughout mammalian evolution we have to suppose that, in man, additional genes for intelligence have arisen there. Once they had appeared their advantage in a hunter-gatherer society would assure male dominance and rapid dissemination throughout the group.[9] In recent correspondence on this subject Ohno philosophised: "Most mammalian species, including our own, are noticeably sexually dimorphic. As a rule such species practice the polygamous, more precisely the polygynous, mating system; after exhaustive combat between adult males, only the victor gains possession of a large number of females. Is it not ironic if the reward of a victor has been to transmit his intelligence only to his daughters and never to his sons. If the main genetic source of intelligence resides on the X chromosome, man, at least, should have organised the matriarchial society with the polyandrous mating system. Perhaps we are still paying for the mistake of organising the patriarchal society of kings and dukes."

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X linked complicated spastic paraplegia, MASA syndrome, and X linked hydrocephalus owing to congenital stenosis of the aqueduct of Sylvius: variable expression of the same mutation at Xq28

Hereditary 'pure' spastic paraplegia is a disorder characterised by progressive spasticity of the legs in otherwise normal subjects. In the majority of families pedigree data are in accordance with autosomal dominant inheritance, but X linked recessive transmission has also been documented.[1] In the 'complicated' form the spasticity may be combined with a variety of one or more symptoms, such as mental retardation, micro- and macrocephaly, epilepsy, and ocular symptoms.[2 3]

In 1974 Blanchine and Lewis[4] delineated, on the basis of clinical and