

# Intelligence and cognitive profile in the fra(X) syndrome: a longitudinal study in 18 fra(X) boys

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**SUMMARY** A longitudinal study of IQ and cognitive profile in 18 fra(X) positive boys is reported. At the time of diagnosis, four of the boys were mildly retarded, seven were moderately retarded, and five were severely mentally retarded. Intelligence was borderline in one child and normal in another. A decline in intellectual performance with age in the fra(X) syndrome indicated in previous studies was not confirmed and we review the reported data on this subject.

In the various studies of the psychological profile of the fra(X) syndrome consideration has been given to the intellectual functioning of these males. In the initial studies a global estimation of their intellectual performance was given with or without further data on exact IQ measurements. In the majority of these reports, however, precise data on the type of IQ tests were not given.<sup>1-9</sup> In their study, McDermott *et al*<sup>10</sup> reported the different types of IQ tests but did not include final results of these tests.

Different types of IQ tests have been used and most frequently reference is made to the Stanford-Binet scale or Terman-Merrill scale and the Wechsler scales.<sup>11-23</sup> In all the studies, cognitive function was evaluated on the basis of these traditional intelligence tests and in only a minority was consideration given to the broader spectrum of cognitive function. In the fragile X syndrome few data are available on the development of cognitive function and performance in relation to age. In most reports the authors discussed the results of cross sectional studies<sup>7 15 17 22 24 25</sup> and in the majority a decline in IQ in relation to age was reported.

The aim of the present study was to determine the fluctuation of IQ with age and to elaborate the different cognitive functions of fra(X) boys.

## Methods and results

In this study intellectual function and cognitive profile of 18 fra(X) positive males\* was analysed.

The fragile X syndrome was diagnosed in 15 boys during observation in De Hondenberg, an observation clinic for mentally retarded and/or behaviourally disturbed children and adolescents in the southern part of the Netherlands.

The three other boys had not been admitted to the clinic. One of them was a brother of a fra(X) patient in De Hondenberg, and he was ascertained through family research. Two males\* had been diagnosed through the external service of the cytogenetics laboratory of De Hondenberg. In the period 1983 to 1986 a fragile X study was performed in 341 patients, 311 males and 30 females. Fra(X) was found in 24 males. Four boys were not included in the study, two because their parents would not give consent and two because their families had emigrated. Two other boys had been tested for intelligence more than once by means of various tests, which made comparison difficult. These boys were therefore excluded. Psychological and clinical data of the 18 boys are summarised in the table.

## INTELLIGENCE

In the 18 boys IQ evaluations were performed at regular intervals using either the Terman-Merrill or Wechsler scales. At the time of diagnosis the IQ level of the 18 fra(X) positive boys varied greatly (table). Intelligence was normal in one boy and borderline in another, and four were mildly, seven moderately, and five severely mentally retarded (AAMD classification). In these last five patients the severe retardation, with IQ measurements below 30, was present from the beginning. Further testing showed no changes in level over time. The fluctuation of the IQs between the ages of four and 17 in the other 13 boys is shown in fig 1.

\*One of the patients is an adult.

TABLE Psychological and clinical features in 18 fra(X) positive boys.

Present age	Age at fra(X) investigation	Percentage of fra(X) positive cells	Degree of mental retardation	Skull centiles
7	4	2	Moderate	75th
9	4	2½	Mild	25th
12	9	3	Moderate	50th
34	33	4	Severe	50th
21	17	4	Moderate	50th
12	7	6	Mild	75th
6	4	10	Severe	80th
8	6	15	Borderline	No data
16	13	15	Moderate	50th
6	4	17	Severe	40th
9	6	19	Moderate	40th
15	13	20	Mild	50th
8	5	24	Mild	97th
8	4	28	Moderate	50th
11	8	30	Not mentally retarded	50th
8	8	32	Severe	10th
13	8	60	Moderate	50th
10	6	62	Severe	10th

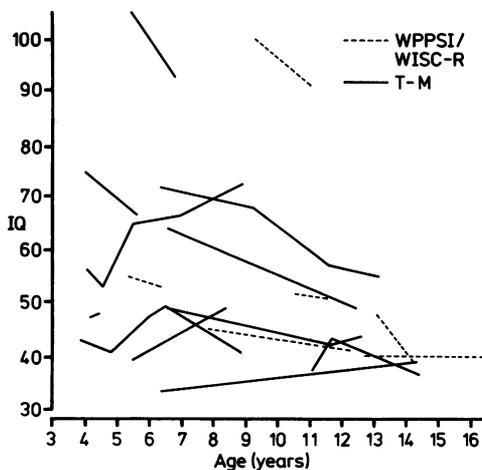


FIG 1 Age variation of IQ in 13 fra(X) positive boys (Terman-Merrill scale and WPPSI/WISC-R tests).

A decline in intellectual performance with age was seen in four boys. In three, however, there was a significant increase in IQ scores, whereas in the remaining six children no fluctuation in IQ was observed (confidence interval 68%). At the 95% confidence level no IQ variation was found in 11 boys. In two of these the increase in IQ score was on the borders of significance. In the other two boys there was a significant decline in intelligence scores.

**VERBAL AND PERFORMANCE INTELLIGENCE TESTS**  
We were able to obtain data on verbal and performance intelligence in five fra(X) boys with

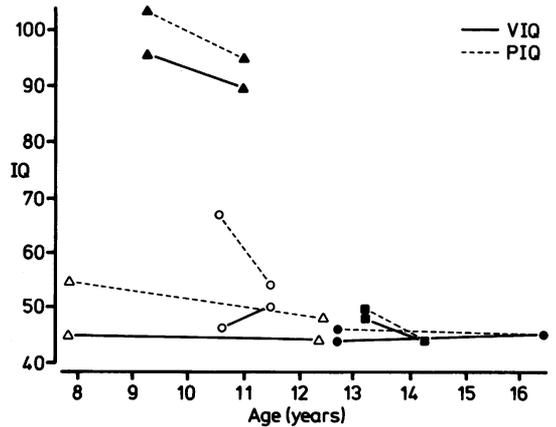


FIG 2 Variation of verbal and performance IQ (WISC-R).

measurements at two different ages with the WISC-R test. These results are summarised in fig 2. The discrepancies between verbal and performance IQ were small with relatively better results in performance tests. This difference, however, was only significant in one evaluation in one boy.

**Discussion**

Precise IQ testing and subclassification according to the AAMD classification of the 18 fra(X) boys in the present study indicated a marked variation in intelligence. In one boy normal intelligence was found and one other showed borderline intelligence. Normal intelligence has rarely been documented after precise IQ testing in the fra(X) syndrome. Veenema *et al*<sup>26</sup> reported two normal intelligent boys in a study of 17 fra(X) positive boys. Fryns *et al*<sup>6</sup> observed normal intelligence in one fra(X) boy in their study of the psychological profile of prepubertal and adolescent fra(X) males.

In a critical review Madison *et al*<sup>27</sup> concluded that most studies on the intellectual performance in the fra(X) syndrome subdivide the patients into different categories on the basis of different types of classification. This may result in important differences in the final classification and subgrouping of the patient material. The AAMD classification was applied in some of the previous studies.<sup>7 23</sup> Madison *et al*<sup>27</sup> also stressed that the variation in results is further increased by the application of different IQ tests in different studies. In the present study IQ testing was performed with the Wechsler scale and the Stanford-Binet test<sup>28-30</sup> and the results of both are presented separately. Different tests were also applied in previous studies.<sup>22 23</sup> Comparison of the

results of different tests may lead to false interpretations; for example, Newell *et al*<sup>16</sup> reported a lower non-verbal IQ (on the Leiter test) compared to the total IQ (Stanford-Binet test). However, underestimation of the intellectual level with the Leiter test is well documented. Few systematic data are available on the variation of intellectual performance in the fra(X) syndrome in relation to age. Most studies report retrospective IQ data obtained on different IQ scales by different persons. The majority of these data suggest a decline in intellectual functioning in relation to age.<sup>7 15 17 19 22-25</sup> Only a few reports include data on longitudinal IQ determinations, mostly on a small number of patients. Rhoads,<sup>19</sup> Partington,<sup>7</sup> and Hagerman *et al*<sup>15</sup> each reported data on the longitudinal follow up of four patients. They all described a decline in intellectual performance. Precise information on the type of IQ tests and the degree of regression was only presented by Hagerman *et al*.<sup>15</sup> Primrose *et al*<sup>21</sup> compared actual IQ scores of 40 fra(X) males with previous IQ measurements on the Stanford-Binet scale. In 21 patients severe retardation (IQ<30) was present on two separate tests. In 10 males a significant decline in IQ was observed over a period of seven to 31 years, whereas a significant increase in intellectual performance was observed in three fra(X) adult males over a period of 11 to 39 years. Borghgraef *et al*<sup>23</sup> noted a decline in IQ in three of the seven fra(X) boys analysed in their study. In these patients, IQ tests (WISC-R or Terman-Merrill) were repeated after a period of three to four years. In the present study we did not observe this decline in intellectual performance with age in the longitudinal follow up of 16 of the 18 fra(X) boys.

In the present study there was no significant difference between the results of the verbal and performance subtests in five fra(X) boys. Up to now, few data have been available on possible discrepancies between verbal and performance intelligence in the fra(X) syndrome. The results of most studies are inconclusive<sup>7 11 12 19 31</sup>; in some patients verbal IQ was lower than performance IQ and the other way round in others. The possible relationship between non-verbal intelligence and verbal expression in fragile X patients was studied by Paul and Leckman<sup>32</sup> and Newell *et al*.<sup>16</sup> Paul and Leckman<sup>32</sup> observed a correlation between verbal expression and non-verbal intelligence (Leiter or WISC-R) while Newell *et al*<sup>16</sup> reported better results in receptive language (PPVT test) than in visual-perceptive tasks. Varley *et al*<sup>20</sup> described a significantly higher verbal IQ score in one fra(X) boy compared to the results on performance IQ tests (WISC-R) and higher scores on the subtests Comprehension and Similarities. From these data the

authors concluded that social competence is relatively well developed in the fra(X) syndrome. Chudley *et al*<sup>18</sup> and Dielkens<sup>31</sup> observed no differences in verbal and performance IQ in their study of 29 and six fra(X) males respectively. The lowest results in subtest scores were observed in Picture Completion, Similarities, and Picture Arrangement. In mildly retarded fra(X) boys, Borghgraef *et al*<sup>23</sup> reported low scores on concentration and attention (Digit span and Coding subtests) and better results on visuospatial perception and synthetic-analytic skills (Block Design and Object Assembly). These differences were not observed in moderately mentally retarded fra(X) boys. With the Kaufman Assessment Battery for Children, Dykens *et al*<sup>33</sup> studied the variable aspects of cognitive functioning. In 14 fra(X) boys, aged between two and 20 years, they observed lower scores on sequential processing (short term memory auditory, visual, and motor skills) compared to the results on simultaneous processing measuring perceptual flexibility and alertness.

Based on the data available, no definite conclusions can be drawn about possible patterns in the development of cognitive profiles in the fra(X) syndrome with age. In most studies the number of young fra(X) boys is very small<sup>15 24 32</sup> or data are reported on one or more fra(X) males in one family.<sup>20</sup> Madison *et al*<sup>27</sup> concluded that these aspects should be studied further in the fra(X) syndrome with the application of verbal and performance IQ tests to augment the general IQ tests.

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