Phenotypic Checklist to Screen for Fragile X Syndrome in People With Mental Retardation

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Abstract: The development of a phenotypic checklist for identifying people with fragile X syndrome is described. The checklist was designed to identify people with developmental disabilities of unknown causes for molecular genetic testing for fragile X syndrome. The list consists of 28 items (7 on physical characteristics and 21 on behavioral features). Validation data were collected for 110 boys and men with fragile X syndrome and for 79 members of a control group, matched for CA, level of cognitive development, and social (mal)adaptation. On the basis of checklist results, those boys who are likely to be diagnosed as having fragile X syndrome can be identified. The screening list can be considered to be a consistent, reliable, and valid instrument.

In recent years interest in fragile X syndrome, a relatively common hereditary disorder, has increased. In 1991, several simultaneous reports indicated that fragile X syndrome involves a trinucleotide repeat sequence in the region containing the FMR-1 gene (Oberlé et al., 1991; Verkerk et al., 1991; Yu et al., 1991). Individuals in the general population show between 6 and 50 trinucleotide repeats, whereas obligate carriers without clinical symptoms of the disorder show 50 to 200 repeats. This expanded region, which is called a "premutation," is meiotically unstable and can expand to a full mutation (>200 repeats) in the next generation by an affected female. Males having an expansion of over 200 repeats develop fragile X syndrome. The full repeat expansion causes methylation of the promoter regions of the gene, and, as a consequence, the gene is not expressed (Pieretti et al., 1991). Turner et al. (1996) estimated fragile X syndrome prevalence to be 1 in 4,000, based on the molecular and not the cytogenetic diagnosis. Fragile X syndrome, then, accounts for about 15% to 20% of persons with X-linked mental retardation. All boys and men with a full mutation have mental retardation, most frequently of a moderate to severel level. A small group of persons with the disorder have mild or profound mental retardation (De Vries et al., 1993; Maes et al., 1994).

In the present study a phenotypic screening list was developed to identify boys and men with fragile X syndrome as efficiently as possible. A screening test is not intended to be diagnostic; it allows a first selection of persons who are likely to be diagnosed as belonging to a certain (syndrome) group. Persons with positive or suspicious findings must be referred to a specialist for diagnosis. In designing this screening list, we acknowledge the importance of early detection and diagnosis of fragile X syndrome. Kan et al. (1990), in a study in the Netherlands, showed that, on average, the etiological fragile X diagnosis had not been made until after the age of 3 years. For about 20% of the 46 fragile X boys in their study, the preliminary diagnosis had not been confirmed until the boys were 11 to 12 years old. We think that efforts aimed at screening people with developmental disabilities for this common disorder are needed. Detection of fragile X syndrome in older children and adults is also of significance for various rea-

sons. For example, families can be made aware of the need for genetic counselling, and caregivers can provide appropriate intervention and support based on the needs of individuals with fragile X syndrome. Therefore, we designed the screening list to be used with males of any age who have general developmental delays of unknown cause.

Table 1 provides an analysis of fragile X checklists that have already been developed. The previous published checklists contain 5 to 17 items. Two of these are concentrated almost exclusively on physical features. Butler et al. (1991), Hagerman, Amiri, and Cronister (1991) as well as Arvio, Peippo, and Simola (1997) included a more balanced combination of physical characteristics and behavioral traits. In several comparative studies, investigators demonstrated that boys and men with fragile X syndrome have a specific behavioral and developmental profile that distinguishes them from other people with mental retardation (Borghgraef, 1991; Crowe & Hay, 1990; Curfs, 1989; Dykens et al., 1988; Einfeld, Hall, & Levy, 1991; Einfeld, Molony, & Hall, 1989; Ferrier et al., 1991; Kemper, Hagerman, & Altshul-Stark, 1988; Maes et al., 1993, 1994; Paul et al., 1987; Reiss & Freund, 1992; Sudhalter et al., 1990; Wolf-Schein et al., 1987). This profile might advance detection of fragile X syndrome at an early stage. We postulated that the typical behavioral characteristics should take a central position and form the core of the present fragile X screening list.

Although the previously mentioned research has convincingly demonstrated that some physical as well as behavioral aspects of fragile X syndrome depend on age or developmental level, none of the developers of existing screening instruments have considered these effects when interpreting the scores. Hagerman et al. (1991) affirmed that some physical manifestations are often not present in prepuberty.

Finally, we believe that there are some methodological problems with the existing screening instruments. Nolin et al. (1991, 1992) and Arvio et al. (1997) developed a two- or three-step program for screening males with mental retardation of unknown cause followed by a selective cytogenetic evaluation. Because only those individuals who had scored above a certain threshold value on the checklist were further screened genetically, it is impossible to determine the instrument's degree of sensitivity and specificity. Butler et al. (1991) and Hagerman et al. (1991) conducted statistical analyses to clarify which traits were more frequently seen in fragile X positive males than in males without fragile X. Although they concluded that certain items had greater differentiating power than did others, they did not attribute a different weight to these items nor did they exclude the nondifferentiating items from their list. Further, their sample was a nondifferentiated group of people showing no clear cause of their mental retardation. Screening scores were prospective: Scores had been given and recorded before the results of genetic studies were known. After genetic tests were completed, scores could be compared between persons who were identified as having fragile X syndrome and those who were not. This method, however, did not allow the authors to check to what degree the fragile X and the nonfragile X group were comparable on certain variables. Using a fragile X and a matched control group and conducting statistical analysis of the scores of both groups would allow authors to demonstrate their checklist's reliability and validity more accurately. If there is a fragile X as well as a control group, those who complete the

Table 1
Overview and Analysis of Existing Screening Lists

Item	Butler et al.,1991	Hagerman et al., 1991	Nolin et al.,1991	Laing et al., 1991	Arvia et al., 1997
No. of specific physical characteristics	6/15	4/13	7/10	3/5	5/17
No. of specific behavioral features	8/15	8/13	2/10	1/5	11/17
Sensitivity (%)	47	87	—	94	—
Specificity(%)	98.3	85	—	77	—
Statistical analysis of validity and/or reliability	+	+	-	-	—

Note. None of these list developers used a matched control group, and none conducted differential weighing of item scores. None of the scores were interpreted on the basis of age or level of mental retardation.

screening list must not know its purpose, in order to gather the data in an unbiased manner.

Method

Participants

Beginning in 1980, researchers at the Centre of Human Genetics in Leuven (Belgium) have been conducting several systematic etiologic–diagnostic studies in facilities for persons with mental retardation. The etiology of the mental retardation of all residents involved in these studies was determined on the basis of a careful examination by a clinical geneticist; an anamnesis of prenatal, developmental, and family history; and a genetic analysis whenever the cause was unknown.

The screening list has been completed for two groups of participants. The first group consisted of 57 boys and 53 men with fragile X syndrome who had been diagnosed on the basis of a cytogenetic and molecular analysis. The control group of 26 boys and 53 men had mental retardation due to other causes; fragile x syndrome had been ruled out on the basis of a genetic analysis. In the control group, there was either no evident cause for their mental retardation and no family history of mental retardation or there were demonstrable cerebral dysfunctions. No members of the control group had another genetic or chromosomal disorder. Table 2 shows that both groups were matched with regard to a number of relevant variables. There were no significant differences (t tests) between the two groups on CA, average level of cognitive development (IQ for children, mental age for adults), or social (mal)adaptation (measured using the Dutch Social Adaptation Scale and Behavioral Problems Scale for Persons with Mental Retardation). The length of time they had been in residential care, however, was significantly lower for fragile X than for the control group, $t(187) = 3.11$, $p < .005$. With regard to level of cognitive functioning, 6.5% of the children had profound; 29.9%, severe, 48.1%, moderate; and 15.6%, mild mental retardation. In the adult group there were 14% with profound; 71%, severe; 21%, moderate; and none, mild mental retardation. All participants came from the same special schools, day care centres, or residential institutions.

Description of the Checklist

The final version of the checklist, which is provided later, consists of 28 items (7 on physical characteristics and 21 on behavioral features). In preliminary research 69 items had been identified, based on the previously mentioned comparative studies of the developmental and behavioral profile of boys and men with fragile X syndrome and on the already existing screening lists for fragile X syndrome. In the final version of the screening list, we included only those items that were significantly more frequent or striking in boys and men with fragile X syndrome compared to people with mental retardation but without fragile X syndrome.

When constructing the final list, we considered the following criteria: (a) The checklist should be easy to use and score, (b) items should be relevant, (c) scoring should be possible on the basis of direct observation, and (d) items should be clearly defined and unequivocal for the person administering the list.

In addition to the core items, some identification data are requested: chronological age (CA), date of checklist administration, diagnosis and level of mental retardation, name and position of the person who administered the

Table 2
Composition of Norm Groups

	Fragile X			Control		
Age[a]/Characteristic	Mean	*SD*	Range	Mean	*SD*	Range
Adults						
MA	3.42	1.27	1.17–6.25	3.50	1.50	0.67–7.00
Social adaptation	6.38	1.04	4.00–9.00	6.34	1.26	2.00–9.00
Behavioral problems	6.12	1.33	2.00–8.25	6.19	1.20	3.00–7.75
Children's IQ	46.63	11.81	19–72	42.56	11.28	20–73
Total group						
CA	26.17	18.70	3.58–67	31.25	17.19	3.50–67
Length of stay in residential facility	10.83	14.61	0.00–60	18.00	16.69	0.00–58

[a]There were 53 adults with fragile X syndrome and 53 control adults, 57 children with fragile X syndrome and 26 control children.

screening list. Finally, some additional observation and test data are entered: percentiles of length, weight, and head circumference at birth and, at the time of screening, number and socio–economic level of family members with mental retardation, as well as results of psychodiagnostic tests and scales previously administered. These additional data are meant to enable more accurate interpretations of the checklist results.

Scoring and Interpretation of Checklist

Any person having medical or psychological–educational qualifications, such as care-providers, special education teachers, nurses, therapists, psychologists, or pediatricians can administer the checklist in any of several settings: childcare facility, nurseries, regular and special classes, health care and rehabilitation centers, or special facilities and programs for persons with developmental disabilities. The screening should be completed exclusively by someone who knows the testee well and who has the necessary information to answer all questions. Personal observations can be supplemented by anamnestic data and information from parents.

To make scoring easier, we provided an explanation of each item, with concrete and observable characteristics and illustrations included. Items pertain to the actual behavior of an individual in his or her daily circumstances. Each item is answered with a *yes* or *no*. The checklist is meant as a screening instrument. If the score is high, the individual should be referred to his or her physician or a genetic counselor. For children, referral is recommended if the score is at least 17; a score of 26 or above indicates that a referral is necessary. When a number of items are answered with the response *Are Not Applicable* (e.g., for a child who cannot yet speak), less strict criteria may be used to determine whether a genetic analysis is necessary. A high score on the checklist alone is not sufficient grounds for a diagnosis of fragile X syndrome.

Standardization, Reliability, and Validity

Because there were several psychometric requirements to validate the checklist, we have undertaken some statistical analysis.

Standardization

A linear regression analysis allowed us to examine which items added most to the discriminatory value of the screening list in indicating fragile X syndrome. We gave a coefficient to each item, varying from 1 (the least predictive of fragile X syndrome) to 7 (the most predictive of fragile X syndrome). These coefficients were directly based on the orientation parameters of the regression analysis (parameters under .10 were given coefficient 1; between .10 and .20, coefficient 2; between .20 and .30, coefficient 3, etc.). Because we assigned coefficients separately for the children (under 18 years) and adults (from 18 years up), we have a child and adult version of the checklist. The highest coefficients for the children were for large, protruding ears (7), macro-orchidism (6), fearfulness (5), and hand biting (3). In addition to hyperextensible joints, we assigned a coefficient of 2 to behavioral features: hyperactivity, impulsivity, hypersensitivity for changes, gaiety/cheerfulness, avoiding eye contact, and echolalia. All other items had a coefficient of 1. If an item is scored positively, the item score is the coefficient's value; if the item is scored negatively, the item score is zero. Item scores are added in a weighed total score.

An individual's score on this checklist may provide a first indication that he or she has fragile x syndrome. Figure 1 and Table 3 contain information that should assist in the interpretation of the total score.

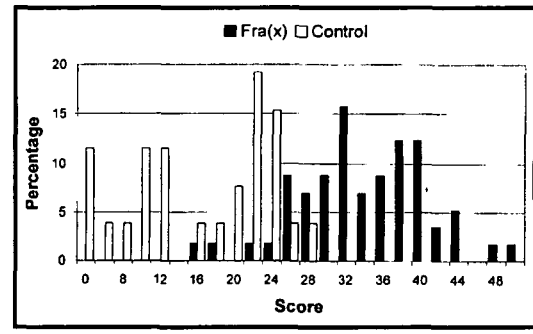


Figure 1. Frequency distribution of scores for children.

Table 3
Risk Percentages for Children to Have Fragile X

Weighed total score	Control	Fragile X
< 17	100	00.0
17 - 25	76.5	23.5
26 - 29	18.0	82.0
> 29	0.0	100.0

Figure 1 shows the frequency distribution of the children's weighed total scores. A child with a certain score on the screening checklist can be easily placed on this scale. This figure can be used to interpret a child's score on the checklist. We discerned three main ranges: a range where fragile X syndrome is to be excluded with a rather high certainty (scores < 17); a range where fragile X syndrome is to be considered likely (scores > 29); and a range in between of overlapping fragile X and control group scores. For example, a child with a total score between 17 and 25 has a 23.5% chance of having fragile X syndrome; with a total score between 26 and 29, the chance increases to 82% (see Table 3).

Reliability

To test the reliability of the screening list, we measured its internal consistency. Cronbach alpha for the total group was .84 for the whole list, .74 for the physical items, and .82 for the behavioral features.

Validity

To determine the validity of the checklist, we first used one-way analysis of variance to examine the discriminatory value of each item. Diagnosis (fragile X syndrome positive or negative) was the independent variable and average item score the dependent variable. Table 4 shows the results of these analyses. For all items a significant difference, $p < .05$, in average item score was found between fragile X and the control group for one or both of the age groups, meaning that all physical features and all behavioral aspects were observed more frequently or more obviously in the fragile X group than in the control group.

In the one-way analysis of variance, the effect of the diagnosis (fragile X syndrome positive or negative) on the average number of positively scored items was highly significant (see Table 5). The average number of positively scored physical features, $F(1, 128) = 89.77$, $p < .0001$, and the average number of positively scored behavioral characteristics, $F(1, 187) =$

Table 4
Variance Analyses for Effect of Diagnosis on Mean Item Scores by Group

	Children		Adults		Total group	
Item	Effect of diagnosis, *F* (*df*)	*p*	Effect of diagnosis, *F* (*df*)	*p*	Effect of diagnosis *F* (*df*)	*p*
1. Narrow and elongated face	0.20 (1,27)	.66	61.35 (1,104)	.0001	49.15 (1,133)	.0001
2. High forehead	0.76 (1,25)	.39	19.91 (1,104)	.0001	21.53 (1,131)	.0001
3. Prominent lower jaw	3.42 (1,25)	.08	19.91 (1,104)	.0001	18.71 (1,131)	.0001
4. Large, protruding ears	31.66 (1,27)	.0001	21.89 (1,104)	.0001	41.49 (1,133)	.0001
5. Macro-orchidism	9.68 (1,26)	.004	147.52 (1,104)	.0001	142.26 (1,132)	.0001
6. Hyperextensible finger joints	0.96 (1,26)	.34	4.61 (1,104)	.03	8.74 (1,132)	.004
7. Hyperextensible joints (other)	0.78 (1,25)	.38	4.24 (1,104)	.04	1.88 (1,131)	.17
8. Hyperactivity	18.24 (1,81)	.0001	1.39 (1,104)	.24	16.05 (1,187)	.0001
9. Sensory oversensitivity	2.75 (1,81)	.1	1.95 (1,104)	.16	6.94 (1,187)	.009
10. Impulsivity	4.13 (1,81)	.04	4.69 (1,104)	.03	12.29 (1,187)	.0006
11. Being chaotic	3.82 (1,81)	.054	6.75 (1,104)	.01	13.21 (1,187)	.0004
12. Shyness	9.17 (1,81)	.003	4.69 (1,104)	.03	14.93 (1,187)	.0002
13. Being too helpful	1.74 (1,81)	.19	4.59 (1,104)	.03	8.95 (1,187)	.003
14. Approach–avoidance conflict	1.31 (1,81)	.26	9.29 (1,104)	.003	11.12 (1,187)	.001
15. Fearfulness	12.85 (1,81)	.0006	0.61 (1,104)	.44	7.15 (1,187)	.008
16. Gaiety, cheerfulness	2.28 (1,81)	.13	5.57 (1,104)	.02	9.26 (1,187)	.003
17. Hypersensitivity for changes	2.80 (1,81)	.10	0.60 (1,104)	.44	4.99 (1,187)	.03
18. Hand biting	9.34 (1,81)	.003	20.06 (1,104)	.0001	31.27 (1,187)	.0001
19. Stereotypic hand movements	2.82 (1,81)	.10	2.43 (1,104)	.12	4.69 (1,187)	.03
20. Flapping hands and arms	4.76 (1,81)	.03	5.57 (1,104)	.02	14.28 (1,187)	.0002
21. Avoiding eye contact	1.68 (1,81)	.20	6.82 (1,104)	.01	7.65 (1,187)	.006
22. Turning away the face	1.64 (1,81)	.20	6.70 (1,104)	.01	9.24 (1,187)	.003
23. Tactile defensiveness	1.03 (1,81)	.31	12.10 (1,104)	.0007	11.50 (1,187)	.0008
24. Rapid speed of language	2.17 (1,81)	.14	3.41 (1,104)	.07	7.85 (1,187)	.006
25. Being talkative	1.36 (1,81)	.25	0.73 (1,104)	.39	3.93 (1,187)	.049
26. Perseveration	0.29 (1,81)	.59	5.62 (1,104)	.02	1.93 (1,187)	.17
27. Echolalia	4.95 (1,81)	.03	2.47 (1,104)	.12	6.84 (1,187)	.01
28. Imitation of own language	0.89 (1,81)	.35	4.68 (1,104)	.03	0.45 (1,187)	.50

Table 5
Means and SDs of Positively Scored Characteristics by Group

No. of positively scored items	Fragile X				Control			
	n	Mean	*SD*	Min.-Max.	*n*	Mean	*SD*	Min.-Max.
Physical features	69	4.11	1.65	0 - 7	61	1.43	1.57	0 - 6
Behavioral characteristics	110	12.53	4.32	2 - 21	79	8.19	4.37	0 - 17
Total	69	16.13	4.92	5 - 26	61	8.80	4.41	0 - 19

45.96, $p < .0001$, were, separately as well as combined, $F(1, 128) = 79.03$, $p < 0001$, significantly higher in the fragile X than in the control group.

Because the whole group was very heterogeneous, we examined whether the total score on the screening list is dependent on age or level of mental retardation.

Level of mental retardation. Independent variables in the two-way analysis of variance were diagnosis (fragile X syndrome positive or negative) and level of mental retardation (profound, severe, moderate, and mild). The level of cognitive development had no significant effect on the number of positively scored items for any of the study participants: total score $F(3,15) = .40$, $p = .75$ (children) and $F(2,100) = .64$, $p = .53$ (adults); physical features, $F(3,15) = 1.56$, $p = .24$ (children) and $F(2,100) = 1.00$, $p = .37$ (adults); and behavioral features, $F(3, 69) = 0.65$, $p = .58$ (children) and $F(2, 100) = 1.15$, $p = .32$ (adults).

Age. The results of the two-way analysis of variance, with diagnosis (fragile X syndrome positive or negative) and age group (0 to 6 years, 6 to 12 years, 12 to 18 years, 18 to 50 years, and over 50 years) as the independent variables, points to a significant effect of age for the behavioral features, $F(4, 178) = 4.76$, $p = .001$, and for the total score, $F(4, 121) = 2.61$, $p = .04$. For the screening list as a whole, children from 6 to 12 years of age had significantly more fragile X characteristics (mean score=18.5) than did the adults from 18 through 50 years (mean score=13.38), $p = .04$, and over 50 years (mean score=11.17), $p = .005$. As to behavioral features the same significant differences were found between children from 6 to 12 years (mean score = 13.51) and adults from 18 years through 50 (mean score = 10.68), $p = .004$, and over 50 years of age (mean score = 8.43), $p = .0001$. The men over 50 years who had fragile X had significantly less typical behavioral features (mean score = 8.43) than did participants in all other age groups (0 to 6 years: mean score = 13.10, $p = .006$; 6 to 12 years: mean score = 13.51, $p = .0001$; 12 to 18 years: mean score = 12.34, $p = .0009$; and 18 to 50 years: mean score = 10.68, $p = .02$). Because there were fewer younger participants, their scores must be interpreted with caution. On the basis of these results, we decided to take the age factor into account when processing the data. The scores on the screening list are, therefore, interpreted separately for the group of children and for the group of adults.

The sensitivity of the scale is measured by the number of boys and men with fragile X syndrome who would have been correctly identified; its specificity, by the number of correctly identified boys and men without fragile X. Of the children who would have been referred with a score of 26 or more, 93% of the boys with fragile X syndrome and 92.3% of the control boys would have been diagnosed correctly; 7% would be false-negatives (boys with fragile X syndrome who were not detected) and 7.7% false-positives (boys without fragile X syndrome who were suspected of having the syndrome). If the criterion for referring were lowered (from score 17 on) more than half of the non-fragile X group would be wrongly identified as having fragile X syndrome (57.5%). In this case there would be no false-negatives in the fragile X group. If the criterion (from score 29 on) were raised, too many persons with fragile X syndrome would be missed (22.8%).

Discussion

The checklist we have discussed is a useful tool for determining whether boys and men with developmental delays of unknown causes should be referred for genetic examination for fragile X. A high checklist score makes it possible to identify those boys and men who are likely to be diagnosed as having fragile X syndrome. The checklist is conceived as a systematic observation instrument that can be easily integrated into everyday clinical practice. The score on the list can in no way replace a cytogenetic or molecular diagnosis. Because genetic testing for fragile X syndrome is expensive, it seems im-

portant to be able to screen appropriately for persons at risk for the syndrome. A screening instrument encourages genetic testing on a limited group with a likely high positive yield. Arvio et al. (1997) recommend a step-by-step procedure successively using a clinical checklist, a clinical examination by a physician, and, finally, a molecular test. In this way, according to these investigators, molecular and cytogenetic examinations may be targeted to the correct subpopulation of males with mental retardation. Phenotypic checklists may be of help when initiating general detection programs in a certain region. The results of such population studies may either confirm or correct the estimation of incidence and prevalence of fragile X syndrome.

When the contents of our checklist is compared with other screening instruments, the family history of mental retardation is missing in our list, although this item proved to be a very important one in identifying the syndrome (Butler et al., 1991; Hagerman et al., 1991; Laing et al., 1991; Nolin et al., 1991, 1992). People with fragile X syndrome usually have other relatives with mental retardation. We asked for the number and category of family members with mental retardation as additional data rather than as part of the checklist because we wanted to restrict the items in our screening list to observable features.

The seven physical features items in the present screening list are also included in other screening instruments. We have found macroorchidism (with a coefficient of 6) and large protruding ears (with a coefficient of 7) to be most predictive of fragile X syndrome. This corresponds with the findings by Butler et al. (1991) and Hagerman et al. (1991). Butler et al. added hyperextensible finger joints, dermatoglyphic abnormalities (Simian crease or Sydney line and plantar crease), and pale blue eyes as very discriminating in identifying fragile X phenotype.

Results of the present study confirm that behavioral features are equally differentiating as the physical characteristics between people with mental retardation with and without fragile X syndrome and form a strong indication for the syndrome. According to Hagerman et al. (1991) and Butler et al. (1991), the behavioral features that most significantly differentiate between individuals with and those without fragile X syndrome are hyperactivity and/or short attention span, stereotyped movements (flapping arms), autistic features (tactile defensiveness, avoiding eye contact), and conversational aspects (perseverations). Our results with regard to significantly higher mean scores on behavioral features for individuals with fragile X syndrome compared to control participants are consistent with those found by Hagerman et al. and Butler et al., with the exception of attention problems. However, we have completed these items with behavioral features on the basis of recent comparative research on persons with and without fragile X syndrome. These pertain to social interaction (shyness, being too helpful, approach–avoidance conflict, fearfulness), temperament (gaiety and cheerfulness, hypersensitivity for changes), communicative idiosyncrasies (rapid speed of language, being talkative, echolalia, palilalia), and behavioral problems (biting hands or arms, impulsivity, sensory oversensitivity).

In the present study we compared the scores on the screening list of a fragile X and a nonfragile X group matched on a number of relevant variables. The results of this analysis are very satisfactory. The screening list can be considered to be a consistent, reliable, and valid instrument that clearly differentiates between people who have mental retardation with and without fragile X syndrome. Physical as well as behavioral characteristics reliably differentiate between boys who have fragile X syndrome and those who do not, regardless of their level of developmental delay. Because we used coefficients for each of the items, the most predictive traits preponderate in the final score. Because we developed two versions of the checklist—one for children and one for adults, the age dependability of diverse characteristics is taken into account.

Detection and diiagnosis of fragile X syndrome requires a multidisciplinary approach (Curfs & Fryns, 1992; de Winter, 1993). From a genetic point of view, an early diagnosis results in appropriate psychosocial advice and genetic counseling for family members. Providing information on the cause of mental retardation in a family often puts an end to many uncertainties. In addition, female carriers of the fragile X gene may be offered prenatal diagnosis. From an educational perspective, once the diagnosis has been made, an early stimulation and home-based program can be started that is focused on the specific behavioral and devel-

opmental needs and strengths of children with fragile X syndrome. In addition, the parents may get educational support in order to make their expectations and interactions meet their child's needs. In this way secondary behavioral problems are prevented. The specific behavioral and developmental profile of persons with fragile X syndrome also has consequences for the nature of interventions and supports. It affects, for example, the organization of the environment, the nature of activities and training programs, and the means of communication and interaction.

Further validation studies of the present screening list, however, are necessary, especially refinement of the list's items and validation data for younger age groups. Although the age at which early detection of fragile X syndrome should take place is 0 to 6, only 5.3% of the children in our sample were diagnosed from 0 to 6 years of age. Verifying the checklist and expanding the standardization data for this age group are, therefore, necessary in order to heighten its value as an early detection instrument.

It would be worthwhile to contemplate the use of this instrument for girls and women who have mental retardation due to fragile X syndrome. At the present time, a comparable screening list is being developed for female carriers of fragile X mutation. The items on the list are based on the behavioral and developmental profile of women with fragile X gene mutation.

We recently sent a questionnaire to all persons who have used the fragile X checklist in the last few years in order to determine who is using this list (kind of service, training, function) and whether it is user friendly (definition of items, method of scoring, coefficients) and efficient (number of clients who have been correctly identified).

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