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9 Developmental issues in fragile X syndrome

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Fragile X syndrome is a recently identified X-linked disorder resulting in mental retardation and characteristic physical, cognitive, and behavioral features. Although data are now accumulating regarding the psychological functioning of fragile X males, previous research has focused almost exclusively on the genetic aspects and physical features of the disorder. As a result, the data are quite limited on the intellectual, adaptive, and behavioral functioning of boys and men with fragile X syndrome, and many questions remain about the development of fragile X males in virtually all areas of functioning.

In addition, the research reports on fragile X syndrome are found largely in the genetics literature, and less accessible to parents, educators, and health professionals who seek guidance with the daily management and education of these individuals. Given this need, and the relative newness of the disorder, this chapter will begin with a brief overview of fragile X syndrome, including its genetic features and enigmas and its physical phenotype. Data on the prevalence of fragile X syndrome, and the intellectual, adaptive, and behavioral functioning of fragile X males will then be presented. These findings will be discussed in relation to the two-group approach in mental retardation, the trajectory of intelligence, and the interplay between genetics and the environment.

Overview of fragile X syndrome

Genetic features

The chromosomal abnormality associated with fragile X syndrome was initially identified in 1969 by Lubs, who observed a pinched or constricted end on the X chromosomes of mentally retarded males in a large pedigree that followed an X-linked inheritance pattern. These chromosomal find-

ings were not replicated until 1977, when Sutherland reported that in order to observe the abnormality on the X chromosome, tissue cells had to be grown in a culture deficient in folate. Even with these procedures, only a small percentage of the cells of affected males manifest the "fragile" site (15–40%), and it is not always consistently observed (Bregman, Dykens, Watson, Ort & Leckman, 1987). Recent advances in molecular genetic marking techniques are refining the accuracy of the fragile X diagnosis (Murphy, Kidd, Breg, Ruddle, & Kidd, 1985). Although there are many forms of X-linked retardation, the diagnosis of fragile X syndrome is generally reserved for cases in which the fragile site is identified through proper cytogenetic or molecular genetic procedures.

Fragile X syndrome is generally assumed to follow a Mendelian X-linked inheritance pattern. In this pattern, an unaffected female carrier has a 50% chance of transmitting the affected X chromosome to her daughters – who then become carriers – and a 50% chance of transmitting the affected X chromosome to her sons, who are affected with the disorder. Recent evidence, however, has pointed to considerable deviation from this pattern. Unlike other recessive X-linked disorders (e.g., color blindness, hemophilia), approximately one-third to one-half of the women carrying the fragile X marker are themselves mildly affected with the disorder, and may exhibit learning disabilities, a history of poor school performance, or mild to moderate mental retardation (Fishburn, Turner, Daniel, & Brookwell, 1983; Hagerman & Smith, 1983; Turner, Brookwell, Daniel, Selikowitz, & Zilibowitz, 1980). Recent estimates (Sherman et al., 1985) suggest that if the carrier female is affected herself, then 50% of her daughters will become carriers and all of her sons will inherit the disorder. If the carrier female is not clinically affected, then sons who inherit the affected X chromosome have a 75% of being clinically impaired, and daughters have a 30% chance of being affected.

In addition, segregation analyses suggest that as many as 20% of males who receive a fragile X chromosome by descent will fail to exhibit the fragile site cytogenetically and will be unaffected with the disorder (Sherman et al., 1985). The existence of these nonpenetrant carrier males has been confirmed using newer recombinant DNA techniques that allow investigators to follow the inheritance of segments of DNA from the affected region of the X chromosome. Although all of the daughters of these nonpenetrant, unaffected males will be carriers, they do not generally manifest clinical impairments. The sons of these males will not be affected with the disorder. Thus, fragile X syndrome presents several deviations from a recessive X-linked inheritance pattern that have important implications for the genetic counseling of families affected with this disorder.

Physical phenotype

Many mentally retarded males with fragile X syndrome exhibit characteristic physical features. Approximately 70% of these males have an elongated face, a high forehead, and enlarged ears (see Bregman, Dykens, Watson, Ort, & Leckman, 1987 for a review). Many of these features become more pronounced after puberty. In addition, several investigators have observed connective tissue dysplasia in some of their fragile X patients. These features include hyperextensible joints, a high arched palate, and mitral valve prolapse (Hagerman, VanHousen, Smith, & McGauran, 1984). Macroorchidism, or enlarged testes, has also been consistently observed in fragile X males, particularly at postpubertal stages of development (see Bregman, Dykens, Watson, Ort, & Leckman, 1987 for a review). The increased frequency of macroorchidism in fragile X syndrome, although not necessarily unique to this form of retardation, has led many investigators to explore the neuroendocrine functioning of fragile X males. These studies do not generally point to abnormal neuroendocrine functioning, although some affected males may exhibit gonadal dysfunction and slight abnormalities in the hypothalamic–pituitary regulation of the thyroid.

Prevalence of fragile X syndrome

Recent estimates of the prevalence of fragile X syndrome in the population (0.73–0.92 per 1,000 males) suggest that it is second only to Down syndrome in terms of a known chromosomal cause of retardation (Herbst & Miller, 1980; Webb, Bundey, Thake, & Todd, 1986). As Down syndrome is rarely transmitted as a genetic disorder from Down syndrome parent to Down syndrome child, fragile X syndrome is thought to be the most common heritable cause of mental retardation. Surveys of retarded populations indicate that fragile X syndrome may account for 2–7% of all cases of retardation among males (Webb, Bundey, Thake, & Todd, 1986). Thus, fragile X syndrome is estimated to be quite prevalent among mentally retarded males. As discussed next, both the prevalence of the disorder and the patterns of its genetic transmission (e.g., affected carrier females) have important implications for the classification of retarded individuals, specifically for the two-group approach.

Fragile X syndrome and the "two-group" approach

In contrast to defect or difference theorists, developmental theorists have generally relied on the "two-group" approach to differentiate among

mentally retarded individuals (Zigler, 1967; 1969). Within this approach, approximately 25% of mentally retarded individuals are assumed to have organic etiologies, and 75% to have nonorganic, or familial retardation (Zigler & Hodapp, 1986). A review of large-scale population studies, however, has identified a 50-50 split between organic and familial retardation (Zigler & Hodapp, 1986). Recently, Zigler and Hodapp (1986) revised this two-group approach, extending the two groups into four groups, and calling for further differentiation of those individuals with organic and nonorganic impairments.

In the expanded classification system of Zigler and Hodapp (1986), 25% of retarded individuals are assumed to have organic impairments with known etiologies, 35% to have familial retardation, 35% are classified as polygenic isolates, and less than 5% are construed as experiencing severe environmental deprivation. The authors acknowledge that these percentages are estimates and are subject to change, and the recent discovery of fragile X syndrome, including its prevalence and pattern of genetic transmission, certainly provides several important sources of change for the percentages noted. For example, Zigler and Hodapp (1986) assert that an "undisputed fact" about nonorganic retardation is "that it tends to run in immediate families" (p. 51). In addition, familial–cultural retardation is defined as existing in those cases in which at least one parent has an IQ below 70, and in which the range of retardation in the affected members is mild to moderate. Fragile X syndrome certainly runs in both immediate and distant family members, and the mean IQ of affected males is in the moderate range (Chudley, 1984).

Approximately 33% of carrier females, including mothers, exhibit learning difficulties or mild to moderate retardation. Thus, it appears that many cases of fragile X syndrome fit the typical description of familial mental retardation. This overlap in clinical description, as well as the estimated prevalence and frequency of fragile X, makes it quite likely that fragile X syndrome will result in a decrease of cases classified as familial–cultural and an increase in cases classified as organic.

Although Zigler and Hodapp's (1986) revised classification system has refined the description of nonorganic retarded individuals, it has not attempted to refine the classification of individuals with organic retardation. Recently, Burack, Hodapp, and Zigler (1988) emphasized the need for further differentiation among organically impaired individuals. These authors note that the predominant tendency in MR research is to classify groups according to level of impairment, not by etiology. Yet, as Burack, Hodapp, and Zigler (1988) demonstrate, classifying groups solely by level of impairment may obscure important differences between various etio-

logical groups. These group differences may be manifest in both psychological and behavioral functioning, including intellectual and adaptive strengths and weaknesses, the trajectories of intelligence throughout development, and patterns of maladaptive behavior. Recent data pertaining to the psychological and behavioral functioning of boys and men with fragile X syndrome provide considerable support for the classification of research groups based on etiology, as opposed to level of impairment. These data are presented next, and are also disscussed in relation to an underlying area of weakness that appears to permeate various domains of functioning in fragile X males.

Intellectual functioning

Although fragile X males display the full range of intellectual impairments from borderline to profound, most are moderately affected, with IQs in the 35–40 range (Chudley, 1984). Affected fragile X males with average or near average IQs have also been reported (Daker, Chidiac, Fear, & Berry, 1981). Several investigators (Chudley, 1984; Herbst, Dunn, Dill, Kalousek, & Krywaniuk, 1981) have reported that fragile X males perform lower on certain subtests of the Wechsler Intelligence Scale for Children-Revised (WISC-R) (e.g., information, digit span, arithmetic) and higher on others (e.g., picture completion, similarities). The implication of these findings, however, remains unclear, as the authors did not advance hypotheses regarding the underlying cognitive processing of their subjects.

Recently, Dykens, Hodapp, and Leckman (1987) systematically examined the intellectual functioning of fragile X males by identifying their strengths and weaknesses and relating them to putative styles of cognitive processing. These authors aimed to measure "two types of mental functioning that have been identified independently by cerebral specialization researchers ... Luria and his followers ... and cognitive psychologists" (Kaufman & Kaufman, 1983, p. 2). The two types of mental functioning are *sequential processing*, or solving problems bit by bit in serial or temporal order, and *simultaneous processing*, or integrating stimuli in a holistic, frequently spatial manner. These processing domains have proven useful in formulating educational strategies that capitalize on individual processing strengths and minimize processing weaknesses.

Utilizing the Kaufman Assessment Battery for Children (K-ABC; Kaufman & Kaufman, 1983), these authors reported that fragile X males exhibited consistent and significant difficulties with sequential-processing tasks. Deficits in sequential processing have also been observed by Kemper,

Hagerman, and Altshul-Stark (1987). This difficulty in sequential processing indicates significant weaknesses in auditory, visual, and motoric short-term memory. Achievement in mathematics also emerged as an area of significant weakness in these males (Dykens, Hodapp, & Leckman, 1987) and is consistent with the association between poor sequential-processing skills and problems in the retention of math facts (Kaufman, Kaufman, & Goldsmith, 1984).

In contrast to their findings of relative weaknesses in sequential processing, Dykens, Hodapp, and Leckman (1987) found significant strengths for fragile X males in simultaneous processing. This strength in simultaneous processing was particularly noteworthy in subjects' abilities to make perceptual inferences, and to complete tasks that required perceptual closure, flexibility and organization. This distinct pattern of relative strengths in simultaneous processing and weaknesses in sequential processing, was evident for all fragile X males in this study.

Although the intellectual profiles identified by Dykens, Hodapp, and Leckman (1987) may be unique to males with fragile X syndrome, additional data are necessary to confirm this hypothesis. Utilizing the K-ABC with Down syndrome subjects, Pueschel, Gallagher, Zartler, and Puezzullo (1987) have reported no particular strengths or weaknesses in the sequential and simultaneous-processing abilities of these children. A significant strength emerged, however, in a sequential task assessing visual–motoric short-term memory. This task emerged as the lowest subtest score for all of the fragile X subjects in the Dykens, Hodapp, and Leckman (1987) study. Thus, what appears to be a significant strength in Down syndrome children is a significant weakness in fragile X boys. Still, the uniqueness of these profiles remains unclear, and more systematic comparisons between Down syndrome, fragile X, and other etiological groups are necessary to address this issue.

Even without clarifying data, however, the identification of specific strengths and weaknesses in the fragile X and Down syndrome samples conflicts with previous analyses of educable and trainable mentally retarded children. Silverstein, Goldberg, Kasner, and Solomon (1984), for example, found no significant strengths or weaknesses in the intellectual functioning of educable mentally retarded children. Similarily, Kaufman and Kaufman (1983) reported no significant difference between sequential and simultaneous processing, and little variability in achievement tests, in groups of educable and trainable mentally retarded children. In these studies, the etiology of the children's retardation was not considered in data analysis. This classification of retarded individuals according to their level of functioning may obscure potential differences in the cognitive

profiles of various etiological groups (Burack, Hodapp, & Zigler, 1988). The identification of specific cognitive profiles in fragile X syndrome, and in other groups such as Down syndrome, confirms the importance of classifying groups on the basis of etiology rather than overall level of impairment. Further refinement of classification, and of intervention approaches with individuals with organic retardation, requires that workers in the field of mental retardation begin to adopt this perspective in their research methodologies.

In addition to confirming the importance of research groups based upon etiology, it may be that the specific pattern of cognitive strengths and weaknesses in fragile X males affects their functioning and development in other domains. Specifically, compromised sequential processing and relative strengths in simultaneous processing may be evident in areas other than intellectual functioning. Indeed, recent evidence suggests that sequential-processing difficulties and strengths in simultaneous processing in fragile X males are found in their linguistic functioning and in their patterns of maladaptive behavior. Sequential-processing deficits may also be apparent in the adaptive behavior skills of these males. The linguistic and adaptive functioning and the maladaptive behavior of fragile X males are presented next, and are discussed in relation to this apparently pervasive sequential-processing defect.

Linguistic functioning

The linguistic functioning of fragile X males has been characterized as disabled, with distinctive problems in auditory memory, reception, and articulation (Howard-Peebles, Stoddard, & Mims, 1979). It has also been described as jocular, abrupt, and repetitive, with rhythmic, litany-like phrasing, echolalia and palilalia, and dysfluent and dyspraxic traits (Jacobs et al., 1980; Paul, Cohen, Breg, Watson, & Herman, 1984; Turner, Brookwell, Daniel, Selikowitz, & Zilibowitz, 1980).

It remains unclear if these language characteristics are unique to fragile X syndrome or shared with other etiological groups. In a comparison of institutionalized fragile X and nonfragile X retarded men, Paul, Dykens, Leckman, Watson, Breg, and Cohen (1987) found no patterns of strength or weakness, or distinctive group differences, in receptive or expressive language functioning.

Areas of significant strength and weakness have been found, however, in studies of noninstitutionalized fragile X boys and young men. Marans, Paul, and Leckman (1987) have reported significant strengths in both expressive and receptive vocabulary of noninstitutionalized fragile X sub-

jects, and relative strengths in vocabulary have also been observed by Sudhalter (1987). In contrast, fragile X males have been found to have significant weaknesses in sentence imitation tasks and in the mean length of utterance (MLU) (Marans, Paul, & Leckman, 1987). Both sentence imitation and longer MLUs require auditory short-term memory and the ability to organize and express words in an orderly, step-by-step, linear manner. As such, they tap many processes inherent in sequential processing. Thus, it appears that the underlying cognitive deficit in sequential processing also manifests itself in the linguistic functioning of many fragile X males. In addition, their linguistic strengths in receptive and expressive vocabulary may be related to their cognitive strengths in simultaneous processing; strengths in both of these domains reflect the ability to understand and label the overall meaning or goal of a task.

Maladaptive behavior and psychopathology

Although many fragile X males have been described as cooperative, cheerful, and pleasant (Chudley, 1984; Herbst, Dunn, Dill, Kalousek, & Krywaniuk, 1980), males with this syndrome have been shown to exhibit significant levels of maladaptive behavior (Dykens, Hodapp, & Leckman, 1989), as well as specific patterns of behavioral difficulties (Bregman, Leckman, & Ort, in press). In particular, problems with aggressive outbursts, hyperactivity, gaze aversion, attention deficits, stereotypy, and self-injurious behavior have been frequently observed (Bregman, Dykens, Watson, Ort, & Leckman, 1987; Fryns, Jacobs, Kleczkowska, & Van den Berghe, 1984; Jacobs et al., 1980; Lejune, 1982; Mattei, Mattei, Aumeras, Auger, & Giraud, 1981).

Many of these maladaptive behaviors may be related to the presence of certain psychiatric disorders in the fragile X population. For example, given the stereotypical behaviors and communication problems in some fragile X boys, several investigators have explored the relationship between fragile X syndrome and infantile autism. Reports of the prevalence of autism in fragile X males are quite variable, with estimates ranging from 7% (Bregman, Leckman, & Ort, in press) to 14% (Fryns, Jacobs, Kleczkowska, & Van den Berghs, 1984) to 47% (Hagerman, Jackson, Levitas, Rimland & Braden, 1986). Numerous investigators have also screened their autistic samples, testing for the fragile X marker in boys already diagnosed with autism. The frequency of fragile X among males with autism is also quite variable, ranging from 15% to none (see Bregman, Dykens, Watson, Ort, & Leckman, 1987 for a review). Thus, there may be a modest degree of overlap in the two syndromes, and it is quite likely that

some of the variability in the literature may be attributable to discrepancies among investigators in their diagnostic procedures and subject samples. These discrepancies make it difficult to ascertain a precise estimate of the degree of overlap between the disorders at present.

Unlike the controversy over the diagnosis of infantile autism, there appears to be a consensus in the literature that many boys and young men with fragile X syndrome exhibit significant problems with attention, hyperactivity, and impulsivity (e.g., Hagerman, Murphy, & Wittenberger, 1987). Indeed, Bregman, Leckman, and Ort (in press) determined that 93% of their noninstitutionalized fragile X sample met the Diagnostic and Statistical Manual of Mental Disorders (DSM-III; American Psychiatric Association, 1980) criteria for Attention Deficit Disorder with Hyperactivity. In addition, these authors found that approximately 29% of their sample met DSM-III criteria for Anxiety Disorder. Anxiety problems were noted to be particularly problematic in interpersonal situations and in the social arena. It appears that these anxiety and attentional problems may characterize both young, noninstitutionalized boys and older institutionalized fragile X men (Dykens, Hodapp, & Leckman, 1989).

It may also be the case that attentional problems may change depending upon the age of the fragile X males. Although additional longitudinal data are needed, it seems that the hyperactive, impulsive, and aggressive symptoms that frequently accompany attentional deficits are less problematic among older fragile X subjects (Dykens, Hodapp, & Leckman, 1989). Thus, attention deficits in fragile X boys have been consistently observed by several investigators, and they may persist in many adults as well, but without the motoric involvement often noted in younger subjects.

It may be that the anxiety disorders noted in some fragile X males contribute to their difficulties in sustaining appropriate levels of attention and concentration. It is also quite likely that these attention deficits are related to the underlying deficit in sequential processing that characterizes many fragile X males. Adequate sequential processing requires some competency in short-term memory functioning; short-term memory is generally impaired when the ability to attend and concentrate is compromised. Although the relationship between these two problematic areas remains unclear, it is hypothesized that they are interdependent in that one deficit may serve to exacerbate the other.

Adaptive functioning

The ability to adapt socially – or to perform "daily activities required for personal and social sufficiency" (Sparrow, Balla, & Cicchetti, 1984, p. 6) –

is essential for the success of retarded persons living in a variety of settings. For example, social adaptation has been identified as more important than IQ for the ultimate life success of retarded individuals living in the community (Baller, Charles, & Miller, 1967; Windle, 1962). In addition, adaptive behavior is critical in determining the success or failure of individuals in group homes (Hill & Bruininks, 1984; Landesman-Dwyer & Sulzbacher, 1981) and in the large institutional setting (King, Raynes, & Tizard, 1971).

In assessing the importance of social adaptation, however, most studies have relied on data from mixed etiological groups. As such, data remain limited regarding the adaptive functioning of specific etiological groups such as fragile X syndrome.

Herbst (1980) noted that there may be a relationship between "social adaptability" and IQ in fragile X males, but did not specify how, or if, social adaptation was measured. Utilizing the Vineland Adaptive Behavior Scales (Sparrow, Balla, & Cicchetti, 1984), which assess communication, daily living, and socializations skills, Dykens, Leckman, Paul, and Watson (1987) compared older fragile X individuals to other residents of a large institution. These authors found that fragile X males exhibited significantly higher domestic daily living skills than their nonspecific retarded and autistic counterparts, and were apt to demonstrate adaptive skills that exceeded mental age (MA) expectations. Further examination of both institutionalized and noninstitutionalized fragile X males (Dykens, Hodapp, & Leckman, 1989) pointed to significant relative strengths in both groups in their daily living skills compared with communication and socialization abilities. Within the daily living skills domain, personal skills (e.g., toileting, grooming) and domestic skills (e.g., cleaning, cooking) were better developed than community skills (e.g., managing money, using a phone).

Although the institutional sample in this study demonstrated particular deficits in expressive and written communication compared with the noninstitutionalized group, the overall pattern of adaptive functioning identified by these authors persisted across samples that varied widely in their residential status, age, and degree of impairment. In addition, Wolff, Gardner, Lappen, Paccia, and Schnell (1987) have also recently reported strengths in domestic and personal daily living skills in a sample of fragile X children and adults. Although these authors did not relate the living status or functioning level of their subjects, it appears that strengths in daily living skills apply to many fragile X males regardless of their age, IQ, and residential status.

This profile of adaptive behavior may be consistent with sequential-processing deficits, and with the apparent strength of these males in tasks

requiring vocabulary and factual knowledge. Achievement tasks tapping skills in vocabulary and general environmental knowledge are similar to daily living skills in that both areas often involve tasks that are susceptible to repeated training (see Baker, 1984). Given the weakness in sequential processing and short-term memory, fragile X males may be particularly adept at performing behaviors that are typically overtrained and that do not necessarily rely upon short-term memory. Thus, although fragile X males exhibit levels of adaptive behavior that are generally commensurate with their levels of cognitive ability (Dykens, Leckman, Paul, & Watson, 1987), their adaptive skills may exceed MA expectations in tasks that are repeatedly taught and that deemphasize sequential processing.

As presented here, the hypothesis of sequential-processing deficits in many males with fragile X syndrome has received support from their profiles of strength and weakness in cognitive, linguistic, and adaptive functioning, as well as from their patterns of maladaptive behavior. This underlying sequential-processing deficit thus appears to pervade many aspects of functioning in these males and should be an important consideration in the development of appropriate intervention strategies for this group. The strengths of many fragile X males in simultaneous processing and in tasks requiring vocabulary and environmental knowledge provide additional guidelines for the development of effective educational tactics and intervention strategies.

Individuals with strengths in simultaneous processing solve problems best by mentally processing many parallel pieces of information at the same time. Simultaneous processing may be particularly important in recognizing the shape and appearance of numbers and letters, understanding the overall meaning of a story or situation, interpreting the overall meaning of visual stimuli such as pictures, charts, diagrams and maps, and visualizing solutions to problems in their entirety (Kaufman, Kaufman, & Goldsmith, 1984). As such, many fragile X males who demonstrate a relative strength in simultaneous processing may respond well to a teaching strategy that emphasizes the overall meaning of a task, or groups of details or images, before breaking down the task or grouping into its component parts. This teaching style might include helping fragile X males to visualize what is to be learned, offering a sense of the whole by appealing to their visual–spatial orientation, and making tasks concrete whenever possible with manipulative materials such as graphs, models, pictures, maps, and diagrams.

Many individuals with relative strengths in simultaneous processing and relative weaknesses in sequential processing exhibit difficulty with word attack skills, decoding and phonetics, the rules of grammar, breaking down

arithmetic problems into their component parts, remembering specific sequences or details of a story, and understanding and following oral instructions or a sequence of steps or rules (Kaufman, Kaufman, & Goldsmith, 1984). As such, fragile X males who exhibit this profile may not respond well to teaching strategies that appeal to their verbal–temporal functioning, that emphasize verbal cues and auditory memory, or that present materials in a step-by-step manner that gradually leads up to the presentation of the entire concept.

The deficits in sequential processing shown by many fragile X males may be exacerbated by overactivity, impulsivity, and poor concentration and attention, particularly in younger boys. In many fragile X youngsters, including those with diagnoses of attention deficit hyperactivity disorder, these behaviors contribute to considerable management problems in both their classroom and home environments. In situations where traditional behavioral modification programs aimed at reducing impulsivity and increasing on-task behavior fail, families and physicians may consider a trial of stimulant medication. In particular, methylphenidate has been noted to improve the attention span of some fragile X boys (Hagerman, Murphy, & Wittenberger, 1987), and clonidine has been reported as effective in other youngsters (Leckman, 1987).

Trajectory of intelligence

The specific profiles of strength and weakness in fragile X syndrome and in other etiological groups offer guidelines as to *how* one may best intervene with these individuals. Of equal importance, however, is *when* one should intervene. It is generally assumed that intervention programs may meet with more success if they are implemented at specific times in an individual's course of development (e.g., early intervention programs), and considerable attention has focused on the timing of programs that optimize cognitive functioning (e.g., Zigler & Seitz, 1982).

The timing of interventions aimed at cognitive functioning have generally been based upon data pertaining to the trajectory of intelligence in normal individuals and in mentally retarded individuals of mixed etiologies. However, proponents of the developmental approach to mental retardation suggest that trajectories of intelligence may differ across various etiological groups (Burack, Hodapp, & Zigler, 1988). For example, Hodapp and Zigler (in press) have reviewed longitudinal studies of Down syndrome children that showed decelerating rates of intellectual development from infancy throughout adolescence. This pattern contrasts with studies of retarded cerebral palsy subjects in which fairly stable IQ's over

time were noted, with some indications of slight increases in IQ over time (e.g., Cruickshank, Hallahan, & Bice, 1976).

These findings contrast with the long-term IQ stability noted in educable children of mixed etiologies over a 4-year span (Silverstein, 1982), and in mildly retarded adults, also of mixed etiology, when followed for a period of 35 years (Ross, Begab, Dondis, Giampiccolo, & Meyers, 1985). Thus, whereas data pertaining to mixed etiological groups point to long-term IQ stability, specific etiological groups may manifest markedly different trajectories of intellectual development. Additional data on the trajectories of IQ in specific etiological groups such as fragile X syndrome could help clarify the issue of IQ stability versus change in retarded populations.

Some reports have noted that the intellectual functioning of many younger boys with fragile X syndrome lies in the borderline or mildly retarded range, whereas adult males are more often severely or profoundly retarded (Hagerman, Kemper, & Hudson, 1985; Opitz, 1984). Thus, there may be a deceleration of IQ in fragile X males that is related to CA (Borghgraef, Fryns, Dielkens, Pyck, & Van den Berghe, 1987). Lachiewicz, Gullion, Spiridigliozzi, and Aylsworth (1987) report that this IQ decline begins in early childhood. In contrast, Dykens, Hodapp, Ort, Finucane, Shapiro, and Leckman (1989) have reported that IQ declines and MA plateaus in the late childhood or early adolescent years (ages 10–15 years). An additional report (Hagerman, Schreiner, Kemper, Wittenberger, Zahn, & Habicht, submitted) indicates that the greatest drop in IQ in their sample occurred between the ages of 8 and 12 years, spanning the age ranges in the two studies noted. Thus, although there is agreement that IQs eventually decline in many fragile X males, the exact point at which this is likely to occur remains unclear. Additional longitudinal and cross-sectional studies with large numbers of fragile X males are needed to precisely delineate the parameters of the age range in which IQ declines and MA plateaus.

The question of why IQ remains relatively stable at early ages but declines in the early teen years remains problematic. Some researchers have speculated that this premature decline in IQ may be related to regulatory factors responsible for the initiation of puberty in that the earliest signs of cognitive plateauing in these males appear to coincide with the earliest signs of their pubertal development (Dykens, Hodapp, Ort, Finucane, Shapiro, & Leckman, 1989). Other researchers, however, have hypothesized that the drop in IQ occurs because the abstract reasoning and symbolic language skills that are stressed in the intellectual assessments of later childhood may be problematic for many fragile X males (Hagerman, Schreiner, Kemper, Wittenberger, Zahn, & Habicht, submitted). These hypotheses raise the question of whether IQ changes are due

to changes in the "developmental tasks" facing the child or to changes in the development of the neurological system. This issue of task versus maturation has been discussed in relation to Down syndrome children (Hodapp & Zigler, in press; see chapter 12) and the development of normal children (McCall, Eichorn, & Hogarty, 1977). Additional longitudinal research should examine the contribution that these or other hypotheses make in explaining the IQ changes observed in fragile X males.

Implications for intervention

Studies of IQ trajectory confirm the importance of classifying research groups by etiology in that identifying differences between IQ trajectories of various groups will ultimately allow for more fine-tuned intervention efforts. Although it is too early to conclude that declines in IQ are an inevitable consequence of fragile X syndrome, findings from these studies may help in planning the timing and intensity of educational and vocational efforts with fragile X males; indeed these findings provide renewed impetus for the "earlier the better" focus of many intervention programs. Parents and teachers should be counseled that these findings do not necessarily signal a deterioration or loss of acquired cognitive skills. Rather, they should be informed about the possibility that in contrast to nonretarded children, whose cognitive development plateaus from 16 to 18 years of age, fragile X boys may plateau at an earlier period, somewhere between the ages of 10 to 15 years. Thus, fragile X children doing comparatively well in their earlier years may ultimately perform lower on IQ tests than previously thought. In addition, parents and educators should be counseled that this decline in IQ may not be apparent in the child's adaptive behavior, and that the relationship between IQ decline and the adaptive functioning of fragile X males remains unknown at present.

The family environment and fragile X syndrome

Although developmental theorists and researchers have traditionally focused on changes and processes within the child alone, there has been an increasing emphasis on the role played by the child's external environment at various points in both normal and atypical development (e.g., Sameroff, chapter 5, this volume). A considerable amount of this work in developmental psychology has been devoted to the child's immediate, interpersonal environment – primarily the family and mother–child interactions.

Fragile X syndrome provides several unique opportunities to examine

environmental issues of concern to developmentalists – such as the child's family environment and mother–child interaction – that are not readily afforded in other retardation syndromes or in families with atypical members.

As previously discussed, approximately one-third to one-half of the females who carry the fragile X marker are themselves affected with the syndrome. These women may manifest mild to moderate mental retardation, or learning problems and disabilities that may be similar to the profiles of cognitive weaknesses manifest by affected males, such as poor attention span, difficulty with numerical reasoning, and auditory short-term memory (e.g., Kemper, Hagerman, Ahmad, & Mariner, 1986). Thus, some boys with fragile X syndrome reside in families in which their mothers and/or female siblings exhibit retardation or learning problems, others may have similarly affected male siblings, and still others may have families in which their mothers, sisters, and/or brothers are not at all affected with the syndrome. These variations in family constellation provide opportunities for researchers to compare mother–child interactions, sibling–child interactions, and so on in families with or without an affected mother or sibling, and to relate the findings to the affected males' intellectual, adaptive, and behavioral functioning. In short, the variable pattern of expression seen in fragile X syndrome provides a unique opportunity to tease apart the effects of the retardation syndrome from surrounding environmental stimulation.

In addition, recent research has suggested that many carrier females exhibit psychological and emotional difficulties such as anxiety (Hagerman & Smith, 1983), psychotic problems and shyness (Fyrns, 1986), and autistic behavior (Hagerman, Chudley, Knoll, Jackson, Kemper, & Ahmad, 1986). Most recently, Reiss, Hagerman, Vinogradov, Abrams, and King (1988) have reported an increase of schizophrenia spectrum disorders and a history of chronic affective disorders in a sample of 35 carrier mothers compared with a matched control group of mothers of developmentally delayed and behaviorally dysfunctional youngsters. Research on mother–child interactions in depressed and schizophrenic mothers in general points to considerable problems in maternal responsiveness to the needs of their children (Tronick & Field, 1986), as well as to deviant maternal communication patterns (Bateson, Jackson, Haley, & Weakland, 1956; Massie, 1982). As no studies have yet been reported that describe mother–child interactions of fragile X females who exhibit psychiatric or cognitive impairments, it is difficult to describe the impact that these maternal problems may have in the development of their sons and daughters affected with fragile X syndrome. It may be hypothesized, however, that the offspring of carrier females with multiple psychiatric and cognitive

difficulties are at increased risk compared with fragile X boys with "normal" mothers. Until research that explores this hypothesis is available, the present findings of increased vulnerability to psychiatric and learning disabilities among some carrier females suggest that intervention efforts need to be carefully tailored to the needs of each individual family. For example, some families may require extra support and involvement from school officials, mental health agencies, outreach programs, and parent aid/education programs, and others will require less intensive or minimal efforts.

Directions for future research

Although data are fast accumulating on the genetic, behavioral, cognitive, adaptive, and maladaptive features of males with fragile X syndrome, many questions remain about their development in all areas of functioning. In addition, there are considerable gaps in our knowledge of carrier females, their profiles of cognitive and behavioral strengths and weaknesses, and the impact that affected mothers and siblings may have on family functioning.

Of particular interest to those concerned with the developmental approach to mental retardation are questions regarding the specificity of the cognitive, adaptive, linguistic, and behavioral profiles previously described, as well as the specificity of the IQ trajectory in fragile X syndrome. Further research is necessary to identify the extent to which these profiles and trajectories are shared by other etiological groups, and to describe how these findings confirm or contradict the extension of the two-group approach in organic retardation. In addition, the implication of the pervasive sequential-processing deficit observed in this syndrome for defect versus developmental theory needs to be described.

Many questions also remain that may have more immediate applicability to educators, parents, and health professionals who intervene on a daily basis with fragile X boys and men. For example, the relationship between the decline in IQ and the adaptive functioning of these males remains unclear, as does the age at which this decline is most apt to occur. The reasons why all boys with fragile X syndrome do not manifest this IQ decline also remain to be elucidated. In addition, there is a need to systematically evaluate the effectiveness of educational efforts and vocational strategies that capitalize on potential strengths in simultaneous processing and minimize the pervasive sequential-processing deficits often observed in these males. Finally, if future research identifies similarities in the cognitive and behavioral profiles of carrier females, nonpenetrant males, and

affected males, then effective intervention strategies that optimize the functioning of all affected family members will have to be developed.

This recommendation for future research will be particularly helpful if it also describes the impact that carrier females with and without psychiatric and cognitive disabilities may have upon family functioning, mother–child interactions, and the development of their offspring affected with fragile X syndrome. Given the nature of these questions, future work in fragile X syndrome will necessarily require collaboration between many fields, including genetics, developmental and clinical psychology, child psychiatry, and special education.

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