

## **OVERVIEW OF BEHAVIORAL PHENOTYPE**

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Fragile X syndrome is an X-linked condition, where the genetic anomaly is transmitted from parent to offspring on the X chromosome. However, the pattern of inheritance is not that of a simple X-linked Mendelian disorder. Only four-fifths of males with the genetic anomaly show cognitive defects, yet about one-third of "carrier" females are themselves learning-disabled (Hagerman and Silverman 1996). Fragile X syndrome has been shown to account for almost 10 per cent of boys with moderate to profound mental retardation and for about 6-10 per cent of otherwise unexplained mild mental retardation (Thake et al. 1987). Recent estimates put its prevalence at between one in 3,000 and one in 6,000 boys and approximately one in 8,000 girls (Turner et al. 1996). It is therefore the most common inherited cause of intellectual impairment and the second most common cause of mental retardation after Down syndrome which is only rarely inherited.

### **Intellectual functioning**

Substantial research has clarified developmental and behavioural correlates. General level of intellectual functioning is very variable but is usually in the mild to moderate mental retardation range corresponding to an IQ of 35-70. There is a verbal/performance discrepancy with relative skills in language areas but particularly special needs with numeracy and visuo-spatial functioning (Curfs et al., 1989). The *rate* of intellectual development remains parallel to that of non-learning disabled peers up until puberty when the discrepancy widens. This is attributed to relative strengths with simultaneous information processing yet specific difficulties in the sequential processing of information which become more marked over time (Hodapp et al. 1991). All these intellectual anomalies are witnessed in female carriers most of whom have average intellectual functioning. Female carriers have also been described as showing "executive function" deficits (Sobesky et al., 1996). These manifest as problems in organizing thinking, difficulties planning ahead and impaired ability to shift from one "mind set" to another. Female carriers may also be more prone to depression (Franke et al., 1996), but do not seem to have emotion-perception or perspective-taking difficulties (Mazzocco et al., 1993).

Recent research confirms that males with the milder genetic abnormality, known as a premutation, may still be affected clinically. They too can show a range of specific learning difficulties as well as social and language impairments and attentional deficits (Mills et al., 2002; Aziz et al., 2003).

### **Social Impairments**

There is an association with autism in that fragile X syndrome accounts for 2-3 per cent of cases of autism (Bailey et al. 1993). Conversely autism can be diagnosed in a substantial minority of children with fragile X syndrome (Turk 1992). People with fragile X syndrome have a stronger association with a characteristic profile of autistic-like features. These include delayed symbolic and imaginative play, delayed echolalia, repetitive speech, hand flapping, hand biting and scratching in response to anxiety or excitement, gaze aversion and social anxiety in the presence of a usually friendly and sociable personality (Turk and Graham 1997). It is often the paradoxical juxtaposition of a friendly, socially responsive and affectionate personality with high levels of social anxiety and the above cluster of autistic-like communicatory and ritualistic/obsessional features which is the hall-mark of fragile X syndrome. Most people with fragile X syndrome have good face and emotion recognition skills (in contrast to people with autism) (Turk & Cornish 1998). They also show "theory of mind" abilities and executive function skill levels consistent with their general level of intellectual functioning (Garner et al., 1999). This again emphasizes the contrasts between fragile X syndrome and autism in many instances.

### **Speech & Language**

Speech is often "cluttered" (rapid and disrhythmic) with frequent dysfluent, rapid, tangential remarks, garbled speech and poor topic maintenance (Ferrier et al. 1991). 50 per cent or so of individuals display "jocular litanic phraseology", so-called because of the humorous quality to the perseverative and repetitive speech which shows up-and-down swings of pitch and palilalia (multiple repetitions of phrases with increasing speed and diminishing volume). Speech disturbance is complicated further by central information processing difficulties, macrognathia (large and protruding jaw) and temporo-mandibular joint laxity. This emphasizes the need for early specialist speech and language evaluation and intervention (Abbeduto and Hagerman 1997). Care must be taken with any plans to eliminate "deviant" speech and language patterns. It has been argued that some of the language impairments such as echolalia and repetitiveness may be serving important functions in maintaining other people's attention while giving the fragile X individual sufficient time to compensate for information processing difficulties (Ferrier et al. 1991).

### **Attentional Deficits & Overactivity**

Children with fragile X syndrome often show unexpectedly extreme levels of inattentiveness, restlessness, fidgetiness, impulsive tendencies and distractibility even when their level of general development is taken into account (Turk 1998). Some are also overwhelmingly overactive. Many of the remainder are very active as well but probably no more so than other children with similar degrees of intellectual impairment who do not have fragile X syndrome. There is evidence that these features do not necessarily improve with age (in contrast to most children with these traits) emphasizing the need for early diagnosis and multi-disciplinary intervention.

### **FraX-E**

FraX-E is a rare variant of fragile X syndrome. It is caused by a similar abnormal gene expansion on the X chromosome's long arm, but one that is even closer to the chromosome's tip. The condition remains under-researched but can manifest with a wide spectrum of affectedness including mild to severe mental retardation, with or without autism (Barnicoat et al., 1997). Conversely individuals can be quite severely affected with severe mental retardation and autism (Turk et al., 2000). A separate DNA test is required to check for FraX-E and this must be requested specifically.

### **Intervention & Support**

The degree of intellectual impairment, and presence or absence of autistic features and attentional deficits, will determine largely the nature of multi-disciplinary intervention required. Teachers must be aware of the implications of often strikingly uneven cognitive profiles, the characteristic trajectory of intellectual development with sequential information processing difficulties, social anxiety, gaze aversion, language anomalies, ritualistic tendencies, difficulties with transitions and changes to routine, and frequent and persisting attentional deficits (Gibb 1992). Sadly, research suggests that educational staff often have little knowledge about learning styles of children with fragile X syndrome, and insufficiently specialized knowledge to ensure that special educational needs are being met fully (Wilson & Mazzocco 1993; York et al., 1999). Follow-up studies are beginning to show that without intensive early support and intervention, many serious cognitive, social, communicatory and other behavioral problems persist (Das & Turk 2002). Thus a combination of medical, psychological, educational and social managements, initiated as early as possible in development following comprehensive evaluation and clarification of special needs profile is required for optimal progress (Turk 1996a). It is also important in preventing the development of avoidable secondary handicaps (Turk 1996b).

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