**Fragile-X Syndrome**

Identifying Neuropsychological Strengths and Weaknesses in Boys and Girls with Fragile-X Syndrome

**SUMMARY**

Fragile-X syndrome is a genetic disorder linked to the X chromosome. It affects approximately 1 per 3000 males and 1 per 6000 females. It is the second most common identifiable cause of moderate-severe learning difficulties in males, and the most common form of learning disability that may be directly inherited.

Dr Kim Cornish and Fehmidah Munir of Queen's Medical Centre, Nottingham, have identified key behavioural and neuropsychological characteristics associated with Fragile-X syndrome, which have clear implications for the development of remedial programmes. They found that:

- Boys with Fragile-X had problems related to deficits in attention (including hyperactivity, irritability and impulsiveness). These problems were often associated with socially unacceptable behaviour such as aggressiveness or swearing.
- Boys with Fragile-X had specific impairments in the ability to select relevant information while ignoring or inhibiting irrelevant information.
- Girls with Fragile-X tended to have difficulties in social relations (e.g. lack of social interaction skills, social withdrawal and severe shyness). There was also a high incidence of depression and anxiety in both young and older girls with Fragile-X.
- In both boys and girls with Fragile-X syndrome, verbal skills were more advanced than non-verbal skills. Girls with Fragile-X had exceptionally poor arithmetic skills which may not always be understood by teachers in mainstream schools.
- The findings of the present study have important implications for the development of future remedial programmes (educational, psychological and medical) for children and young adults with Fragile-X syndrome. While the research has highlighted a number of weaknesses in their cognitive and behavioural profile, it has also identified a number of important strengths which need to be developed and encouraged to ensure each individual reaches their full potential.

**BACKGROUND**

**Genetic cause**

The disorder is associated with an X chromosome fragile site at Xq27.3. Research in the early nineties indicated a candidate gene, the FMR1 gene, characterised by multiple repeats that appear to lengthen dramatically in affected individuals. In the general population, this triple repeat contains between 5 and 50 triple repeats, whereas in affected individuals the region becomes greatly expanded to between 200
and 2000 triple repeats, the gene becomes methylated and FMR-1 mRNA fails to be transcribed. This is known as the 'full-mutation'. It is the loss of function of this gene that is associated with the clinical manifestations of the syndrome. An intermediate stage between the normal and fully mutated gene, the 'pre-mutation' explains the existence of 'normal transmitting males' and 'carrier females'.

Degree of learning disability

Over 90% of all males with the FMR1 full-mutation will have learning disabilities, usually in the mild to moderate ranges, compared with females with the full mutation, who present with a wider degree of intellectual impairment with over a third functioning within the normal range of abilities.

THE RESEARCH

Dr Cornish and colleagues studied 30 children (aged 7 to 15 years) and 30 young adults (aged 18 to 30 years) all with Fragile-X syndrome. Each participant was tested individually using a set of neuropsychological tests (e.g. memory, attention, face recognition, spatial skills, motor skills, verbal skills). They were also assessed on scales of behavioural functioning (e.g. social problems, aggression, hyperactivity, mood problems), communication and daily living skills.

THE FINDINGS

- In boys with Fragile-X the ability to select relevant information while ignoring or inhibiting irrelevant information was specifically impaired. The results of the study also indicated that hyperactivity but not attention problems decrease with age. However, other behaviour problems including aggressive behaviour, delinquency and social problems increased in intensity with age.
- Girls with Fragile-X tended to have difficulties in social relations (lack of social interaction skills, social withdrawal and severe shyness). Unfortunately, these features appear to continue from childhood into early adulthood and may severely interfere with the establishment of peer/parent/romantic relationships. The researchers also found a high incidence of depressive illness and anxiety in both young and older girls.
- In both boys and girls with Fragile-X syndrome, verbal skills (articulation, comprehension and vocabulary skills) were more advanced than non-verbal skills (emotion perception, face recognition, visuo-spatial skills).
- Of particular concern were the exceptionally poor arithmetic skills in girls with Fragile-X. This weakness needs to be addressed urgently particularly as many girls will attend mainstream schools where teachers may be unaware that poor maths skills is a feature of the syndrome rather than a symptom of laziness or an unwillingness to try harder.
- Girls in this study also consistently reported problems in other areas of the curriculum particularly in geography and physical education. Poor motor coordination, reduced short-term memory and impaired visuo-spatial skills observed in many girls with Fragile-X may explain why they can often struggle at school even though their overall intellectual ability may be within the normal range.
The study also found that the ability to hold information in mind (short-term memory skill) is a major difficulty for both boys and girls with Fragile-X syndrome, with many teachers and parents reporting a high level of inattentiveness and restlessness in the child or young adult with Fragile-X. The neuropsychological findings further suggest that the ability to recall and remember verbal information may be less impaired than the ability to recall abstract, non-verbal information.

The findings indicated no relationship between the molecular characteristics (number of CGG repeats) of the disorder and cognitive impairment in either boys or girls. This indicates that cognitive ability was not correlated with size of CGG repeat (i.e. a higher repeat did not imply lower cognitive functioning), a finding that has considerable implications for future genetic counselling and prenatal diagnoses.

THE IMPLICATIONS

Educational

Boys with Fragile-X may benefit from teaching strategies which aim to strengthen their ability to focus on the task at hand and inhibit potential distractors.

For both boys and girls with Fragile-X, teaching and 16 year plus training need to focus on encouraging and developing the relative strengths in verbal ability rather than concentrating on specific weaknesses. This seems particularly relevant as verbal skills continue to increase at a much faster rate of development than non-verbal skills. It might also be beneficial to develop teaching strategies that take into account the relative strength in verbal memory and try and reduce the impact of a much greater impaired non-verbal memory.

For girls with Fragile-X, patterns of weakness in arithmetic, visuo-spatial skills, and poor motor coordination need to be recognised and acknowledged by the school, therapist, parent or affected girl herself so that appropriate provision can be offered. Otherwise, repeated failure to achieve competence on cognitive skills such as arithmetic may perpetuate and further increase the level of social anxiety and low self-esteem that already characterises girls with Fragile-X.

Social / emotional

For girls with Fragile-X, the establishment of appropriate counselling services may help alleviate emotional problems by addressing the reasons for their depression. Also specific training programmes that could promote their cognitive strengths and increase their confidence and self-esteem may be of great benefit to young adult women with Fragile-X syndrome.

Medical

When providing genetic counselling to young women with Fragile-X, it is crucial that clinical geneticists take into account their problems in short-term memory processing and social avoidance. Both these aspects of their profile could severely affect the amount of information that is assimilated and subsequently processed. Genetic counsellors should also note the lack of association between molecular characteristics and cognitive ability.
Further reading:


For further information contact:

The Fragile X Society

This support group was formed in May 1990 to provide support and information to Fragile-X families and has published a number of publications describing specific aspects of Fragile-X syndrome including behaviour, education approaches and genetics. For more information please contact the society at:

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