Cytogenetic Anomalies in Poor Scholastic Children

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ABSTRACT

Poor scholastic performance is a symptom, where the child scores poor marks which remain below the class average or backwardness in relation to the average attainment for that age and grade. The underlying cause may be genetic in nature in many cases showing variability in symptoms and genetic defects. Many human genetic disorders are caused by missing or duplicated pieces of genetic material or chromosome, known as a copy number variant (CNV). Chromosome disorders can be observed by the light microscope and they are known to occur at the molecular level of magnitude in the genetic material. This still has a role in identifying large scale copy number variant disorders practiced by many hospital laboratories for diagnosis of genetic disorders.

INTRODUCTION

Poor scholastic performance may be intellectual disability (ID), which is characterized by significant limitations in both intellectual functioning and adaptive behavior that begin before the age of 18 years, affects neatly 1.5 to 2% of the population in the world. Intelligence was one of the first human traits to be the target of genetic research even before psychology emerged as a scientific field. The correlation between DNA sequence and behavioral differences such as intelligence is considered causal because DNA variations can lead to behavioral differences but behavioral differences do not change DNA sequences (Deary *et al.* 2006).

Academic underachievement of children is a big concern among parents and teachers in present day competitive society. The underlying cause of scholastic

backwardness should be identified in order to provide appropriate remedy so that the academic performance of such children can be made better.

GENETIC GROUNDWORK

Changes in chromosomal copy number were first recognized as a cause of intellectual disability in 1959, when it was discovered that an extra copy of chromosome 21 is the cause of Down's syndrome (Lejeune *et al.* 1959). Trisomy 21 remains the most important chromosomal cause of intellectual disability. Steady advances in chromosome-banding techniques facilitated the detection of unbalanced rearrangements, including translocations, large deletions or duplications, and supernumerary marker chromosomes.

Single-gene causes have also been identified for a number of intellectual disability syndromes and include both autosomal and X-Iinked genes, with the fragile X syndrome being the most common of inherited syndromes caused by a single-gene defect leading to this phenotype in male patients. Genetic testing was first introduced as a clinical tool in the 1960s with the advent of chromosomal karyotyping. This test allows the chromosomes to be visualized under a common microscope. Special stains applied to the chromosomes captured in metaphase give each chromosome a characteristic pattern of stripes, or "banding pattern." Most banding pattern tests have a resolution limit of about 550-650 'bands'. Trained professionals are able to view photographs from banding tests and determine whether all or part of a chromosome is missing, duplicated, or abnormally located.

DIAGNOSIS OF INTELLECTUAL DISABILITY

A diagnosis of intellectual disability is usually made when IQ testing reveals an IQ of less than 70, which means that often the diagnosis is not made until late childhood or early adulthood. However, most persons with intellectual disability (ID) are identified early in childhood on the basis of apprehension about developmental

delays, which may include motor, cognitive, and speech delays (Mefford *et al.* 2012). Karande and Kulkarni (2005) reported that around 20% of school children have scholastic backwardness. Factors associated with scholastic backwardness include physical illnesses, below average intelligence, learning disorders, attention hyperactivity disorder and psychiatric disorders (Pratinidhi *et al.* 1992, Mogasale *et al.* 2012).

CHROMOSOME DEFICIENCIES IN MENTAL SUB LEVEL

The minimum size of disrupted chromosome that can be detected by chromosome banding is approximately 5 to 10 Mb, and such cytogenetically visible rearrangements are responsible for 10 to 15% of cases of intellectual disability (Ropers, 2008). It was soon recognized that some patients with syndromic forms of intellectual disability also had deletions in the same chromosomal region, a finding that resolved the molecular cause of micro deletion syndromes, including the Prader-Willi and Angelman syndromes with deletion of 15qll-ql3 (Butler *et al.* 1986), the Williams-Beuren syndrome with deletion of 7qll.23 (Perez Jurado *et al.* 1996) and the Smith-Magenis syndrome with deletion of 17pl2 (Smith *et al.* 1986). It was also noted that 1 to 3% of patients with autism had a maternally inherited duplication involving 15qll-ql3 (Hogart *et al.* 2010).

Several novel micro deletions have been identified in patients who have intellectual disability. Heterozygous deletions of 17q21.31, which were described by three groups simultaneously, are associated with moderate-to-severe intellectual disability, hypotonia, facial dysmorphic features, occasional cardiac and renal abnormalities, and seizures (Koolen *et al.* 2006; Sharp *et al.* 2006; Shaw-Smith *et al.* 2006). The deletion is 500 to 650 kb in size and is not detectable by routine karyotyping. All 17q21.31 deletions that have been identified are de novo, and the deletion has never been seen in healthy control subjects. Its prevalence is estimated to

be approximately 1 in 16,000 persons.75 Deletions of 15q24 are much rarer, but patients with 15q24micro deletions also have an intellectual disability syndrome with recognizable features. Common features include developmental delay and intellectual disability that is usually moderate to severe.

In 1963 a review in Science of genetic research on intelligence was influential in showing the convergence of evidence from family, twin, and adoption studies pointing to genetic influence (Erlenmeyek and Jarvik, 1963). During the 1960s, environmentalism was beginning to diminish in psychology and the stage was set for increased acceptance of genetic influence on intelligence (Plomin and Spinath, 2004).

CONCLUDING REMARKS

In last two decade, the learning disability movement has picked up momentum swift in India, and more and more children with this condition are being identified. There is dearth of epidemiological studies in India to determine the exact prevalence of scholastic backwardness. Moreover, studies are required to better understand genetic basis if any, in different cases of poor scholastic performance among children.

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