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GENETICS BASIS OF LEARNING DISABILITIES: Mini Overview

Maheen Waqar* and Erum Shoeb

Department of Genetics. University of Karachi, Karachi-75270, Pakistan.
**Corresponding author. E-mail: maheenwaqarfarooq@gmail.com; erumsh@uok.edu.pk*

ABSTRACT

Learning Disability (LD) is said to affect the abilities of brain to receive, process and store information causing difficulties for an individual to read, write or learn. Learning disabilities may have environmental reasons like prenatal exposure to alcohol or postnatal exposure to lead, but most of the learning disabilities are genetic. Fragile-X syndrome is one of the leading causes of learning disabilities, which is the reason why LD is more common in males than females. The present review is an attempt to highlight genetic factors involved which might facilitate earlier screening of LDs through molecular identification.

Key-words: Learning disability, genetics, fragile X-syndrome, pediatric patients.

The term learning disability is used to describe limited or slow development of intellectual functioning (Thomas and Wood, 2003). The causes of learning disabilities can be divided into two areas: Genetic and Environmental, although these may overlap at times (AAMR 1992, Russell 1985).The cause for one individual may not be the same as for another, and in many cases it may not be obvious.A learning disability can be caused by any condition that impairs the development of the brain either before birth, during birth or within the childhood years (book). Among the spectrum of issues of concern in learning disabilities, the inability to read and comprehend is a major obstacle to learning and may have long-term educational, social, and economic implications (AAP, 1998).

Learning disabilities often called learning difficulties are more frequently genetic. This review emphasizes over the genetic facts that result in learning disabilities in childhood or adult age. The aim of this review is to substantiate that not all thedisabilities/disorders are due to environmental reasons; there are some that are genetic that is, inherited by the family.

Learning disability is a terminology used to label people that function at an intellectual level that is significantly lower than the average level of people in the society (Thomas and Woods, 2003). Learning disability is a descriptive concept, not a disorder. It has been suggested that several hundred different causes have been discovered. Predominantly LDs are caused by a difference in brain structure that is present at birth.A long held and totally valid view has been that the conditions leading to severe and profound learning disability have identifiable pathologies, including genetic disorders (Walter, 2000).Learning disabilities can impact how someone learns to read, write, hear, speak, and calculate and are often hereditary.

GENETIC FOUNDATION FOR LEARNING DISABILITIES:

A popular theory is that learning disabilities are genetically transmitted. Mental disorders almost always involve more than one gene. Studies have shown that one mental disorder can be caused by different genes on different chromosomes in different populations. It now appears that specific mental disorders are related to different sets of genes that vary across families and ethnic groups.

Genes associated with mental disorders do not always show the same degree of penetrance, which is defined as the frequency with which a gene produces its effects in a specific group of people. Penetrance is expressed as a percentage. For example, a gene for manic depression may have 20% penetrance, which means that 20% of the members of the family being studied are at risk of developing the disorder.

There have been major advances in the past few years in our understanding of the X-linked learning disabilities. The most common of these is the fragile-X syndrome, but the number of other gene defects that are now recognized to be linked with learning disability is increasing rapidly (Robertshaw and MacPherson, 2006).

A series of conditions associated with learning disability has been regionally mapped to the X-chromosome. Much work has been done with regard to the role of the X-chromosome in intelligence (Turner, 1996; Lehrke, 1997). Many different genetic defects involving the X-chromosome have been described resulting in lowered intelligence. This topic has been explored further by Gecz and Mulley (2000) and Partington *et al.* (2000). More than 150 genes associated with X-linked learning disability have now been identified.

The fact that there are more men than women with learning disability has been known for over a hundred years and is mainly due to X-linked disorders (Walter, 2000).Since males are hemizygous for X-linked genes, all X-linked genes are expressed in males whether recessive or dominant. In contrast females having two X chromosomes get

expression of only dominant X-linked genes and recessive genes are expressed in females only when present in double dose, i.e., when contributed by both the parents. The most common of these disorders is fragile-X syndrome, with a prevalence of 1:4000 males and approximately 1:8000 females (Turner, 1996).

It has been known that the risk a child will have a reading problem is increased from four to thirteen times if one of the parents has a similar problem.Every child is born with unique genetic combination, thereby having unique abilities to learn. Variation in developmental processes is usual but delay in achieving certain developmental milestones, when most other aspects of development are normal, could be a sign of a learning disability.Such delays may include problems with language, motor delays, or problems with socialization. While there is no direct cure for a learning disability, early screening and intervention from specialists can often provide great benefits. LDs arethe most common handicapping condition ofchildhood (with an estimated incidence of 15% or greater), relatively little is knownabout their etiology (Pennington and Smith, 1983).The etiology of these difficulties is multifactorial, reflecting genetic influences and abnormalities of brain structure and function. The child with LD has difficulty with processing skills such as memory, visual perception, auditory perception, or thinking; and as a result has trouble achieving in at least one subject such as reading, writing or counting (Lerner, 2003).

"Learning disability" tends to conjure images of problems with language, particularly reading and writing although it can also apply to specific difficulties in math, reasoning, attention, and organizational abilities (Henry, 1999). Adults with learning disabilities may not have difficulties with language per se, but instead do not effectively process the nonverbal elements of social interaction (Henry, 1999). Heredity plays an important role in the development of learning disabilities. Learning disabilities may also be inherited by adults and children, just like genetic disorders.

Learning disabilities have become an increasing personal and public concern (AAP, 1998). There are a number of reasons for finding out the possible cause of a person's learning disabilities. One is that often individuals and their families want to know, and have a right to do so. There are also health factors. It is important to distinguish between learning disability and physical or mental health problems which may well be treatable.Characteristics associated with learning disabilities may contribute to social skills deficits. A disproportionate number of juvenile offenders have learning disabilities; a number of researchers believe that many of them get into trouble because they do not fully understand the implications of their inappropriate actions (Henry, 1999).

Learning Disabilities may be genetic or due to certain environmental conditions as prenatal exposure to alcohol, perinatalcomplications, postnatal exposure to lead (Needleman, 1980). These can result in underdevelopment of the brain. Certain learning disabilities, such as specific dyslexia, hold out the long-term prospect for being understood at all levels of analysis, including the genetic, neurobiological, neuropsychological, environmental, and functional (Pennington and Smith, 1983). Some steps inthe direction of this kind of understandinghave already been taken for simpler behaviors.The neural bases of some well-established developmental milestones are beginning to be understood, mainly in terms of regional cycles of myelination in particular parts of the developing brain (Konner, 1982; Yakovlev and Lecours, 1967).

Familial disorders associated with learning disability often do not show simple Mendelian inheritance. Partial penetrance, parent-of-origin effects and anticipation occur and in some cases, for example Fragile-X, occurs together (Walter, 2000). It is now estimated that X-linked learning disability has a prevalence of 2.6:1000 population, accounting for over 10% of all cases of learning disability (Stevenson and Swartz, 2002).

Intellectual and developmental disabilities such as autistic spectrum disorders (ASDs) and Attention deficit hyperactivity disorder (ADHD) are heterogeneous disorders that have diverse etiologies. It is very clear from the previous studies that genetic factors can conceivably alter braindevelopment through a large number of different pathways, including interaction between aspecific genetic change and a particular environment (Pennington and Smith, 1983).

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