International Journal for Life Sciences and Educational Research
Vol.1(2), pp. 57 - 63, July- 2013
Available online at http://www.ijlser.com
E-ISSN : 2321-1229; P – ISSN : 2321-1180

Review Article

Causes of mental retardation: environmental or genetic

Monika Panchani
Department of Zoology, Vallabh Govt.College, Mandi

Article History : Received 05 June 2013, Accepted 28 June 2013

Abstract

Tremendous advancements have seen in the past decade in the diagnosis of mental retardation. In present scenario prevalence of mental retardation is also increasing so more research has to be carried out to unearth the causes of mental retardation which will help in treatment and reduction in its prevalence. Mental retardation is the most common developmental disorder which is affecting almost 3% of the population. Mental retardation (MR) is a particular state of functioning that begins in childhood and is characterized by decreased intelligence and adaptive skills. The causes of mental retardation need not be present at birth. Mental retardation may be acquired during later development (but prior to eighteen years of age). Causes of mental retardation are numerous and include genetic and environmental factors. They are usually grouped into: (i) prenatal, (ii) perinatal (around the time of birth) and (iii) postnatal causes. In at least 30 to 50 percent of cases, physicians are unable to determine etiology. It is noted that diagnostic capability-clinical and laboratory-must be increased for 50% reduction in the prevalence of severe mental retardation to be achieved in the foreseeable future.

Keywords: Mental retardation (MR), Prenatal, Perinatal, Postnatal causes Environmental and Genetic factors.

Introduction

Mental retardation is one of the common problems in children with major implications for a nation's health, education and community services. World Health Organization estimates that 10% of the whole population has some form of mental disability and 1% suffers from severe incapacitating mental disorders (WHO, 1989). A mentally defective person is a person who is incapable of managing himself and his affairs, or being taught to do so, and requires supervision, control and care for his own welfare and welfare of the community. It is identified by significantly sub-average intellectual functioning resulting in or associated with concurrent impairment in adaptive behaviours and manifested during the developmental period (Grossman, 1983).

Causes

Mental retardation is a complex condition, which may be caused by the interaction of many factors. In about 75% of cases, the exact cause is never known. In at least 30 to 50% of cases, physicians are unable to determine etiology despite a thorough evaluation (Baird and Sadovnick, 1985). Comprehensive family history is the first and most important step in the diagnosis of mental retardation. Previous Gynecologic and obstetric history may reveal infertility or fetal loss (Matson and Sevin, 1994). Complications of prematurity, especially in extremely low-birth-weight infants, or postnatal exposure to lead can also cause mental retardation (Piecuch *et al.,* 1997).

Many environmental and genetic factors can cause mental retardation, including premature

*Corresponding Author : Monika Panchani, Email : monaharipanchani@gmail.com

birth, premature birth infections, chromosomal abnormalities and a single gene mutation (Kins-Bourne and Graf, 2000). They are usually grouped into: (i) prenatal, (ii) perinatal (around the time of birth) and (iii) postnatal causes. Prenatal causes include congenital infections such as cytomegalo-virus, toxoplasmosis, herpes, syphilis, rubella and human immunodeficiency virus; prolonged maternal fever in the first trimester; exposure to antico-nvulsants or alcohol; and untreated maternal phenyl-ketonuria (Stromme and Hagberg, 2007).

Toxoplasma infection (toxoplasmosis) is caused by a parasite, *Toxoplasma gondii.* This parasite is found in warm-blooded animals and mostly associated with cats in the United States and Canada. It can also be introduced through undercooked meats that are infected with the parasite. The parasite can live in the ground, so it can also be spread if an individual swallows the parasite by accidentally ingesting dirt while engaged in activities like gardening. The symptoms emerge as the baby shows signs of jaundice, rashes, and an enlarged liver and spleen. Toxoplasmosis has a profound effect on the baby's central nervous system.

Rubella that causes German measles is commonly associated with mental retardation in infants. The symptoms present after birth and include mental retardation, and even death in rare cases. Another virus, cytomegalovirus is common and everyone has contracted it by the time he or she reaches adulthood. Five percent of babies who contract the virus have significant developmental problems including blindness and brain damage. Herpes simplex is a sexually transmitted disease that an infant can contract from the mother during pregnancy or childbirth resulting in significant brain damage and possibly death.

Perinatal causes include prematurity complications infection, late pregnancy (complications of pregnancy, diseases in the mother such us heart and kidney disease and diabetes and placental dysfunction), during delivery (labour), severe pre-maturity, very low birth weight, birth (Kolevzon *et al.,* 2007).

Postnatal problems may occur during infancy and childhood period. It involves brain infection such as tuberculosis, Japanese encephalitis, and bacterial meningitis, as well as head injury, chronic lead exposure, severe and prolonged malnutrition and gross under stimulation (Leonard and Wen, 2002 and Zoghbi, 2003). Physical brain trauma is a possible cause of mental retardation. Physical brain trauma may be caused by abuse or by any injury to an infant or child's head. Shaken baby syndrome is a condition resulting from damage caused when a caregiver shakes an infant. In this case, the child's brain makes contact with the skull while it is shaken, resulting in bruising, nerve damage, and swelling.

On the basis of nature of factors such as environmental and genetic, causes may be categorized into two types as: (i) Environmental causes (ii) Genetic causes

(i) Environmental causes:

Environmental exposure can affect a child via pre or post-natal (before or after birth) exposure. There are numerous environmental factors that often contribute to mental retardation. Iodine deficiency affecting approximately 2 billion people worldwide is the leading preventable cause of mental disability in areas of the developing world where iodine deficiency is endemic. Lack of adequate availability of iodine from the mother restricts the growth of the brain of the foetus, and leads to a condition called hypothyroidism. More common than full fledged cretinism, as retardation caused by severe iodine deficiency called, is a mild impairment of intelligence (Gaitan and Dunn, 1992). India is the most outstanding, with 500 million suffering from iodine deficiency, 54 million from goitre, and 2 million from cretinism. Among other nations affected by iodine deficiency, China

and Kazakhstan have begun taking action, whereas Russia has not (McNeil, 2006).

Toxins such as lead and mercury affect the mental health. Mercury can be found in polluted air and water. Young children sometimes eat paint which may contain lead affecting the growth of children by damaging the brain (The Arc, 1993). Another heavy metal that affects foetal development is lead. While lead can be introduced to the foetus prior to birth through the mother's food and environmental conditions. Exposure to poisons like lead or mercury may also affect mental ability (Aicardi, 1998 and Daily *et al.,* 2000).

Exposure to certain types of disease or toxin diseases like whooping cough, measles, or meningitis can cause mental disability if medical care is delayed or inadequate. Exposure to radiation during pregnancy can also cause mental retardation. Behavioural or societal factors such as poverty, malnutrition, maternal drug and alcohol use, as well as severe stimulus deprivation can contribute to mental retardation (Mc Laren and Bryson, 1987). Smoking can also contribute to mental retardation. When a pregnant woman smokes, her fetus does not receive an adequate supply of oxygen. In addition to an inadequate oxygen supply, the fetus of a smoking woman is exposed to a number of harmful substances contained in cigarette smoke. The emotional and motivational factors, may influence the performance of individuals, and account for certain behavioural differences between those of the same mental age (Zigler and Hodapp, 1991).

The other common cause of mental retardation in industrialized nations is foetal alcohol syndrome (FAS) with an incidence rate of 1 in 100 births. Fetal alcohol syndrome (FAS) and neural tube defects are the prenatal factors which can cause mental retardation in the foetus. FAS is caused by excessive drinking by the mother during pregnancy. Neural tube defects in the foetus spine does not close normally, fluid may collect in the brain, producing a condition known as hydro-cephalus (Smith, 1993).

Sociological factors, poor diet, poor health practice and poor housing may lead to mental retardation. Children in poor families may become mentally retarded due to malnutrition, unhygienic environment, inadequate medical care and environmental health hazards (The Lancet, 2008).

Environmental mental retardation can be prevented by reducing the effects of environ-mental factors. Reducing the exposure to lead mercury and other toxins may reduce the mental retardation affected by them.

(ii) Genetic causes

Genetic studies have indicated that genes often play an important role in the development of mental disorders, via developmental pathways interacting with environmental factors. Over 350 inborn errors of metabolism have been identified, most of which lead to mental retardation (Scriver, 1995). Up to 60% of severe mental retardation can be attributed to genetic causes making it most common cause in case of severe mental retardation (Moser, 1995).

Numerical or structural chromosome abnormalities are responsible for 10-20% of the mild mental retardation (MMR) and 40% of the severe mental retardation (SMR). Children with non chromosomal defects, including central nervous system defects and all types of organ and system defects, are at substantially increased risk for all levels of mental retardation. Children with chromosomal and other structural birth defects are at a substantially increased risk for having mental retardation (MR) by 7 years of age compared with children born without a birth defect. Children with birth defects are at an especially increased risk of having severe mental retardation (Laura *et al.,* 2003).

The most common genetic disorders that have been shown to cause mental retardation are Trisomies. The common ones are trisomy 21

(Down's syndrome), trisomy 13 (Edward's Syndrome) and trisomy 18 (Patau's Syndrome). In trisomy 21, which causes Down's syndrome, the affected child inherits three chromosomes 21's, often due to non-disjunction of chromosomes during meiosis. Just like mental retardation in general, Down syndrome is associated with a broad spectrum of intellectual and adaptive functioning. Each down case is unique. Some individuals function quite well and demonstrate relatively good social skills, while others face profound challenges in social and intellectual situations. The chances of having a baby with Down syndrome do increase with the mother's age. At maternal age 20-24 the probability is one in 1562, at age 35-39 the probability is one in 214, and above age 45 the probability is one in 19 (Huether, 1998).

Sex linked chromosomal aberration are seen in Klinefelter's Syndrome (47, XXY; extra copy of the X chromosome) and Turner's syndrome (45, X0; Knox or Y chromosome). The other two mentally retarded related syndromes are Prader-Willi and Angelman's Syndrome. Both have distinct phenotypes but occur due to a deletion of the 15th Chromosome at q13 region. Prader-Willi manifests itself when the paternal copy gets deleted and Angelman's when it occurs in the maternal copy. Uniparental disomy, wherein both of the chromosomes (in this case the 15th) are inherited from one parent. In addition to the 15th Chromosome, uniparental disomy is also seen on chromosomes 4, 6, 7, 11, 14, 16 and 21. Mascari *et al.,* (1992) demonstrated uniparental disomy in 20 percent of the thirty cases of Prader-Willi Syndrome.

The most common inherited causes of mental retardation are Fragile X Syndrome (Batshaw, 1997). Fragile X is the most common genetic cause of mental retardation in males, who tend to be affected more severely than females who have the syndrome. Since females have two X chromosomes, the disorder is less pronounced in girls. So long as females have a working copy of the FRM1 gene, the abnormal copy is not expressed. Even so, Fragile X does remain a significant cause of mental retardation in females as well as males.

Fragile X syndrome involves a genetic abnormality of the FRM1 gene located on the long arm of the X (sex-determining) chromosome. Here the expansion in the number of trinucleotide repeats (CGG), beyond a certain number, causes inactivation of the gene via methylation. The resultant loss of the protein FMRP causes mental retardation. The role of FMRP likely underlies some of the behavioural and developmental symptoms of FRAXA patients (Zalfa and Bagni, 2004).

X-linked mental retardation (XLMR) is a common cause of moderate to severe intellectual disability in males. XLMR is very heterogeneous, and about two-thirds of patients have clinically indistinguishable non-syndromic (NS-XLMR) forms. X-linked mental retardation (XLMR) affects 1.8 per thousand male births and is usually categorized as "syndromic" (MRXS) or "non-specific" (MRX) forms according to the presence or absence of specific signs in addition to the MR. Up to 60 genes have been implicated in XLMR and certain mutations can alternatively lead to MRXS or MRX. Mutations in X-linked genes account for more males than females affected with mental retardation. Causative mutations have been identified in both syndromic XLMR and in the genetically heterogeneous non-syndromic forms of XLMR, without a clear clinical phenotype other than cognitive deficit. About 20 non-syndromic XLMR genes and 25 syndromic XLMR genes have been identified. Non syndromic XLMR proteins include 5 distinct classes: trans-membrane receptors, small GTPases effectors or regulators, enzymes and translational regulators (Bahi-Buisson *et al.,* 2006).

Nonspecific X linked mental retardation (MRX) is mental retardation in persons of normal physical appearance who have no recognizable features apart from a characteristic pedigree.

There is clinical variability in the degree of mental retardation within families and genetic heterogeneity, based on gene localization, between families (Kerr *et al.,* 1991). Genes causing X-linked mental retardation (XLMR) have been localized and cloned, namely 38 genes of the 136 known syndromic conditions and 19 for the non-syndromic conditions. XLMR explains the 20 % excess of males over females (Helga *et al.*, 2005).

Mutations in genes account for 50% of the families with NS-XLMR (Hans-Hilger and Ropers, 2006).

The genetic defects associated with X-linked mental retardation (XLMR) in males have revealed tens of genes important for normal brain development and cognitive functioning in men. Beside gene deletions, an increase in gene dosage due to genomic duplications seems to contribute to causality more (Bauters *et al.,* 2008).

These are some of the genetic causes which lead to mental retardation. Other genetic disorders lead to syndromes with mental retardation such as Williams syndrome, Angelman syndrome, Cockayne and Cri du Chat Syndromes and many more. Williams syndrome, is a genetic condition that is a cause of mental retardation. The cause of the disorder is a mutation of chromosome 7; a fragment of chromosome 7 is missing in the individual's genetic make-up. The mutation seems to be random rather than inherited. Williams syndrome is not nearly as common as Down syndrome. Angelman syndrome is chromosomal in nature and is associated with neurological problems. The genetic disorder involves the absence of inactivity of a certain group of genes that control ubiquitin, a protein present on chromosome 15q11-13. The abnormal chromosome are typically inherited, but some cases seem to be caused by spontaneous genetic mutation. Cockayne and Cri du Chat Syndromes. This rare genetic disorder involves defective CSA and CSB genes on chromosome 5. CSA and CSB genes or proteins that are key components used by the body for DNA repair. Cri du Chat Syndrome, like Cockayne syndrome, is caused by an irregularity on chromosome 5.

In case of genetic causes diagnosis is highly dependent on a comprehensive personal and family medical history, a complete physical examination and a careful developmental assessment of the child. Effective counseling of the affected individuals and their family members can be done. Thus better prevention, management, monitoring and indeed treatment of these disorders can be possible. These will guide appropriate evaluations and referrals to provide genetic counseling, resources for the family and early intervention programs for the child (Rutter, 2006).

Knowledge of the causes of mental retardation is fundamental to developing prevention strategies. Environmental mental retardation can be prevented by adopting some methods such as avoiding exposure to causal factors and bringing positive change in behavioural factors. Increased diagnostic capability-clinical and laboratory-must be increased if a 50% reduction in the prevalence of severe mental retardation has to be achieved in the foreseeable future.

References

Aicardi, J. 1998. The aetiology of developmental delay. *J. Semin. Pediatr. Neurol.,* 5 (1): 15 - 20.

Bahi-Buisson, N., Chelly, J. and Portes, V. 2006. Update on the genetics of X- linked mental retardation*. J. Revue neurologique.,* 162(10): 952 - 63.

Baird, P.A. and Sadovnick, A.D. 1985. Mental retardation in over half-a-million conservative live births: An epidemiological study. *American Journal of Mental Deficiency*., 89 : 323-330.

Batshaw, M.L. 1997. Children with disabilitie: A medical primer (4Ed) Baltimor: Paul, H Brookes Publishing Co.

Bauters, M., Weuts, A., Vandewalle, J ., Nevelsteen, J., Marynen, P., Van Esch, H. and Froyen, G. 2008. Detection and validation of copy number variation in X-linked mental retardation. *J. Cyto. Geno. Research.,* 123 (1-4): 44-53.

Daily, D.K., Adinger, H.H. and Holmes, G.E. 2000. Identification and evaluation of mental retardation. *Am. Fam. Physician.,* 61: 1059-1067.

Gaitan, E. and Dunn, J.T. 1992. Epidemiology of iodine deficiency. *J. Trends in endo and metabolism*., 3(5) : 170 – 175.

Grossman, H. 1983. Classification in mental retardation (3rd ed.) American Association on Mental Deficiency. Washington DC.

Hans-Hilger and Ropers. 2006. X-linked mental retardation: many genes for a complex disorder. *J. Curr. Opinion in genetics & development*., 16(3) : 260 - 9.

Helga Rehder and Barbara Fritz. 2005. Genetic causes of mental retardation. *J. Wiener Medizinische Wochenschrift.,* 155 (11-12): 258 -67.

Huether, C.A. 1998. Maternal age specific risk rate estimates for Down syndrome among live birth in Whites and other races from Ohio and metropolitan Atlanta. *J. Med. Genet*., 35: 482 - 490.

Kerr, B., Turner, G., Mulley, A., Gedeon, M and Partington. 1991. Non-specific X linked mental retardation. *J. Med. Genetics*., 28 (6): 378 - 82.

Kinsbourne, M. and Graf, W.D. 2000. Disorders of mental development, in: child neurology (Eds. J. H. Menkes and H.B. Sarnat). Lippincott Williams and wilkins. Philadelphia: pp. 1155 – 1211.

Kolevzon, A., Gross, R. and Reichenberg, A. 2007. Prenatal and Perinatal Risk Factors for Autism: A Review and Integration of Findings. *J. Arch. Pediatr. Adolesc. Med.,* 161 (4): 326-333.

Laura, L., Jelliffe, Pawlowski., Gary, M., Shaw, Verne., Nelson., John and Harris, A. 2003. Risk of mental retardation among children born with birth defects. *J. Archives of pediatrics & adolescent medicine.* 157(6): 545 - 50.

Leonard, H. and Xingyan Wen, X. 2002. The epidemiology of mental retardation: Challenges and opportunities in the new millennium. *J. Men. Retar. Devel. Disab. Res. Rev.,* 8(3): 117-134.

Mascari, M.J., Gottleib, W. and Rogan, P.K. 1992. The frequency of uniparental disomy Dopamine neurons derived from embryonic stem cells function in an animal model of Parkinson's disease. *J. Nature.,* 418 : 50-56.

Matson, J.L. and Sevin, J.A. 1994. Theories of Dual Diagnosis in Mental Retardation. *J. Cons and Clin Psychol.,* 62(1): 6-16.

McLaren, J. and Bryson, S. 1987. Review of Recent Epidemiological Studies of Mental Retardation: Prevalence, Associated Disorders, and Etiology. *Am. J. Men. Retardation.,* 92(3): 243-254.

McNeil, D.G. 2006. In Raisingthe World's I.Q., the Secret's in the Salt. New York Times.

Moser, H.G. 1995.. A role for gene therapy in mental retardation. Mental Retardation and Developmental Disabilities Research Reviews: *J. Gene Therapy*., 1 : 4 - 6.

Piecuch, R.E., Leonard, C.H., Cooper, B.A and Sehring, S.A. 1997. Outcome of extremely low birth weight infants (500 to 999 grams) over a 12-year period. *J. Pediatrics.,* 100: 633 - 39.

Rutter, L.Q. 2006. First Diagnosis of Severe Mental and Physical Disability: A Study of Doctor–Parent Communication. *J. Child Psychology & Psychiatry*., 35(7): 1273-1287.

Scriver, C.R. 1995. The metabolic and molecular bases of inherited disease Seventh edition). McGraw Hill, New York.

Smith, R. 1993. Children with mental retardation: A Parent's Guide. Bethesda, MD: Woodbine House.

Stromme, P. and Hagberg, G. 2007. A etiology in severe and mild mental retardation: a population-based study of Norwegian children. *J. Dev. Med. & Child Neurol.,* 42(2): 76-86.

The Arc. 1993. Health problems diseases like whooping cough, measles. *J. Psychol. Med*., 29 (40): 769 - 89.

The Lancet. 2008. Iodine deficiency-way to go yet. 372 : 88.

World Health Organization (WHO) 1989. World Health Organization Training in the community for people with disabilities. Geneva.

Zalfa, F. and Bagni, C. 2004. Molecular insights into mental retardation: multiple functions for the Fragile X mental retardation protein? *Curr. Issues Mol. Biol*., 6(2): 73-88.

Zigler, E. and Hodapp, R. 1991. Behavioral functioning in individuals with mental retardation. *J. Ann. Rev. Psychol*., 42:29-50

Zoghbi. 2003. Postnatal Neurodevelopment Disorders: Meeting at the Synapse? *J. Science*., 302: 826 - 830.

****