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REVIEW ARTICLE

Autism Spectrum Disorder: Lost In Space

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ABSTRACT

Pervasive developmental disorders (PDD) is a developmental neurological disorders. PDD consist of Autism, Asperger syndrome, Pervasive developmental disorder not otherwise specified Rett's disorder and childhood disintegrative disorder. The incidence of the disease has been increased in past one decade when compared to earlier, which is due to increased awareness of the disease. The diagnosis of the PDD mainly by diagnostic and statistical manual of mental disorder(DSM) published by American psychiatric association. DSM V the pervasive development disorders were considered into single autism like spectrum of disorders. Autism spectrum disorder is not completely curable and hence requires lifelong management. Educational and behavioral interventions are more successful when compared to medications alone. Early interventions have more positive results. The present review articles describes regarding the Pervasive developmental disorders, prevalence of autism worldwide, individual countries ,their characteristic features, diagnosis by DSM IV and DSM V, causative factors involved and management.
Keywords*: Pervasive developmental disorder, Autistic spectrum of disorder, Autism, Rett's disorder, Child hood disintegrative disorder.*

INTRODUCTION

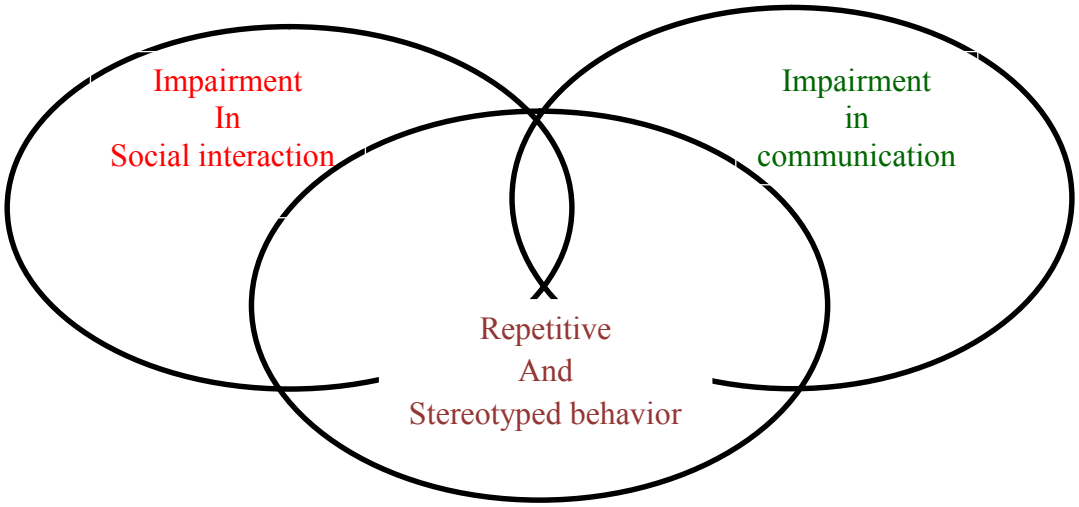
Autism is one among the five neurological disorders, considered under pervasive developmental disorders (PDD).[1]PDD are developmental disorders of brain in which the individual suffer from severe and pervasive impairment in thinking, feeling, language and ability to relate to others.[2] The other four disorders considered under PDD are Asperger's syndrome, Pervasive developmental disorder not otherwise specified (PDD NOS), Rett's disorder and childhood disintegrative disorder.[3] Autism is characterized by impairment in social interaction, communication and stereotyped repetitive behavior. Individuals with autism have very low IQ. Asperger's syndrome is similar to autism in which the individual have average or above average IQ.Pervasive developmental disorder not otherwise specified, also been described as atypical autism is one in which only few autistic behaviors are present, but sufficient criteria's not present to be diagnosed as autism. There are no biological markers for the diagnosis of the pervasive developmental disorders except for Rett's disorder which is characterized by mutations of the methyl-CpG-binding protein 2 (MeCP2) gene. Childhood disintegrative disorder is very rare in which child develops the features of autism after 3-4 years, initially being normal before.[4]

The term Autism was originally used by Bleuler in 1911 to describe "withdrawal from the social relations into a rich family type seen in individuals with schizophrenia"[5]. Autism word is been derived from Greek word '*autos*' (self) and 'ismos' (condition). Leo Kanner in 1943 for the first time described autism disorder among 11 cases and defined it "as enclosure in one's self".[5]

Approximately 67 million people are affected at present by autism around the world. The prevalence of Autistic Disorder among children worldwide at present is 12 per 1,000 . In the USA,1 in 110 children are diagnosed with autism. The prevalence of autism in other countries like in Australia 6.25 in 1000 ,China 1.1 in 1000 , Denmark 9 in 1000 ,India 1 in 250 ,Japan 3 in 1000 , Mexico 2 to 6 per 1000 ,Canada 1 in 154 ; Sweden 1 in 188 ,Finland 1 in 833 , Denmark 1 in 833 , Iceland 1 in 769 , Philippines 500,000 children and in Thailand 180,000 children. There has been increase in the autism cases from the last decade which is due to increase awareness about the disease rather than actual cause.[6]

Autism also termed as childhood autism or classical autism, is diagnosed by the behavioral abnormalities in child before the age of three years or it can be diagnosed more early at the age of 18 months.[7]The male

children are affectedmore when compared to female in a ratio of 3-4:1. Autism is mainly characterized by impairment of social interaction, communication and repetitive stereotyped behavior. The impairment of social interaction includes aloofness, inability to make friends, seeking others company but decreased ability in maintaining mutual interaction, social passiveness, indifferent eye movements, inability to understand social rules, making embracing comments unintentionally, impaired use of nonverbal behaviors to regulate social interaction, lack of spontaneously sharing enjoyment with others. Impairment in communication implies delay in or lack of development of the language without any compensatory forms of communication, difficulty in initiating or maintaining conversation and stereotyped or idiosyncratic use of language. The repetitive activities includesthe interest that are extremely narrow, which are unusual and intense. They are usually adherent to routine activities and intolerance to change stereotyped repetitive motor activities like hand flapping and persistent pre occupation with objects. Autism is also accompanied by other common features such as decreased intellectual ability, epilepsy, unusual sensory responses to particular sound or tactile sensations, angry outbursts, anxiety and self-injurious behavior.[8]



Pervasive developmental disorder: DSM IV

There exist no biological markers for the diagnosis of the autism. The diagnosis is mainly by the behavioral characteristics.Diagnostics and statistical manual of mental disorders (DSM) published by American psychiatric association is used for diagnosis. Infantile autism was first included in DSM III. Later DSM III was updated to DSM IV in 1994 and revised in 2000.According to DSM IV for diagnosing a case as at least 6 criteria's had to be fulfilled with a minimum of two in 1st and minimum of one in 2nd and 3rd.[9]

1) DSM Criteria for an Autism Diagnosis: Impairment in social Interaction
   Must meet 2 of the following:
   a. Marked impairment in multiple nonverbal behaviors (e.g., eye contact, facial expressions)
   b. Failure to develop peer relationships for age
   c. Lack of spontaneous seeking to share enjoyment, interests or achievement with others
   d. Lack of social or emotional reciprocity
2) DSM Criteria for an Autism Diagnosis:Impairmentin Communication
   Must meet 1 of the following:
   a. Delay in, or total lack of, the development of spoken language (not accompanied by an attempt to compensate through alternative modes of communication)
   b. Marked impairment in ability to initiate or sustain conversation with others
   c. Stereotyped and repetitive use of language
   d. Lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level
3) DSM Criteria for an Autism Diagnosis: Restricted Repetitive and Stereotyped Patterns of Behavior, Interests, and Activities

Must meet 1 of the following:

   a. Encompassing preoccupation with one or more stereotyped and restricted patterns of interest that's abnormal in intensity or focus

b. Inflexible adherence to specific, non-functional routines or rituals
c. Stereotyped and repetitive motor mannerisms (e.g., hand flapping, rocking)

Persistent preoccupation with parts of objects

The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) was published by the American Psychiatric Association (APA) in May 2013. The new edition introduced major revisions to the diagnostic criteria for autism spectrum disorder (ASD).[10]

With regard to the diagnosis of pervasive developmental disorders DSM-5 has introduced several major changes, which include

(1) Converging the diagnostic groups previously considered under the category of PDDs into a single diagnosis of ASD

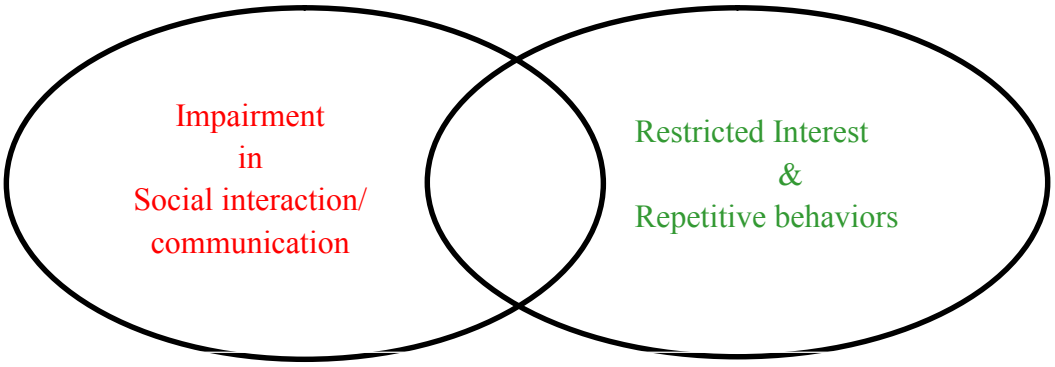
(2) Merging the social and communication impairment symptom domains required for the diagnosis of autism into a single domain, thus reducing the symptom domains involved in diagnosis from 3 to 2

(3) Expanding the "restricted, repetitive behaviors" symptom domain to include abnormalities in sensory processing;

(4) Relaxing the age at onset criterion.[11]

The main concept of the DSM V was the merging of three domain in DSM IV that is1) impairment in social interaction, 2) impairment in communication and 3)restricted and repetitive patterns of interests and activities to two main domain that is

1) Social communication deficits and 2) Restricted interests and repetitive behaviors



Autism Spectrum disorder: DSM V

The shift from 3 to 2 symptom domains in the definition of ASD was proposed because, deficits in communication and social behaviors were considered inseparable and more accurately considered as a single set of symptoms with contextual and environmental specificities. The category of restrictive, repetitive behaviors has been expanded to include sensory symptoms, which have long been observed in individuals with autism, but were not part of the diagnostic criteria under DSM-IV. This new criterion describes hypersensitivity or hyposensitivity to sensory input or an unusual interest in sensory cues.Sensory signals don't get organized into appropriate responses, which is a functional disorder than a structural disorder. Due to the sensory abnormality the child with autism feels like, "lost in space". According to DSM V, 2 or more restrictive, repetitive behavior symptoms must be present, instead of a single symptom as required under the DSM-IV definition. Under the new DSM-5 definition, the age at onset criterion for the diagnosis of ASD has been relaxed to state that symptoms must be present in early childhood not compulsory to be under 3 years of age.

The individual's current level of symptom severity also forms part of the diagnosis, and the new criteria bring a recognition that this can change over time, or in different contexts. These are:[12]

Level 3: Requiring very substantial support

Social communication:

- Severe deficits in verbal and nonverbal social communication skill
- Severe impairment in functioning
- Very limited initiation of social interaction
- Minimal response to social overtures from others.

Restricted Interest And Repetitive Behavior:

- Preoccupation
- Fixated rituals or repetitive behavior markedly interfering in functioning

- Marked distress when rituals or routines are disrupted.
- Very difficult to redirect from fixated interests and returns to it quickly.

LEVEL 2: Requiring substantial support

Social communication:

- Marked deficits in verbal and nonverbal social communication skill
- Social impairment apparent in place even with support
- Limited initiation of social interaction
- Reduced or abnormal response to social overtures from others.

Restricted Interest And Repetitive Behavior:

- Preoccupation or fixated interests appear frequently enough to be obvious to the casual observer
- Interferes functioning in a variety of context
- Distress and frustration are apparent when interrupted
- Difficult to redirect from fixated interest.

LEVEL 1: Requiring support

Social communication:

- Without supports in place, deficits in social communication cause noticeable impairment.
- Has difficulty in initiating social interaction
- Demonstrates clear example of atypical or unsuccessful response to social overtures of others.
- May appear to have decreased interest in social interaction

Restricted Interest And Repetitive Behavior:

- Rituals and repetitive behaviors causes significant interference with function
- Resist attempt by other to interrupt rituals and repetitive behavior
- Resist attempt to be redirected from fixated interest.

Causative Factors:

As there is no singleperfect cause for the autism.Many postulates have been putforthwhich may describe the development of the autism. They include genetic causes, environmental risk factors, physiological abnormalities, physical abnormalities, and psychological abnormalities.

Genetic Factors:

There are many evidences to prove the involvement of genetic component in the development of autism. Twin and family studies have shown that the autism is heritabledisorder. The mechanism is complex and involves the interaction between many genes. At present the complex genetic influences are taught to have higher influence in development of autism when compared single gene disorders or chromosomal abnormality, which accounts only for the 5-10%.

In monozygotic twins probability of the both children developingASD is 60% ; probability is very less if the twins are dizygotic. The rate of incidence of ASD in singleton siblings is 2-6% which is high when compared to the general population. Several genes may interact together to produce susceptibility for the ASD. These genes aremost commonly found on chromosomes 2, 7, 16 and 17. The genetic findings do not rule out the possibility that some form of gene environment interactioninvolvement is necessary in pathogenesis. Single gene disorders orchromosomal abnormalities areseen in 10% of individuals with ASDs. These include untreated phenylketonuria, tuberoussclerosis, fragile X syndrome (FRAXA), Turner's syndrome, duplication and inverted duplication of chromosome 15q11-q15.[13]

Environmental factors:

A variety of environmental factors have been implicated in the development of the autism in the children. The environmental factors may act at various stages such as prenatal period, perinatal period of the infant or childhood period.

Maternal viral infection in the first trimester and bacterial infection in the second trimester are associated with development of autism in the offspringlater. Rubellainfection in first 8 weeks after conception results in development of autism in the child after birth. Maternal immune activation due to prenatal viral exposure lead to an increase in maternal IL-6 levels and alteredgene expression, which potentially could precipitate autistic behavior and neuropathology in the offspring.[14] The use of thalidomide by the mother leads to the development of autism in the offspring. Misoprostol, a prostaglandin analogue used for prevention of gastric ulcers and in some countries as an abortifacient, is associated with development of autism following unsuccessful abortion attempts. Similarly prenatal exposure to valproic acid, ananti-convulsant also results in autism. Acetaminophen in overdose has also been suggested to cause autism.[15] Increased frequencyin males than in females raises the possibility of a role for sex hormones in the development or expression of autistic traits. Estrogens and progesterone have neuroprotective functions

by reducing the consequences of brain injury.[16]The environmental and genetic damage caused to the brain may be ameliorated by these hormones in case of females but not in males. Thus females are expected to show fewer sequel of neural damage than males. Anatomical, functional and psychomotor disturbances have been seen in the offspring of mothers who have experienced carbon monoxide (CO) poisoning. The fetus is highly sensitive to any decrease in oxygen carrying capacity and often dies even when the mother survives CO intoxication with no adverse effects herself. If the fetus survives the chronic CO exposure, then later after birth may develop autism.[17]

In childhood bacterial, parasitic or viral infection in the CNS are associated with development ASD symptoms. Cytomegalovirus infection ,congenital rubella virus infection and herpes simplex virus encephalitis are the most common viral infections which may cause development into autism.It has been hypothesized that ASDs may be causally related to the existence of persistent infection. Many viruses, such as herpes simplex, varicella zoster, and Epstein-Barr virus, persist in the human body throughout life.These viruses are all large DNA viruses, with a very stable genome that is able to be maintained or be latent in the cells that harbor them, which allows their presence not to be detected by the host immune system.At present there is no complete evidence that such persistent infections are causally related to autism.[18] The potential risk between MMR vaccination and development of ASD has been questioned by number of experts. The aforementioned reviews were unanimous in their conclusions that a causal link between the MMR vaccine and "autistic colitis" and ASDs was not proven and that current epidemiological evidence did not support this proposed link. More extensive research would be necessary to provide evidence for the biological possibility of a suggested causal link between viral infections and ASDs.[19]Exposure to mercury during the critical periods of early development can lead to a variety of developmental problems affecting motor skills such as walking and speech. It has been suggested that some of the sensory, neurological, motor, behavioral and other dysfunctions associated with mercury intoxication are similar to traits associated with ASDs.Methyl mercury is the form most commonly associated with risk of developmental effects. In serious cases of methylmercury exposure of the developing fetuses, the effects can be delayed, including retardation ofdevelopmental milestones such as walking and talking and more severe effects such as brain damage with mental retardation, incoordination and inability to move. Early exposure to thiomersal,a preservative containing approximately 49% ethylmercurybeen used successfully as a preservative in vaccines, may be implicated as a risk factor for ASDs. Children with behavioral and/or developmental problems have higher blood lead levels.[20]

Physiological Abnormalities:

The Gastro-Intestinalsystem has considerable involvement in the development of ASD. It has been postulated that altered intestinal permeability canresult in adverse events occurring in the central nervous system, which might result indevelopmental regression. It remains unclear whether such compromised gastrointestinalfunction is a cause of ASD, or it reflects one facet of the disorder in a subpopulationof affected individuals.At present there are no epidemiological data toindicate the incidence or prevalence of gastrointestinal problems within the population of individualswith ASDs.[21]

The nutrient intake of children with ASDs as a group has been found to be adequate and typicalof well-fed American children; these children showed no evidence to toxicity or deficiencies in the minerals or nutrients. There are many case reports of clinical improvement in children with ASDs placed on gluten and/or casein free diets.Theseinvestigations are based upon studies reporting that during proteolysis of casein in the gastrointestinal tract

β-casomorphines were created, and they were biologically active with both endorphin effects and immune regulatory properties. Similarlygluteomorphins were also produced from wheat proteins. Although it is possible to provide a biological hypothesis to explain the possible beneficial effects of gluten and casein free diets in ASDs, thereno properly controlled studies described in peer-reviewed journals.Abnormalities in the composition of the enteric flora have been suggested to occur in ASDs,and antibiotic and antifungal therapies have been used – although usually in commercial, nonacademic, centers. Such suggestions of enteric dysbiosiswere initially based on reports of the onset of ASDs after antibiotic treatment for otitis media.A leading proponent of the theory that bacterial and fungal overgrowth contributes to autism spectrum disorder been reports of production of various gliotoxins by Candida albicans. One bacterial species which has been suggested as pathogenic in ASDs is Clostridium tetani, with cognitive abnormalities proposed to be induced by the action of clostridial neurotoxins absorbed from the intestine.[22]

Heavy metals are increased in the blood and urine of autistic subjects .Study conducted on blood and urine from 503 patients with autism, Asperger's syndrome, or atypical autism, and compared their results to samples from neurotypical controls. The analyses revealed that 85% of the patients exhibited severely

elevated Cu:Zn ratios and 99% showed evidence of a metal- metabolism disorder, suggesting defective metallothionein. Defective metallothionein might be responsible for the greater amount of blood mercury found in autistic children compared to neurotypical controls. Metallothionein plays an important role in the development and continued function of the immune response, in neuronal development, and in the detoxification of heavy metals.Many classic symptoms of autism may be explained by a metallothionein defect, including gastrointestinal tract problems, heightened sensitivity to toxic metals, and abnormal behaviors. Porphyrinuria in children with autism is considered a marker of heavy metal toxicity.Individuals with severe autism had increased mercury-intoxication-associated urinary porphyrins.[23]

Physical Abnormalities:

There are no known physical markers of ASDs. ASDs can co-occur with other conditions.Research on brainabnormalities has been hampered by the small number of brain samples available for study.Each has reported some specific findings not yet replicated elsewhere. Brain weight is increased in an as yet uncertain proportion of individuals with ASDs; decreased Purkinje cell number is seen in the majority of cases; developmental abnormalities of the inferior olive are a common observation. Similarly head circumference is increased in a proportion ofindividuals .There is some preliminary evidence for a disproportion in the grey matter to white matter ratio and also some suggestion of regional variability in increased brain volume .There is some debate as to the mechanisms underlying these increases in brain weight and volume.Thus it is unclear whether the underlying abnormality is overproduction of cells, which subsequently do not undergo selective cell death, or whether the primary problem is a failure of synaptic pruning.[24]

Functional abnormalities:

Studies have shown relatively low activity in the cerebral cortex, but there is littleagreement as to which areas of the brain are specifically affected. A common finding, though one not specific to ASDs, is reduced activation of the frontal lobes – thought to be crucial areas for the control of complex behavior.There may also be abnormalities in the limbic system, involved in processing of socio-emotional information.Taken together with the EEG findings and the association with epilepsy, it appears that ASD is associated with abnormal cortical organization, although the extent to which this a localized versus generalized phenomena is currently unclear. Many claims of abnormalities in neurotransmitter systems have either not replicated or are internally inconsistent.[25]An elevation in blood serotonin is a relatively consistent finding in the field andappears to reflect increased storage in platelets rather than abnormal synthesis. Some studies havealso observed hyperserotonaemia in relatives. Claims of an association between ASDs and a particular variant of the serotonin transporter gene have so far not been replicated and there is no association between serotonin levels and behavior in individuals with ASDs. Metabolites of serotonin in the CSF are unremarkable and neither genetic nor post-mortem studies have found evidence of receptor abnormalities.A recent positron emission tomography (PET) imaging studyhas demonstrated that the normal pattern of high brain serotonin synthesis capacity in childhood may be disrupted in ASDs, but it is unclear whether this finding is connected to unusual levels of platelet serotonin or is secondary to abnormal brain development.[26]Results of studies of the dopaminergic and noradrenaline systems are contradictory. There is no evidence of a consistent elevation of dopamine or its metabolites in plasma or urine, nor of noradrenaline, although it has been suggested that the sympathetic nervous system might be hyper-responsive to stress.There are very recent studies of the cholinergic and GABAergic. Systems in small numbers of individuals with ASDs, but the reported abnormalities must be considered preliminary. Studies of plasma opioids have produced inconsistent findings and there is just one report of extremely abnormal endorphin fragments in ASDs. Although naltrexone appears to have some effect in reducing hyperactivity, it has no clear effect upon core autistic symptoms. In summary, further investigation of the relationship between brain serotonin synthesis and other indices of serotonergic function appears warranted.There is also scope for further postmortem work examining the rote of the GABAergic andglutaminergic systems, as both neurotransmitters have been implicated in the pathogenesis of epilepsy. Future studies will need to utilize IQ matched controls to determine which abnormalities are specific to ASDs as well as genetically sensitive designs.The possibility that genes may act through effects on the intrauterine environment also merits further investigation.[27]

Management:

ASD are neurodevelopmental disorders. They do not have complete cure and hence they require chronic lifelong treatment.Interventions to be targeted towards core features of ASDs such asimpairment in social reciprocity, deficits in communication, and restricted, repetitive behavior.Minimizingthe core features,

associated deficits, maximizing functional independence and quality of life, alleviating family distress, facilitating development and learning, promoting socialization, reducing maladaptive behaviors are the primary goals of treatment. The interventionsin the management of autism are mainly educational and medical.[28]

Educational Intervention:

Education interventions are the corner stone of the management of the ASDs. These interventions are directed most commonly towards communication, social skills, day to day activities, academics and maladaptive behavior.

1) Applied Behavior Analysis: Applied behavior analysis (ABA) is the process of applying interventions that are based on the principles of learning derived from experimental psychology research to systematically change behavior and to demonstrate that the interventions used are responsible for the observable improvement in behavior. ABA focuses on the reliable measurement and objective evaluation of observable behavior within relevant settings including the home, school, and community. ABA methods are used to increase and maintain desirable adaptive behaviors, reduce interfering maladaptive behaviors, narrow the conditions under which they occur, teach new skills, and generalize behaviors to new environments and situations.

Children who receive early intensivebehavioral treatment have been shown to make substantial, sustained gains in IQ, language, academic performance, and adaptive behavior as well as somemeasures of social behavior.[29]

2) Structured Teaching:

Important elements ofstructured teaching include organization of the physical environment, predictable sequence of activities, visual schedules, routines with flexibility, structured work,activitysystems, and visually structured activities. There is an emphasis on both improving skills of individuals with ASDs and modifying the environment to accommodatetheir deficits.[30]

3) Developmental Models:

Developmental models are based on use of developmental theory to organize hypotheses regarding the fundamental nature of ASDs and design approaches to address the deficits. It is basedlargely on remediating key deficits in imitation, emotion sharing, theory of mind, and social perception by using play, interpersonal relationships, and activities to foster symbolic thought and teach the power of communication.[31]

4) Speech and Language Therapy:

Children with ASDs have deficits in social communication and treatment by a speech-language pathologist usually is appropriate. Most children with ASDs can develop useful speech.Chronologic age, lack of typical prerequisite skills, failure to benefit from previous language intervention, and lack of discrepancy between language and IQ scores should not exclude a child fromreceiving speech-language services. Speech-language pathologists are likely to be most effective when they train and work in close collaboration with teachers, support personnel, families and the child's peers to promote functional communication in natural settings throughout the day. Use of augmentative and alternative communication modalities, including gestures, sign language, and picture communication programs, often is effective in enhancing communication.[32]

5) Occupational Therapy and Sensory Integration Therapy:

Traditional occupational therapy often is provided topromote development of self-care skills like dressing,manipulating fasteners, using utensils, personal hygiene and academic skills like cutting with scissors, writing. Occupational therapists also may assist in promoting development of play skills, modifying classroom materials and routines to improve attention and organization,and providing prevocational training. Sensory integration (SI) therapy often is used alone or as part of a broader program of occupational therapy for children with ASDs. The goal of SI therapy is not to teach specific skills or behaviors but to remediate deficits in neurologic processing and integration of sensory information to allow the child to interact with the environment in a more adaptive fashion.[33]

MEDICATIONS:

The underlying neurological problem associated with autism is not cured by the medications. Medications are given to manage the behavioral manifestations of the disorder such as hyper activity, impulsivity, attention difficulties and in few cases anxiety. Medications help by decreasing the above symptoms and thereby help in obtaining maximum benefits from the educational and behavioral interventions.

1) Antipsychotics:

These are the drugs most commonly used in autism patients. This drug reduces hyper activity, repetitive behavior and aggression in some autism patients. The newer antipsychotic drugs such as olanzapine, respiridone and quitipine are most commonly used.

2) Antidepressants:

Selective serotonin reuptake inhibitor are found to be effective against depression, obsessive compulsive disorder,anxiety, repetitive behaviors, irritability, tantrums and aggression in the autism patients. The most commonly used SSRIs are fluoxetine, fluoaxamine, sertraline, paroxetine.

3) Stimulants:The drugs used in the treatment of the attention deficit hyperactive disorder may find useful in some autism patients by increasing the person's ability to concentrate, pay attention, reducing impulsivity and hyperactivity. Drugs most commonly used are methylphenidate and amphetamines.

4) Dietary Interventions:

Dietary interventions are of the principle that the food allergies or deficiency in certain vitamins and minerals may be the cause for the autism symptoms.Diets being gluten free and casein free have been helpful in some autism patients.Vitamin b6 supplementation with magnesium is also found helpful in some .

5) Others:

Other many drugs may also help the autistic patients .Anticonvulsants are helpful managing seizures ,Alpha 2 adrenergic agonist are helpful in managing hyper activity and behavioral problems in some autism patients. Buspirone and propranolol have also been found useful.

CONCLUSION

Autism being one of the pervasive developmental disorders according to DSM IV later grouped under autistic spectrum of disordered under DSM V is a developmental neurological disorder. The components in the DSM IV is been grouped to two components mainlyImpairment inSocial interaction/ communication and Restricted Interest and repetitive behaviors. The incidence has been increased in the recent years most commonly due to increased awareness of the disease. The management is mainly by educational, behavioral intervention and to a lesser extent by medication .Early diagnosis and intervention helps in improving the condition of the patient by reducing the behavioral symptoms.Hence more awareness and education has to be provided for both the medical practitioners and the general public regarding the early diagnosis of the condition.

REFERENCES

1. Klin A, Lang J, Cicchetti DV. J Autism DevDisord. 2000; 30(2):163–67.
2. Chakrabarti S, Fombonne E. Pervasive developmental disorders in preschool children. JAMA.2001;285: 3093-99.
3. Rossignol D A. Novel and emerging treatments for autism spectrum disorders: A systematic review. Annals of Clinica l Psychiatry 2009;21(4):213-36.
4. Rice C. Prevalence of autism spectrum disorders—autism and developmental disabilities monitoring network,14 sites, United States, 2002. MMWR. 2007;56 :12-28.
5. Nylander N, LugnegardT,Haller Back MU. Autism spectrum disorders and schizophrenia disorders in adults. Clinical neuropsychiatry.2008;5(1):43-5
6. Fombonne, E. Epidemiological surveys of autism and other pervasive developmental disorders : an update. Journal of Autism and Developmental Disorders.2003; 33(4): 365-82
7. Baird G, Charman T, Baron-Cohen S, et al. A screening instrument for autism at 18 months of age: a 6-year follow-up study. J Am Acad Child Adolesc Psychiatry. 2000;39:694-702.
8. Kanner L. Autistic disturbances of affective contact. Nervous Child 1943;2: 217–50.
9. American Psychiatric Association. Diagnostic andstatistic manual of mental disorders (DSM-IV-TR). 4th ed [Test revision]. Washington DC: AmericanPsychiatric Association.
10. Hazen E P, McDougle C J, Volkmar F R.Changes in the Diagnostic Criteria for Autism in DSM-5: Controversies and Concerns.J Clinical Psychiatry 2013, July, 74(7): 739.
11. McPartland JC, Reichow B, Volkmar F R.Sensitivity and specificity of proposed DSM-5 diagnostic criteria for Autism Spectrum Disorder. Journal of the American Academy of Child & Adolescent Psychiatry.2012;51, 368-83.
12. Amaze.Information Sheet:Changes to the Diagnostic Criteria for Autism Spectrum Disorder.2013:1-3
13. Muhle R; Stephanie V. Trentacoste BA, Isabelle Rapin. PEDIATRICS. 2004;113 (5):472-86.
14. Chess S. Follow-up report on autism in congenital rubella. J. AutismChild.Schizophr. . 1977; 7:69–81.
15. Helen V. Ratajczak. Theoretical aspects of autism: Causes—A review. Journal of Immunotoxicology, 2011; 8(1): 68–79
16. Cohen BS,Hammer J.. Is autism an extreme form of the "malebrain"? Adv. Infancy Res. 1997;11:193–217.
17. Geier D A , Kern J K , Garver C R, Adams J B, Audhya T, Nataf R, and Geier M R. Biomarkers of environmental toxicity and susceptibility in autism. J. Neurol. Sci. 2009; 280:101–108.
18. Singh V K, Lin S X, Yang V C. Serological association of measlesvirus and human herpesvirus-6 with brain autoantibodies in autism. Clin.Immunol.Immunopathol.1998; 89:105–108.

19. DeStefano F. Vaccines and autism: evidence does not support a causal association. Clin.Pharmacol.Ther. 2007;82:756–759.
20. Desoto M C, HitlanR. T. Blood levels of mercury are related to diagnosis of autism: a reanalysis of an important data set. J. Child Neurol .2007 22:1308–1311.
21. Jyonouchi H, Geng L, Ruby A, et al. Evaluation of an association between gastrointestinal symptoms and cytokine production against common dietary proteins in children with autism spectrum disorders. J Pediatr. 2005;146:605-610.
22. Geier D A., and Geier M. R. A clinical and laboratory evaluation of methionine cycle-transsulfuration and androgen pathway markers in children with autistic disorders.Horm. Res. 2006;66:182–188.
23. London E A. The environment as an etiologic factor in autism: a new direction for research. Environ. Health Perspect.2000;108 (3):401–404.
24. Aylward E H , Minshew N J, Field K , Sparks B. F , and Singh N. Effects of age on brain volume and head circumference in autism. Neurology.2002; 59:175–183.
25. Bauman M L, Kemper T. L.Neuro-anatomic observations of the brain in autism. In: *The Neurobiology of Autism*, Baltimore: Johns Hopkins University Press. 1994;119–145.
26. Chugani D C, Muzik O, Behen M, Rothermel R, Janisse J. J, Lee J, Chugani H T.Developmental changes in brain serotonin synthesis capacity in autistic and nonautistic children. Ann. Neurol.1999; 45:287–295.
27. Ornitz EM. The functional neuroanatomy of infantile autism.Int. J. Neurosci.1983. 19:85–124.
28. Levy SE, Hyman SL. Novel treatments for autistic spectrum disorders. Ment Retard DevDisabil Res Rev. 2005;11:131-142.
29. Charlop M. H ,Schreibman L, Thibodeau, M. G. Increasing spontaneous verbal responding in autistic children using a time delay procedure. Journal of Applied Behavior Analysis.1985;18(2), 155–166.
30. Dawson G ,Osterling, J. Early intervention in autism. In M. J. Guralnick (Ed.), The effectiveness of early intervention .1997:307–26.
31. Krantz P J. Zalewski S, Hall L, Fenski E, McClannahan L E. Teaching complex language to autistic children. Analysis & Intervention in Developmental Disabilities.1981; 1(3) : 259–297.
32. Marcus L M, LansingM, Andrews C E, Schopler E. Improvement of teaching effectiveness in parents of autistic children. Journal of the American Academy of Child Psychiatry.1978;17(4): 625–639.
33. Schopler E, Mesibov G, Baker A. Evaluation of treatment for autistic children and their parents. Journal of the American Academy of Child Psychiatry.1982;21(3), 262–67.
34. AkankshaM,SahilK,PremjeetS,BhawnaK.Autism spectrum disorders. IJRAP.2011 ;2(5): 1541-56.

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