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# Functional Aspects of Autism Spectrum Disorder Review

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**Abstract** **Review Article**

A budding body of research has investigated the functional development of brain in Autism Spectrum Disorder (ASD).Brain progress trajectories are different in autism spectrum disorder .Autism spectrum disorder (ASD) is a set of neurodevelopmental disorders characterized by a deficit in social behaviors and nonverbal interactions such as reduced eye contact, facial expression, and body gestures in the first three years of life. It is not a single disorder, and it is broadly considered to be a multi-factorial disorder resulting from genetic and non-genetic risk factors and their interaction. Genetic studies of ASD have identified mutations that interfere with typical neurodevelopment in utero through childhood. These complexes of genes have been involved in synaptogenesis and axon motility. Recent developments in neuroimaging studies have provided many important insights into the pathological changes that occur in the brain of patients with ASD in vivo. Especially, the role of amygdala, a major component of the limbic system and the affective loop of the cortico-striato-thalamo-cortical circuit, in cognition and ASD has been proved in numerous neuropathological and neuroimaging studies. Besides the amygdala, the nucleus accumbent is also considered as the key structure which is related with the social reward response in ASD. Although educational and behavioral treatments have been the mainstay of the management of ASD, pharmacological and interventional treatments have also shown some benefit in subjects with ASD. Also, there have been reports about few patients who experienced improvement after deep brain stimulation, one of the interventional treatments. The key architecture of ASD development which could be a target for treatment is still an uncharted territory. Further work is needed to broaden the horizons on the understanding of ASD.

**Keywords:** Autistic Disorders, Review, Neurobiology, Amygdala.



## INTRODUCTION

Autism spectrum disorder (ASD) is a developmental disorder categorized by deficits in social communication and repetitive and stereotyped interests and behaviors [1]. Autism is among the most enigmatic disorders of child development, with a dramatic increase in prevalence from 1 in 500(0.20%) and incidence rate is approximately 1 in90,666 in 2018(according to Rehabilitation council of India) [2]. While the global burden of ASD is currently unknown, in the United States, the annual societal cost of the condition was recently predicted to be $126 billion and $34 billion in the UK [3].

Currently, one of the most burdensome complaints among parents of children with autism is disrupted sleep, with more than 40–80% of children experiencing sleep problems, compared with 25–40% in typically developing children (TYP) [4,5].

The neuropathological basis of autism has not been determined, and much of the work has focused on autism is due to dysfunction of mesolimbic (dopaminergic) brain areas (ventromedial prefrontal cortex, medial temporal lobe, striatum and limbic thalamus) because damage to these brain regions can cause features of autism (impaired social and emotional functioning, stereotyped behaviors, mannerisms and obsessionist) .This hypothesis is supported by studies which have reported that (i) in animals, social deficits and stereotypical behavior are associated with damage to the medial temporal lobe in infancy[7] (ii) in humans, autistic-type patterns of behavior are associated with abnormalities in the temporal lobe caused by other neurodevelopmental disorders (e.g. tuberous sclerosis) [8]and (iii) individuals with autism are impaired on `frontal' executive tasks [9].Non-limbic areas such as the parietal lobe have also been suggested as important in etiology because the inattention of children with autism to salient social cues resembles inattention and neglect following parietal lobe damage [10]. Some

children with autism are also impaired on neurological tests sensitive to parietal dysfunction [11]. Other investigators have proposed that developmental abnormalities of the cerebellum [12] or dysfunction of cerebellar–cortical serotonergic pathways are patho-aetiological factors for autism [13]. Consistent with this, acquired cerebellar lesions have been associated with deficits in social and emotional behavior, executive dysfunction and obsessionality [14].

Reviews of the literature on social deficits in autism have appeared recently [15], so the relevant studies are only summarized here. A study of Social Behavior is the earliest descriptions of the social impairment in autism [16, 17]. These take the form of clinical impressions. These include lack of "apparent affection" ,withdrawal from people , lack of attention to people ,noncommunicative use of language ,lack of communicative gestures ,treating parts of people as detached Objects, lack of eye contact ,treating people as inanimate objects ,lack of behavior appropriate to cultural norms ,attention to the nonsocial aspects of people ,lack of awareness of the feelings of to others ,and lack of savories-faire [18]. This escalation and economic problem identify individuals with ASD as one of the highest priority populations for clinical research and treatment development.

The following are the list of some conducts found in autism children:

- They prefer to be alone.
- They never respond to their name and seems like deaf.
- Never show eye contact.
- Difficult in mingling with same age children.
- They do not point to ask for something.
- They never try to attract others by their activity.
- They never imitate adults ‘action
- Rarely or never use gestures.
- Extreme fear
- They enjoy flapping, spinning, rotating objects
- Show extreme distress in others

Behavioral studies have shown that typically developing (TD) children inherently value and pursue social stimuli such as a hug or smile from a parent [19]. In contrast, individuals diagnosed with autism spectrum disorders (ASD) appear indifferent to faces and social interactions [20].Clinical observations and previous studies suggest the hypothesis that early developmental dysfunction of brain pathways linking social stimuli and reward [21] lead to autistic individuals’ deficits in social and emotional reciprocity [22].

Dopaminergic projections from the ventral tegmental area (VTA) to cortico limbic regions are important in mediating the effects of reward on behavior [23], and neuroimaging studies have shown that neural activity in regions of the brain where dopaminergic neurons project, including the ventral medial prefrontal cortex, ventral striatum, posterior cingulate and precuneus, are modulated by eye contact, a social reward signal [24]. Dysfunctions in this pathway that may contribute to the lack of social motivation in ASD have also been previously explored using behavioral [25], event-related potential (ERP), event-related potential (ERP) [26] and structural imaging studies [27].

Our brain is endowed with the ability to detect and respond to simple social signals such as eye contact, as well as to infer from more complex behaviors intrinsically social qualities of other people such as fairness or cooperation. Individuals suffering from high-functioning autism spectrum disorders (HFASD), a neurodevelopmental disorder, are impaired in understanding social cues and in responding to them. These patients generally have normal language or general intellectual abilities, yet in everyday life they avoid eye contact and do not spontaneously interact with people [28]. On formal tests of social cognitive skill, they show specific impairments in understanding the intentions of others and lack of fast intuitive judgments about social contexts [29]. The pathogenesis of autism is unclear, although mutations in genes implicated in synaptogenesis have been identified [30] and different neurochemical, neurophysiological, and neuropathological abnormalities have been demonstrated in these patients [31]. An interesting current hypothesis has implicated oxytocin in the etiology of autism, and in the social disorders that are the hallmark of HF-ASD [32].

There are many kinds of treatment available for autism such as Behavior and communication approaches, dietary approaches and Medication, Complementary and alternative medicines. [33]Applied Behavior analysis, Physical therapy improves gross motor skills and helps to handle sensory integration issues [34]. Occupational therapy helps to treat sensory issues, sensory integration therapy, speech therapy improves communication skills.

Epidemiological survey of handicapped children in the London revealed that social impairment is not restricted to autism but is also found among other mentally handicapped people [35]. They found that 21.2 of every 10,000 children aged under 15 years in the area exposed impairments of reciprocal interaction and, of these, 4.9 had a history of typical autism. Furthermore, they found that the social impairment could be distinguished into three types: social aloofness, passive interaction, and active-but-odd interaction. This latter description referred to social behavior that was undertaken mainly to indulge some repetitive, idiosyncratic preoccupation, showing no interest in the other person's needs. Pharmacological treatment can help ameliorate some of the behavioral symptoms of ASD, including irritability, aggression and self-injuries

behavior. Additionally, by reduce interfering disruptive behavior.

Social adaptation requires specific cognitive and emotional competences. Individuals with high-functioning autism or with asperger syndrome cannot understand or engage in social situations despite preserved intellectual abilities. Recently, it has been suggested that oxytocin, a hormone known to promote mother-infant bonds, may be implicated in the social deficit of autism. The behavioral effects of oxytocin with autism, in a simulated ball game where participants interacted with fictitious partners, found that after oxytocin inhalation, patients exhibited stronger interactions with the most socially cooperative partner and reported enhanced feelings of trust and preference. Also, during free viewing of pictures of faces, oxytocin selectively increased patients' gazing time on the socially informative region of the face, namely the eyes. Thus, under oxytocin, patients respond more strongly to others and exhibit more appropriate social behavior and affect, suggesting a therapeutic potential of oxytocin through its action on a core dimension of autism [36]. Risperidone is the first FDA approved medication for the treatment of symptomatic condition associate with ASD children and adolescence, including aggressive behavior deliberate self-injury and temper tantrums.

Loneliness and friendship were examined in 22 high- functioning children with autism and 19 typically developing children equated with the autistic children for IQ, CA, gender, mother's education, and ethnicity. Children between the ages of 8 and 14 were asked to report on both their understanding and feelings of loneliness and the quality of their friendship. Compared to typically developing children, children with autism were both lonelier and had less complete understandings of loneliness. Although all children with autism reported having at least one friend, the quality of their friendships was poorer in terms of companionship, security, and help. Fewer associations were found between loneliness and friendship for the autistic than for the non- autistic children, suggesting less understanding of the relation between loneliness and friendship. Implications of these results are discussed for conceptualizing the social deficits in autism [37].

Thus, the finding that lesions to discrete brain areas may result in clinical symptoms that are also present in people with autism recommends a neurobiological basis and implicates dysfunction of the mesolimbic areas, parietal cortex and cerebellum. However, the studies only provide partial insight into the biological basis of autistic disorder.

## OUTCOME

The main goal of Autism Research is to learn more about, what causes Autism and to develop drugs that can improve the quality of life of people living with this ailment in different levels. The prevalence of Autism is increased significantly, this increase may be largely attributed to broader diagnostic criteria and one of the key goals is to enable a new level of research that was not possible previously on animal studies. Receiving an accurate Autism spectrum diagnosis at younger age is associated with more positive functional outcomes in later life as a result of ASD diagnosis and receipt of the above targeted treatment. Since pragmatically there is no amble evidence in support of Autism care and permanent cure.

The above situation inspired me to contribute something constructively to address the society afflicted by this disorder which is not adequately analyzed hitherto considering the density of this disorder and mental agony encountered by the parents' siblings of the Autism affected kids is inexplicable. Here again according to my understanding Autism is more prone among boys as compared with girls (4:1) ratio remarkably seemingly alarming hence requiring at most care to be attached to identify remedial medicines are explored in a quickest pace to reduce further Autism penetration across the globe.

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## REFERENCES

1. Baio J. Prevalence of autism spectrum disorder among children aged 8 years-autism and developmental disabilities monitoring network, 11 sites, United States, 2010.
2. World Health Organization. Comprehensive and coordinated efforts for the management of autism spectrum disorders. Report of executive board. Retrieved May. 2013 Apr 8;11:2014.
3. Mindell JA, Meltzer LJ. Behavioural sleep disorders in children and adolescents. Ann Acad Med Singapore. 2008 Aug 1;37(8):722-8.
4. Reynolds AM, Malow BA. Sleep and autism spectrum disorders. Pediatric Clinics. 2011 Jun 1;58(3):685-98.
5. Damasio AR, Maurer RG. A neurological model for childhood autism. Archives of neurology. 1978 Dec 1;35(12):777-86.
6. Webster MJ, Bachevalier J, Ungerleider LG. Connections of inferior temporal areas TEO and TE with parietal and frontal cortex in macaque monkeys. Cerebral cortex. 1994 Sep 1;4(5):470-83.
7. Malkova L, Bachevalier J, Webster M, Mishkin M. Effects of neonatal inferior prefrontal and medial temporal lesions on learning the rule for delayed nonmatching-to-sample. Developmental neuropsychology. 2000 Dec 1;18(3):399-421.

8. Bolton PF, Griffiths PD. Association of tuberous sclerosis of temporal lobes with autism and atypical autism. The Lancet. 1997 Feb 8;349(9049):392-5.
9. Ozonoff S, Jensen J. Brief report: Specific executive function profiles in three neurodevelopmental disorders. Journal of autism and developmental disorders. 1999 Apr 1;29(2):171-7.
10. Zwaigenbaum L, Bryson S, Rogers T, Roberts W, Brian J, Szatmari P. Behavioral manifestations of autism in the first year of life. International journal of developmental neuroscience. 2005 Apr 1;23(2-3):143-52.
11. Cook Jr EH, Courchesne RY, Cox NJ, Lord C, Gonen D, Guter SJ, Lincoln A, Nix K, Haas R, Leventhal BL, Courchesne E. Linkage-disequilibrium mapping of autistic disorder, with 15q11-13 markers. The American Journal of Human Genetics. 1998 May 1;62(5):1077-83.
12. Courchesne E, Yeung-Courchesne R, Hesselink JR, Jernigan TL. Hypoplasia of cerebellar vermal lobules VI and VII in autism. New England Journal of Medicine. 1988 May 26;318(21):1349-54.
13. Chugani DC, Muzik O, Rothermel R, Behen M, Chakraborty P, Mangner T, Da Silva EA, Chugani HT. Altered serotonin synthesis in the dentatothalamocortical pathway in autistic boys. Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society. 1997 Oct;42(4):666-9.
14. Schmahmann JD, Sherman JC. The cerebellar cognitive affective syndrome. Brain: a journal of neurology. 1998 Apr 1;121(4):561-79.
15. Baron-Cohen S. Social and pragmatic deficits in autism: Cognitive or affective. Journal of autism and developmental disorders. 1988 Sep 1;18(3):379-402.
16. Kanner L. Autistic disturbances of affective contact. Nervous child. 1943 Apr;2(3):217-50.
17. Eisenberg L, Kanner L. Childhood schizophrenia: Symposium, 1955: 6. Early infantile autism, 1943–55. American Journal of Orthopsychiatry. 1956 Jul;26(3):556.
18. Wing L, Gould J. Severe impairments of social interaction and associated abnormalities in children: Epidemiology and classification. Journal of autism and developmental disorders. 1979 Mar 1;9(1):11-29.
19. Dawson G, Toth K, Abbott R, Osterling J, Munson J, Estes A, Liaw J. Early social attention impairments in autism: social orienting, joint attention, and attention to distress. Developmental psychology. 2004 Mar;40(2):271.
20. Kishida KT, De Asis-Cruz J, Treadwell-Deering D, Liebenow B, Beauchamp MS, Montague PR. Diminished single-stimulus response in vmPFC to favorite people in children diagnosed with Autism Spectrum Disorder. Biological psychology. 2019 Jul 1; 145:174-84.
21. Dawson G, Osterling J, Rinaldi J, Carver L, McPartland J. Brief report: Recognition memory and stimulus-reward associations: Indirect support for the role of ventromedial prefrontal dysfunction in autism. Journal of autism and developmental disorders. 2001 Jun 1;31(3):337-41.
22. Capps L, Sigman M, Mundy P. Attachment security in children with autism. Development and psychopathology. 1994;6(2):249-61.
23. McClure SM, Daw ND, Montague PR. A computational substrate for incentive salience. Trends in neurosciences. 2003 Aug 1;26(8):423-8.
24. Kishida KT, De Asis-Cruz J, Treadwell-Deering D, Liebenow B, Beauchamp MS, Montague PR. Diminished single-stimulus response in vmPFC to favorite people in children diagnosed with Autism Spectrum Disorder. Biological psychology. 2019 Jul 1; 145:174-84.
25. Dawson G, Webb SJ, McPartland J. Understanding the nature of face processing impairment in autism: insights from behavioral and electrophysiological studies. Developmental neuropsychology. 2005 Jun 1;27(3):403-24.
26. Dawson G, Bernier R, Ring RH. Social attention: a possible early indicator of efficacy in autism clinical trials. Journal of neurodevelopmental disorders. 2012 Dec;4(1):11.
27. Courchesne E, Pierce K, Schumann CM, Red cay E, Buckwalter JA, Kennedy DP, Morgan J. Mapping early brain development in autism. Neuron. 2007 Oct 25;56(2):399-413.
28. Baron-Cohen S, Wheelwright S, Hill J, Raste Y, Plumb I. The "Reading the Mind in the Eyes" Test revised version: a study with normal adults, and adults with Asperger syndrome or high-functioning autism. The Journal of Child Psychology and Psychiatry and Allied Disciplines. 2001 Feb;42(2):241
29. Dalton KM, Nacewicz BM, Johnstone T, Schaefer HS, Gernsbacher MA, Goldsmith HH, Alexander AL, Davidson RJ. Gaze fixation and the neural circuitry of face processing in autism. Nature neuroscience. 2005 Apr;8(4):519.
30. Klin A, Jones W, Schultz R, Volkmar F, Cohen D. Visual fixation patterns during viewing of naturalistic social situations as predictors of social competence in individuals with autism. Archives of general psychiatry. 2002 Sep 1;59(9):809-16.
31. Klin A, Volkmar FR, Sparrow SS. Asperger syndrome. Guilford Press; 1997.
32. Frith U. Emanuel Miller lecture: Confusions and controversies about Asperger syndrome. Journal of child psychology and psychiatry. 2004 May;45(4):672-86.
33. Durand CM, Betancur C, Boeckers TM, Bockmann J, Chaste P, Fauchereau F, Nygren G, Rastam M, Gillberg IC, Anckarsäter H, Sponheim E. Mutations in the gene encoding the synaptic scaffolding protein SHANK3 are associated with

autism spectrum disorders. Nature genetics. 2007 Jan;39(1):25.

34. Jamain S, Quach H, Betancur C, Råstam M, Colineaux C, Gillberg IC, Soderstrom H, Giros B, Leboyer M, Gillberg C, Bourgeron T. Mutations of the X-linked genes encoding neuroligins NLGN3 and NLGN4 are associated with autism. Nature genetics. 2003 May;34(1):27.
35. Waterhouse L, Fein D, Modahl C. Neurofunctional mechanisms in autism. Psychological review. 1996 Jul;103(3):457.
36. Bauminger N, Kasari C. Loneliness and friendship in high- functioning children with autism. Child development. 2000 Mar;71(2):447-56.