 DOI: 10.18231/2455-8559.2017.0017

Neurobiology of Autsim Spectrum Disorders

Gowri Devi.M[1], Tejas Gayal[2,*]

[1]HOD, [2]DNB Resident, Dept. of Academics, Asha Hospital, Hyderabad, Telangana

***Corresponding Author:**
Email: tejas.gayal@gmail.com

Introduction

Neurobiology has been a great interest of research in last few decades in the field of psychiatry. Day by day we are moving towards associating various psychiatric disorders to its point of origin related to structural neuro-anatomy of brain. Newer imaging modalities like Functional MRI, Positron emission tomography (PET) scan and Single photon emission tomography (SPECT) are being used more often by clinicians to assess the structural as well as functional neuroanatomical changes that are frequently associated with certain psychiatric disorders. This area has been under extensive research thus giving us insight into anatomical defects associated with disorders; Thus unraveling various evidences and explanations to the clinical symptomatology that occurs in a particular condition. As the research is progressing, slowly but surely we are moving towards evidence based answers to the way patients present and why as to certain behaviors are associated with its structural correlates.

Although a lot of studies have concluded various anatomical correlates for adult psychiatric disorders; much work is to be done yet into the common childhood disorders like Attention deficit hyperactivity disorder (ADHD), Autism spectrum disorders (ASD), Intellectual disability (ID) and Specific learning disabilities (SLD).

It has been proven that symptomatic patients who have associated structural abnormalities may present with even more severe symptoms and is usually associated with a poorer prognosis. Thus identifying the patients early, especially those with associated structural abnormalities becomes crucial considering its prognostic implications. If identified early and intervened with appropriate management for the disorder, chances of improvement and better outcome increase significantly.(1)

Overview of Genetics & Neurobiology of Asd

What we already know – Autism spectrum disorders have multifactorial etiologies which include mainly; Genetic, Biological and Immunological factors. Genetic factors play a predominant role in etiopathogenesis as we all know. In general up to 15% of ASD cases are associated with a known genetic mutation. Some family studies demonstrate as much as 50% increased rates, especially in families having two or more children affected with ASD. Large twin studies demonstrated concordance rates up to 36% in monozygotic pairs; although the heterogeneity of expression points to the multifactorial genetic transmission. Two genetic markers - elevated platelet 5-HT & m-TOR (mammalian target of rapamycin) are disrupted in ASD.(2)

Some co morbidities are highly associated with ASD. Most common inherited cause is fragile X syndrome (present in 2-3% of total ASD cases).

Specific Biomarkers

Multiple biomarkers have been extensively studied and their roles in influencing neuronal functions have been documented in some of the studies. First identified biomarkers is elevated platelet serotonin through serotonin transporter. Because of the key role played by serotonin in brain development, it may lead to functional alteration thus leading to certain abnormalities. Another gene implicated is m-TOR , which is especially involved when ASD is associated with co morbid genetic conditions like Fragile X syndrome, neurofibromatosis, hamartoma.(3)

Structural & Functional Aspects

Studies depict increased total brain volumes in children younger than 4 years while after the age of 5 years they may show macrocephaly. Specific structures documented to be involved are amygdala and striatum. Interestingly these studies have shown increase in the size of these structures initially followed by decrease; as the child grows.

Functionally the studies focus on face perception, neutral face tasks, communication impairments, working memory and repetitive behaviors. FMRI studies have shown so far that there is a definite increase in amygdaloid arousal along with abnormal activation of right temporal lobe. Atypical patterns in frontal lobe have also been documented especially in cases involving deficits in social-emotional reciprocation.(4)

Recent Advances & Newer Studies

Extensive research and studies have been performed recently, especially over last decade trying to understand the underlying structural and functional abnormalities in brain. As mentioned earlier, amygdala and hippocampus which mediate emotional perception and regulation have been the areas which have been

implicated in etiopathogenesis. Studies indicating increased volume of these structures in adolescence also correlate with functional imaging studies which support the increased activity in these centers. The studies which implicated abnormal neurocircuitary in patients especially in early life were associated with worse prognosis and more commonly showed repetitive stereotypical behaviors which were observable in first year of life. Diffusion tensor imaging (DTI) studies in developing children in ASD showed abnormal integrity in white mater in general along with specific defects in corpus callosum, internal capsule and middle cerebellar peduncles. Children with ASD have also shown reduced Fractional anisotropy (FA) and increased radial diffusion in white mater along with the above mentioned segments in internal capsule and corpus callosum. Other findings which were associated in DTI were (i) increased mean diffusion (MD) in whole brain and specifically in anterior and posterior limbs of internal capsule. (ii) Reduced axial diffusion in body of corpus callosum. (iii) Reduced FA in middle cerebellar peduncle.

Thus if the findings are corroborated, it suggests diffuse structural changes in white mater. Abnormal corpus callosal findings are indicative of impaired inter-hemispheric transfer. DTI studies strengthen the already established findings of impairments in subcortical tracts in ASD. While the defects in internal capsule can be correlated with abnormal sensorimotor functioning.[(5)]

Salient Findings in Various Studies Over Last Few Years

A) Anterior insula and anterior cingulate gyrus are the key structures involved in salience networks. Abnormal functioning of these salience networks seems to be the reason for impairment in socio-emotional reciprocation as well repetitive behavior in ASD.
B) Significant over activity in primary sensory and emotion processing areas of brain like primary sensory cortices, amygdala and prefrontal cortex have been implicated in exaggerated negative responses to sensory stimuli in children with ASD.
C) Some parents of children with ASD may have increased activation of the amygdala and fusiform gyrus in response to faces.
D) Higher order sensory processing defects may be due to the structural abnormalities in connectivity including myelination.
E) Brain circuitry maturation appears to be abnormal as the children with ASD grow up.
F) Basic deficits in processing of sensory information may be correlated to specific dysfunction in white mater, neuro-circuitary and organization in the associated area of the brain, dealing with that particular sensation.[(6)]

Acknowledgements – Nil
Conflict of Interest – Nil
Source of Funding – Nil

References

1. Sparks BF, Friedman SD, Shaw DW, et al. Brain structural abnormalities in young children with autism spectrum disorder. Neurology. 2002 Jul 23;59(2):184–92.
2. Kaplan and Sadock's Synopsis of Psychiatry: Behavioral Sciences/Clinical Psychiatry 2014 Benjamin J. Sadock,Virginia Alcott Sadock, Pedro Ruiz eds.(11th ed) 2014.
3. Goldani AAS, Downs SR, Widjaja F, Lawton B, Hendren RL. Biomarkers in Autism. Front Psychiatry. 2014;5:100.
4. Limbic Circuitry in Patients With Autism Spectrum Disorders Studied With Positron Emission Tomography and Magnetic Resonance Imaging |Am J Psychiatry.2000; 157(12):1994-2001.
5. Charles JM, Carpenter LA, Jenner W, Nicholas JS. Recent Advances in Autism Spectrum Disorders. Int J Psychiatry Med. 2008 Jun 1;38(2):133–40.
6. Jeremy Willsey, Matthew State. Autism spectrum disorders: from genes to neurobiology. Current Opinion in Neurobiology 2015;30:92-99.