

Autism Spectrum Disorder and the Role of Serotonin

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Abstract:- Neurotransmitters assumes a significant part in Autism Spectrum Disorder and helps to forward signals from one to another part of the brain. About in 25% Patients detailed with ASD found expanded 5-HT levels, the condition is called Hyper serotoninemia which was the first biomarker distinguishes in ASD. The biological function of 5HT is more complex and multifaceted. It transmits messages between nerve cells. Although serotonin considered as a mood stabilizer but excess concentration of serotonin in brain can lead to excessive nerve cells activity. Expansion in Serotonin receptor thickness and serotonergic innervation and serotonin union with age assumes a vital part for the improvement of Brain. Specific serotonin reuptake inhibitors are drugs solid and all the more inadequately endured in those kid patients experienced ASD when contrasted with grown-ups with in a similar sort of analysis. Conversely, SRI organization or transient tryptophan consumption in human and grown-up rodents adjust inversion learning and other intellectual measures applicable to the dull or enthusiastic conduct saw in ASD.

Keywords:- (ASD) Autism Spectrum Disorder, Hyperserotonemia, 5-HT, Serotonin.

I. INTRODUCTION

Autism Spectrum Disorder (ASD), impacts on overall nervous system and affects physical, mental, social or emotional health of an individual and also includes repetitive patterns and limited behaviour. The term Spectrum in ASD refers to a variety of symptoms and severity status. It is a disorder accompanying with the developmental growth of brain which appears in childhood showing some predefined symptoms that hold extraordinary ways of recount to folks and of delayed in language or tongue developmental issues, social and behavioural challenges. The problem may be a mild, severe or in between of them. In advance studies the experts have recognized about differ types of the disease, Autistic disorder, pervasive development disorder, Asperger's syndrome, but now as combined named as Autism spectrum disorder. During last 2 decades, the ASD cases have remarkably increases from 2-5% per 10K children. In comparison with the female children patients, male children patients are around 4 times more. In the reality, ASD cases having diversified etiologies in their behaviour pattern and an important feature associated with the possibility of trite mechanism. ASD appears in early childhood stage and causes problems in normal functioning in society, in schools, at work place etc., presently there is no care for ASD and early treatment of the disorder may affect the lives of many children in society.

II. SEROTONIN

Central nervous system comprises of Serotonin which ultimately having performance both as a Neurotransmitter and also as regional hormone in peripheral vascular system. Serotonin conferred in full concentration in platelets within then blood. More over 90% of the total amount in then body is conferred in the enterochromaffin cell in the gut. In the localised regions of the midbrain, 5HT is present in very high centration which act as transmitter in the CNS. From dietary 5 Hydroxytryptophan by tryptophan hydroxylase, 5HT is formed, then 5 HT by a non-specific decarboxylase & is transported into cells by a particular Serotonin uptake carrier (SERT). Monoamine Oxidase degrades into 5-Hydroxyindoleacetic acid which is eliminate in urine. The biological function of 5HT is more complex and multifaceted. It transmits messages between nerve cells. Although serotonin considered as a mood stabilizer but excess concentration of serotonin in brain can lead to excessive nerve cells activity. Expansion in Serotonin receptor thickness and serotonergic innervation and serotonin union with age assumes a vital part for the improvement of Brain.

Elsewhere, serotonin also helps to maintain normal health of bones, sleep, sexual functions, digestion of food, regulation of mood and blood clotting in the body. 5HT or serotonin is often also known as “feel-good” chemical.

III. HYPERSEROTONEMIA AND AUTISM SPECTRUM DISORDER

Increased 5-HT level is the state of Hyper serotoninemia, it is also termed as Serotonin syndrome which is a group of of different symptoms and sometimes may occur due to certain types of serotonergic medication therapy. The severity may result to death. The consecutive use of more than two serotonergic medication includes selective serotonin reuptake inhibitor, serotonin norepinephrine reuptake inhibitors, monoamine oxidase inhibitor, tricyclic antidepressant, amphetamine, pethidine, tramadol, dextromethorphan, buspirone, cocaine, metoclopramide, L-tryptophan, triptans etc. Hyper serotoninemia is the state of increased 5-HT levels. The phenomenon found among subjects with Autism spectrum disorder, reported in about 25% of the subjects. (1). Serotonin synthesis efficiency in non-autistic kids was >200% as comparison to matured values until the age of 5 years and then it diminishes toward matured values. Serotonin synthesis efficiency in autistic kids increased gradually between the ages 2 years to 11 years to values one and a half times adult average values. (2)

During infancy, humans experience a period of high brain serotonin capacity. This developmental progress is disrupted in ASD subjects with some brain regions more severely impacted. (2) Serotoninemia was found as a

biomarker in autism spectrum disorder (ASD) introduce the extensive acceptance of 5-HT as neurotransmitter. (3) There is an essential relationship found between 5-HT_{1A} receptor to brain regions accountable for abnormalities in autism. In the adult brain, 5HT_{1A} receptor binding and immunoreactivity are high in limbic brain regions (including lateral septum, CA1 and dentate gyrus in hippocampus, frontal and entorhinal cortex). (4) Drugs targeting serotonin receptors, particularly 5-HT_{1A} and HT_{2A}, shown promise for increasing social interaction or decreasing cognitive rigidity, (5,6) More complete understanding of the temporal and spatial influences of altered 5-HT function on ASD-relevant behaviour may yield new opportunities for rescue experiments, however we are already having potential targets.

The alteration in serotonergic innervation & serotonin receptor density and serotonin synthesis with age suggest that serotonin plays a role in the adult brain, 5HT_{1A} receptor binding and immunoreactivity are high in limbic brain regions (including lateral septum, CA1 and serrate gyrus in hippocampus, frontal and entorhinal cortex). (4) Drugs targeting serotonin receptors, distinctly 5-HT_{1A} and HT_{2A}, shown covenant for growing (prenominal) social interaction or diminishing cognitive inflexibility, (5,6) More entire perception of the transitory and spatial influences of change 5-HT activity on ASD-relieving behaviour may furnish new opportunities for rescue experiments, however we are already having influential targets. The alteration in serotonergic innervation & serotonin receptor density and serotonin synthesis with age suggest that serotonin plays an essential role in the growth of brain. (5) Indeed, there is a body of record that serotonin settle several aspects of brain development, including regulation of cell division, differentiation, neurite outgrowth and synaptogenesis. Serotonin control brain development by regulation of nourishing factors and by immediate regulation of activity dependent plasticity.

IV. CONCLUSION

About more than exploration of 50 years with rigorous studies, autism spectrum disorder has not completely perceived its relationship with excessive concentration of 5HT or serotonin in brain, hyper serotoninemia biomarker. Serotonin syndrome which is a group of different symptoms and sometimes may occur due to certain types of serotonergic medication therapy. The severity may result to death. The consecutive use of more than two serotonergic medication includes selective serotonin reuptake inhibitor, serotonin norepinephrine reuptake inhibitors, monoamine oxidase inhibitor, tricyclic antidepressant, amphetamine, pethidine, tramadol, dextromethorphan, buspirone, cocaine, metoclopramide, L-tryptophan, triptans etc. The effect of change in 5-HT take-up or breakdown on tactile advancement was seen as obviously formative and may not identified with the designated medicines in adulthood. Serotonin also helps to maintain normal health of bones, sleep, sexual functions, digestion of food, regulation of mood and blood clotting in the body. 5HT or serotonin is often also known as “feel-good” chemical.

Subjects with a type of ASD, Specific serotonin reuptake inhibitors (SSRIs) i.e. Venlafaxine, Fluoxetine or fluvoxamine are recommended which respond a constructive outcome on generalized and monotonous conduct, social shortages, correspondence problems and interests. (7).

Specific serotonin reuptake inhibitors (SSRIs) like Fluvoxamine, Fluoxetine and venlafaxine are recommended in subjects with a type of ASD and shows a constructive outcomes on generalized and monotonous conduct, interests, social shortages and correspondence problems. (7) Nevertheless, SSRIs appear to be less strong and are all the more inadequately endured by kids experiencing ASD than by grown-ups with in the equivalent diagnosis. (8) interestingly, momentary tryptophan consumption or SRI organization in grown-up rodents and human modifies inversion learning and other intellectual measures applicable to the dull or impulsive conduct saw in ASD. (9)

More complete comprehension of the fleeting and spatial impacts of modified 5-HT work on ASD-applicable conduct might yield new freedoms for salvage tests.

Finally, it was concluded that, adjustments of the guideline of serotonin combination with the age in ASD subject uniquely kids along with a significant job of serotonin in post pregnancy mental health stage recommends a methodology for the pharmacological treatment of ASD.

REFERENCES

- [1.] Levitt, P. Serotonin and the autisms: A red flag or a red herring? *Arch. Gen psychiatry* 2011.,68,1093-1094.
- [2.] *Molecular psychiatry* (2002), 7, S16-S17. Doi:10.1038/sj.mp.4001167
- [3.] Kolk GE Jr, Long JP. Serotonin as a neurotransmitter: a review. *Comp Biochem physiol C*. 1988 91:251-257.
- [4.] Chugani DC et al. *Ann Neurol* 1999; 45:287-295
- [5.] Edwards DJ, Chugani DC, Chugani, HT, Chehab J, Malian M, Aranda JV. Pharmacokinetics of buspirone in autistic children. *J Clin pharmacol*. 2006; 46:508-514.
- [6.] File SE, Gonzalez LE, Andrews N. Comparative study of pre- and postsynaptic 5-HT_{1A} receptor modulation of anxiety in two ethological animal tests. *J Neurosci*. 1996; 16:4810-4815.
- [7.] Kumar, B.; Prakash, A.; Sewal, R K.; Medhi, B.; Modi, M. Drug therapy in autism: A present and future perspective. *Pharmacol. Rep* 2012, 64, 1291-1304.
- [8.] Doyle, C A.; McDougle, C. J. Pharmacologic treatments for the behavioral symptoms associated with autism spectrum disorders across the lifespan. *Dialogues Clin. Neurosci*. 2012, 14, 263-279.
- [9.] Clarke HF, Dalley JW, Crofts HS, Robbins TW, Roberts AC. Cognitive inflexibility after prefrontal serotonin depletion. *Science*. 2004; 304:878-880.
- [10.] Hona Quack, Madeleine R. Bronus and Margot Van de Bor: *The Dynamics of Autism Spectrum Disorder: How Neurotoxic compounds and Neurotransmitters interact* 2013.