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Therapeutics regulation of Autism Spectrum Disorder- The Gut Effect

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Development of autism is related to something fundamental- alteration in biological machinery triggered by functions of gut microbiome

Globally 1 out of every 68 children are impacted by autism spectrum disorder (ASD). In India alone, this neurodegenerative disorder affects 1% to 1.5% of children in the age band of 2 to 9 years.

The current set of interventions adopted by healthcare practitioners are restricted to behavioural therapies & pharmaceutical strategies. The oral administration of drugs includes antidepressants, Aripiprazole & more that impact the concentration of serotonin in the brain. However studies have found that these drugs may lead to hyperactivity & aggression & trigger side effects such as nausea, vomiting, weight gain & increased appetite.

Although autism is sometimes coined as a genetic disorder, scientists & researchers have found that genes just tell the potential or the risk. Having autism related genes does not translate into development of autism in 95% of the situations. Development of autism is related to something fundamental- alteration in biological machinery triggered by functions of gut microbiome.

Gut-Brain Axis & role of microbiome

Gut contains millions of nerve cells that form its own nervous system- enteric nervous system (ENS), also referred to as the second brain. ENS & central nervous system are connected via vagus nerve & form gut brain axis. The communication between gut & brain via gut brain axis regulates behaviour & cognitive responses. Trillions of microbes living in the gut stimulate production of serotonin(approx.. 90%) & various other beneficial metabolites that regulate emotions & behaviour & have neuro-protective effects. However, certain pathogenic microbes in the gut stimulate production of neurotoxins that can pass through the vagus nerve highway & block production of neurotransmitters in the brain, thereby precipitating behavioural deficits & increasing risk of autism.

Early microbial colonisation

Microbial colonisation in offspring starts even before the child is born inside the mother's womb in placenta & amniotic fluid. During pregnancy, the mother's gut microbiota regulates bioavailability of various biochemicals & nutrients that support offspring brain development. Some specific microbial consortium in mother’s gut releases certain metabolites that influences

development of foetal brain.

Post birth, certain bacterial species are passed on in infants from breast milk of lactating mothers. The composition of microbiome in the child stabilises in 2-3 years & plays a key role in brain development of infant.

Oral administration of antibiotics, stress & wrong dietary choices of expectant mothers can disrupt their microbiome which can have far fetched impact on brain health of the offspring. Production of certain metabolites due to imbalanced gut such as trimethylamine-N-oxide (TMAO),imidazole propionate (IP), 3-indoxyl sulphate (3-IS) can cross the blood brain barrier & impact neuron development in child.

The Gut microbiome immune system link

70% of our immune system lies around our gut lining & our gut microbes are constantly training immune cells to differentiate between friend or foe, evidencing the role of gut microbiome in immune responses. Studies have found that blocking of a pro-inflammatory molecule- IL17a produced by the immune system of expectant mothers opens up new avenues for prevention of autism.

Mode of Delivery & Breastfeeding

Children born via vaginal delivery have more healthy & diverse gut microbiome composition as compared to those born via caesarean section delivery. Vaginal births are exposed to mother’s vaginal & gut microbiome while C-section births acquire microbes from mother’s skin flora & environmental microorganisms. Studies have found that C-sections born have altered gut microbial composition in early infancy which might delay neurological adaptation in infants with 23% high risk of developing autism. Therefore breastfeeding becomes all the more important for children born through C-section.

Breast milk contains specific sugar Human Milk Oligosaccharides (HMO) which cannot be digested by infants. Rather HMO is metabolised by infant's gut microbiome & synthesised into beneficial short chain fatty acids that promote immune system & brain development. Infants fed with formula milk alters their microbiome composition with potential for growth of pathogenic microbes which can release proinflammatory molecules impacting brain development

Scientists believe that promoting balanced gut microbiome of mother through right dietary choices, minimal use of antibiotics & regulating stress levels goes a long way in promoting healthy neonatal brain development.

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