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Letter to the Editor

Gut microbiota: friend or foe

Sir,

Comprising of trillions of various bacteria, protozoan, fungi and viruses, the gut microbiota live in human body as a super complex ecosystem mostly in gastro intestinal tract (70%). Apart from GI tract they also inhabit skin, mouth and sexual organs as an essential ecological community of commensal, symbiotic or even pathogenic relationship. These microbiota interplay with bodily immune, endocrinal, metabolic and nervous system and produces various pathological changes responsible for disease etiology.[1] These microbiota play a major role in digestion and absorption of macro molecules, maturation of immune system, protection of gut and behavioural development of an individual. In gut disorders like inflammatory bowel disease (IBD) or irritable bowel syndrome (IBS) the altered brain axis is responsible for disorders like depression, anxiety, schizoaffective disorders, autistic spectrum disorders, multiple sclerosis and parkinson's disease.[2]

The injudicious use of antimicrobials and the stress influences these gut microbiota and act either via dysbiosis (an imbalance between beneficial bacteria like Bifidobacterium, lactobacilli and colonization of harmful bacteria) or by stimulation of hypothalamic pituitary adrenal axis (HPA). The stress induced persistent stimulation of this HPA axis releases glucocorticoids from hypothalamus and sympathetic hormones (adrenaline and nor adrenaline) via sympathetic branches of autonomic nervous system. These neuro endocrinal products binds to the receptors present on immunocytes like lymphocytes, monocytes, macrophages and produces dysregulation of cell mediated immunity. Furthermore neuroactive substances like Histamine and GABA released by the bacteria also stimulates the peripheral neurons via vagal sensory neurons which in turn help in localization of infection corresponding to the host defense.[3,4] The central nervous system alters motility, permeability and secretion by neuroendocrinal, autonomic and HPA axis which ultimately modulate the gut microbiota composition.

The most common neuropsychiatric disorder related with these altered gut microbiota are depression and anxiety. Increased serotonin levels and expression of C-Fos protein by campylobacter jejuni in various brain nuclei like amygdala, hypothalamus, stria terminalis alter the brain gut axis. In disorders like ulcerative colitis and crohn's disease, the altered population of bacteroids and acinetobacter liberates the toxins which decreases the level of 5HT and Brain neurotrophic factor (BNF) which contributes to the associated depression in these diseases. Plants like aloe-vera and the use of probiotic Bifidobacterium produces their beneficial therapeutic effect by changing neurotransmitter, neuromodulators and growth factors in these psychiatric disorders.[5,6]

The autistic spectrum disorder of childhood is caused by genetic, environmental, stress factor and recently altered microbiota in form of significant colonization of clostridium tetani, clostridium sporogens and desulfovibrio are also implicated in its etiology. The metabolites of these bacteria (especially Indole 3 propionic acid) affects the mitochondrial functioning and energy failure affecting the brain gut axis. The use of hyperbaric oxygen therapy (HBOT) reduces mitochondrial dysfunction, oxidative stress and brings about the improvement in behavioral and gut functioning in these patients. Similarly, by elimination of bacterial neurotoxin, vancomycin produces its substantial but transient effect in autistic behavior.[7]

The gut microbiota also plays a significant role in myelination of prefrontal cortex. The auto immune trigger in multiple sclerosis is also related to altered gut microbiota. In Remitting and Relapsing multiple sclerosis (RRMS) several gut microbiota especially Bacteroidetes and aldercrcutzia are relatively less in number than the general population. These microbiota alters the metabolism of phytoestrogens and bile acid so the resultant metabolite produces intense inflammatory response which accounts for autoimmune etiology of RRMS. Parkinson's disease (PD) a degenerative disorder of nervous system is associated with imbalance between a prevotellaceae and entero bacterias (reduced abundance of prevotellaceae and increased abundance of entero bacterias). This imbalance is responsible for increased postural instability and gait difficulty with other motor impairments. The prevotellaceae bacteria induces mucine synthesis by intestinal mucosa and production of neuroactive short chain fatty acids. The reduced concentration of these bacteria result in increased gut permeability, decreased mucin synthesis with miscoding of excessive expression of alpha – synuclein. This miscoded alpha- synuclein affecting basal ganglion, forebrain and brain stem is responsible for the symptoms of gastroparesis like bloating and constipation even before the onset of motor symptoms in PD.9 The gastroparesis an impaired gut motility predispose for small intestinal bacterial overgrowth (SIBO). Independently SIBO worsen the motor functions by altering absorption of Levodopa, disrupting the mucosal barrier and intense immune system stimulation. The colonization of H. Pylori in parkinson's patients further deteriorates the motor functioning by intense neutrophilic response and decreased secretion of acetyl choline (Ach) so is the increased antral muscle tone.10 Similarly altered brain gut axis is associated with diseases like stroke and alzheimer's, dementia. This opens the new

frontiers in understanding the etiology of these disorders in relation to gut microbiota.

Mediterranean diet is the answer to get the optimal composition of gut microbiota. This balanced diet (comprising of fruit, vegetables, legumes, meat, fish and olive oil) by restoring the intestinal permeability, reducing endotoxemia, restore harmony of brain gut axis with an overall positive metabolic effect. 11 This is probably the simplest and cheapest way to attain a balanced brain gut axis which helps to treat and prevent the deterioration linked with altered gut microbiota. Therefore, this review advocates the need for further research with an insight that an optimal gut microbiota would enable to improve the treatment strategies for many of the neuropsychiatric disorders.

Ansh Chaudhary[1]*, Shubhi Shubhangi Bhatnagar[2], Meghna Prashant Nair[2], Bhupendra Chaudhary[3]

[1]Department of Medicine, Bharati Vidyapeeth Medical College and Research Centre, Pune, Maharashtra, India

[2]Department of Medicine, Dr. D.Y. Patil School of Medicine, Navi Mumbai, Maharashtra, India

[3]Department of Neurology, Jaswant Rai Super Speciality Hospital, Meerut, Uttar Pradesh, India

***Correspondence to**
Dr. Ansh Chaudhary
Email: doctorabpl567@gmail.com

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