Anecdote on Microbiome Diet-Neurotransmitter Triangle, A Classical View

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Abstract: Biological importance of the gut microbiome is evident from the early stages of life the human gut microbiota develops after birth and contributes to the development of the immune system in newborns. The gut microbiome gradually reaches an adult-like configuration by the age of 3–6 years old and remains stable throughout adulthood. The food we consume has a profound and multifaceted impact on our neurotransmitter systems. By supporting a healthy gut microbiome, our diet can be a powerful tool for modulating our mood, cognitive function and overall mental well-being. Gut Microbiota functions in digestion of complex carbohydrates and fiber, production of short-chain fatty acids (SCFAs) like butyrate, acetate, propionate, synthesis of vitamins K and B, modulation of immune responses and communication with the brain via the gut–brain axis. Bacteria use neurotransmitters to communicate with the central nervous system and release molecules into the bloodstream that regulate physiological processes in the intestinal wall. Neurotransmitters including 5-hydroxytryptamine, dopamine, gamma-aminobutyric acid and glutamate are essential transductors in the Gut-Brain Axis. The composition of the gut microbiota is shaped by diverse factors including age, genetics, dietary habits, environmental exposures, psychological stress, infections, concurrent medical conditions, antibiotic use and lifestyle influences such as smoking, alcohol consumption, stress, sleep, and exercise. Stress triggers the hypothalamic-pituitary-adrenal axis, increasing cortisol, alter gut motility, permeability and microbial balance. Stress leads to reduced diversity of beneficial bacteria, overgrowth of pro-inflammatory microbes, increased gut permeability and negative impact on serotonin production. Targeting the gut microbiome represents a promising approach for managing mental disorders such as depression, schizophrenia, Alzheimer disease, Autism and generalized anxiety disorders. Microbiome-based therapeutic interventions including probiotics, prebiotics, fecal microbiota transplant and dietary interventions have become potential strategies. World Health Organization advises a total of 4 mg/kg of tryptophan is achieved daily. The unique alkaloid neferine derived from the seed of lotus plant has therapeutic effects. Lactobacillus may be the gut microbial target of neferine in alleviating depression. Aerobic exercise is hypothesized to have beneficial effect on the gut microbiome, as it promotes a diverse microbiome with increased levels of beneficial Firmicutes and reduced amounts of Bacteroides compared to sedentary individuals, whereas excessive endurance exercise in athletes can cause dysbiosis. Ancient Tamil literatures describe ideas of probiotic foods, herbs, lifestyle that map onto the modern concepts of the gut–brain connection. They repeatedly link digestion, diet, bodily balance and mental state, a conceptual precursor to today's gut–microbiome ideas. The convergence of ancient observations like Kuruntokai and Akanānūru, Mukkuttram such as Vali, Azhal, Iyam, Siddha and Thirukkural with contemporary gut–brain science suggests a long-standing recognition in Tamil culture that nourishment is both a physiological and psychological determinant of human well-being. Contemporary science supports the gut–brain axis. Modern medical reviews describe mechanisms linking gut microbes, vagus nerve signalling, immune mediators and neurotransmitter production, the physiological framework that makes the ancient observations plausible today. Author shares for future directions by plotting milestones at developmental stages.

Key words: Gut Microbiome, Diet, Neurotransmitters, Stress, Lifestyle, Bacteria, Psychobiotics, Body-Mind connection, Ancient Literatures and Well-Being.

Gut microbiome – Inception

The biological importance of the gut microbiome is evident from the early stages of life. The human gut microbiota develops after birth and contributes to the development of the immune system in newborns. Furthermore, microbial colonization in the gastro intestinal tract of infants enables the production of essential amino acids and vitamins, which begins around 4 months of life. The gut microbiome gradually reaches an adult-like configuration by the age of 3–6 years old and remains stable throughout adulthood. Notable biological functions of the adult gut microbiome include regulation of nutrient harvest from the diet, regulation of immunity and auto-immunity, maintenance of intestinal barrier integrity, cholesterol metabolism, transformation of bile acids (BAs), production of antimicrobial peptides and drug metabolism. Recent studies have revealed that the human gut microbiome is a major determinant of plasma metabolome, potentially playing a more dominant role than genetics. [1]

Gut microbiome – Castle

The term 'microbiota' refers to microbial communities including bacteria, archaea, eukaryotes, and viruses that are present in a host. A metagenomics analysis of the gut microbiome in 124 individuals, a cohort composed of healthy subjects, overweight subjects, and inflammatory bowel disease patients revealed that 99 % of the genes were bacterial, and 1000 to 1150 species were identified across the entire cohort. Each individual hosted at least 160 bacterial species and over three million microbial genes. [2, 3]

Gut microbiome - Flowering

Since the intrauterine environment is sterile, microbial colonization begins only at birth. During vaginal delivery, infants are initially exposed to maternal microbes within the birth canal, initiating colonization of various body sites, including the gastrointestinal tract, oral cavity, skin, and conjunctiva, predominantly by bacterial genera such as Bifidobacterium, Lactobacillus, and Prevotella. In contrast, infants delivered via cesarean section primarily acquire microbes resembling those found on maternal skin and environmental surfaces, with initial gut colonization predominantly reflecting external environmental and maternal skin-associated bacteria. The composition of infant gut microbiota reflects the bacterial profile from the external environment and maternal skin, with the delivery method significantly influencing initial microbial colonization. At this developmental stage, breastfed infants typically exhibit less microbial diversity in their gut compared to those who are formula-fed, yet they maintain a more stable microbial composition. The introduction of solid foods represents a significant shift, leading to an increased diversity within the gut microbiota. During this period, there is a notable rise in the prevalence of anaerobic bacteria, especially Firmicutes. By the age of

three, the composition of the gut microbiome begins to closely resemble that of an adult. [4]

In adulthood, although a stable "core microbiota" persists, the composition of the gut microbial community remains sensitive to a range of intrinsic and extrinsic factors, including dietary patterns, lifestyle choices, psychological stress, medications especially antibiotic usage and environmental exposures. These factors may induce alterations in microbiome structure and function. With aging, the gut microbiome undergoes structural changes named dysbiosis, one of the 12 updated hallmarks of aging.[4,5]

Gut microbiome - Prologue

Gut Microbiota functions in digestion of complex carbohydrates and fiber, production of short-chain fatty acids (SCFAs) like butyrate, acetate, propionate, synthesis of vitamins (e.g., vitamin K, certain B vitamins), modulation of immune responses and communication with the brain via the gut–brain axis.[6]

Chronic stress triggers the hypothalamic-pituitary-adrenal (HPA) axis, increasing cortisol levels, which can alter gut motility, permeability, and microbial balance. Stress leads to reduced diversity of beneficial bacteria, overgrowth of pro-inflammatory microbes, increased gut permeability and negative impact on serotonin production about 90% of serotonin is produced in the gut. [7]

Emerging evidence highlights the pivotal role of the gut microbiota in the production of neuroactive compounds, modulates immune and inflammatory responses, and influences stress regulation. Diet, lifestyle habits, and stress management strategies are key determinants of microbial diversity and stability. Adopting dietary patterns rich in fiber, fermented foods, polyphenols omega-3 fatty acids supports beneficial bacteria alongside regular physical activity, adequate sleep, and mindfulness practices, has been shown to promote a balanced gut ecosystem. Such measures may contribute to improved mood regulation, reduced anxiety, and enhanced cognitive function, positioning gut health as a promising avenue for mental health promotion. A high intake of processed foods, sugars, and unhealthy fats can cause dysbiosis, leading to inflammation and impaired mental well being.[8]

The effect of dietary components on gut microbiome is expressed in Table.1.

Table 1: Diet links to Gut Microbiome

Dietary Component	Effect on Gut Microbiota
High-fiber foods (fruits, vegetables, legumes, whole grains)	Promote growth of beneficial bacteria (e.g., Bifidobacterium, Lactobacillus) and SCFA production
Fermented foods (yogurt, kefir, sauerkraut, kimchi)	Supply live probiotics and enhance microbial diversity

Polyphenol-rich foods (berries, green tea, dark chocolate)	Increase beneficial bacteria and reduce harmful ones
Omega-3 fatty acids (fatty fish, flaxseeds, chia seeds)	Anti-inflammatory effects, support microbiota balance
Excessive sugar & processed foods	Promote dysbiosis (overgrowth of harmful microbes)
High saturated fat diets	Linked to reduced beneficial bacteria and increased gut inflammation

Gut microbiome dovetails Neurotransmitters

World Health Organization advises a total of 4 mg/kg of tryptophan is achieved daily.

Bacteria use neurotransmitters to communicate with the CNS and release molecules into the bloodstream that regulate physiological processes in the intestinal wall.
Neurotransmitters, including 5-hydroxytryptamine (5-HT), dopamine (DA), gamma-aminobutyric acid (GABA), and glutamate, are essential transductors in the Gut-Brain Axis.
This bidirectional communication involves neural, immune, and metabolic pathways, linking gut health to mood regulation, cognition, and stress response.[9,10]
The precursor nutrient for specific neurotransmitters along the food pyramid is shown in Table.2. and Table.3.

Table.2: Diet links to Neurotransmitters

Neurotransmitter	Function	Precursor Nutrient	Food Sources
Serotonin	Mood regulation, sleep, appetite	Tryptophan	Turkey, chicken, eggs, cheese, soy, tofu, nuts, seeds, bananas, oats
Dopamine	Motivation, reward, motor control	Tyrosine (from phenylalanine)	Dairy, meats (beef, chicken), fish, soy, avocados, bananas, almonds
Norepinephrine	Focus, alertness, stress response	Tyrosine	Fish, poultry, dairy, eggs, nuts, legumes
GABA	Calming, anti-anxiety	Glutamate, Vitamin B6	Tomatoes, spinach, brown rice, soybeans, lentils, fermented foods (kimchi, yogurt)

Acetylcholine	Learning, memory, muscle movement	Choline	Eggs (yolks!), liver, soybeans, fish, chicken, cruciferous vegetables
Glutamate	Main excitatory neurotransmitter	Glutamine (amino acid)	Cheese (Parmesan), tomatoes, soy sauce, mushrooms, meat broth
Endorphins	Pain relief, pleasure	Stimulated by exercise & certain foods	Dark chocolate, spicy foods (chili peppers), ginseng, exercise itself
Histamine	Immune function, wakefulness, digestion	Histidine	Meat, fish, eggs, dairy, fermented foods

Table.3: Nutrients bind to Neurotransmitters

Nutrient	Role in Neurotransmitter Function	Food Sources
Vitamin B6	Cofactor for GABA, serotonin, dopamine	Chickpeas, bananas, tuna, chicken, potatoes
Folate (B9)	Required for serotonin and dopamine synthesis	Leafy greens, legumes, citrus fruits, fortified cereals
Vitamin B12	Essential for myelin and neurotransmitter regulation	Meat, eggs, dairy, fortified cereals
Magnesium	Helps regulate GABA and glutamate activity	Nuts, seeds, dark chocolate, leafy greens
Zinc	Modulates GABA and glutamate receptors	Shellfish, meat, legumes, pumpkin seeds
Iron	Required for dopamine synthesis	Red meat, spinach, lentils, fortified grains
Omega-3 fatty acids	Supports neuronal health and neurotransmission	Fatty fish (salmon, sardines), walnuts, flaxseeds

Gut microbiome network with Psychiatry

A pivotal study from Stanford supports the "opponency hypothesis": dopamine serves as an accelerator, while serotonin acts as a brake in reinforcement learning. This interplay is critical for adaptive behavior and holds implications for treating disorders like addiction and depression.

Numerous bacterial species, including Streptococcus, Lactobacillus, Klebsiella, and Escherichia coli have reportedly expressed serotonin-synthesizing properties via tryptophan synthetase mediation. Since 90% of serotonin synthesis occurs peripherally in the distal gastro intestinal tract, it is of no surprise that forthcoming research is linking tryptophan metabolism, and serotonin host levels to the gut microbiota.[11]

It has also become clear that tryptophan and serotonin are centrally integrated in the pathogenesis of many neurological and psychiatric disorders such as depression and anxiety

Higher susceptibility to schizophrenia and suicidal behavior is linked to specific polymorphisms in the tryptophan hydroxylase1 enzyme, plausibly due to impairment in the tryptophan to serotonin conversion pathway. Furthermore, low levels of the serotonin metabolite: 5-hydroxyindole acetic acid in the cerebrospinal fluid were associated with suicidal and aggressive behavior.[10]

Several investigations have shown that L-dopa supplementation allows Enterococcus faecium in the gastrointestinal tract to convert L-dopa into dopamine. Taking Lactobacillus plantarum for 12 weeks decreased stress and anxiety in stressed individuals compared to a placebo group and this was associated with alterations along the brain neurotransmitter pathways of serotonin and dopamine-norepinephrine.[10]

A study explored the unique alkaloid neferine derived from the seed of the lotus plant has therapeutic effects. Lactobacillus may be the gut microbial target of neferine in alleviating the symptoms of depression. The consumption of Bacillus coagulans can lessen the anxiety and depression. The alteration of the gut-brain axis' microbiome may be responsible for the reversal of emotional behavior after treatment with Bacillus coagulans.[12]

According to human studies to date, the gut microbiome is altered in major depression. The expression of Gamma Amino Butyric Acid was changed in the brain by Lactobacillus rhamnosus, which decreased depression and anxiety. One of the products of Blautia-dependent arginine metabolism is the gut microbial neurotransmitter Gamma Amino Butyric Acid, its increase was linked to a lower risk of Alzheimer Disease. Due to its inverse relationship, the abundance of M schaedleri may be associated with the development of postpartum depression.[10]

Enteric glutamatergic signaling links to depression, Alzheimer disease, Autism and other neuropsychological disorders. The GI tract of ASD patients has a considerable rise in the numbers of Desulfovibrio species, Lactobacillus species, and Clostridium perfringens.

Many studies show that gut microbiota alteration in Autism individuals may improve their behavior. The Ketogneic diet is a high-fat, appropriate-protein, low-carbohydrate diet that may be used to treat many neurological and psychiatric disorders. The

mechanism behind still unclear, Ketogenic diet may improve symptoms by altering the gut microbiome composition.

Kang et al showed significant improvements regarding both gastrointestinal and behavioral symptoms in children with Autism that were still detectable two years after discontinuing the microbiota transfer therapy treatment. Probiotics and Fecal Microbiota Transplant demonstrates effect on gastrointestinal symptom and improve behavior problems. However, until today, much remains to be discovered about the role of the microbiota-gut-brain axis in Autism.[10,13]

Inference

Understanding how the gut-brain axis works has led to the development of novel therapeutic approaches aimed at targeting the gut microbiota to improve brain disorders symptoms. Microbiome-based therapeutic interventions, including probiotics, prebiotics, Fecal Microbiota Transplant and dietary interventions have all been explored as potential strategies aimed to support mental well-being.[14]

Future research should aim to dissect the intricate interactions within the microbiota-gut-brain axis, identify specific microbial strains with significant neuroactive effects, understand the precise molecular mechanisms of gut-brain communication, and assess the long-term impacts of microbiota-modulating therapies across various patient demographics.[1]

Dysbiosis has been linked to mood disorders, anxiety, and impaired cognitive function. Dietary choices, stress management, and lifestyle interventions that support microbial diversity can enhance neurotransmitter balance and promote neurological well-being. Understanding this bidirectional communication opens new avenues for preventive and therapeutic strategies targeting both gut and brain health.[15]

Essence

The connection between food sources and neurotransmitters is a fascinating and complex area of research. The food we consume has a profound and multifaceted impact on our neurotransmitter systems. By providing the essential building blocks, co-factors, and supporting a healthy gut microbiome, our diet can be a powerful tool for modulating our mood, cognitive function, and overall mental well-being.[1]

The composition of the gut microbiota is shaped by diverse factors, including age, genetics, dietary habits, environmental exposures, psychological stress, infections, concurrent medical conditions, antibiotic use, and other lifestyle influences.[3]

The use of psychobiotics constitutes combining probiotics, live organisms possessing therapeutic effects, with prebiotics, food that can be processed by the probiotics in the colon, to produce metabolites that sustain the gut microbiome leading to health benefits across the gut-brain axis.

Targeting the gut microbiome represents a promising approach for managing mental disorders such as depression, schizophrenia, anxiety disorders like generalized anxiety disorder and autism.[10]

Gut microbiota acts as a central player in the diet–stress–health triangle. A high-fiber, polyphenol-rich, minimally processed diet plus consistent stress management like mindfulness, yoga, breathing exercise, adequate sleep, moderate exercise, nature friendliness, laughter fosters both a balanced gut ecosystem and emotional well-being. This is the essence which even fits the western world.[16]

Gut microbiome True-Blue

Ancient Tamil literatures and traditional Tamil and Siddha medical texts describe ideas of probiotic foods, herbs, lifestyle that map onto the modern concepts of the gut–brain connection (gut microbiota → neurotransmitters →mood). They repeatedly link digestion, diet, bodily balance and mental state, a conceptual precursor to today's gut–microbiome ideas.[17]

Contemporary science supports the gut–brain axis. Modern medical reviews describe mechanisms linking gut microbes, vagus nerve signalling, immune mediators and neurotransmitter production, the physiological framework that makes the ancient observations plausible today.[5]

Literary and medical contexts articulate a holistic understanding of the interdependence between diet, bodily balance, and emotional state, reflecting an empirical awareness of the body–mind connection. Sangam poetry in the Kuruntokai and Akanānūru depicts how specific foods, meal sequences, aromas, and social contexts of eating shape sensations of comfort, rest, joy, and intimacy. Siddha medical texts emphasize the maintenance of Agni, digestive or metabolic fire and the equilibrium of the three Mukkuttram such as Vali, Azhal, Iyam as foundational to physical health and mental clarity. Improper diet or impaired digestion disrupts humoral balance, leading to both somatic ailments and disturbances of mood or cognition, a conceptual analogue to modern models in which diet modulates the gut microbiome, influencing neurochemical pathways such as serotonin, dopamine, and gamma amino butyric acid synthesis. The convergence of these ancient observations with contemporary gut–brain science suggests a long-standing recognition in Tamil culture that nourishment is both a physiological and psychological determinant of human well-being.[18,19,20,21]

Ancient literatures parallels with modern gut-brain science as depicted in Table.4.

Table.4. Ancient literatures parallels with modern gut-brain science

Ancient Tamil	Modern gut–brain science parallel
Kuruntokai 63 – Sequence of eating sour mango then tart gooseberry, followed by rest ("eat a little and sleep")	Meal composition and timing influence satiety hormones, gut motility, and neurotransmitter production (e.g., serotonin) that affect sleep and mood.
Akanānūru 141 – Fragrant household as a source of joy and emotional well-being	Sensory food cues (aroma) and social eating environments influence limbic system activity via olfactory–vagal pathways, shaping mood and emotional bonding.
Siddha – Agni (digestive/metabolic fire)	Efficient digestion supports optimal nutrient breakdown and absorption; adequate precursors (tryptophan, tyrosine) for neurotransmitters are made available to the brain.
Siddha – Mukkuttram balance (Vali, Azhal, Iyam)	Homeostasis of gut microbiota, immune modulation, and autonomic regulation maintains mental stability; dysbiosis is linked to anxiety and depression.
Kuruntokai 156 – Ritual food vessels and seasonal abundance bringing household joy	Seasonal diets and traditional fermented foods can increase microbiome diversity, linked to better mood regulation and resilience to stress.
Thirukkural 942 – Eat only after earlier food is digested	Avoiding overeating and allowing digestive rest supports circadian alignment of gut microbiota and reduces inflammatory signalling that can impair brain function.

Gut microbiome- Atonement

In recent decades, studies have revealed complex relationships between hosts and their microbial communities, impacting various physiological processes beyond energy metabolism and digestion, including cognitive functions, emotional regulation, and behavioral outcomes. Since the pioneering study by Sudo et al. demonstrating that the maturation of brain functions related to stress responses is decisively influenced by gut microbiota, discoveries concerning the relationship between gut microbiota and the brain have surged exponentially.[5]

Changes in the human diet, including dietary patterns, habits, and food processing, have greatly influenced gut health. Moreover, modern life and its impact on the gut microbiome have also made fundamental changes to the spectrum of human illnesses,

shifting focus from traditional infectious diseases towards increasingly frequent mental diseases, such as depression. Integrating probiotics into daily consumption emerges as a crucial aspect of this modern strategy, as they can support gut microbial balance and play a role in the holistic treatment of mental conditions.[22]

Lifestyle choices such as smoking, alcohol consumption, stress, sleep, and exercise heavily influence the gut microbiome. Aerobic exercise is hypothesized to have a beneficial effect on the gut microbiome, as it promotes a diverse microbiome with increased levels of beneficial Firmicutes and reduced amounts of Bacteroides compared to sedentary individuals, whereas excessive endurance exercise, such as in athletes, can cause dysbiosis.[15,23, 24, 25]
Author suggests future directions on gut microbiome in Indian context as explained by Table.5.

Table.5. Suggested Future Directions on Gut Microbiome –Indian Context

Life Course						
At Birth	**Infant**	**Toddler**	**Pre School**	**School age**	**Adolescence and Adulthood**	**Aging**
Parenthood preparation for normal vaginal delivery. Private and Public sector Hospitals particulary Obstetrics and Gynaecological department, Maternity centres, Neonatal units and Paediatric departments to highlight on Living Life on	Exclusive Breast feeding. Formula feeding. Lactational counseling to teach on inclusion of microbiome	Universal immunization programme to blend with Nutritional Education on Microbiome Health Care Delivery system at Balvadi to program value based curriculum with	School organizations and Homes to cultivate values by a feather touch Thirukkural, Sangam literatures on healthy life style through Good Habbits Primary and Subcentre health centre level to plan awareness talks on gut	School Health Programmes on Food-Mood Journal towards microbiome form traditional literatures. Child Education classesor Course on Healthy life, Learn Psychobiotics, Probiotics, Prebiotics. Pracitce of Yoga, stress management	Exercise Yoga Meditation Cautious with medication	Day scheduling Walking Diet Yoga Grandparenthood to grandchildren, the cultural values processing. Elderly care takers to udate on microbiome essential for

Micerobiome		microbiome based teaching by Health workers.	microbiome during early life periods by Medical officers, nurses and health assistants	strategies and Habbits along with Peer group. Child-Parent sessions on Microbiome-Diet-Neurotransmitters triangle		aging risks

The cultural observations preserved in these verses thus provide a historical lens on the intuitive recognition that nourishment is not only a physical process but also a determinant of emotional and mental well-being.[26]

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