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REVIEW ARTICLE OPEN ACCESS

The Gut-Brain Axis: Microbial and Medicinal Effects on Mental Health and Neurodegeneration

Mohd. Sharique Katchhi[1], Bhagya Venkanna Rao[2]*, Babiker Bashir Haroun Baraka[2] and Shilpa Borehalli Mayegowda[3]

[1]Department of Pharmacy Practice, KLE College of Pharmacy, Bengaluru, Karnataka, India.
[2]Department of Pharmacology, KLE College of Pharmacy, Bengaluru, Karnataka, India.
[3]Department of Psychology, Christ-Deemed to be University, Bengaluru, Karnataka, India.

Abstract

This comprehensive review explores the intricate connections between microbial entities and various neuropsychiatric disorders, revealing the profound impact of viruses, bacteria, and therapeutic drugs on mental health. Extensive research has uncovered compelling evidence linking microbial elements to conditions such as depression, anxiety, schizophrenia, Parkinson's disease, stroke, bipolar disorder, obsessive-compulsive disorder (OCD), dementia, and Alzheimer's disease. Viral infections, including influenza A (H1N1), varicella-zoster virus, herpes simplex virus, and human immunodeficiency virus/received immune deficiency syndrome (HIV/AIDS), are implicated in the development and exacerbation of depression and anxiety. The review delves into the neuroinflammatory mechanisms triggered by viruses, shedding light on their role in conditions like schizophrenia, Parkinson's disease, and stroke. Moreover, bacterial involvement in psychiatric disorders is underscored, with dysbiosis in the gut microbiota associated with depression, anxiety, and schizophrenia. The dysregulation of neurotransmitter pathways and bidirectional communication along the gut-brain axis provides insights into the complex microbial modulation of mental health. Additionally, the review discusses the impact of therapeutic drugs on neuropsychiatric conditions, highlighting certain antiepileptic drugs, antibiotics, and other medications linked to increased risks of depression, anxiety, and cognitive issues. It emphasizes the importance of understanding the psychotropic effects of therapeutic drugs to optimize treatment strategies. Furthermore, investigations into the influence of microbes on neurodegenerative diseases reveal potential connections between the gut microbiota and conditions such as dementia and Alzheimer's disease. This review concludes by advocating for a holistic approach in psychiatry, recognizing the multifaceted role of viruses, microorganisms, and therapeutic medicines in shaping the landscape of neuropsychiatric disorders.

Keywords: Neuropsychiatric Disorders, Microbial Influences, Viruses, Bacteria, Therapeutic Drugs

***Correspondence:** bhagyavrao.klecop@gmail.com

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INTRODUCTION

Neuropsychiatry, the interdisciplinary discipline of neurology and psychiatry, has witnessed a paradigm shift in recent years as research sheds light on the complicated interaction between microbial factors and diverse neuropsychiatric disorders.[1] This burgeoning location of research is unveiling novel insights into the etiology, progression, and remedy of conditions inclusive of depression, anxiety, schizophrenia, Parkinson's disease, bipolar sickness, and obsessive-compulsive sickness (OCD). In parallel, microbial involvement in psychiatric situations has received recognition, with increased research addressing the function of gut dysbiosis in schizophrenia, bipolar sickness, and different mental fitness situations.[2] Additionally, global health projects underscore the requirement to think about the role of therapeutic capsules on mental well-being, aligning with emerging evidence suggesting that positive medications can also contribute to the improvement of depressive and irritating signs. This advent set the stage for a comprehensive exploration of the difficult relationships among viruses, microorganisms, therapeutic pills, and neuropsychiatric disorders, integrating proof from respectable resources.[3] As we delve into the complexities of this dynamic interplay, a deeper understanding of these relationships may also pave the manner for transformative advancements inside the analysis and control of neuropsychiatric conditions, providing a desire for stepped-forward intellectual fitness results on a global scale.

Depression

Depression is a mental health disorder where there is a constant feeling of sadness, hopelessness, and a lack of interest or pleasure in daily activities or may cause suicidal tendencies in severe cases. It is ranked as the single largest contributor to global disability with a 7.5% mark in 2015.[4]

Bacteria induced depression

The elaborate relationship between intestine bacterial groups and mental fitness has emerged as a charming location of study, in particular in information on the link between bacterial composition and improved melancholy.[5] Research has revealed noteworthy modifications in the gut microbiota, including a decrease in useful *Bifidobacteria* and *Lactobacillus*, coupled with an increase in potentially dangerous bacterial species.[6] These alterations correlate with depression, dropping mild on the impact of the intestine-brain axis. The transplantation of gut microorganisms into healthful mice has proven a correlation between microbial stability and depressive signs.[7] Additionally, experiments supplementing mice with beneficial bacteria have shown promising effects on depression,[8] highlighting the capacity for microbiota-based interventions. Further unraveling the mechanisms at play, it has been found that microorganisms play a pivotal position in the production of brief-chain fatty acids.[9] These molecules play an important role in neurotransmitter production, impacting both neuroendocrine function and the anxious machine.[10,11] The production of brief-chain fatty acids by way of microorganisms holds the key to knowing their acute and continual results on mind shape and features. This elaborate interaction among gut bacteria and intellectual health provides a compelling road for future studies and therapeutic interventions like transplanting healthy fecal microbiota,[12] this may new insights into the complex etiology of depression and pave the way for revolutionary processes to its prevention and treatment.

Virus induced depression

Recent investigations into the intestine have unveiled intriguing connections between viral changes and depressive states. Notably, people experiencing depression exhibit discernible adjustments of their gut viral composition,[13] emphasizing the capacity role of viruses in influencing mental health. One virus that has garnered attention in this context is the Adenovirus, with studies suggesting its potential to result in depressive signs and symptoms.[14] The impact of viruses on temper regulation is similarly elucidated by way of their have effect on neurotransmitter production. Viral infections may additionally disrupt the sensitive stability of neurotransmitters, contributing to the dysregulation of mood-related pathways.[15] Moreover, the function of viruses in instigating neuroinflammation has been implicated

as a key mechanism main to despair.[16] Viral-brought neuroinflammation might also cause a cascade of occasions that adversely affect neural circuits associated with mood and emotional law. In a promising revelation, research has verified that antiviral treatments can cause a reduction in depressive symptoms. This finding underscores the capacity therapeutic implications of concentrating on viral infections inside the management of despair, starting new avenues for using antiviral therapy which has shown a significant decrease in anxiety.[17]

Other microbes induced depression

The difficult courting between microbial entities and mental fitness extends past microorganisms and viruses, encompassing fungi, yeast, and parasites. *Candida albicans*, a not-unusual yeast, has been associated with inducing depression in women,[18] highlighting the numerous effects of microorganisms on mental well-being. Conversely, research has indicated that positive yeast traces can enhance melancholy signs and symptoms, suggesting a nuanced role of yeast in mental health.[19] Parasite infections, even as historically taken into consideration outside of the central nervous system (CNS), have emerged as potential contributors to mental illness.[20] The infection caused by parasitic infections impacts the brain and CNS through multiple pathways, the blood-mind barrier, activation of the vagus nerve, and immune responses. Surprisingly, harmless parasite *Toxoplasma gondii* has been implicated in suicide attempts.[21] Expanding therapeutic horizons, mycotherapy, or using fungi for treatment, has shown promise in addressing mood disorders.[22]

Drug induced depression

The impact of medications on mental health, especially depression, is a critical consideration in clinical practice. Antiepileptic drugs, barbiturates, vigabatrin, and topiramate exhibit depressive signs, affecting up to 10% of patients. Zonisamide, although information is restrained, indicates temper issues may additionally rise in about 7% of excessive dosage instances. Conversely, tablets like phenytoin, carbamazepine, and lamotrigine present decreased dangers (<1%) and might have fine effects on temper. Mechanisms underlying these results consist of GABA neurotransmission potentiation, folate deficiency, and pharmacodynamic interactions, emphasizing the importance of cautious tracking, particularly in people with a record of depression or familial predisposition.[23] Beyond antiepileptics, steroids like corticosteroids, various calcium channel blockers, and glycosides like digoxin have been continuously linked to depression through properly conducted research. Psychostimulant has withdrawal effects which can cause outstanding depression-like symptoms.[24] Additionally, beta-blockers, interferon alpha, and acne treatments like isotretinoin have been related to depressive results,[25] highlighting the want for cautious attention to intellectual fitness implications while prescribing or withdrawing these medicinal drugs (Table 1).

Anxiety

Anxiety is a normal and adaptive human reaction to stress or threats, characterized by feelings of nervousness, worry, and uneasiness. It is a natural part of the body's "fight-or-flight" response, preparing an individual to deal with a challenging situation. However, when anxiety becomes excessive, persistent, and disproportionate to the situation at hand, it can develop into an anxiety disorder. Indian epidemiological studies have reported prevalence of anxiety in India to be 5.6%-16.5%.[26]

Bacteria induced anxiety

The interplay between the intestine microbiota and mental health has grown. Recent studies showed that the intestine microbiota impacts neurotransmitter modulation.[27] The intestine microbiota composition in people with Stress-Anxiety Disorder (SAD) has identified wonderful microbial patterns, with improved tiers of *Anaeromassili bacillus* and *Gordonibacter* genera in SAD sufferers and a higher abundance of *Parasutterella excrementihominis* in healthy controls.[28] Furthermore, investigations into the impact of psychosocial stress on conduct and intestinal permeability have found a connection between pressure, gut characteristics, and mental health. Short-chain fatty acid (SCFA) remedy confirmed an excellent capacity to mitigate pressure-precipitated adjustments, enhancing

praise in search of behavior and reducing anxiety- and depressive-like behaviors. The impact of the gut microbiota on pressure signaling receptors in the hypothalamus and hippocampus emphasizes the complex relationship between intestine microbial stability and intellect.[29] Ampicillin exposure results in gastrointestinal inflammation mediated by *K. oxytoca*. Notably, remedy with lactobacilli has shown the ability to suppress neuroinflammation, supplying a glimpse into the therapeutic possibilities of microbial interventions.[30] The efficacy of fecal microbiota transplantation has shown alleviation in depressive symptoms underlines the dynamic position of the intestine microbiota.[31]

Virus induced anxiety

The complex relationship between viral infections and mental health has gained substantial attention in recent studies. Influenza A (H1N1), herpes simplex virus, human immunodeficiency virus (HIV), varicella-zoster virus, and hepatitis C, have been identified as precipitating factors in anxiety and melancholy.[32] The historical observations of the influenza epidemic, in which infected people displayed psychiatric disorders comparable to schizophrenia or melancholy, laid the foundation for understanding the linkages between viral sicknesses and mental illnesses.[33] Further research on intense acute respiratory syndrome (SARS-CoV-2) infection, causing COVID-19, has discovered a giant boom in early put-up-infection tension, depression, and sleep disturbances. Gender, earlier anxiety and depression signs and symptoms, and inpatient treatment had been identified as threat factors, with correlations located between mental health signs and inflammatory parameters.[34] Additionally, investigations into the neurological sequelae of SARS-CoV-2 contamination have recognized the virus's spike protein as a potential contributor to cognitive decline and anxiety-like behavior.[35] Animal studies related to Theiler's Murine Encephalomyelitis Virus (TMEV), support the perception of virus-prompted tension, with infected animals showing behaviors indicative of tension-like responses in diverse behavioral checks.[36] These findings collectively underscore the intricate impact of viral infections on intellectual health.

Other microbes induced anxiety

The rising field of studies exploring the connection between diverse microbes and tension underscores the profound impact of microorganisms on intellectual health. *Candida albicans*, a not unusual yeast, has been related to elevated anxiety-like conduct and altered pressure hormone production, in particular an expanded basal production of corticosterone (CORT) and dysregulation following acute stress.[37] Conversely, the administration of an oral sake yeast complement has proven neurobehavioral defensive results, on the whole through the activation of central A1 receptors.[38] Parasitic infections in addition amplify the spectrum of microorganisms influencing tension. Acanthocephalan parasites, regarded for infecting a diverse range of hosts, including human beings, were shown to effect the general anxiety-like circuitry in their intermediate hosts.[39] Similarly, episodes of mild malaria were related to alterations in mind cytokine profiles, specific behavioral dysfunction, microglial activation in the hippocampus, and a brief suppression of person hippocampal neurogenesis.[40] The contamination with *Plasmodium berghei* ANKA, a malaria-inflicting parasite, ended in lengthy-lasting disturbances, including memory-associated behavioral changes and a traumatic-like phenotype in mice.[41] These findings collectively emphasize the complex courting among microbial infections, starting from yeast to parasites, and tension-related behaviors. The diverse mechanisms through which these microbes exert their affect underscore the complexity of the intestine-mind axis and the ability for targeted interventions to modulate intellectual fitness consequences. As studies on this subject progress, a deeper knowledge of these microbe-precipitated anxiety mechanisms may additionally provide novel healing avenues for individuals tormented by anxiety problems.

Drug induced anxiety

The initiation of a new antidepressant regimen has been determined to cause emergent tension in a few sufferers, resulting in a new reason for the prescription of antianxiety medicines. This phenomenon is more familiar among young adults and women.[42] Additionally, opioids were related to an elevated chance of hysteria. The use of opioids, while effective in pain management,

seems to have an unintentional aspect effect of heightening anxiety tiers in a few people.[43] These observations underscore the importance of vigilant tracking and personalized strategies in prescribing medicinal drugs, in particular for those at risk of drug-triggered tension (Table 2).

Schizophrenia

Schizophrenia is a chronic and severe mental disorder that affects thought processes, perceptions, emotions, and behavior. Those with schizophrenia frequently experience symptoms like hallucinations, delusions, disorganized thinking, impaired cognitive functions, and challenges in social and occupational functioning. In India, which has a population of approximately 1.1 billion, the prevalence of schizophrenia is around 3 per 1000 individuals.[44]

Bacteria induced schizophrenia

Emerging studies show a compelling connection between bacterial translocation, immune machine dysregulation, and the manifestation of signs and symptoms in deficit schizophrenia. Increased bacterial translocation, coupled with deficits in the compensatory immune-regulatory gadget (CIRS), has been recognized as an ability driving force of poor signs and symptoms and neurocognitive impairments in individuals with deficit schizophrenia.[45] Notably, bacterial infection and translocation have been related to accelerated aggression in schizophrenia sufferers.[46] The observation posits that modification in the intestine microbiota composition leads to schizophrenia pathogenesis, especially by influencing tryptophan-kynurenine metabolism.[47] The findings propose that an imbalance in intestinal plants may lessen shielding elements at the same time as raising neurotoxins and inflammatory mediators, leading to neuronal and synaptic damage and in the end inducing schizophrenia.[48] While considering the capacity healing use of physiobiotics to deal with schizophrenia signs and symptoms, challenges arise due to psychophysiological variables, restricting the applicability of this method.[49] Nevertheless, understanding the elaborate interplay between gut microbiota and schizophrenia pathogenesis offers valuable insights, paving the manner for focused interventions that address the microbial element of this complicated intellectual health sickness.

Virus induced schizophrenia

Virus-precipitated schizophrenia is a complicated and intriguing location of research that explores the potential links between various viral infections and the improvement of schizophrenia in affected people. Numerous viruses, such as influenza virus, herpes simplex viruses 1 and a couple of others (HSV-1 and HSV-2), cytomegalovirus (CMV), Epstein-Barr virus (EBV), retrovirus, COVID-19, Borna virus, had been implicated in disrupting the everyday maturation of the fetal brain. These viruses can also exert their impact actively or through immune-induced mediators like cytokines, ultimately contributing to the onset of schizophrenia.[50] Studies display that prenatal viral infections will have a ways-accomplishing effect, disrupting the structure and gene expression of important tissues consisting of the placenta, hippocampus, and prefrontal cortex. Interestingly, the deleterious outcomes located in uncovered offspring occur without the presence of viral RNAs inside the goal tissues.[51] Individuals born seropositive for viral sellers show off a drastically accelerated threat of growing schizophrenia, emphasizing the potential role of viral infections as an etiological factor.[52,53] Despite methodological challenges, converging proof underscores the multiplicity of consequences that the influenza virus, specifically, will have on both prenatal and postnatal processes. Disruptions in these methods might also contribute to an increased danger of growing schizophrenia or acute psychoses in adulthood.[54] While the right pathogenesis of schizophrenia and the unique contribution of viral infections remain undefined, ongoing research sheds light on the complex interplay between viral exposures at some stage in crucial developmental periods and the subsequent chance of psychiatric problems.

Other microbes induced schizophrenia

The difficult courting between the human microbiome and intellectual health has won attention, specifically regarding the position of yeast species like *Saccharomyces cerevisiae* and *Candida albicans*. In a bad microbiome, an imbalance in these commensal yeast species has

been found, with increased degrees related to schizophrenia. This highlights the ability influence of intestine microbiota on mental fitness results.[55] Interestingly, red yeast rice (RYR), recognized for its lipid-decreasing results, gives extra benefits as it exhibits antioxidant and anti-inflammatory houses. Beyond its conventional use, RYR supplementation emerges as a promising method for addressing symptoms associated with schizophrenia.[56] The antioxidant and anti-inflammatory outcomes of RYR may contribute to mitigating the impact of fungal imbalances inside the microbiome, probably influencing the complicated interplay among the intestine and the brain. The capability link among fungal exposures, microbiome imbalance, and intellectual health underscores the importance of considering holistic methods in addressing conditions like schizophrenia. While RYR supplementation holds promise, in addition studies is needed to clarify the appropriate mechanisms and set up the efficacy of this method. Integrating insights from microbiome research into mental health strategies opens new avenues for information and probably treating situations that involve elaborate interactions between the intestine and the vital worried machine.

Drug induced Schizophrenia

The association between addictive drug use or the misuse of prescribed medicinal drugs and the onset of psychosis underscores a complex interplay between substances and mental health. Psychotic symptoms, including hallucination, anhedonia, and disrupted executive capabilities, regularly show up in individuals dealing with drug-induced psychoses (DIP). These signs carefully reflect the ones observed in schizophrenia.[57] Notably, many drugs like Barbiturates, alcohol, atropine, both at once and via withdrawal effects, can set off a psychic reaction corresponding to Bonhoeffer's "exogenous reaction syndrome," characterized with the aid of impaired focus, memory, orientation, and consciousness.[58] However, the psychoses discussed here showcase minimal or absent impairment of consciousness, similar to idiopathic psychoses like schizophrenia. Research comparing stimulant-induced cocaine and phencyclidine (PCP)-caused psychoses with idiopathic schizophrenia well-known shows both similarities and distinctions. While positive First Rank Schneiderian Symptoms (FRSS) are commonplace, disparities exist. Cocaine-induced psychosis is connected extra with severe suspiciousness and paranoia, while PCP-prompted psychosis is characterized by means of delusions of bodily energy, altered sensations, and uncommon reviews.[59] These findings emphasize the need for an integrative model considering various psychogenic capsules to comprehensively recognize psychotic signs in schizophrenia. Tailoring pharmacologic interventions to unique components of those signs may additionally enhance treatment efficacy, offering a nuanced approach to drug-triggered and idiopathic psychosis (Table 3).

Parkinson's disease

Parkinson's disease is a neurodegenerative disorder that mainly impacts movement. It is marked by the gradual loss of dopamine-producing neurons in the brain, especially in the substantia nigra region. Dopamine is a neurotransmitter that plays a crucial role in regulating movement and coordination. It is estimated that about 10 million people worldwide (around 0.3% of the global population) and 1% of individuals over the age of 60 are affected by Parkinson's disease.[60]

Bacteria induced Parkinson's disease

Emerging studies suggests an ability hyperlink among bacterial interest and the improvement of Parkinson's sickness (PD). Specifically, an expanded presence of hydrogen sulfide (H_2S)-producing bacteria inside the colon, especially from the *Desulfovibrionaceae* and *Enterobacteriaceae* households, can also contribute to PD pathogenesis.[61] These microorganism, observed in better amounts within the microbiome of people with PD, release H_2S, which could penetrate cellular membranes and trigger occasions within cells, including the release of cytochrome c from mitochondria and an increase in reactive oxygen species. These methods may also cause the formation of alpha-synuclein oligomers and fibrils, feature of PD. Moreover, the examine highlights the potential function of *P. gingivalis*, a bacterium allied with gum ailment, in PD pathology. The presence of *P. gingivalis* LPS and gingipain protease in odd blood clotting found in PD samples indicates a potential hyperlink between this bacterium and PD,

warranting further investigation.[62] They have a look at additionally notes that influenza infections may also elevate PD hazard via selling the overgrowth of H_2S-generating bacteria within the colon and duodenum. Furthermore, medicinal drug with L-dopa and entacapone, generally utilized in PD treatment, impacts the propotional abundance of specific bacterial genera, which includes *Peptoniphilus, Finegoldia, Faecalibacterium, Fusicatenibacter, Anaerococcus, Bifidobacterium, Enterococcus,* and *Ruminococcus*.[63] There is elaborate dating between intestine microbiota and medicine in individuals with PD.[64] Overall, those findings recommend an ability position of microorganism-caused processes in the systemic inflammation and hypercoagulable pathology related to Parkinson's disease.

Virus induced Parkinson's disease

The difficult connections between Parkinson's sickness (PD), viral infections, and the impact of COVID-19, emphasizing the parallels among RNA viral pathways and neurodegenerative tactics in PD. The Braak hypothesis, detailing the onset and progression of PD, aligns with the pathogenic nature, molecular mechanisms, and symptom development found in SARS-CoV-2 infection and COVID-19.[65] Growing evidence supports the idea that viral infections and resulting viral-mediated neuroinflammation may contribute to the development of idiopathic Parkinson's disease (PD). Viruses have been found to affect α-synuclein oligomerization and the autophagic clearance of abnormal intracellular protein aggregations, both of which are crucial in the pathogenesis of PD. A study examined the effects of viral neuroinflammatory priming on α-synuclein aggregate-induced neuroinflammation and neurotoxicity in the rat nigrostriatal pathway. The administration of a viral mimetic (poly I) worsened α-synuclein aggregate-induced neuropathological and behavioral effects, suggesting a potential role for viral infections in the etiology and pathogenesis of PD.[66] Despite over 2 hundred years in view that its first description, the precise motive of PD remains elusive. Recent epidemiological research has reignited scientific hobby in exploring microbial interactions with the crucial apprehensive device, difficult the previously disregarded affiliation among positive viral infections and neurodegenerative illnesses.[67] PD is characterized through the revolutionary lack of dopaminergic neurons, and the interaction between genetic and environmental factors can also contribute to ailment susceptibility.[68] Inflammation, particularly immune dysfunctions, is increasingly more recognized as a part of the neurodegenerative process in PD, shedding mild on the capability nexus between environmental and genetic elements and the position of unusual immune feature in sickness development.

Other microbes induced Parkinson's disease

A currently discovered melatonin analogue, 6-hydroxy-N-acetyl-β-oxotryptamine, derived from the marine fungus *Penicillium* sp. KMM 4672, demonstrated neuroprotective consequences in Parkinson's disorder (PD) cell fashions.[69] Alongside other compounds from various fungi, it exhibited various levels of safety against neurotoxicity induced through 6-hydroxydopamine and paraquat. The new melatonin analogue confirmed advanced effectiveness in comparison to melatonin itself. Additionally, changes in risky natural compounds (VOCs) and fungal composition were observed in PD sufferers, indicating a distinct metabolome and mycobiome. This suggests that fungal dysbiosis may make a contribution to the pathogenesis of Parkinson's ailment.[70]

Drug induced Parkinson's disease

Drug-caused Parkinsonism (DIP) ought to be suspected whilst sufferers undergoing drug remedy showcase parkinsonian symptoms along with tension, tremors, or postural instability. This condition, a commonplace purpose of secondary Parkinsonism, is regularly linked to antipsychotic medications, different neuroleptics, and calcium-channel blockers. The threat is dose-established, mainly with dopamine D_2 striatal occupancy, even though 2nd generation bizarre antipsychotics pose a decrease chance. Other implicated pills include antidepressants, antivirals, anti-arrhythmics, lithium, and valproic acid. Symptoms typically regress about three months after discontinuation of the causative drug, however in some cases, they persist, main to an idiopathic Parkinson's disorder diagnosis.[71] A take a look at discovered that DIP sufferers, specifically men, face an expanded

risk of developing idiopathic Parkinson sickness (IPD). The affiliation is noteworthy within the first 12 months of observe-up, and sure capsules, like calcium channel blockers, may also increase the danger of IPD in DIP patients. This underscores the importance of cautious tracking for potential IPD occurrence in individuals who expand DIP. The hyperlink among DIP and IPD shows a triggering impact through causative capsules on people with underlying subclinical IPD pathology (Table 4).[72]

Stroke

A stroke, or cerebrovascular accident (CVA), is a medical condition resulting from an interruption of blood supply to a specific area of the brain. This can occur due to a blockage in the blood vessels (ischemic stroke) or bleeding into the brain tissue (hemorrhagic stroke). The interruption of blood flow deprives brain cells of oxygen and nutrients, causing cell damage or death. Between 1990 and 2019, there has been a 70% increase in stroke cases.[73]

Bacteria induced stroke

Changes in gut microbiota composition, known as gut dysbiosis, along with impaired intestinal permeability, can affect the signaling profile of intestinal bacterial metabolites to the brain. Metabolites derived from the microbiota, such as short-chain fatty acids (SCFAs), bile acids (BAs), trimethylamine N-oxide (TMAO), lipopolysaccharides (LPS), and phenylacetylglutamine (PAGln), can have both beneficial and harmful effects on organs outside the gut, including the brain. These metabolites are increasingly recognized as biomarkers and mediators of ischemic stroke (IS), although their specific roles are still not fully understood.[74] Exploring these merchandise and metabolites in-intensity may additionally unveil novel healing avenues for IS. Studies have proven that stroke induces gut permeability and bacterial translocation, mainly in younger mice, with differing bacterial species seeding in peripheral organs among young (*Escherichia*) and elderly (*Enterobacter*) mice. Aged mice showcase a more pronounced septic response characterized by continual hypothermia, weight reduction, and immune dysfunction publish-stroke as compared to their younger counterparts.[75] Furthermore, research related to ampicillin-handled mice discovered an affiliation between microbiota signature, decreased gut irritation, lengthy-time period favorable consequences, ameliorated stereotypic conduct, and diminished brain tissue loss.[76] These findings propose that centered change of the microbiome, particularly specializing in microbial enzymatic pathways, could doubtlessly serve as a preventive approach for people at high chance of stroke, emphasizing the important function of the intestinal microbiota in brief- and long-time period results of ischemic stroke.

Virus induced stroke

Virus-induced strokes represent a complex and multifaceted component of cerebrovascular pathology. Influenza virus infection, for example, triggers a cytokine cascade that exacerbates ischemic mind harm and heightens the hazard of intracerebral hemorrhage following tissue plasminogen activator remedy. A promising healing method involves α7 nicotinic acetylcholine receptor agonists to mitigate cytokine production inside the proinflammatory context of stroke.[77] Several viruses were implicated in stroke pathogenesis, with varicella zoster virus (VZV), cytomegalovirus (CMV), and human immunodeficiency virus (HIV) being distinguished examples. VZV, particularly, has been linked to ischemic and hemorrhagic strokes, aneurysms, arterial ectasia, and cerebral arterial dissection. CMV is suggested to contribute to the formation of arteriosclerotic plaques in cerebral arteries, even as HIV may additionally boom stroke danger, doubtlessly through either HIV contamination or opportunistic VZV contamination in immunocompromised people.[78] Hepatitis C virus (HCV) contamination has also emerged as an issue related to an extended hazard of stroke, as indicated via a meta-evaluation. This locating underscores the want for further prospective cohort studies to establish the affiliation and unravel the underlying biological mechanisms.[79] Furthermore, herpes simplex virus (HSV) infections, which includes meningitis or encephalitis, can complicate the evolution of ischemic strokes. Clinicians must recall HSV as a capability cause, in particular in younger sufferers with ischemic strokes of unknown beginning. Overall, expertise the various methods wherein viral infections

contribute to stroke pathophysiology is essential for correct clinical diagnoses and the development of targeted healing techniques.[80]

Other microbes induced stroke

Consider ischemic stroke secondary to Central Nervous System (CNS) fungal infections in sufferers with recurrent or innovative cryptogenic strokes, regardless of immune popularity and cerebrospinal fluid profile. Distinct characteristics exist for CNS yeast and mold infections, warranting precise diagnostic techniques. Depending on scientific suspicion, a comprehensive diagnostic method, including spinal fluid evaluation and biopsy, must be pursued for correct identification and appropriate management.[81]

Drug induced stroke

Drug abuse, together with stimulants like amphetamines and cocaine, poses a significant chance for each hemorrhagic and ischemic strokes. Substances like "crack" cocaine can also result in acute ischemic and hemorrhagic strokes, even as cocaine hydrochloride is extra associated with hemorrhagic strokes. Cannabis, synthetic cannabinoids, and opioids/heroin have conflicting findings concerning their association with stroke. Anabolic androgenic steroids are linked to cardiotoxicity and atherothrombotic phenomena, increasing the chance of ischemic stroke.[82] Additionally, oral and intravenous medicines, including oral contraceptive tablets and anticoagulants, can precipitate drug-prompted strokes, making toxicological screening critical, in particular in young stroke sufferers (Table 5).[83]

Other Psychiatric and Neurodegenerative disorders

Bipolar Disorder

Bipolar disorder, a complex spectrum of mood problems characterized with the aid of fluctuations in temper and electricity tiers, has been associated with vast changes inside the gut microbiome. The bidirectional verbal exchange among the microbiome, intestine, and brain, known as the microbiome-intestine-brain (MGB) axis, performs a crucial position in retaining physical and intellectual health. Recent research has furnished initial proof of intestine microbial adjustments in individuals with bipolar ailment, highlighting the ability involvement of the MGB axis within the pathogenesis of this condition.[84] On the pharmacological front, the use of antidepressants in bipolar disorder poses challenges. Unlike in unipolar melancholy, wherein the threat of switching into mania with antidepressants is minimum, individuals with bipolar sickness, even when treated with temper stabilizers, may additionally face a better hazard of such temper shifts. Some studies advocate that tricyclic antidepressants may also double the incidence of manic switches. Additionally, cycle acceleration has been located in a subgroup of patients on preservation treatment with tricyclic antidepressants. Despite the capacity risks related to antidepressant use in bipolar ailment, determining the maximum judicious remedy set of rules remains a mission. Clinical trials comparing unique processes, which include adjunctive temper stabilizers as opposed to unimodal antidepressants, are eagerly awaited to establish comparative danger-gain ratios. Identification of scientific and biological markers for antidepressant responsivity holds promise for refining remedy strategies and choosing the simplest modality for coping with depression breaking via prophylaxis with mood stabilizers in bipolar disease (Table 6).[85]

Table 1. Summary of Microbes and Drugs Inducing Depression

Microorganism	Effect on Depression
Bifidobacteria and *Lactobacillus*	Decrease in their count, increase risk of depression
Adenovirus	It triggers depressive symptoms
Toxoplasma gondii	It reportedly induce society
Fungi	Mycotherapy, fungi treatment to cure depression
Candida albicans	It induces depression in women
Summary of Drugs Inducing Depression	
Class Of Drugs	Drug inducing Depression
Anticonvulsants	Barbiturates, Vigabatrin, Topiramate
Steroids	Corticosteroids
Anticancer	Interferon alpha
Cardiac Glycosides	Digoxin
Psychiatry	Psychostimulants
Anti-acne	Isotretinoin

Table 2. Summary Of Microbes and drug inducing Anxiety

Microorganism	Effect on Anxiety
Anaeromassili bacillus	Increases in Anxiety
Gordonibacter genera	Increases in Anxiety
Candida albicans	Cause increase in Anxiety
Oral Yeast Supplements	Help in controlling anxiety
Acanthocephalan & Malaria Parasite	Cause Alteration in anxiety related behaviour
Influenza	Increase Anxiety
Varicella-zoster virus	Increase Anxiety
Herpes simplex virus	Increase Anxiety
HIV	Increase Anxiety
SARS-CoV-2	Spike protein affect Anxiety
Hepatitis C	Increase Anxiety
Summary of Drug Inducing Anxiety	
Class Of Drugs	Drug inducing Anxiety
Anti-depressant	New regimen of antidepressants
Analgesics	Opioids

Table 3. Summary of Microbe and Drugs inducing Schizophrenia

Microorganism	Effect on Schizophrenia
Gut Bacteria	Decreases in Schizophrenia patients
Influenza Virus	Prenatal and postnatal infection, increases the chances of infection in adulthood
Herpes simplex Virus 1 & 2	Increases the chances of Schizophrenia
Cytomegalovirus	Increases the chances of Schizophrenia
Ebola Virus	Increases the chances of Schizophrenia
Retrovirus	Increases the chances of Schizophrenia
Covid-19	Increases the chances of Schizophrenia
Borna Virus	Increases the chances of Schizophrenia
Candida albicans	Increases the chances of Schizophrenia
Saccharomyces cerevisiae	Increases the chances of Schizophrenia
Red Yeast	Supplementations decrease Schizophrenia symptoms
Fungus	Increase risk for Schizophrenia
Summary of Drugs Inducing Schizophrenia	
Class Of Drugs	Drugs inducing Schizophrenia
CNS - Depressant	Barbiturates, Alcohol, Atropine
CNS - Stimulant	Cocaine & Phencyclidine

Obsessive compulsive disorder

Obsessive-Compulsive Disorder (OCD) is a persistent intellectual health condition characterized by way of intrusive mind (obsessions) and repetitive behaviors or intellectual acts (compulsions) completed to relieve misery. These rituals can significantly impair every day functioning and quality of existence. In the area of immunological strategies, a specific subtype known as Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) hyperlinks OCD to streptococcal infections like scarlet fever or strep throat. Referred to as the "autoimmune OCD subtype," PANDAS

Table 4. Summary Of Microbes and Drugs inducing Parkinson's disease

Microorganism	Effect on Parkinson's Disease
Desulfovibrionaceae	Increases the risk for Parkinson's Disease
Enterobacteriaceae	Increases the risk for Parkinson's Disease
P. Gingivalis	Increases the risk for Parkinson's Disease
Covid-19	Increases the risk for Parkinson's Disease
Influenza	Increases the risk for Parkinson's Disease
Melatonin from fungus Penicillium	Neuroprotective in Parkinson's Disease
Summary of Drug Inducing Parkinson's Disease	
Class Of Drug	Drugs Inducing Parkinson's Disease
Antidepressants	Tricyclic Antidepressants
Anticonvulsants	Valproic Acid

Table 5. Summary of Microbes and Drug inducing Stroke

Microorganism	Effect on Stroke
Gut Bacteria	Decrease in case of stroke
Influenza	Increases the risk of stroke
CNS fungal Infection causer	Increases the risk of stroke
Summary of Drug causing Stroke	
Class Of Drug	Drug Causing Stroke
CNS Stimulants	Amphetamines, Cocaine
Analgesics	Opioids, Cannabis

Table 6. Summary of Microbes and Drugs Causing other Psychiatric and Neurodegenerative Disorders

Disorder	Microbes	Drugs
Bipolar Disorder	Gut Microbiota	Tricyclic antidepressants
Obsessive-Compulsive Disorder	Streptococcal Infections	2nd generation antipsychotics
Dementia	*Treponema pallidum*	benzodiazepines, antihypertensives and drugs with anticholinergic activity
Alzheimer's Disease	Herpes simplex virus type 1 (HSV1), Chlamydia pneumoniae, spirochaete bacteria, and fungal infections	-

is characterized by the onset of OCD signs and symptoms following such infections, highlighting the capability position of immunological elements in OCD pathophysiology.[86] Additionally, second-generation antipsychotics (SGAs), mainly clozapine, olanzapine, and risperidone, have been related to de novo emergence or precipitation of obsessive-compulsive symptoms (OCS) in people with schizophrenia. Case reports recommend a hyperlink between these SGAs and comorbid OCS, probably compromising the general treatment blessings and hindering the recuperation manner in sufferers with schizophrenia.[87]

Dementia

Dementia is a huge term describing a set of cognitive disorders characterized by memory loss, impaired reasoning, and a decline in different mental abilities that intrude with everyday life. It is regularly related to structural and purposeful mind abnormalities. In the context of microbial causes, spirochete microorganism, specifically *Treponema pallidum*, are connected to syphilitic dementia, leading to the deposition of gray rely in various brain areas. Spirochete colonies, located in the cerebral brain, are involved in the pathology of syphilitic dementia.[88] On the drug-induced front, over 10% of patients attending memory clinics can also experience iatrogenic dementia. Benzodiazepines, anti-hypertensives, and drugs with anticholinergic residences are frequently implicated, potentially producing distinct styles of neuropsychological deficits.[89]

Alzheimer's disease

Alzheimer's sickness (AD) is a neurodegenerative disorder characterized by neuronal loss, synaptic dysfunction, and the accumulation of amyloid-β (Aβ) peptide and atypical tau protein, main to cognitive decline and reminiscence loss. It is the most common cause of dementia among the aged. Researchers and clinicians raised concerns regarding the role of particular microbes in AD progression. Studies implicate herpes simplex virus type 1 (HSV1), *Chlamydia pneumoniae*, spirochaete bacteria, and fungal infections inside the etiology of AD. The concept suggests that persistent or latent infections, together with HSV1, can also contribute to the improvement of Alzheimer's, challenging conventional perspectives on its causative elements.[90]

CONCLUSION

Presents a comprehensive overview of the microbe, the drug causes psychiatric and global concern regarding neuropsychiatric disorders. Our review concludes that the correlation between neuroscience and microbiology highlights the important role of microbial entities in shaping neuropsychiatric disorders. This convergence has highlighted the bidirectionality along the gut-brain axis; any impact viral infections may have on neuroinflammatory processes and mental health issues can arise from dysbiosis caused by bacteria. By understanding how these relationships intertwine with viruses, bacteria, and therapeutic

drugs, we can develop new approaches to treatment and individualized interventions in psychiatry. Thus, this comprehensive outlook is instrumental in enhancing care strategies and improving mental health outcomes for persons with neurologic-psychiatric complaints.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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All datasets generated or analyzed during this study are included in the manuscript.

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Not applicable.

REFERENCES

1. Steinert T. Psychiatry shifting to a new paradigm. *Indian J Med Res.* 2020;152(4):329-331. doi: 10.4103/ijmr.IJMR_3913_20
2. Goswami A, Wendt FR, Pathak GA, et al. Role of microbes in the pathogenesis of neuropsychiatric disorders. *Front Neuroendocrinol.* 2021;62:100917. doi: 10.1016/j.yfrne.2021.100917
3. Tango RC. Psychiatric side effects of medications prescribed in internal medicine. *Dialogues Clin Neurosci.* 2003;5(2):155-165. doi: 10.31887/DCNS.2003.5.2/rcasagrandetango
4. Lim GY, Tam WW, Lu Y, Ho CS, Zhang MW, Ho RC. Prevalence of depression in the community from 30 countries between 1994 and 2014. Scientific reports. 2018;8(1):2861. doi: 10.1038/s41598-022-19021-x
5. Liu L, Wang H, Chen X, Zhang Y, Zhang H, Xie P. Gut microbiota and its metabolites in depression: from pathogenesis to treatment. *EBioMedicine.* 2023;90:104527. doi: 10.1016/j.ebiom.2023.104527
6. Li J, Wang J, Wang M, et al. *Bifidobacterium*: a probiotic for the prevention and treatment of depression. *Front Microbiol.* 2023;14:1174800. doi: 10.3389/fmicb.2023.1174800
7. Knudsen JK, Michaelsen TY, Bundgaard-Nielsen C, et al. Faecal microbiota transplantation from patients with depression or healthy individuals into rats modulates mood-related behaviour. *Sci Rep.* 2021;11(1):21869. doi: 10.1038/s41598-021-01248-9
8. Gao J, Zhao L, Cheng Y, et al. Probiotics for the treatment of depression and its comorbidities: A systemic review. *Front Cell Infect Microbiol.* 2023;13:1167116. doi: 10.3389/fcimb.2023.1167116
9. Silva YP, Bernardi A, Frozza RL. The role of short-chain fatty acids from gut microbiota in gut-brain communication. *Front Endocrinol*. 2020;11:25. doi: 10.3389/fendo.2020.00025
10. O'Riordan KJ, Collins MK, Moloney GM, et al. Short chain fatty acids: Microbial metabolites for gut-brain axis signalling. *Mol Cell Endocrinol.* 2022;546:111572. doi: 10.1016/j.mce.2022.111572
11. Mirzaei R, Bouzari B, Hosseini-Fard SR, et al. Role of microbiota-derived short-chain fatty acids in nervous system disorders. *Biomed Pharmacother.* 2021;139:111661. doi: 10.1016/j.biopha.2021.111661
12. Hu B, Das P, Lv X, et al. Effects of 'healthy' fecal microbiota transplantation against the deterioration of depression in fawn-hooded rats. *mSystems*. 2022;7(3):e0021822. doi: 10.1128/msystems.00218-22
13. Wu J, Chai T, Zhang H, et al. Changes in gut viral and bacterial species correlate with altered 1,2-diacylglyceride levels and structure in the prefrontal cortex in a depression-like non-human primate model. *Transl Psychiatry.* 2022;12(1):74. doi: 10.1038/s41398-022-01836-x
14. Karimi Z, Chenari M, Rezaie F, Karimi S, Parhizgari N, Mokhtari-Azad T. Proposed pathway linking respiratory infections with depression. *Clin Psychopharmacol Neurosci.* 2022;20(2):199-210. doi: 10.9758/cpn.2022.20.2.199
15. Udina M, Navines R, Egmond E, et al. Glucocorticoid receptors, brain-derived neurotrophic factor, serotonin and dopamine neurotransmission are associated with interferon-induced depression. *Int J Neuropsychopharmacol.* 2016;19(4):pyv135. doi: 10.1093/ijnp/pyv135
16. Yu X, Wang S, Wu W, et al. Exploring new mechanism of depression from the effects of virus on nerve cells. *Cells.* 2023;12(13):1767. doi: 10.3390/cells12131767
17. Durcan E, Hatemi I, Sonsuz A, Canbakan B, Ozdemir S, Tuncer M. The effect of direct antiviral treatment on the depression, anxiety, fatigue and quality-of-life in chronic hepatitis C patients. *Eur J Gastroenterol Hepatol*. 2020;32(2):246-250. doi: 10.1097/MEG.0000000000001501
18. Irving G, Miller D, Robinson A, Reynolds S, Copas AJ. Psychological factors associated with recurrent vaginal candidiasis:a preliminary study. *Sex Transm Infect.* 1998;74(5):334-338. doi: 10.1136/sti.74.5.334
19. Mikkelsen K, Hallam K, Stojanovska L, Apostolopoulos V. Yeast based spreads improve anxiety and stress. *J Funct Foods.* 2018;40:471-476. doi: 10.1016/j.jff.2017.11.034
20. Lampard-Scotford AR, McCauley A, Kuebel JA, Ibbott R,

Mutapi F. Impact of parasitic infection on mental health and illness in humans in Africa: A systematic review. *Parasitology.* 2022;149(8):1003-1018. doi: 10.1017/S0031182022000166

21. Bak J, Shim SH, Kwon YJ, et al. The Association between Suicide Attempts and *Toxoplasma gondii* Infection. *Clin Psychopharmacol Neurosci.* 2018;16(1):95-102. doi: 10.9758/cpn.2018.16.1.95
22. Meade E, Hehir S, Rowan N, Garvey M. Mycotherapy: Potential of fungal bioactives for the treatment of mental health disorders and morbidities of chronic pain. *J Fungi*. 2022;8(3):290. doi: 10.3390/jof8030290
23. Mula M, Sander JW. Negative effects of antiepileptic drugs on mood in patients with epilepsy. *Drug Saf.* 2007;30(7):555-567. doi: 10.2165/00002018-200730070-00001
24. Patten SB, Love EJ. Drug-induced depression. *Psychother Psychosom*. 1997;66(2):63-73. doi: 10.1159/000289110
25. Patten SB, Barbui C. Drug-induced depression: a systematic review to inform clinical practice. *Psychotherapy and psychosomatics.* 2004;73(4):207-15. doi: 10.1159/000077739
26. Manjunatha N, Jayasankar P, Suhas S, et al. Prevalence and its correlates of anxiety disorders from India's National Mental Health Survey 2016. *Indian J Psychiatry*. 2022;64(2):138-142. doi: 10.4103/indianjpsychiatry.indianjpsychiatry_964_21
27. Huang F, Wu X. Brain neurotransmitter modulation by gut microbiota in anxiety and depression. *Front Cell Dev Biol.* 2021;9:649103. doi: 10.3389/fcell.2021.649103
28. Butler MI, Bastiaanssen TFS, Long-Smith C, et al. The gut microbiome in social anxiety disorder: Evidence of altered composition and function. *Transl Psychiatry.* 2023;13(1):95. doi: 10.1038/s41398-023-02325-5
29. van de Wouw M, Boehme M, Lyte JM, et al. Short-chain fatty acids: microbial metabolites that alleviate stress-induced brain-gut axis alterations. *J Physiol.* 2018;596(20):4923-4944. doi: 10.1113/JP276431
30. Jang HM, Lee HJ, Jang SE, Han MJ, Kim DH. Evidence for interplay among antibacterial-induced gut microbiota disturbance, neuro-inflammation, and anxiety in mice. *Mucosal Immunol.* 2018;11(5):1386-1397. doi: 10.1038/s41385-018-0042-3
31. Meyyappan AC, Forth E, Wallace CJK, Milev R. Effect of fecal microbiota transplant on symptoms of psychiatric disorders: a systematic review. *BMC Psychiatry.* 2020;20(1):299. doi: 10.1186/s12888-020-02654-5
32. Coughlin SS. Anxiety and Depression: Linkages with viral diseases. *Public Health Rev.* 2012;34(2):7. doi: 10.1007/BF03391675
33. Tomonaga K. Virus-induced neurobehavioral disorders: mechanisms and implications. *Trends Mol Med*. 2004;10(2):71-7. doi: 10.1016/j.molmed.2003.12.001
34. Yyldyzeli SO, Kocakaya D, Saylan YH, et al. Anxiety, depression, and sleep disorders after COVID-19 infection. *Cureus.* 2023;15(7):e42637. doi: 10.7759/cureus.42637
35. Oh J, Cho WH, Barcelon E, Kim KH, Hong J, Lee SJ. SARS-CoV-2 spike protein induces cognitive deficit and anxiety-like behavior in mouse via non-cell autonomous hippocampal neuronal death. *Sci Rep*. 2022;12(1):5496. doi: 10.1038/s41598-022-09410-7
36. Umpierre AD, Remigio GJ, Dahle EJ, et al. Impaired cognitive ability and anxiety-like behavior following acute seizures in the Theiler's virus model of temporal lobe epilepsy. *Neurobiol Dis.* 2014;64:98-106. doi: 10.1016/j.nbd.2013.12.015
37. Markey L, Hooper A, Melon LC, et al. Colonization with the commensal fungus *Candida albicans* perturbs the gut-brain axis through dysregulation of endocannabinoid signaling. *Psychoneuroendocrinology*. 2020;121:104808. doi: 10.1016/j.psyneuen.2020.104808
38. Bozorgi H, Rashidy-Pour A, Moradikor N, Zamani M, Motaghi E. Neurobehavioral protective effects of Japanese sake yeast supplement against chronic stress-induced anxiety and depression-like symptoms in mice:Possible role of central adenosine receptors. *Psychopharmacology* (Berl). 2024;241(2):401-416. doi: 10.1007/s00213-023-06496-3
39. Cozzarolo CS, Perrot-Minnot MJ. Infection with an Acanthocephalan helminth reduces anxiety-like behaviour in crustacean host. *Sci Rep*. 2022;12(1):21649. doi: 10.1038/s41598-022-25484-9
40. Guha SK, Tillu R, Sood A, et al. Single episode of mild murine malaria induces neuroinflammation, alters microglial profile, impairs adult neurogenesis, and causes deficits in social and anxiety-like behavior. *Brain Behav Immun.* 2014;42:123-37. doi: 10.1016/j.bbi.2014.06.009
41. de Sousa LP, de Almeida RF, Ribeiro-Gomes FL, et al. Long-term effect of uncomplicated *Plasmodium berghei* ANKA malaria on memory and anxiety-like behaviour in C57BL/6 mice. *Parasit Vectors*. 2018;11(1):191. doi: 10.1186/s13071-018-2778-8
42. Li Z, Pfeiffer PN, Hoggatt KJ, Zivin K, Downing K, Ganoczy D, Valenstein M. Emergent anxiety after antidepressant initiation: a retrospective cohort study of Veterans Affairs Health System patients with depression. *Clin Ther.* 2011;33(12):1985-1992.e1. doi: 10.1016/j.clinthera.2011.11.010
43. Leung J, Santo T, Colledge-Frisby S, et al. Mood and anxiety symptoms in persons taking prescription opioids:A systematic review with meta-analyses of longitudinal studies. *Pain Med.* 2022;23(8):1442-1456. doi: 10.1093/pm/pnac029
44. Loganathan S, Murthy RS. Living with schizophrenia in India: Gender perspectives. *Transcult Psychiatry.* 2011;48(5):569-84. doi: 10.1177/1363461511418872
45. Maes M, Kanchanatawan B, Sirivichayakul S, Carvalho AF. In Schizophrenia, increased plasma IgM/IgA responses to gut commensal bacteria are associated with negative symptoms, neurocognitive impairments, and the deficit phenotype. *Neurotox Res*. 2019;35(3):684-698. doi: 10.1007/s12640-018-9987-y
46. Wang C, Zhang T, He L, et al. Bacterial translocation associates with aggression in Schizophrenia inpatients. *Front Syst Neurosci.* 2021;15:704069. doi: 10.3389/fnsys.2021.704069
47. Zhu F, Guo R, Wang W, et al. Transplantation of microbiota from drug-free patients with schizophrenia causes schizophrenia-like abnormal behaviors and dysregulated kynurenine metabolism in mice. *Mol*

Psychiatry. 2020;25(11):2905-2918. doi: 10.1038/s41380-019-0475-4

48. Yuan X, Kang Y, Zhuo C, Huang XF, Song X. The gut microbiota promotes the pathogenesis of schizophrenia via multiple pathways. *Biochem Biophys Res Commun.* 2019;512(2):373-380. doi: 10.1016/j.bbrc.2019.02.152
49. Munawar N, Ahsan K, Muhammad K, et al. Hidden role of gut microbiome dysbiosis in Schizophrenia: Antipsychotics or psychobiotics as therapeutics? *Int J Mol Sci*. 2021;22(14):7671. doi: 10.3390/ijms22147671
50. Kotsiri I, Resta P, Spyrantis A, et al. Viral infections and Schizophrenia: A comprehensive review. *Viruses*. 2023;15(6):1345. doi: 10.3390/v15061345
51. Fatemi SH, Folsom TD, Rooney RJ, et al. The viral theory of schizophrenia revisited: abnormal placental gene expression and structural changes with lack of evidence for H1N1 viral presence in placentae of infected mice or brains of exposed offspring. *Neuropharmacology*. 2012;62(3):1290-1298. doi: 10.1016/j.neuropharm.2011.01.011
52. Kneeland RE, Fatemi SH. Viral infection, inflammation and Schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry.* 2013;42:35-48. doi: 10.1016/j.pnpbp.2012.02.001
53. Kim JJ. Viral Infections as ethiological factors of Schizophrenia. *Psychiatry Investigation.* 2007;4(2):61.
54. Kepinska AP, Iyegbe CO, Vernon AC, Yolken R, Murray RM, Pollak TA. Schizophrenia and influenza at the centenary of the 1918-1919 Spanish influenza pandemic:Mechanisms of psychosis risk. *Front Psychiatry.* 2020;11:72. doi: 10.3389/fpsyt.2020.00072
55. Severance EG, Gressitt KL, Stallings CR, et al. Probiotic normalization of *Candida albicans* in schizophrenia: A randomized, placebo-controlled, longitudinal pilot study. *Brain Behav Immun.* 2017;62:41-45. doi: 10.1016/j.bbi.2016.11.019
56. Bruno A, Pandolfo G, Crucitti M, et al. Effect of red yeast rice on cognitive functioning in Schizophrenia: Data from a pilot study. *J Clin Psychopharmacol*. 2019;39(3):210-213. doi: 10.1097/JCP.0000000000001025
57. Ham S, Kim TK, Chung S, Im HI. Drug Abuse and Psychosis: New Insights into Drug-induced Psychosis. *Exp Neurobiol.* 2017;26(1):11-24. doi: 10.5607/en.2017.26.1.11.
58. Davidson K. Drug-induced psychoses and their relationship to Schizophrenia" in {Eds.) Kamali D, Bartholini G, Richter D, Schizophrenia Today. New York: Pergamon Press Ltd., 1976. doi: 10.1016/B978-0-08-020928-9.50015-3
59. Rosse RB, Collins JP Jr, Fay-McCarthy M, Alim TN, Wyatt RJ, Deutsch SI. Phenomenologic comparison of the idiopathic psychosis of schizophrenia and drug-induced cocaine and phencyclidine psychoses:a retrospective study. *Clin Neuropharmacol*. 1994;17(4):359-369. doi: 10.1097/00002826-199408000-00008
60. Surathi P, Jhunjhunwala K, Yadav R, Pal PK. Research in Parkinson's disease in India: A review. *Ann Indian Acad Neurol.* 2016;19(1):9-20. doi: 10.4103/0972-2327.167713
61. Murros KE. Hydrogen sulfide produced by gut bacteria may induce Parkinson's disease. *Cells.* 2022;11(6):978. doi: 10.3390/cells11060978
62. Adams B, Nunes JM, Page MJ, et al. Parkinson's disease: A systemic inflammatory disease accompanied by bacterial inflammagens. *Front Aging Neurosci.* 2019;11:210. doi: 10.3389/fnagi.2019.00210
63. Weis S, Schwiertz A, Unger MM, et al. Effect of Parkinson's disease and related medications on the composition of the fecal bacterial microbiota. *NPJ Parkinsons Dis.* 2019;5:28. doi: 10.1038/s41531-019-0100-x
64. Parashar A, Udayabanu M. Gut microbiota: Implications in Parkinson's disease. *Parkinsonism Relat Disord.* 2017;38:1-7. doi: 10.1016/j.parkreldis.2017.02.002
65. Rosen B, Kurtishi A, Vazquez-Jimenez GR, Moller SG. The intersection of Parkinson's disease, viral infections, and COVID-19. *Mol Neurobiol.* 2021;58(9):4477-4486. doi: 10.1007/s12035-021-02408-8
66. Olsen LK, Cairns AG, Aden J, et al. Viral mimetic priming enhances α-synuclein-induced degeneration: Implications for Parkinson's disease. *Brain Behav Immun.* 2019;80:525-535. doi: 10.1016/j.bbi.2019.04.036
67. Olsen LK, Dowd E, McKernan DP. A role for viral infections in Parkinson's etiology? *Neuronal Signal.* 2018;2(2):NS20170166. doi: 10.1042/NS20170166
68. Caggiu E, Arru G, Hosseini S, et al. Inflammation, infectious triggers, and Parkinson's disease. *Front Neurol.* 2019;10:122. doi: 10.3389/fneur.2019.00122
69. Yurchenko EA, Menchinskaya ES, Pislyagin EA, et al. Neuroprotective cctivity of some marine fungal metabolites in the 6-hydroxydopamin- and paraquat-induced Parkinson's disease models. *Mar Drugs.* 2018;16(11):457. doi: 10.3390/md16110457
70. De Pablo-Fernandez E, Gebeyehu GG, Flain L, et al. The faecal metabolome and mycobiome in Parkinson's disease. *Parkinsonism Relat Disord.* 2022;95:65-69. doi: 10.1016/j.parkreldis.2022.01.005
71. Bohlega SA, Al-Foghom NB. Drug-induced Parkinson's disease. A clinical review. *Neurosciences* (Riyadh). 2013;18(3):215-21.
72. Jeong S, Cho H, Kim YJ, Ma HI, Jang S. Drug-induced Parkinsonism: A strong predictor of idiopathic Parkinson's disease. *PLoS One.* 2021;16(3):e0247354. doi: 10.1371/journal.pone.0247354
73. Feigin VL, Brainin M, Norrving B, et al. World Stroke Organization (WSO): Global Stroke Fact Sheet 2022. *Int J Stroke*. 2022;17(1):18-29. doi: 10.1177/17474930211065917
74. Zhang W, Dong XY, Huang R. Gut microbiota in ischemic stroke: Role of gut bacteria-derived metabolites. *Transl Stroke Res.* 2023;14(6):811-828. doi: 10.1007/s12975-022-01096-3
75. Crapser J, Ritzel R, Verma R, et al. Ischemic stroke induces gut permeability and enhances bacterial translocation leading to sepsis in aged mice. *Aging*. 2016;8(5):1049-1063. doi: 10.18632/aging.100952
76. Benakis C, Poon C, Lane D, et al. Distinct commensal bacterial signature in the gut is associated with acute and long-term protection from ischemic stroke. *Stroke.* 2020;51(6):1844-1854. doi: 10.1161/STROKEAHA.120.029262

77. Muhammad S, Haasbach E, Kotchourko M, et al. Influenza virus infection aggravates stroke outcome. *Stroke.* 2011;42(3):783-791. doi: 10.1161/STROKEAHA.110.596783
78. Nagel MA, Mahalingam R, Cohrs RJ, Gilden D. Virus vasculopathy and stroke:an under-recognized cause and treatment target. *Infect Disord Drug Targets.* 2010;10(2):105-111. doi: 10.2174/187152610790963537
79. Huang H, Kang R, Zhao Z. Hepatitis C virus infection and risk of stroke:a systematic review and meta-analysis. *PLoS One*. 2013;8(11):e81305. doi: 10.1371/journal.pone.0081305
80. Zis P, Stritsou P, Angelidakis P, Tavernarakis A. Herpes simplex virus type 2 encephalitis as a cause of ischemic stroke: Case report and systematic review of the literature. *J Stroke Cerebrovasc Dis.* 2016;25(2):335-339. doi: 10.1016/j.jstrokecerebrovasdis.2015.10.002
81. George P, Ramiro JI, Gomes JA, Newey CR, Bhimraj A. Central nervous system fungal infection-related stroke:A descriptive study of mold and yeast-associated ischemic stroke. *J Stroke Cerebrovasc Dis*. 2020;29(6):104759. doi: 10.1016/j.jstrokecerebrovasdis.2020.104759
82. Tsatsakis A, Docea AO, Calina D, et al. A mechanistic and pathophysiological approach for stroke associated with drugs of abuse. *J Clin Med.* 2019;8(9):1295. doi: 10.3390/jcm8091295
83. Siddiqui FM, Qureshi AI. Medication-induced stroke. In:Tsiskaridze A, Lindgren A, Qureshi AI, eds. *Treatment-Related Stroke:Including Iatrogenic and In-Hospital Strokes*. Cambridge University Press; 2016:227-240. doi: 10.1017/CBO9781139775397.023
84. Lai J, Jiang J, Zhang P, et al. Gut microbial clues to bipolar disorder: State-of-the-art review of current findings and future directions. *Clin Transl Med.* 2020;10(4):e146. doi: 10.1002/ctm2.146
85. Post RM, Denicoff KD, Leverich GS, Frye MA. Drug-induced switching in bipolar disorder:epidemiology and therapeutic implications. *CNS Drugs.* 1997;8:352-365. doi: 10.2165/00023210-199708050-00002
86. Bendriss G, MacDonald R, McVeigh C. Microbial reprogramming in obsessive-compulsive disorders:A review of gut-brain communication and emerging evidence. *Int J Mol Sci.* 2023;24(15):11978. doi: 10.3390/ijms241511978
87. Fonseka TM, Richter MA, Muller DJ. Second generation antipsychotic-induced obsessive-compulsive symptoms in schizophrenia:a review of the experimental literature. *Curr Psychiatry Rep.* 2014;16(11):510. doi: 10.1007/s11920-014-0510-8
88. Yadav P, Lee YH, Panday H, et al. Implications of microorganisms in Alzheimer's disease. *Curr Issues Mol Biol.* 2022;44(10):4584-4615. doi: 10.3390/cimb44100314
89. Starr JM, Whalley LJ. Drug-induced dementia. Incidence, management and prevention. *Drug Saf.* 1994;11(5):310-317. doi: 10.2165/00002018-199411050-00003
90. Itzhaki RF, Lathe R, Balin BJ, et al. Microbes and Alzheimer's disease. *J Alzheimers Dis.* 2016;51(4):979-84. doi: 10.3233/JAD-160152