REVIEW ARTICLE

Bridging Neurotransmitter Functions and Psychological Disorders: A Detailed Review

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ABSTRACT
Neuropharmacology, the branch of medical science, deals with the action of various pharmacological agents on the nervous system. Neurotransmitters are the endogenous chemical substances released from neurons, through which neurons are capable to communicate with each other through-out the body. There are numerous neurotransmitters are present in the body such as acetylcholine, noradrenalin, adrenaline, dopamine, serotonin, glutamate, GABA (γ-amino butyric acid), aspartate, glycine and histamine etc. These neurotransmitters are actively involved in almost all the physiological process in the body. Upregulation or downregulation of these neurotransmitters results in abnormal physiological or disease states. Therefore, a number of pharmacological agents are developed to regulate the level of neurotransmitters in brain and are employed to treat these neurological diseases or disorders.
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INTRODUCTION
Neuropharmacology is the branch of medical science, deals with the action of various pharmacological agents or drugs on nervous system. Neuropharmacology includes both human and animal studies.[1]This article emphasizes on different types of neurological diseases or disorders and the use of numerous pharmacological agents to treat/cure/prevent various neurological diseases or disorders such as Bipolar disorder (depression/mania), epilepsy, schizophrenia, parkinsonism etc. The term neuropharmacology is obtained from two individual term "neuro + Pharmacology", indicating the use of pharmacological agents against neurological imbalances.[2]
The branch of neuropharmacology is interconnected with other branches of science such as molecular biology, cellular biology, biochemistry, neurophysiology etc.[3]Apart from all other branches of science, neuropharmacology focuses on the concept behind the development of diseases or disorders of nervous system and how they can be treated.[4]

NEUROTRANSMITTER
Acetylcholine (Ach)
Ach was the first identified neurotransmitter, discovered in 1800s but its structure was found in 1920s. Dietary choline and acetyl coenzyme A act as the precursor for the synthesis of Ach in cholinergic neurons, catalyzed by choline acetyltransferase.[5] Numerous mechanisms regulate the synthesis of Ach in cholinergic neurons:

a. Amount of dietary choline available
b. Feedback mechanism- production of higher amount of Ach itself inhibits the synthesis of Ach in nerve terminal, on the other hand, depletion of Ach itself increase Ach neuronal secretion.[6]

Acetylcholinesterase is the enzyme that causes break down of Ach into acetate and choline. Whenever the concentration of ach is reduced due to hydrolytic break down, anticholinesterases (such as neostigmine, physostigmine etc) are required. Ach is major neurotransmitter in motor system. In substantia nigra,Ach act as cofactor in dopaminergic neurotransmission. The major transmission area for Ach is basal forebrain, where cholinergic nerve fibers are projected from medial septal nucleus to limbic cortex as well as in hippocampus. Therefore, Ach regulates memory, concentration, learning process, emotions and cognitive functions. It also regulates neuroendocrine functions. In periphery, Ach regulates the contraction of smooth muscles.[8, 9]
In 1970, it was found that Ach neurotransmission is decline with the age and results in Alzheimer's disease.[10]

Catecholamines: Noradrenaline, Adrenaline and Dopamine
In1920, Walter Cannon and his colleagues discovered monoamine neurotransmitters such as Noradrenaline, Adrenaline and Dopamine monoamine neurotransmitters.[11] They found in their research that on the stimulation of sympathetic nerve, these monoamines are released.[12] Therefore, they are also known as sympathomimetic amines and are involved in stimulation

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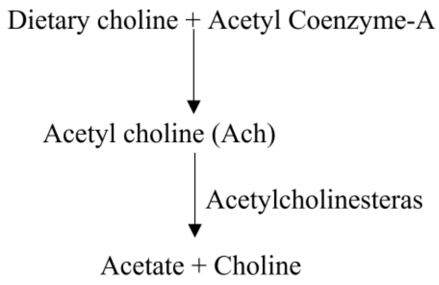
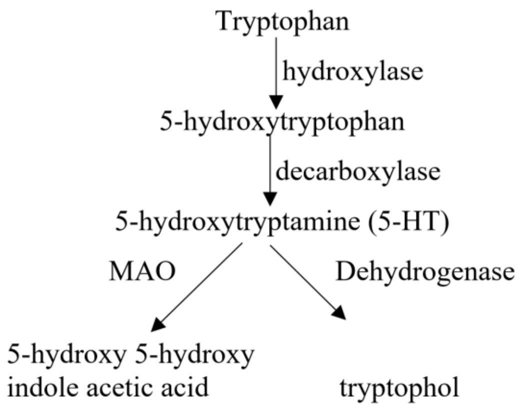
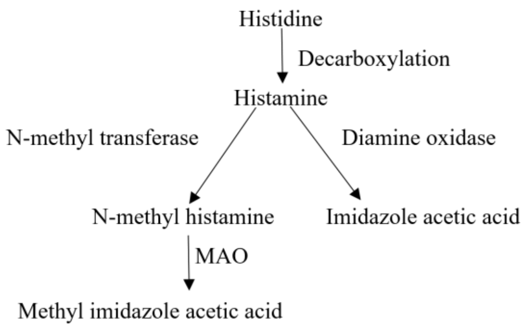


Schematic diagram 1: Synthesis and destruction of acetylcholine[7]



Schematic diagram 2: Synthesis and metabolism of 5-HT



Schematic diagram 3: Synthesis and destruction of Histamine

of nervous system and different stimulatory process such cardiac stimulation.

Chemically their structure consists of a Catechol nucleus (a benzene ring along with two -OH groups), a single -NH_2 (amine) group and a single chain aliphatic amine. Tyrosine is the substrate and tyrosinase is the key enzyme for biosynthesis of these three monoamines. Tyrosinase hydroxylate the tyrosine to DOPA, which upon decarboxylation gives dopamine.[13,14] Furthermore, dopamine is β-hydroxylated to noradrenaline and noradrenaline methylated to adrenaline. Noradrenaline, adrenaline and dopamine, all of the three catecholamines have specific physiological function.[15] Likewise, 5-HT, dopaminergic neurons have control function over the neurotransmission of dopamine, noradrenaline and adrenaline exerted through the control over tyrosinase, the rate limiting enzyme. Mono-amino oxidase (MAO) can degrade catecholamine in synaptic vesicles. After formation, catecholamine control various functions of central nervous system for instances, Dopamine transmission in nigrostriatal system (substantia nigra to basal ganglia) control motor functions, in mesolimbic system it controls affectivecognitive functions and emotions, in mesocortical system it involves in arousal, motivation and attention.[16]Dopamine also regulates the secretion of prolactin, sexual functions as well as fertility.

Table 1: Various neurotransmitters found in central nervous system[28]

Type of neurotransmitter	Examples
Amines	Acetylcholine (Ach)
	Dopamine (DA)
	Noradrenaline
	Adrenaline
	Serotonin (5-HT)
Circulating hormones	Insulin
	Glucagon
	Calcitonin
	Angiotensin
Pituitary peptides	Growth Hormone (GH)
	Corticosteroid (ACTH)
	Oxytocin
	Vasopressin
	Lipotropin
	Melanocyte stimulating hormone
Opioid peptides	Kyotrophin
	Dynorphin
	Met-enkephalin
	Leu-enkephalin
	β-Endrophin
Amino acids	Aspatic acid
	Glycine
	Glutamic acid
	GABA (γ-animo butyric acid)
Gestrointestinal hormones	Gastrin
	Motilin
	Substance P
	Secretin
	Cholecystokinin
	Vasoactive intestinal peptide

Sympathomimetic neurotransmitters regulate myriad central processes such as concentration, learning, memory, attention, arousal, attention, appetite. Peripherally, they are involved in the regulation of numerous cardiac functions such as heart rate, blood pressure as well as in smooth muscles relaxation, dilatation of pupil etc.[17]

Serotonin

5-hydroxytryptamine (5-HT) or serotonin is a well-known neurotransmitter. In 1940, 5-HT was discovered in gastrointestinal mucosa, chemically it is similar to amino acid tryptophan, found in all vertebrate as well as

Table 2: Different types of receptors and their subtypes and location[41]

Receptors	Subtypes	Locations
Cholinergic receptors	Muscarinic (M1-5)	
	M_1	CNS, autonomic ganglia&gastric gland
	M_2	Heart, visceral smooth muscles
	M_3	Eye, glands & smooth muscles
	M_4	Sensory nerve endings, CNS
	M_5	CNS
	Nicotinic (N)	
	N_N	Autonomic ganglia, CNS
	N_M	Neuromuscular junction
Adrenergic receptors	α_1	Post-junctional on effector organ
	α_2	CNS, platelets, blood vessels, β-cells of pancreas
	β_1	CVS, kidney (JG cells)
	β_2	Smooth muscles, blood vessels, liver, GIT
	β_3	Adipose tissues
Dopaminergic receptors	D_1	CNS: Straitum, Prefrontal cortex, Hippocampus
	D_2	Substantia nigra, Straitum, Prefrontal cortex, Pituitary Gland
	D_3	Nucleus accumbens, Ventral tegmental area, Limbic system
	D_4	Prefrontal cortex, Amygdala, Limbic system
	D_5	Prefrontal cortex, Hippocampus, Hypothalamus
Glutaminergic receptors	NMDA	Hippocampus, Striatum, Cerebral cortex, Spinal cord
	Kainate	Cerebellum, Thalamus, Spinal cord
	AMPA	Hippocampus, Striatum, Cerebral cortex, Cerebellum, Spinal cord
Histamine receptors	H_1	Smooth muscles, blood vessels, heart, GIT
	H_2	Gastric glands, blood vessels, CNS, CVS
	H_3	CNS, lungs, blood vessels, ileum
	H_4	Basophils, eosinophils, mast cells
Serotonergic receptors	$5HT_{1A,B,C,D,E,F}$	Hippocampus, substantia nigra, basal ganglia, raphe nuclei
	$5HT_2$	Visceral & vascular smooth muscles, cerebral neurons, platelets
	$5HT_3$	NTS (nucleus tractus solitarious), area postrema,myenteric plexus, somatic & autonomic nerve endings
	$5HT_{4-7}$	Smooth muscles, gut, CNS, mucosa
Opioid receptors	μ	Thalamus, area postrema, NTS, periaqueductal gray & nucleus ambiguous
	γ	Myenteric plexus, limbic areas
	κ	CNS, spine areas

invertebrate including scorpions, ocean crustaceans and wasps etc.[18] It is found in almost all the body parts, for instances 90% of total 5-HT in a human body is found in G.I.T., 8% in the platelets (blood) and remaining 2% is found in CNS. It is synthesized in neuronal terminal end and transferred to the synaptic vesicles afterwards, released at the synapse and interact either with the receptors present on nearest neuron (act as specific neurotransmitter) or with the auto-receptors from their original neuron (initiate a process called as re-uptake).[19,20] Re-uptake results in decrease concentration of neurotransmitter at the synapse and reuptake also control the generation and transportation of further neurotransmitter from the neuron. Nerve cells can enhance the 5-HT transmission directly by decreasing the auto-receptor generation, less amount of serotonin will be destroyed, if lesser number of auto-receptors are present there. Initially, serotonin is synthesized from tryptophan, after hydrolysis tryptophan converted into L-5-hydroxytryptophan. Afterwards, L-5-hydroxytryptophan decarboxylated to serotonin.[21] Serotonin is responsible for a number of deportment processes such as sleep patter, anxiety, appetite, regulation of mood etc.[22] Therefore, imbalance in the synthesis, release and reuptake pattern of 5-HT results in different type of disorders which includes, anxiety, schizophrenia, OCD (obsessive compulsive disorder), depression, neuro-degenerative disorders, post-traumatic stress disorder, insomnia etc.[23]

Amino acid neurotransmitters: Glutamate, GABA (γ-animo butyric acid), Aspartate and glycine

Initially in 1880, GABA was considered as a bioproduct of plant metabolism. However, in late 1950s, it was considered as a mammalian tissues constituent and exist in brain as well as spinal cord in the large quantity. Later on, it was found that GABA is an inhibitory neurotransmitter, synthesized from L-glutamate after decarboxylation in the presence of glutamate decarboxylase enzyme. Glutamate decarboxylase and cofactor, vitamin B_6 (Pyridoxine) are the rate limiting factors for GABA synthesis with in the neurons. Being an inhibitory neurotransmitter, it decreases the activity of nervous system. Due to hyperpolarization, GABA is involved in the regulation of insomnia, anxiety

Table 3. Various neurological conditions, their pharmacotherapies and side effects

Neurological condition	Pharmacotherapy	Side effects
Depression	TCA e.g. imipramine, desipramine, amitriptyline and nortriptyline etc., SSRIs e.g. fluoxetine, citalopram, fluvoxamine, paroxetine sertraline etc., SNRIs e.g. venlafaxine, duloxetine, Atypical antidepressants e.g. trazodone, mianserine etc.	Dry-mouth, urinary hesitency, weight gain, seizures, postural hypertension, sedation, blurred vision etc.
Mania	Lithium carbonate	Polyuria, thirst, vomiting, nausea, tremors, motor incoordination, ataxia, slurred speech etc.
Anxiety	Azapirones e.g. gepirone, buspirone, ispapirone, BZPs, β-blockers, anti-histaminic	Dizziness, nausea, headache, tachycardia, depression etc.
Parkinsonism	Levodopa, COMTinhibitors e.g. tolcapone, entacapone,MAO-B inhibitors e.g. rasagiline, selegiline peripheral DOPA decarboxylase inhibitors e.g. carbidopa, benserazide	dyskinesia, tachycardia, angina-pectoris, nausea, vomiting by stimulation CTZ, decrease prolactin release, behavioral changes
Epilepsy	valproic acid, phenytoin, carbamazepine, phenobarbitone, lamotrigine, gabapentin, topiramate, vigabatrin, tiagabine and primidone	Anorexia, vomiting, nausea, heart burn, loose motion, alopecia, cleft palate, osteomalacia, gum hypertrophy, megaloblastic anemia etc.
Chronic pain syndrome	Analgesics- nimesulide, aspirin etc. Antispasmodics- chlorzoxazone, cyclobenzaprine etc.	Peptic ulcer, hypersensitivity, idiosyncrasy, salicylates poisoning etc.

and epilepsy etc. although GABA also exhibits depolarization in the neurons of spinal cord but hyperpolarization action of GABA is more prominent in central cortical neurons.[24] Glycine is also an inhibitory neurotransmitter, found in mammalian tissues and proteins. It is synthesized from serine after hydroxy-methylation. In different parts of CNS such as cerebellum, substantia nigra and striatum neurons etc., glycine exhibits inhibitory effect. It causes relaxation of facial and mastication muscles, respiratory and cardiac muscles, also regulates cutaneous, visual, vestibular functions.[25] Aspartate and glutamate are the non-essential amino acids, act as excitatory neurotransmitters. Glutamate is a synthesized in body as a byproduct of glucose metabolism or Kreb's cycle. Glutamate act as a precursor for GABA and also act as excitatory neurotransmitter in spinal cord and major parts of central nervous system, involve in memory, learning and oxygenation process of neurons. Aspartate is another excitatory neurotransmitter but less characterized.[26]

Histamine

Histamine is one of the another amino-acid derived neurotransmitter, synthesized from histidine. MAO-B enzyme degrade histamine by methylation. It is secreted from mast celland responsible for inflammation and allergic reaction. Histamine also regulates sleep and arousal pattern, appetite, memory and learning, pain, sexual behavior, heart rate and blood pressure etc.[27]

PSYCHOLOGICAL DISORDERS

Depression

Major depression and mania, bothare the bipolar disorder. Depression is characterized by sadness, blue mood, low energy, loss of interest, decrease appetite, slow cognition and even suicidal thoughts. According to WHO, approximately 15% of total world population is suffering from depression.[29] "Monoamine hypothesis" of depression suggests that deficiency of monoamine (such as serotonin, nor-adrenaline) neurotransmission by decrease in biosynthesis, degradation by MAO enzyme and neuronal re-uptake leads to less availability of monoamine on postsynaptic neuron. Therefore, monoamine re-uptake inhibitors such as nor-adrenaline and serotonin re-uptake inhibitor are used in the treatment of depression.[30,31] Initial pharmacological therapy of depression includes iproniazid (1950), which was the first pharmacological agent that affect monoamine reuptake or elevate moodand also used against tuberculosis. Afterward, MAO inhibitors were introduced,which inhibit MAO enzyme, prevent monoamine degradation and monoamine i.e. serotonin, noradrenaline are available on postsynaptic neuron. There are 2 subtypes of MAO enzyme: MAO-A and MAO-B. Among them, MAO-A is responsible for deamination of nor-adrenaline and serotonin. Clorgyline, moclobemide and cimoxatone are the pharmacological agents that selectively inhibits MAO-A enzyme and prevent the deamination of mono-amines.[32] Tricyclic antidepressants (TCA) are the widely used, efficacious, potent pharmacological agents against depression. They prevent neuronal reuptake of monoamine (serotonin and nor-adrenaline) and increase the availability of monoamine on post synaptic neuron. TCA includes various pharmacological agents such as imipramine, desipramine, amitriptyline and nortriptyline etc. Desipramine selectively block reuptake of nor-adrenaline and others have mixed effect (block reuptake of both serotonin and nor-adrenaline). Apart from inhibition of serotonin and Nor-adrenaline, TCA also inhibits histamine and Ach receptors and results in a number of unwanted reactions including dryness of mouth and eyes, hallucination, constipation, urinary hesitancy etc.[33]Due to antagonistic action of α-receptor, TCA causes cardiac arrhythmia, blood pressure etc. In 1980, new class of antidepressants was introduced namely selective serotonin reuptake inhibitors (SSRIs). Fluoxetine was the first SSRIs, more potent and efficacious than TCA without inhibition Ach and histamine receptors. SSRIs exhibits their action by strongly inhibiting the serotonin (5-HT) reuptake at the presynaptic neuron. After fluoxetine, four more SSRIs were synthesized and marketed citalopram, fluvoxamine, paroxetine and sertraline. They have same mechanism of action as Fluoxetine. All the SSRIs are effective against depression, OCD (obsessive compulsive disorder), panic disorder and anxiety etc.[34]

Some atypical antidepressants such as venlafaxine,bupropionwas also synthesized, at lower dose, venlafaxine inhibits reuptake of 5-HT but at higher dose it inhibits both nor-adrenaline and 5-HT as well as dopamine re-uptake. In some individual's venlafaxine causes headache, agitation, insomnia and hypertension. Bupropion is anotheratypical antidepressant, block both nor-adrenaline and dopamine reuptake. Bupropion exhibits various gastrointestinal and sexual side effects. Therefore, mirtazapine was introducedas atypical antidepressant which block α-2 adrenergic receptor on nor-adrenaline postsynaptic neuron as well as serotonergic neuron andenhance the amount of 5-HT and nor-adrenaline. Additionally, it blocks 5HT-2 and 5HT-3 receptors and minimize the gastrointestinal and sexual side effects associated with bupropion.[35,36] A number of antidepressant drugs with great potency, safety and efficacy are available in the market.

Mania

Bipolar disorder (mania) is also another type of mood disorder, occurs only in 1% of the total population, characterized by mood swings from uncontrol excitement, agitation to psychotic delusions and depression. Variety of bipolar disorders are there, in which mood swings from manic excitement to depression, mania to euthymia etc. Etiology of mania is not clear, it may occur genetically or noradrenergic and serotonergic systems may also cause manic excitements. It has also been observed that TCAs stimulates mood swing from depression to mania. Over excitement of dopaminergic system also cause manic excitements.[37]

Pharmacotherapy of mania includes a single pharmacological compound i.e. lithium carbonate which was initially introduced in 19th century against arthritis and gout. But in late 1940s, lithium carbonate was found effective against mania.[38,39] The mechanism of action includes:

i) By inhibiting inositol monophosphatase, it inhibitshydrolysis of inositol-1-phosphate and decrease the availability of free inositol for the production of inositol triphosphate and diacylglycerol.
ii) Modulation of nor-adrenaline and serotonin release, by increasing the re-uptake of noradrenaline (or decrease the release of nor-adrenaline on presynaptic neuron) and increasing the amount of 5-HT (also increase the amount of tryptophan, 5-HT precursor). Both of these actions contribute to minimizing nor-adrenergic activity and counteract the manic excitement.

However, some interactions and adverse reaction are also there, including metabolism of lithium which occur in kidney not in liver. In kidney, lithiuminteracts with variety of pharmacological agents such as NSAIDS, ACE (Angiotensin converting enzyme inhibitors and also with antibiotics. Lithium also exhibits some kind of adverse effects affecting gastrointestinal tract, thyroid gland, dermatologic as well as cardiac system. Therefore, some antiepileptic drugs such as valproic acid, gabapentin, lamotrigine and carbamazepine are also used against mania to stabilize mood.[40]

NEUROLOGICAL DISORDERS

Parkinsonism

It is a movement disorded characterized by bradykinesia, rigidity, stiffness, tremors, loss of control on movements, gait, mask like face, sialorrhea, slow movements and at last loss of movements etc.[42]The etiology of parkinsonism includes degeneration of dopaminergic neuron in substantia nigra (nigrostriatal pathway) leading to decrease in amount of dopamine. Therefore, dopamine and its congeners such as levodopa are utilized in the pharmacotherapy of parkinsonism.[43]

The mechanism of action of levodopa includes, transmission of levodopa through BBB from periphery to central nervous system.Dopa-decarboxylase causes decarboxylation of levodopa to dopamine in CNS. Furthermore, MAO-B and COMT (catechol-O-methyl transferase) causes degradation of dopamine.[44] Therefore, inhibitors of MAO-B(i.e.selegeline) and COMT (i.e. tolcapone, entacapone) are used in the pharmacotherapy of parkinsonism.Carbidopa, benserazide are act peripherally to inhibit dopa-decarboxylase and prevent peripheral degradation of levodopa to dopamine.

It exhibits a variety of adverse reactions including dyskinesia, tachycardia, angina-pectoris, nausea, vomiting by stimulation CTZ, decrease prolactin release, behavioral changes etc.[45]

Epilepsy

Convulsions occur due to abnormal discharge of neurons in the CNS. The etiology of epilepsy includes paroxysmal stimulation of neurons, activity of GABA channels and modulated due to Na^+, Ca^{++} channel current. On the basis of clinical manifestations seizures may be of two types: generalized and partial seizures. Furthermore, generalized and partial seizures are also divided into subcategories: tonic-clonic, myoclonic, atonic, absence generalized seizures as well as simple and complex partial seizures. Tonic clonic seizures affect the whole body while partial seizures only affect one arm or one leg only.[46]

A number of pharmacological agents are used against tonic clonic seizures such as valproic acid, phenytoin, carbamazepine, phenobarbitone, lamotrigine, gabapentin, topiramate, vigabatrin, tiagabine and primidone etc. There are three major mechanisms of action for all the antiepileptic drugs including:

i. prolongation of sodium channel inactivation during the depolarization phase of action potential.

ii. Prevention of T- type calcium current in brain
iii. Potentiate the activity of GABA - chloride channel complex and result in hyper-repolarization.[47]

Different antiepileptic pharmacological agents exhibittheir action by one of the above-mentioned pathways. Carbamazepine and phenytoin prolong the sodium channel inactivation, phenobarbitone potentiate the effect of GABA -chloride channel complex, ethosuximide inhibits type-T calcium current in CNS. Valproic acid is the drug which act by all of above-mentioned mechanism, including prolong sodium channel inactivation, inhibit type-T calcium current and potentiate GABA - chloride channel complex effect.[48, 49]

Chronic pain syndrome

Chronic pain syndrome includes any type of severe pain in any part of body such as joints, skeletal tissues, muscles known as musculoskeletal pain or pain generated due to damage of nerve tissues known as neuropathic pain.[50]Arthritis is a type of musculoskeletal pain, affecting only single muscle, myofascial pain affects a set of muscles and fibromyalgia affects various body parts. Non-steroidal anti-inflammatory drugs (such as nimesulide, aspirin etc.) antispasmodics (such as chlorzoxazone, cyclobenzaprine etc.) are widely employed against chronic pain syndrome.[51, 52]

RESULTS

The review highlights and identifies the vital role of neurotransmitters including serotonin, acetylcholine, dopamine, GABA and glutamate in the regulation of various physiological pathways. Each neurotransmitter exhibits different type of neurological functions such as cognition, motor function, sensory processing and mood regulation. Dysregulation of neurotransmitters level results in numerous psychological conditions i.e. bipolar disorder: depression and mania, anxiety disorders and schizophrenia etc. They may also result in neurodegenerative disorders such as Alzheimer's and Parkinson's disease. Through research it has been proven that both downregulation and upregulation of any particular neurotransmitters may results in abnormal physiological states, thus impacting cognitive and mental health. Pharmacological compounds such as GABAergic drugs, dopamine agonists, and selective serotonin reuptake inhibitors (SSRIs) etc. are aim to restore the balance of these neurotransmitters, providing significant improvements in managing neurological conditions.

DISCUSSION

There is a complex relationship exists between dysfunction of neurotransmitters and psychological disorders, while knowing the fact that each and every neurotransmitter contributed differently to the mental-health. For instances Dopamine, involved in the pathophysiology of schizophrenia and the addiction as well. Serotonin imbalances contributes to mood disorders like anxiety and depression, However the major inhibitory-neurotransmitter GABA, contributed to conditions like generalized anxiety disorder and epilepsy etc.

Moreover, the role of aspartate and glutamate in neuronal damage and excitotoxicity conditions has been a critical area of focus in neurodegenerative diseases. Glutamate receptor antagonists are being investigated for their potential to treat conditions such as Alzheimer's and Parkinson's disease. The therapies based on neurotransmitters have been shown maximum efficacy, but the challenges remain as such in achieving targeted drug delivery with minimal or no side-effects. There is a complex-interplay in between neurotransmitters and their respective receptors, variations in brain chemistry at individual level which creates complications in the therapeutic landscape.

FUTURE DIRECTIONS

In the field of neuropharmacology, the future research must be focused on the following aspects:

i. 1.Novel-Pharmacological moiety: This aspect includes the discovery or development of more selective chemical compounds that can target with a required or specific neurotransmitter along with lesser side effects. For instances, a new class of drugs targeting serotonin-transporter or GABA-receptor, may results in the better management of depression or anxiety.
ii. 2.Personalized Medicine: Understanding the environmental and genetic factors that contributes to the dysfunction of neurotransmitter, paving the way for personalized pharmacological-interventions tailored to an individual's unique neurochemical profile.
iii. 3.Neuroplasticity and Regeneration: The research must be focused on neurotransmitters role in influencing neuroplasticity as well as the regeneration ability of CNS. These types of therapies will not only help in curing or managing the symptoms but also promoting the long-term recovery and mental health.

CONCLUSION

Neurotransmitters plays a vital role in the regulation both pathological as well as functions of central nervous system. Dysregulation in the system of neurotransmitters generates a variety of psychological conditions. Pharmacological compounds, targeting the selective neurotransmitter imbalances have been proven effective in restoring a wide cluster of neurological and psychiatric-conditions. However, numerous challenges involving adverse effects, treatment-resistance, and individualized responses are remain in question since a long time. Future research should be continued with the refine-strategies of treatment, focused on more targeted, effective and personalized interventions to improve outcomes for individuals suffering from neurotransmitter-related disorders.

REFERENCES

1. Jocham G, Ullsperger M. Neuropharmacology of performance monitoring. Neurosci Biobehav Rev. 2009 Jan;33(1):48-60. doi: 10.1016/j.neubiorev.2008.08.011. Epub 2008 Aug 22. PMID: 18789964.

2. Henderson BJ, Lester HA. Inside-out neuropharmacology of nicotinic drugs. Neuropharmacology. 2015 Sep;96(Pt B):178-93. doi: 10.1016/j.neuropharm.2015.01.022. Epub 2015 Feb 4. PMID: 25660637; PMCID: PMC4486611.
3. Rammsayer TH. Neuropharmacological evidence for different timing mechanisms in humans. Q J Exp Psychol B. 1999 Aug;52(3):273-86. doi: 10.1080/713932708. PMID: 10467900.
4. Tallman JF. Neuropsychopharmacology at the new millennium: new industry directions. Neuropsychopharmacology. 1999 Feb;20(2):99-105. doi: 10.1016/S0893-133X(98)00104-3. PMID: 9885790.
5. Bozarth MA, Pudiak CM, KuoLee R. Effect of chronic nicotine on brain stimulation reward. I. Effect of daily injections. Behav Brain Res. 1998 Nov;96(1-2):185-8. doi: 10.1016/s0166-4328(98)00050-3. PMID: 9821554.
6. Blokland A. Acetylcholine: a neurotransmitter for learning and memory? Brain Res Brain Res Rev. 1995 Nov;21(3):285-300. doi: 10.1016/0165-0173(95)00016-x. PMID: 8806017.
7. Callaway, E., Halliday, R., & Naylor, H. (1992). Cholinergic activity and constraints on information processing. *Biological Psychology, 33*(1), 1–22. https://doi.org/10.1016/0301-0511(92)90002-C
8. Yamadori A, Yoshida T, Mori E, Yamashita H. Neurological basis of skill learning. Brain Res Cogn Brain Res. 1996 Dec;5(1-2):49-54. doi: 10.1016/s0926-6410(96)00040-7. PMID: 9049070.
9. Michael D. Kopelman (1986) The cholinergic neurotransmitter system in human memory and dementia: A review, The Quarterly Journal of Experimental Psychology Section A: Human Experimental Psychology, 38:4, 535-573, DOI: 10.1080/14640748608401614
10. Dunne, M. P., & Hartley, L. R. (1985). *The effects of scopolamine upon verbal memory: evidence for an attentional hypothesis. Acta Psychologica, 58(3), 205–217.* doi:10.1016/0001-6918(85)90020-4
11. Rammsayer TH. On dopaminergic modulation of temporal information processing. Biol Psychol. 1993 Sep;36(3):209-22. doi: 10.1016/0301-0511(93)90018-4. PMID: 8260566.
12. Dayan L, Finberg JP. L-DOPA increases noradrenaline turnover in central and peripheral nervous systems. Neuropharmacology. 2003 Sep;45(4):524-33. doi: 10.1016/s0028-3908(03)00190-4. PMID: 12907313.
13. Trantham-Davidson H, Neely LC, Lavin A, Seamans JK. Mechanisms underlying differential D1 versus D2 dopamine receptor regulation of inhibition in prefrontal cortex. J Neurosci. 2004 Nov 24;24(47):10652-9. doi: 10.1523/JNEUROSCI.3179-04.2004. PMID: 15564581; PMCID: PMC5509068.
14. Riba J, Rodríguez-Fornells A, Morte A, Münte TF, Barbanoj MJ. Noradrenergic stimulation enhances human action monitoring. J Neurosci. 2005 Apr 27;25(17):4370-4. doi: 10.1523/JNEUROSCI.4437-04.2005. PMID: 15858063; PMCID: PMC6725119.
15. Mundorf ML, Joseph JD, Austin CM, Caron MG, Wightman RM. Catecholamine release and uptake in the mouse prefrontal cortex. J Neurochem. 2001 Oct;79(1):130-42. doi: 10.1046/j.1471-4159.2001.00554.x. PMID: 11595765.
16. Moore RY, Bloom FE. Central catecholamine neuron systems: anatomy and physiology of the norepinephrine and epinephrine systems. Annu Rev Neurosci. 1979;2:113-68. doi: 10.1146/annurev.ne.02.030179.000553. PMID: 231924.
17. Laakso A, Pohjalainen T, Bergman J, Kajander J, Haaparanta M, Solin O, Syvälahti E, Hietala J. The A1 allele of the human D2 dopamine receptor gene is associated with increased activity of striatal L-amino acid decarboxylase in healthy subjects. Pharmacogenet Genomics. 2005 Jun;15(6):387-91. doi: 10.1097/01213011-200506000-00003. PMID: 15900211.
18. Czyrak, A., Czepiel, K., Maćkowiak, M., Chocyk, A., & Wędzony, K. (2003). *Serotonin 5-HT1A receptors might control the output of cortical glutamatergic neurons in rat cingulate cortex. Brain Research, 989(1), 42–51.* doi:10.1016/s0006-8993(03)03352-3
19. Deng PY, Poudel SK, Rojanathammanee L, Porter JE, Lei S. Serotonin inhibits neuronal excitability by activating two-pore domain k+ channels in the entorhinal cortex. Mol Pharmacol. 2007 Jul;72(1):208-18. doi: 10.1124/mol.107.034389. Epub 2007 Apr 23. PMID: 17452494.
20. Gardier AM, Malagié I, Trillat AC, Jacquot C, Artigas F. Role of 5-HT1A autoreceptors in the mechanism of action of serotoninergic antidepressant drugs: recent findings from in vivo microdialysis studies. Fundam Clin Pharmacol. 1996;10(1):16-27. doi: 10.1111/j.1472-8206.1996.tb00145.x. PMID: 8900496.
21. Peroutka SJ, Synder SH. Relationship of neuroleptic drug effects at brain dopamine, serotonin, alpha-adrenergic, and histamine receptors to clinical potency. Am J Psychiatry. 1980 Dec;137(12):1518-22. doi: 10.1176/ajp.137.12.1518. PMID: 6108081.
22. Vitiello B, Martin A, Hill J, Mack C, Molchan S, Martinez R, Murphy DL, Sunderland T. Cognitive and behavioral effects of cholinergic, dopaminergic, and serotonergic blockade in humans. Neuropsychopharmacology. 1997 Jan;16(1):15-24. doi: 10.1016/S0893-133X(96)00134-0. PMID: 8981385.
23. Hjorth S, Bengtsson HJ, Kullberg A, Carlzon D, Peilot H, Auerbach SB. Serotonin autoreceptor function and antidepressant drug action. J Psychopharmacol. 2000 Jun;14(2):177-85. doi: 10.1177/026988110001400208. PMID: 10890313.
24. Puig MV, Santana N, Celada P, Mengod G, Artigas F. In vivo excitation of GABA interneurons in the medial prefrontal cortex through 5-HT3 receptors. Cereb Cortex. 2004 Dec;14(12):1365-75. doi:

10.1093/cercor/bhh097. Epub 2004 May 27. PMID: 15166106.
25. Ji H, Shepard PD. Lateral habenula stimulation inhibits rat midbrain dopamine neurons through a GABA(A) receptor-mediated mechanism. J Neurosci. 2007 Jun 27;27(26):6923-30. doi: 10.1523/JNEUROSCI.0958-07.2007. PMID: 17596440; PMCID: PMC6672239.
26. Michels G, Moss SJ. GABAA receptors: properties and trafficking. Crit Rev Biochem Mol Biol. 2007 Jan-Feb;42(1):3-14. doi: 10.1080/10409230601146219. PMID: 17364682.
27. Benatoui R, Bairi A, Tahraoui A. Modulatory effect of harmine on spatial memory, fertility via MAO inhibition, preventing anemia and anti-nociception upon footshock stress at three stages of pregnant rats. Universal Journal of Pharmaceutical Research 2021; 6(5):35-45. DOI: https://doi.org/10.22270/ujpr.v6i5.671
28. Bozarth MA, Pudiak CM, KuoLee R. Effect of chronic nicotine on brain stimulation reward. I. Effect of daily injections. Behav Brain Res. 1998 Nov;96(1-2):185-8. doi: 10.1016/s0166-4328(98)00050-3. PMID: 9821554.
29. Tsuang MT, Taylor L, Faraone SV. An overview of the genetics of psychotic mood disorders. J Psychiatr Res. 2004 Jan;38(1):3-15. doi: 10.1016/s0022-3956(03)00096-7. PMID: 14690766
30. De Bruijn ER, Sabbe BG, Hulstijn W, Ruigt GS, Verkes RJ. Effects of antipsychotic and antidepressant drugs on action monitoring in healthy volunteers. Brain Res. 2006 Aug 11;1105(1):122-9. doi: 10.1016/j.brainres.2006.01.006. Epub 2006 Feb 24. PMID: 16499887.
31. Gardier AM, Malagié I, Trillat AC, Jacquot C, Artigas F. Role of 5-HT1A autoreceptors in the mechanism of action of serotoninergic antidepressant drugs: recent findings from in vivo microdialysis studies. Fundam Clin Pharmacol. 1996;10(1):16-27. doi: 10.1111/j.1472-8206.1996.tb00145.x. PMID: 8900496.
32. Hjorth S, Bengtsson HJ, Kullberg A, Carlzon D, Peilot H, Auerbach SB. Serotonin autoreceptor function and antidepressant drug action. J Psychopharmacol. 2000 Jun;14(2):177-85. doi: 10.1177/026988110001400208. PMID: 10890313.
33. von Knorring AL, Cloninger CR, Bohman M, Sigvardsson S. An adoption study of depressive disorders and substance abuse. Arch Gen Psychiatry. 1983 Sep;40(9):943-50. doi: 10.1001/archpsyc.1983.01790080025003. PMID: 6615156.
34. Sturt E, Kumakura N, Der G. How depressing life is--life-long morbidity risk for depressive disorder in the general population. J Affect Disord. 1984 Oct;7(2):109-22. doi: 10.1016/0165-0327(84)90029-6. PMID: 6238066.
35. Torgersen S. Genetic factors in moderately severe and mild affective disorders. Arch Gen Psychiatry. 1986 Mar;43(3):222-6. doi: 10.1001/archpsyc.1986.01800030032003. PMID: 3954541.
36. Oyeniran Taiwo O, Opeyemi A, Ejiogu DC. New era of medicine: role of nutraceuticals in treatment and prevention of various diseases. Universal Journal of Pharmaceutical Research. 2017, 2(5), 60-63.
37. Maier F, Merkl J, Ellereit AL, Lewis CJ, Eggers C, Pedrosa DJ, Kalbe E, Kuhn J, Meyer TD, Zurowski M, Timmermann L. Hypomania and mania related to dopamine replacement therapy in Parkinson's disease. Parkinsonism Relat Disord. 2014 Apr;20(4):421-7. doi: 10.1016/j.parkreldis.2014.01.001. Epub 2014 Jan 12. PMID: 24467817.
38. Gitlin MJ, Mintz J, Sokolski K, Hammen C, Altshuler LL. Subsyndromal depressive symptoms after symptomatic recovery from mania are associated with delayed functional recovery. J Clin Psychiatry. 2011 May;72(5):692-7. doi: 10.4088/JCP.09m05291gre. Epub 2010 Jun 29. PMID: 20673560.
39. Brooks JO 3rd, Hoblyn JC. Secondary mania in older adults. Am J Psychiatry. 2005 Nov;162(11):2033-8. doi: 10.1176/appi.ajp.162.11.2033. PMID: 16263839.
40. Young W. Review of lithium effects on brain and blood. Cell Transplant. 2009;18(9):951-75. doi: 10.3727/096368909X471251. Epub 2009 May 13. PMID: 19523343.
41. El-Zine MAY, Ali MAA, Al-Shamahy HA. Prevalence of cns tumors and histological recognition in the operated patients: 10 years' experience in Yemen. Universal Journal of Pharmaceutical Research 2021; 6(2):20-27. DOI: https://doi.org/10.22270/ujpr.v6i2.563
42. Roze E, Coêlho-Braga MC, Gayraud D, Legrand AP, Trocello JM, Fénelon G, Cochen V, Patte N, Viallet F, Vidailhet M, Pollak P, Apartis E. Head tremor in Parkinson's disease. Mov Disord. 2006 Aug;21(8):1245-8. doi: 10.1002/mds.20918. PMID: 16673401.
43. Postuma RB, Aarsland D, Barone P, Burn DJ, Hawkes CH, Oertel W, Ziemssen T. Identifying prodromal Parkinson's disease: pre-motor disorders in Parkinson's disease. Mov Disord. 2012 Apr 15;27(5):617-26. doi: 10.1002/mds.24996. PMID: 22508280.
44. Boeve BF, Silber MH, Ferman TJ, Lucas JA, Parisi JE. Association of REM sleep behavior disorder and neurodegenerative disease may reflect an underlying synucleinopathy. Mov Disord. 2001 Jul;16(4):622-30. doi: 10.1002/mds.1120. PMID: 11481685.
45. Curran T, Lang AE. Parkinsonian syndromes associated with hydrocephalus: case reports, a review of the literature, and pathophysiological hypotheses. Mov Disord. 1994 Sep;9(5):508-20. doi: 10.1002/mds.870090503. PMID: 7990846.
46. Karimi I, Yakhchalian N, Fathi M, Miraghaee SS. Pharmacogenomic considerations for prescribing the antidepressant fluoxetine: A review in personalized medicine. Universal Journal of Pharmaceutical Research 2022; 7(3):74-80. DOI: https://doi.org/10.22270/ujpr.v7i3.779

47. Fiest KM, Sauro KM, Wiebe S, Patten SB, Kwon CS, Dykeman J, Pringsheim T, Lorenzetti DL, Jetté N. Prevalence and incidence of epilepsy: A systematic review and meta-analysis of international studies. Neurology. 2017 Jan 17;88(3):296-303. doi: 10.1212/WNL.0000000000003509. Epub 2016 Dec 16. Erratum in: Neurology. 2017 Aug 8;89(6):642. doi: 10.1212/WNL.0000000000004317. PMID: 27986877;
48. Keezer MR, Bell GS, Neligan A, Novy J, Sander JW. Cause of death and predictors of mortality in a community-based cohort of people with epilepsy. Neurology. 2016 Feb 23;86(8):704-12. doi: 10.1212/WNL.0000000000002390. Epub 2016 Jan 15. PMID: 26773074.
49. Galanopoulou AS. GABA(A) receptors in normal development and seizures: friends or foes? Curr Neuropharmacol. 2008 Mar;6(1):1-20. doi: 10.2174/157015908783769653. PMID: 19305785; PMCID: PMC2645547.
50. Udogadi NS, Divine O, Edeaghe E. Integrating genomic discoveries into forensics: A mini review. Universal Journal of Pharmaceutical Research 2022; 7(1):50-54. DOI: https://doi.org/10.22270/ujpr.v7i2.750
51. Chabal C, Jacobson L, Mariano A, Chaney E, Britell CW. The use of oral mexiletine for the treatment of pain after peripheral nerve injury. Anesthesiology. 1992 Apr;76(4):513-7. doi: 10.1097/00000542-199204000-00005. PMID: 1312797.
52. Dahl JB, Kehlet H. Non-steroidal anti-inflammatory drugs: rationale for use in severe postoperative pain. Br J Anaesth. 1991 Jun;66(6):703-12. doi: 10.1093/bja/66.6.703. PMID: 2064886.