Review Article

ROLE OF NEUROTRANSMITTERS IN THE HUMAN BODY

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ABSTRACT:
A number of neurotransmitters are released in the body. Acetylcholine plays a role in the control of sleep and wakefulness, movements, memory and learning. Dopamine has a role in reward, behavior, and addiction. Hyperactivity of dopaminergic receptors is involved in some type of psychosis. Locus ceruleus and norepinephrine are involved in REM sleep. Serotonin is involved in the control of sleep, intake of food, remodeling of bone, reproductive behavior, emotional states, temperature and sensory perception. Substance P is the neurotransmitter in the slow pain pathway. Excessive glutamate receptor activation may give rise to Parkinson's disease and Alzheimer's disease. Degeneration of GABA secreting neurons results into Huntington's chorea. Brain histamine takes part in the regulation of wakefulness, sexual behavior, blood pressure, drinking, pain threshold and anterior pituitary hormones. Nitric-oxide takes part in the control of long term behavior and memory. Opioid neurotransmitters inhibit cerebral neurons involved in the perception of the pain.
Conclusion. It is concluded that neurotransmitters are involved in the regulation of many body functions and their disturbances lead to many diseases.

Key Words. Neurotransmitters, Catecholamines, Serotonin, Dopamine

INTRODUCTION:

Neurotransmitters have been the focus of research for the last many years. The role of important neurotransmitters has been reviewed.

Acetyl-choline is a small molecule neurotransmitter present in synaptic vesicles in nerve terminals of cholinergic neurones. Acetyl choline is formed by the reaction of acetyl – Co A with choline catalyzed by choline acetyl transferase. It is released from postganglionic parasympathetic nerve fibers, postganglionic sympathetic nerve fibers supplying sweat glands and also is the neurotransmitter at the neuromuscular junction. It is also present in preganglionic sympathetic and parasympathetic nerve endings. It is also released by gigantocellular neurons in upper brain stem. Corticostriate fibers release acetyl choline in caudate and putamen. Imbalance of acetyl choline and dopamine in caudate and putamen results into Parkinson's disease.[1] Acetyl choline plays a role in the regulation of sleep and wakefulness, movements, memory and learning.[2,3]

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Acetyl choline is removed from synapses by the enzyme acetyl cholinestrase. Cholinergic receptors are of two types; muscarinic and nicotinic. Muscarenic receptors are present on effectors supplied by parasympathetic postganglionic nerve fibers and sympathetic postganglionic fibers supplying sweat glands. Nicotinic receptors are present at synapses between preganlionic sympathetic and parasympathetic neurons and at muscle membrane in the neuromuscular junction.[4,5] Defects in cholinergic pathways in the brain are involved in senile dementia and Alzheimer's disease.[6] Treatment with long term acting anticholinestrase improves cognitive functions in these patients.[7]

Catecholamines

Catecholamines include norepinephrine, epinephrine, and dopamine.[7] Norepinephrine is released from postganglionic sympathetic nerve fibers, also secreted by the adrenal medulla. Norepinephrine secreting neurons are located in locus ceruleus.[8] Nerve fibers from locus ceruleus pass to the spinal cord, cerebellum, paraventricular nuclei and supraoptic nuclei of the hypothalamus, thalamus and neocortex.[9,10] Epinephrine is

secreted from the adrenal medulla.[1] Hypothalamus contains a high concentration of nor-epinephrine.[11]

Dopamine is secreted by nigrostriate fibers in caudate and putamen and is involved in motor control. Its deficiency leads to Parkinson's disease. Catecholamines are synthesized by hydroxylation and decarboxylation of the amino acid tyrosine. Norepinephrine is converted into epinephrine by phenyl ethanolamine –N– methyl transferase (PNMT).[2]

Catecholamines are metabolized by monoamine oxidase (MAO) and catechol-o-methyl transferase (COMT) into metanorepinephrine, metanephrrine and vanillylmandelic acid (VMA).[2] Monoamine oxidase inhibitors have been used in patients of depression.[6] In pheochromocytoma, excretion of VMA increases in the urine.[12] In the limbic subcortical region, dopamine is involved in emotion and behavior.[13] In human beings, with age, there is a gradual loss of dopamine receptors in basal ganglia. Hyperactivity of dopaminergic synapses may be involved in some types of psychosis.[7] Cocaine abuse leads to excessive dopamine activity.[13] Locus ceruleus and nor epinephrine are involved in REM sleep.[14]

Substance P. It is the neurotransmitter in the transmission of slow pain impulses from the periphery to the spinal cord. It is a polypeptide containing 11 amino acids. It is found in high concentration in migrostriatal system.[15] It is also present in the hypothalamus to be involved in neuroendocrinal regulation. It is released by nerve fibers involved in axon reflex.[2]

Serotonin:

Serotonin (5–hydroxytryptamine) is secreted by nerve fibers arising from raphe nuclei located at the junction of pons and medulla oblongata. Raphe nuclei are a part of the analgesia system. From raphe nuclei, nerve fibers project to the hypothalamus, the limbic system, neocortex, cerebellum and spinal cord.[2] Serotonin is involved in the control of sleep, intake of food, remodeling of bone, reproductive behavior and emotional states[6] body temperature and sensory perception.[7]

Glycine causes both excitation and inhibition in the brain and spinal cord. It is responsible for direct inhibition in the brain and spinal cord by increasing Cl^- conductance. The action of glycine is antagonized by strychnine. Glycine is involved in postsynaptic inhibition.[1,2]

Glutamate

It is the major excitatory neurotransmitter in the brain and spinal cord and is responsible for 75% of excitatory transmission in the central nervous system. In Kreb's cycle, alpha keto glutarate is converted into glutamate by the enzyme GABA transaminase. Another pathway for the formation of glutamate is that glutamine is converted into glutamate by the enzyme glutaminase.[2] Glutamate binds with glutamate receptors permitting Na^+ and Ca^{++} influx resulting into fast excitatory postsynaptic membrane potential (EPSP).[16,17] Glutamate accumulates in the infarcted area of the brain to produce excitotoxic damage and cell death. Excessive glutamate receptor activation may give rise to some neurodegenerative disorders such as Parkinson's disease and Alzheimer's disease.[18,19]

Gamma-Aminobutyric Acid (GABA)

It is the major inhibitory neurotransmitter in the brain. Its formation involves decarboxylation of glutamate by the enzyme glutamate decarboxylase. Nerve fibers from caudate and putamen that pass to globus pallidus and substantia nigra secrete GABA at their nerve endings. Degeneration of GABA secreting neurons in caudate and putamen results into Huntington's chorea. It is metabolized by transamination of GABA to succinic semialdehyde and then to succinate in the citric acid cycle. GABA receptors are metabotropic that K^+ efflux and Cl^- influx to produce inhibitory postsynaptic membrane potential (IPSP).[20] GABA receptors are of 3 types; $GABA_A$,

$GABA_B$, and $GABA_C$.[21, 22] Benzodiazepines, Barbiturates increase Cl^- conductance produced by $GABA_A$ receptors. These drugs have antianxiety activity and are used as sedatives, muscle relaxant and anticonvulsant.[23]

Histamine:
Histamine secreting neurons are found in the posterior hypothalamus, their nerve fibers project to parts of the cerebral cortex and spinal cord. It is also present in gastric mucosa, mast cells and blood basophils. Histamine is formed by decarboxylation of histidine.[2]
There are 03 types of histamine receptors (H_1, H_2, and H_3). H_3 receptors mediate the release of histamine and other transmitters via a G-protein. Brain histamine is involved in wakefulness, sexual behavior, blood pressure, drinking, pain threshold and regulation of secretion of anterior pituitary hormones. Histamine H_2 receptors have a role in the regulation of cells of the immune system.[2]
Nitric oxide (Nitric oxide) secreted by nerve fibers in parts of the brain that control long term memory and behavior.[2] Its synthesis starts from arginine and this reaction is catalyzed by NO synthase. It activates guanalyl cyclase. It is not stored in vesicles but is synthesized on demand at postsynaptic sites.[2]
Nitric oxide is involved in transmission between inhibitory motor neurons of the enteric nervous system and gastrointestinal smooth cells. Also acts as a neurotransmitter in the brain.[7] Nitric oxide takes part in learning, development, penile and clitoral erection, sensory and motor modulations in cardiovascular system.[24]
Opioid peptide neurotransmitters are enkephalins, endorphins, and dynorphins. These are secreted by neurons in the central nervous system and intrinsic neurons of the gastrointestinal tract. These inhibit cerebral neurons and are involved in the perception of pain.
Opioid peptides bind to opioid receptors present in the brain and gastrointestinal tract.[25,26] These are present in substantia gelatinosa. When injected into the brain, these exert analgesia effect. These are metabolized by enkephalinase A, enkephalinase B and aminopeptidase.[2]

The feeling of pleasure on listening to music in due to the neurotransmitter dopamine released in the brain. There is also the release of endorphins and nitrous oxide while listening to music Endorphins result into an emotional response to music and nitrous oxide lead to vasodilation and blood pressure reduction.[27,28]

CONCLUSION:

It is concluded that neurotransmitters are involved in the regulation of many body functions and their disturbances lead to many diseases.

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