Chapter 1

Central Nervous System

INTRODUCTION

The drugs that act on the central nervous system (CNS) influence the lives of everyone at all times. These drugs can selectively relieve pain, reduce fever, suppress disordered movement, induce sleep or arousal, and reduce the desire to eat or ally the tendency to vomit. Selectively, acting drugs can be used to treat anxiety, mania, depression, or schizophrenia and do so without altering consciousness.

Monoamines were the first identified central nervous system transmitters. The pathways of noradrenergic, dopaminergic, and serotonergic neurons in laboratory animals were produced and the same basic features have been confirmed in human brain. Neurotransmitters are categorized according to their chemical nature, that is, amino acids, amines, monopeptide, and purines.

The electrophysiological signs of action in the CNS falls into two categories (i) excitatory (produce depolarization) and (ii) inhibitory (produces hyperpolarization) in the neurons. Some of these that modulate the CNS are called neuromodulators. The excitatory action is produced by glutamate, aspartate, and other biogenic catecholamines. Inhibitory action is produced by GABA and glycine. The neuromodulators are circulating steroid hormones, locally released adenosine, and other purines. The neurotransmitters are discussed in the section on 'Functional Aspects'.

Amino Acids

There is a wide spread of GABA, glycine, and glutamate regulation seen in CNS. GABA releases correlate with the frequency of the nerve stimulation, which produce increased Cl^- ion conductance to produce inhibition through hyper-polarization and mediates presynaptic inhibition. GABA ergic system present in the cerebral cortex, olfactory bulb, hippocampus, and lateral septal muscles. GABA receptors exist in A and B types. Glycine is another inhibitory amino acid, prominent in the brain stem and the spinal cord. Glutamate and aspartate are found abundantly in the brain, and they are extremely powerful excitatory neurotransmitter acts through *N*-methyl D-aspartate (NMDA) receptor. Activation of NMDA receptors produces long-term potentiating in hippocampus and at high concentration, glutamate produces excitotoxicity leading to neurotoxic signs.

Adrenergic Pathway in CNS

The cell bodies of noradrenergic neurons occur in small clusters in pons and medulla and send extensively branched axons to many prominent clusters in locus cerulus. There is a close relationship between moods and states of arousal; depressed individuals are usually lethargic and unresponsive to external stimuli. The catecholamine hypothesis of affective disorders suggested that depression results from a functional deficiency of nor-adrenaline in certain parts of the brain, while mania results from an excess, and the blood pressure regulation in CNS mediated through α_2 auto receptors.

Functional Aspects of Dopamine

Dopamine is a neurotransmitter as well as a leading precursor of noradrenaline. It is degraded in a similar fashion to noradrenaline. They are connected with nigrostriatal pathway, which is important in motor control, mesolimbic pathways running from groups of cells in the midbrain to parts of the limbic system. Parkinson's disease is associated with a deficiency of nigrostriatal dopaminergic neurons. Behavioural effects of an excess dopamine activity constitute stereotyped behaviour patterns and can be produced by dopamine releasing agents.

Functional Aspects of 5-HT

The precise localization of the 5-HT neurons in the brain stem and throughout the brain parts regulates the hallucinations, behavioural changes, sleep, wakefulness, mood, feeding behaviour, and control of sensory transmission. The 5-HT receptors are concentrated in the midline raphe nuclei in the pons and medulla projecting diffusely to cortex, limbic system, hypothalamus, and spinal cord similar to noradrenergic neuron. They exert inhibitory or excitatory effects on individual neurons, acting either presynaptically or postsynaptically.

Cholinergic Transmission in CNS

Acetylcholine is widely distributed in the basal forebrain nuclei, septohippocampal projections; short interneuron in striatum and nucleus accumbans. Both nicotinic and muscarinic acetylcholine receptors are found predominantly in the CNS. The former mediate the central effects of nicotine through nicotinic receptors mainly located in presynapse. Muscarnic receptors appear to mediate main behavioural effects associated with acetylcholine such as arousal, learning, and memory. Certain neurodegenerative diseases, that is, dementia and Parkinson's disease are associated with abnormalities of cholinergic pathways.

Other Neurotransmitters and Functions in CNS

Histamine is another neurotransmitter, histaminergic neurons originate in a small area of hypothalamus and have a wide distribution. Histamine is active on waking hours and histaminic receptor antagonists are strongly sedative and antiemetic.

In purines, adenosine triphosphate (ATP) and adenosine are present. ATP is converted into adenosine diphosphate (ADP) and adenosine mono phosphate (AMP). Adenosine mainly exerts inhibitory effects through

A_1 and A_2 receptors resulting in sedative, anti-convulsant, and neuro-protective effect; it also acts as a safety mechanism.

These neurotransmitters and the functional aspects are necessary to maintain the homeostasis in the brain and many drugs act on these functions to alter the CNS activity and produce sedative, hypnosis, antianxiety, depression, antiepileptic, and anaesthetic actions.