Glutamate is the main excitatory transmitter in the brain and spinal cord, and it has been calculated that it is the transmitter responsible for 75% of the excitatory transmission in the brain. Synthesis: Glutamate is formed by reductive amination of the Krebs cycle intermediate -keto glutarate in the cytoplasm. Receptors: Glutamate receptors are of two types: metabotropic receptors and ionotropic receptors. The metabotropic receptors are G protein-coupled receptors that increase intracellular IP3 and DAG levels or decrease intracellular Ca2+ levels. The ionotropic receptors are ligand-gated ion channels that resemble nicotinic cholinergic receptors and GABA and glycine receptors. There are three general subtypes, the kainate receptors, AMPA receptors, and NMDA receptors. The three all allow for cationic currents in response to glutamate stimulation.

GABA is the major inhibitory mediator in the brain, including being responsible for presynaptic inhibition. Synthesis: GABA, which exists as gamma-aminobutyrate in the body fluids, is formed by decarboxylation of glutamate. The enzyme that catalyzes this reaction is glutamate decarboxylase (GAD), which is present in nerve endings in many parts of the brain. Receptors: The GABA and GABA receptors are ion channels made up of five subunits surrounding a pore, and allow the influx of Cl-. The GABA receptors are metabotropic and are coupled to heterotrimetric G proteins that increase conductance in K+ channels, inhibit adenyl cyclase, and inhibit G protein-dependent pathways. Synthesis: GABA, which exists as gamma-aminobutyrate in the body fluids, is formed by decarboxylation of glutamate. The enzyme that catalyzes this reaction is glutamate decarboxylase (GAD), which is present in nerve endings in many parts of the brain. Receptors: The GABA and GABA receptors are ion channels made up of five subunits surrounding a pore, and allow the influx of Cl-. The GABA receptors are metabotropic and are coupled to heterotrimetric G proteins that increase conductance in K+ channels, inhibit adenyl cyclase, and inhibit G protein-dependent pathways.

Acetylcholine is a major neurotransmitter in the peripheral nervous system, and it is also present in the brain. Fibers that release ACh are called cholinergic fibers. Acetylcholine is the transmitter at the neuromuscular junction, in autonomic ganglia, and in postganglionic parasympathetic nerve-target organ junctions and some postganglionic sympathetic nerve-target junctions. It is also found within the brain, including the basal forebrain complex and pontomesencephalic cholinergic complex. These systems may be involved in regulation of sleep-wake states, learning, and memory (hence anticholinesterases in dementia). Synthesis: Acetylcholine is synthesized from choline and acetyl coenzyme A in the cytoplasm of synaptic terminals and stored in synaptic vesicles. Receptors: At the neuromuscular and autonomic ganglia, the ACh receptors are ligand-gated ion channels which are located in skeletal muscle, on postganglionic sympathetic nerve terminals, and on the cardiac muscle of the heart. These nicotinic receptors are comprised of two main types of subunits, alpha and beta. The alpha and beta subunits are each made up of several copies of these subunits, which form a complex that allows for the influx of sodium and potassium ions. Synthesis: Acetylcholine is synthesized from choline and acetyl coenzyme A in the cytoplasm of synaptic terminals and stored in synaptic vesicles. Receptors: At the neuromuscular and autonomic ganglia, the ACh receptors are ligand-gated ion channels which are located in skeletal muscle, on postganglionic sympathetic nerve terminals, and on the cardiac muscle of the heart. These nicotinic receptors are comprised of two main types of subunits, alpha and beta. The alpha and beta subunits are each made up of several copies of these subunits, which form a complex that allows for the influx of sodium and potassium ions.

Serotonin (5-hydroxytryptamine; 5-HT) is a major neurotransmitter in the brain, including being responsible for presynaptic inhibition. Synthesis: Serotonin is synthesized from tryptophan and stored in synaptic vesicles. Receptors: Serotonin receptors are of two types: 5-hydroxytryptamine receptors and alpha receptors. The 5-hydroxytryptamine receptors are G protein-coupled receptors that increase intracellular IP3 and DAG levels or decrease intracellular Ca2+ levels. The alpha receptors are metabotropic and are coupled to heterotrimetric G proteins that increase conductance in K+ channels, inhibit adenyl cyclase, and inhibit G protein-dependent pathways. Synthesis: Serotonin is synthesized from tryptophan and stored in synaptic vesicles. Receptors: Serotonin receptors are of two types: 5-hydroxytryptamine receptors and alpha receptors. The 5-hydroxytryptamine receptors are G protein-coupled receptors that increase intracellular IP3 and DAG levels or decrease intracellular Ca2+ levels. The alpha receptors are metabotropic and are coupled to heterotrimetric G proteins that increase conductance in K+ channels, inhibit adenyl cyclase, and inhibit G protein-dependent pathways.