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Describe in details the synthesis of two known neurotransmitters.

**Synthesis of Dopamine**

Dopamine is synthesized from the amino acid tyrosine, which is taken up into the brain via an active transport mechanism. Tyrosine is produced in the liver from phenylalanine through the action of phenylalanine hydroxylase. Tyrosine is then transported to dopamine containing neurons where a series of reactions convert it to dopamine. Within catecholaminergic neurons, tyrosine hydroxylase catalyzes the addition of a hydroxyl group to the meta position of tyrosine, yielding L-dopa. This rate-limiting step in catecholamine synthesis is subject to inhibition by high levels of catecholamines (end- product inhibition). Because tyrosine hydroxylase is normally saturated with substrate, manipulation of tyrosine levels does not readily impact the rate of catecholamine synthesis. Once formed, L-dopa is rapidly converted to dopamine by dopa decarboxylase, which is located in the cytoplasm.

Phenylalanine → L-Tyrosine → L-DOPA → Dopamine

**Synthesis of Norepinephrine and Epinephrine**

Norepinephrine is the primary neurotransmitter for postganglionic sympathetic adrenergic nerves. It is synthesized inside the nerve axon, stored within vesicles, then released by the nerve when an action potential travels down the nerve. The synthesis of Norepinephrine:

1. The amino acid tyrosine is transported into the sympathetic nerve axon.
2. Tyrosineis converted to DOPA by tyrosine hydroxylase (rate-limiting step for Norepinephrine synthesis). DOPA is converted to dopamine by DOPA decarboxylase.
3. Dopamine is transported into vesicles then converted to norepinephrine by dopamine β-hydroxylase (DBH), transport into the vesicle can by blocked by the drug reserpine.

**Epinephrine** is synthesized from norepinephrine in a synthetic pathway shared by all catecholamines, including L-dopa, dopamine, norepinephrine, and epinephrine.Epinephrine is synthesized via methylation of the primary distal amine of norepinephrine by phenylethanolamine N-methyltransferase (PNMT) in the cytosol of adrenergic neurons and cells of the adrenal medulla (so-called chromaffin cells). PNMT is only found in the cytosol of cells of adrenal medullary cells. PNMT uses S-adenosylmethionine (SAMe) as a cofactor to donate the methyl group to norepinephrine, creating epinephrine.For norepinephrine to be acted upon by PNMT in the cytosol, it must first be shipped out of granules of the chromaffin cells. This may occur via the catecholamine-H+ exchanger VMAT1. VMAT1 is also responsible for transporting newly synthesized epinephrine from the cytosol back into chromaffin granules in preparation for release.

