

Name: Ekpo Mfonido E

Mat.no: 18/mhs03/017

Dept: Anatomy

Course: Cellular Biochemistry

QUESTION:

Describe in details the synthesis of one named neurotransmitter

## 1.DOPAMINE SYNTHESIS

Dopamine is synthesized from the amino acid tyrosine; the majority of circulating tyrosine originates from dietary sources, but small amounts are derived from hydroxylation of phenylalanine by the liver enzyme phenylalanine hydroxylase .

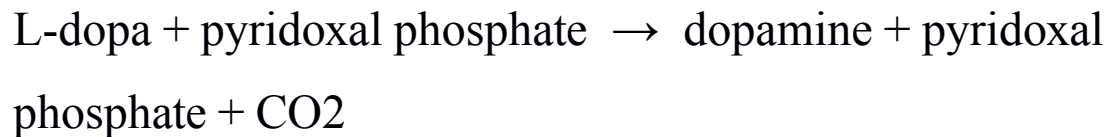
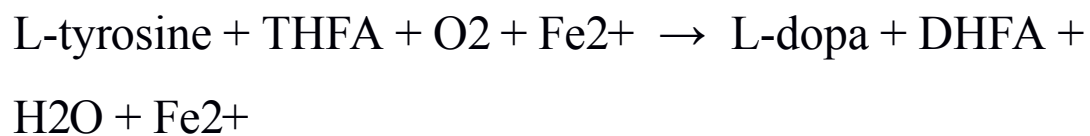
Blood-borne tyrosine is taken up into the brain by a low-affinity amino acid transport system and subsequently from brain extracellular fluid into dopaminergic neurons by high- and low-affinity amino acid transporters.

Tyrosine is converted to dopamine by the enzymes tyrosine hydroxylase (TH) and l-amino acid decarboxylase (AADC) also called dihydroxyphenylalanine (DOPA) decarboxylase (DDC).

The aromatic amino acid hydroxylases 2000

TH activity is the most critical factor that controls dopamine synthesis, and considerable efforts have been devoted to understanding activation/inactivation of this enzyme. Assignment of the human tyrosine hydroxylase gene to chromosome 1984

As previously said, AADC is the second and terminal enzyme in dopamine biosynthesis. The enzyme uses pyridoxal phosphate as a cofactor and can convert both DOPA to dopamine and 5-hydroxytryptophan to serotonin [5-hydroxytryptamine (5-HT)]. Aromatic L-amino acid decarboxylase modulation and Parkinson's disease 1995  
The following is the complete reaction:



So for L-dopa formation, L-tyrosine, THFA (tetrahydrofolic acid), and ferrous iron are essential and for dopamine biosynthesis from L-dopa, pyridoxal phosphate is essential.

The activity of the enzyme rises and falls according to how much pyridoxal phosphate there is. Besides two enzymes being required for the formation of dopamine from L-tyrosine (L-tyrosine >>> L-dopa >>> dopamine),

three coenzymes are also required. They are : THFA (for L-tyrosine to L-dopa), pyridoxal phosphate (for L-dopa to dopamine), and NADH (for the formation of THFA and Pyridoxal phosphate). The cofactor tetrahydrobiopterin (BH<sub>4</sub>) donates the hydrogen atom needed for hydroxylation of tyrosine to DOPA.

Because pterin also serves as a cofactor for other monooxygenases as well as nitric oxide synthase, its availability is a determinino factor in the control of TH activity. Regulation of pteridine-requiring enzymes by the cofactor tetrahydrobiopterin 1999

## 2. SYNTHESIS OF SEROTONIN

Serotonin is an example of a monoamine neurotransmitter, a chemical messenger that is passed between nerve cells. This hormone is mainly found in the gastrointestinal tract, the platelets and the central nervous system of animals and is thought to contribute to a sense of well being and happiness.

Serotonin is synthesized from the amino acid L-tryptophan via a short metabolic pathway that involves two major enzymes. These enzymes are:

Tryptophan hydroxylase (TPH)

Amino acid decarboxylase

The reaction in this pathway that is mediated by tryptophan hydroxylase is the rate limiting step, meaning that if this enzyme is blocked, the synthesis of serotonin would be stopped. Tryptophan hydroxylase exists in two forms - TPH1 and TPH2. While TPH1 is found in several tissues, TPH2 is specifically found in nerves of the brain. Serotonin transporter protein called SERT or 5HTT is responsible for carrying serotonin from the synaptic cleft to its target nerve. This transporter acts as a regulator of serotonin levels and mutations in the 5HTT gene have

been shown to disrupt serotonin uptake. Serotonin regulates many important bodily functions ranging from sleep, mood, appetite and eating habits as well as influencing anxiety levels, suicidal tendencies, and our ability to learn and memorize things.

The 5-HTT protein is an important target of many antidepressant therapies. There are two forms of 5-HTT genes, the long form and the short form. Studies have shown that people with two long forms of the 5-HTT genes are less likely to suffer from depression compared with people who have one short and one long copy of the gene or two short copies.

While serotonin in its primary form cannot reach the brain since it cannot cross the blood–brain barrier, the serotonin precursors tryptophan and its metabolite 5-hydroxytryptophan (5-HTP) do cross this barrier and reach the brain. These agents can be taken as dietary supplements to increase levels of serotonin in the brain.

