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DEPT: PHYSIOLOGY

MATRIC NO: 17/MHS05/018

COURSE CODE: BCH 308

ASSIGNMENT TITLE: NEUROCHEMISTRY

Describe in details the synthesis of two named neurotransmitters

Neurotransmitters

- Acetylcholine
- Gamma Amino- butyric Acid (GABA)

1. ACETYLCHOLINE-

It is a neurotransmitter between axons and striated muscle at the neuromuscular junction. Neurons that synthesize and release acetylcholine are known as cholinergic neurons.

Acetylcholine is synthesized from choline and acetyl- CoA through the action of an enzyme: choline acetyl- transferase in neuronal /nerve terminal cytoplasm where the enzyme is located. Coenzyme A is synthesized in the mitochondria and accesses choline acetyl- transferase following transport across the mitochondrial membrane into the cytoplasm. In addition to its synthesis in the liver, choline employed in acetylcholine production is derived from dietary sources. There is a carrier system in capillary endothelial cells that is responsible for transport of choline, in its free and phospholipid forms, into the brain. Hydrolysis of choline- containing phospholipids may also liberate choline that is used in acetylcholine synthesis. As choline acetyl- transferase is not saturated by concentrations of acetyl coenzyme A and choline that are estimated to be present in the nerve

terminal, it appears that the rate of acetylcholine synthesis is dependent on precursor availability. Enzyme activity is also regulated by product inhibition by binding at an allosteric site on choline acetyltransferase, acetylcholine inhibits its activity. In addition, mass action and neuronal activity influence the rate of acetylcholine formation. Short-term regulation of enzyme activity is partly achieved by phosphorylation induced by protein kinases. There are no very specific and potent inhibitors of the enzyme and it should be noted that pharmacological blockade of this step (e.g. with naphthyl vinyl pyridine) in the life-cycle of acetylcholine produces a less profound effect on the transmitter than does inhibition of choline transport.

Acetylcholine is then incorporated into synaptic vesicles and stored therein.

2. GAMMA AMINO- BUTYRIC ACID (GABA)-

GABA is a naturally occurring amino acid that acts as a neurotransmitter in brain and spinal cord. It balances the brain by inhibiting over excitation.

GABA Like other amino acids, it has a carboxylic (- COOH) group and an amino group (- NH₃). It is a derivative of glutamate, a non-essential amino acid that is abundantly present in the body. It is primarily synthesized from glutamate in the inhibitory neurons. These inhibitory neurons which produce GABA are referred to as GABAergic neurons via decarboxylation reaction catalyzed by the enzyme glutamate decarboxylase (GAD) with Pyridoxal phosphate (the active form of vitamin B₆) as a cofactor. This process converts glutamate (the principal excitatory neurotransmitter) into GABA (the principal inhibitory neurotransmitter) and stored in vesicles in axon terminals.

GABA can also be synthesized from putrescine by diamine-oxidase and

aldehyde dehydrogenase.