Editorial

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Norepinephrine: Structure, Function, and Biochemical Mechanisms

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Editorial

Nor Epinephrine (NE), also known as Nor Adrenaline (NA) or noradrenalin, is an organic molecule in the catecholamine family that acts as both a hormone and a neurotransmitter in the brain and body. In the United Kingdom, the name "noradrenaline," derived from Latin words meaning "at/near the kidneys," is more generally used; in the United States, "norepinephrine," derived from Greek origins with the same meaning, is usually favoured. The drug's international nonproprietary name is also "norepinephrine." Norepinephrine's general role is to mobilise the brain and body for action. The release of norepinephrine is lowest during sleep, rises during awake, and reaches significantly higher levels under stressful or dangerous conditions, in the so-called fight-or-flight response. Walter Cannon, who popularised the idea of a sympathoadrenal system preparing the body for fight and flight, and his colleague Arturo Rosenblueth proposed a theory of two sympathins, sympathin E (Excitatory) and sympathin I (Inhibitory), responsible for these actions early in the twentieth century. Between 1934 and 1938, Belgian pharmacologist Zénon Bacq, as well as Canadian and US-American pharmacologists, proposed that noradrenaline could be a sympathetic transmitter. Hermann Blaschko and Peter Holtz separately discovered the norepinephrine biosynthetic pathway in the vertebrate body in 1939.

Norepinephrine raises arousal and alertness, promotes vigilance, improves memory formation and retrieval, and concentrates attention in the brain; it also increases restlessness and anxiety. Norepinephrine raises heart rate and blood pressure, causes glucose to be released from energy storage, increases blood flow to skeletal muscle, decreases blood flow to the gastrointestinal system, and inhibits bladder voiding and gastrointestinal motility in the remainder of the body. A number of therapeutically significant medications work by modifying the effects of noradrenaline systems.

Noradrenaline is commonly used as an injectable medication to treat critically low blood pressure. Beta blockers, which block noradrenaline receptors and so counteract some of its effects, are commonly used to treat glaucoma, migraine, and a variety of cardiovascular conditions. Alpha blockers are used to treat a variety of cardiovascular and psychiatric problems by blocking a separate set of noradrenaline effects. Alpha-2 agonists frequently have a sedative effect and are commonly employed as anesthetic enhancers in surgery as well as in the treatment of drug or alcohol addiction. Many major psychiatric medicines have considerable impacts on the brain's noradrenaline systems, resulting in side effects that can be beneficial or harmful. Norepinephrine is a phenethylamine and a catecholamine.

The main difference between it and epinephrine is that epinephrine has a methyl group connected to its nitrogen, whereas norepinephrine contains a hydrogen atom in place of the methyl group. The prefix nor is derived from the word "normal," and it is used to denote a demethylated substance. A sequence of enzymatic processes in the adrenal medulla and postganglionic neurons of the sympathetic nervous system produce norepinephrine from the amino acid tyrosine. While tyrosine is converted to dopamine mostly in the cytoplasm, dopamine -monooxygenase converts dopamine to norepinephrine primarily within neurotransmitter vesicles. The metabolic route is as follows:

Phenylalanine → Tyrosine → L-DOPA → Dopamine → Norepinephrine

Dopamine is the direct precursor of norepinephrine, and it is produced indirectly from the essential amino acid phenylalanine or the non-essential amino acid tyrosine. As these amino acids are found in practically every protein, they are obtained through the consumption of protein-containing foods, with tyrosine being the most prevalent. Norepinephrine is rapidly metabolized to different metabolites in animals. The first stage in the breakdown might be catalysed by either monoamine oxidase (most notably monoamine oxidase A) or COMT. The breakdown can then progress in a number of ways.

Vanillylmandelic acid or a conjugated version of MHPG are the main end products, both of which are assumed to be physiologically inactive and eliminated in the urine. Norepinephrine, like many other biologically active chemicals, exerts its actions by binding to and activating receptors on the surface of cells. There are two large categories of norepinephrine receptors known as alpha and beta adrenergic receptors. Alpha receptors are classified as subtypes 1 and 2; beta receptors are classified as subtypes 1,2, and 3. Inside the brain, norepinephrine acts as a neurotransmitter and is regulated by a set of mechanisms shared by all monoamine neurotransmitters. The vesicular monoamine transporter transports norepinephrine from the cytosol into synaptic vesicles after it has been synthesized (VMAT)

Norepinephrine has been found in a wide range of animal species, including protozoa, placozoa, and cnidaria (jellyfish and

related species), but not in ctenophores (comb jellies), which have quite different neurological systems than other animals. It is found in most deuterostomes (vertebrates, for example), but in protostomes (arthropods, mollusks, flatworms, nematodes, annelids, and so on), it is substituted by octopamine, a chemical with a similar manufacturing mechanism.