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Assignment Question: Describe in detail, the synthesis of two named neurotransmitters

Solution

Neurotransmitters

A neurotransmitter is defined as a chemical messenger that carries, boosts, and balances signals between neurons, or nerve cells, and other cells in the body. These chemical messengers can affect a wide variety of both physical and psychological functions including heart rate, sleep, appetite, mood, and fear. Billions of neurotransmitter molecules work constantly to keep our brains functioning, managing everything from our breathing to our heartbeat to our learning and concentration levels.

How Neurotransmitters Work

In order for neurons to send messages throughout the body, they need to be able to communicate with one another to transmit signals. However, neurons are not simply connected to one another. At the end of each neuron is a tiny gap called a synapse and in order to communicate with the next cell, the signal needs to be able to cross this small space. This occurs through a process known as neurotransmission.

In most cases, a neurotransmitter is released from what's known as the axon terminal after an action potential has reached the synapse, a place where neurons can transmit signals to each other.

When an electrical signal reaches the end of a neuron, it triggers the release of small sacs called vesicles that contain the neurotransmitters. These sacs spill their contents into the synapse, where the neurotransmitters then move across the gap toward the neighboring cells. These cells contain receptors where the neurotransmitters can bind and trigger changes in the cells.

After release, the neurotransmitter crosses the synaptic gap and attaches to the receptor site on the other neuron, either exciting or inhibiting the receiving neuron depending on what the neurotransmitter is.

Neurotransmitters act like a key, and the receptor sites act like a lock. It takes the right key to open specific locks. If the neurotransmitter is able to work on the receptor site, it triggers changes in the receiving cell.

Sometimes neurotransmitters can bind to receptors and cause an electrical signal to be transmitted down the cell (excitatory). In other cases, the neurotransmitter can actually block the signal from continuing, preventing the message from being carried on (inhibitory).

So what happens to a neurotransmitter after its job is complete? Once the neurotransmitter has had the designed effect, its activity can be stopped by different mechanisms.

It can be degraded or deactivated by enzymes

It can drift away from the receptor

It can be taken back up by the axon of the neuron that released it in a process known as reuptake

Neurotransmitters play a major role in everyday life and functioning. Scientists do not yet know exactly how many neurotransmitters exist, but more than 60 distinct chemical messengers have been identified.1

What They Do

Neurotransmitters can be classified by their function:2

Excitatory neurotransmitters: These types of neurotransmitters have excitatory effects on the neuron, meaning they increase the likelihood that the neuron will fire an action potential. Some of the major excitatory neurotransmitters include epinephrine and norepinephrine.

Inhibitory neurotransmitters: These types of neurotransmitters have inhibitory effects on the neuron; they decrease the likelihood that the neuron will fire an action potential. Some of the major inhibitory neurotransmitters include serotonin and gamma-aminobutyric acid (GABA).

Some neurotransmitters, such as acetylcholine and dopamine, can create both excitatory and inhibitory effects depending upon the type of receptors that are present.

Modulatory neurotransmitters: These neurotransmitters, often referred to as neuromodulators, are capable of affecting a larger number of neurons at the same time. These neuromodulators also influence the effects of other chemical messengers. Where synaptic neurotransmitters are released by axon terminals to have a fast-acting impact on other receptor neurons, neuromodulators diffuse across a larger area and are more slow-acting.

Types

There are a number of different ways to classify and categorize neurotransmitters. In some instances, they are simply divided into monoamines, amino acids, and peptides.3

Neurotransmitters can also be categorized into one of six types:

Amino Acids

Gamma-aminobutyric acid (GABA) acts as the body's main inhibitory chemical messenger. GABA contributes to vision, motor control, and plays a role in the regulation of anxiety. Benzodiazepines, which are used to help treat anxiety, function by increasing the efficiency of GABA neurotransmitters, which can increase feelings of relaxation and calm.

Glutamate is the most plentiful neurotransmitter found in the nervous system where it plays a role in cognitive functions such as memory and learning. Excessive amounts of glutamate can cause excitotoxicity resulting in cellular death. This excitotoxicity caused by glutamate build-up is associated with some diseases and brain injuries including Alzheimer's disease4 , stroke, and epileptic seizures.

Peptides

Oxytocin is both a hormone and a neurotransmitter. It is produced by the hypothalamus and plays a role in social recognition, bonding, and sexual reproduction.5 Synthetic oxytocin such as Pitocin is often used as an aid in labor and delivery. Both oxytocin and Pitocin cause the uterus to contract during labor.

Endorphins are neurotransmitters than inhibit the transmission of pain signals and promote feelings of euphoria. These chemical messengers are produced naturally by the body in response to pain, but they can also be triggered by other activities such as aerobic exercise.6 For example, experiencing a "runner's high" is an example of pleasurable feelings generated by the production of endorphins.

Monoamines

Epinephrine is considered both a hormone and a neurotransmitter. Generally, epinephrine (adrenaline) is a stress hormone that is released by the adrenal system. However, it functions as a neurotransmitter in the brain.7

Norepinephrine is a neurotransmitter that plays an important role in alertness is involved in the body's fight or flight response. Its role is to help mobilize the body and brain to take action in times of danger or stress. Levels of this neurotransmitter are typically lowest during sleep and highest during times of stress.

Histamine acts as a neurotransmitter in the brain and spinal cord.8 It plays a role in allergic reactions and is produced as part of the immune system's response to pathogens.

Dopamine plays an important role in the coordination of body movements. Dopamine is also involved in reward, motivation, and additions.9 Several types of addictive drugs increase dopamine levels in the brain. Parkinson's disease, which is a degenerative disease that results in tremors and motor movement impairments, is caused by the loss of dopamine-generating neurons in the brain.

Serotonin plays an important role in regulating and modulating mood, sleep, anxiety, sexuality, and appetite. Selective serotonin reuptake inhibitors, usually referred to as SSRIs, are a type of antidepressant medication commonly prescribed to treat depression, anxiety, panic disorder, and panic attacks. SSRIs work to balance serotonin levels by blocking the reuptake of serotonin in the brain, which can help improve mood and reduce feelings of anxiety.10

Purines

Adenosine acts as a neuromodulator in the brain and is involved in suppressing arousing and improving sleep.

Adenosine triphosphate (ATP) acts as a neurotransmitter in the central and peripheral nervous systems.11 It plays a role in autonomic control, sensory transduction, and communication with glial cells. Research suggests it may also have a part in some neurological problems including pain, trauma, and neurodegenerative disorders.

Gasotransmitters

Nitric oxide plays a role in affecting smooth muscles, relaxing them to allow blood vessels to dilate and increase blood flow to certain areas of the body.

Carbon monoxide is usually known as being a colorless, odorless gas that can have toxic and potentially fatal effects when people are exposed to high levels of the substance. However, it is also produced naturally by the body where it acts as a neurotransmitter that helps modulate the body's inflammatory response.12

Acetylcholine

Acetylcholine is the only neurotransmitter in its class. Found in both the central and peripheral nervous systems, it is the primary neurotransmitter associated with motor neurons.13 It plays a role in muscle movements as well as memory and learning.

What Happens When Neurotransmitters Do Not Work Right

As with many of the body's processes, things can sometimes go awry. It is perhaps not surprising that a system as vast and complex as the human nervous system would be susceptible to problems.

A few of the things that might go wrong include:

Neurons might not manufacture enough of a particular neurotransmitter

Too much of a particular neurotransmitter may be released

Too many neurotransmitters may be deactivated by enzymes

Neurotransmitters may be reabsorbed too quickly

When neurotransmitters are affected by disease or drugs, there can be a number of different adverse effects on the body.

Diseases such as Alzheimer's, epilepsy, and Parkinson's are associated with deficits in certain neurotransmitters.

Health professionals recognize the role that neurotransmitters can play in mental health conditions, which is why medications that influence the actions of the body's chemical messengers are often prescribed to help treat a variety of psychiatric conditions.

For example, dopamine is associated with such things as addiction and schizophrenia. Serotonin plays a role in mood disorders including depression and OCD.10 Drugs, such as SSRIs, may be prescribed by physicians and psychiatrists to help treat symptoms of depression or anxiety. Medications are sometimes used alone, but they may also be used in conjunction with other therapeutic treatments including cognitive-behavioral therapy.

Drugs That Influence Neurotransmitters

Perhaps the greatest practical application for the discovery and detailed understanding of how neurotransmitters function has been the development of drugs that impact chemical transmission. These drugs are capable of changing the effects of neurotransmitters, which can alleviate the symptoms of some diseases.

Agonists vs Antagonists: Some drugs are known as agonists and function by increasing the effects of specific neurotransmitters. Other drugs and referred to as antagonists and act to block the effects of neurotransmission.14

Direct vs Indirect Effects: These neuro-acting drugs can be further broken down based on whether they have a direct or indirect effect. Those that have a direct effect work by mimicking the neurotransmitters because they are very similar in chemical structure. Those that have an indirect impact work by acting on the synaptic receptors.

Drugs that can influence neurotransmission include medications used to treat illness including depression and anxiety, such as SSRIs, tricyclic antidepressants, and benzodiazepines.

Illicit drugs such as heroin, cocaine, and marijuana also have an effect on neurotransmission. Heroin acts as a direct-acting agonist, mimicking the brain's natural opioids enough to stimulate their associated receptors. Cocaine is an example of an indirect-acting drug that influences the transmission of dopamine.15

Identifying Neurotransmitters

The actual identification of neurotransmitters can actually be quite difficult. While scientists can observe the vesicles containing neurotransmitters, figuring out what chemicals are stored in the vesicles is not quite so simple.

Because of this, neuroscientists have developed a number of guidelines for determining whether or not a chemical should be defined as a neurotransmitter:16

The chemical must be produced inside the neuron.

The necessary precursor enzymes must be present in the neuron.

There must be enough of the chemical present to actually have an effect on the postsynaptic neuron.

The chemical must be released by the presynaptic neuron, and the postsynaptic neuron must contain receptors that the chemical will bind to.

There must be a reuptake mechanism or enzyme present that stops the action of the chemical.

Neurotransmitters play a critical role in neural communication, influencing everything from involuntary movements to learning to mood. This system is both complex and highly interconnected. Neurotransmitters act in specific ways, but they can also be affected by diseases, drugs, or even the actions of other chemical messengers.

Biosynthesis of Selected Neurotransmitters

(1). Glutamate;

(2). Norepinephrine

In neuroscience, glutamate refers to the anion of glutamic acid in its role as a neurotransmitter: a chemical that nerve cells use to send signals to other cells. It is by a wide margin the most abundant excitatory neurotransmitter in the vertebrate nervous system.[1] It is used by every major excitatory function in the vertebrate brain, accounting in total for well over 90% of the synaptic connections in the human brain. It also serves as the primary neurotransmitter for some localized brain regions, such as cerebellum granule cells.

Biochemical receptors for glutamate fall into three major classes, known as AMPA receptors, NMDA receptors, and metabotropic glutamate receptors. A fourth class, known as kainate receptors, are similar in many respects to AMPA receptors, but much less abundant. Many synapses use multiple types of glutamate receptors. AMPA receptors are ionotropic receptors specialized for fast excitation: in many synapses they produce excitatory electrical responses in their targets a fraction of a millisecond after being stimulated. NMDA receptors are also ionotropic, but they differ from AMPA receptors in being permeable, when activated, to calcium. Their properties make them particularly important for learning and memory. Metabotropic receptors act through second messenger systems to create slow, sustained effects on their targets.

Because of its role in synaptic plasticity, glutamate is involved in cognitive functions such as learning and memory in the brain.[2] The form of plasticity known as long-term potentiation takes place at glutamatergic synapses in the hippocampus, neocortex, and other parts of the brain. Glutamate works not only as a point-to-point transmitter, but also through spill-over synaptic crosstalk between synapses in which summation of glutamate released from a neighboring synapse creates extrasynaptic signaling/volume transmission.[3] In addition, glutamate plays important roles in the regulation of growth cones and synaptogenesis during brain development.

Biosynthesis

Glutamate is a major constituent of a wide variety of proteins; consequently it is one of the most abundant amino acids in the human body.[1] Under ordinary conditions enough is obtained from the diet that there is no need for any to be synthesized. Nevertheless, glutamate is formally classified as a non-essential amino acid, because it can be synthesized from alpha-Ketoglutaric acid, which is produced as part of the citric acid cycle by a series of reactions whose starting point is citrate. Glutamate cannot cross the blood-brain barrier unassisted, but it is actively transported out of the nervous system by a high affinity transport system, which maintains its concentration in brain fluids at a fairly constant level.[4]

Glutamate is synthesized in the central nervous system from glutamine as part of the glutamate–glutamine cycle by the enzyme glutaminase. This can occur in the presynaptic neuron or in neighboring glial cells.

Glutamate itself serves as metabolic precursor for the neurotransmitter GABA, via the action of the enzyme glutamate decarboxylase.

Synthesis of Norepinephrine

The retention of H3-norepinephrine in the rat brain after the injection of H3-norepinephrine into the lateral ventricle of the brain was severely reduced 6 hr after a single injection of reserpine. The ability to retain small amounts of H3-norepinephrine in the brain recovered rapidly between 24 and 48 hr after reserpine at a time when the animals were recovering from the most obvious behavioral effects of the drug. During this period the endogenous norepinephrine content of the brain was markedly depressed and rose only slowly to 40% of normal levels after 8 days. In reserpine-treated rat brains the accumulation of H3-norepinephrine could be inhibited by pretreatment with a second dose of reserpine or increased by treatment with an inhibitor of monoamine oxidase. Treatment of reserpinized animals with amphetamine or DMI produced changes in the metabolism of H3-norepinephrifle which indicate that these drugs are still able to inhibit norepinephrine uptake in such animals. These results are consistent with other studies which suggest that the primary action of reserpine is to impair the intracellular storage of norepinephrine rather than to inhibit the uptake of norepinephrine into adrenergic neurons. The small amount of H3-norepinephrine retained in the brains of 24-hr reserpinized animals was resistant to release by amphetamine or by the administration of an additional dose of reserpine. After the administration of C14-tyrosine or H3-dopamine into the lateral ventricle of normal or reserpinized rat brains it was possible to demonstrate that all the enzymatic steps involved in the biosynthesis of norepinephrine can occur in reserpinized animals.