Lecture #06 Neuromodulatory Systems

Question 1: Which correctly matches a neuromodulator with its principal nucleus of origin?

a) Serotonin, Hypothalamus

b) Dopamine, Hypothalamus

c) Acetylcholine, Hypothalamus

d) Serotonin, Raphe nuclei

e) Histamine, Locus Coeruleus

HINT:

Consider the neurotransmitter thought to be involved in depression

EXPLANATION:

Serotonin is produced by the widespread raphe nuclei and sent by long ascending and descending axons throughout the central nervous system.

Acetylcholine::Basal forebrain, two pontine nuclei.

Dopamine::substantia nigra pars compacta, ventral tegmental area.

Histamine::tuberomammillary nucleus of hypothalamus.

Norepinephrine::locus coeruleus.

Serotonin::raphe nuclei of brainstem.

ANSWER: ['Serotonin, Raphe nuclei']

Lecture #06 Neuromodulatory Systems

Question 2: What is the most universal aspect of a neuromodulator's action?

a) It is G protein coupled

b) It has rapid onset

c) It has rapid termination

d) It originates from billions of widely dispersed cell bodies

e) It has precisely placed synapses

HINT:

Contrast neuromodulators with neurotransmitters that act directly to alter ion channels

EXPLANATION:

Direct ion channel neurotransmission is inherently rapid and discrete. It is delayed only by cleft transport and action upon binding at receptors, and it does not spread beyond the closely apposed pre- and post-synaptic elements. Neuromodulators may be released at axonal varicosities located at a distance from their site of action, rather than at discrete synapses. Neuromodulators are also called second messenger neurotransmitters. They act via G protein coupled mechanisms that alter enzymatic activity and thus indirectly, slowly, and profoundly alter neuronal excitability. There are many G protein coupled actions. The most common action is via adenylate cyclase and protein kinase to phosphorylate membrane proteins and thus alter membrane properties.

ANSWER: ['It is G protein coupled']

Lecture #06 Neuromodulatory Systems

Question 3: Where are the raphe nuclei located?

a) Midbrain (mesencephalon)

b) Brainstem midline

c) Dorsolateral pontine tegmentum

d) Basal forebrain

e) Hypothalamus

HINT:

The serotonergic nuclei are among the most widespread of neuromodulator nuclei

EXPLANATION:

Raphe refers to the midline seam of the brainstem. Serotonergic raphe nuclei are narrow structures found from medulla through midbrain along the raphe. The raphe nuclei appear very big from a lateral view, but small and thin when looking up or down the brainstem.

ANSWER: ['Brainstem midline']

Lecture #06 Neuromodulatory Systems

Question 4: Which neuromodulator is released by stimuli that predict reward?

a) Histamine

b) Serotonin

c) Norepinephrine

d) Acetylcholine

e) Dopamine

HINT:

Reward prediction involves the same neuromodulator as internal reward itself

EXPLANATION:

Reward prediction involves the same neuromodulator as internal reward itself. Dopamine is a catecholamine neurotransmitter that has major functions in motor behavior and internal reward mechanisms. Dopamine is produced mainly in the midbrain by the substantia nigra pars compacta and the ventral tegmental area, which have long ascending axons that terminate throughout the higher brain regions. Loss of dopamine with degeneration of the substantia nigra in Parkinson's disease results in reduced motor abilities. Replacement of dopamine as a therapy for Parkinson's disease can result in inappropriate reward-seeking behavior.

ANSWER: ['Dopamine']

Lecture #06 Neuromodulatory Systems

Question 5: What disease is believed to result from loss of cell bodies of cholinergic neuromodulatory neurons?

a) Alzheimer's

b) Parkinson's

c) Pick's

d) Hemiballismus

e) Huntington's

HINT:

hint

EXPLANATION:

Alzheimer's disease is believed to result from loss of cholinergic neuromodulatory neurons, leading to depression of the cerebral cortex. There is little effective treatment for Alzheimer's disease, with most promising treatments acting on the cholinergic neuromodulatory system.

ANSWER: ["Alzheimer's"]

Lecture #06 Neuromodulatory Systems

Question 6: Where is the locus coeruleus located?

a) Ventral pons

b) Dorsal medulla

c) Ventral medulla

d) Dorsal midbrain

e) Dorsal pons

HINT:

The locus coeruleus is the primary source of norepinephrine in the brain

EXPLANATION:

Norepinephrine is produced by neurons of the locus coeruleus in the dorsolateral pons, which have long ascending and descending axons that provide norepinephrine throughout the brain. Norepinephrine is a major arousal neuromodulator. The locus coeruleus is an important component of the ascending reticular activating system.

ANSWER: ['Dorsal pons']

Lecture #06 Neuromodulatory Systems

Question 7: Where are the cell bodies of dopaminergic neurons?

a) Substantia nigra (SNc)

b) Basal forebrain

c) Raphe nuclei

d) Tuberomammillary nucleus

e) Locus coeruleus

HINT:

Dopamine loss accompanies Parkinson's disease

EXPLANATION:

Dopamine is a catecholamine neurotransmitter that has major functions in motor behavior and internal reward mechanisms. Dopamine is produced mainly in the midbrain by the substantia nigra pars compacta and the ventral tegmental area, which have long ascending axons that terminate throughout the higher brain regions. Loss of dopamine with degeneration of the substantia nigra in Parkinson's disease results in reduced motor abilities. Replacement of dopamine as a therapy for Parkinson's disease can result in inappropriate reward-seeking behavior.

ANSWER: ['Substantia nigra (SNc)']

Lecture #06 Neuromodulatory Systems

Question 8: 5-hydroxytryptamine (5HT) is which neuromodulator?

a) Serotonin

b) Dopamine

c) Norepinephrine

d) Acetylcholine

e) Histamine

HINT:

Consider alternate names for amine neuromodulators

EXPLANATION:

Serotonin is made from tryptophan. Tryptophan is converted to 5 hydroxytryptophan (5 HTP) by tryptophan hydroxylase. 5 HTP is converted to serotonin (5HT, 5 hydroxy tryptamine) by 5 HTP decarboxylase. Monoamine oxidases break down the amine neurotransmitters.

ANSWER: ['Serotonin']

Lecture #06 Neuromodulatory Systems

Question 9: Where are the cell bodies of noradrenergic (norepinephrinergic) neurons?

a) Tuberomammillary nucleus

b) Substantia nigra (SNc)

c) Locus coeruleus

d) Raphe nuclei

e) Basal forebrain

HINT:

Identify the nucleus that produces norepinephrine

EXPLANATION:

Norepinephrine is produced by neurons of the locus coeruleus in the dorsolateral pons, which have long ascending and descending axons that provide norepinephrine throughout the brain. Norepinephrine is a major arousal neuromodulator. The locus coeruleus is an important component of the ascending reticular activating system.

ANSWER: ['Locus coeruleus']

Lecture #06 Neuromodulatory Systems

Question 10: Where are the cell bodies of cholinergic neuromodulatory neurons?

a) Substantia nigra (SNc)

b) Locus coeruleus

c) Tuberomammillary nucleus

d) Raphe nuclei

e) Basal forebrain

HINT:

Alzheimer's disease is believed to result from loss of cholinergic neuromodulatory neurons

EXPLANATION:

Acetylcholine acts as an arousal neuromodulatory neurotransmitter. Neuromodulatory acetylcholine is produced mainly by the neurons of the basal forebrain, in areas including the nucleus basalis of Meynert, and also in two nuclei of the pontine tegmentum, the pedunculopontine nucleus and the laterodorsal tegmental nucleus. The pontine acetylcholine neurons are involved in the wake-sleep cycle, with acetylcholine levels being high during wakefulness and rapid eye movement sleep (REM sleep) and low during slow wave sleep.

ANSWER: ['Basal forebrain']

Lecture #06 Neuromodulatory Systems

Question 11: Which neuromodulator is found in the pedunculopontine and laterodorsal tegmental nuclei of the pons?

a) Muscarine

b) Gamma Amino Butyric Acid (GABA)

c) Acetylcholine

d) Histamine

e) Galanin

HINT:

The same neurotransmitter is found in the basal forebrain

EXPLANATION:

Acetylcholine acts as an arousal neuromodulatory neurotransmitter. Neuromodulatory acetylcholine is produced mainly by the neurons of the basal forebrain, in areas including the nucleus basalis of Meynert, and also in two nuclei of the pontine tegmentum, the pedunculopontine nucleus and the laterodorsal tegmental nucleus. The pontine acetylcholine neurons are involved in the wake-sleep cycle, with acetylcholine levels being high during wakefulness and rapid eye movement sleep (REM sleep) and low during slow wave sleep.

ANSWER: ['Acetylcholine']

Lecture #06 Neuromodulatory Systems

Question 12: What disease results from loss of substantia nigra (SNc) neurons?

a) Parkinson's

b) Pick's

c) Huntington's

d) Hemiballismus

e) Alzheimer's

HINT:

The direct and indirect pathways of the basal ganglia are both affected, but the root cause lies elsewhere

EXPLANATION:

The substantia nigra pars compacta has dopamine neurons that release dopamine in the striatum at D1 and D2 receptor-expressing striatal projection neurons, depressing the excitatory direct pathway and enhancing the inhibitory indirect pathway. Important basal ganglia disease correlations are:

Parkinson's disease::substantia nigra pars compacta

Huntington's disease::D2 striatal neurons

Hemiballism::subthalamic nucleus

ANSWER: ["Parkinson's"]

Lecture #06 Neuromodulatory Systems

Question 13: Which is a prominent inhibitory peptide neuromodulator?

a) Histamine

b) Acetylcholine

c) Galanin

d) Gamma Amino Butyric Acid (GABA)

e) Muscarine

HINT:

hint

EXPLANATION:

Known inhibitory neuromodulator neurotransmitters are less numerous than excitatory ones. The main inhibitory neurotransmitter throughout the central nervous system is gamma amino butyric acid or GABA. Glycine is also an inhibitory amine neurotransmitter. The most prominent inhibitory peptide neurotransmitter is galanin, which is widespread in the nervous system. Galanin inhibits the excitatory neuromodulators and promotes sleep.

ANSWER: ['Galanin']

Lecture #06 Neuromodulatory Systems

Question 14: Which neuromodulator is most directly associated with reward prediction?

a) Substance P

b) Norepinephrine

c) Dopamine

d) Serotonin

e) Acetylcholine

HINT:

The reward neurotransmitter is also vital for motor activity

EXPLANATION:

Dopamine is a catecholamine neurotransmitter that has major functions in motor behavior and internal reward mechanisms. Dopamine is produced mainly in the midbrain by the substantia nigra pars compacta and the ventral tegmental area, which have long ascending axons that terminate throughout the higher brain regions. Loss of dopamine with degeneration of the substantia nigra in Parkinson's disease results in reduced motor abilities. Replacement of dopamine as a therapy for Parkinson's disease can result in inappropriate reward-seeking behavior.

ANSWER: ['Dopamine']

Lecture #06 Neuromodulatory Systems

Question 15: What disorder results from loss of the subthalamic nucleus?

a) Hemiballismus

b) Huntington's

c) Parkinson's

d) Alzheimer's

e) Pick's

HINT:

The subthalamic nucleus is part of the indirect pathway of the basal ganglia

EXPLANATION:

Important basal ganglia disease correlations are:

Parkinson's disease::substantia nigra pars compacta

Huntington's disease::D2 striatal neurons

Hemiballism::subthalamic nucleus

ANSWER: ['Hemiballismus']

Lecture #06 Neuromodulatory Systems

Question 16: Which enzyme is required for production of norepinephrine but not dopamine?

a) Dopamine beta hydroxylase

b) Tyrosine hydroxylase

c) Dopa decarboxylase

d) 5-HTP decarboxylase

e) Tryptophan hydroxylase

HINT:

norepinephrine is one metabolic step beyond dopamine

EXPLANATION:

The amine neurotransmitters are generally made from amino acids with a hydroxylase enzyme followed by a decarboxylase enzyme, with further steps to make additional neurotransmitters. Tyrosine is converted by tyrosine hydroxylase to levodopa, l-dopa, which is converted by dopa decarboxylase to dopamine. If dopamine beta hydroxylase is present, dopamine is converted to norepinephrine. Further steps can follow for epinephrine, etc. Serotonin is made from tryptophan. Tryptophan is converted to 5-hydroxytryptophan (5 HTP) by tryptophan hydroxylase. 5-HTP is converted to serotonin (5 HT) by 5 HTP decarboxylase. Monoamine oxidases break down the amine neurotransmitters. Catechol-O-methyl transferase (COMT) breaks down the catecholamine neurotransmitters dopamine and norepinephrine.

ANSWER: ['Dopamine beta hydroxylase']

Lecture #06 Neuromodulatory Systems

Question 17: Cocaine and amphetamines share which neuromodulatory action?

a) Increase of the duration and spatial extent of dopamine action

b) Reduction of symptoms of schizophrenia

c) Reduction of the duration and spatial extent of dopamine action

d) Increasing the activity of the serotonin transporter

e) Increasing the activity of the dopamine transporter

HINT:

Cocaine and amphetamines act at catecholaminergic synapses

EXPLANATION:

Cocaine and amphetamines have multiple actions, most directly affecting dopamine and norepinephrine. They reduce reuptake of dopamine and norepinephrine by reducing activity of the dopamine transporter (DAT) and norepinephrine transporter (NET). This increases the duration and spatial extent of dopamine and norepinephrine action. Cocaine and amphetamines mimic internal reward mechanisms that act via dopamine release.

ANSWER: ['Increase of the duration and spatial extent of dopamine action']

Lecture #06 Neuromodulatory Systems

Question 18: Which is a common feature of the initial synthetic step for Dopamine and Serotonin?

a) 5-HTP

b) Tryptophan amino acid

c) Tyrosine amino acid

d) Monoamine oxidase

e) Hydroxylase enzyme

HINT:

Dopamine is synthesized from tyrosine, serotonin from tryptophan

EXPLANATION:

The amine neurotransmitters are generally made from amino acids with a hydroxylase enzyme followed by a decarboxylase enzyme, with further steps to make additional neurotransmitters. Tyrosine is converted by tyrosine hydroxylase to levodopa, l-dopa, which is converted by dopa decarboxylase to dopamine. If dopamine beta hydroxylase is present, dopamine is converted to norepinephrine. Further steps can follow for epinephrine, etc. Serotonin is made from tryptophan. Tryptophan is converted to 5 hydroxytryptophan (5 HTP) by tryptophan hydroxylase. 5 HTP is converted to serotonin (5HT, 5 hydroxy tryptamine) by 5 HTP decarboxylase. Monoamine oxidases break down the amine neurotransmitters. Catechol-O-methyl transferase (COMT) breaks down the catecholamine neurotransmitters dopamine and norepinephrine.

ANSWER: ['Hydroxylase enzyme']

Lecture #06 Neuromodulatory Systems

Question 19: What is the effect of blocking DAT or NET (SLC6A2)?

a) Increased acetylcholine levels

b) Decreased catecholamine levels

c) Decreased acetylcholine levels

d) Increased catecholamine levels

e) Decreased arousal

HINT:

Some drugs act primarily in this manner

EXPLANATION:

Cocaine and amphetamines have multiple actions, most directly affecting dopamine and norepinephrine. They reduce reuptake of dopamine and norepinephrine by reducing activity of the dopamine transporter (DAT) and norepinephrine transporter (NET). This increases the duration and spatial extent of dopamine and norepinephrine action. Cocaine and amphetamines mimic internal reward mechanisms that act via dopamine release.

ANSWER: ['Increased catecholamine levels']

Lecture #06 Neuromodulatory Systems

Question 20: Which is a feature of direct ion channel neurotransmission that is not shared by neuromodulators?

a) Phosphorylation of membrane proteins

b) Amplification of effects by enzymes that convert multiple molecules

c) Wide variety of potential ultimate effects

d) Rapid and discrete action

e) Control of overall neuronal excitability

HINT:

Contrast neuromodulators with neurotransmitters that act directly to alter ion channels

EXPLANATION:

Direct ion channel neurotransmission is inherently rapid and discrete. It is delayed only by cleft transport and action upon binding at receptors, and it does not spread beyond the closely apposed pre- and post-synaptic elements. Neuromodulators may be released at axonal varicosities located at a distance from their site of action, rather than at discrete synapses. Neuromodulators are also called second messenger neurotransmitters. They act via G protein coupled mechanisms that alter enzymatic activity and thus indirectly, slowly, and profoundly alter neuronal excitability. There are many G protein coupled actions. The most common action is via adenylate cyclase and protein kinase to phosphorylate membrane proteins and thus alter membrane properties.

ANSWER: ['Rapid and discrete action']

Lecture #06 Neuromodulatory Systems

Question 21: Which is a second location of the cell bodies of dopaminergic neurons?

a) Substantia nigra pars reticulata (SNr)

b) Striatum

c) Horizontal limb of the diagonal band of Broca (HDB)

d) Nucleus basalis of Meynert

e) Ventral tegmental area (VTA)

HINT:

The secondary area of dopamine cell bodies is near the primary area

EXPLANATION:

The ventral tegmental area (VTA) is located in the midbrain. The VTA is medial and partly ventral to the substantia nigra pars compacta. A summary of neuromodulator areas and transmitters is:

Acetylcholine::Basal forebrain, two pontine nuclei.

Dopamine::substantia nigra pars compacta, ventral tegmental area.

Histamine::tuberomammillary nucleus of hypothalamus.

Norepinephrine::locus coeruleus.

Serotonin::raphe nuclei of brainstem.

ANSWER: ['Ventral tegmental area (VTA)']

Lecture #06 Neuromodulatory Systems

Question 22: What disease progresses from loss of the D2 striatal neurons?

a) Pick's

b) Alzheimer's

c) Parkinson's

d) Hemiballismus

e) Huntington's

HINT:

An early part of the indirect pathway of the basal ganglia is involved

EXPLANATION:

Important basal ganglia disease correlations are:

Parkinson's disease::substantia nigra pars compacta

Huntington's disease::D2 striatal neurons

Hemiballism::subthalamic nucleus

ANSWER: ["Huntington's"]