NBL 355-655 Module 14 Review Q&A

The information in this study guide is derived directly from Chapters 3 and 4 of Essential of Modern Neuroscience and selective Wikipedia articles.

*1. What are the divisions, functions, inputs to and outputs from the amygdala?*

The amygdala is a subcortical almond-shaped group of nuclei derived located deep and medially within each temporal lobe. Part of the limbic system, the amygdala is an integration center that is critical for the processing of emotion, including emotional reactions, emotional communication, emotional memory, motivation, and decision making. The amygdala is interconnected with numerous cortical and subcortical areas, receiving inputs from all the senses via the thalamus and cerebral cortex and from the hypothalamus and brainstem. Connections to these areas allow the amygdala to process information from sensory areas and areas associated with behavior and autonomic function. The amygdala interacts directly with other parts of the limbic system, generating autonomic emotional reactions particularly related to survival, such as fear and the fight-or-flight response. In addition, the amygdala is involved in processing of other emotions, such as anger, pleasure, and motivation. It’s also involved in the modulation of a variety of cognitive functions, such as attention and perception and is responsible for providing emotional content to long-term declarative memories.

Composed of approximately 13 nuclei, the amygdala is functionally divided into 3 major interconnected regions: the basolateral complex, the corticomedial nuclear group, and the central nucleus. The largest subdivision, the basolateral complex, has reciprocal connections with the cerebral cortex, thalamus, and hippocampus. Information from the olfactory system is received by the corticomedial nuclei. The corticomedial nuclei and central nucleus provide direct outputs to the hypothalamus, and the central nucleus also provides direct output to brainstem areas that control expression of innate behaviors and associated physiologic responses.

*2. What are the divisions, functions, inputs to and outputs from the hippocampus?*

The medial temporal lobe contains the hippocampus and associated cortical structures that are critical for encoding long-term declarative and spatial memory and the transmission of memories to other cortical regions for long-term memory storage. Declarative memory includes semantic memory (for facts) and episodic memory (for events). The hippocampus has also been implicated in navigation and spatial cognition. The hippocampus looks similar to a seahorse or ram’s horn. The hippocampus is part of cerebral cortex but is allocortex with only 3-4 layers. The main input to the hippocampus is from the entorhinal cortex. The entorhinal cortex is reciprocally connected with many cortical and subcortical structures including sensory areas, thalamic nuclei, medial septal nucleus, hypothalamus, and brainstem. The main output from the hippocampus is to the subiculum, which projects to numerous areas including the prefrontal cortex, hypothalamus, entorhinal cortex, amygdala, nucleus accumbens and other areas.

Since different neuronal cell types are neatly organized into layers in the hippocampus, it has frequently been used as a model system for studying neural plasticity known as long-term potentiation (LTP), which was initially discovered to occur in the hippocampus. LTP is widely believed to be one of the main neural mechanisms by which memories are encoded and probably stored in the brain. In Alzheimer's disease (and other forms of dementia), the hippocampus is one of the first regions of the brain to suffer damage; memory loss and disorientation are included among the early symptoms in AD.

*3.What are the divisions, functions, inputs to and outputs from the hypothalamus?*

The single hypothalamus lies beneath the thalamus and anterior to the midbrain. The overarching function of the hypothalamus is integration and control of body functions for survival and reproduction. The hypothalamus acts as an integrator to regulate basic life- and species-sustaining functions such as fluid and electrolyte balance, drinking and feeding behavior, energy metabolism, thermoregulation, stress responses, and sleep–wake cycles, as well as sexual behavior and reproduction. To produce control over so many bodily functions, the hypothalamus uses 3 major outputs: the behavioral, autonomic, and endocrine systems.

The hypothalamus receives sensory inputs necessary for the detection of changes in both the internal and external environments and controls behaviors related to those inputs. The hypothalamus receives direct sensory inputs from all the sensory systems. In addition, regions within the hypothalamus contain sensors for blood sugar, temperature, and ion levels and receptors for stress and appetite hormones. As part of the limbic system, the hypothalamus receives inputs from the hippocampus, amygdala, and cingulate cortex, which provide highly processed sensory and salience information from the rest of the cerebral cortex. These inputs to the hypothalamus contribute to a range of emotional responses, feelings, and expressions, as well as behaviors such as aggression and motivational behaviors, such as drinking, feeding, and sexual behaviors.

Well interconnected with the brainstem and spinal cord, the hypothalamus is also involved in control of the autonomic nervous system (ANS). Hypothalamic neurons send axons directly to the preganglionic neurons in both the sympathetic and parasympathetic ANS. In addition, the hypothalamus has extensive outputs to adjust brainstem circuits that regulate autonomic output. The hypothalamus links the nervous system to the endocrine system via the pituitary gland, which releases hormones into the bloodstream and consequently controls many physiologic functions of the body. Some neurons the hypothalamus send their axons to form the posterior pituitary where they secrete oxytocin and vasopressin directly into the circulation. Other neurons in the hypothalamus send axons that release hypothalamic hormones, which act on the anterior pituitary to regulate secretion of specific anterior pituitary hormones into the circulation. Another key function of the hypothalamus is regulation of body functions in concert with the daily light–dark cycle, in which the suprachiasmatic nucleus is responsible for entraining circadian rhythms to the day–night cycle.

*4.What are the divisions, functions, inputs to and outputs from the brainstem?*

Considered one of the most primitive parts of the human brain, the brainstem (or brain stem) is the structure most important to life. In the human brain the brainstem is composed of the midbrain, the pons, and the medulla oblongata. The brainstem contains nuclei, which are essential for automatic, reflex, and autonomic functions that are critical for survival, and white matter tracks that connect the forebrain with the cerebellum and spinal cord. The white matter tracts are involved in transmission of motor impulses that control the body and head and the largest majority of sensory tracts. In addition, 10 of the 12 pairs of CNs emerge directly from the brainstem, with nuclei involved in both somatic motor and sensory functions of the head, face, and neck and in autonomic parasympathetic functions. The brainstem also contains nuclei involved in essential automatic processes, including breathing and nuclei for the control of cardiac, vascular and respiratory function, helping to control heart rate, blood pressure and breathing rate. It also contains the reticular formation, a group of nuclei located from the upper midbrain to the lower medulla that function in arousal, alertness, sleep and wakefulness, consciousness, and other motor and sensory functions.

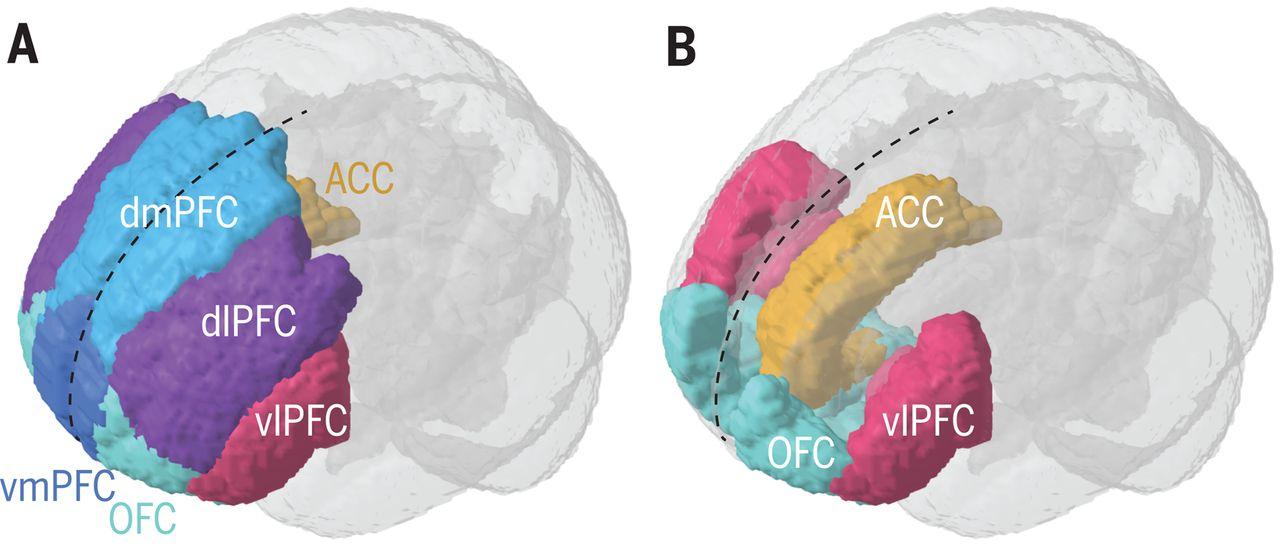
In Module 12 we learned that the midbrain contains the substantia nigra and ventral tegmental area, two regions that contain dopaminergic neuron cell bodies that contribute to the basal ganglia and are involved in motor control, and motivation and reward pathways. The pons contains the locus coeruleus, which contains the cell bodies of norepinephrine neurons (noradrenergic neurons). The Raphe nuclei, which contain the cell bodies or serotonergic neurons, are located in the midbrain, pons and medulla.

*5. What are the divisions, functions, inputs to and outputs from the prefrontal cortex?*

An important role of the frontal lobe is to produce cognitive functions that orchestrate thoughts with the selection of appropriate actions to achieve particular goals. The two major areas in the frontal lobe are the motor cortex and the prefrontal cortex. We already covered the motor cortex in Module 13. It is the function of the prefrontal cortex to predict outcomes, project future consequences resulting from current activities, work toward a defined goal, make expectations based on actions and evaluate the consequences of a particular course of action, differentiate among conflicting thoughts, determine similarities and differences between things or events, choose between good (or better) and bad (or worse) actions, suppress impulses, and override and control socially unacceptable responses.

The prefrontal cortex is involved in what are termed *executive functions*, including attentional control, short-term working memory, self-control and moderation of social behavior, decision making, judgment, planning, reasoning, problem solving, and abstract thinking, as well as the expression of emotion and personality. These cognitive functions require the prefrontal cortex but also involve other cortical and subcortical regions as well. Though we often think about the prefrontal cortex as mainly involved in the executive functions of decision making and problem solving, it also has major roles in cognitive, behavioral and emotional control.

The prefrontal cortex can be divided into four main regions (also called domains) and each of these regions consists of particular gyri and sulci, and have specific functions. There are two regions in the dorsal prefrontal cortex: the dorsolateral prefrontal cortex (dlPFC) and dorsomedial prefrontal cortex (dmPFC). There are two regions in the ventral prefrontal cortex. One is the ventromedial prefrontal cortex (vmPFC), which is considered anatomically synonymous with the orbitofrontal cortex (OFC), and will be referred to as the OFC/vmPFC. The other is the ventrolateral prefrontal cortex (vlPFC).



The prefrontal cortex is highly interconnected with much of the brain, including extensive connections with other cortical, subcortical, and brainstem regions. The prefrontal cortex receives massive inputs from the somatosensory, visual, and auditory sensory association cortices and also from the thalamus. The dorsal prefrontal cortex is especially interconnected with brain regions involved with attention, cognition, and action, whereas the ventral prefrontal cortex interconnects with brain regions involved with emotion.

Dorsal Regions: The DLPFC has connections with the OFC/vmPFC, thalamus, basal ganglia, hippocampus, and association areas of the temporal, parietal, and occipital lobes. An important function of the DLPFC is executive functions, such as working memory, decision making, planning, cognitive flexibility, inhibition, and abstract reasoning. However, the DLPFC is not exclusively responsible for these executive functions. All complex mental/cognitive activity requires the additional cortical and subcortical circuits with which the DLPFC is connected. The DLPFC is also the highest cortical area that is involved in motor planning, organization and regulation. The dmPFC is identified to play a variety of roles including processing a sense of self, integrating social impressions, theory of mind, morality judgments, empathy, decision making, altruism, fear and anxiety information processing, and top-down motor cortex inhibition. The dmPFC also modulates or regulates emotional responses and heart rate in situations of fear or stress and plays a role in long-term memory.

Ventral regions: The OFC/vmPFC has direct connections to the thalamus, amygdala, and cingulate cortex of the limbic lobe and are thought to be involved in impulse control and to provide the emotional and reward components to decision making, planned behavior, and memory. Other functions include the processing of risk and fear, as it is critical in the regulation of amygdala activity. It also plays a role in the inhibition of emotional responses, and in the process of decision making, self control, and the cognitive evaluation of morality. The vlPFC is thought to play a critical role in motor inhibition and spatial attention. Also, the vlPFC is the end point of the ventral pathway (stream) that brings information about the stimuli's characteristics.

Note in the figure where the anterior cingulate cortex (ACC) is located. Though the ACC is not a part of the prefrontal cortex, the ACC lies in a unique position in the brain, with connections to both the “emotional” limbic system and the “cognitive” prefrontal cortex.

*6. What is the connectome?*

A connectome is a comprehensive map of neural connections in the brain, and may be thought of as its "wiring diagram". The wires are the axons, and bundles of axons are tracts in the CNS. The three types of tracts are the association, commissural and projection tracts. More broadly, a connectome would include the mapping of all neural connections within an organism's nervous system. The production and study of connectomes, known as connectomics, may range in scale from a detailed map of the full set of neurons and synapses within part or all of the nervous system of an organism to a macro scale description of the functional and structural connectivity between all cortical areas and subcortical structures. The term "connectome" is used primarily in scientific efforts to capture, map, and understand the organization of neural interactions within the brain. Research has successfully constructed the full connectome of the roundworm C. elegans, and partial connectomes of a mouse retina and mouse primary visual cortex have also been successfully constructed. The ultimate goal of connectomics is to map the human brain. This effort is pursued by the Human Connectome Project, sponsored by the National Institutes of Health (NIH), whose focus is to build a network map of the human brain in healthy, living adults.

*7. Describe neuroplasticity. What is BDNF?*

Neuroplasticity, also known as neural plasticity, or brain plasticity, is the ability of neural networks in the brain to change through growth and reorganization. These changes range from individual neurons making new connections, to systematic adjustments like cortical remapping. Examples of neuroplasticity include circuit and network changes that result from learning a new ability, environmental influences, practice, and psychological stress.

Neuroplasticity was once thought by neuroscientists to manifest only during childhood, but research in the latter half of the 20th century showed that many aspects of the brain can be altered (or are "plastic") even through adulthood. However, the developing brain exhibits a higher degree of plasticity than the adult brain. Activity-dependent plasticity can have significant implications for healthy development, learning, memory, and recovery from brain damage.

Structural plasticity is often understood as the brain's ability to change its neuronal connections. New neurons are constantly produced and integrated into the central nervous system throughout the life span based on this type of neuroplasticity. Researchers nowadays use multiple cross-sectional imaging methods (i.e. magnetic resonance imaging (MRI), computerized tomography (CT)) to study the structural alterations of the human brains. This type of neuroplasticity often studies the effect of various internal or external stimuli on the brain's anatomical reorganization. The changes of grey matter proportion or the synaptic strength in the brain are considered as examples of structural neuroplasticity. Structural neuroplasticity is currently investigated more within the field of neuroscience in current academia.

Functional plasticity refers to brain's ability to alter and adapt the functional properties of neurons. The changes can occur in response to previous activity (activity-dependent plasticity) to acquire memory or in response to malfunction or damage of neurons (reactive plasticity) to compensate a pathological event. In the latter case the functions from one part of the brain transfer to another part of the brain based on the demand to produce recovery of behavioral or physiological processes. Regarding physiological forms of activity-dependent plasticity, those involving synapses are referred to as synaptic plasticity. The strengthening or weakening of synapses that results in an increase or decrease of firing rate of the neurons are called long-term potentiation (LTP) and long-term depression (LTD), respectively, and they are considered as examples of synaptic plasticity that are associated with memory. More recently it has become clearer that synaptic plasticity can be complemented by another form of activity-dependent plasticity involving the intrinsic excitability of neurons, which is referred to as intrinsic plasticity. This, as opposed to homeostatic plasticity does not necessarily maintain the overall activity of a neuron within a network but contributes to encoding memories.

At the beginning of the connectome project, it was thought that the connections between neurons were unchangeable once established and that only individual synapses could be altered. However, recent evidence suggests that connectivity is also subject to change, termed neuroplasticity. There are two ways that the brain can rewire: formation and removal of synapses in an established connection or formation or removal of entire connections between neurons. Both mechanisms of rewiring are useful for learning completely novel tasks that may require entirely new connections between regions of the brain.

BDNF is a neurotrophic factor that acts on certain neurons, helping to support survival of existing neurons, and encouraging growth and differentiation of new neurons and synapses. During development BDNF promotes neuronal survival, and stimulates axonal branching, dendritic growth, and refinement of synapses in an activity-dependent manner. BDNF promotes the formation of both excitatory and inhibitory synapses and increases their maturation. In the adult brain BDNF has been shown to modulate synaptic transmission and plasticity.

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