NBL 356-656 Module 7 Review Q&A

1. *What is cognition and what are the main cognitive functions/domains? Would you consider emotion to be a cognitive function?*

Cognitive functions include attention and perception, both short term working memory and long term memory, executive functions and language. From Wikipedia, cognition is “the mental action or process of acquiring knowledge and understanding through thought, experience, and the senses.” The main cognitive functions/domains include attention, visual-spatial perception, long term memory, core/basic executive functions (such as inhibition, working memory and cognitive flexibility), higher order executive functions (such as planning, organizational skills, judgment and evaluation, reasoning, computation, problem solving, decision making and fluid intelligence), and the comprehension and production of language. Higher order executive functions require the simultaneous use of multiple basic executive functions and include planning and fluid intelligence (e.g., reasoning and problem solving). Some neuroscientists think that emotion can affect or is a component of several of the cognitive functions listed, but generally don’t consider emotion to be a cognitive function per se.

1. Define attention, selective attention and divided attention.

Attention is the behavioral and cognitive process of selectively concentrating on a discrete stimulus while ignoring other perceivable stimuli. Attention is the ability of our brains to focus its resources on whatever you want to focus on and perceive. It allows us to consciously or unconsciously focus more energy on something while letting other things slack in the background. Attention involves primarily the prefrontal cortex integrating information and communicating back to the sensory cortices to focus attention on specific things. Selective attention is the ability of our brains to focus its attention on one thing over everything around it. Selective attention is the ability to select from many factors or stimuli and to focus on only the one that you want while filtering out other distractions. Divided attention is the ability to process two or more responses or react to two or more different demands simultaneously. Divided attention is the ability of the brain to quickly switch between focusing its attention on several different things at the same time.

1. *What are large-scale brain networks, the default mode network, salience network and executive control network?*

Cognition is thought to result from the dynamic interactions of distributed brain areas operating in large-scale brain networks. The large-scale brain networks are connections of various brain regions that have been shown to be functionally linked in various functionalities. This is essentially a network of different brain regions connected by white matter tracts and working together to process and react to information.

The default mode network (DMN) is one of the resting-state networks, and has been associated with cognitive processes that are directed toward the self, such as introspection and autobiographic memory. The DMN’s integrity appears to be crucial for mental health. For example, patients with Alzheimer’s disease or other psychiatric conditions show disruptions of functional connectivity within the brain regions of the DMN. The DMN is the activity of the brain when we are not focusing on anything. It could be related to daydreaming or our stream of consciousness and could be the brain’s baseline activity of processing the environment.

The term salient refers to anything (person, behavior, trait, etc.) that is prominent, conspicuous, or otherwise noticeable compared with its surroundings. A salient feature can be thought of as the “figure” that stands out against the “ground” of all other nonsalient features. Saliency means the quality of being particularly noticeable or important; prominence. The salience network is formed by the coordination of the anterior insula and the dorsal anterior cingulate cortex. It is involved in detecting salient stimuli, such as bright colors or fast movement. This allows us to focus on the exogenous cues that stick out most to us.

The ECN functions in working memory, cognitive tasks that require externally-directed attention, integration of sensory and memory information, relational integration, response inhibition, task-set switching and the regulation of cognition and behavior. The ECN is often used to study the functional mechanism of executive function changes in patients, and several research teams have found a close correlation between executive function changes and the ECN.

1. *Why is memory the cognitive function/domain that has been the most intensely studied and yielded the most information about underlying mechanisms?*

Some possible ideas: A) Specific human brain injuries affect specific types of memory. B) Animal model studies have been used extensively to study memory. C) Clinical importance-dementias, neurodevelopmental disorders, and brain injury.

1. *Define memory and define the three main processes (encoding, storage and retrieval) thought to be involved in long term memory.*

Memory (in this case, referring to long term memory) is the process in which information is encoded, stored, and retrieved. A memory is a lasting representation that is reflected in thought, experiences, or behaviors.

Encoding or registration: receiving, processing, and combining of received information

Storage: creation of a permanent record of the encoded information

Retrieval, recall, or recollection: calling back the stored information in response to some cue for use in a process or activity

1. *What are the “three stages of memory” (or three types of memory systems)? What is the Atkinson–Shiffrin multistore memory model and what was so significant about it? What is the engram/memory trace?*

From Wikipedia: “The Atkinson–Shiffrin model (also known as the multi-store model or modal model) is a model of memory proposed in 1968 by Richard Atkinson and Richard Shiffrin. The model asserts that human memory has three separate components:

a sensory register (sensory memory), where sensory information enters memory,

a short-term store, also called short-term or working memory, which receives and holds input from both the sensory register, and a long-term store, where information that has been rehearsed in the short-term store is held indefinitely. The model is notable for the significant influence it had in stimulating subsequent memory research.”

From Wikipedia: “Engrams are theorized to be means by which memories are stored as biophysical or biochemical changes in the brain (and other neural tissue) in response to external stimuli. The existence of engrams is posited by some scientific theories to explain the persistence of memory and how memories are stored in the brain. The existence of neurologically defined engrams is not significantly disputed, though their exact mechanism and location has been a focus of persistent research for many decades.”

1. *What are the features of sensory memory and what brain regions are involved? What are the four types of sensory memory (modalities)?*

Sensory memory is very short term (it decays very quickly, on the order of hundreds of milliseconds to seconds), modality specific, weakly dependent on attention (can be conscious or unconscious), and very detailed with a high capacity. It has three well characterized subdivisions: iconic memory, echoic memory, and haptic memory, and though not well studied, olfactory and taste (gustatory) sensory memory are expected to occur as well. Iconic memory involves the occipital lobe (visual cortex), echoic memory involves the temporal lobe (auditory cortex), and haptic memory involves the parietal lobe (somatosensory cortex).

1. *Information is passed from sensory memory into short term memory via the process of attention. Again, what is attention? What are the features of short term memory and what brain regions are involved? What techniques can extend the capacity and duration of short term memory?*

From Wikipedia: “Attention is the behavioral and cognitive process of selectively concentrating on a discrete aspect of information, whether deemed subjective or objective, while ignoring other perceivable information. It is the taking possession by the mind in clear and vivid form of one out of what seem several simultaneous objects or trains of thought.”

“Short-term memory is the capacity for holding, but not manipulating, a small amount of information in mind in an active, readily available state for a short period of time.”

Primary Brain Regions - Prefrontal cortex, parietal lobe, temporal lobe

Short Term Memory Features

• Temporary recall of information that is being processed

• Retains approximately 7 pieces of information for 15-20 seconds (though this number was found for college students and has been revised for older adults to be about 4-5 pieces of info)

• It requires sensory memory and attention

• It involves short term storage of information

• There is agreement that short term memory involves (and requires) the prefrontal cortex. STM also requires other brain regions for sensing and transmitting incoming and retrieved information, attention, etc. Recently, “Researchers found persistently active neurons in the medial frontal lobe as well as the medial temporal lobe. The neurons remained active even after the patient stopped looking at an image or object. Until now, the medial temporal lobe was thought to be involved only in the formation of new long-term memories. Now, however, the new findings show that both areas of the brain are critical for maintaining short-term memory and rely upon the ongoing activity of the neurons for memorization.”

Rehearsal can extend the duration of STM, and the technique of chunking (dividing information into smaller groups that have some type of meaning or association with each other and/or prior memory) can improve the capacity of STM.

1. *Define working memory. How does short term memory relate to working memory? What brain regions are involved in short term working memory?*

From Wikipedia: “Working memory is a cognitive system with a limited capacity that is responsible for temporarily holding information available for processing. Working memory is important for reasoning and the guidance of decision making and behavior. Working memory is often used synonymously with short-term memory, but some theorists consider the two forms of memory distinct, assuming that working memory allows for the manipulation of short term stored information, whereas short-term memory only refers to the short-term storage of information.” Thus STM is a component of working memory.

Working memory involves the prefrontal cortex (PFC), parietal cortex and possibly the temporal cortex. Regarding the PFC: “One view was that the dorsolateral areas are responsible for spatial working memory and the ventrolateral areas for non-spatial working memory. Another view proposed a functional distinction, arguing that ventrolateral areas are mostly involved in pure maintenance of information, whereas dorsolateral areas are more involved in tasks requiring some processing of the memorized material.” “There is an emerging consensus that most working memory tasks recruit a network of PFC and parietal areas.” “This has led some researchers to argue that the role of PFC in working memory is in controlling attention, selecting strategies, and manipulating information in working memory, but not in maintenance of information. The maintenance function is attributed to more posterior areas of the brain, including the parietal cortex. Other authors interpret the activity in parietal cortex as reflecting executive functions, because the same area is also activated in other tasks requiring attention but not memory.”

1. *Describe the short term working memory model of Baddeley and Hitch, and explain the components.*

The original model of Baddeley & Hitch had three main components; the central executive, which acts as supervisory system and controls the flow of information to and from its subservient systems: the phonological loop and the visuo-spatial sketchpad. The phonological loop stores verbal content, whereas the visuo-spatial sketchpad retains visuo-spatial data. Both subservient systems only function as short-term storage centers. In 2000 Baddeley added a third subservient system to his model, the episodic buffer, which temporarily retains information recalled from long term memory that is relevant to the task at hand.

1. *What are the cellular (circuit) mechanisms proposed to be involved in short term working memory?*

Persistent firing of neurons within neural networks (for seconds to minutes) is thought to underlie short term working memory. From Wiki “neuronal microcircuits within PFC are able to maintain information in working memory through recurrent excitatory glutamate networks of pyramidal cells that continue to fire throughout the delay period.” And “It has been speculated that synchronous firing of neurons involved in working memory oscillate with frequencies in the theta band (4 to 8 Hz).” Thus, working memory is thought to involve persistent network activity, but not any biochemical or persistent molecular changes to the neurons or synapses in those networks.

1. *What are the characteristics of long term memory?*

Long term memory is characterized by a very large, perhaps unlimited, capacity. It is very long term, and can involve life-long storage and access/retrieval. It does not involve continued circuit activity but requires long term biochemical and morphological changes to neurons and synapses. LTM involves epigenetic, transcriptional and translational dependent changes in gene expression that results in biochemical, physiological and structural changes in synaptic connections, and new connections.

13. *What are the two main types of long term memory, and what are the sub-domains of each? Which regions of the brain are involved in each type of long term memory encoding?*

The two main types of LTM are called declarative (explicit) memory and non-declarative (implicit)memory. The subdomains of declarative/explicit memory are semantic, episodic and spatial memory and all three require the medial temporal lobe (including the hippocampus) for encoding these types of LTM. The subdomains of non-declarative/implicit memory (and the brain region involved in encoding) are: procedural memory (striatum and cerebellum), priming (prefrontal cortex), classical conditioning- emotional memory (amygdala), classical conditioning-muscle reflex (cerebellum) and non associative learning (reflex circuits).

14. *Where are long term memories stored?*

Long term memories are thought to be stored in neural circuits throughout the cerebral cortex.

15. *What are the main functions of the hippocampus (be specific)? Is the hippocampus where the majority of long term memories are stored?*

Functions of hippocampus include learning/encoding of long term declarative/explicit memories, including synaptic consolidation and early systems consolidation (transfer to cortex), spatial memory and navigation, and emotions. It has been hypothesized that the hippocampus is also required for the retrieval of some episodic and contextual memories. Synaptic plasticity in the hippocampus is thought to be involved in encoding declarative and spatial memory. Dr. Paul King suggests, “Two emerging views on the hippocampus in theoretical neuroscience is that it is a temporary store for new memories, which are later transferred to the cerebral cortex, and that it is responsible for generating coding schemes (like a database index or file compression "dictionary") to support efficient, compact, and organized representations in the cerebral cortex.” Long term memories are not thought to be stored in the hippocampus, but rather are stored in neuronal circuits throughout the cerebral cortex.

16. *Who was patient HM and what happened to him and why? What type of amnesia did he suffer? What key types of information did studies with patient HM provide?*

Henry Molaison (HM) was an epilepsy patient who underwent a bilateral medial temporal lobectomy to stop the seizures. This removed ~ 2/3 of his hippocampi, the parahippocampal cortices, the entorhinal cortex, piriform cortices and his amygdala. Postmortem analysis demonstrated that after the surgery the remaining portion of his hippocampi atrophied. Upon awakening from his surgery many of his existing memories remained intact but he lost the ability to form new explicit memories. He could still learn procedural tasks such as mirror tracing which is important because it suggested 1) a division of different types of long term memory in the brain as well as 2) revealing the importance of the hippocampus in processing new declarative memories. It also suggested that 3) working memory and sensory memory are anatomically separated from the encoding of explicit memory into long term memory. And 4) the majority of declarative memories are not stored in the hippocampus or require the hippocampus for retrieval. Retrograde amnesia is forgetting of events that happened in the past while anterograde amnesia, which HM suffered, is a deficit in the formation of new memories.

17. *The hippocampus is part of the cerebral cortex. What type of cortex is it? What are the main inputs to the hippocampus? What are the main outputs from the hippocampus? What are the additional minor inputs into CA1 of the hippocampus from the brainstem and basal forebrain?*

There are two types of cerebral cortex, allocortex and neocortex. The hippocampus is a type of allocortex, and is specifically a type of archicortex (primitive cortex), which is defined as cortex that only has three or four layers (instead of the six layers that defines neocortex). The main inputs to the hippocampus come from the entorhinal cortex. The entorhinal cortex receives inputs from the perirhinal cortex and the parahippocampal cortex.

In addition to its main input from CA3, the CA1 dendrites of the hippocampus receive additional minor inputs from the locus coeruleus, medial septal nucleus (cholinergic inputs), raphe nuclei, and the substantia nigra. Thus, neurons located in the basal forebrain and a variety of brainstem nuclei send cholinergic, dopaminergic, noradrenergic and serotonergic signals to the hippocampus. CA1 axons provide the main outputs from the hippocampus to the subiculum, amygdala, lateral septum, entorhinal cortex, and various areas of cortex.

18. *What is the definition of long-term potentiation (LTP)? How and where was it first discovered? Where else has it now been shown to occur?*

LTP is an activity dependent increase in synaptic strength (synaptic response) that persists for 30 minutes or more; LTP was first published from studies in vivo hippocampus in perforant pathway by Bliss & Lomo (1973); LTP has been extensively studied in CA3-CA1 synapse Schaffer Collateral; LTP Lasts 30 minutes to several hours in a hippocampal slice in vitor; LTP can last days or weeks in vivo. LTP has been demonstrated to occur in the hippocampus, neocortex, amygdala, striatum and cerebellum.

19. *What are the three main circuit “pathways” in the hippocampus? What types of neurons are dentate granule, CA1 and CA3 neurons, and what types of synapses do they form?*

Perforant pathway – Entorhinal cortex neurons project axons to granule neurons in the dentate gyrus. Mossy fiber pathway – Dentate gyrus granule neurons project axons called mossy fibers to pyramidal neurons in CA3 of the hippocampus. Schaffer Collaterals – CA3 neurons project axons to CA1 dendrites. The entorhinal cortex neurons that project to the DG, the dentate granule neurons in the dentate gyrus, the CA3, and CA1 pyramidal neurons are all glutamatergic neurons. The majority of the synapses are excitatory synapses on dendritic spines. Also there are a variety of GABAergic (inhibitory) interneurons in the hippocampus (which regulate the excitatory neurons).

20. *How is LTP measured electrophysiologically at the hippocampal CA3-CA1 synapse (Schaffer collateral)? What is a dendritic fEPSP and somatic population spike? Why are these downward responses (more negative) if they are excitatory?*

LTP is studied in the Schaffer collateral using a stimulating electrode to stimulate the CA3 axons to induce them to all fire action potentials at the same time, and uses an extracellular recording electrode to measure the dendritic excitatory post synaptic potentials from the population of dendrites, in response to the stimulated axons. A somatic population spike also occurs at the cell bodies (because there is so much dendritic excitation that action potentials are generated by the CA1 neurons). The extracellular recordings have a downward deflection due to the movement of Na+ ions into the neurons via AMPA receptor (and NMDA receptor) activity. The recording electrode is outside of the dendrites, so it reports the movement of Na+ to the inside of the cell (during the EPSP the outside of the membrane becomes more negative). LTP studies measure the CA1 population dendritic EPSPs or population spikes in response to presynaptic CA3 action potentials.

21. *Why is the hippocampus such a useful preparation to measure LTP? What are the roles of the different regions of the hippocampus?*

The hippocampus is required for long term memory encoding/acquisition and consolidation. It is an excellent area to measure LTP because one can stimulate the hippocampus at excitatory synapses and measure the plasticity at these synapses. The hippocampus can be extracted quickly and easily from rats and mice and slices remain viable for hours in oxygenated artificial cerebrospinal fluid. Moreover, basic extracellular electrophysiology techniques are easily applied to the investigation of synaptic function in hippocampal slices. Because all the neurons are connected in a very specific and repetitive way, one knows exactly which axons and where they are to stimulate, and which area to record in. And because so many neuronal axons can be stimulated simultaneously, it produces a very strong electrical response (from thousands of synapses) that can be easily measured with an extracellular electrode.

Rodent dorsal hippocampus (human posterior hippocampus) is proposed to be involved in encoding declarative memories and spatial memory. Rodent ventral hippocampus (human anterior hippocampus) is proposed to be involved in stress, emotion (such as fear conditioning) and affect.

22. *What is Hebb’s postulate and what does Hebbian mean?*

Hebb’s postulate: “neurons that fire together wire together” Long term potentiation is considered a Hebbian process because there is coincident activity in the presynaptic neuron and the postsynaptic neuron. A process is Hebbian if it is input specific. This is another way of stating Hebb’s hypothesis: When the presynaptic axon from neuron A is active (firing action potentials) and, at the same time, the postsynaptic neuron B is strongly activated (by that input from A or by additional synaptic inputs), then the synapse on B formed by the presynaptic axon A will be strengthened. (In the tetanus experiment, the presynaptic inputs from CA3 axons (in the Schaffer collateral pathway) provides both the presynaptic input (glutamate), and since it is so robust, it provides the strong activation of the postsynaptic neuron. Under physiological conditions, the input pathway would probably not provide enough stimulation on its own to robustly depolarize the postsynaptic cell. Rather the depolarization of the postsynaptic dendrites would involve many additional concomitant synaptic inputs.) The corollary is also true. When the presynaptic axon is active and, at the same time, the postsynaptic neuron is only weakly activated by that or other inputs, then the synapse formed by the presynaptic axon is weakened in LTD.