Emotion, Reward, and Mood

Limbic System: Gross Anatomy
1. The **limbic system** is a generic term for a collection of brain structures involved in memory & emotion.
   a. The major components of the limbic system are:
      i. **Amygdala**
      ii. **Hippocampus**
      iii. Medial cortical areas, specifically:
         1. **Cingulate cortex**
         2. **Entorhinal cortex**
         3. **Orbitofrontal cortex (OFC)**
         4. **Medial pre-frontal cortex** (mPFC).

Limbic System: Microscopic Anatomy
1. Hippocampus:
   a. **Dentate gyrus**
      i. The **input center** of the hippocampus.
         1. Receives input from **entorhinal cortex** (which gets input from other cortical areas)
   b. Cornu ammonis 3 (**CA3**)
   c. Cornu ammonis 1 (**CA1**)
   d. **Subiculum**
      i. The **output center** of the hippocampus.
      ii. Axons from these cells coalesce to form the **fimbria** (which turns into the **fornix**).
         1. The fimbria/fornix projects to cortex and many other places.
2. Amygdala:
   a. Lateral nucleus (L)
      i. An **input center** of the amygdala.
      ii. Has cytoarchitecture **similar to cortex**.
   b. Basal nucleus (B)
      i. An **input center** of the amygdala.
      ii. Has cytoarchitecture **similar to cortex**.
      iii. **Receives projections from cholinergic cells of the nucleus basalis of Meynert.**
   c. Central nucleus (Ce)
      i. **Output** center of the amygdala
      ii. Has a cytoarchitecture **similar to striatum**.
         1. This makes sense since it sits just inferior to the globus pallidus.
Limbic System: Circuitry

1. Hippocampus:
   a. Inputs:
      i. Information we want to learn goes from sensory cortex → entorhinal cortex → dentate gyrus
   b. Processing:
      i. Dentate gyrus → CA3 → CA1 → Subiculum
   c. Outputs:
      i. Subiculum → fimbria/fornix → cortex (“learned” information is stored into memory).
      ii. Subiculum → entorhinal cortex (“learned” information modulates input at start of circuit).

2. Amygdala:
   a. Inputs:
      i. “Significant” sensory stimuli go from sensory cortex → basal (B) & lateral (L) nuclei.
   b. Processing:
      i. There are many connections between the amygdala nuclei that do this.
   c. Output:
      i. The central nucleus receives processed info from other amygdala nuclei.
      ii. It initiates “emotional” (especially “fear”) responses…
         1. Directly:
            a. Ce → PAG (organize stress response).
            b. Ce → hypothalamus (induce hormone secretion).
            c. Ce → dorsal nu. of X; ventrolateral medulla (engage autonemics)
         2. Indirectly:
            a. Ce+B+L → (ventral striatum and/or MD thalamus) → mPFC → engage autonemics
            b. Ce+B+L → (ventral striatum and/or MD thalamus) → OFC → assign value or “significance” to sensory stimuli (to be discussed in addiction lecture).
Function of Amygdala and Hippocampus, together and separately.

1. Lesions of large parts of the temporal lobe (both amygdala & hippocampus) cause “psychic blindness.”
   a. Individuals become very passive, lacking fear and anger responses.
      i. For example, monkeys with such damage will approach live snakes.
   b. Individuals have no sense of objects’ significance.
      i. For example, monkeys with such damage try to eat inedible things like sticks, screws, etc.
   c. Individuals don’t learn about objects
      i. For example, they keep trying to eat sticks, screws, etc., over and over.

2. Lesions of the hippocampus produce memory deficits.

3. Lesions of the amygdala produce fear deficits.

4. Amygdala, MD thalamus, and mPFC have altered activity in depressed patients.
   a. Electrical stimulation of the mPFC seems to relieve depression.

What Have Experiments Taught Us About the Function of the Amygdala and its Associated Structures?

1. Amygdala:
   a. Involved in fear
      i. Stimulation of the amygdala has been shown to produce fear in patients.
      ii. Lesions of the amygdala block expression and recognition of fear.
   b. Involved in adapting behavioral & visceral responses to “emotional” situations.
      i. The classic example is **potentiation of the startle reflex**.
         1. First, how does the startle reflex (jumping in response to a loud sound) work?
            a. Sound signals travel from the cochlea to the cochlear nuclei.
            b. The cochlear nuclei project to the reticular formation.
            c. Reticular formation projects to spinal cord motor neurons to make us jump
   1. The amygdala doesn’t drive the startle response, but rather modulates it based on the emotional state of the animal.
      a. For example, if we were to put a mouse into a fearful state (by showing it a light that it knew would be followed by an electric shock), the animal will jump A LOT when a loud sound is played. If the amygdala is lesioned bilaterally, the extra jump due to the fearful state will not occur (i.e. the animal does not develop fear in the absence of the amygdala).
         i. In other words, the amygdala modulates the startle reflex circuitry to be more active during a fearful state.
         ii. Here’s a real life example:
            1. If a door slams while you are working on the computer, you might jump a little bit.
            2. If the door slams while you are sitting alone in the dark watching a scary movie (or in other words, are in a fearful state), you will jump A LOT!

2. mPFC:
   a. Interconnected with amygdala and other limbic structures.
   b. Cortical activation of autonomics
      i. Stimulating mPFC causes changes in blood pressure and respiratory rate.
      ii. mPFC activates autonomic responses during hypoglycemia.
         1. As you’ll learn next year, these include sweating and tachycardia.
            a. They are the body’s way of telling a person, “Go eat some food!”
   c. Implicated in mood disorders
      i. mPFC hyperactive in major depression
      ii. Deep brain stimulation in mPFC can relieve intractable depression.

3. Ventral Striatum & Ventral Pallidum
   a. Connected to amygdala, etc, to medial prefrontal cortex, and mediadorsal thalamus.
   b. Involved in turning on or off various emotional states, preferences, and moods.
4. The ventromedial prefrontal cortex was damaged in **Phineas Gage**
   a. He was a 1840s railroad worker who had a steel rod shot into his head by an aberrant explosion on the jobsite.
   b. His personality changed dramatically:
      i. He went from being a responsible person to being reckless, irresponsible, and vulgar.
5. Similar damage in ventromedial cortex in modern patients produces similar deficits.
   a. Damage causes abnormal “skin conductance responses” (SCRs) during “gambling tasks.”
      i. What is a skin conductance response?
         1. It is subconscious sweating due to emotional (often negative) stimuli.
      ii. What is a gambling task?
         1. Subjects are made to select playing cards from different decks.
            a. Each card has a dollar reward or penalty written on it.
            b. Some decks reward the subject in the long run; others penalize.
               i. Normal subjects have SCRs when drawing from bad decks.
               ii. Patients with OFC damage don’t show SCRs when drawing from bad decks, and pick from them without reservation.
   b. These patients lack the visceral reaction to emotional stimuli
   c. They also make markedly inappropriate and foolish choices.
   d. Without the visceral response they appear to lack a “warning signal” about bad choices.