COGS17 Neurobiology of Cognition

Lecture 11: Learning and Memory

LEARNING = The development of a permanent change in behavior based on experience

- **Law of Effect**: Stimulus/Context/Act associated with Reinforcement, will be repeated = "Conditioning"
  - Classical Conditioning = Developed association between stimuli
    - e.g. Dog salivates to Food. Pair Food (Pos Reinforcer=StimA) w/Bell (Conditioned Stimulus=StimB); Soon dog salivates to Bell alone, via association between Stim A & Stim B
  - Operant Conditioning = Developed association between stimulus and response
    - e.g. If pigeon pecks (Response) Target (Cond Stimulus) gets Food (Pos Reinf); Soon pecks often
    - e.g. While pigeon pecking target, Shocked (Neg Reinforcer) but only when Light (Conditioned Stim) on; Soon pigeon will stop pecking (Cond Resp) whenever light comes on (thus avoiding aversive shock)
  - **Temporal Contiguity** critical in both – i.e. above events must Co-Occur to become associated in learner's mind
    - Presumably, it is this co-occurrence that leads to the **neural co-activity** of the stimulated circuits
- **Hebbian Cell Assemblies** (proposed by Hebb as the fundamental neural process involved in Learning)
  = Co-activated neural circuits involved in learning and retrieval of associations (Fire Together:Wire Together)
  - Mechanisms responsible include structural or metabolic changes in NT availability, release, and/or reception
  - In contemporary computational models, involves development of "weighting" changes across Neural Nets

Long-Term Potentiation (LTP) (Semi-)permanent structural and connectivity changes, via variety of mechanisms:

- Post-Synaptic: Include structural changes in Receptor Sites, Dendritization, etc.
  - e.g. **Hippocampus** in the Rat, in which the best-studied mechanisms of LTP involve…
    - Cells w/multiple types of **Glutamate** Receptor Sites on the same cell; Some sites harder to trigger than others
      - **AMPA** Receptor Sites respond well to Glutamate (Ionotroipic: Allow Na+ in to excite Post-Synaptic cell)
      - **NMDA** Receptor Sites only respond to Glutamate if cell already partially hypo-polarized by above
      - Typically Magnesium ions (**Mg++**) block these gates that, when opened, allow Na+ & Ca++ to enter
    - When Post-Synaptic cell is massively stimulated by Glutamate from multiple Pre-Synaptic cells…
      - AMPA receptors reduce polarity of cell, evict Mg++, allowing NMDA Receptors to also respond
    - Ca++ influx helps **change structure** of **Post-Synaptic** cell, increasing its future responsiveness to Glutamate
      - e.g. New AMPA receptors form, or old ones are made even more responsive
      - e.g. Some NMDA Receptors are changed into the easier-to-stimulate AMPA receptors
      - e.g. Activates enzymes in cell that break protein "bridges" that structure dendritic spines, splitting them to form **new dendritic branches** (increased surface area) lined with AMPA Receptors

Other structural changes include…

- Pre-Synaptic: - **Retrograde Messengers** (e.g. Nitrous oxide) from Post-Syn cell that prolong NT release
  - **Perforation** = division, expansion of "Active Zone" of Pre-Syn by out-growth from surface of Post-Synaptic cell
- Genetic: Activity can turn on transcription of DNA to RNA, then translation of RNA into proteins
  - e.g. Such proteins may change #, size, & distribution of NT vesicles, or other relevant metabolic processes in cell
- Neurogenesis: Rare in NS overall, but common in Hippocampus, esp re temporal-based and spatial learning

MEMORY- The active process of retrieval of something learned

Different types of memory appear to be mediated by different areas of the brain

- **Spatial** - **Hippocampus:** Recall of specific locations, spatial judgments of familiarity
- **Procedural** - **Cerebellum & Striatum** (Basal Ganglia): Motor Skill, How to do it (peck a target, ride a bike)
- **Declarative** - **Hippocampus & Mediodorsal Thalamus:** Episodic (personal history), Semantic/Associative (facts)

Spatial Memory:

- Hippocampus esp active in rat learning a maze, developing a **Cognitive Map** of its environment
  - **Place Cells** in Hippocampus are differentially active when rat is in different, familiar locations
- Birds that cache thousands of seeds & must remember locations during winter (e.g. Clark's Nutcracker) have much larger Hippocampus than non-caching relatives (e.g. Scrub Jay)
  - Also larger in Humans who have extensive spatial experience (e.g. taxi drivers, bushmen)
- Humans show more activity (e.g. via PET scans) in Hippocampus while answering questions that depend on spatial information (e.g. re: locations in or routes through city) than nonspatial (e.g. Who's Who)
- Plus, damage to Hippocampus impairs formation/use of spatial memory (e.g. ability to navigate, to map)

Procedural Memory:

e.g. Rat in an "F" Maze (learns to run from base of F, turn right into one of two perpendicular arms for reward)
- Condition A = Go forward as long as floor is rough, then turn right (Requires Sensorially-Cued Procedure)
- Condition B = Go to same arm where rewarded on last trial (Requires Rule-Based Spatial)

- **Cerebellum** damage interferes with performance in Cond A (**Procedural** Memory) but not Cond B, while Hippocampus damage interferes with perf in Cond B (Declarative/Spatial Memory) but not on Cond A
- Also implicated in some cases of **Classical Conditioning** involving Procedural Memory
  - e.g. Rabbits: Tone (Conditioned Stim) + Puff of air at eye (Neg Reinf) =>Blink; Later Tone Alone=>Blink
  - Damage to (or temporary suppression e.g. via cooling of) **Lateral Interpositus** nucleus (**LIP**) of Cerebellum
    => Even with extensive conditioning, rabbits never learn Tone + Blink association
  - Damage to or suppression of **Red Nucleus** of Midbrain's Tegmentum (i.e. Motor site that LIP projects to)
    => Rabbit not show blink response until suppression wears off, then does show response
    - So learned/stored in Cerebellum but not expressed without Midbrain participation
- **Striatum** (Caudate Nucleus & Putamen, input circuits of Basal Ganglia) also implicated in Procedural Memory
  - **NMDA-Antagonist** injected into Striatum interferes with rat recall of Cued Procedures
  - As discussed previously, Basal Ganglia involved in selecting/integrating/ordering motor activity
  - Plus note role of **Amygdala** (well connected to Basal Ganglia) in both Procedural and Declarative memory!

Declarative Memory

- For cued **facts** or past **personal episodes**, perceptual input first processed by cortical sensory areas, then to "**Medial Temporal Lobe**" (Hippocampus & associated structures), then to **Mediodorsal Thalamus**, then to **Prefrontal Cortex** ("**Working Memory**") interconnected to other higher cortical areas
- **Hippocampus** not just involved in spatial memory, but also in consolidating & retrieving declarative memories
  e.g. Match-To-Sample task (Shown Sample stimulus, subject picks which of 2 Alternatives matches Sample)
  - Train rat on MTS until proficient; After rat learns task, lesion its **Hippocampus**
  - Test w/novel stimuli, must apply "**rule**" (i.e. Pick alt that matches sample); Performance impaired
- **Mediodorsal Thalamus** (like Hippo.) damage more likely to impact declarative than procedural memory
  - e.g. Connections from Thalamus to Prefrontal Cortex appear damaged in **Korsakoff's Syndrome**
    - Chronic alcoholism >> vitamin B1 (Thiamine) deficiency, required for cells to metabolize glucose
    - Anterograde amnesia (cannot form new memories) & Confabulation (make up stories based on current cues)
- **H.M.** Famous epilepsy patient had Hippocampus, Amygdala & some Temporal Cortex removed
  - Personality & IQ fairly intact, but suffered severe **Anterograde Amnesia** (+ some Retro for time near trauma)
    - Couldn't remember people he'd just met, page he'd just read; parents moved, couldn't find his way home
    - Could be taught a simple associative task (e.g. word + photo), so Working Memory still OK
    - But could not recall it 15 min later - So Hippocampus may act to **consolidate** some types of memories
  - W/repetitive training, learned new skills (e.g. "Tower of Hanoi" puzzle) but not recall having learned them
    - So H.M. shows Long-Term Procedural (Skill) Memory but not Declarative (Fact) Memory
- **Amygdala** itself also plays critical role in **Consolidation** of temporary associations into Long-Term Memories
  - Block NMDA receptors in Basolateral Amygdala, prevent learning; But after learning, blocker has no effect !
  - Emotion facilitates memory formation (Although extremes of emotion or stress can impair learning/memory)
    - e.g. Arbitrary list of words easy to forget, except few "taboo" words that evoked emotional response

NOTE! Such memories **not stored** in Hippo. or Thalamus, but areas are necessary to consolidate/retreieve those memories
- e.g. Memory for familiar faces disrupted by damage to **Fusiforme Gyrus (**of IT Cortex) = **Prosopagnosia**
- e.g. Memory for well-learned words, voices disrupted by damage to **Dorsal Temporal Cortex**
- e.g. Memory for activity in praxic space (within hands' reach, from egocentric view) in **Posterior Parietal**