COGS 107B – Systems Neuroscience

Nicole La Grange      Section: Fri 11am-12      OH: Friday 9am-11
Today’s Schedule

Lecture 7: Neuromodulatory Systems
Lecture 7: Neuromodulatory Systems & Drugs of Abuse

Principle of the week:

**Functional Anatomy**: Brain processes are not static. Brain changes the way it responds to sensory information coming in.
Neuromodulators

Norepinephrine/Noradrenaline – NE/NA
Dopamine - DA
Serotonin - 5HT
Histamine – HA
Acetylcholine – Ach
characteristics of brain neuromodulatory systems:

1. small groups of neurons (10’s of thousands) sharing the same neurotransmitter (i.e., neuromodulator) - Small but Powerful

2. projections, via unmyelinated fibers, to widespread regions of the brainstem and forebrain - Unmyelinated (slower movement of information).

3. neurotransmitter binding to receptors generates, through phosphorylation, long-lasting (100+ ms) changes in properties of voltage-gated ion channels - Long lasting effects (due to phosphorylation).

4. firing activity of neuromodulatory neurons is strongly impacted by sleep/wake state (exception for dopamine) - Change a lot across stages of sleep.

5. neuromodulatory neurons receive input from a number of different sources, but all receive input from prefrontal cortex - All receive information from the PFC (side note: humans have large PFC relative to other animals).

6. low firing rates (mean approx. 0-6 Hz)

7. influence the neuronal responses to ionotropic excitatory and inhibitory inputs as opposed to directly mediating excitatory or inhibitory responses (i.e., alter the ‘functional anatomy’ of the brain) – Example of Functional Anatomy: metabotropic receptor effects can change functioning of inotropic receptors.
## Neurotransmitter Receptor Types

<table>
<thead>
<tr>
<th>Ionotropic</th>
<th>Metabotropic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receptor is on an ion channel. NT activates the channel itself.</td>
<td>NT binds to receptor → activation of cascade of biochemical events that will change property of ion channel.</td>
</tr>
<tr>
<td>Two types:</td>
<td>Depends of context. Neuromodulatory. NE, 5-HT, DA, HA, ACh</td>
</tr>
<tr>
<td>Excitatory → EPSPs</td>
<td></td>
</tr>
<tr>
<td>Inhibitory → IPSPs</td>
<td></td>
</tr>
</tbody>
</table>
Iontropic vs. Metabotropic Post Synaptic Potentials

Iontropic: Quicker and Shorter

Metabotropic: Slower and Longer Lasting
Properties of Neuromodulatory Systems

1. Small Groups of Neurons
   - Tens of thousands that produce the NT.

2. Unmyelinated Projections
   - To brainstem and forebrain.

3. Phosphorylation
   - Long-lasting (100+ms) changes in properties of voltage-gated ion channels.

4. Firing Impacted by Sleep/Wake Cycle
   - Except DA.

5. Input from PFC
   - ALL receive info from prefrontal cortex.

6. Low Firing Rates
   - 0 – 6Hz.

7. Functional Anatomy
   - Don't excite or inhibit directly but change the way in which a neuron responds to input.
Neuromodulatory systems

**neuromod. system**

**Noradrenergic (NE):**
main nucleus is the **locus coeruleus** in the pons.

**Dopaminergic (DA):** **ventral tegmental area** and **substantia nigra** area (both in midbrain) – note more localized projections.

Projects everywhere, but mainly to Basal ganglia and prefrontal cortex.

**projection pattern**

---

dopamine

norepinephrine
Neuromodulatory systems

**neuromod. system**

**Cholinergic (ACh):** pontine and basal forebrain groups. Reaches all parts of the brain.

**Serotonergic (5-HT):** several raphe nuclei distributed in brainstem

**Histaminergic (HA):** the ‘forgotten one’ – neurons localized to **posterior hypothalamus**
Local Vs. Global

- Local (Ach) vs global (NE)
- Local: nuclei project to individual locations
- Global: nuclei project to multiple locations
Iontropic vs. Metabotropic Receptor Dynamics

Metabotropic result: activation of protein kinases that phosphorylate ion channels thereby changing membrane potential and/or membrane potential responses to activation of ionotrophic receptors
Potential Changes to Ion Channels

- **ion selectivity** – e.g., Na+, Ca++, K+, Cl-
- **gating** – e.g., by voltage, ligand
- **kinetics** – e.g., open-time
- **state** – e.g., activated, inactivated, deinactivated, persistent, phosphorylated
- **distribution** – e.g., in dendrites, at axon hillock
NE Alters How Neurons Respond to Stimulation.

NE results in less excitatory response (especially in 1b).
alteration of ion channel kinetics through changes in phosphorylation.

- Oxo-M: Ach substitute
- No effect when neurons are bathed in it.
- In general, with current injection, you get more action potentials than baseline.
- If you stimulate again with an increased current (while in Oxo-M), the neuron will continue firing after the stimulus is removed.
- This is an example of a neuron ‘remembering’ a stimulus.
- It is the result of changes in K+ channel kinetics from phosphorylation. (K+ channel closes quicker).
Lecture 8: Spatial Cognition

Principles of the week:

**Frames of Reference**: Coordinate system. How you refer to the space. Always know which one you are using.

**Reentry**: Anatomical concept. Structure sends projections back to the region from which it received information.
Depth Perception

- depth perception from **motion parallax** (close looks faster than far).
- depth perception from **texture gradient**
- depth perception from **occlusion**
- depth perception from **retinal disparity** (stereopsis). Further away eyes don’t have to converge, close up they do.
What is spatial cognition?

Exploration of how we flexibly construct and utilize knowledge of space, both with respect to the outside world and ourselves.
Spatial Frames of Reference: What coordinate system are we defining space by?

1. **Egocentric reference frame**
   - Retinal space
   - Hand space
   - Trunk space
   - Etc.

2. **Allocentric (world-centered)**

3. **Route-centered**

4. **Object-centered**

**Egocentric:** Locations are defined by their relationships to the individual/animal
Spatial Frames of Reference: What coordinate system are we defining space by?

1. **Egocentric reference frame**
   - Retinal space
   - Hand space
   - Trunk space
   - Etc.

2. **Allocentric (world-centered)**

3. **Route-centered**

4. **Object-centered**

**Egocentric:** Locations are defined by their relationships to the individual/animal
Spatial Frames of Reference: What coordinate system are we defining space by?

1. Egocentric reference frame
   - Retinal space
   - Hand space
   - Trunk space
   - Etc.
2. Allocentric (world-centered)
3. Route-centered
4. Object-centered

Egocentric: Locations are defined by their relationships to the individual/animal
Spatial Frames of Reference: What coordinate system are we defining space by?

1. Egocentric reference frame
   - Retinal space
   - Hand space
   - Trunk space
   - Etc.

2. Allocentric (world-centered)

3. Route-centered

4. Object-centered

Allocentric: Locations are defined by their relationships to the landmarks and boundaries of the observable environment
Spatial Frames of Reference: What coordinate system are we defining space by?

1. Egocentric reference frame
   - Retinal space
   - Hand space
   - Trunk space
   - Etc.
2. Allocentric (world-centered)
3. Route-centered
4. Object-centered

Route-centered: Locations are defined by their relationships to the sequences of actions that collectively construct a trajectory through an environment, regardless of the position of the trajectory.
Spatial Frames of Reference: What coordinate system are we defining space by?

1. Egocentric reference frame
   - Retinal space
   - Hand space
   - Trunk space
   - Etc.

2. Allocentric (world-centered)

3. Route-centered

4. Object-centered

Route-centered: Locations are defined by their relationships to the sequences of actions that collectively construct a trajectory through an environment, regardless of the position of the trajectory.
Spatial Frames of Reference: What coordinate system are we defining space by?
1. Egocentric reference frame
   - Retinal space
   - Hand space
   - Trunk space
   - Etc.
2. Allocentric (world-centered)
3. Route-centered
4. Object-centered: Locations are defined by their positions relative to the subparts of the object.
Spatial Frames of Reference:
What coordinate system are we defining space by?

1. **Egocentric reference frame**
   - Retinal space
   - Hand space
   - Trunk space
   - Etc.

2. **Allocentric** (world-centered)

3. **Route-centered**

4. **Object-centered**: Locations are defined by their positions relative to the subparts of the object.
Spatial representations within the brain

**Hippocampus** and connected structures: neurons exhibit spatially responsivity in distinct spatial reference frames.

The hippocampus proper = dentate gyrus (DG) + CA3 + CA1

**Hippocampus** and connected structures: spatial responses of neurons within these structures are critical for effective navigation and spatial memory, indicating that the observed spatial activity generates a representation of an environment for future use.
intrahippocampal and extrahippocampal connections (with cortex) exhibit patterns of *convergence*, *divergence*, and *reentry* at multiple scales.

**Trisynaptic pathway:**
1. EC → DG
2. DG → CA3
3. CA3 → CA1

EC  →  DG  →  CA3  →  CA1
intrahippocampal and extrahippocampal connections (with cortex) exhibit patterns of convergence, divergence, and reentry at multiple scales.

**Reentry:** structure sends projections back to the region from which it receives information.

Special form of reentry found in hippocampus:

Autoassociation (DG & CA3)
Distinct forms of Spatial Representations: Head-direction cells of Postsubiculum (PS)

- Tracking directional heading in the frame of reference: ‘head direction’ cells
- Different neurons have different preferred directions (all directions are represented)
- Firing is tuned to the orientation of the animals head relative to the boundaries of the environment
Distinct forms of Spatial Representations: Head-direction cells of Postsubiculum (PS)

**Head-direction cells:**

- Firing is tuned to the orientation of the animal's head relative to the boundaries of the environment (i.e., not to magnetic north)
- Directional tuning may differ completely across two different environments provided that they are perceived as different
Head Direction Cells

Found in many areas including: Post Sibiculum and Medial Entorhinal Cortex (MEC)

Builds up from vestibular input from the medial vestibular nucleus.
Distinct forms of Spatial Representations: Grid cells of the medial Entorhinal Cortex (mEC)

- Neurons of the mEC exhibit multiple firing fields in any given environment
- Such fields are arranged according to the nodes of a set of ‘tesselated’ triangles
- Grids rotate with the boundaries of the environment (Allocentric)

- Neighboring grid cells have similar grid orientations and spacing (topography)

Medial Entorhinal Cortex
Grid Cells
Allocentric Space
Universal
Distinct forms of Spatial Representations: Place cells of Hippocampus (HPC)

- Discrete firing fields that reflect the (X,Y) coordinate of the animal in the environment.
- These ‘place cells’ are found in most HPC sub-regions.
- Different neurons map different positions (all positions are represented).
- Rotation of the environment boundaries = rotation of the place fields (Allocentric)

All Regions of Hippocampus Place Cells Allocentric Space

Sugar et al., 2011
Distinct forms of Spatial Representations: Place cells of Hippocampus (HPC)

- Given that different hippocampal neurons bear different place fields, the firing rates of those neurons at any given time can be used to predict the animal’s position in the environment.
- For a set of neurons, the firing rates across the full set describe the ‘pattern’ of activity across the full population – this is called a ‘population firing rate vector’.
- All brain regions appear to register information according to such ‘population’ patterns.
Distinct forms of Spatial Representations: Place cells of Hippocampus (HPC)

- Given that different hippocampal neurons bear different place fields, the firing rates of those neurons at any given time can be used to predict the animal’s position in the environment.

- For a set of neurons, the firing rates across the full set describe the ‘pattern’ of activity across the full population – this is called a ‘population firing rate vector’.

- All brain regions appear to register information according to such ‘population’ patterns.
Distinct forms of Spatial Representations: Place cells of Hippocampus (HPC)

- Given that different hippocampal neurons bear different place fields, the firing rates of those neurons at any given time can be used to predict the animal’s position in the environment.
- For a set of neurons, the firing rates across the full set describe the ‘pattern’ of activity across the full population – this is called a ‘population firing rate vector’.
- All brain regions appear to register information according to such ‘population’ patterns.
Applications of ‘Where’ and ‘What’ Pathways

area VIP of parietal cortex: bringing together personal spaces of the somatosensory and visual systems

along the ‘where’ pathway: area MST integrates optic and vestibular ‘flow’