COGS 107B Section

Wednesday 1-2PM in CSB 004  (Office hours Wednesday 2-3PM)
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Lecture 15

MOTOR CONTROL
We talked a bit before about motor system - alpha motor neurons, etc.

We will move beyond, and on to PFC and attention in next lecture

In transitioning, we will show how in PFC, the brain exhibits an embodied nature

Principle: **population code**

- We saw this in the midterm question where there were 4 neurons firing at different rates in different positions - the pattern of firing was the population code for position

- We will examine it in terms of motor control, and how it gives a different idea of what primary motor cortex is doing
Motor homunculus: on a strip of cortex in precentral gyrus, stimulation causes twitches in various muscles of body; positions corresponding to particular muscles

Image: movie, Robo cop

- Cop gets gunned down by villain Clarence, but they save part of brain and embody it in a robot body, becomes cop again
- Movie was prophetic in some ways; back then, there were no neural prosthetics

Now, there are prosthetics developed by people like Andy Schwartz...

- Electrodes go into motor cortex of a quadriplegic patient, and patient uses brain activity to control robotic arm w/ 10 degrees of freedom
- Now, it's progressing: use touch sensors in hand to stimulate sensory homunculus to associate w/ grabbing of items
- Comes with moral issues, some of which were addressed in Robo cop
Motor neurons and muscle fibers

- We’ll start by discussing the organization at the level of muscles and what the system is composed of.
- **Alpha motor neurons** in ventral horn of spinal cord are the final pathway to muscles.
  - Provide projections to **extrafusal muscle fibers** of individual muscles.
  - Synapse on muscles itself, at **nicotinic** (ionotropic) receptors (ACh).
  - Cause depolarization and Ca influx, which cause actin and myosin molecules to crawl across each other, which scrunch and contract the muscle.
Alpha motor neurons exit spinal cord at multiple different levels to innervate muscles at different parts of body

- [No need to memorize stuff long diagram on right]
- **Cauda equina** - broadening of outputs that lead to full extent of lower limbs

For any single alpha motor neuron, projection is only to **one muscle**

- Within that muscle, we can have projection to **multiple individual fibers**
- But, only to **one type of fiber**
Fiber Types

- **Slow-twitch (aerobic):**
  - 50 ms – longer to reach peak force
  - Relatively small force
  - Non-fatiguing (aerobic)
  - Useful for tonic movements, as in maintaining posture
  - Innervated by type S motor neurons

- **Fast-twitch (glycolytic):**
  - 25 ms – shorter to peak force
  - Large force
  - Fatigue easily (glycolysis)
    - Kind that produces lactic acid when you’re sore
  - Useful for quick powerful movements, e.g. jerk
  - Innervated by type F motor neurons, capable of high firing rates
Central pattern generators

- If we record from muscles themselves, see a pattern for walking
  - Figure depicts, in black, activations across time of 6 different muscles of lower limbs as a person walks
- Common, repeatedly utilized behaviors like walking, chewing, withdrawal, etc. imply workings of central pattern generators
  - Exist generally in and around brainstem reticular formation
  - Made up of muscle synergies that evolve over time
Muscle synergies

- **Muscle synergies** = patterns of muscles - which are active, not active, partially active, etc.
  - Similar to population code of neurons
- Already discussed muscle synergies w/ reach to grasp task (image)
  - Muscle synergies change in order to accomplish more efficient reach
- Synergies can be part of **central pattern generators** that are “built in” and create repeated patterns, but can also be adapted to accomplish new tasks
  - In fact, central pattern generators themselves have to adapt all the time as we age and such
- E.g., walking pattern repeats, but also changes over time
  - Varies from left side to right side of body
Anatomy of muscle synergies

How do we get muscle synergies activated? What components control this collection?

Start with the spinal cord

- We have alpha motor neurons that are the last part of the whole thing, projecting and synapsing on muscles to activate
- Also within ventral horn of spinal cord, there are many different types of interneurons

**Spinal cord interneurons**: cell bodies, axons, dendrites all lie within spinal cord

- Complex network
- Some excitatory, some inhibitory
- Interconnected with selves and with alpha motor neurons
- May have axons which cross comissure (to other side) and/or extend into other segments
  - Ventral horn interneurons on right side of body can influence ventral horn interneurons on left side of body, to coordinate left and right muscle activity in tandem
- Recipients of both converging and diverging primary motor cortex inputs
Four systems

- Inputs reaching into ventral horn spinal cord interneuron/alpha motor neuron network are broken down into 4 groups
  - **Corticospinal** (primary motor cortex output)
    - Reaches all the way down to ventral horn of spinal cord
  - **Vestibulospinal**
    - Vestibular nucleus takes in all info from vestibular system, and outputs to spinal cord to directly impact activity - presumably as a reflex, for example
  - **Reticulospinal** (mesencephalic locomotor region)
    - Mesencephalic = midbrain
    - Produces central pattern generator for walking
    - If you disconnected brainstem from rest of forebrain, and you stimulate in this area, you still get walking behavior
  - **Rubrospinal**
    - Receives output from cerebellum
Side note…

- New data is showing the extent to which corticospinal system is, at the same time, part of the other 3 systems as well
- Same neurons also project to other 3 areas of brainstem
- All a huge system that takes up a lot of the brain
Convergence and divergence of corticospinal axons

- We will concentrate on the corticospinal system.
- In the motor homunculus (primary motor cortex)...
  - Pick individual neuron and fill with black dye
  - Dye will fill dendrites and all axons
- Schematic image of primary motor cortex neuron’s (dyed) axons reaching into ventral horn of spinal cord
  - Sections of horn correspond to outputs of alpha motor neurons to different muscles
- Corticospinal neuron’s axon terminals are diverging to influence multiple alpha motor neurons
  - These alpha motor neurons, in turn, innervate different muscles
    - I.e., a single motor cortex neuron can activate several different muscles
You can see, if you stimulate neuron to fire single action potential and record from diff muscles of forearm, it will produce a synergy of a sort

- E.g., activate 4/6 muscles – see graphs to the right

Any alpha motor neuron has a convergence from different areas of motor homunculus

- There are singular alpha motor neurons of spinal cord which reach to actual thumb, others to forefinger
- Along motor cortex, there’s a part that corresponds to thumb, part to forefinger
  - These areas are located next to each other
- On diagram, see triangles – these represent many of those primary motor cortex neurons: some that correspond to thumb, and some to forefinger
- Most of the forefinger corticospinal (motor cortex) neurons contact forefinger alpha motor neuron, but a few contact the thumb motor neuron
  - And vice versa
Center-out experiment

- **Center-out task**
  - Monkey seated in chair, holding lever (like a bigger joystick)
  - Receives command to move in one of 8 different directions
  - Record muscles as animal reaches in the different directions

- As he moves in one of those directions, the movement has a sort of **pattern** associated
  - Starts out fast, reaches peak, then as it approaches target, slows down
  - Muscle has different patterns that correspond to the 8 different directions
  - E.g., triceps muscle strongly active as reaches forward - extends elbow
    - Activated strongly for that direction, more weakly for movements that pull back (flexion at elbow)
Georgopoulos looked at patterns in primary motor cortex corresponding to these movements.

- Any particular neuron fires in different amounts for each direction.

- Draw vectors – arrows with lengths corresponding to firing rate of a neuron – for each direction.
  - Use action potential rasters (tic marks), for a single neuron during 5 separate reaches to 8 different directions from the center point, as data.
  - Apply circular statistics that put all data together mathematically to find the average vector.
  - This vector shows the neuron’s directional tuning, or preferred direction.

- Every direction is equally represented by different primary motor cortex neurons.
Put all primary motor cortex neurons together into one plot/one analysis

- Image: each of the 8 plots is a **population firing rate vector** for a direction
- Each line within each of 8 plots corresponds to a specific neuron
- Each line’s orientation is pointing in direction of its preferred tuning
- Length of the line corresponds to firing rate
  - Hence why red line is short for northern directions and long for southern

By considering the firing rate of all recorded neurons at any given time (i.e., the population rate vector), the associated direction of movement can be predicted

- This is how prosthetics use brain activity to determine direction to move
Furthermore, according to G. and Schwartz, primary motor cortex is literally encoding direction of movement.

- "Because primary motor cortex projects through the rubrospinal and reticulospinal systems and through network of interneurons in spinal cord, it doesn't necessarily have to specify individual muscles to be moved"
  - It can specify just the direction of movement
  - Specifies direction and speed of movement, and the conversion to particular muscles which will accomplish is achieved in the reticulospinal system and/or the interneuron system of ventral horn and spinal cord

- This is controversial – not everyone believes this
  - E.g. Prof. Nitz/ others believe that it specifies particular muscle syner

- This is still a major argument in the field
  - Controversy continues because, when you try to set the muscle activity patterns in the directions of movements against each other, you don't get a clean answer
Robo-monkey: interfacing the activity patterns of monkey motor cortex neurons with a robot arm – monkeys learn to generate activity patterns that will control a robot arm.

- Monkey in chair, researchers recording brain.
- Monkey is using primary motor cortex activity to move the robotic arm to pick up piece of food.
  - Robot arm & ‘fingers' pinching a piece of food – monkey subsequently moves food to mouth.
Controlling the controller: premotor cortex drives activity patterns in motor cortex and is, in turn, driven by both prefrontal and parietal cortices.

- If M1 is controller of what movements will happen, then prefrontal and premotor are part of controlling the controller.
- Continuum: prefrontal → premotor → primary motor cortex.

Several regions (don’t need to memorize, but they’re listed in image) that can be considered premotor or prefrontal cortex:

- Highly connected with parietal cortex.
- Project into primary motor cortex.
- Premotor cortices hooked up with prefrontal cortex as well.
Premotor cortex in navigating rats exhibits more abstract relationships to action – mapping of action, sequence-dependence of action mapping, and mapping of action plans.

**Experiment**
- Record in premotor cortex of rat
- Rat is on track maze; start at bottom and move out - make 3 L/R choices in row
  - This means there are 3 actions to decide and implement
  - 8 different goal sites

In premotor cortex, can see neurons whose activities relate to actions
- When animal makes right turns, neuron is highly activated
- **Action mapping neurons**: map actual actions at the current moment
But, in same area, neighboring neurons are **action planning neurons**
- For these, activity is related to action, but **not the one of the moment**
- Fires as animal runs straight, but only when animal is **about to** turn right

**Sequence-dependent action mapping neurons**
- E.g., a neuron fires after the **last** turn, if it’s a right
- Depends on where the action is in the sequence of actions

Representation of action becomes more “abstract”
Activity may reflect the position of an action in an action sequence
- Sequence-dependent action mapping is seen in monkeys as well

Train monkeys to trace different shapes on screen with finger
- Sits, screen shows image, some delay, then monkey copies image starting at a dot

Recordings from 2 different neurons
- Image: firing rate is stronger wherever the line is depicted as wider
First neuron’s data
- Note that these are all cases where neuron is moving more or less to west/ northwest, and at end of sequence
- Doesn’t fire a lot again when monkey starts going same direction again, because it’s not the end of sequence

Second neuron’s data
- Fires more near the beginning of sequence, primarily for west/ southwest
- Note: labels for final segment vs first segment are Not reversed on slide (no typo)
- Monkey is drawing on screen in a counter clockwise pattern
Dissociating the premotor and motor cortex III

- 'Mirror neurons' of the premotor cortex – activity maps actual as well as witnessed behaviors of the same type

- Ex 1 - peanut grab
  - Monkey reaches to tray to receive something like peanut
    - Neuron fires a lot in relation to that act
  - Researcher went to reach for peanut
    - Neuron also fired a lot for this act, even though it wasn’t moving itself

- Ex 2 - peanut crack
  - Monkey cracks open peanut
    - Neuron fires a lot
Monkey grasps a ring
  - Baseline firing

Human reaches for peanut, grabs, and cracks peanut
  - Neuron fires a lot

Human reaches for peanut, grabs, and cracks peanut, & monkey has headphones
  - Can’t hear cracking of peanut
  - Neuron still fires a lot

Monkey can’t see peanut grabbing/ cracking, but can hear it
  - Neuron still fires a lot!

Anything that relates to action of cracking peanut causes firing
  - Relatively specific to motor act itself, whether or not monkey does itself
Ex 3 - block

- Person reaches for block
  - Neuron fires a lot
- Person reaches, but block isn’t there
  - Very little firing
- Block is put down, screen prevents monkey from seeing block, person reaches for it
  - Neuron fires a lot
- Nothing is placed there, screen covers, person reaches (for nothing)
  - Neuron does not fire

Activity patterns correspond to actions, but also to inferred or mirrored actions - concept of action
Firing properties related to more abstract features of a motor task

- Dorsolateral prefrontal cortex neurons mark the beginning and ending of a behavioral episode
- Continuum from premotor to PFC - they have different names, but it’s not like there’s a definitive line
- Graybiel experiment
  - Monkey makes saccades from fixation point to targets on screen
    - Saccades from target to target as they appear
  - Number of eye movements = number of targets
  - Different trials have him saccade to different directions
Across trials, PFC neurons have activity corresponding to each instance of movement:
- Firing peak during fixation, and then for each movement to target
- Not specific to direction or anything - just responds to the act of saccading

At the end of 4 saccades, there’s an extra peak of firing:
- No matter the amount of saccades in between, there’s always firing at end of a sequence
- Also occurs at beginning (fixation)
- Abstract encoding of start and end
  - It’s not even part of the task to know beginning/ end, it just happens
Firing properties related to more abstract features of a motor task III

- Dorsolateral prefrontal cortex neurons ‘count’
- Nieder experiment
  - Monkey stares at fixation point on screen
  - Blobs of different shapes and sizes in various amounts will appear on screen in different places
    - Monkey must remember the number of blobs that appeared
  - Delay period
  - Another screen appears, with 2 images of blobs, equally as varied as before
    - Monkey supposed to select image with correct amount, regardless of other features
“Numerosity” of 3 – “threeness” – concept of 3, irrespective of medium that expresses it

Specific PFC neurons have more activity for certain numerosities over others

Side note: Monkeys can learn to associate numerosity with symbols (like typed number 3)
  - Nitz argues: associating symbols with concepts = the rudiments of language
Dorsolateral prefrontal cortex neurons map action sequence categories

Tanji experiment
- Seats monkey in front of panel
- Panel has button (pushed), key (turned), and ring (pulled)
  - 3 potential actions
  - Light above each of them
- At beginning of trial, light sequence occurs
  - Do respective actions in order
  - E.g., 2 flashes above button and 2 above ring = push-push-pull-pull
Findings

- Prefrontal neurons have delay activity that corresponds to categories of movement
  - Categories are different patterns of movements (AABB, ABAB, or AAAAA)
- E.g., AABB sequence: neuron would fire a lot for push-push-pull-pull, or pull-pull-push-push, etc.
- This is an emergent property of the system
The whole body schema is in posterior parietal cortex, but PFC best reflects your outlook on the world.

**Top-down processing**: PFC and how it controls rest of brain
- E.g., PFC changes to some extent how primary visual cortex takes in visual info by LGN
- Kind of akin to functional anatomy

This isn’t really a lecture on attention (difficult concept to nail down), but we’ll talk about it
- Think of working memory in PFC while understanding that slide
- How it might account for attentional effects we’ll see
On attention:

“Everyone knows what attention is. It is the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thought. Focalization, concentration, of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others, and is a condition which has a real opposite in the confused, dazed, scatterbrained state which in French is called distraction, and Zerstreutheit in German.”
Premotor cortex – a more indirect role in motor control
- Activity, as in primary motor cortex, may directly reflect present action
- Activity accompanies actions as well as planning for actions
- Action-related activity may depend on ordering of actions in a sequence
- Activity may reflect perceived actions as opposed to actual movements (as in ‘mirroring’)

As we move forward from primary motor cortex into premotor cortex, we still have activity (dynamics) related to actions, but in a more abstract way
- So much so that they can even be said to represent concepts
More review

-Covered in previous lecture:
- Firing properties related to more abstract features of a motor task I: dorsolateral prefrontal cortex neurons mark the beginning and ending of a behavioral episode

-Also covered in previous lecture:
- Firing properties related to more abstract features of a motor task IV: dorsolateral prefrontal cortex neurons map action sequence categories
  - Side note: not all possible combinations (categories) were shown
The pattern of efferent projections from prefrontal cortex suggests three different pathways by which prefrontal cortex can enact ‘top-down’ influences on other regions of cerebral cortex (e.g., in some forms of attention):

- Direct projections
- Projections to neuromodulatory systems
- Projections to thalamus

What do all these connections mean?

- Emergent encoding of categories of sequences in PFC
  - But what happens with it?
- Well, rest of brain is influenced by PFC
PFC has direct projections to most other areas of cortex
  - Including premotor, posterior parietal, inferotemporal cortex
  - Areas referred to as associative because they get projections from a lot of other areas of cortex
    - E.g., parietal gets from somatosensory, auditory, visual
  - PFC also reaches other cortices by the thalamus
    - Extensive projections into thalamus, which then project out to other areas of cortex
  - PFC also has major pathway to influence rest of brain through neuromodulatory systems
    - We discussed how these systems change functional anatomy of info processing of different regions of cortex, and how they alter spike timing dependent plasticity rules
Through all these different pathways, PFC is impacting many things:

- What you can learn
- The very processing of things like sensory info and motor output info
- Now that we have anatomy, we need to connect it to dynamics
General working memory experimental design

- Working memory: general experimental design
  - Monkey fixates on screen
  - Stimulus, e.g. green dot flashes on screen
  - Impose delay period of diff times
    - Anywhere from a few seconds to a minute
  - Then, give some cue that indicates “go”
  - Monkey does something, e.g. saccade to indicate memory of where stimulus was

- Under the circumstances, you see working memory firing patterns
  - Example with Stimulus 1 and Action 1, and Stimulus 2 and Action 2
A certain neuron fires a lot right after stimulus 1, maintaining firing while decrementing over time until time of action
- For Stimulus 2, neuron doesn’t fire - specific to this particular stimulus
- During delay period, has a working memory for the stimulus - stimulus delay type of working memory PFC neuron

Another neuron fires little for stimulus 1, but as time goes on during delay for action 1, it increments in firing right up until the action, when it peaks
- For stimulus 2 and action 2, neuron doesn’t really fire at all
- These neurons are specific for the action
- Delay action type of working memory PFC neuron
If you were to switch stimulus 1 to be paired with action 2...
- The first neuron would fire + decrement over delay, because it only cares about the stimulus
- Conversely, if you do stimulus 2 + action 1, it would not fire

If you were to switch stimulus 2 to be paired with action 1...
- The second neuron would increment firing during delay, because it only cares about the action
- Conversely, if you do stimulus 1 + action 2, it would not fire

During delay period, there is a cognitive process that is transitioning of perception of stimulus into appropriate action
An example: prefrontal ‘top-down’ influences on parietal cortex during an oculomotor delayed response task

- Inactivation of prefrontal cortex via cooling depresses ‘working memory’ responses of parietal cortex neurons and increases errors

Goldman-Rakic experiment

- Recording in parietal cortex
  - Also has working memory processes

- Monkey stares at fixation cross, then a cue comes up, then delay, then monkey saccades to location of target
Single neuron activity data

- Activity during delay period for all trials – target site was in 8 different regions in visual field
- Parietal neuron has delay-period activity specific to the N and NW targets
  - Looks like delay action neuron
  - Neuron fires more when target is in north/northwest

Delay-period activity for the same neuron is depressed when prefrontal cortex is inactivated

- If PFC is inactivated, the working memory activity of this neuron for those 2 regions almost completely returns to baseline
  - This was done in old school way of inactivation: put probe and run cold water through it to cool down PFC so neurons couldn’t fire

Working memory processes as it appears in other areas of brain is actually dependent on PFC

- Working memory processes of PFC are being broadcast and influencing rest of brain
Firing properties related to more abstract features of a motor task II

- Dorsolateral prefrontal cortex neurons track time intervals
- Interval timing task
  - Monkey presses and holds a key for 1-2 seconds until cue appears
  - Cue is a colored bar on screen, associated with particular time intervals
    - Think of the time intervals as stimulus in this exp.
  - Bar will appear on screen in one of three colors for 2 seconds
    - Once it appears, clock starts running
      - I.e., these 2 seconds count as part of the time cue indicates to hold button
  - E.g., if blue bar comes up, monkey is supposed to wait 8 seconds before releasing the key he’s been pressing
    - Pink is 4 seconds, yellow is 2 seconds
  - Later, after these standard task cues, do reverse task cues
    - Change rules for task - i.e., blue = 4s, pink = 8s
Side note: When you vocalize internally (mentally count “aloud”), areas like Broca’s area (premotor area related to speech) are active.

When rat has to solve this problem of waiting certain part of time, rat does similar thing:

- Does sequence of actions that takes the right amount of time

Individual prefrontal neurons respond for different cued time intervals:

- Some build responses leading to key release time, some decrement responses following cue onset

Graphs: firing neuron on y axis, time on x axis:

- The time the bar is up on screen shown by colored bar
- Movement onset at the end
6 neurons are represented (3 shown in images)

- First neuron responds to 8s interval
  - Therefore, it responds to blue bar in standard trial and pink in reverse
  - Remember, interval = stimulus – color of cue does not matter
  - Decrements response starting from cue presentation up until action

- Second neuron responds to 4s interval
  - Therefore, it responds to pink, then blue, bars

- Other neurons (delay action type, not shown in lecture slides online)
  increment response to peak at movement onset
  - Like before, one of these neurons is specific to, e.g., 8s interval only

- Rate at which neurons ramp up/ down their activity relates to interval
The timing of attention

• The timing of attention – a role for prefrontal mapping of time intervals?
• Recording in V4 region of visual cortex
• Relates time to attention
• Consider possibility that effects we see here of time on attention might be mediated by PFC acting on V4
  • PFC is very important player in how we play attention, both with respect to covert attention and overt attention
Task
- On any given trial, 4 items will show up on screen
  - Same item (bar) in diff orientations
- Monkey will be cued as to which ones to pay attention to
  - E.g., to bars 1 & 2
- Pay attention to whether or not any of their orientations change
- Both are in receptive field (RF) for a particular neuron
  - Other two are outside that RF
- Next screen (e.g. bar 4 changes, but monkey should ignore because it’s not 1 or 2)
- Next screen (e.g. bar 2 changes orientation - now monkey releases key)
Activity of single neurons in visual cortex (area V4) responding to a visual stimulus fire more if their response field (RF) overlaps the region of the visual field that must be attended (‘attend in’ vs. ‘attend out’)

- On trial of paying attention to 1 and 2 (inside RF), firing pattern starts a lot, then less but continuous, then ramps up again
- On trial where to pay attention to 3 and 4 (outside RF), firing pattern starts a lot, then less – drops down without ramping up again

Difference between those patterns are the **attention index**

- Initial is same, but not the end - it increases
- Subtracting the ‘attend out’ from the ‘attend in’ firing rate curve yields the ‘attention index’, which measures the difference in response to the stimulus due to attention
- **Change probability** graph
  - The probability that the orientation will change *varies across time*
  - The ‘attention index’ changes in accord with the probability that the stimulus will change orientation – that is, attention has a temporal component

- **Conditional probability** (aka hazard function) - tells you what probability is, at any given moment in time after start of trial, the change will happen, assuming it hasn't happened already

- Monkey’s attentional process picks up on this hazard function
  - Hazard function has same shape as attention index

- Only sort of pay attention at beginning, and increase attention as it becomes more likely for change to occur