ANATOMY REVIEW: Basal Ganglia

Motor dysfunction 2: Spinal cord injury and subcortical motor disorders

- A group of **subcortical nuclei**
- caudate, putamen, globus pallidus

Basal ganglia

- clinically, subthalamic nucleus and substantia nigra included
• These structures are grouped together because
  – they are highly interconnected anatomically
  – functionally, they share an importance in motor disturbances called dyskinesias, characterized by involuntary purposeless movements

CIRCUITRY
As with cerebellum, basal ganglia act indirectly
• Highly interconnected

• Input from cortex to neostriatum (putamen, caudate)
**Output** to cortex from globus pallidus and substantia nigra, via thalamus

- **tonic inhibition of thalamus**
- one pathway (D1) **disinhibits**, second pathway (D2) **inhibits**
- projections from cortex go on to influence descending systems controlling body, limb, and eye movements

**Parkinson’s disease**

- Caused by degeneration of pathways from substantia nigra to rest of basal ganglia and thalamus.

**Symptoms include**

- Muscle rigidity
- Akinesia
- Resting tremor
- Shrinkage of handwriting, bradykinesia, athetosis
See deterioration of dopaminergic cells in substantia nigra
- Normally lose a bit every year due to aging, but in Parkinson’s have > 70% gone

• Exact causes unknown
  – genetic, ‘free radical oxidation’, immune, particular toxin
  • Case of ‘frozen addicts’

• Chorea: rapid involuntary movements
  – seen in Huntington’s Disease
  • genetic, deterioration of caudate nucleus (arrows)
• These dyskinesias suggest that the basal ganglia are important in postural adjustments, control of motor output, and initiation of movements.
  – Overall, however, basal ganglia function poorly understood

Basal ganglia and Parkinson’s
• Various surgical interventions are proving helpful
• Example: Pallidotomy (lesion of the globus pallidus)

– some recovery of function
– faster movements & faster deceleration as hone in on target

Pre-op

Post-op

Cerebellar dysfunction

- Review, Gross anatomy:

Cerebellar nuclei

- Information passes through these between brainstem and rest of cerebellum

Cerebellum overview

Regulatory system within a regulatory system
One way to understand what it does under normal circumstances is to look at the difficulties experienced by patients with cerebellar damage.

Cerebellum of a (former) alcoholic
Cerebellar atrophy

Cerebellar dysfunction
• Hypotonia: abnormally low muscle tone.
• Dysmetria: limb movements fall short of, or overshoot, their goal; poor control over the range and direction of movement.
• Ataxia: stumbling gait, resulting from limb incoordination and improper timing of muscular efforts. The patient has a tendency to fall over, unless they walk with widely spread legs.
• Intention (essential) tremor: this occurs during a voluntary limb movement.

An example of improper muscle activity timing
• normal interaction between contraction patterns of different muscles altered when cerebellum inactivated.

Normal situation
-reduced cerebellar output

Suggests cerebellum involved in
  • control of posture and muscle tone
  • coordination, timing, and correction of movements
  • initiation and production of motor activity

Spinal cord injury (SCI) and the search for a paralysis cure
  • Three approaches presently dominating paralysis research
    – Minimization of damage
    – regeneration/reconnection
    – bypassing the damage altogether

Three problems
  • Death
  • Disruption
  • Demyelination

Source: Miami Project to Cure Paralysis
Minimization of damage following SCI

• **Problem 1: Cell death following injury**
  – Can occur hours/days/weeks post-injury

• **Therapeutic goal: neuroprotection**
  – Steroid administration asap
  – Growth factors (proteins)
  – Lower body temperature
  – Moderate inflammation response

• **Problem 2: disruption of nerve pathway**
  – Unlike peripheral nerves, axons in the brain and spinal cord cannot regenerate

• **Therapeutic goal: regrowth, ‘bridge the gap’**
  – Prepare graft using peripheral helper cells (schwann)  
    • Mary Bunge, Miami Project to Cure Paralysis

One problem this research is encountering is getting the graft past the bridge and onto the spinal tissue
• Instead of patching disruption, a second approach is to REPLACE damaged nerves
  - Use of fetal cells successful in animal research

• Problem 3: Demyelination
  – Also get with some spinal cord injuries
  – Again, trying to trigger Remyelination using Schwann cells from the periphery

A different approach to curing paralysis: bypass the damage altogether
• tap into existing circuitry externally
• In cats, can stimulate circuits directly with neurotransmitter to restore locomotion

Could you do this in people?
• In 2002, Nature reported a study using lower back stimulation resulting in a partially paralysed man walking
  – Pen-width electrodes implanted in lower back, gave low level stimulation to spinal cord
  – He can walk up to a kilometer, after a lot of training
• So, a combination of physical and chemical stimulation might allow access to central pattern generators in spinal cord
Third approach: neuroprosthetics
• Bypass damage....bypass body altogether
• Use cortical signals to drive robotics

![Diagram of neuroprosthetics process]

- Review: Motor cortex neurons show "directional tuning" for a given movement direction
  - More complex whole-arm movements

![Graph showing neuronal activity and direction]

Populations of cells may encode the direction of movement in space

![Graph showing population vector and neuronal discharge]

At present can train monkey with implanted array to move cursor
- 2D vs 1D movement seen in Kennedy work

7-30 MI cells
Donoghue Lab, Brown University, Providence, RI

Next step: decode neural signals to drive separate arm directly
- mirror animal's own arm as it pushed buttons on a panel or chased an almond across a tabletop
  - The neural activity provided velocity and direction of movement, fed into a computer
  - At this stage, animal unaware of robot, but eventually would want to train to use 'brain' to move prosthesis

Recently it's been shown that even 5 years post-injury, quadraplegics asked to "move" show cortical activation of appropriate areas

- So the brain signals are there, although some evidence that it can be lost if mental imagery not kept up