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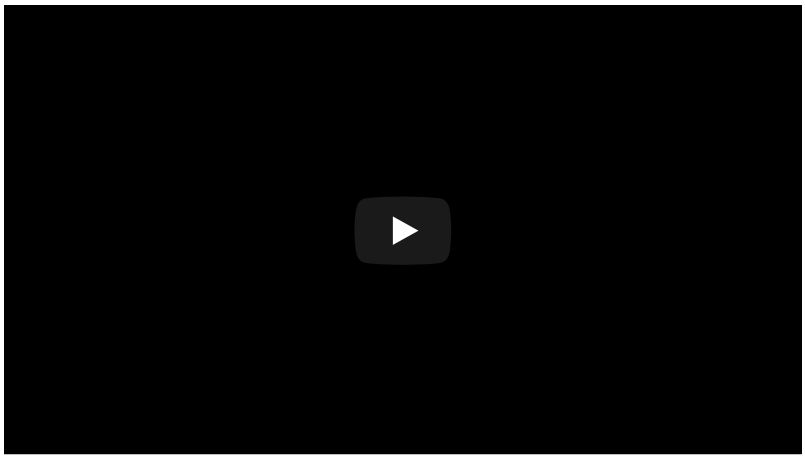
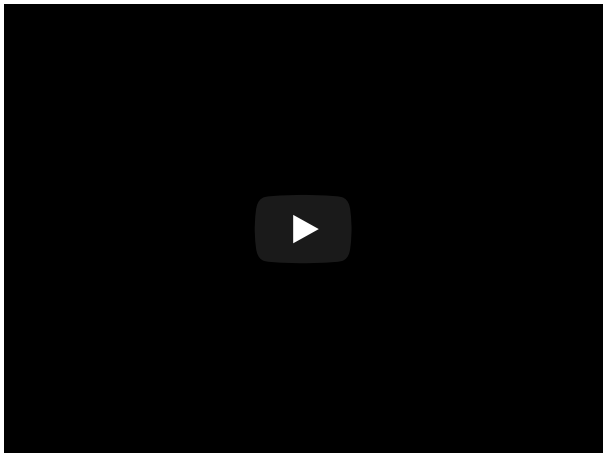
Rick Gilmore

2021-10-27 14:21:16

- For fun
- Output types
  - Types of movements
- Motor system anatomy
  - Key ‘nodes’
  - Projection pathways
- Muscles
  - Functional classes
    - Agonist/antagonist pairs
  - Anatomical types
  - How skeletal muscles contract
    - Skeletal muscle fiber types
  - Muscles as sensory organs
    - Two fiber types
    - Monosynaptic stretch (myotatic) reflex
- Disorders of movement
  - The Faces of Parkinson’s
  - Huntington’s
    - Clinical trial focused on gene therapy
- The big picture
  - The “real” reason for brains
  - What does motor cortex activity encode?
  - What does the cerebellum do?
  - Systems perspective
- References

For fun

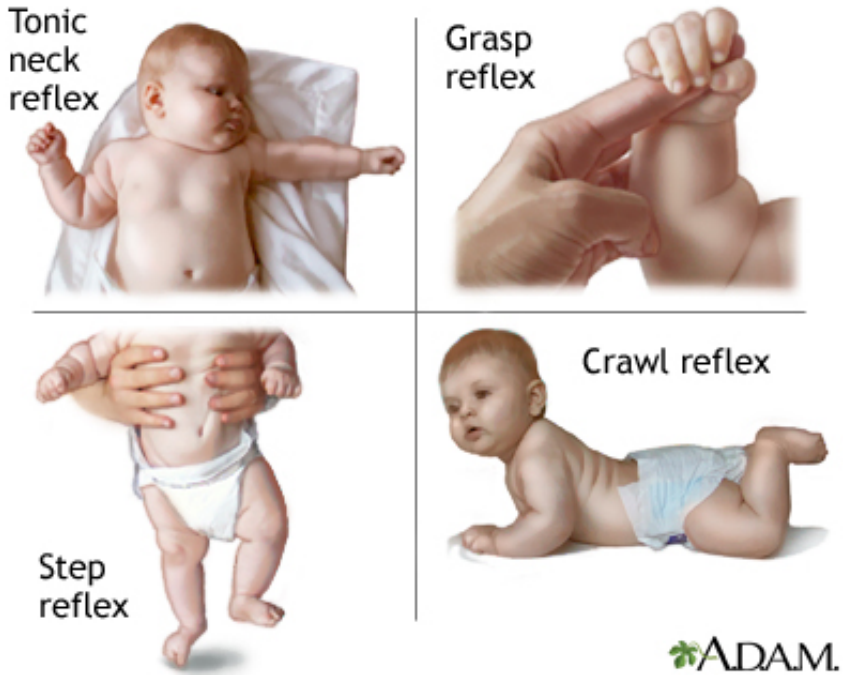




Output types

- What types of outputs are there?
- How are they produced?
  - By the muscles
  - By the nervous system
- Outputs include
  - Movements, vocalizations, facial expressions, gestures
  - Autonomic responses
  - Endocrine responses

Types of movements



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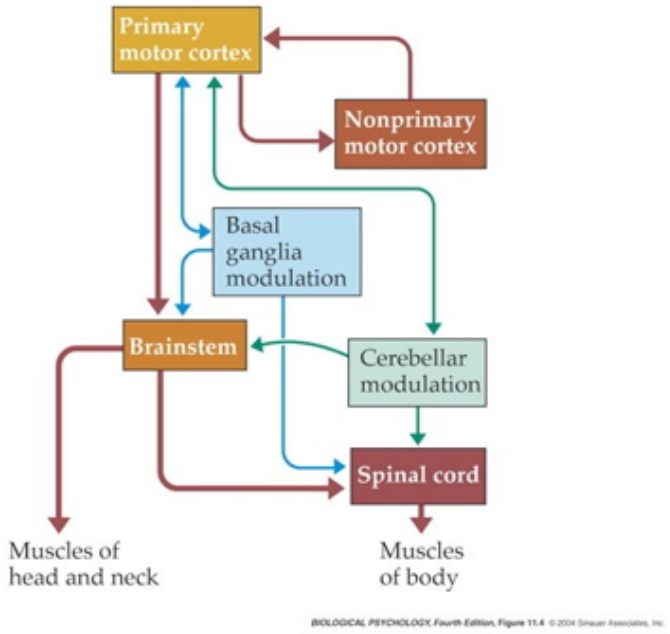
- Reflexes
  - Simple, highly stereotyped, unlearned, rapid, acquired early
- vs. planned or voluntary actions
  - Complex, flexible, acquired, slower
- Discrete (reaching) vs. rhythmic (walking)
- Ballistic (no feedback) vs. controlled (feedback)

Motor system anatomy

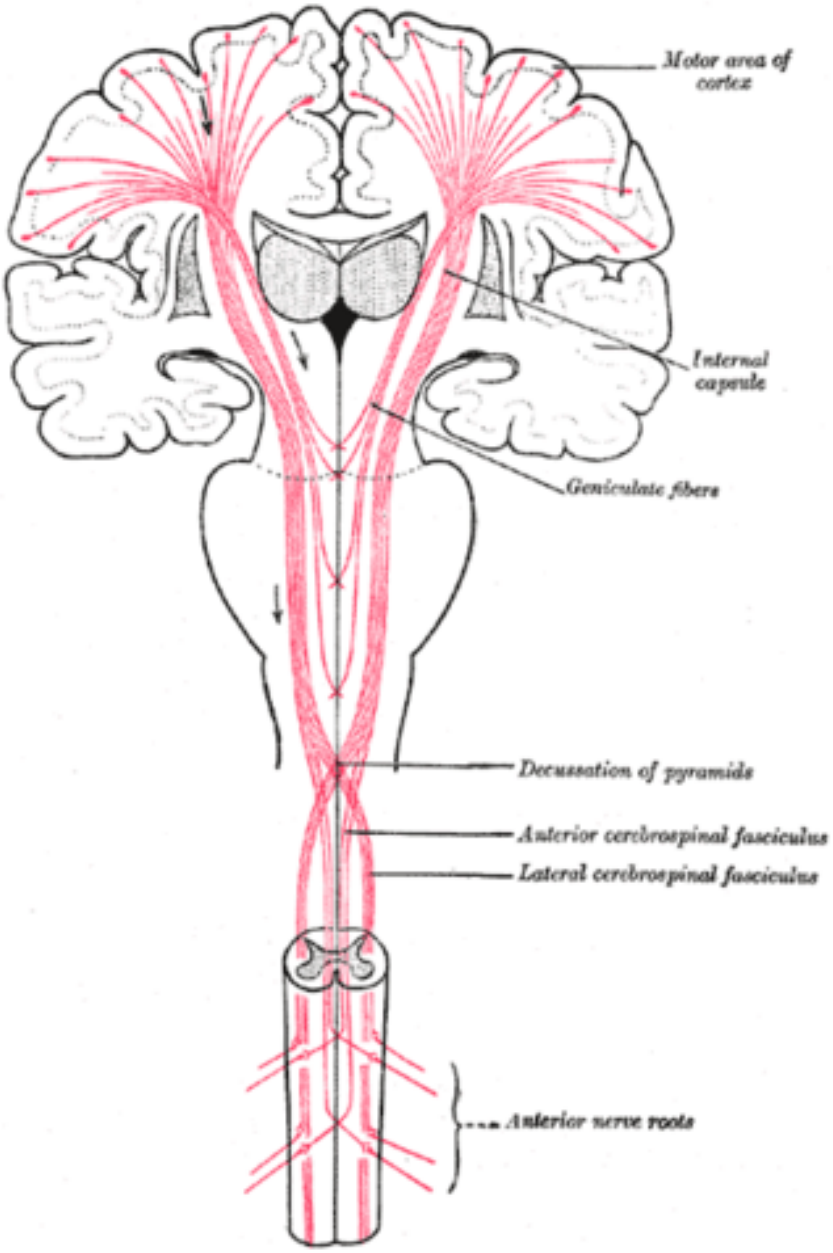
Key ‘nodes’



- Primary motor cortex (M-I)
- Non-primary motor cortex
- Basal ganglia
- Brain stem
- Cerebellum
- Spinal cord

Projection pathways

- Pyramidal tracts
  - Pyramidal cells (Cerebral Cortex Layer 5) in primary motor cortex (M1)
  - Corticobulbar (cortex -> brainstem) tract
  - Corticospinal (cortex -> spinal cord) tract
- Crossover (decussate) in medulla
  - L side of brain ennervates R side of body



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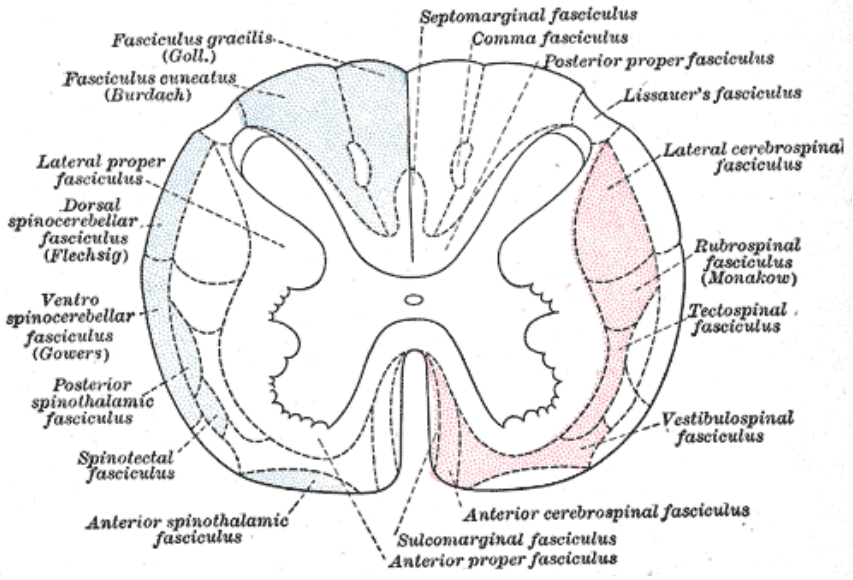


Source: Wikipedia

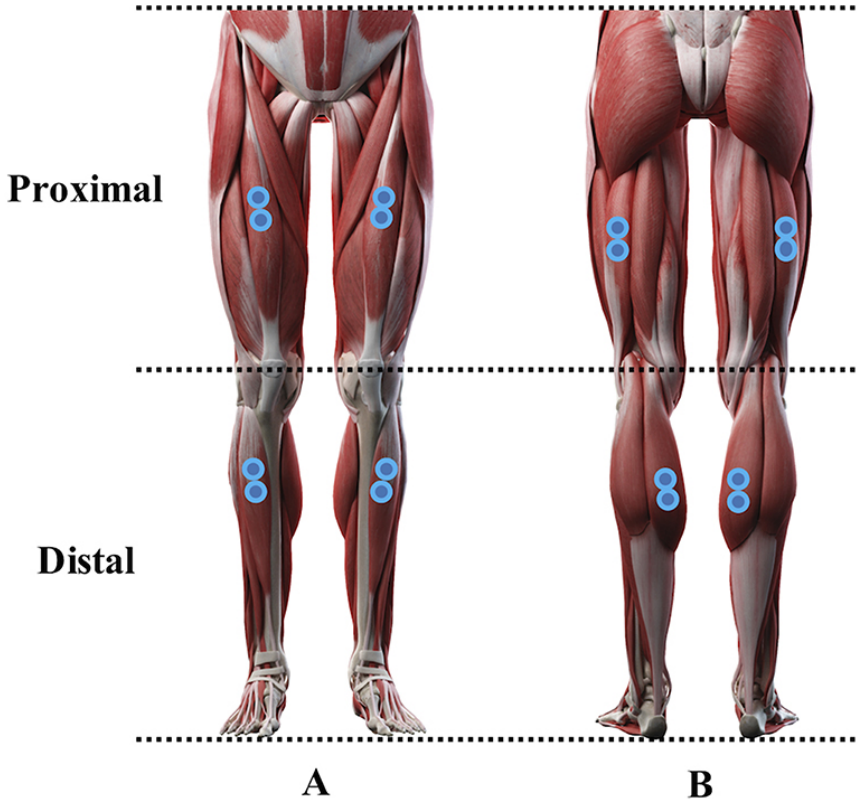
- Extrapyramidal system
  - Tectospinal tract
  - Vestibulospinal tract
  - Reticulospinal tract
- Involuntary movements
  - Posture, balance, arousal

Muscles

- Generate forces
- In one direction

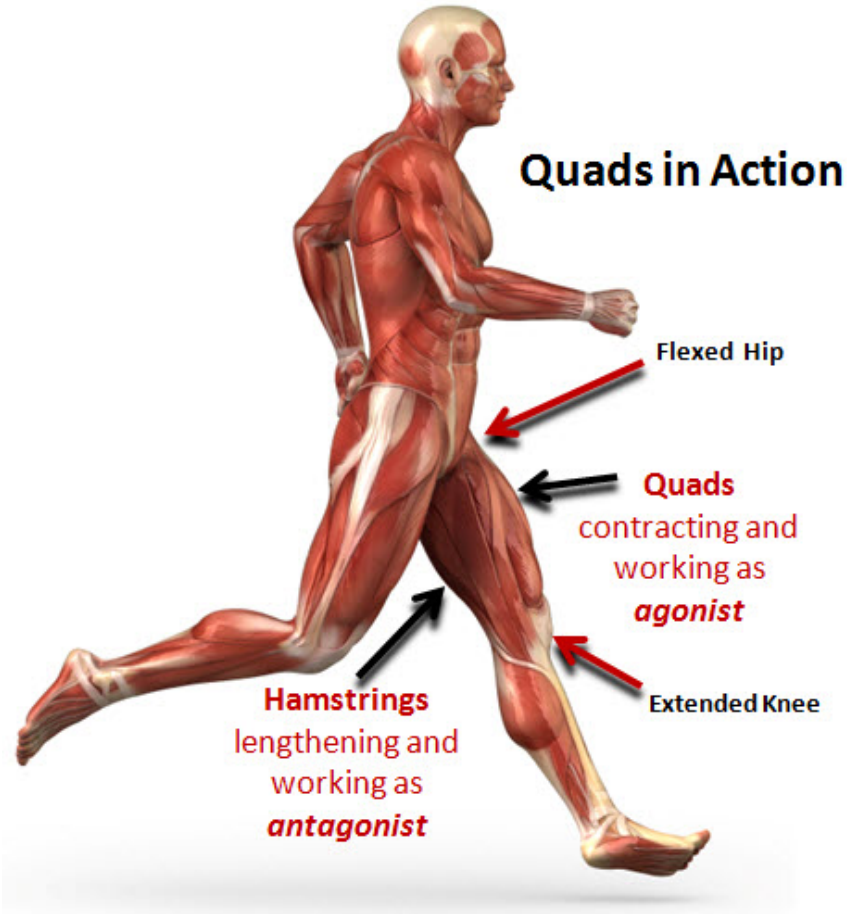
Functional classes

- Axial
  - Trunk, neck, hips
- Proximal
  - Shoulder/elbow, pelvis/knee
- Distal
  - Hands/fingers, feet/toes

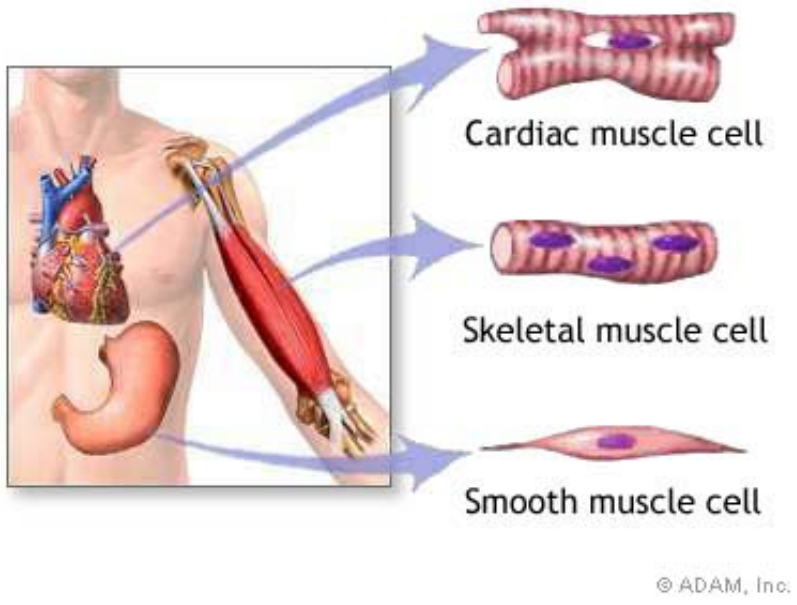


(Cantú, Nantel, Millán, Paquette, & Côté, 2019) (https://doi.org/10.3389/fneur.2019.00951)

Agonist/antagonist pairs



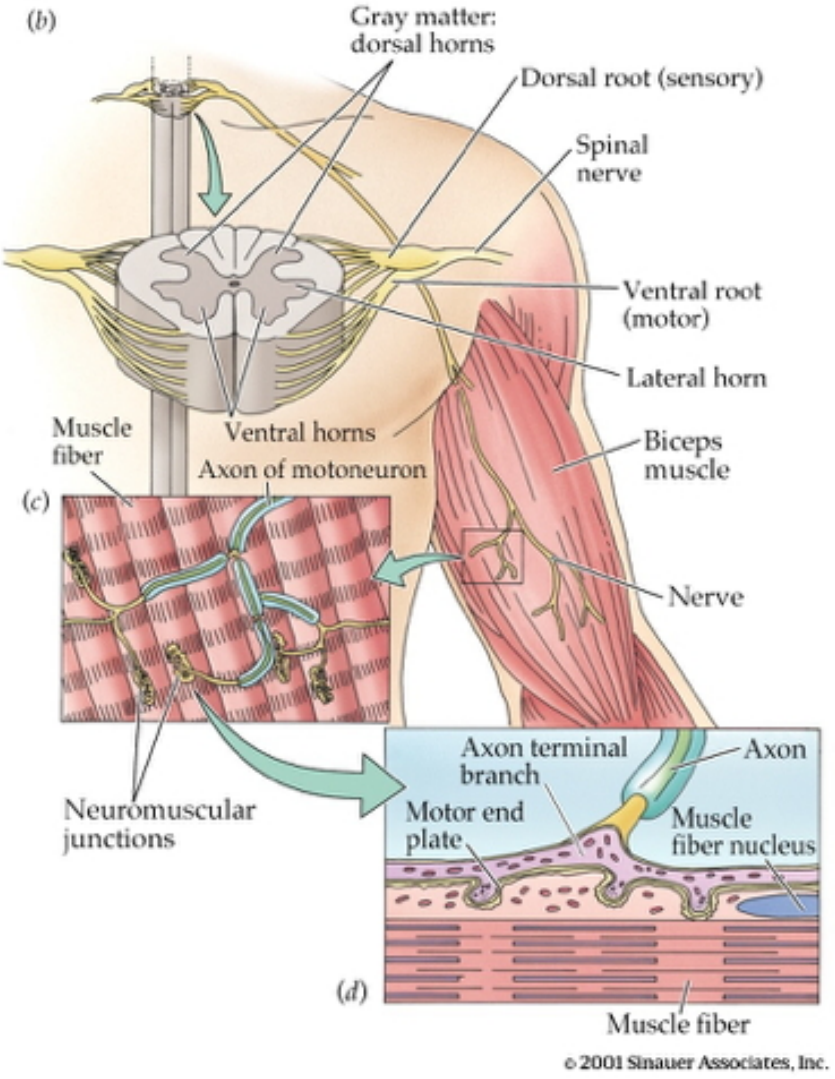
Anatomical types



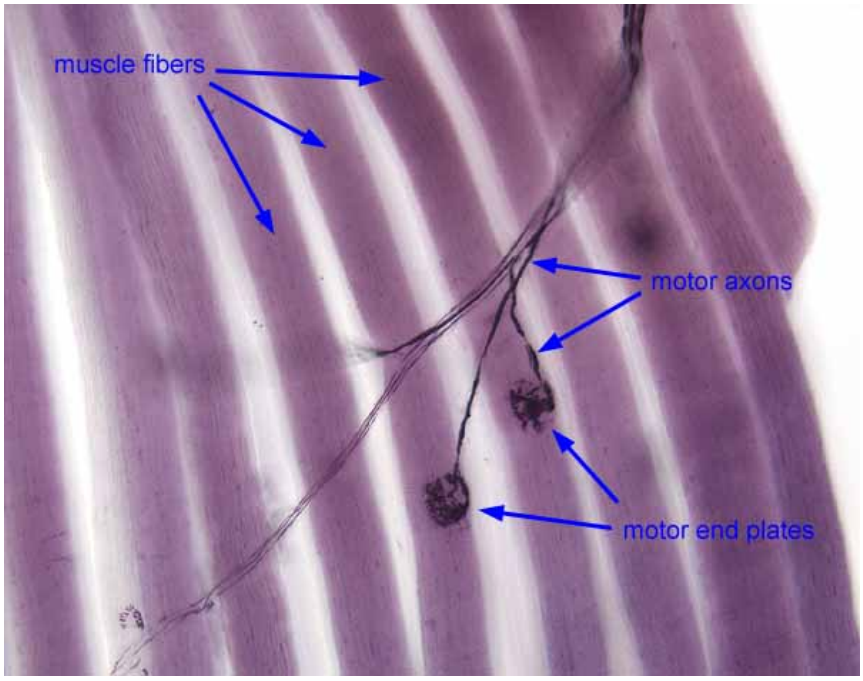
- Cardiac
- Striated (striped)
  - Skeletal
  - Voluntary control, mostly connected to tendons and bones
- Smooth
  - Arteries, hair follicles, uterus, intestines
  - Regulated by ANS (involuntary)

How skeletal muscles contract

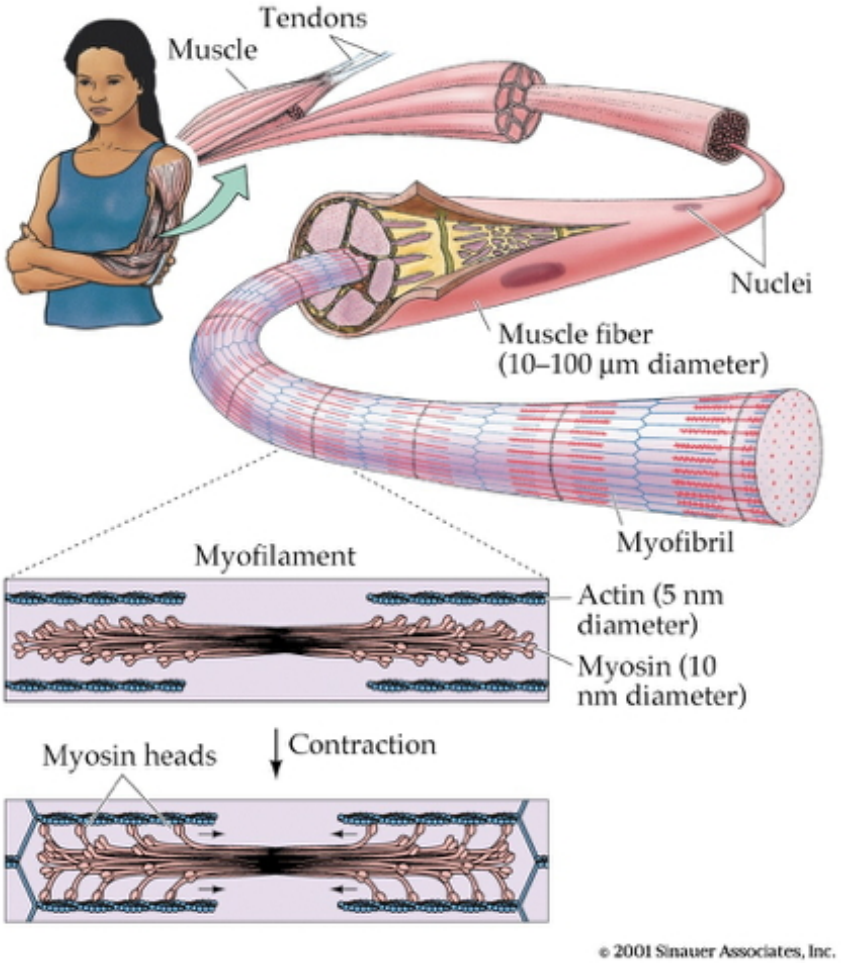
- Motoneuron (ventral horn of spinal cord)
- Projects to muscle fiber
- Neuromuscular junction
  - Synapse between motor neuron and muscle fiber
  - Releases ACh

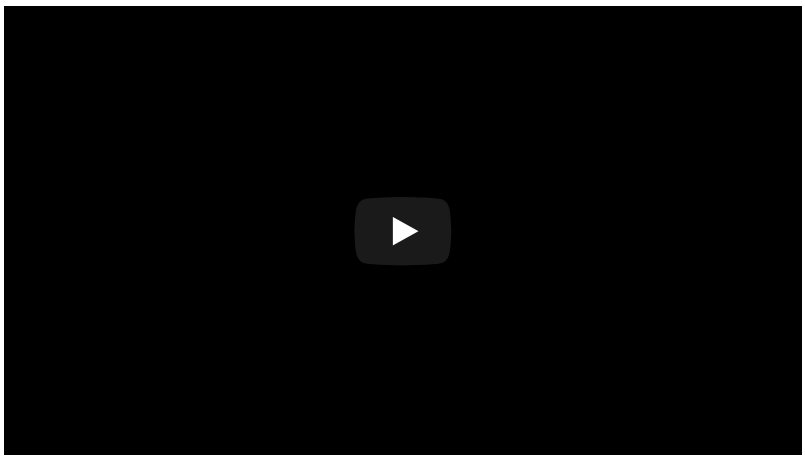


- Motor endplate
  - Contains nicotinic ACh receptors
- Activation produces excitatory endplate potential
  - Muscle fibers depolarize
  - Depolarization spreads along fibers like an action potential
  - Ca++ released from intramuscular stores



- Muscle fibers contain bundles of myofibrils called sarcomeres
- Myofibrils
  - Contain actin & mysosin proteins
  - “Molecular gears”
- Bind, move, unbind in presence of Ca++, adenosine triphosphate (ATP)



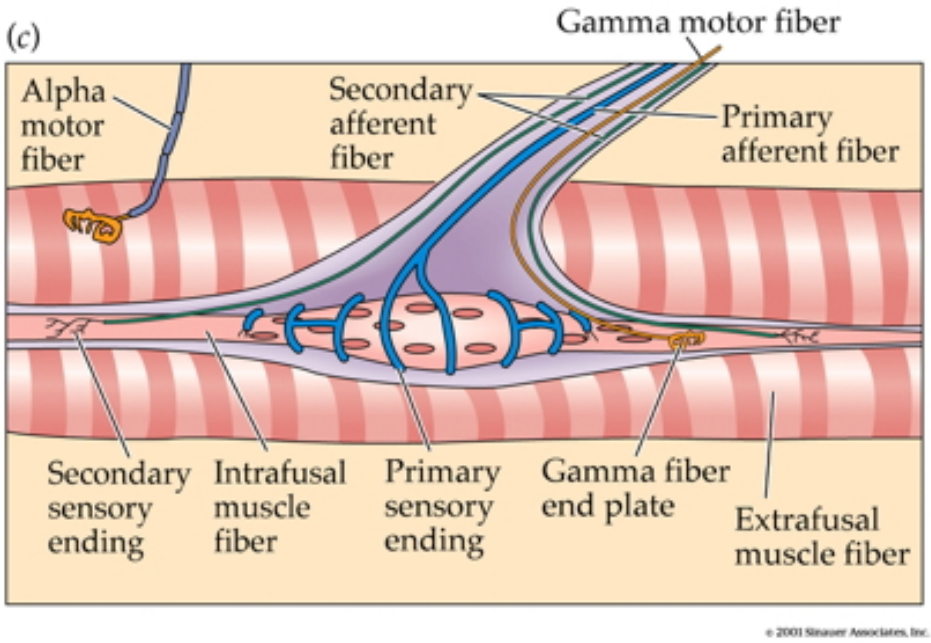


Skeletal muscle fiber types

- Fast twitch/fatiguing
  - Type II
  - White meat
- Slow twitch/fatiguing
  - Type I
  - Red meat

Muscles as sensory organs

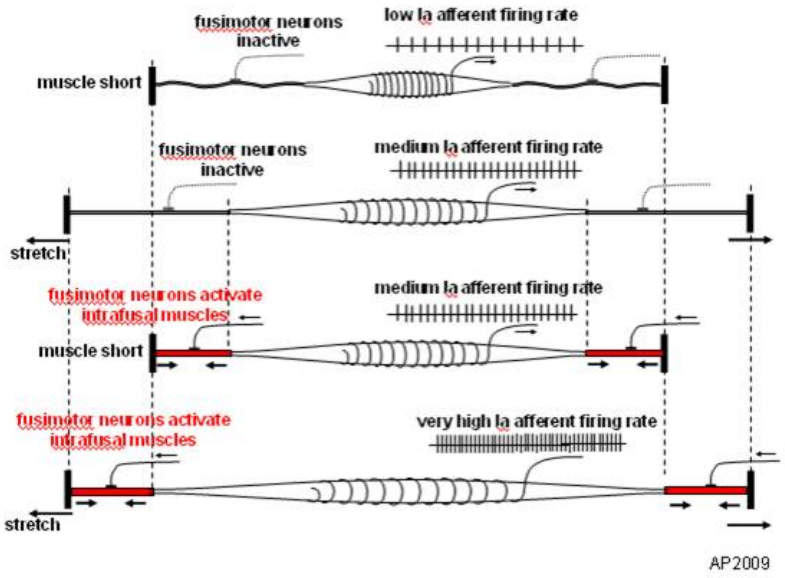
Two fiber types



- *Intrafusal* fibers
  - Sense muscle length and change in length, e.g. “stretch”
  - Also called muscle spindles
  - Provide muscle proprioception (perception about the self, a form of interoception)
  - Ennervated by by primary Ia afferents (sensory output from muscle); also secondary Type II fibers
  - Ennervated by gamma (γ) motor neurons (motor input)
- *Extrafusal* fibers
  - Generate force
  - ennervated by alpha (α) motor neurons

Monosynaptic stretch (myotatic) reflex

- Muscle stretched (length increases)
- Muscle spindle in intrafusal fiber activates
- Ia afferent sends signal to spinal cord
  - Activates alpha (α) motor neuron
- Muscle contracts, shortens length



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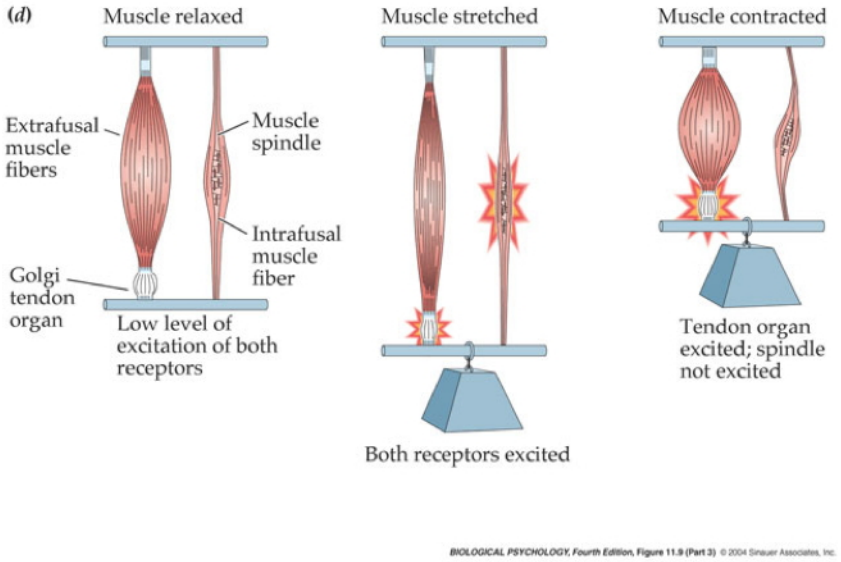
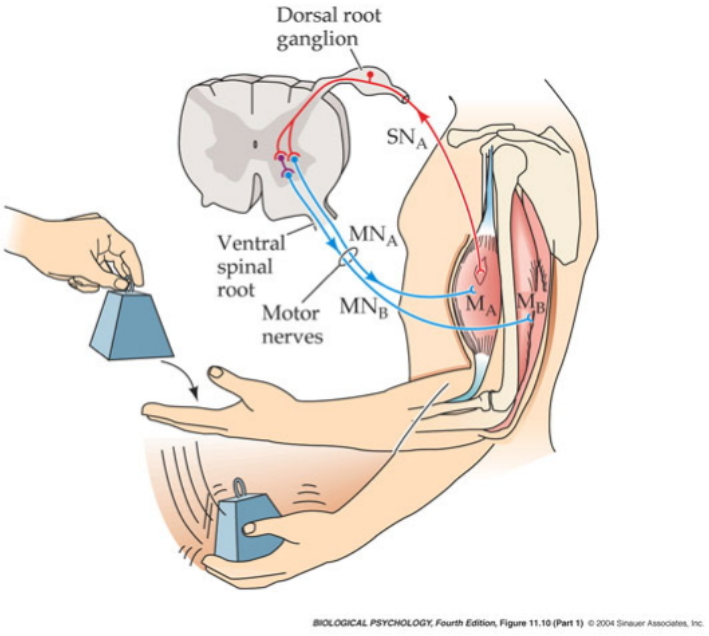
- Gamma (γ) motor neuron fires to take up 'slack' in intrafusal fiber





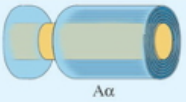
Why doesn't antagonist muscle respond?

- Polysynaptic inhibition of antagonist muscle
- Prevents/dampens tremor

Speed of sensory information propagation

- Brain gets fast(est) propagating sensory info from spindles

TABLE 8.2 *Fibers That Link Receptors to the CNS*

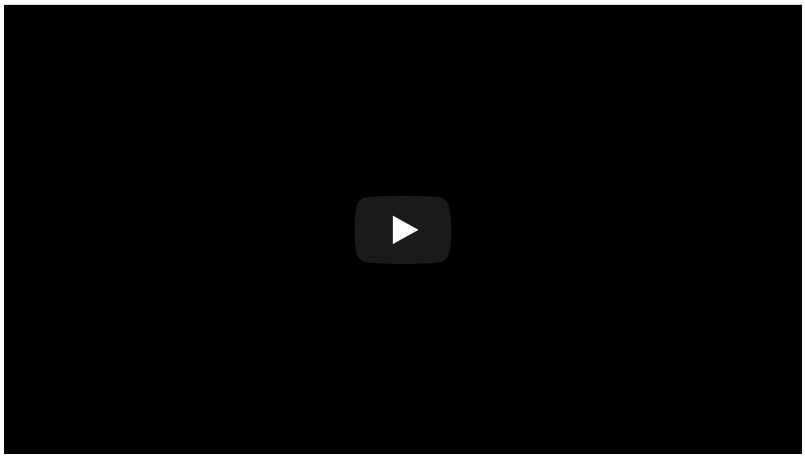
Sensory function(s)	Receptor type(s)	Axon type	Diameter (μm)	Conduction speed (m/s)
Proprioception (see Chapter 11)	Muscle spindle	 Aα	13–20	80–120
Touch (see Figures 8.12 and 8.13)	Pacinian corpuscle, Ruffini's ending, Merkel's disc, Meissner's corpuscle	 Aβ	6–12	35–75
Pain, temperature	Free nerve endings; VRL1	 Aδ	1–5	5–30
Temperature, pain, itch	Free nerve endings; VR1, CMR1	C	0.02–1.5	0.5–2

BIOLOGICAL PSYCHOLOGY, Fourth Edition, Table 8.2 © Sinauer Associates, Inc.

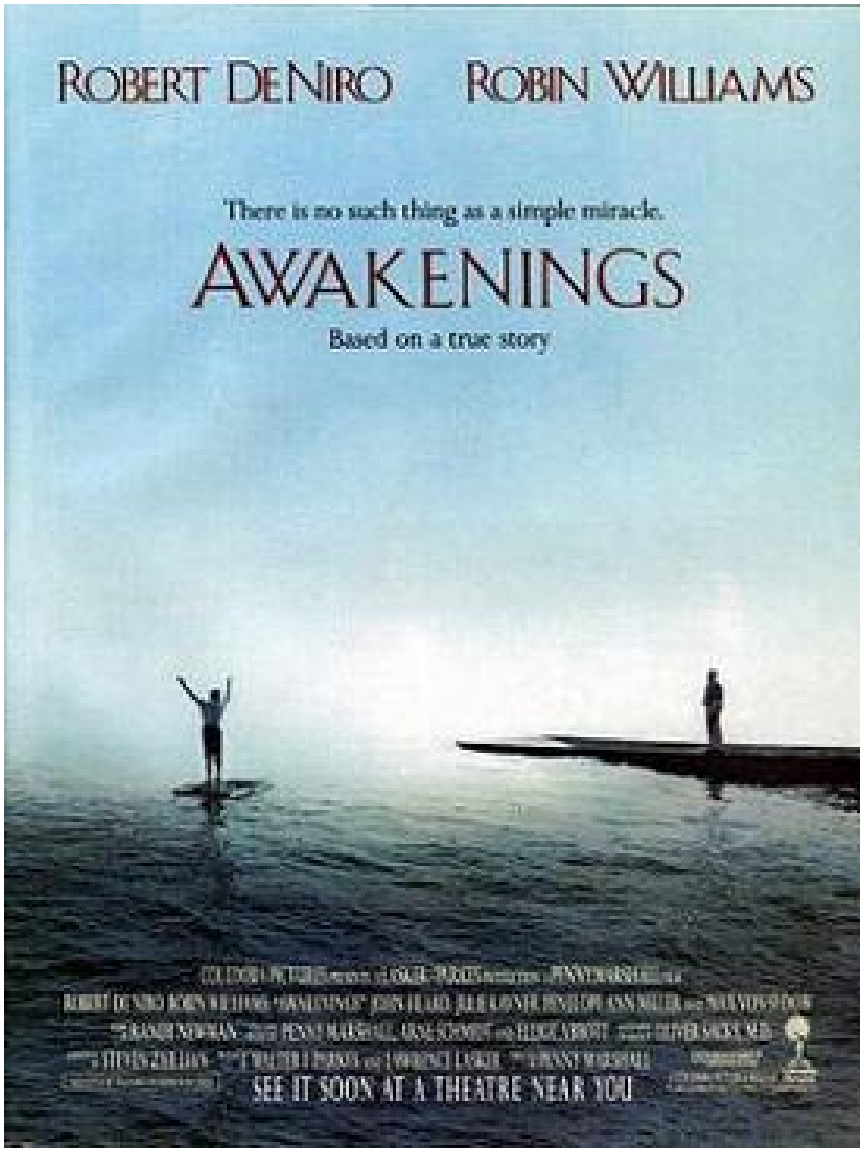
Disorders of movement

- Parkinson's
- Huntington's

The Faces of Parkinson's



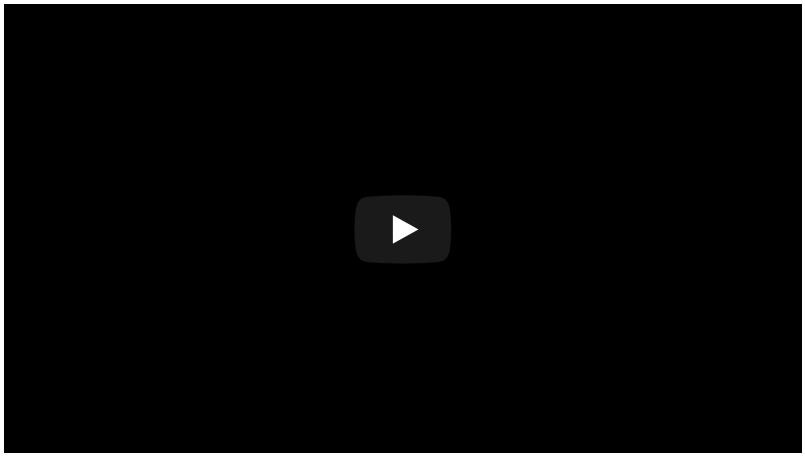
- Slow, absent movement, resting tremor
- Cognitive deficits, depression
- DA Neurons in substantia nigra degenerate
- Treatments
  - DA agonists
  - DA agonists linked to impulse control disorders in ~1/7 patients (Ramirez-Zamora, Gee, Boyd, & Biller, 2016) (http://doi.org/10.1586/14737175.2016.1158103)
  - Levodopa (L-Dopa), DA precursor



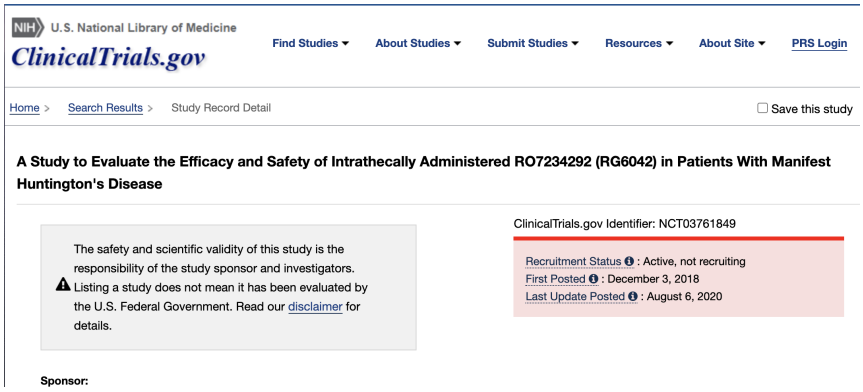
Huntington's

- Formerly Huntington's Chorea
  - "Chorea" from Greek for "dance"
  - "Dance-like" pattern of involuntary movements

- Cognitive decline
- Genetic + environmental influences
- Disturbance in striatum
- No effective treatment
- But progress in an animal model targeting abnormal protein products (Li et al., 2019) (https://doi.org/10.1038/s41586-019-1722-1)



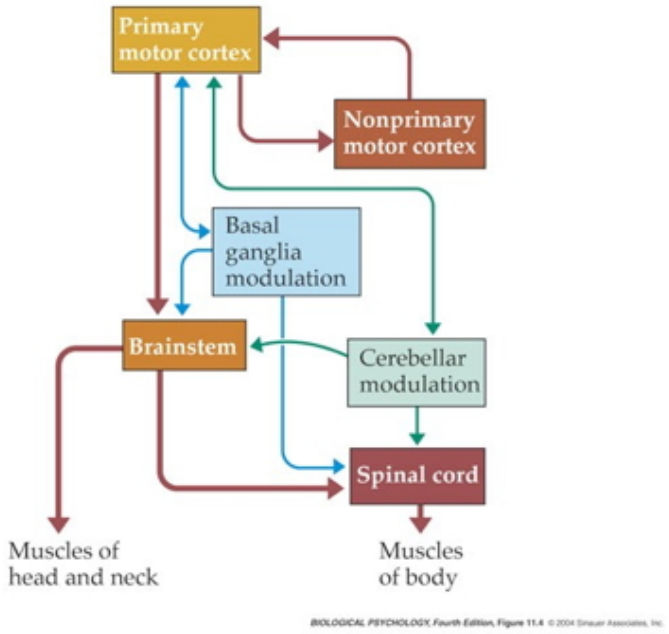
Clinical trial focused on gene therapy



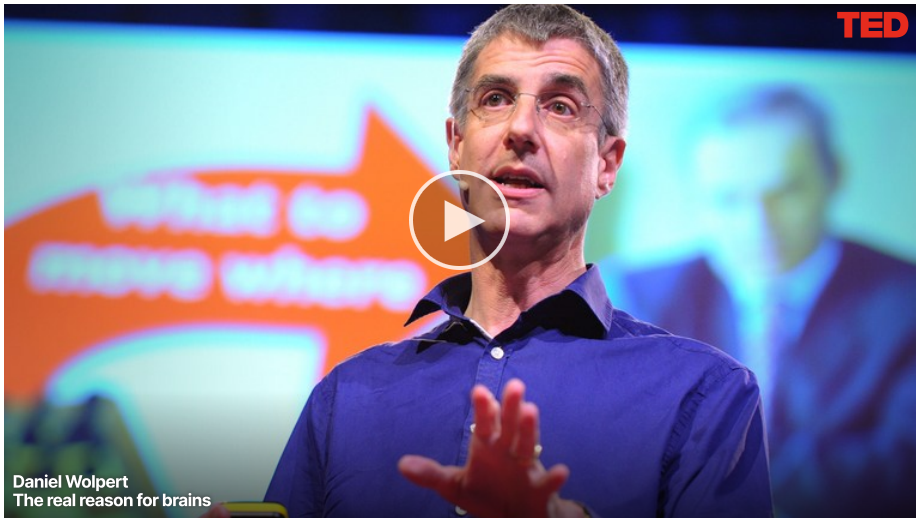
https://clinicaltrials.gov/ct2/show/study/NCT03761849 (https://clinicaltrials.gov/ct2/show/study/NCT03761849)

The big picture

- Control of movement determined by multiple sources
- Cerebral cortex + basal ganglia + cerebellum + spinal circuits

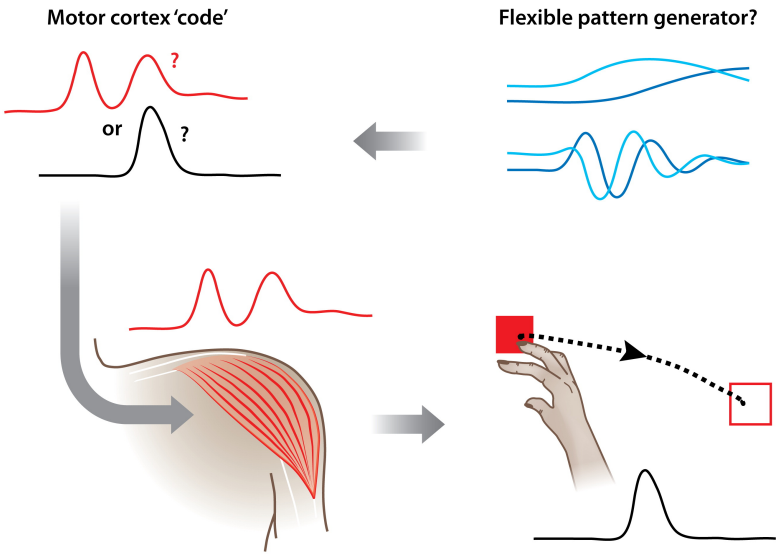


The “real” reason for brains



What does motor cortex activity encode?

Muscle activity? Limb velocity? Or…?



Shenoy KV, et al. 2013.
Annu. Rev. Neurosci. 36:337–59

Shenoy et al., 2013 (http://dx.doi.org/10.1146/annurev-neuro-062111-150509)

Cortical Control of Arm Movements: A Dynamical Systems Perspective

Annual Review of Neuroscience

Vol. 36:337-359 (Volume publication date July 2013)
First published online as a Review in Advance on May 29, 2013
https://doi.org/10.1146/annurev-neuro-062111-150509

What does the cerebellum do?

- Predict future sensory states? (Ito, 2008) (http://doi.org/10.1038/nrn2332)

Systems perspective

- Cognitive/affective states
- Nervous system states
- Muscle states
- Actions
- Consequences of actions on world states
- Sensory states

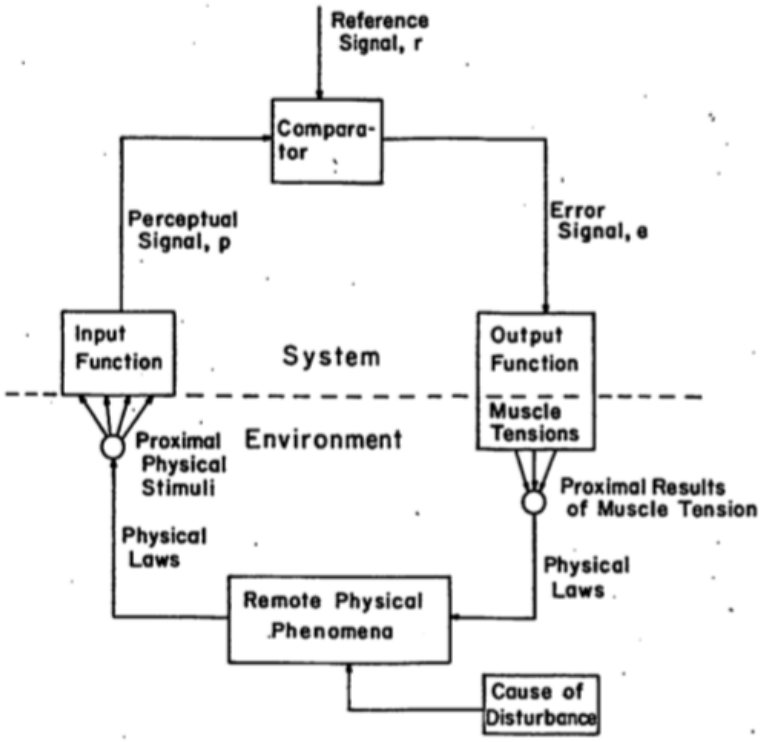


FIGURE 5.2. *General model of a feedback control system and its local environment.*

(Powers, 1973) (http://www.pctresources.com/Other/Reviews/BCP_book.pdf)

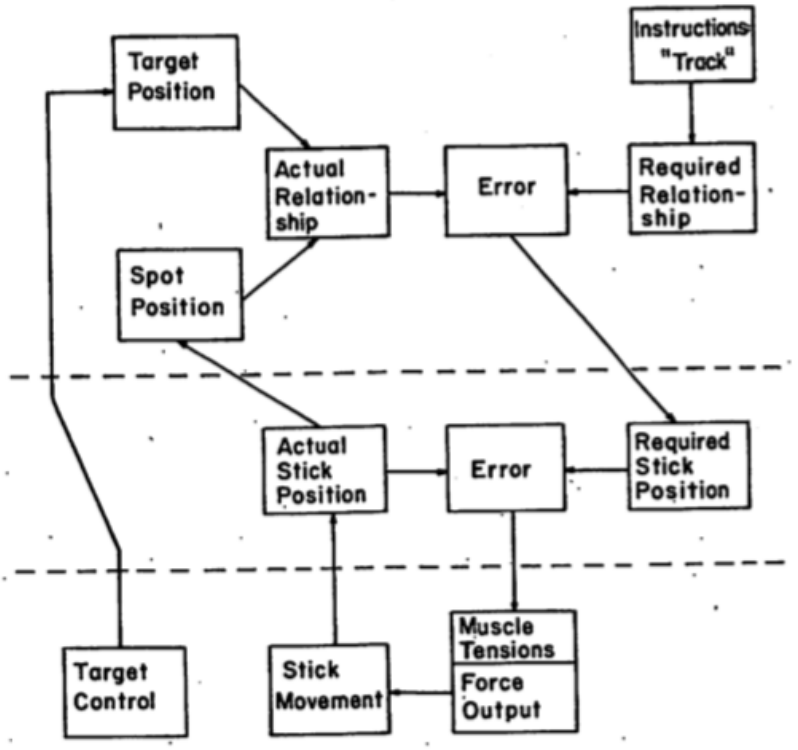


FIGURE 5.1. *A two-level model of feedback relationships in a tracking experiment.*

(Powers, 1973) (http://www.pctresources.com/Other/Reviews/BCP_book.pdf)

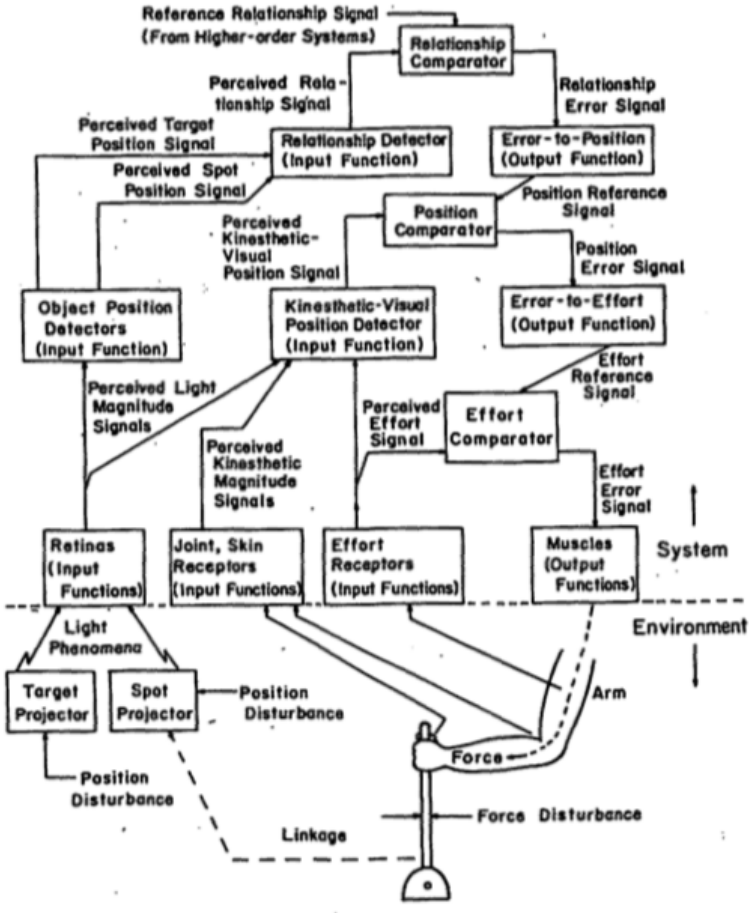


FIGURE 6.1. *A, three-level control-system model of a person in the tracking situation.*

(Powers, 1973) (http://www.pctresources.com/Other/Reviews/BCP_book.pdf)

The New York Times

PHYS ED

Something in the Way We Move

We may each have a movement "signature" that, like our face or fingerprints, is unique to us.

Barton Silverman/The New York Times

https://www.nytimes.com/2019/10/23/well/move/something-in-the-way-we-move.html (https://www.nytimes.com/2019/10/23/well/move/something-in-the-way-we-move.html)

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Li, Z., Wang, C., Wang, Z., Zhu, C., Li, J., Sha, T., … Lu, B. (2019). Allele-selective lowering of mutant HTT protein by HTT-LC3 linker compounds. *Nature*, *575*(7781), 203–209. https://doi.org/10.1038/s41586-019-1722-1 (https://doi.org/10.1038/s41586-019-1722-1)

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Ramirez-Zamora, A., Gee, L., Boyd, J., & Biller, J. (2016). Treatment of impulse control disorders in parkinson's disease: Practical considerations and future directions. *Expert Rev. Neurother.*, *16*(4), 389–399. https://doi.org/10.1586/14737175.2016.1158103 (https://doi.org/10.1586/14737175.2016.1158103)