**Physiology 844 – Neurophysiology**

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**Required textbook and other material**

Rothwell, John C. Control of Human Voluntary Movement. Aspen: Rockville, MD, 1994.
Cheney, P.D. Core Syllabus, Neurophysiology of motor system function
Additional research papers will be used to supplement specific topics and will be listed with each topic.

**Objectives**

R = Rothwell text

**Topic I: Mechanical Properties of Muscle**

Supplemental original papers (required reading for all):

Bizzi E, Giszter SF, Loeb E, Mussa-Ivaldi FA, Saltiel P. (1995) Modular organization of motor behavior in the frog's spinal cord. *Trends Neurosci.* 18:442-446.

Overduin, S.A., d'Avella, A., Roh, J. and Bizzi, E. (2008) Modulation of muscle synergy recruitment in primate grasping. *J. Neuroscience* 28: 880-892.

Dominici et al., (2011) Locomotor primitives in newborn babies and their development. *Science* 334: 997-999.

1. Diagram a mechanical model of muscle. What actual structures in muscle may the individual components in the model correspond to? (R. p. 9-10)

2. Draw a diagram illustrating the length-tension relationship of muscle for active contraction and passive stretch. (R. p. 11) What is the contribution of passive tension? How does the time course of twitch tension vary with muscle length? Compare this to the relation between joint position and torque determined for the tibialis anterior muscle in humans. (R. p. 18)

3. Explain the characteristic features of the length-tension relationship of muscle in terms of interactions between actin and myosin filaments. Account for 1) the ascending portion of the curve, 2) the peak, and 3) the descending portion of the curve. (R. p. 11)

4. Contrast the muscle tension resulting from synchronous versus asynchronous electrical stimulation of the muscle nerve. Which condition most closely matches natural activation of muscle by the CNS. (R. p. 16-17) How does fusion frequency (frequency at which muscle tension record becomes smooth as muscle nerve frequency is increased) vary with muscle length. (R. p. 18)

5. List some consequences for movement control of the length-tension and force-velocity relationships of muscle. (R. p. 22-23)

6. What is the end-point equilibrium hypothesis of movement control? Describe an experiment by Bizzi and colleagues that supports this hypothesis. (R. p. 25-28)

7. Describe the meaning of "convergent force field" as defined by Bizzi and colleagues and describe an experiment in the frog associated with spinal cord microstimulation used to demonstrate these force fields. (Bizzi et al., p. 442-443)

8. What is meant by the term “motor primitive” as used by Bizzi and colleagues? How many primitives can be demonstrated by stimulating the premotoneuronal circuitry of the frog spinal cord?

9. How might a relatively small number of motor primitives be capable of producing movements to a large number of final equilibrium points. Describe the results of the experiment by Bizzi and colleagues in which multiple spinal cord sites were stimulated simultaneously. (Bizzi et al., p. 443-444)

10. Explain the objective of the study by Overduin and others and the approach based on hand grasping in the monkey. (Overduin et al., p. 880-882, Figs. 1 & 2)

11. Explain in conceptual terms the method used by Overduin to extract muscle synergies from EMG activity (Overduin et al., p. 882 and others as needed)

12. Summarize the EMG patterns obtained during object grasping in the monkey. How much variability in EMG patterns could be accounted for based on identified synergies? (Overduin et al., Figures 3 and 4)

13. Explain the reconstruction of EMG activity patterns using identified muscle synergies and summarize the results. (Overduin et al., Figures 5-7)

14. Briefly summarize the extent to which amplitude and timing coefficients varied with object properties. What was the overall conclusion about muscle synergies in primate grasping? Are these synergies primate versions of the primitives described in the frog? (Overduin et al., p. 886-891, Figures 8 & 9)

15a. Explain what is meant by “locomotor primitives” and alternative hypotheses about the development of these basic patterns of muscle activation associated with locomotion. Describe the methods used to dissociate these alternatives. (Dominici et al., 2011, neonate locomotion movie)

15b. Explain the basic muscle activation patterns found in neonates compared to toddlers, preschoolers and adults. (Dominici et al. 2011, Figures 1 and 2)

16. How do these basic patterns compare to patterns derived from EMG data in other species? What are the implications for evolution of human locomotion in relation to other vertebrates? (Dominici et al., 2011, Figure 4)

**Topic II: Properties of Motor Units and Muscle Fatigue**

Supplemental original research paper (required reading for all):

> Mochizuki, Ivanova and Garland (2005) Synchronization of motor units in human soleus muscle during standing postural tasks. *J. Neurophysiology* 94: 62-69.

1. Define motor unit. Name two methods by which the innervation ratio of a muscle can be determined. How is the distribution of muscle fibers innervated by a single motoneuron determined? (R. pp. 32-34) Name three physiological types of motor units. How are they identified? How does conduction velocity and motoneuron size vary with the type of motor unit? (R. p. 30-35, Figs. 3.2, 3.3)

2. Summarize the histochemical and biochemical characteristics of S, FF, and FR motor units. (R. pp. 36-38, Table 3.1)

3. What is “input resistance” and how does it affect the membrane voltage change associated with injected current? How would it affect EPSP size? (R. p. 40-42 & Cheney Syllabus). What is the relationship between injected current and motoneuron firing rate? How is repetitive firing influenced by after-hyperpolarization? How does after-hyperpolarization vary with cell soma size? (R. p. 40-42)

4. Define the principle of orderly recruitment of motor units according to size. This is also referred to as the "size principle". How does EPSP size vary with motoneuron soma size? How does EPSP size for motor unit type vary with tetanic tension? (R. p. 44-50) Name two mechanisms by which force gradation occurs during voluntary movement and the relative importance of each mechanism in small hand muscles as compared to large axial muscles. (R. pp. 60-62)

5. What is the classical explanation of the underlying mechanism of orderly recruitment proposed by Henneman? (R. p. 46-50) (Hint: It is based on the input resistance of motoneurons of different sizes.) Summarize the properties of different motor unit types. What is the extent of recruitment of different medial gastrocnemius motor unit types in relation to various motor activities in the cat (R. Fig. 3.9). Discuss an example in which cat ankle extensor muscles are preferentially recruited for specific types of movement, e.g., paw shakes. (R. p. 56-57)

6. List the different ways in which Henneman and colleagues experimentally activated motor units and found that orderly recruitment applied. (R. p. 48-49). Name two exceptions to orderly recruitment of motor units. (R. p. 49). Describe data from human motor unit recording showing deviations from a "fixed" recruitment order (R. Fig. 3.14). Explain a mechanism for reversal of the normal recruitment order. (R. Fig. 3.11)

7. List and explain four factors, in addition to motoneuron input resistance, that could affect the order in which motoneurons are recruited in relation to a synaptic input. (R. pp. 44-48)

8. Explain the method used to determine the twitch tensions of individual motor units in humans during voluntary movement. Does orderly recruitment according to size apply to human voluntary movements? (R. pp. 52-55)

9. What is motor unit synchronization and how is it detected? What can this type of data reveal about the organization of synaptic input to motoneurons? (R. p. 57-62)

10. Outline the changes that occur in EMG and motor unit recordings from muscles undergoing partial denervation followed by reinnervation. What is the explanation of these changes? (R. pp. 65-70)

11. What are the possible sources of muscle fatigue and give examples of when central and peripheral mechanisms may come into play. (R. p. 62-65)

12. Explain the rational and method used to test for bilateral control from descending systems of soleus muscle motor units in human standing (Mochizuki et al., JNP, 2005; pp 62-64).

13. Explain the primary results of the study (Mochizuki et al., JNP, 2005; pp 64-65, Figs 1-3).

14. Review and explain the main points in the Discussion, particularly relative to the possible roles of the corticospinal and vestibulospinal systems in controlling soleus motor units during postural sway (Mochizuki et al., JNP, 2005; pp 65-68).

**Topic III: Muscle spindle structure, receptor properties and function.**

1. Diagram and explain the current view of the structure of the muscle spindle. To what extent is the static and dynamic gamma innervation independent? What are the diameters of the motor and sensory axons innervating the spindle? (Rothwell, pp. 74-76)

2. Contrast the functional properties of muscle spindle primary and secondary afferents. How are recordings from spindle afferents made in anesthetized animals? What does each receptor signal to the CNS? (Rothwell, pp. 76-81, Fig. 4.6)

3. Contrast the actions of static and dynamic gamma motoneurons on spindle afferent responses to large ramp stretches. How are static and dynamic gamma motoneurons identified? (Rothwell, pp. 81-83, Fig. 4.3, all parts, Figs 4.4, 4.6, 4.7)

4. Contrast the responses of spindle afferents to large ramp stretches versus small amplitude sinusoidal stretches. Discuss the possible functional implications of the high sensitivity of spindle afferents to small stretches. (Rothwell, pp. 84-86, Figs 4.8, 4.9)

5. Diagram the structure of the Golgi Tendon Organ showing its relation to extrafusal muscle and tendon. Based on early experiments by B.H.C. Matthews, it was thought that GTO's have a very high threshold for activation. This view of the GTO is no longer tenable. Summarize the functional properties of the Golgi tendon organ that contradict the early conclusions of Matthews. (Rothwell pp. 87-91)

6. List the receptors found in joints that may have a role in kinesthesia and/or the control of muscle activity. Summarize the location and functional properties of these receptors. Are joint receptors responsible for joint position sense? Why? What other receptor might contribute? (Rothwell pp. 91-94)

7. Excluding the muscle spindle and Golgi tendon organ, list the receptors found in muscle and summarize their properties. (Rothwell, pp 91-92) Name the four main types of sensory receptors found in skin and summarize their properties. Summarize evidence that cutaneous receptors are important in the control of movement. (Rothwell, pp 94-96)

8. Describe a method for recording from afferent fibers in peripheral nerves of awake subjects. Which fibers are most easily recorded? Briefly summarize the properties of human muscle spindle and Golgi tendon organ afferents in relation to findings in the cat. Rothwell, pp. 96-98)

9. Briefly summarize the properties of human cutaneous mechanoreceptors and joint receptors afferents in relation to findings in the cat. (Rothwell, pp. 98-100)

10. Explain a method for electrical stimulation of single axons in peripheral nerve. Summarize the perceptual responses elicited by stimulation of different types of sensory afferent axons. (Rothwell, pp. 100-102)

11. Do spindle afferents contribute to joint position sense? Discuss evidence from tendon pulling experiments in humans and the Matthew's experiment of limb position matching in the presence of vibration. (Rothwell, pp. 102-104)

12. Summarize evidence concerning the role of joint receptors and cutaneous afferents to a sense of movement and joint position. Does the contribution of these receptors vary depending on the joint? (Rothwell, pp. 104-105)

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**Topic IV: Spinal cord reflexes (Rothwell Chapters 5 & 6)**

Supplemental original research paper (required reading for all):

> Hospod, V., Aimonetti, JM, Roll, JP, Ribot-Ciscar, E. Changes in human spindle sensitivity during a proprioceptive attention task. *J. Neuroscience 27: 5172-517, 2007.*

1. Summarize the classification of sensory afferent axons. (Rothwell, pp. 108-109; Advanced Neuroscience Syllabus Tables pp. 18-19)

2. Summarize the synaptic connections of spindle Ia afferents with motoneurons in the spinal cord. What is the evidence based on latency measurements for a monosynaptic connection between spindle Ia

afferents and motoneurons? Is it all monosynaptic? What is the synaptic delay for a monosynaptic connection? (Rothwell, pp. 110-113)

3. What are Ia Inhibitory interneurons? How were these neurons identified? What are the inputs to these neurons? (Rothwell, pp. 114-116)

4. Summarize the synaptic connections of spindle Ib afferents in the spinal cord. Explain the experiment Laporte and Lloyd used to demonstrate Ib inhibition of agonist muscles. (Rothwell, pp. 116-118)

5. Discuss the conflicting data concerning synaptic effects of spindle group II afferents on motoneurons. (Rothwell, pp. 118-120)

6. What are flexor reflex afferents (FRAs)? What is the minimum latency for muscle responses to stimulation of FRAs? Does stimulation of FRAs always produce flexion? What are the contralateral effects from stimulation of FRAs? (Rothwell, pp. 120-122)

7. What is a Renshaw cell? What are its synaptic connections within the spinal cord and give supporting evidence based on intracellular recording? Discuss possible functions of Renshaw cells. (Rothwell, pp. 123-125)

8. What is presynaptic inhibition and how has it been identified experimentally in the terminals of spindle Ia afferents? (Rothwell, pp. 125-127)

9. What is the H-reflex? Explain why the H-reflex amplitude decreases with stimulus intensity. (Rothwell, pp. 129-131)

10. What are long latency stretch reflexes? Summarize the evidence supporting a transcortical pathway mediating long latency stretch reflexes. (Rothwell, pp. 131-134)

11. What is the tonic vibration reflex? What is the mechanism by which the TVR may suppress tendon and H-reflexes in the same muscle? (Rothwell, pp. 134-136)

12. Explain the follow-up servo theory of motor control advanced by Merton. What were thought to be the advantages of this mechanism? (Rothwell, pp 136-138, Fig. 6.5)

13. What did the follow up servo theory predict about the timing of activation of different efferent and afferent neurons? What did evidence from direct recording of spindle afferents in humans show? What is meant by alpha-gamma coactivation? (Rothwell, pp 139-140, Fig. 6.6)

14. What is meant by the gain of the stretch reflex? How might it be quantified? Characterize the gain of the stretch reflex at distal forelimb muscles in humans? What are the implications for the follow up servo theory? (Rothwell, pp 139-140, Fig. 6.7)

15. Summarize the background and goal of the study by Hospod et al. (J. Neuroscience 27: 5172-5178).

16. Explain the methods used to test the role of muscle spindle responses during drawing movements of the foot. You will need to consult a previous paper (Bergenheim, 2000) for a clear understanding of the behavioral task. How were afferents classified as group I or group II (show the relevant figure)? (J. Neuroscience 27: 5172-5178)

17. Show and explain figures from the paper that present evidence supporting the view that muscle spindle primary afferents responses during the letter recognition task are different than the control condition. What happened with secondary afferents? Did the subjects perform better on the recognition trials when changes occurred in activity of primary afferents? (J. Neuroscience 27: 5172-5178)

18. How did the authors interpret the results? How might increased variability aid in detection of position changes? (J. Neuroscience 27: 5172-5178)

**Topic V: Spinal cord reflexes continued (Rothwell Chapters 5 & 6)**

19. What are the advantages of alpha-gamma coactivation? Is there evidence that alphas and gammas can be activated independently in humans? How has this issue been studied in humans? (Rothwell, pp 140-143)

20. Summarize what is known about alpha gamma coactivation in the cat. Can alphas and gammas be activated independently? Summarize the factors that affect alpha-gamma coactivation. What happens to gamma activity when the cat performs novel movements? What are the patterns of activity of gamma's directly recorded during jaw movements? (Rothwell, pp 143-145, Fig. 6.8).

21. Explain a method for demonstrating reciprocal Ia inhibition in humans. What is a complication of this method and how can it be overcome? (Rothwell, pp. 145-147, Fig. 6.9)

22. Explain a method for demonstrating Ib inhibition in humans. What effect does cutaneous input have on Ib reflexes? What might be the function role of this modulation? (Rothwell, pp. 147-149, Fig. 6.10)

23. Explain two methods of demonstrating presynaptic inhibition in humans (skip #3 in text). How does the strength of presynaptic inhibition change during different phases of muscle contraction? (Rothwell, pp. 149-152, Fig. 6.11)

24. Summarize the properties of human flexion reflexes. What is the latency of responses to stimulation of the sole of the foot? Does the flexion reflex always produce flexion? What is a good rule of thumb that applies? (Rothwell, pp 153-157, Fig. 6.12)

25. Explain the movement paradigm used by Johansson and Westling to investigate the role of cutaneous afferents in finger grip. (Rothwell, pp. 157-158, Fig. 6.14)

26. Summarize the results obtained in the grip force paradigm in terms of discharge from primary sensory afferents, blocking cutaneous afferents with local anesthetics, brief electrical stimulation and unexpectedly changing the load. (Rothwell, pp. 158-163, Fig. 6.15)

27. Summarize the pathophysiology of spinal reflexes associated with decerebrate rigidity. (Rothwell, pp. 162-164)

28. Summarize the pathophysiology of spinal reflexes associated with spasticity. (Rothwell, pp. 164-168)

29. What is the clasp-knife phenomenon? Explain how the method of clinical testing might contribute the perception of a clasp-knife phenomenon. What receptor types most likely mediate the clasp-knife phenomenon? (Rothwell, pp. 168-169; Fig. 6.17)

30. Summarize the pathophysiology of spinal reflexes associated with Parkinson's disease. (Rothwell, pp. 170-172; Fig. 6.18)

31. Summarize the movement capabilities of deafferented human subjects. Is vision important? What types of situations are more dependent on somatosensory feedback? (Rothwell pp 173-178, Figs. 6.20, 6.21)

**Topic VI: Ascending and descending pathways of the spinal cord.**

Required reading for everyone: Rothwell text, Chapter 7 and Lemon review pp. 195-204.

Additional papers:

Lemon RN. Descending pathways in motor control. Ann. Rev. Neurosci. 31:195-218, 2008.

Jankowska E and Edgley SA. How can corticospinal tract neurons contribute to ipsilateral movements? A question with implications for recovery of motor function. *Neuroscientist* 12: 67-79, 2006.

Riddle CN, Edgley SA, Baker, SN. Direct and indirect connections with the upper limb motoneurons from the primate reticulospinal tract. J. Neurosci. 29: 4993-4999, 2009.

Turton A, et al. Lemon RN. Contralateral and ipsilateral EMG responses to transcranial magnetic stimulation during recovery of arm and hand function after stroke. Electroencephalography & Clin Neurophysiol. 101: 316-328, 1996.

1. Diagram the major features of the following ascending pathways and compare their functional properties (e.g., modalities of sensory information transmitted): 1) dorsal-column medial lemniscal pathway, 2) spinocervical and 3) spinothalamic pathway. (Rothwell p. 183-189, Figs 7.1, 7.2, 7.3)

2. Diagram the major anatomical features of the dorsal spinocerebellar tract, cunneocerebellar tract, ventral spinocerebellar tract and rostral spinocerebellar tract. List and compare the principal functional properties of these pathways. (Rothwell pp.189-190, plus diagrams to be identified by student)

3. Diagram the major anatomical features of the corticospinal (pyramidal) tract. List the key properties of this tract. (Rothwell pp 191-195, Figs 7.5, 7.6, additional figures are welcome)

4. Explain the methods of transcranial electrical and magnetic stimulation of the brain. Illustrate how these methods can be used to measure central and peripheral conduction velocity in humans (Rothwell, pp. 203-205, Fig. 7.12a; An explanation of transcranial stimulation is in Chapter 9. Refer to the full pdf copy of the Rothwell text, pp 303-306)

5. Explain the changes in central corticospinal conduction time with age. How do changes in central conduction compare to changes in peripheral conduction? (Rothwell pp. 203-205, Fig. 7.12b) Explain the rationale for concluding that the startle reflex in humans must be mediated by a tract other than the corticospinal tract? (Rothwell, pp. 205-207, Fig. 7.13)

6. Diagram the major anatomical features of the rubrospinal tract. List the key properties of this tract. (Rothwell pp 195-196, Fig 7.7, additional figures are welcome)

7. Diagram the major anatomical features of the vestibulospinal tract. List the key properties of this tract. (Rothwell pp. 196-198, additional figures are welcome)

8. Diagram the major anatomical features of the reticulospinal tract. List the key properties of this tract. Briefly summarize what is known about the tectospinal and interstitiospinal tracts. Summarize the categorization of descending systems and their pattern of termination in the spinal cord. (Rothwell pp. 198-199)

9. Does the reticulospinal system act only on proximal and axial muscles? Discuss evidence that it can have powerful effects on distal muscles. (Riddle et al. paper, Figure 3 only and Discussion section)

10. What is the propriospinal system? Describe its organization and inputs. What is the evidence supporting a specific role of these neurons in reaching movements. (Rothwell pp. 199-203, Figs. 7.10, 7.11)

11. Summarize the differences in the role of the propriospinal system in different species. State a general conclusion about species differences in descending control of motoneurons. (Lemon review, pp. 203-204).

12. Review 10 key properties of descending pathways. Comment on what is known and unknown? (Lemon review, Table 1, p. 197)

13. Summarize the categorization of descending systems into dorsolateral and ventromedial systems. What is the emotional motor system? (Lemon review, Figure 1, pp. 198 – 200).

14. List the multiple functions of the corticospinal system. Is the corticospinal system only a motor pathway? Discuss the evidence? (Lemon review, p. 201)

15. Discuss the suggestion that the main function of descending pathways is to modulate central pattern generators (CPGs). What is the corticomotoneuronal system? Summarize differences in the coticomotoneuronal system in primates compared to rodents, cats and raccoons. (Lemon review, pp. 201-202, Figure 2).

16. What is the ipsilateral corticospinal tract? Compare the distribution of ipsilateral and contralaterally projecting corticospinal terminations. (Jankowska review, Figures 1 and 2 only.)

17. By what descending neural circuits might cortical output neurons exert ipsilateral actions? (Jankowska review, Figures 3 and 5 only)

18. Is there evidence that the ipsilateral corticospinal system may be involved in motor compensation for unilateral damage to motor cortex. (Turton et al., Figure 5 and Discussion section 4.5)

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**Topic VII: Postural Control**

1. List and explain the functions the postural control system must perform. List the vestibular receptor organs and explain the basic mechanism of mechanoelectric transduction. (Rothwell p. 211-217, Figs 8.1, 8.2, Cheney syllabus)

2. Using a diagram, summarize the neural connections of the vestibular system (Rothwell pp.216, plus diagrams to be identified by student.)

3. Summarize the factors involved in maintaining quiet stance, i.e., standing upright posture including the roles of visual, vestibular, and somatosensory feedback as well as the length-tension properties of muscle. (Rothwell pp 216-221, Fig. 8.3)

4. Summarize the reactions and EMG responses to forward and backward translation of a platform on which the subject is standing. Explain the difference between “ankle strategy” and “hip strategy” and how these are evoked. What happens with the subject in a quadrapedal position? (Rothwell pp 222-225, Fig 8.5)

5. Describe the EMG responses and adaptations to rotations of a platform on which the subject is standing. (Rothwell pp. 225-227, Figure 8.6)

6. Summarize the evidence supporting a primary role of somatosensory receptors in mediating responses to platform translation and rotation. Explain evidence supporting a role of visual input on short

latency responses to platform translation. What is the effect of vestibular loss and anesthesia of the foot? (Rothwell pp. 198-199)

7. Describe the types of postural responses to changing visual input. What relative weighting does the postural control system appear to give different sensory inputs? Is the influence of the visual system necessarily slow? (Rothwell pp. 229-230, Fig. 8.8)

8. Explain the types of actions on the postural system that can be mediated by the vestibular system. (Rothwell, pp. 230-234, Figs. 8.9, 8.10)

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**Topic VIII: Properties of cortical motor areas**

Research paper
Kakei, S, Hoffman, DS, Strick PL (1999) Muscle and movement representations in the primary motor cortex. *Science* 285: 2136-2139.

General reference
Cheney, P.D. Behlaj-Saif, M. Boudrias, M.H. (2004) Principles of corticospinal system organization and function. Clinical Neurophysiology of Motor Neuron Diseases. In: Handbook of Clinical Neurophysiology, Vol. 4, A. Eisen, Editor.

1. Describe the laminar (6 layers, etc) structure of cerebral cortex and the basic vertical and lateral patterns of connectivity. What are Broadman's subdivisions of the cerebral cortex? (pp. 243-248, Figs 9.1, 9.2, 9.3)

2. Summarize thalamic inputs to cortical motor areas and postcentral (somatosensory) cortex. (Rothwell pp. 249-251, Fig. 9.4)

3. Summarize the main conclusions from the motor cortex mapping work of Woolsey and colleagues. How was the data collected? (Rothwell pp 252-254, Fig. 9.6)

4. Identify and explain four different methods of electrical activation of motor cortex. What are three major points that emerge from studies of electrical stimulation of motor cortex? How does the map for a single muscle change with stimulus intensity and how does this map compare with maps of evoked movements? (Rothwell pp 255-256, Fig. 9.7)

5. Summarize the results from intracellular recording from motoneurons combined with electrical stimulation of the cortical surface. What is a cortical colony? (Rothwell pp 256-259, Fig. 9.8)

6. Explain the method of spike triggered averaging of EMG activity. What have we learned about the organization of connections from cortical cells to motoneurons? How does this compare with results from anatomical labeling of axons? What is single pulse ICMS (stimulus-triggered averaging of EMG activity?). (Rothwell pp 260-263, Figs 9.9, 9.10, 9.11)

7. What is meant by neural plasticity? Explain an experiment by Sanes and Donoghue demonstrating that cortical output maps obtained with ICMS can change rapidly after peripheral nerve transection. Where does plasticity occur? (Rothwell pp 264-267; Figs. 9.12, 9.13)

8. Ed Evarts pioneered the technique of recording the activity of single neurons in awake monkeys. Summarize his findings concerning the timing of pyramidal tract neuron (PTN) discharge, the relation of discharge to load and preparatory (set) related activity. (Rothwell pp. 268-273; Figs 9.14, 9.15, 9.16)

9. Explain how the potential contribution of the corticomotoneuronal system to motoneuron firing might be calculated. Are all corticomotoneuronal cells activated equally well for tasks that involve there target muscles? (Rothwell, pp. 273-275, Fig. 9.17)

10. Explain the classic neuronal population experiments of Apostolos Georgopoulos demonstrating directional tuning of motor cortex cell discharge. How is directional tuning affected by external loads? (Rothwell pp 275-279; Figs 9.18, 9.19)

11. How does the motor cortex neuronal population vector shift during the delay period during a normal and "mentally rotated" movements (Rothwell, pp. 279-281; Fig. 9.20)

12. Describe the basic relationship between motor output and sensory input in primary motor cortex. (Rothwell, pp 281-283; Figs 9.21)

13. What are transcortical stretch reflexes. Summarize evidence from spike triggered averaging that the cortex participates in these reflexes. (Rothwell pp. 283-285; Fig. 9.22)

14. Name and summarize the properties of non-primary (secondary) cortical motor areas. Summarize the results of electrical stimulation mapping of secondary cortical motor areas. (Rothwell pp 285-286; Cheney et al., Handbook of Clinical Neurophysiology chapter review, Table 1)

15. Summarize the results from lesion studies suggesting that premotor cortex is important for visually cued movements whereas SMA is important for executing movement sequences. (Rothwell pp 286-288, Fig. 9.23)

16. Summarize the results of unit recording experiments that support a role for premotor cortex in visually cued movements (sensory guided) and SMA in movement sequences. (Rothwell pp 288–291, Figs 9.24, 9.25)

17. Research paper presentation. Discuss the background and rationale for the study. Define and explain the research question/issue to be studied. Why is this question/issue important? Explain the methods used to address the experimental questions or issues. Did the methods seem adequate? What were the limitations of the methods? (Kakei et al, 1999)

18. Research paper presentation. Summarize and explain the results that were obtained. Do the results definitively address the questions/issues posed in the introduction? Were there weaknesses/limitations in the data obtained? What were the conclusions from the study? Were the conclusions justified based on the data obtained? In what way did the study advance the field? (Kakei et al, 1999)

**Topic IX: Cerebellum**

Review paper

**Strick, PL, Dum RP, Fiez JA (2009) Cerebellum and nonmotor function. Annual Review of Neuroscience 32: 413-434.**

1. Describe the three major subdivisions of the cerebellum and how these divisions correspond with afferent terminations. (Rothwell, pp. 321-324, Figs. 10.1 (clearer examples of anatomy are available on the web), 10.2, 10.3, 10.4)

2. Summarize the organization of major afferent inputs to the cerebellum. List the sources of mossy fiber and climbing fiber inputs. Summarize the somatotopy of afferent input to the cerebellum (Rothwell, pp 325-328, Figs 10.5, 10.6)

3. Review the basic neuronal circuitry of the cerebellum including mossy fibers, granule cells, parallel fibers, Purkinje cells, deep nuclear cells, climbing fibers and transmitters. (Rothwell, p. 328-331; Figs 10.7, 10.8)

4. Name the two types of Purkinje cell spikes. What is their ionic basis and how are they recognized in extracellular recordings? (Rothwell, pp 331-334, Fig. 10.9)

5. Summarize the efferent connections of different divisions of the cerebellum. (Rothwell, pp. 335-337, Fig. 10.11)

6. Discuss and explain three theories of cerebellar function. (Rothwell, pp. 355-357)

7. Summarize evidence from the timing of neuronal discharge, relation to perturbations, cooling experiments and anatomy supporting the view that dentate neurons (neo or cerebrocerebellum) are involved in the initiation of voluntary movement while interpositus neurons are involved in feedback control of movement. (Rothwell, pp. 337-341, Figs 10.12)

8. Formulate a general conclusion from studies of the relationship between the discharge of cerebellar neurons and movement parameters. Summarize the data relevant to this issue. (Rothwell, pp. 341-345, Fig. 10.14)

9. Discuss the impairments associated with reversible inactivation of cerebellar nuclei in primates. Explain evidence that the cerebellum is more involved with coordination of movements involving multiple joints rather than single joint movements. (Rothwell pp 347-351, Figs ~~10.16~~, 10.17)

10. List and explain the major deficits in humans associated with cerebellar lesions (ataxia [This is a general term lumping together various abnormalities including intention tremor, dysmetria, dysdiadochokinesis.], hypotonia, asynergia, postural disturbance. Explain a useful way of explaining cerebellar deficits based on sagittal subdivisions (Rothwell pp 357-359, Figs 10.19, 10.20)

11. Summarize deficits in stretch reflexes, ballistic movements, slow movements and movement timing. (Rothwell pp. 359-365, Figs. 10.21, 10.22)

12. What is meant by the term “motor learning”? Give examples. Describe two experimental paradigms implicating the cerebellum in motor learning. (Rothwell pp. 351-355, 366-368, Figs. 10.18, 10.23)

13. Summarize the old view and new view of cerebro-cerebellar function based on knowledge of connections revealed with the use of neurotropic viruses as tracers. Explain how the neurotropic virus technique works. (Strick review, pp 413-416, Figures 1-2).

14. Summarize the organization of output channels from the dentate nucleus (Strick review, pp 416-419, Figures 4-5).

15. Describe the main features of the macro-architecture of cerebro-cerebellar loops? (Strick review, pp 420-421, Figure 7).

16. What is the full extent of cerebellar influence over the cerebral cortex and how is this different from older views? Explain an argument that has been raised by Glickstein and Doron (2008) suggesting that regions of prefrontal cortex targeted by dentate are actually concerned with eye movements. What is the cerebro-limbic circuit? (Strick review, pp 422-423).

17. Summarize the functional evidence supporting a cognitive role of the cerebellum and the pitfalls and weaknesses of this evidence (Strick review, pp 423-425).

18. Explain three perspectives on how the cerebellum might influence cognition and affect. (Strick review, pp 425-426).

**Topic X: Basal Ganglia**

Research paper
Liliana Garcia, Giampaolo D'Alessandro, Bernard Bioulac and Constance Hammond (2005) High-frequency stimulation in Parkinson's disease: more or less? Trends in Neurosciences 28: 209-216.

Objectives
1. Identify the structures that comprise the basal ganglia and diagram their intrinsic connections, inputs and outputs. (Rothwell pp 373-379, Figs 11.1, 11.2)

2. Summarize what has been learned about basal ganglia somatotopic organization and function from unit recording in the basal ganglia nuclei. Use information flow through the motor circuit of the basal ganglia, thalamus and cortex to illustrate somatotopic segregation of information. (Rothwell, pp. 379-381, 383, Figs 11.4, 11.6)

3. One hypothesis of basal ganglia function is that it disinhibits other areas of the motor system and "allows" movements to occur. Discuss the evidence supporting this point of view. How does the hypothesis of Mink and Thach differ from this hypothesis? (Rothwell pp. 384-388, Figs 11.8, 11.9) Austin

4. Summarize what is known about the activity of basal ganglia neurons during limb movements in relation to a third hypothesis of basal ganglia function. (Rothwell pp. 388-390)

5. What are the classic symptoms of Parkinson's disease? Briefly describe the nature of these symptoms? (Rothwell pp. 398-400). What is MPTP and explain its significance to Parkinson's disease? (Rothwell 395)

6. Explain the alterations in neuronal activity in the MPTP model of Parkinson's disease and how it might be corrected (Rothwell Fig. 11.14)

7. Explain the effects of reversible pallidal lesions produced by cooling (Rothwell pp 393-395, Fig. 11.13)

8. What is Huntington's disease? What is the genetic defect? Explain the potential neural circuit dysfunction in Huntington's chorea using diagrams like those in Fig. 11.14 of Rothwell. This will require speculation. (Rothwell, pp 410-411)

9. Briefly explain the possible mechanisms of rigidity in Parkinson's disease. (Rothwell pp. 401-402; Fig. 11.17)

10. Briefly explain the possible mechanisms of tremor in Parkinson's disease. (Rothwell pp. 402-405; Fig. 11.18)

11. Briefly explain the possible mechanisms of akinesia/bradykinesia in Parkinson's disease. (Rothwell pp. 405-410; Fig. 11.20)

12. Briefly describe the method of deep brain stimulation (DBS) and evidence supporting the "Less Hypothesis" of its mechanism of action. (Garcia et al., 2005; pp 209-212, Figs 1 and 2).

13. Explain the "More Hypothesis" mechanism of action of DBS and evidence supporting it (Garcia et al., 2005; pp 212-214, Fig. 4).

14. Explain the hypothesis that a high frequency stimulation of the subthalamic nucleus restores a prokinetic rhythm of firing with oscillations in the 70 Hz range (Garcia et al., 2005; pp 214-215).