Medical Neuroscience | Tutorial Notes

Modulation of Movement by the Cerebellum

MAP TO NEUROSCIENCE CORE CONCEPTS[1]

NCC1. The brain is the body's most complex organ.

NCC3. Genetically determined circuits are the foundation of the nervous system.

NCC4. Life experiences change the nervous system.

LEARNING OBJECTIVES

After study of the assigned learning materials, the student will:

1. Identify and discuss the basic parts of the cerebellum.
2. Characterize in general terms the major functions performed by the cerebellum.
3. Sketch the major inputs and output of the cerebellum.
4. Describe the circuitry involved in the main excitatory loop and inhibitory side-loop through the cerebellum.
5. Discuss the means by which circuitry in the cerebellum aid to increase the success of volitional motor performance.
6. Describe the clinical signs and symptoms associated with cerebellar damage.

TUTORIAL OUTLINE

I. Introduction

  A. although the cerebellum's elegant neural circuitry has been known for nearly a century, a general understanding of function has been slow in coming

    1. it is a massive brain structure (~10% of entire brain) and it contains ~50% of all the neurons in the entire CNS

    2. nevertheless, symptoms of cerebellar damage (e.g., ataxia; see below) are relatively minor

  B. general sense of cerebellar function

    1. *"error correction"* = integrates executive commands with sensory feedback regarding the external and internal environment for the moment-to-moment adjustment of behavior

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[1] Visit **BrainFacts.org** for *Neuroscience Core Concepts* (©2012 Society for Neuroscience) that offer fundamental principles about the brain and nervous system, the most complex living structure known in the universe.

2. learns new behavioral programs (both motor and non-motor behaviors) when errors are numerous
3. coordinates ongoing multi-jointed movements (motor agility)
4. assists the premotor cortex in planning movements when motor learning has been stored and errors are few
5. coordinates ongoing sequential cognitive processes (cognitive agility)

II. The circuitry

A. Overview of the basic components of the cerebellum

1. overall organization (see **Figure 19.1A-C**[2] and **Table 19.1**)

a. major parts

(i) cerebellar cortex

(ii) deep cerebellar nuclei

(iii) cerebellar peduncles

b. three functional divisions (see **Figure 19.4** and **19.5**)

(i) **spinocerebellum**: receives proprioceptive information from muscle spindles, as well as visual and auditory information

(ii) **cerebrocerebellum** (also called the neocerebellum): mainly related to processing in the cerebral cortex

(iii) **vestibulocerebellum** (also called the flocculonodular lobe): receives and sends input to the vestibular nuclei; closely related to vestibular function

c. two levels of processing

(i) **cerebellar cortex**

(ii) **deep cerebellar nuclei** (the dentate nucleus, the interposed nuclei, and the fastigial nucleus)

B. a closer look at cerebellar circuits

1. functional overview of inputs to the cerebellum

a. "executive" signals relayed from widespread parts of cerebral cortex in the frontal and parietal lobes via the **pontine nuclei**: *conveys the commands for (motor) behavior*

b. "feedback" signals from proprioceptive systems: *conveys sensory information about ongoing behavior*

c. "learning" signals derived from the **inferior olivary nucleus** of the medulla: *facilitates adaptation (error correction)*

2. anatomical overview of inputs to the cerebellum (see **Figure 19.3**)

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[2] Figure references to Purves et al., *Neuroscience, 5th Ed.*, Sinauer Assoc., Inc., 2012. [click here]

a. two types of afferent projections (see **Figure 19.9** and **19.10**)

(i) **mossy fibers**

- quantitatively, the most important source of input
- all inputs from brainstem and spinal cord, except inputs from the inferior olivary nucleus

(ii) **climbing fibers**

- distinct inputs from the **inferior olivary nucleus**
- modulate the output of the cerebellar cortex

b. both types of afferents *terminate in the cerebellar cortex and the deep cerebellar nuclei*

3. inputs reflect tripartite organization of cerebellum

a. *spinocerebellum*

(i) proprioceptive information about *ipsilateral* body, mainly signals related to muscle spindles (see *Lab Guide*, **Appendix 1**)

(ii) for lower extremities, relayed via second order neurons in **dorsal nucleus of Clark** (thoracic cord)

(iii) for upper extremities, relayed via second order neurons in the **external cuneate nucleus**

(iv) also receives visual and auditory signals from brainstem processing centers

(v) axons of second order neurons reach cerebellum as mossy fibers through the *ipsilateral* inferior cerebellar peduncle

b. *cerebrocerebellum*

(i) receives highly processed **sensory information** (somatic sensory, visual, auditory) and **executive commands** from widespread regions of the *contralateral* cerebral cortex

(ii) relayed via corticobulbar fibers that terminate in the ipsilateral pontine nuclei in the base of the pons

(iii) axons of pontine neurons *decussate* and project to the cerebellar cortex as mossy fibers through the middle cerebellar peduncle

c. *vestibulocerebellum*

(i) information about the **position** and **movements of the head**

(ii) inputs come mainly from **vestibular nuclei** in the brainstem

(iii) axons of second order neurons reach cerebellum as mossy fibers through the *ipsilateral* inferior cerebellar peduncle

4. this arrangement of inputs means that *the cerebellar hemisphere is concerned with the ipsilateral side of the body*

5. cerebellar processing

   a. organization of the cerebellar cortex

      (i) principal neurons: **Purkinje cells**

      - provides output from cerebellar cortex to deep cerebellar nuclei (and vestibular nuclei)
      - *inhibitory*; use GABA as neurotransmitter
      - high level of tonic activity at rest that is modulated during movements (see **Figure 19.11**)

      (ii) interneurons

      - **granule cells**
        - receive mossy fiber input
        - give rise to **parallel fibers** that synapse on Purkinje cells (and other interneurons)
        - excitatory (glutamatergic)
      - other inhibitory interneurons are present (stellate cells, basket cells, Golgi cells)

   b. flow of information through cerebellum circuits: *processing through a main excitatory loop and an inhibitory side-loop*

      (i) mossy fiber inputs

      - mossy fibers send a collateral to neurons in the deep nuclei of the cerebellum (= main excitatory loop)
      - also synapse in cortical glomeruli (encapsulated, specialized synaptic complexes) containing dendrites of granule cells and other interneurons
      - provide the information about the executive command and the feedback sensory cues that are fundamental to cerebellar processing

      (ii) climbing fiber inputs

      - make powerful synaptic contacts on the proximal dendrites of Purkinje cells (hence, “climbing”)
      - climbing fibers also send a collateral to neurons in the deep nuclei of the cerebellum
      - provide the “contextual” information to the cerebellum (especially the Purkinje cells) for learning

      (iii) granule cells drive an elongated “beam” of Purkinje cells via their lengthy parallel fibers

(iv) Purkinje cells integrate parallel fiber and climbing fiber inputs and send inhibitory projections to the deep cerebellar nuclei (= inhibitory side-loop)

- lateral parts of cerebellar cortex (mainly cerebrocerebellum) projects to the **dentate nucleus**
- paramedian parts of the cerebellar cortex (lateral spino-cerebellum) project to the **interposed nuclei**
- medial cerebellar cortex (medial spino-cerebellum) project to **fastigial nucleus**
- and flocculonodular lobe (vestibulocerebellum) projects directly to vestibular nuclei

(v) thus, deep cerebellar nuclei are *excited* by mossy (and climbing) fiber inputs and *inhibited* by Purkinje cell inputs

(vi) strength of Purkinje cell output to deep cerebellar nuclei is subject to use-dependent modification (plasticity):

- pairing of climbing fiber activation and parallel fiber activity leads to a *depression* of Purkinje cell responses to parallel fibers
- this means that activation of this inhibitory side-loop may be *weakened* and, therefore, the output for the deep cerebellar nuclei may be *strengthened*
- this is the cellular basis of learning in the cerebellum

C. outputs of cerebellar (see **Figures 19.6-8**): *arise from the deep cerebellar nuclei*

1. ascending output is directed toward thalamocortical circuits (see **Figure 19.6**)

a. dentate nucleus (and interposed nuclei)

(i) sends its axons out of the cerebellum through the superior cerebellar peduncle, which then *decussate*

(ii) most dentate axons project directly to the contralateral **ventral lateral complex of the thalamus**

- influence thalamocortical circuits concerned with motor control and cognition in the motor cortex and prefrontal cortex, respectively
- adjusts the planning and mental rehearsal of complex motor movements and other cognitive tasks involving the sequencing of multiple steps

2. "descending" output is directed toward brainstem circuits (see **Figure 19.7**)

a. fastigial nuclei

(i) project to medial upper motor neuron systems in the brainstem reticular formation

(ii) output adjusts the control of posture, balance, gaze (i.e., typical "medial" functions)

b. each deep cerebellar nucleus also projects to the red nucleus, which in turn provides feedback signals to the source of the learning signals, the inferior olivary nucleus (see **Figure 19.6**; see also **Figure 19.3**)

3. vestibulocerebellum (an exceptional division of the cerebellum)

a. as noted above, Purkinje cells in the flocculonodular lobe project directly to vestibular nuclei in the brainstem

b. vestibular nuclei, as you know, then project to lower motor circuits that govern eye movements and posture (see **Figure 19.7**)

III. Cerebellar function

A. *coordination of ongoing, **multi-jointed** movement* (error correction)

1. control of stability

2. actively damp oscillations

B. *learning of new movements*

1. adaptation of hand-eye coordination (Friday PM's session)

2. learning can be remarkably specific

a. type of movements

b. body parts involved

C. *initiation and planning of movements*

D. *cognition*

1. timing judgements

2. sequencing of multiple steps (e.g., pegboard puzzle)

3. acquisition of mental skills that require repeated practice (cognitive agility)

IV. Cerebellar lesions: deficits in coordinating movements

A. because of the arrangement of inputs and outputs of the cerebellum, clinical (motor) signs of cerebellar lesions are *always **ipsilateral*** to the lesion

B. cerebellar **ataxia**: incoordination of ongoing movements

1. intentional tremor: tremor during movement

2. dysmetria: instability of a limb as it approaches a target (overshooting or undershooting)

3. rapid, repetitive movements impaired

4. decomposition of movements

C. cognitive deficits are possible (impairments of cognitive agility)

STUDY QUESTIONS

Q1. Which of the following events are critical for motor learning in the cerebellum?

A. insertion of new AMPA receptors in the dendritic spines of Purkinje neurons
B. insertion of new GABA receptors in the dendritic spines of Purkinje neurons
C. removal of GABA receptors from the dendritic spines of Purkinje neurons
D. activation of climbing fibers
E. induction of long-term potentiation at the parallel fiber-Purkinje neuron synapse

Q2. Which of the following signs and symptoms is indicative of dysfunction in cerebellar modulation of movement?

A. hyporeflexia
B. hypereflexia
C. rigidity
D. flaccidity
E. ataxia
F. atonia
G. spasticity