Neural Integrators, particularly the Oculomotor Neural Integrator

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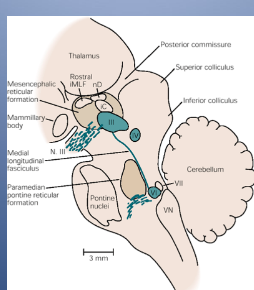
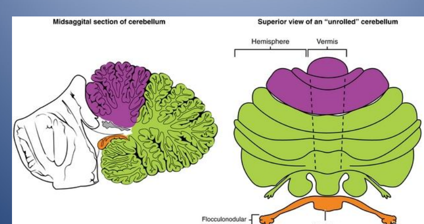
Neural Integrators, particularly the Oculomotor Neural Integrator

- (i) Cerebellum structure and function in motor learning;
- (ii) An alternative view from Alain Berthoz;
- (iii) The cerebellum and primitive reflexes;
- (iv) The Neural Integrator, view from Dick Bruenech.
- (v) Conclusions

Cerebellum position



Cerebellar Structure



Cerebellar Signatures of Vestibulo-Ocular Reflex Motor Learning

Blazquez PM, Hirata Y, Heiney SA, Green AM, Highstein SM (2003)

Blazquez et al studied the vestibulo-ocular reflex (VOR) as it was is an excellent way to study the possible cerebellar roles in motor learning.

- New VOR gains can be induced (learned) by the wearing of minifying or magnifying lenses, and learning requires the presence of the cerebellum.
- Within the cerebellum the Purkinje cells change their head velocity, head position, eye position and eye velocity sensitivities after learning.

Cerebellar Signatures of Vestibulo-Ocular Reflex Motor Learning (2003)

P.M. Blazquez, Y. Hirata, S. A. Heiney, A. M. Green, S. M. Highstein

- These combined changes at the Purkinje cell level contribute to a net modulation that is appropriate to support the new VOR gains.
- The mechanisms involved in VOR adaptation require changes in head-related and oculomotor-related sensitivities are necessary for maintenance of VOR performance over the full range of head movement.

Cerebellar Signatures of Vestibulo-Ocular Reflex Motor Learning (2003)

P.M. Blazquez, Y. Hirata, S. A. Heiney, A. M. Green, S. M. Highstein

- Importantly, the changes in the eye position parameter suggest the involvement of the neuronal integrator pathways in VOR learning.
- Purkinje cells in Flocculus (FL) show changes in both eye and head signals, indicating that FL is an essential node for reflex performance after VOR adaptation.

The Vestibulo-Ocular Reflex as a model for motor learning: what is the role of the cerebellum?

Blazquez PM, Hirata Y, Highstein SM (2004)

- Motor systems are under a continuous process to maintain behaviour throughout developmental changes and disease, a process called motor learning.
- The main targets for motor learning are the cerebellum and it's target neurons in the brainstem.

The Vestibulo-Ocular Reflex as a model for motor learning: what is the role of the cerebellum?
Blazquez PM, Hirata Y, Highstein SM (2004)

- Learning can be divided into

(i) acutely acquired over a few hours, and
(ii) chronically acquired over longer periods.
Both chronic and motor learning have three phases; acquisition, consolidation and retention.

- The cerebellum has a clear role in retention, but this paper, working with mice, showed it has a part in acquisition of motor learning too.

Cerebellar function: Coordination, learning or timing?
M. D. Mauk, J. F. Medina, W. L. Nores, T. Ohyama. (2000)

- The cerebellum is associated with motor coordination through learning with timing. Motor learning and timing are neither mutually exclusive nor even separate mechanisms.
- The cerebellar functions of coordination through sensorimotor integration, and of motor learning, are also intertwined.
- To alter movements properly requires the ability not only to adjust outputs, but to adjust output with the proper delays relative to the inputs.

Cerebellar function: Coordination, learning or timing?
M. D. Mauk, J. F. Medina, W. L. Nores, T. Ohyama. (2000)

Cerebellar contributions to saccades

- As well as studying the VOR, studying saccades can show the interrelations between sensorimotor coordination, learning and timing in the cerebellar Purkinje cell responses.
- The data on saccade systems, adaptation of the vestibulo-ocular reflex and eyelid conditioning are all consistent with the view that a basic property of cerebellar processing is to use temporally specific learning to improve motor performance.

New Encyclopedia of Neuroscience
M Goldman, A Compte, X Wang (2007)

This is the ‘How does it happen at neuron level?’ section.

Time integration involves two basic operations.

- (i) during stimulation, a neural integrator needs to additively increase or decrease its output in response to excitatory or inhibitory input signals, respectively.
- (ii) a neural integrator should have a memory capability to store the running total of inputs.

…but…not quite the whole story…

New Encyclopedia of Neuroscience
M Goldman, A Compte, X Wang (2007)

- As there is leakage of neuronal currents out of the membrane which tends to make a neuron forgetful.
- As a result, the duration over which a neuron can temporally sum incoming synaptic potentials is limited by its membrane time constant.
- To achieve long integration times, most models therefore incorporate tuned positive feedback that serves to offset the intrinsic leakage of membrane currents.

New Encyclopedia of Neuroscience
M Goldman, A Compte, X Wang (2007)

(a) Network integrator models: rate code

- In some neural integrator networks two opposing populations of cells are responsible for accumulating the input.
- Inputs to these populations are typically arranged in a "push-pull" manner such that, when one population is excited ("pushed") by the external input, the other population is inhibited ("pulled").
- The oculomotor integrator is an example of such a push-pull organisation.

New Encyclopedia of Neuroscience
M Goldman, A Compte, X Wang (2007)

- In the oculomotor neural integrator, external commands that encode the velocity of an intended eye movement are sent through excitatory connections to one cell population and through inhibitory connections to the opposing population.
- The network integrates these inputs into sustained differences in firing rate between the two populations.

New Encyclopedia of Neuroscience
M Goldman, A Compte, X Wang (2007)

(b) Network integrator models: location code

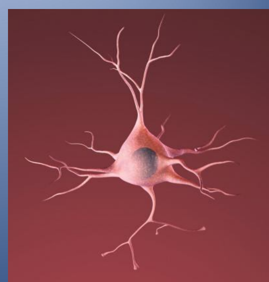
- Neural networks in which the encoded feature is specified by the peak location of the network activity profile (location code).
- The head-direction system is a good example of having neural integrators using a location code.
- When an animal turns its head, the angular velocity signal carried by vestibular inputs is integrated over time by head-direction cells into a positional signal, and the latter is sustained internally when the animal keeps the head directions fixed.

New Encyclopedia of Neuroscience

M Goldman, A Compte, X Wang (2007)

(c) Single-neuron integrator models

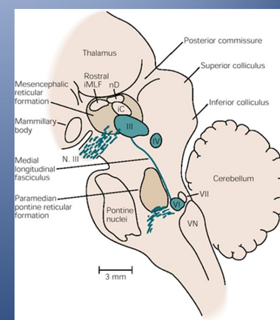
Neural integrators can also reside in the internal biochemical machinery of a single neuron.



Learning-Induced Plasticity in Deep Cerebellar Nucleus.

Obyama T, Nores W, Medina J, Rieusch F, Mauk (2006)

- Eyelid conditioning and adaptation of the VOR are both forms of cerebellar motor learning that induce plasticity at two sites,
- ie in the cerebellum and also in their target neurons in the deep cerebellar/vestibular nuclei.



(ii) An alternative way to look at neural integration

The Brain's Sense of Movement

Berthoz A (2000)

- Rather than considering the neural integrator in terms of a complex combination of multiple signals to integrate their messages,
- Berthoz considered integration in the literal mathematical sense of progression from the derivative of a variable of movement to it's integral;
- ie, of acceleration to velocity,
- or of velocity to position.
- Studying the VOR is a good example to understand how the nervous system manages to handle speed and precision at the same time.

The Brain's Sense of Movement

Berthoz A (2000)

- The vestibular receptors are accelerometers (measuring degrees per sec per sec) that detect movements very rapidly.
- But the command that displaces the eye in its socket necessarily produces a rotation, specified as degrees of angular measure;
- So, although the brain gains from an early, dynamic piece of information, it must transform it by delaying it, to control the position of the eye with respect to the environment: it must be subjected to low-pass filtering, or integration.

The Brain's Sense of Movement
Berthoz A (2000)

- An initial filtering, or first integration (going from acceleration to velocity), is carried out at the level of the receptors themselves.
- They have viscoelastic properties that delay the signals in a variable manner according to the rapidity of the movement.
- But a second integration must take place in the brain to go from velocity to position.

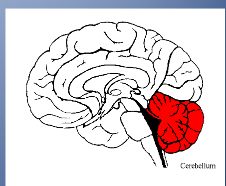
The Brain's Sense of Movement
Berthoz A (2000)

- A part of integration is certainly carried out at the level of the vestibular nuclei, for the response to rotation is delayed at this level.
- If the head is briefly rotated, the fibres of the vestibular receptors respond very quickly, and their response diminishes spontaneously after about 5 to 12 seconds once the head has stopped moving.
- The neurons of the vestibular nuclei do not stop firing until about 20 to 25 seconds afterwards.
- A supplementary integration intervenes between the vestibular nuclei and the movement of the eyes, at the cerebellum.

(iii) The Cerebellum and primitive reflexes
Body Posture
Magnus R 1924

On removal of the cerebellum

- all the primitive reflex responses remained intact,
- the loss of the cerebellum affected the animal's posture, balance and movement.
- None of the primitive reflexes were to be found in, or relayed through, the cerebellum.



A cerebellar model for predictive motor control tested in a brain-based device
J. L. McKinstry, G. M. Edelman, J. L. Krichmar. (2006)

- The cerebellum is critical for accurate adaptive control and motor learning.
- A theory of the cerebellum, consistent with much of the neurophysiological, behavioural, and imaging data regarding motor control, proposed that the cerebellum learned to replace reflexes with a predictive controller.
- This predictive controller produced a correct motor control signal earlier than less adaptive reflex responses.

A cerebellar model for predictive motor control tested in a brain-based device
J. L. McKinstry, G. M. Edelman, J. L. Krichmar. (2006)

Adaptive cerebellar functions that are subject to this type of control include:-

(i) eye – blink conditioning,
(ii) the vestibular – ocular reflex,
(iii) smooth pursuit eye movements,
(iv) saccadic eye movements,
(v) arm movements,
(vi) grip force adjustments.

A cerebellar model for predictive motor control tested in a brain-based device
J. L. McKinstry, G. M. Edelman, J. L. Krichmar. (2006)

- In this model, they incorporated a learning rule in which the synapses onto a Purkinje cell (PC) or onto a cell in the deep cerebellar nuclei (DCN) became eligible for plasticity only after a fixed delay from the onset of suprathreshold presynaptic activity.
- This delayed eligibility trace learning rule was formulated to shape cerebellar responses to anticipate and avoid an impending motor error.

A cerebellar model for predictive motor control tested in a brain-based device
J. L. McKinstry, G. M. Edelman, J. L. Krichmar. (2006)

- The results of this study suggested that a delayed eligibility trace rule may account for the predictive ability of the cerebellum in motor control tasks under real-world conditions.
- Their findings provided additional support for the theory that the cerebellum can learn to replace an arbitrary reflexive neural control system with a more adaptive, predictive controller or “preflex”.

(iv) Bruenech R Course Notes
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When we look at the neuro-anatomical organisation of the oculomotor system we have neurons with specialist sensitivities eg head position, eye velocity etc, at each level.

Subnuclear
EOM
EOM nuclei
Supranuclear
Cortical - Sup Colliculus, Cerebellum, Vestibular Apparatus, FEF, PEF, MT/MST.

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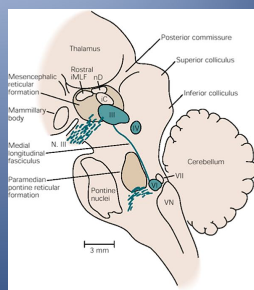
Superior Colliculus,
Cerebellum,
Vestibular Apparatus,



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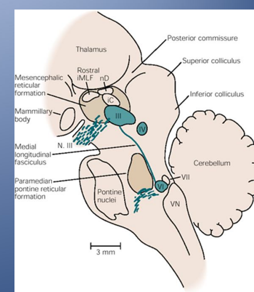
- FEF, Frontal Eye Fields, control of voluntary eye movements.
- PEF, Parietal Eye Fields, voluntary and reflexive saccades.
- MT, Medial Temporal area, detection of movement.
- MST, Medial Superior Temporal area, computes optical flow.



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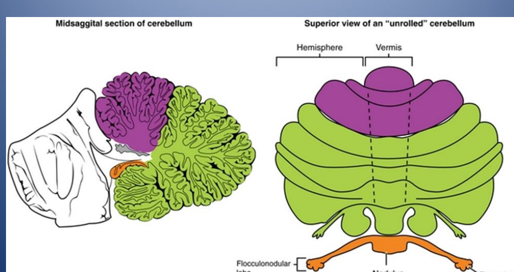
Where does this happen in the cerebellum?



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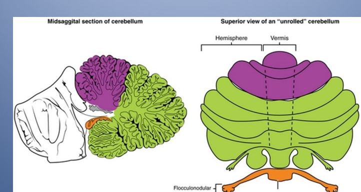

The cerebro-cerebellar pathway to the cerebellar hemispheres receives cortical input from all cortical levels, including the visual cortex.

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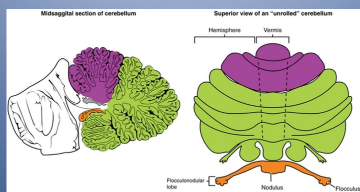

The Vestibulo-cerebellar pathway to the Flocculus receives vestibular input from all the SCCs,
with the efferent fibres from the Flocculus going to the vestibular nucei and motor neurons serving the EOM.

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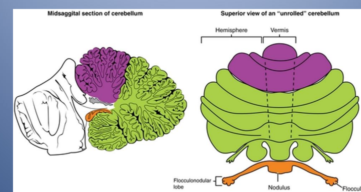

The Ocular proprioception, and the spino-cerebellar pathway somatic proprioceptive information from the proprioceptors in the somatic muscles, are received in the vermis of the cerebellum.

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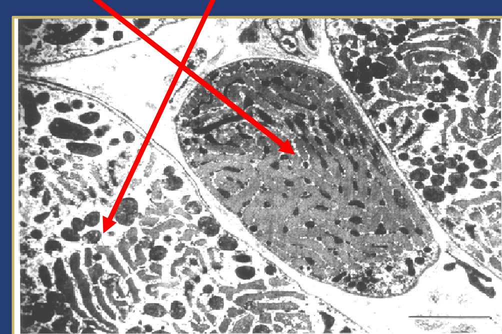
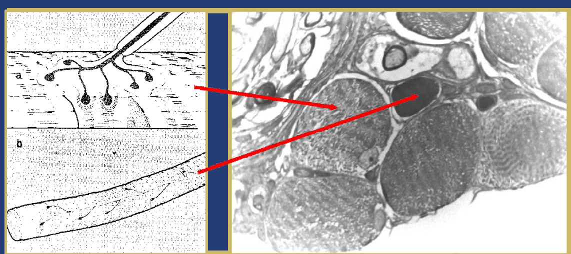
- Ocular proprioception comes from the innervated myotendinous cylinders (IMCs) of the distal tendons of the EOM giving information on eye position,
- and the ciliary body smooth muscle giving information on the state of the accommodation system.

Felderstuktur and Fibrillenstruktur fibres in human extraocular muscles



Bruenech et al. (2003) Motor units in human extraocular muscles

Felderstuktur and Fibrillenstruktur fibres in human extraocular muscles

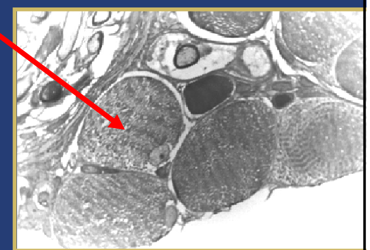


Bruenech et al. (2003) Motor units in human extraocular muscles

Muscle fibres in human extraocular muscles

FIBRILLENSTRUKTUR—STRIATED MUSCLE

- Fast, twitch
- Large diameter
- Peripheral nuclei
- Abundant sarcoplasm
- Single motor endplate
- Rapid, fast fatigue
- Constitute 80%



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Muscle fibres in human extraocular muscles

FELDERSTRUKTUR—SMOOTH MUSCLE

- Slow, tonic
- Small diameter
- Some central nuclei
- Little sarcoplasm
- Many local terminals
- Slow, slow fatigue
- Constitute 20%

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- We are not born with innervated myotendinous cylinders (IMCs), but learn and develop them during activity in early life.
- The receptors are immature under 5 years old.
- Inactivity early in life will not develop the IMCs.
- Stimulation and movement are key to development of IMCs.

(v) Conclusions

Neural Integrators

- Can take acceleration information and integrate it to velocity at the receptor level, and from velocity to position at a second integration in the brain.
- There is a pause in the pathway for integration to take place.

Cerebellum

- Has a key role in all movement information coordination, together with other supranuclear areas - Cortical - Sup Colliculus, Vestibular Apparatus, FEF, PEF, MT/MST.

Conclusions

Cerebellum

- Achieves motor learning and coordination with relation to position and timing.
- Uses temporally specific learning to improve motor performance.
- Learning in the cerebellum induces plasticity in other sites.
- The cerebellum is the coordinator of proprioceptive information from the body and eyes, together with vestibular input.

Conclusions

- Primitive reflexes are not relayed through the cerebellum,
- but the motor learning from the primitive reflexes, to more complex movement patterns and voluntary control, is mediated through the actions of cerebellar motor learning.
- Predictive controllers are developed in the cerebellum for many movement patterns including:-

Conclusions

(i) eye – blink conditioning,
(ii) the vestibular – ocular reflex,
(iii) smooth pursuit eye movements,
(iv) saccadic eye movements,
(v) arm movements,
(vi) grip force adjustments.

The quality of Cerebellar control of learning of movement and timing

The quality of Cerebellar control of learning of movement and timing

depends upon

The sensitivity and accuracy of ocular proprioception

The quality of Cerebellar control of learning of movement and timing

depends upon

The sensitivity and accuracy of ocular proprioception

which depends upon

The number and maturity of the Innovated Myotendinous Cylinders in the EOM

The quality of Cerebellar control of learning of movement and timing

depends upon

The sensitivity and accuracy of ocular proprioception

which depends upon

The number and maturity of the IMCs in the EOM

which depends upon

The stimulation that was received from motor learning in the first five years of life

The quality of Cerebellar control of learning of movement and timing

depends upon

The sensitivity and accuracy of ocular proprioception

which depends upon

The number and maturity of the IMCs in the EOM

which depends upon

The stimulation that was received from motor learning in the first five years of life

which depends upon

The learning from the primitive reflexes in the first year of life, gaining voluntary control of movements, and developing predictive controllers in the cerebellum

The quality of Cerebellar control of learning of movement and timing

depends upon

The sensitivity and accuracy of ocular proprioception

which depends upon

The number and maturity of the IMCs in the EOM

which depends upon

The stimulation that was received from motor learning in the first five years of life

which depends upon

The learning from the primitive reflexes in the first year of life, voluntary control and predictive controllers

which depends upon

The quality of Cerebellar control of learning of movement and timing

Conclusions

- So, why is it important for us to think about this?
- What affect does it have on our day to day practise?
- How does it affect our thinking about OVT?

- How does motor learning, ocular proprioception, timing, position, spatial understanding etc fit into our OVT?

Conclusions

- How does motor learning, ocular proprioception, timing, position, spatial understanding etc fit into our OVT?

EVERYWHERE!!

Bruenech R Course Notes
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Possible roles for Ocular proprioception?

- Development of Binocular vision,
- Ocular alignment,
- Long term tuning of the efferent signal,
- Hand – eye coordination,
- Understanding of space
- Depth perception,
- Attention span,
- Balance,
- Visual orientation,
- Motion detection, etc, etc.