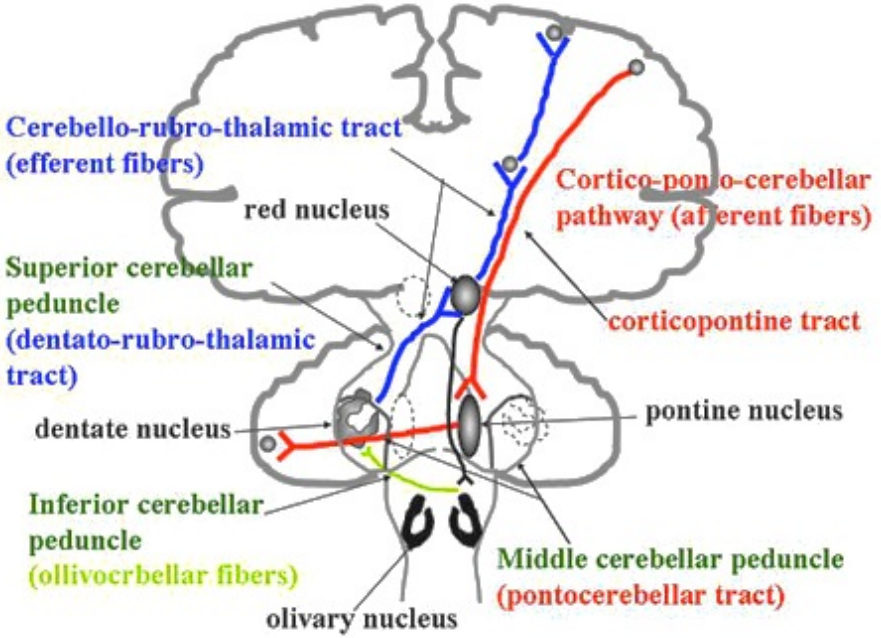
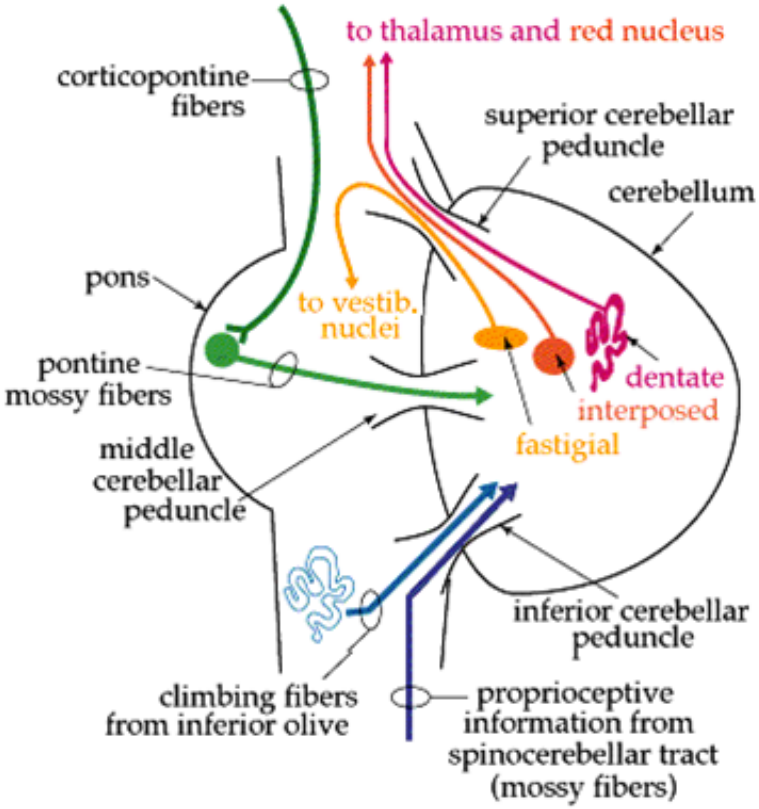
Cerebellar Peduncle Pathways





Virtual Neuroanatomy

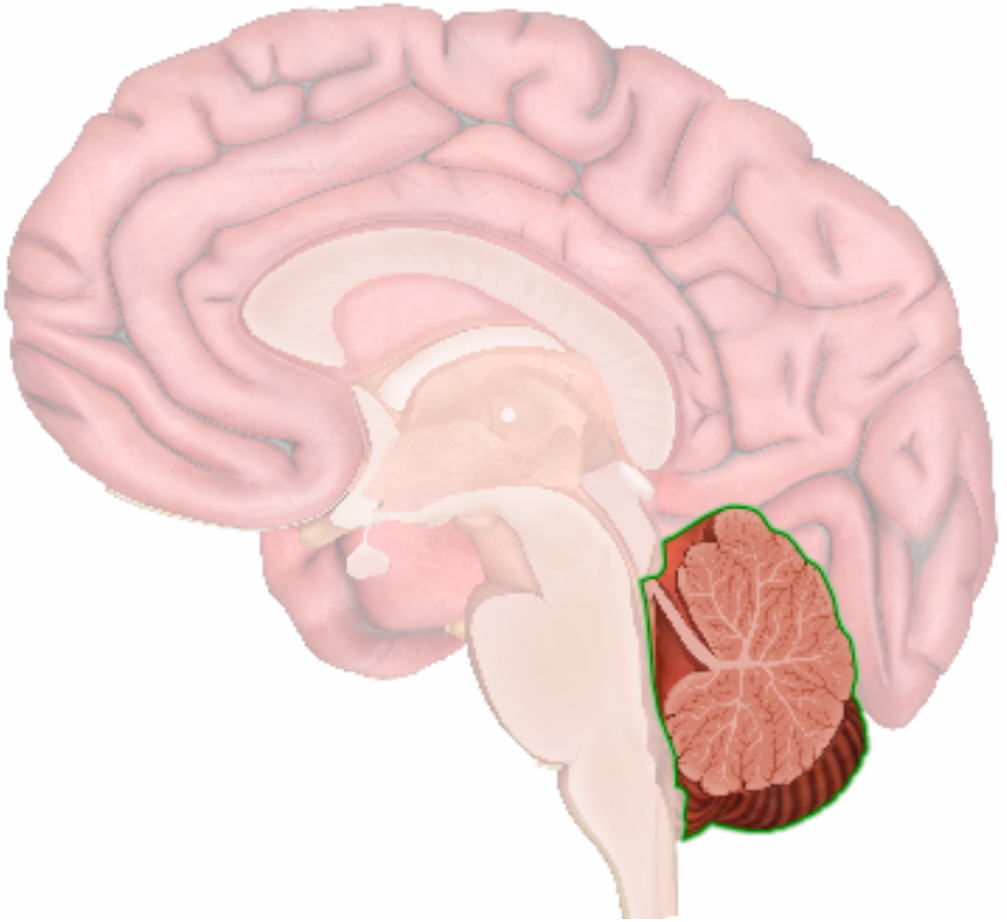
10/14/2014

Outline

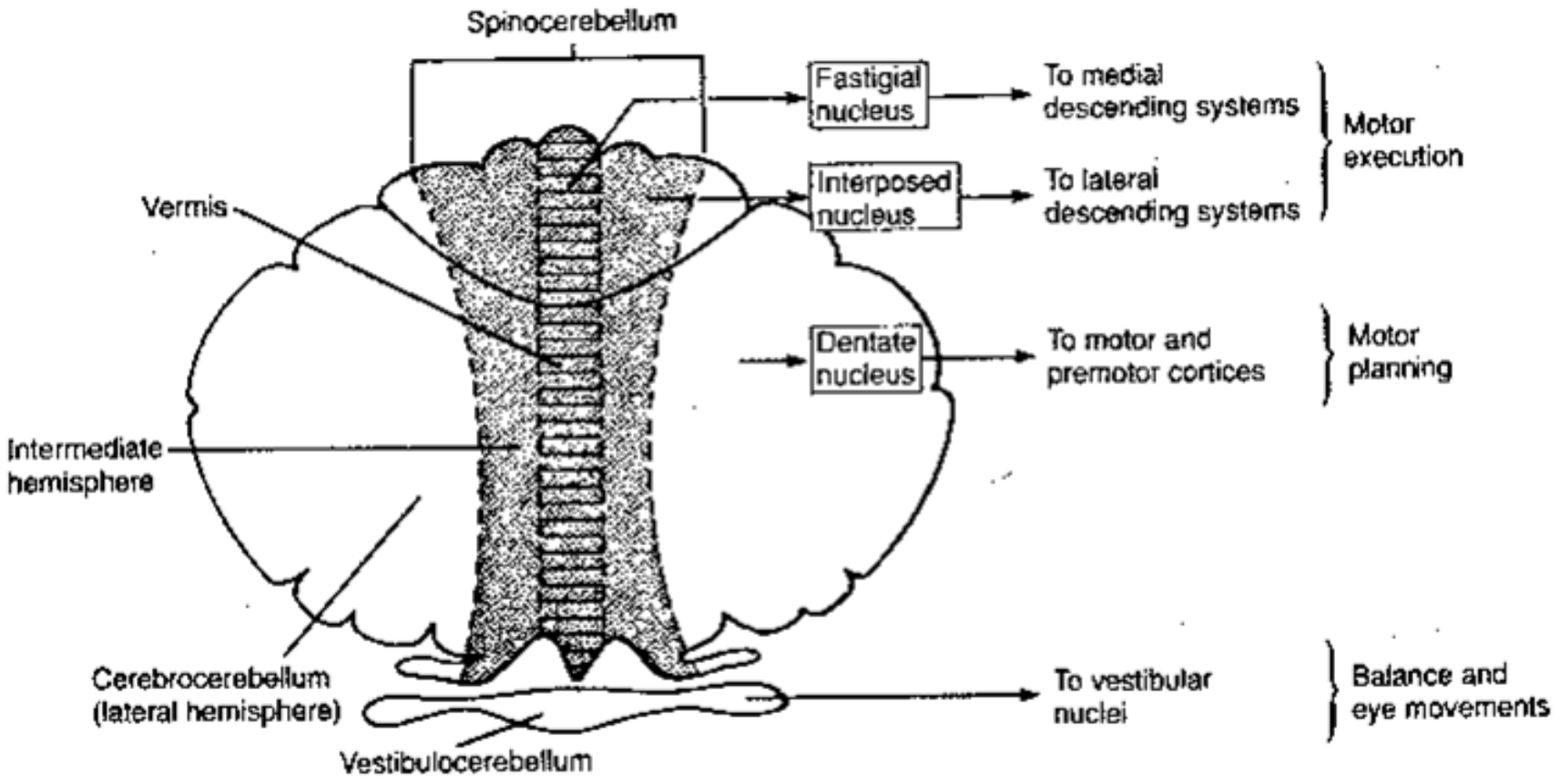
- Overview
- Afferents & Efferents
- Neurophysiology
- Neurochemical Systems
- Physiological Correlates
- Behavioral Correlates
- Clinical Pathologies

Overview

Cerebellum

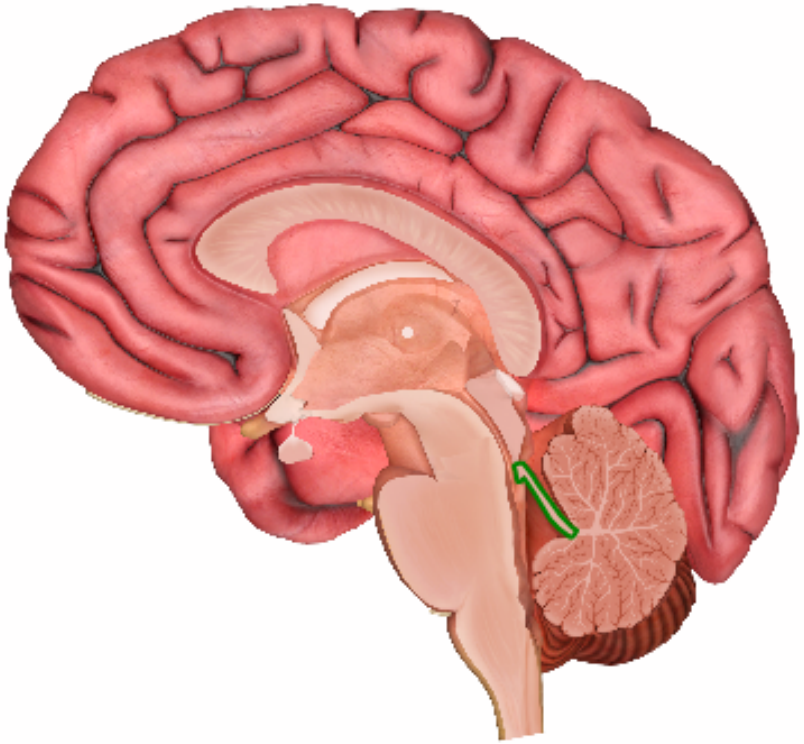


Cerebellar Hemispheres



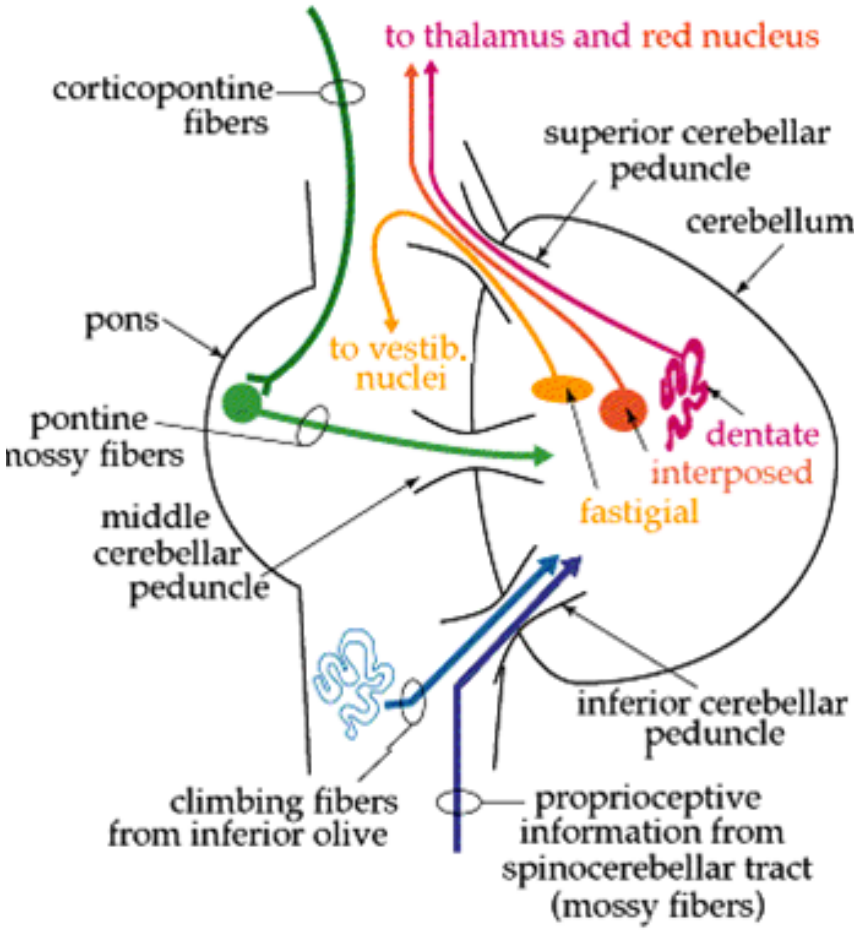
(From Principles of Neural Science, 5th ed)

Cerebellar Peduncles (CP)



Three main fiber bundles that allow **communication** between the **cerebellum** and other regions of the **Central Nervous System**

CP Pathways



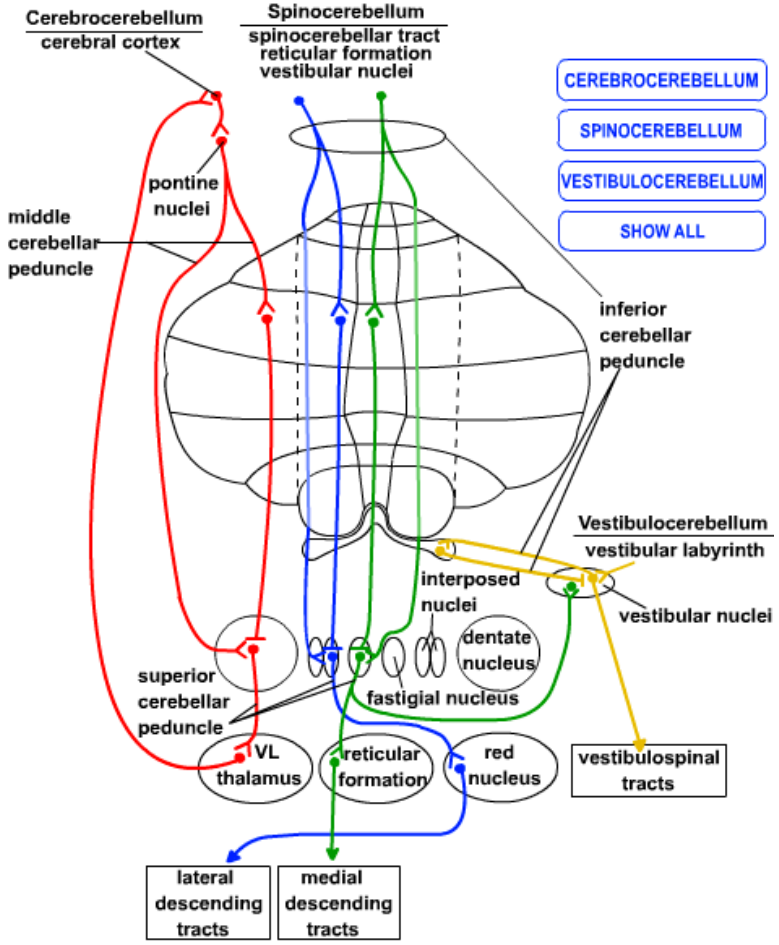
- Integration and analysis of sensory and motor information
- Input
  - **Inferior Peduncle** (ICP)
    - Where am I?
  - **Middle Peduncle** (MCP)
    - Where do I want to be?
    - Association areas
- Output
  - **Superior Peduncle** (SCP)
    - Convey information to cortex

(Retrieved from http://www.eneurosurgery.com/cerebellum.html)

Afferents and Efferents

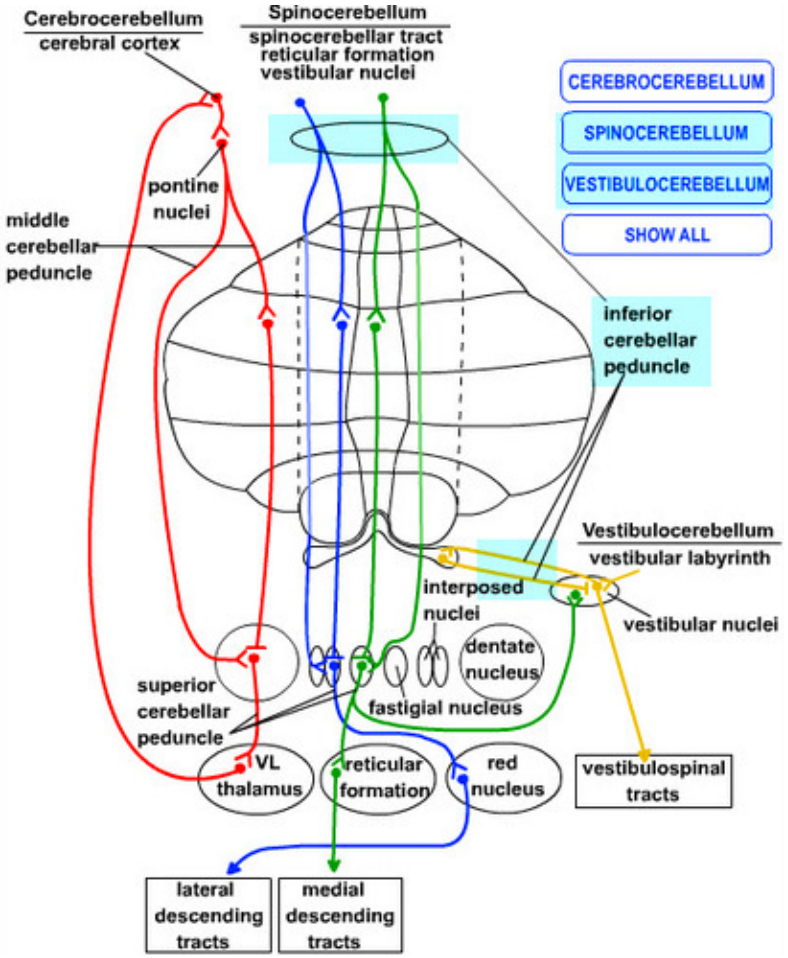
Inputs and Outputs

- Afferent fibers
  - Spinal Cord
  - Cerebral Cortex
  - Vestibular Nerve
- Efferent fibers from deep cerebellar nuclei
  - Thalamus
  - Red Nucleus
  - Reticular Formation
  - Vestibular Nucleus



(From Neuroscience Online, Chapter 5

ICP Pathway



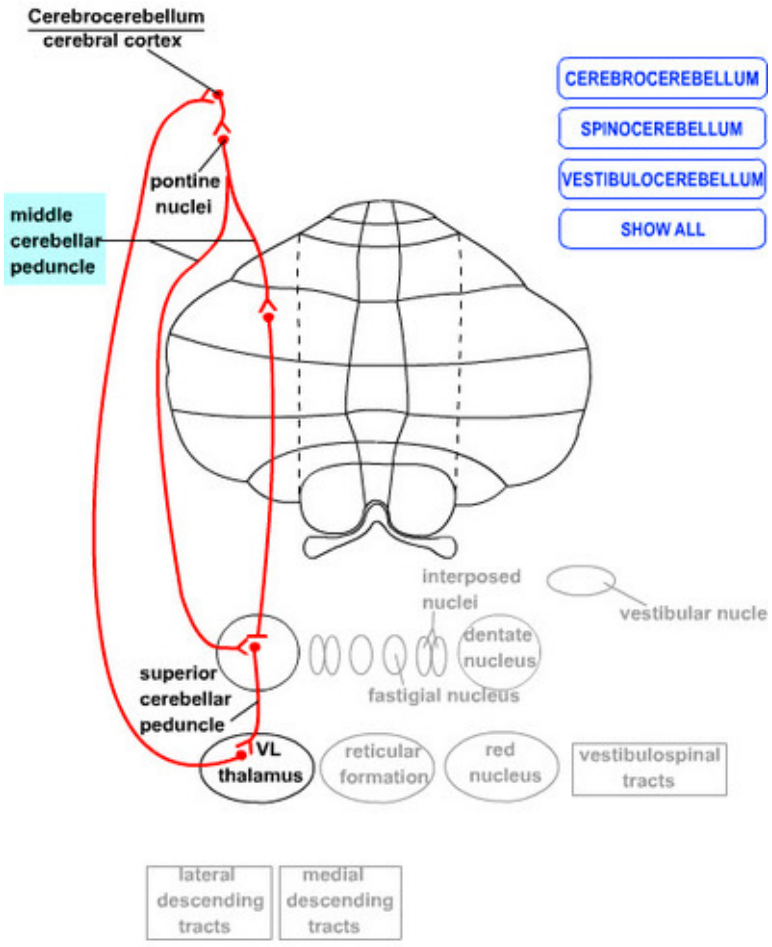
Primarily Afferents

- Spino-cerebellar
- Cuneo-cerebellar
- Vestibulo-cerebellar
- Olivo-cerebellar
- Reticulo-cerebellar

Some Efferents

- Cerebello-vestibular
- Cerebello-reticular

MCP Pathway

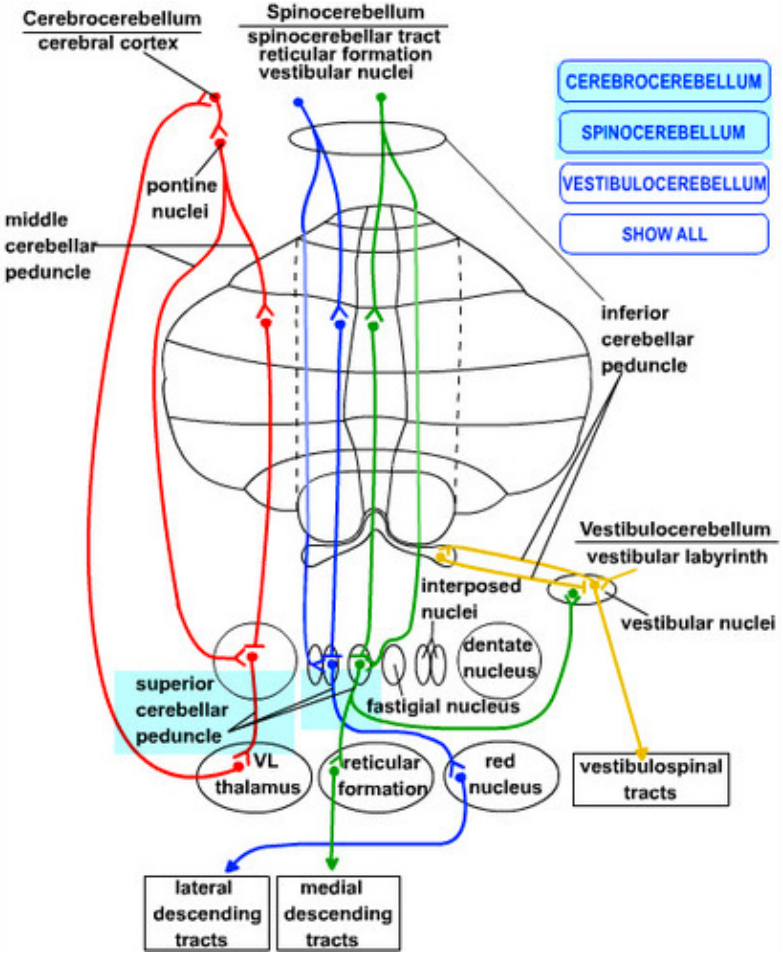


LARGEST OF THE 3 CEREBELLAR PEDENCLES

Exclusive Afferent

Cortico-ponto-cerebellar

SCP Pathway



Primarily Efferent Fibers
(Major Output)

Dento-rubro-thalamic

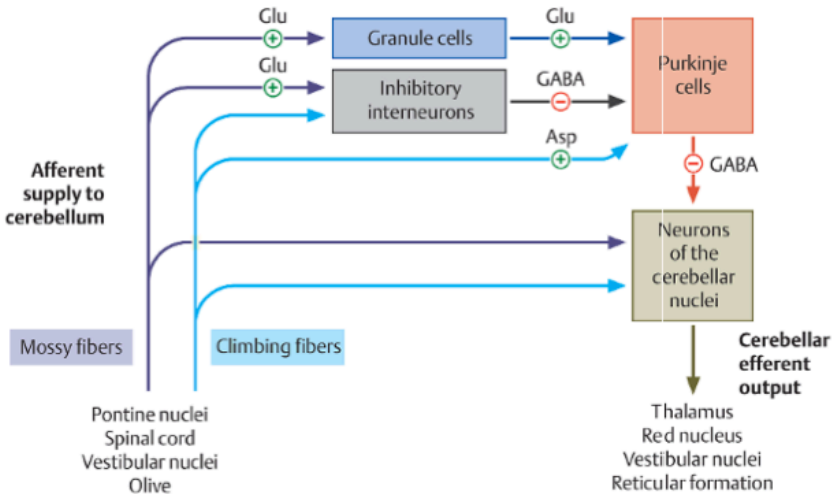
Globose-emboliform-rubral

Some Afferent Fibers

Spino-cerebellar

Neurochemical Systems

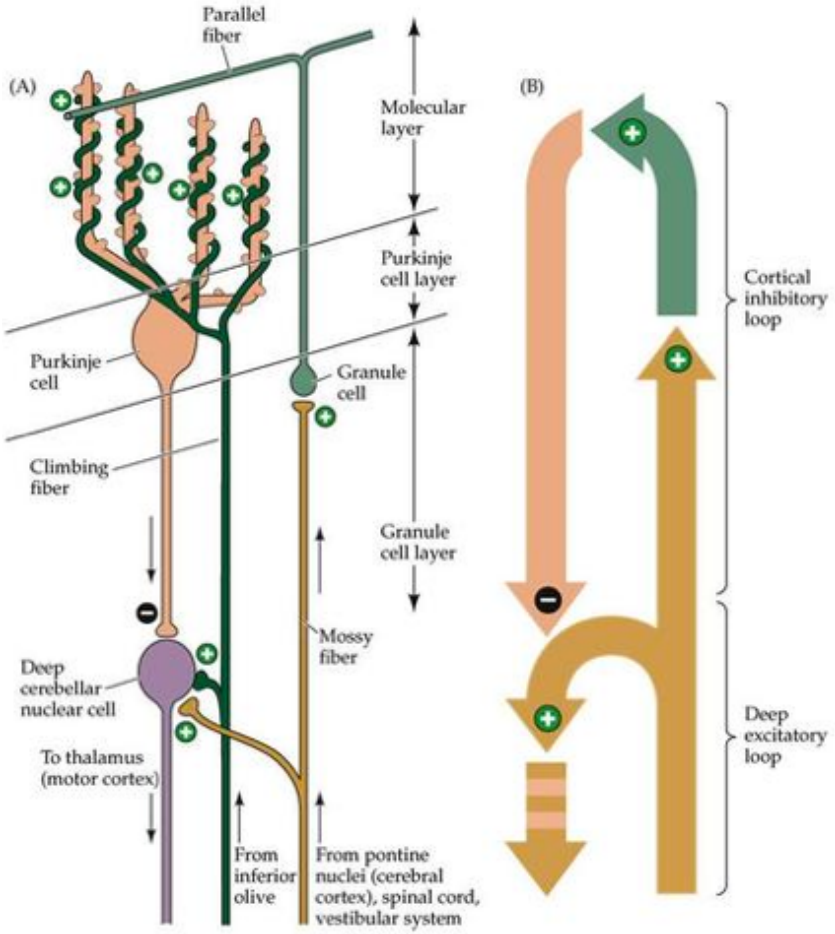
Neurochemical Systems



- Excitatory
  - Glutamate
    - Mossy Fibers
    - DCN (contralateral)
  - Aspartate
    - Climbing Fibers
- Inhibitory
  - GABA
    - Purkinje
  - Glycinergic
    - DCN (ipsilateral)

(From Duus' Topical Diagnosis in Neurology, 5th ed)

Cerebellar Circuits

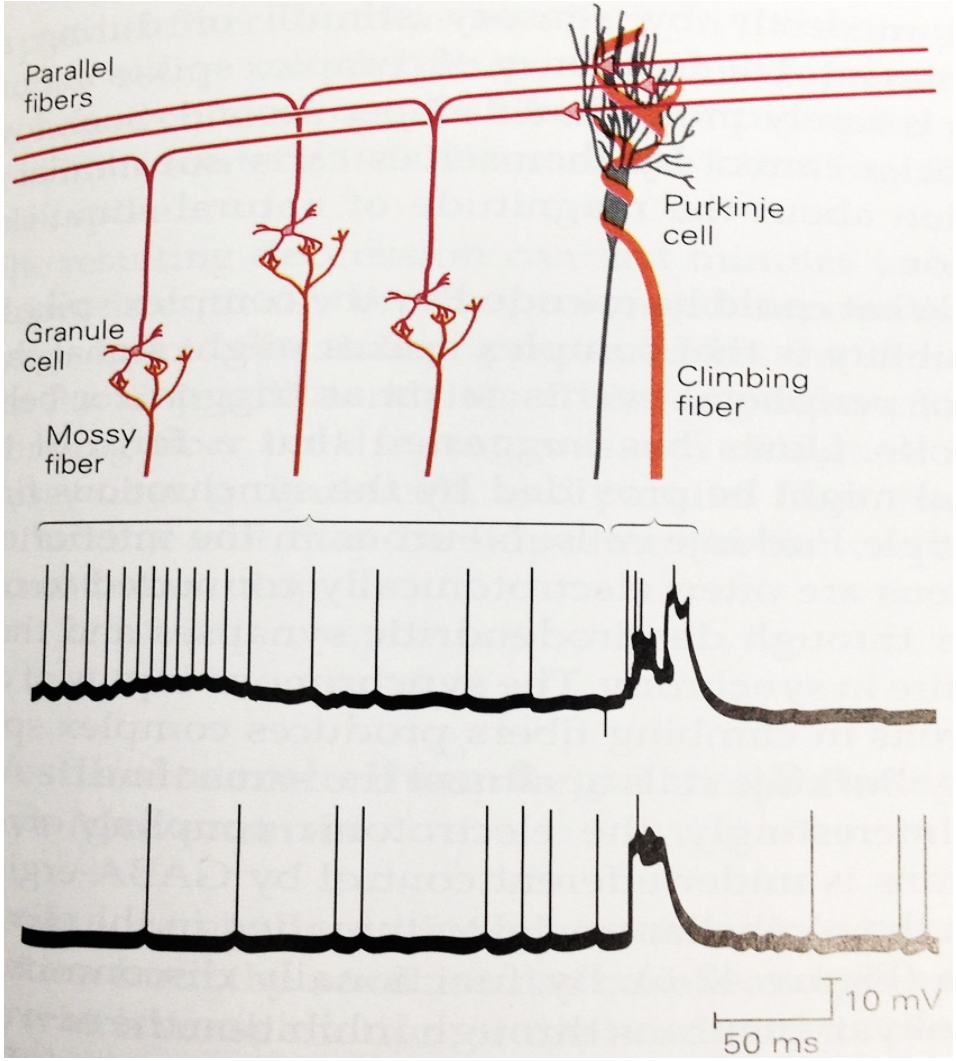


- Three Cerebellar Layers
  - Molecular
  - Purkinje cell
  - Granule cell

(From Neuroscience, 4th Ed)

Neurophysiology

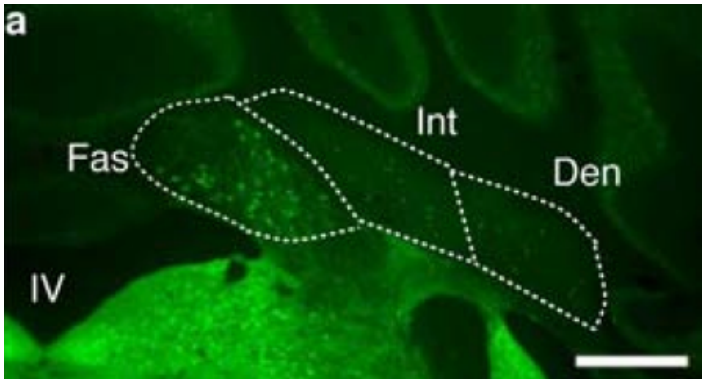
Simple vs. Complex Patterns of Firing



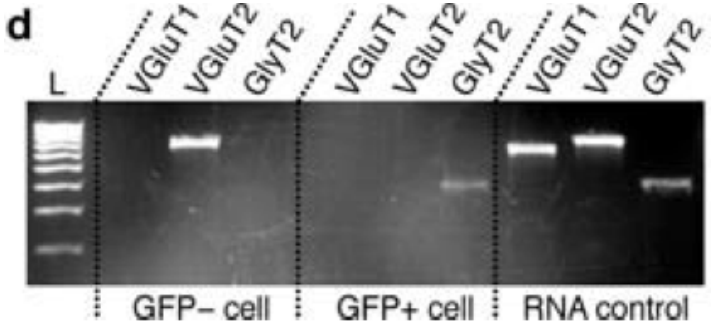
(From Principles of Neural Science, 5th ed)

- Mossy – Purkinje
  - Brief EPSP
- Climbing – Purkinje
  - Prolonged depolarization

Physiological Characteristics Output

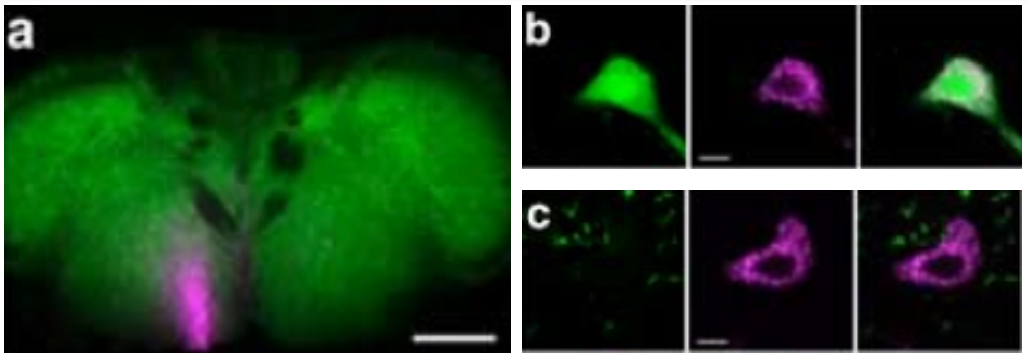


Identification of Glycinergic neurons in fastigial nuclei

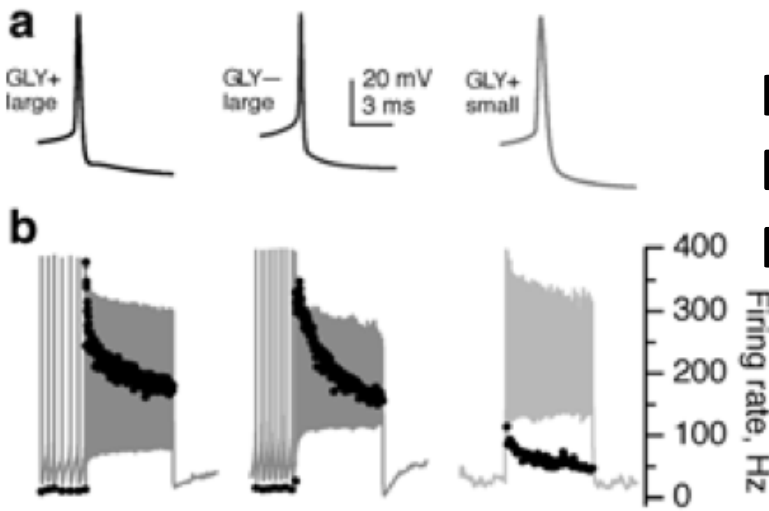


Most fastigial neurons are Glu, however some are Gly

(From Bagnall et al. 2009)



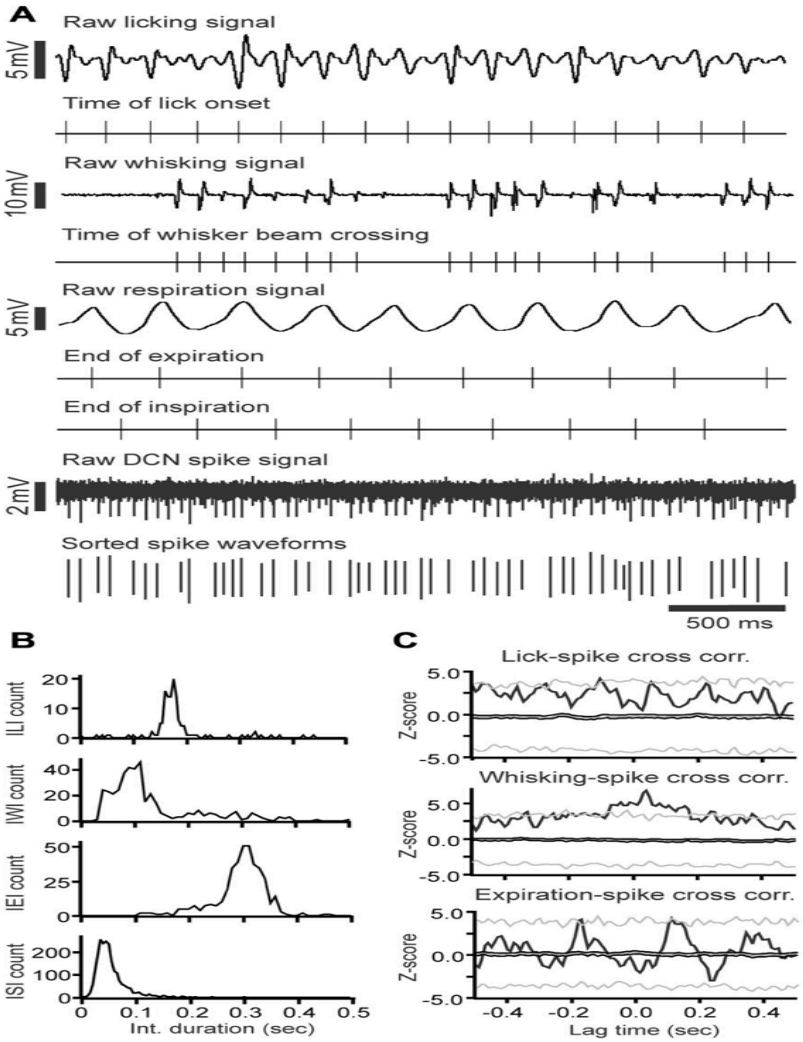
1. Gly neurons project to ipsilateral brainstem
2. Glu neurons project to contralateral regions

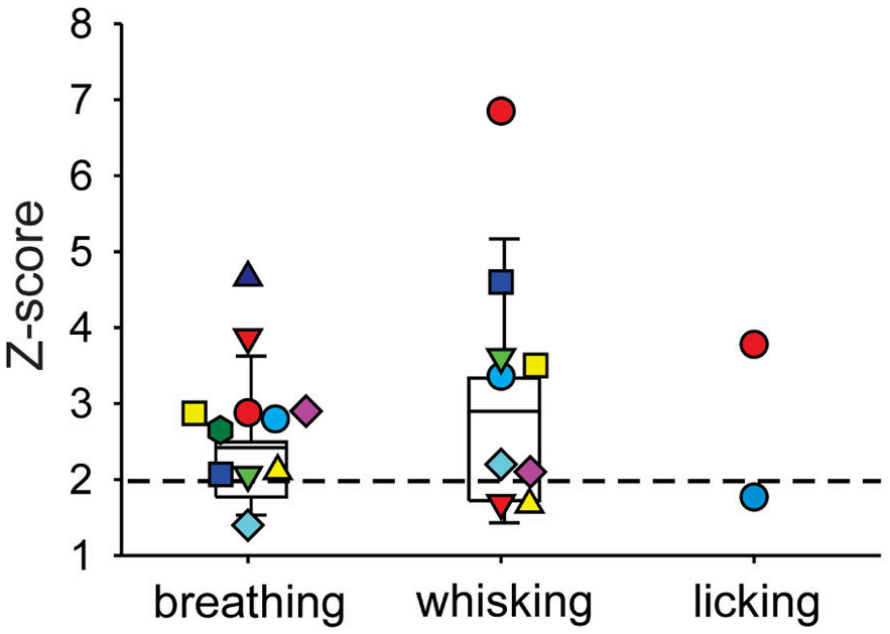


High Baseline Firing Rates

Physiological Correlates

Orafacial and Respiration



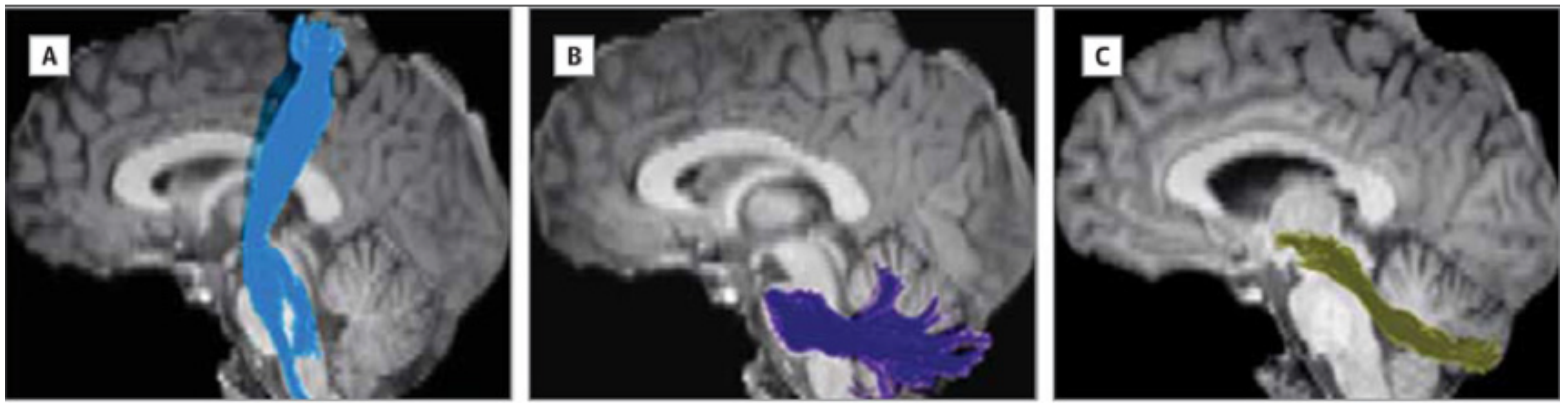


DCN spike activity correlated with Respiration, Licking, and Whisking

(From Lu et al. 2013)

Behavioral Correlates

Motor Correlations

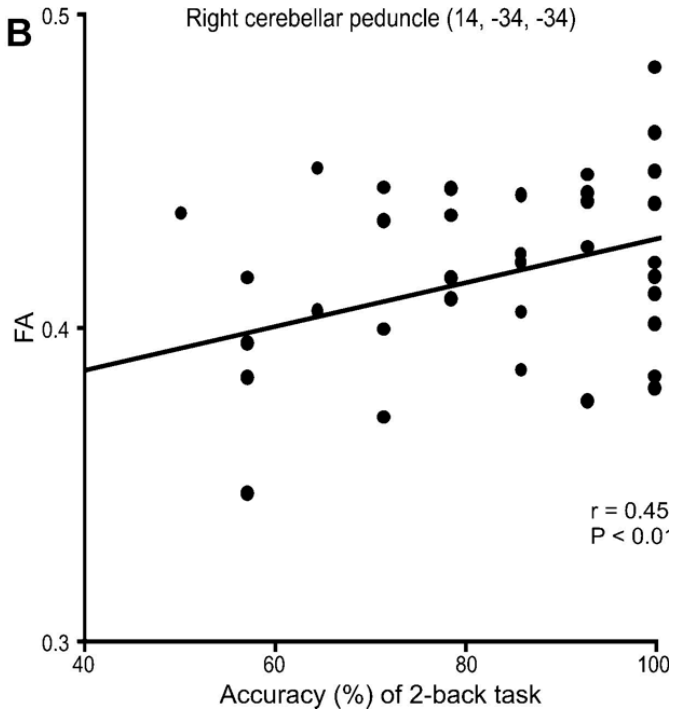


	Behavioral Dyscontrol Scale 2			Purdue Pegboard Dexterity Test		
		Fragile X-Associated Tremor/ Ataxia Syndrome			Fragile X-Associated Tremor/ Ataxia Syndrome	
Behavioral Tests, Groups	Healthy Controls	Negative	Positive	Healthy Controls	Negative	Positive
No. of participants	32	25	35	29	25	32
Explained variance of X, %	28.9	14.5	28.4	24.7	17.3	24.8
Explained variance of Y, %	37.0	42.3	47.0	34.9	36.6	51.5
Correlation (Y, predicted Y)						
R	0.41	0.42	0.55	0.31	0.02	0.56
P value	.02	.037[b]	<.001	.10	.91	<.001

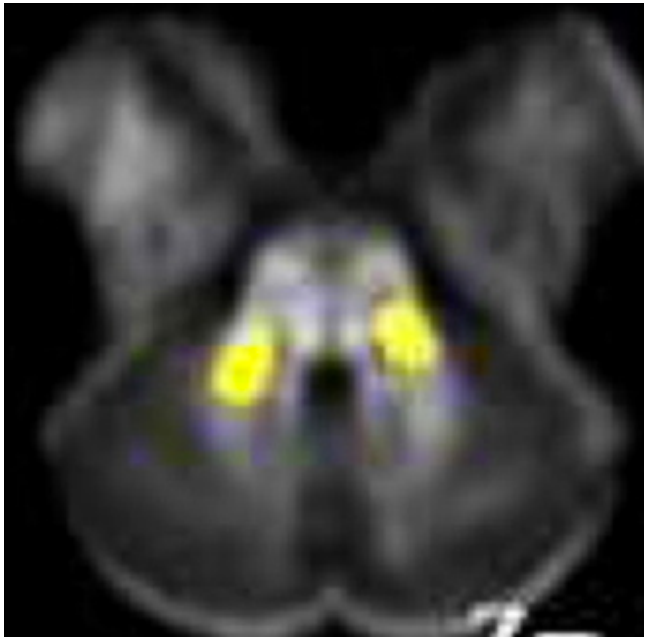
SCP predicts Motor scores for both Normal controls & individuals with FXTAT

(From Wang et al. 2013)

Cognitive Function



Bilateral CP related to Sustained Attention & Working Memory



(From Takahashi et al. 2010)

Educational Outcomes Hearing Loss

	Performance IQ	Full IQ	Verbal IQ	Vocabulary T-score	IEP	Speech-language therapy	Language standard score
AUDITORY ROIs							
NH ($n = 20$)							
No statistically significant correlations							
UHL ($n = 29$)							
FA left Heschl's gyrus	−0.159	0.047	0.367	0.355	−0.522†	−0.167	0.262
Right UHL only ($n = 13$)							
No statistically significant correlations							
Left UHL only ($n = 16$)							
No statistically significant correlations							
NON–AUDITORY ROIs							
NH ($n = 20$)							
No statistically significant correlations							
UHL ($n = 29$)							
MD right posterior limb of the internal capsule	−0.038	−0.171	−0.485†	−0.435*	0.448*	0.343	−0.462*
FA left middle cerebellar peduncle	−0.072	0.275	0.474*	0.342	−0.324	−0.632†	0.270
FA left uncinate fasciculus	−0.569†	−0.554†	−0.358	−0.406*	0.265	0.192	−0.438*
FA left middle cingulate gyrus	0.056	0.156	0.223	0.150	−0.075	−0.460*	0.130
Right UHL only ($n = 13$)							
MD right middle cerebellar peduncle	−0.595	−0.086	−0.905†	−0.795*	0.252	0.504	−0.738*
FA left uncinate fasciculus	−0.819†	−0.841††	−0.451	−0.338	−0.254	0.178	−0.576*
FA right uncinate fasciculus	−0.720†	−0.725†	−0.566*	−0.524	0.380	0.579	−0.736†
Left UHL only ($n = 16$)							
MD left middle cerebellar peduncle	0.147	−0.377	−0.430	−0.328	0.412	0.866††	−0.355
FA left middle cerebellar peduncle	−0.019	0.580*	0.606*	0.455	−0.454	−0.784†	0.517

Statistical significance was considered to be $p < 0.004$ for auditory ROIs and $p < 0.003$ for non-auditory ROIs.

**$p < 0.05$; †$p < 0.01$; ††$p < 0.001$.*

IQ, intelligence quotient; IEP, individualized education plan.

(From Rachakonda, Shimony, Coalson, & Lieu 2014)

Clinical Relations

Spearman Correlation Between the Absolute Value of the Percentage Changes of FA Value in MCP and That of Clinical Scores (n = 17)[a]

The Absolute Value of Percentage Reduction of FA Value in MCP	The Absolute Value of Percentage Reduction of NIHSS, r_s (P)	The Absolute Value of Percentage Change of FMS, r_s (P)	The Absolute Value of Percentage Change of BI, r_s (P)	The Limb Ataxia Scores of ICARS at W12, r_s (P)
Contralateral	**−0.43 (.04)**	**−0.51 (.03)**	−0.30 (.09)	**0.48 (.03)**
Ipsilateral	**−0.52 (.03)**	**−0.59 (.02)**	−0.24 (.19)	**0.73 (.01)**

Abbreviations: FA, fractional anisotropy; MCP, middle cerebellar peduncle; NIHSS, National Institutes of Health Stroke Scale; FMS, Fugl-Meyer scale; BI, Barthel Index; ICARS, International Cooperative Ataxia Rating Scale; W12, 12th week.

[a]The percentage changes of FA value: ([W12 FA value − W1 FA value]/W1 FA value × 100%); the percentage changes of clinical scores: ([W12 scores − W1 scores]/W1 scores × 100%). The significant values are in boldface.

Pathological changes in MCP correlates with Lesser Motor Gains

(From Liang et al. 2014)

Clinical Pathologies

Sources of Injury

- Genetics
  - Inherited cerebellar degeneration
- Lesions
  - Tumor, stroke, etc
- Toxins
  - Ethanol, chemotherapy, antiepileptic drugs
- Autoantibodies
  - Autoimmune disorders

Cerebellar Ataxia

Damage or degeneration of nerve cells in focal regions of the cerebellum

Damage to vestibular, fastigial nuclei & vestibulo-cerebellum

Loss of neurons in the intermediate, dentate nuclei & associated cortex

Atrophy of transverse fibers of pons & MCP

(From Vedolin et al. 2013)

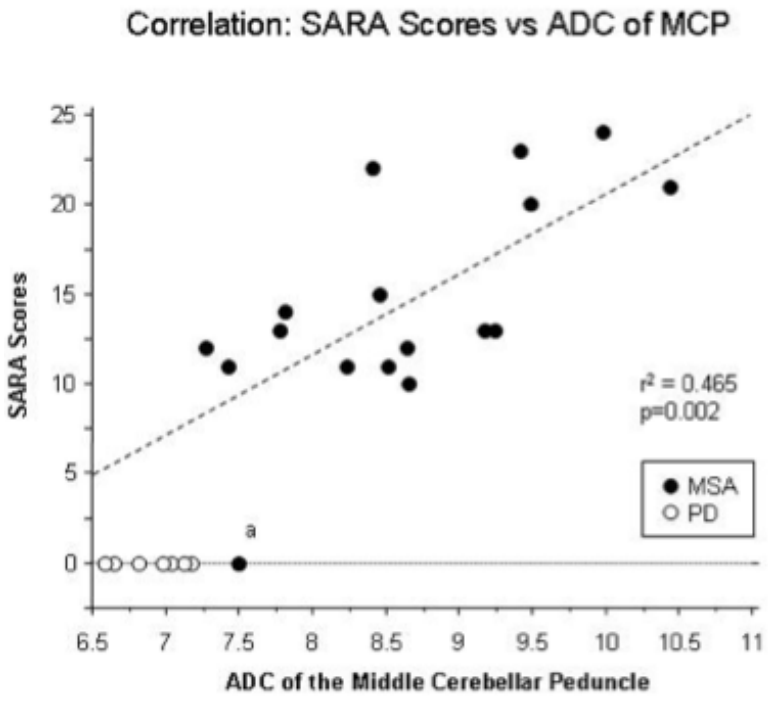
Motor Dysfunctions

Limb movement		
Dyssynergia	Finger to nose Heel shin	Ability to move joints simultaneously/ decomposition of multijoint movements
Dysmetria	Finger to finger test Great toe–finger test (have trunk supported to isolate any limb dysfunction)	Speed of motion Variability of spatial path Over/undershoot
Tremor Kinetic Intention Postural	Holding a position, e.g. (1) arms outstretched with palms down; (2) index to index (hold two index fingers medially) Move to/from target (see tests above) Assess writing/spiriography	Tremor amplitude and frequency Assess for titubation ~3 Hz tremor of the head
Disdiadochokinesia	Alternating pronation–supination Alternating wrist flexion/extension while tapping the thigh Ankle dorsi-plantarflexion	Rate of movement
Asthenia and hypotonia	Passive motion of the limb Test muscle strength	Assess resistance to motion Assess strength
Balance and gait dysfunction		
Balance and gait dysfunction	Stand with eyes open/closed Stand in tandem/on one foot Balance in response to perturbation, volitional upper/lower limb Walking	Rate, direction and amplitude of sway (± vision) and phase between upper and lower body Size of response to postural perturbation Walking – accuracy of foot placement/ degree of sway/time in double stance/ stride length/base of support
Oculomotor		
Nystagmus (e.g. gaze-evoked; downbeat; rebound nystagmus) Fixation deficits (e.g. flutter; macroscopic oscillations)	Ability to fixate into finger ~30 cm away with gaze in primary position and when looking at eccentric targets and on returning gaze to midline	Ocular alignment/presence of nystagmus (rhythmic oscillatory movements of the eyes) type/presence of eye movements (e.g. flutter/ocular bobbing)
Saccadic smooth pursuit Poor vestibulo-ocular reflex cancellation	Follow a target moving up/down/side to side Hold arms together out in front with thumbs pointing up. Fixate gaze on the thumbs while sitting in a chair that is moved side to side	Number of catch-up saccades Ability to maintain gaze fixation
Dysmetric saccades	Ability to rapidly shift gaze from one eccentric target to another (up and down/side to side)	Latency, velocity and precision (over/under-shoot of the target as seen by the need to make more than one saccade to reach the target)
Reduced velocity of divergent eye movement	Ability to shift gaze from targets close to and far away from subject. Ability to follow targets moving to and from target	Latency, velocity and precision
Abnormal vestibulo-ocular reflex and optokinetic response	Sit on a chair and fixate an earth fixed target while the chair rotates side to side Look at an optokinetic drum (ask patient to count the stripes)	Ability to fixate on the target Movement of the eyes in the direction of rotation and re-alignment to the midline
Dysarthria		
	Ability to maintain sustained vowel phonation; repeat syllables Repeat a sentence speech/read a standard passage of text	Intelligibility; rhythm; speed; presence of hesitations, accentuation of syllables and addition/omission of pauses

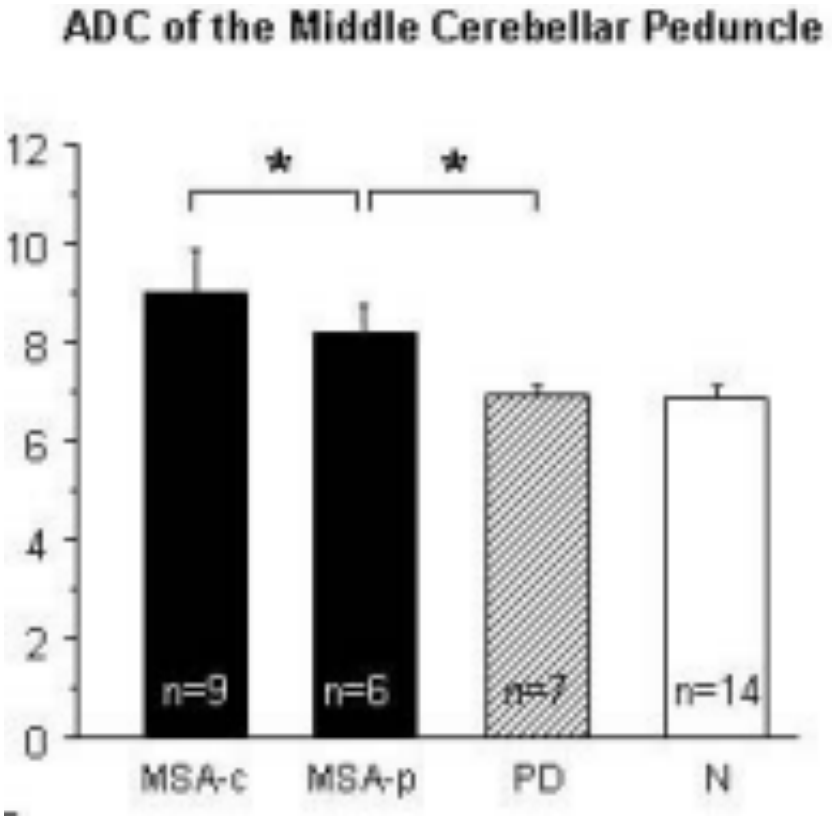
- Spino-cerebellum
  - Gait impairment
- Vestibulo-cerebellum
  - Impaired eye movements
- Cerebro-cerebellum
  - Voluntary, planned movement impairment

(From Fundamental Neuroscience, 4th ed)

Multiple System Atrophy



Increase in ADC value of the middle cerebellar peduncle precedes the appearance of cerebellar ataxia.

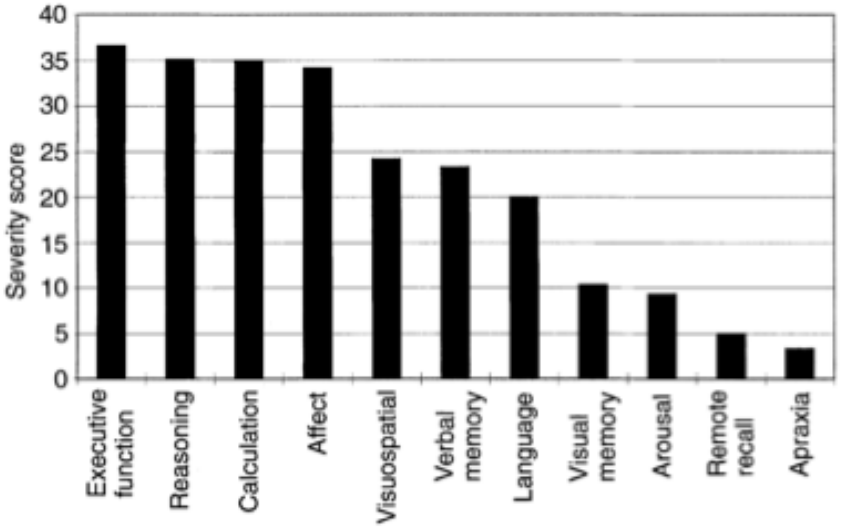


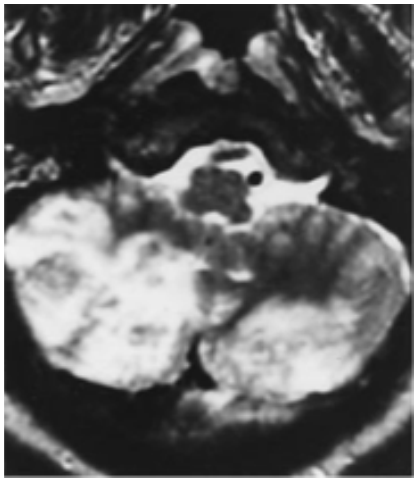
DTI can separate MSA-p from PD even when the patient shows parkinsonism only.

(From Park et al. 2009)

Cerebellar Cognitive Affective Syndrome

- Overall disturbance in cognitive functioning
  - Impaired spatial cognition
  - Personality changes
  - Executive functioning impairment
  - Linguistic impairments





Posterior Lobe = Severe Symptoms

(From Schmahmann & Sherman 1998)

Summary

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