Functional anatomy of the cerebellum

International Parkinson and Movement Disorder Society – European Section
Diagnosis and Treatment of Cerebellar Ataxias
July 13th 2026

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Martha and Robert Fogelman Endowed Chair in Ataxia and Cerebellar Neurology
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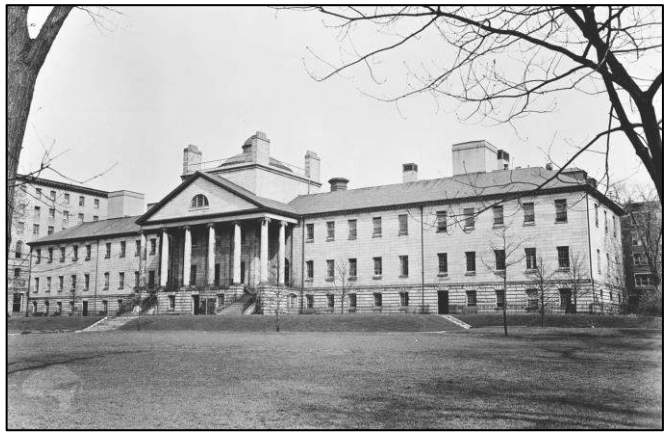
Professor of Neurology, Harvard Medical School



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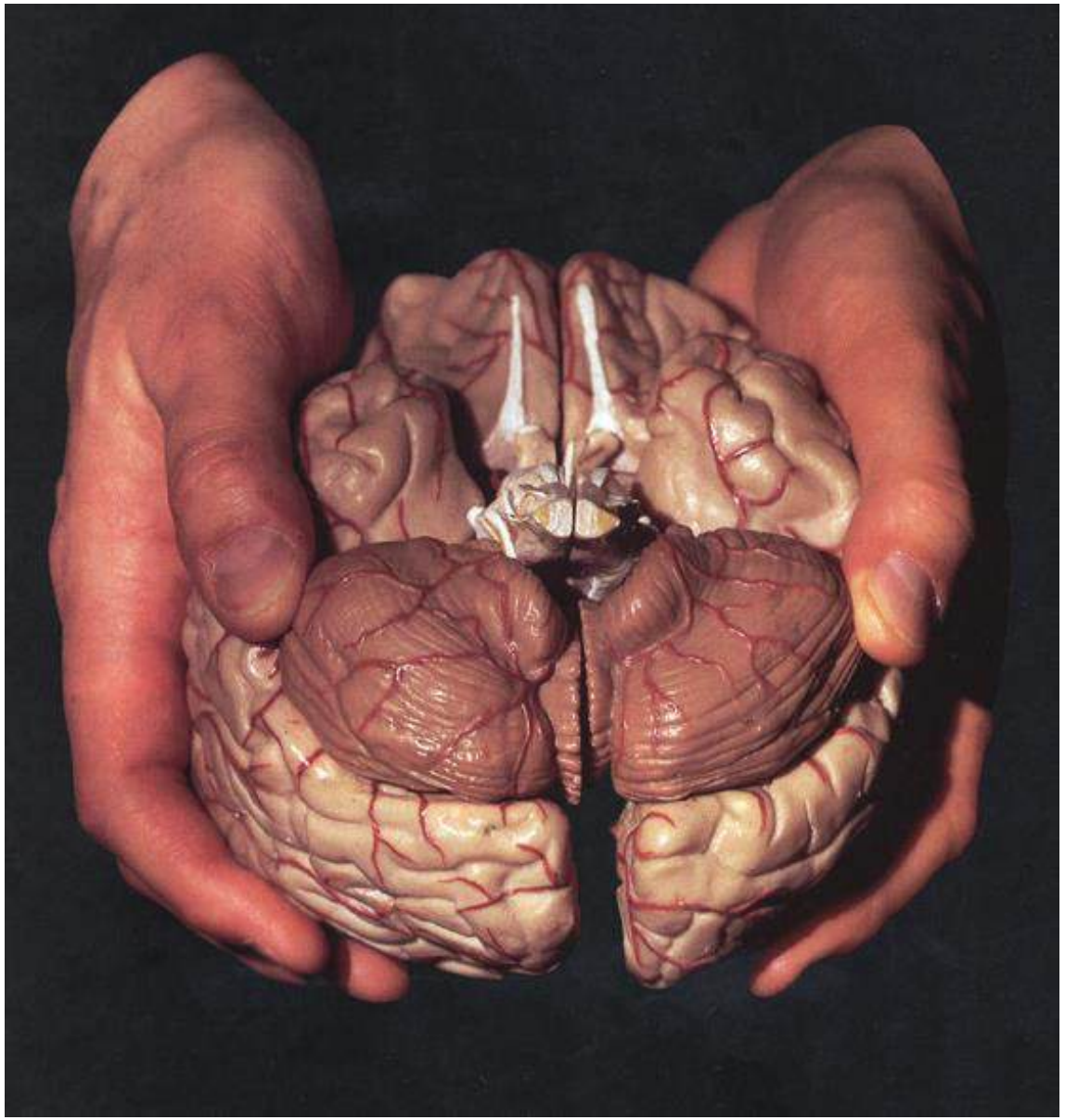
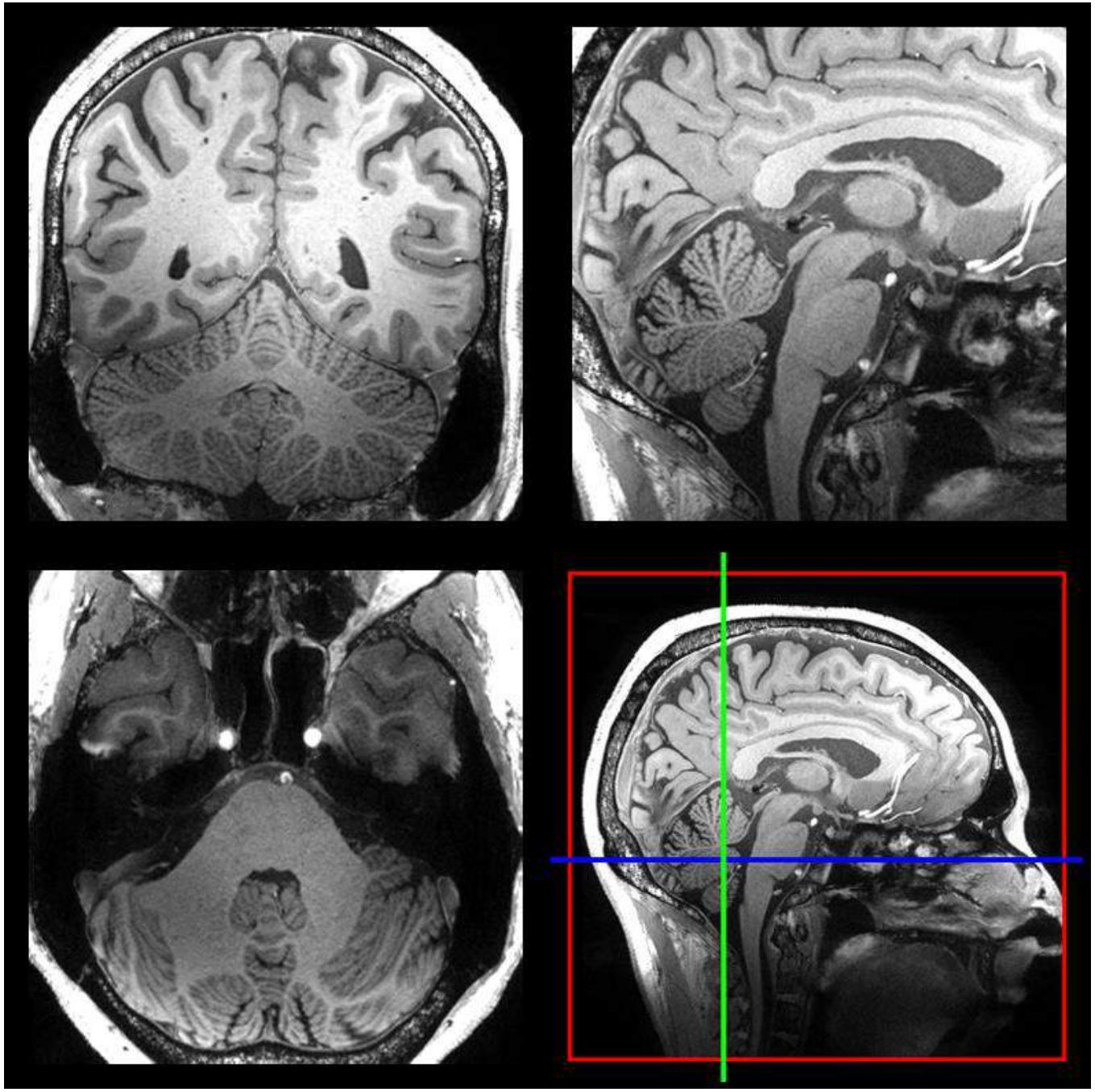
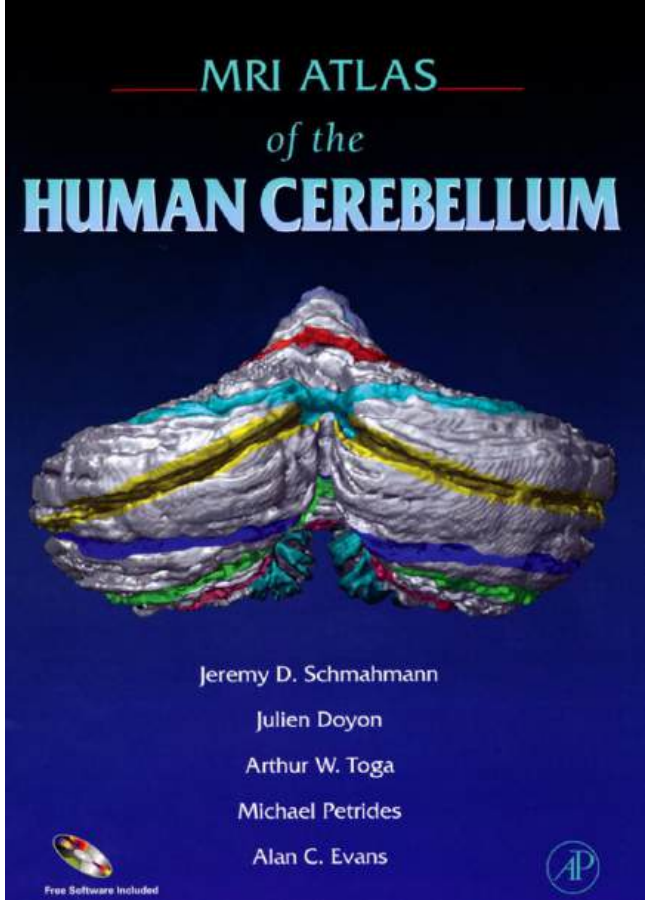
International Parkinson and Movement Disorder Society European Section



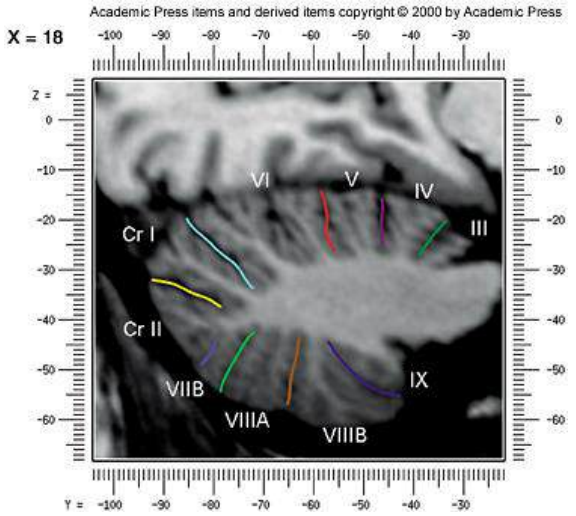
from The Sorcerer's Apprentice.
Jonathan Leonard, Harvard Magazine, 1999

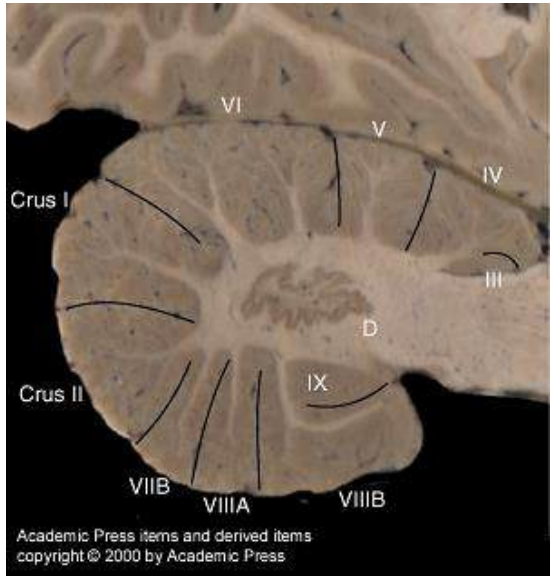


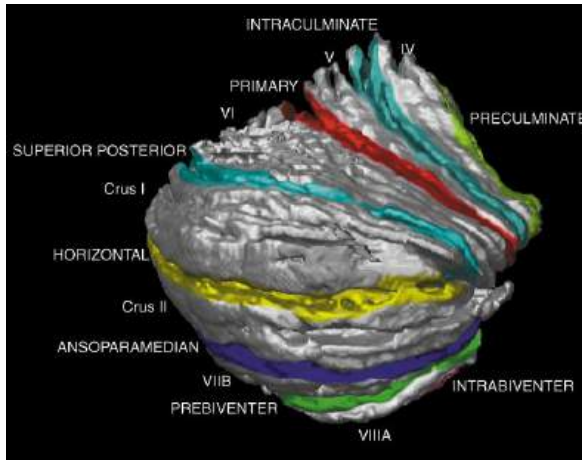
Gray's Anatomy 42e. Courtesy Bruce Fischl, Andre van Kouwe, Otto Rapalino, Jonathan Polimeni.
Laboratory for Computational Neuroimaging, Martinos Center for Biomedical Imaging, Massachusetts General Hospital

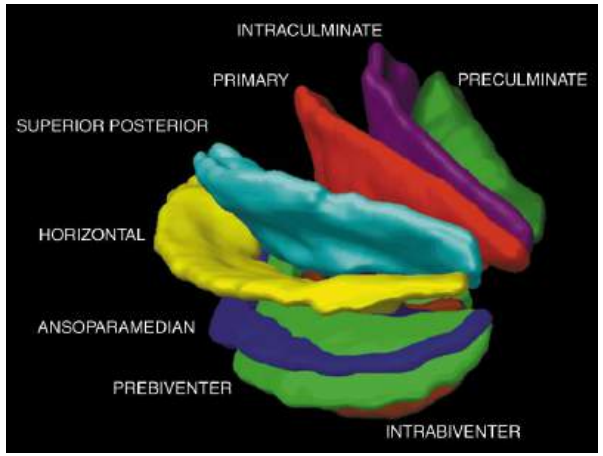


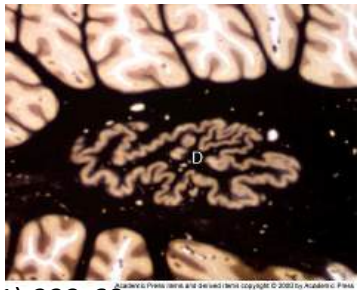
VERMIS Lobule	FISSURE	HEMISPHERE Lobule
I,II		I,II
	Precentral	
III		III
	Preculminate	
IV		IV
	Intraculminate	
V		V
	Primary	
VI		VI
	Superior Posterior	
VIIAf		Crus I
	Horizontal	
VIIAt		Crus II
	Ansoparamedian	
VIIB		VIIB
	Prepyramidal/Prebiventer	
VIIIA		VIIIA
	Intrabiventer	
VIIIB		VIIIB
	Secondary	
IX		IX
	Posterolateral	
X		X



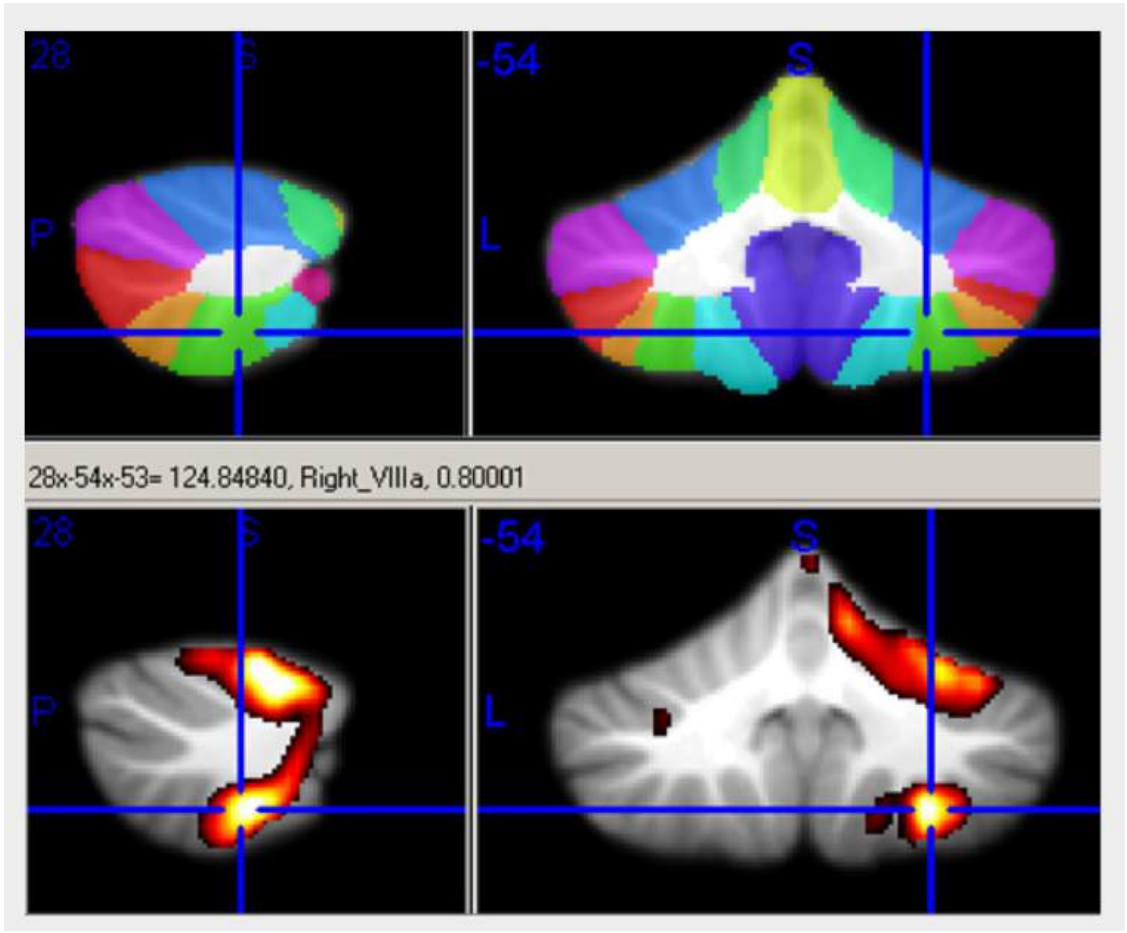




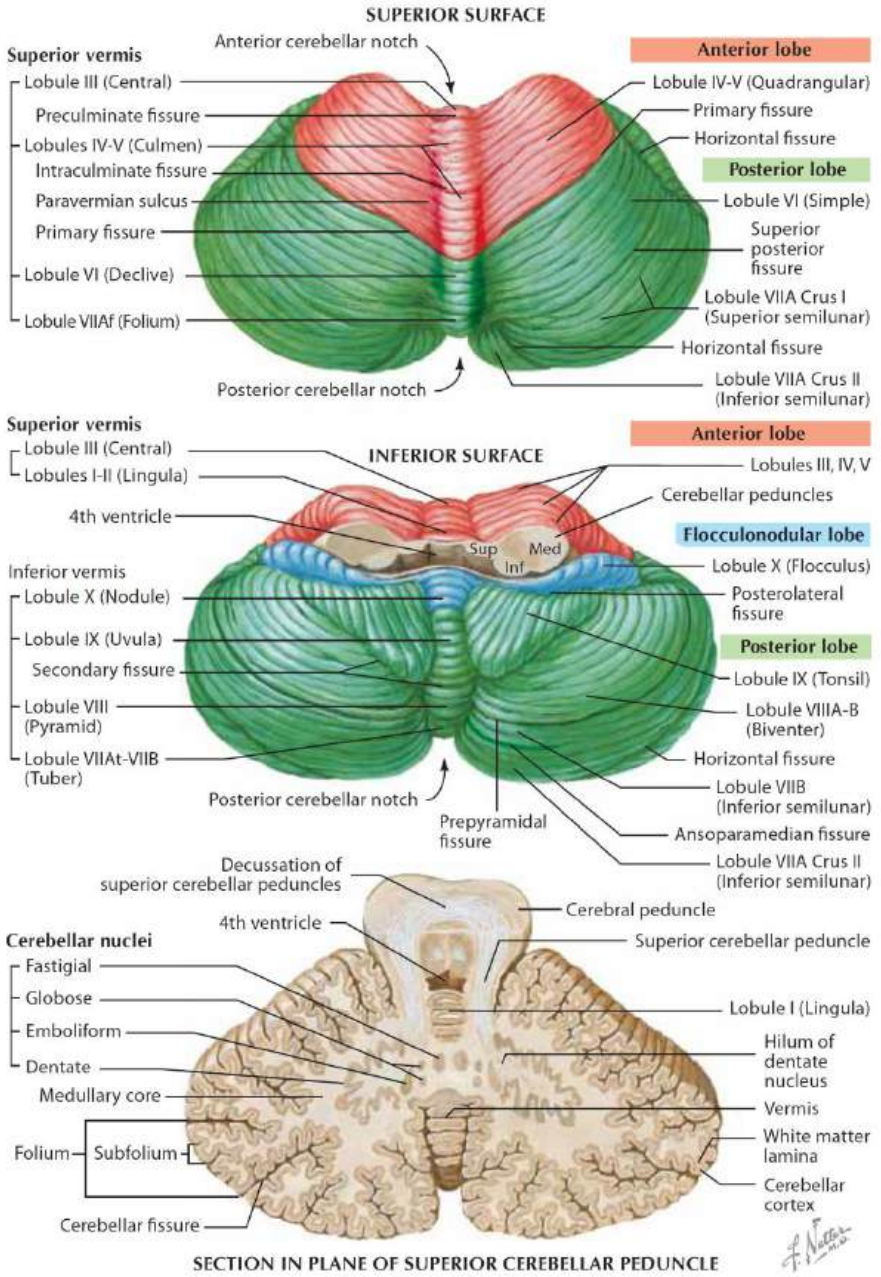




Academic Press. 2000. Also, Schmahmann et al. Neuroimage. 1999;10(3 Pt 1):233-60.

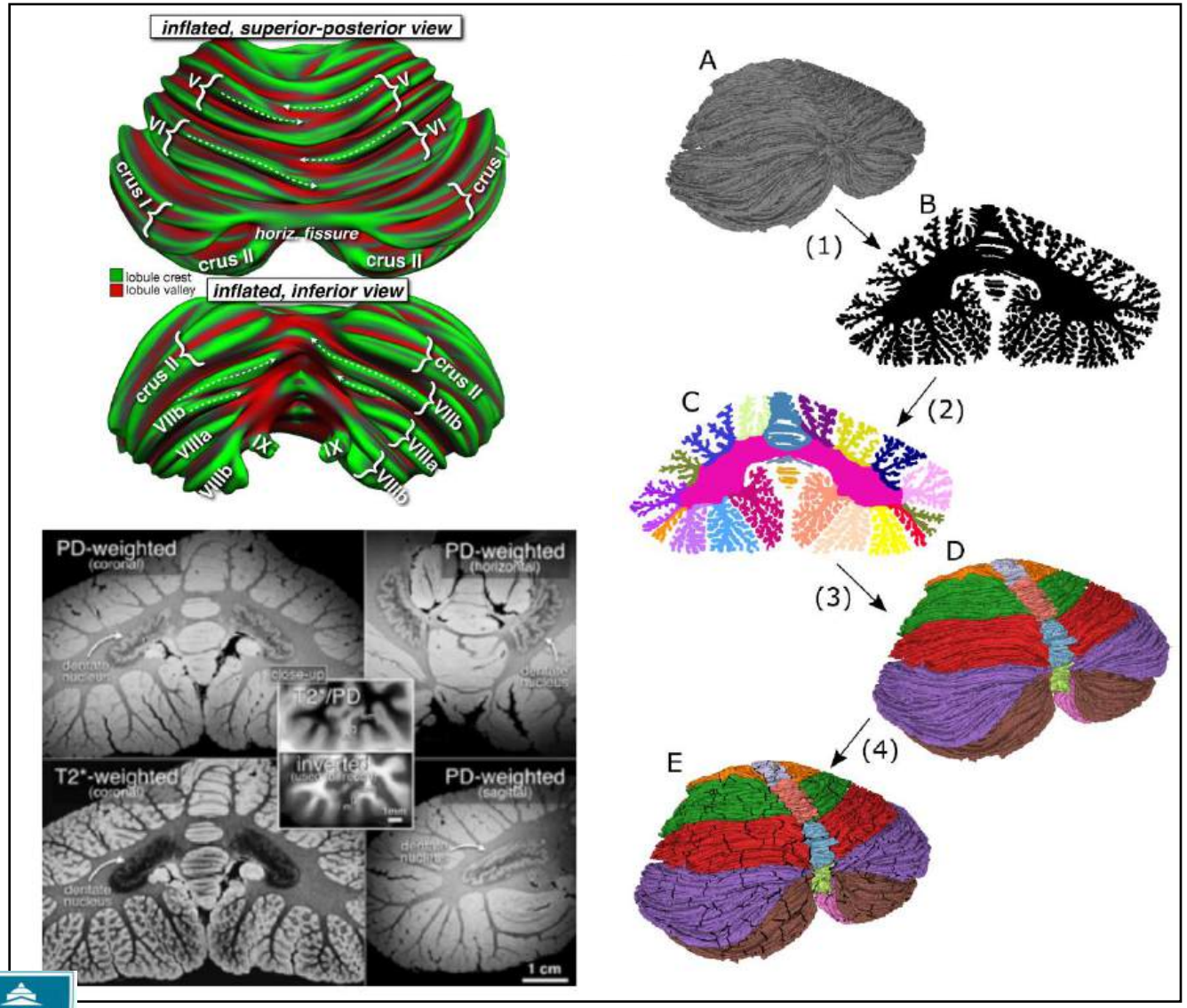


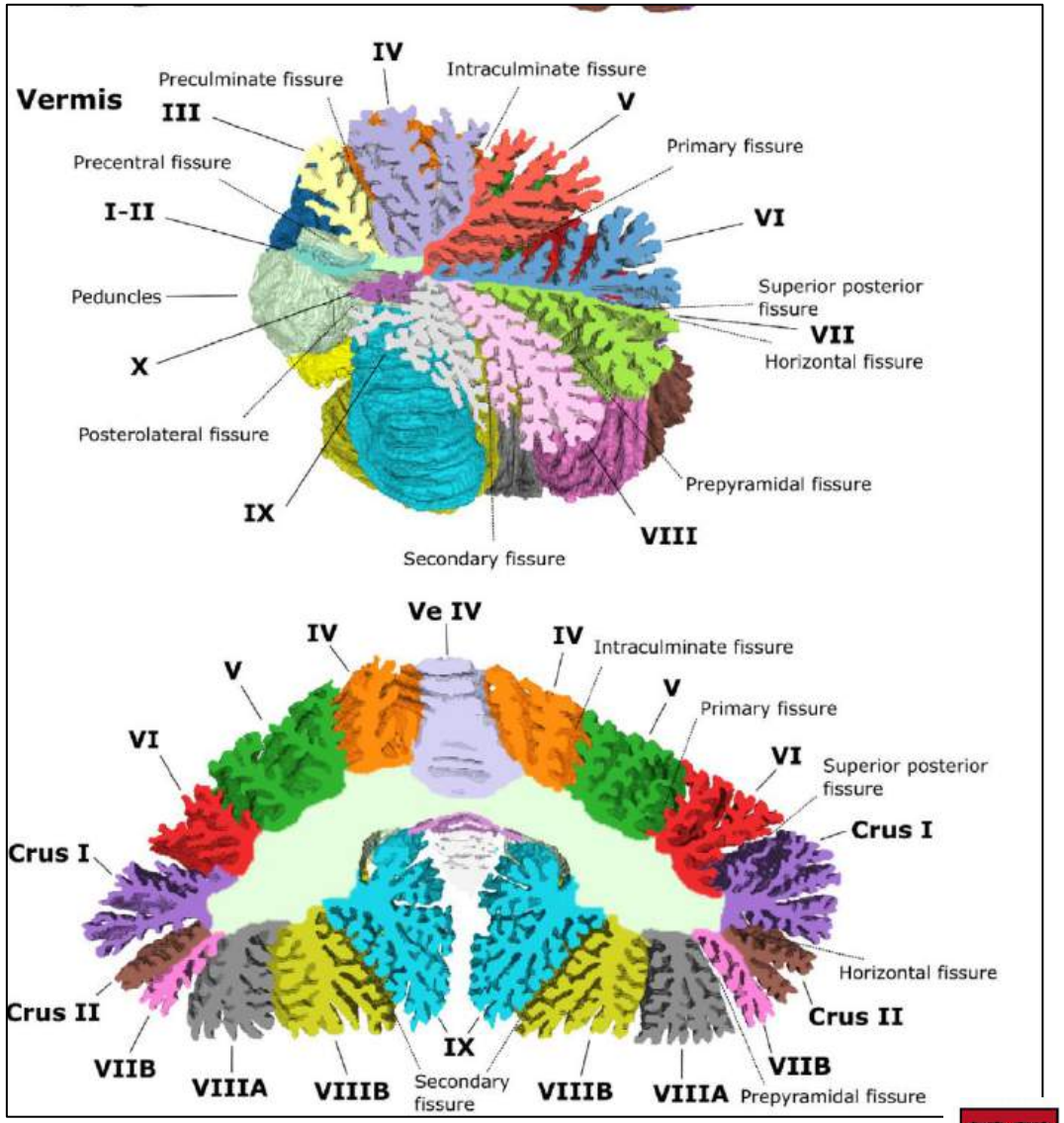
SUIT Atlas: diedrichsenlab.org/imaging/propatlas



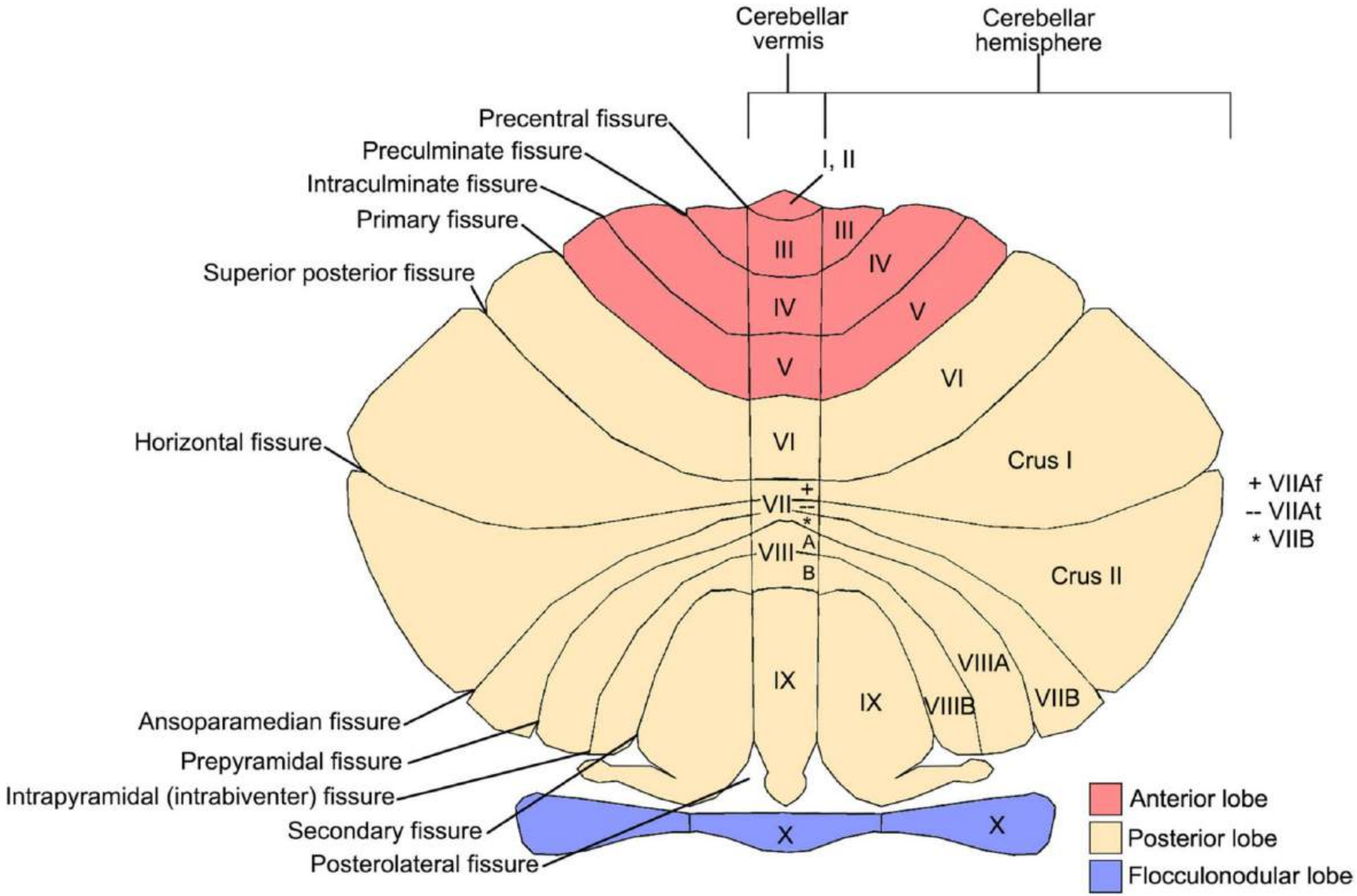
Netter, 2nd edition. Volume 7

A Digital Anatomical Atlas of the Human Cerebellum at Subfolial Resolution

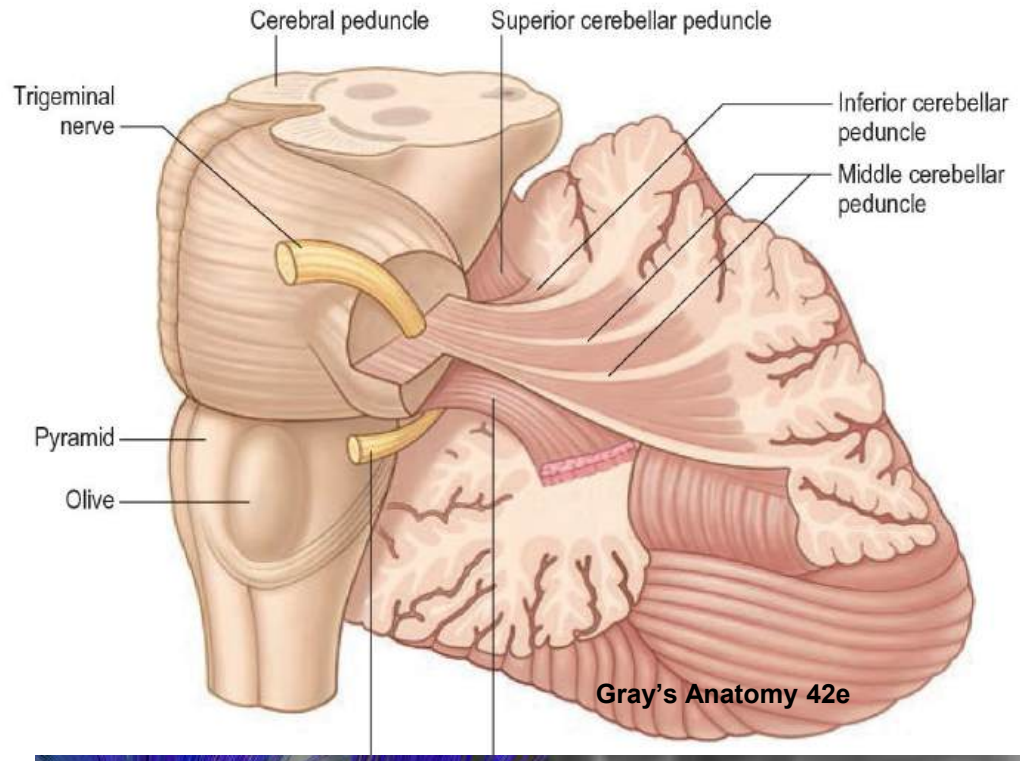




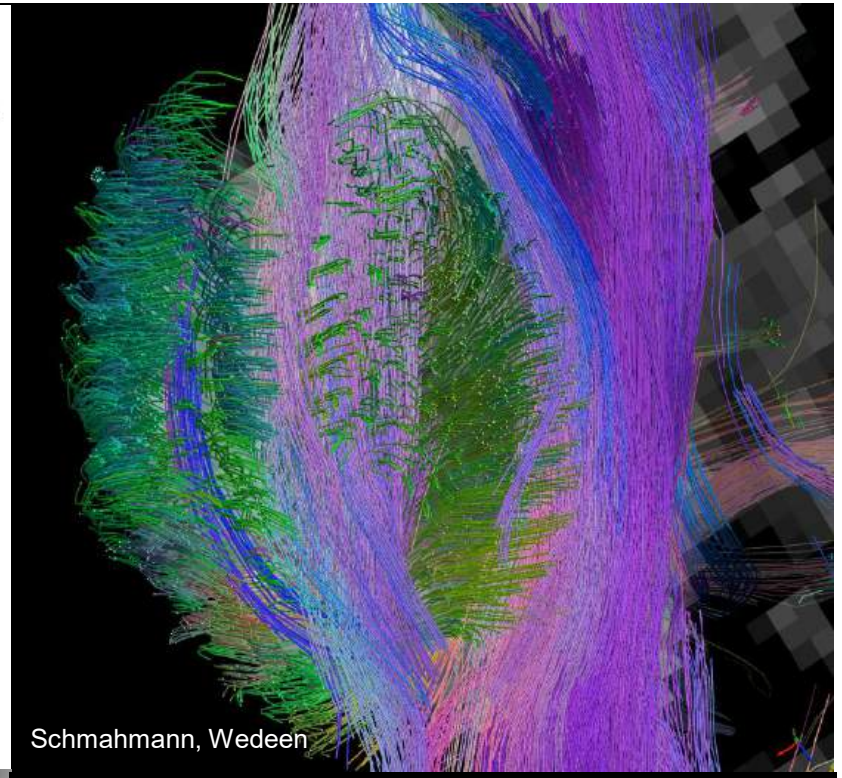
Samuelsson JG, Schmahmann JD, Sereno MI, Rosen B, Hämäläinen MS. Hum Brain Mapp. 2026 Mar;47(4):e70497.



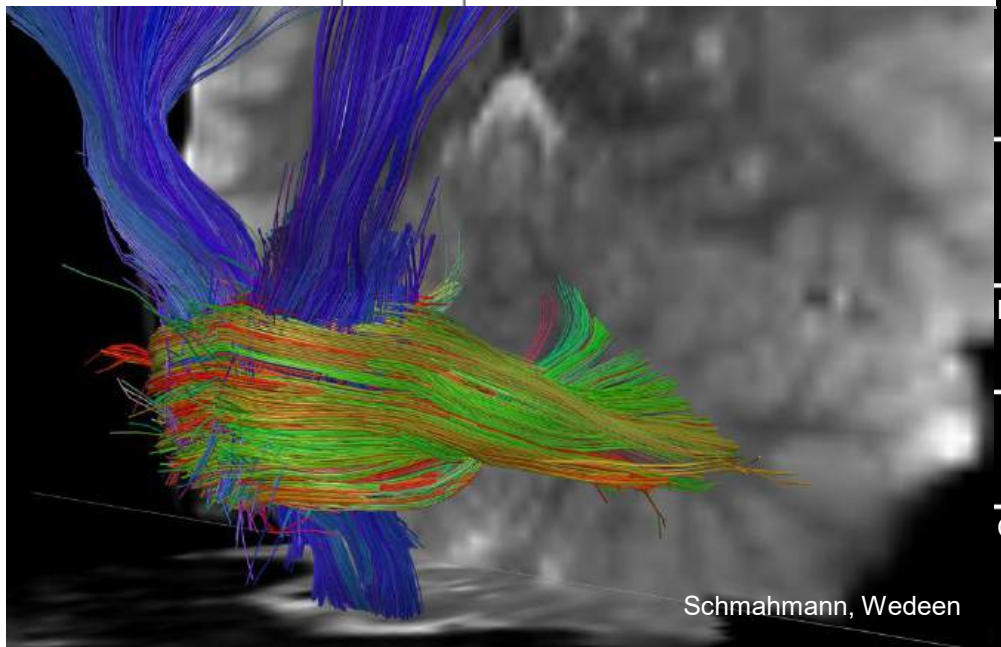
Schmahmann, in D'Mello and Stoodley, 2015



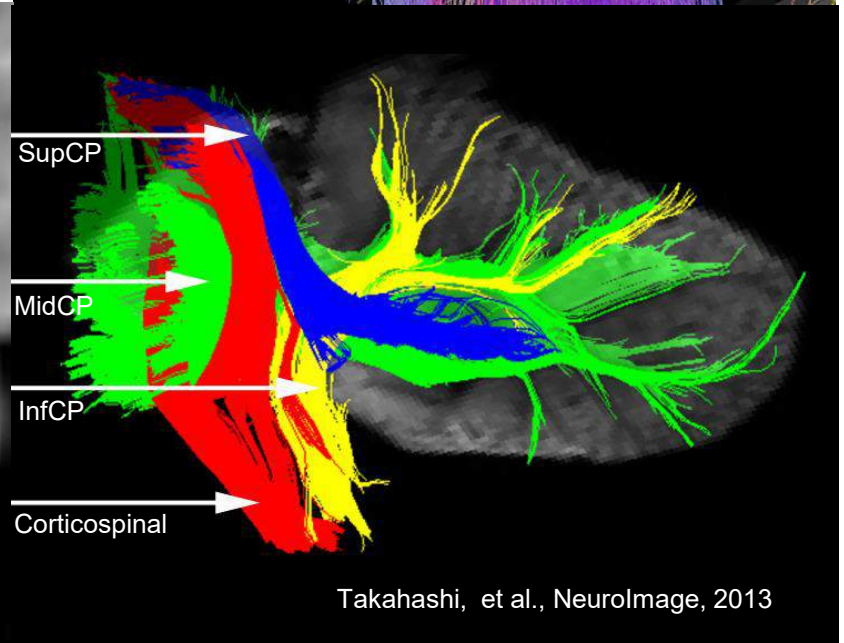
Gray's Anatomy 42e



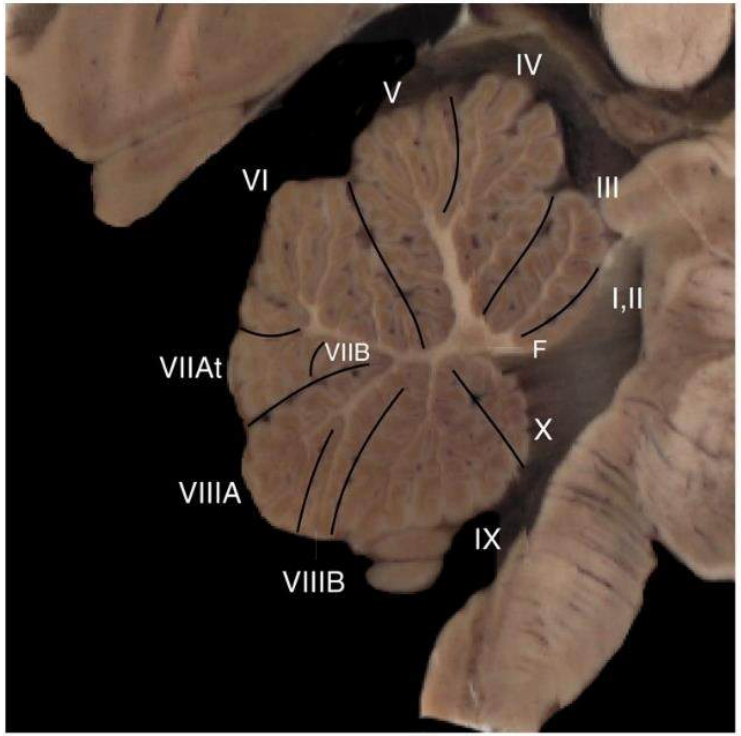
Schmahmann, Wedeen

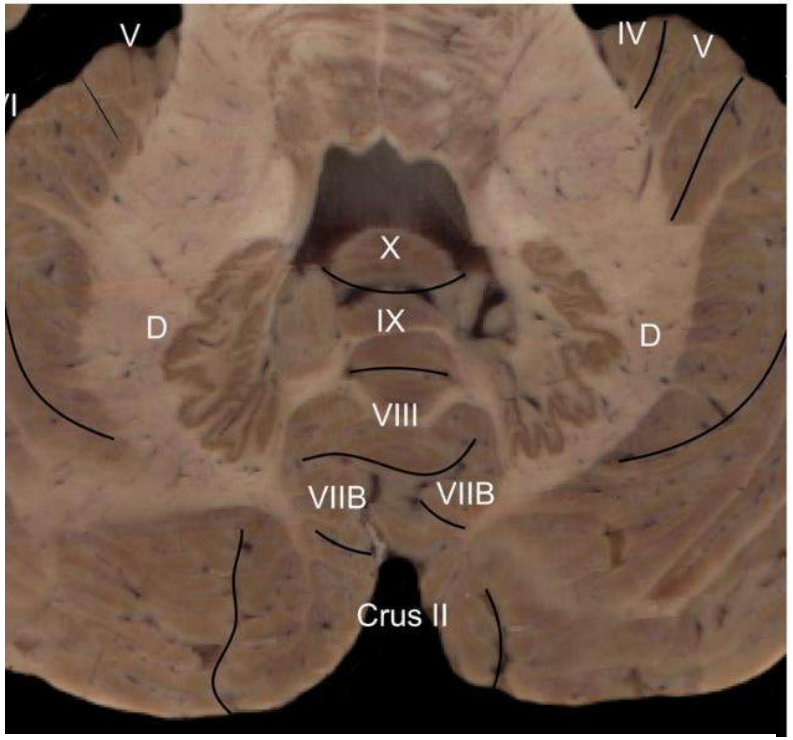


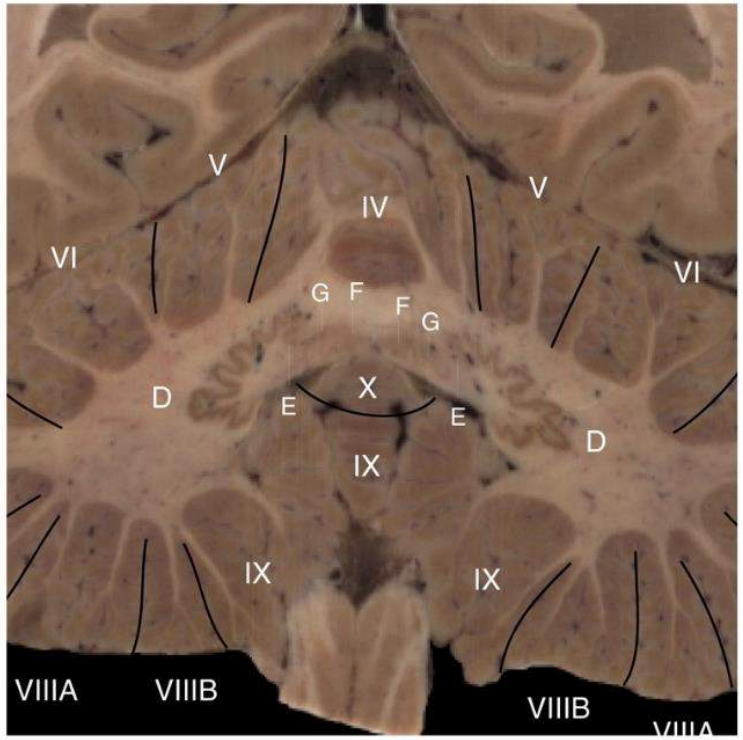
Schmahmann, Wedeen

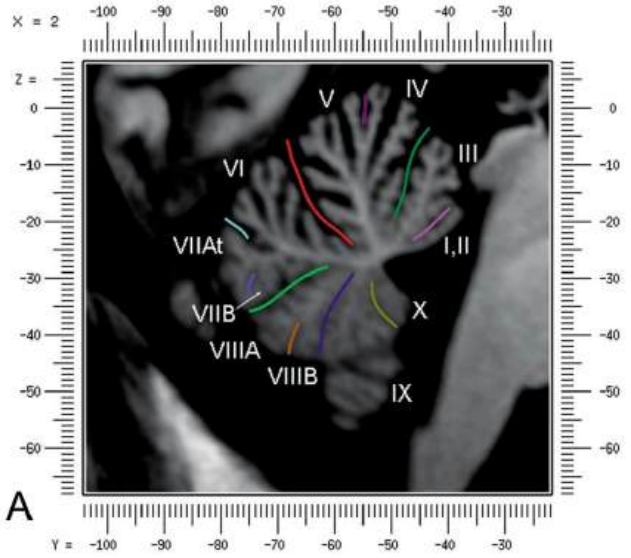


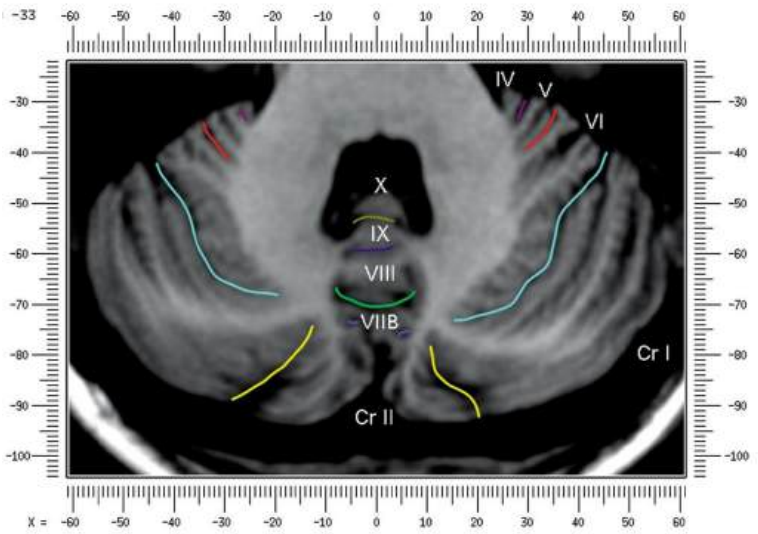
Takahashi, et al., NeuroImage, 2013

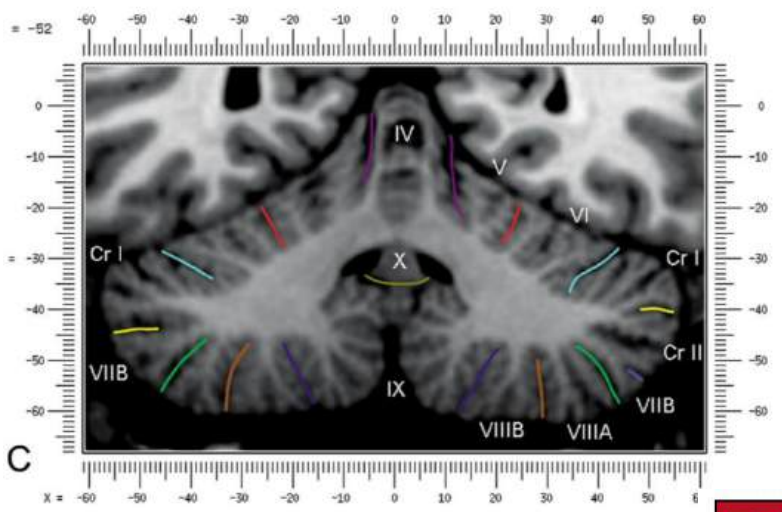






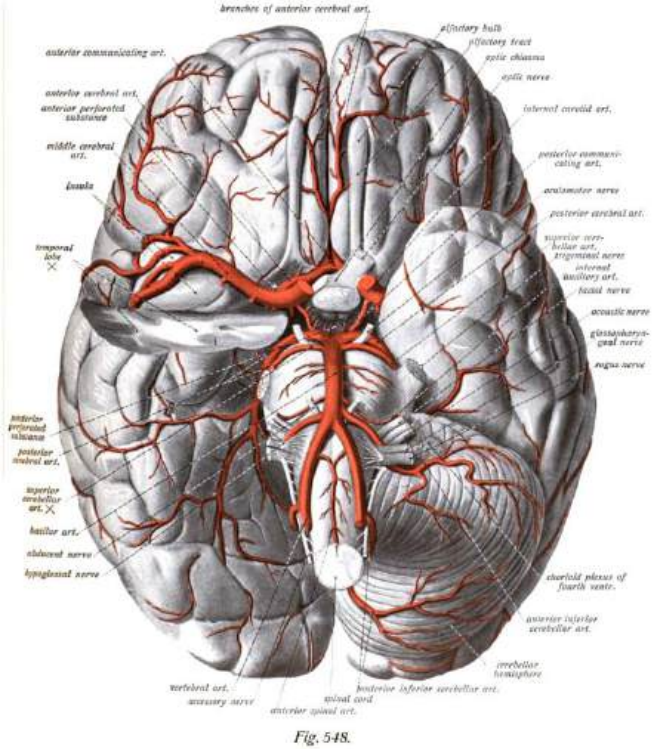






Schmahmann, Doyon, Toga, Petrides, Evans, 2000

SCA, AICA, PICA



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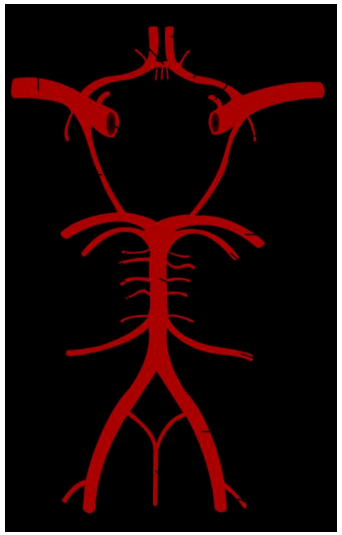
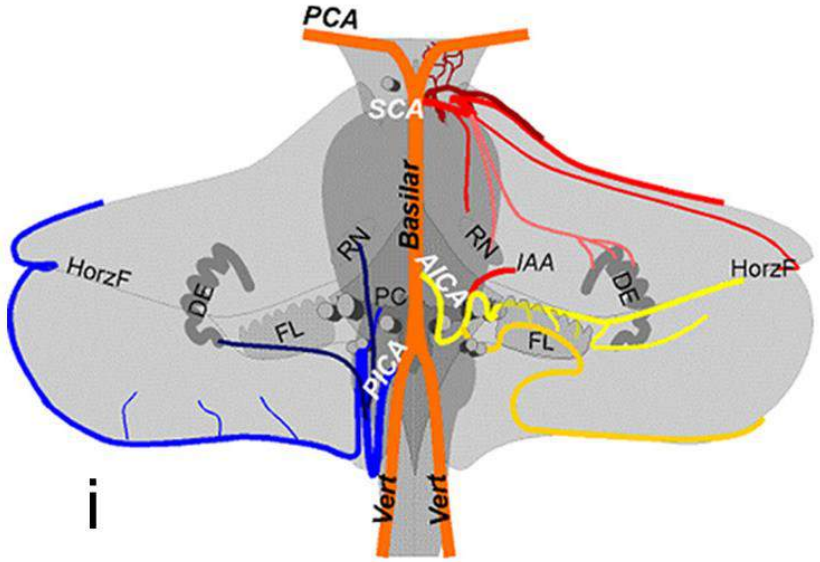
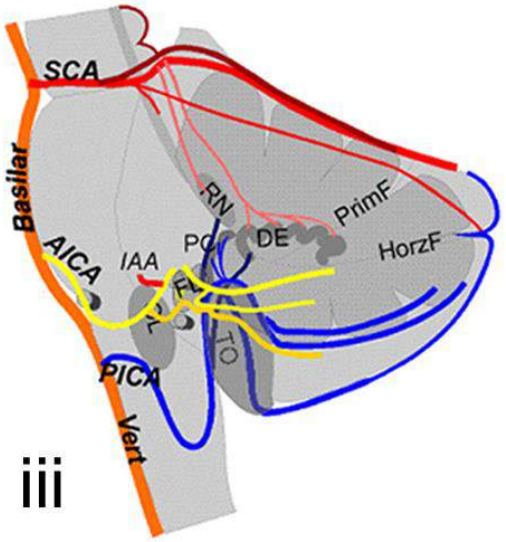
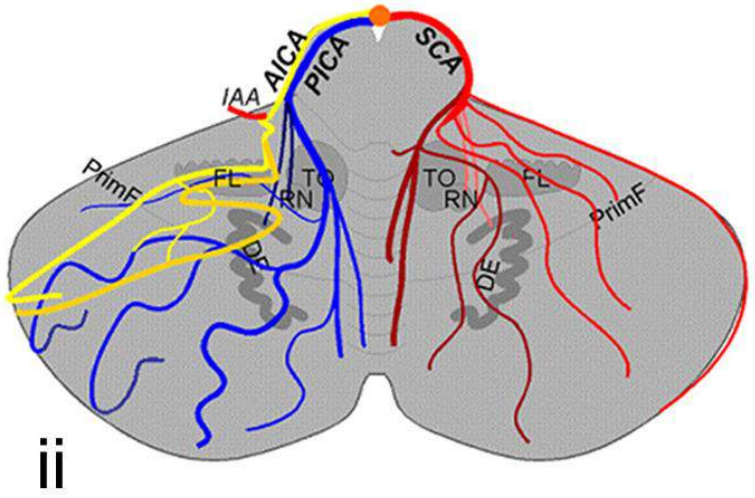


Gray's Anatomy



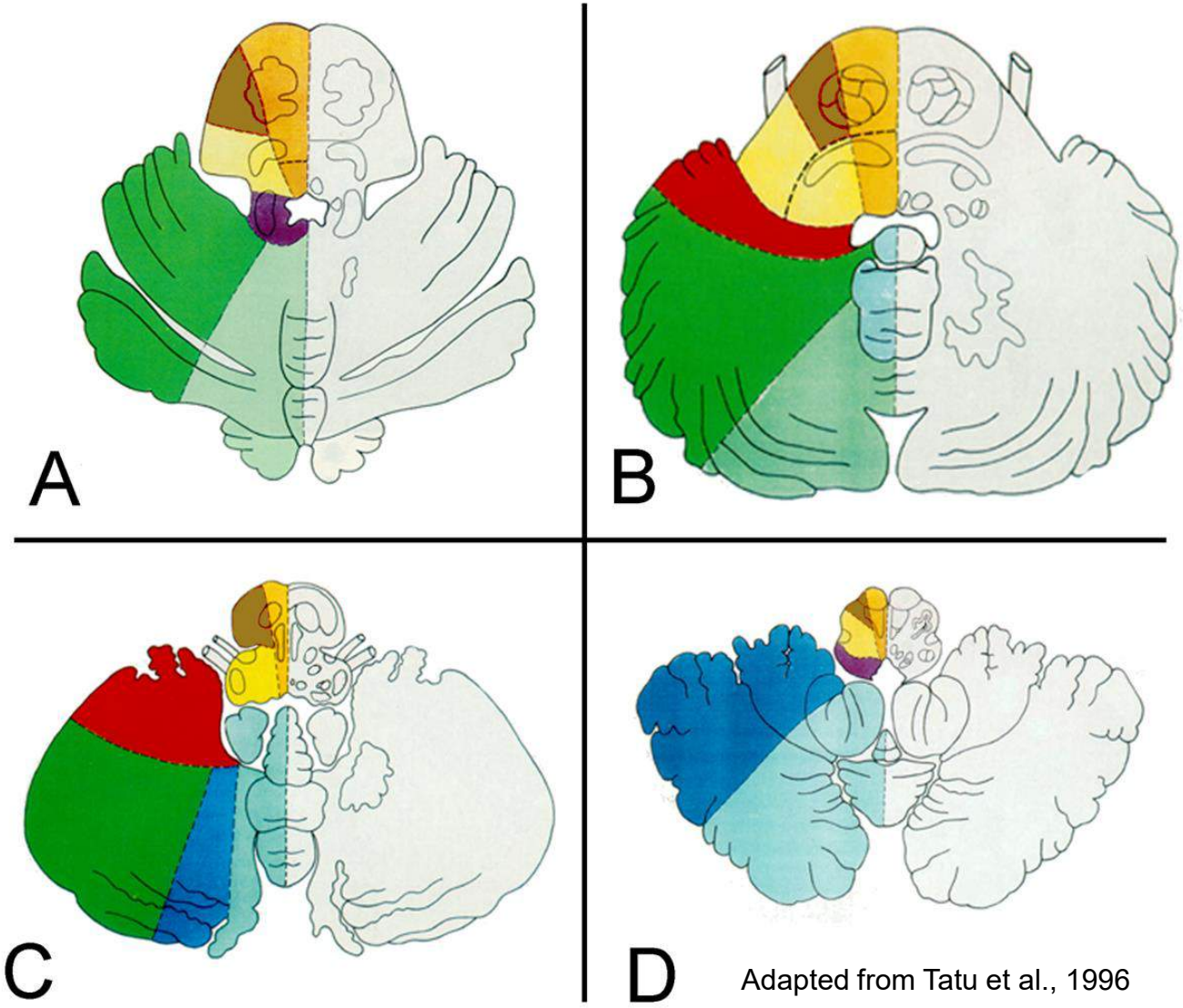




Legend	
Vert	*Vertebral Artery*
Basilar	*Basilar Artery*
PCA	*Posterior Cerebral Artery*
SCA	*Superior Cerebellar Artery*
AICA	*Anterior Inferior Cerebellar Artery*
PICA	*Posterior Inferior Cerebellar Artery*
IAA	*Internal auditory artery*
HorzF	Horizontal fissure
PrimF	Primary fissure
DE	Dentate nucleus
FL	Flocculus
OL	Olive
PC	Plexus choroideus
RN	Roof nuclei
TO	Tonsil

Andreas Luft, in Schmahmann, 2000

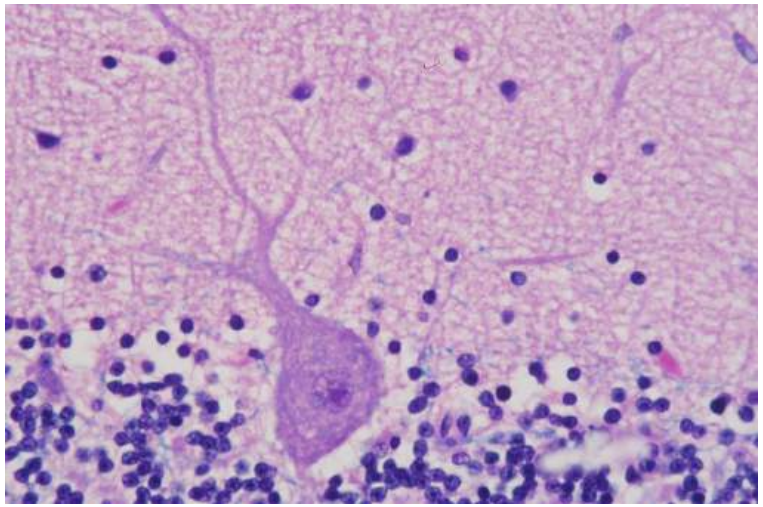
Motor deficit following cerebellar stroke

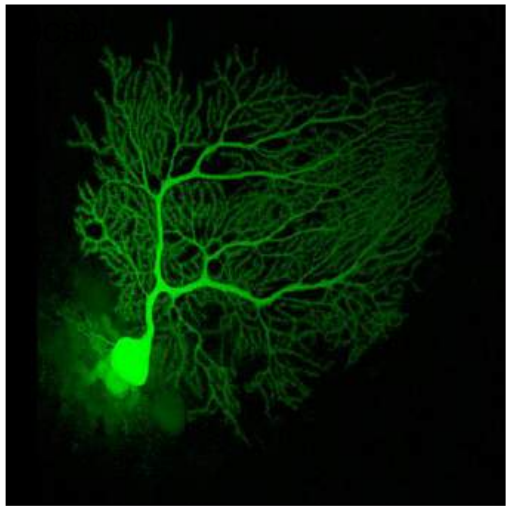


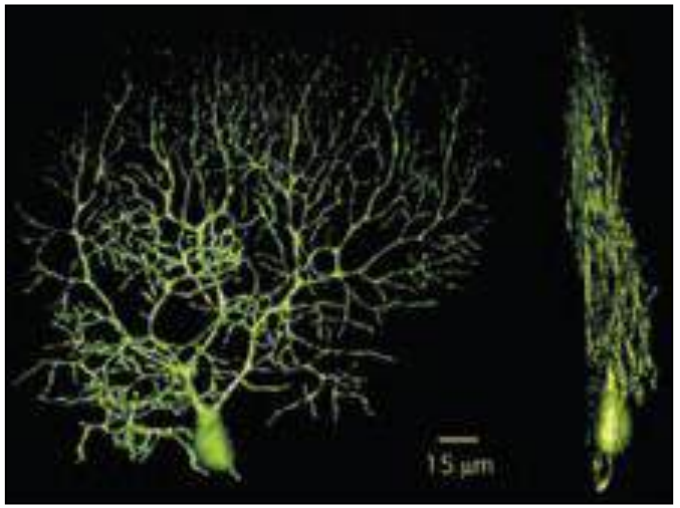
Adapted from Tatu et al., 1996

Schmahmann et al., Neuroscience 2009

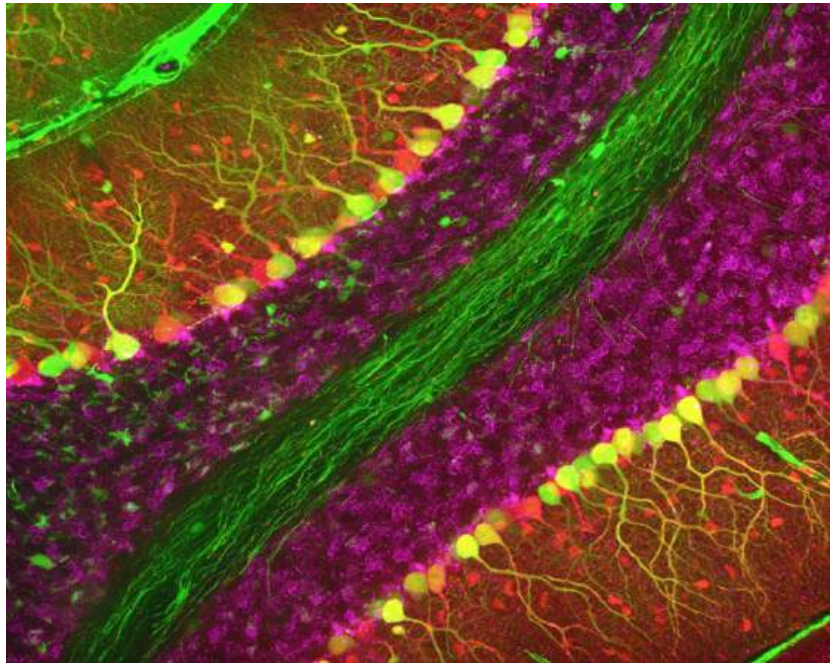
Purkinje Cell



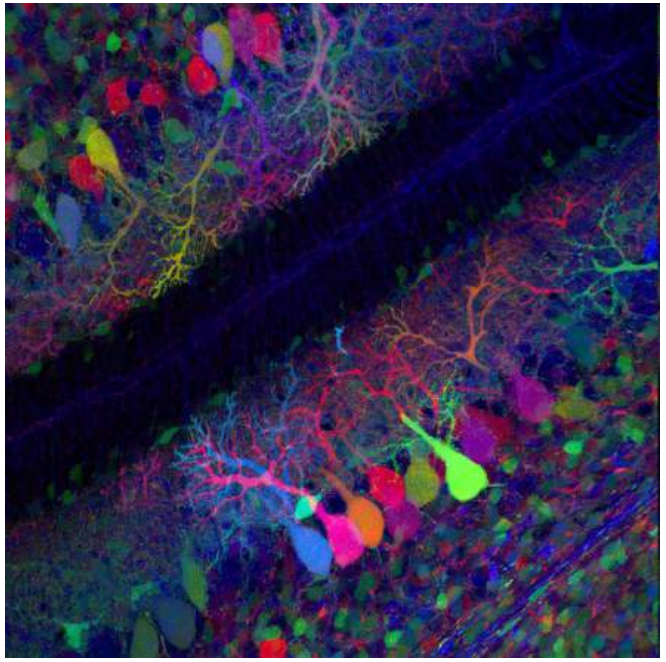




Rossi et al, J Neurophysiol 1995



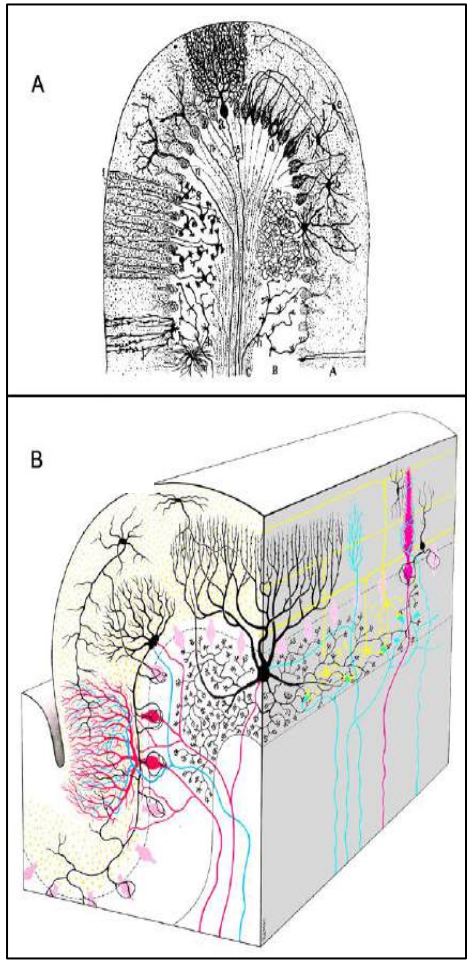
Jennifer Jahncke, Oregon Health & Science University



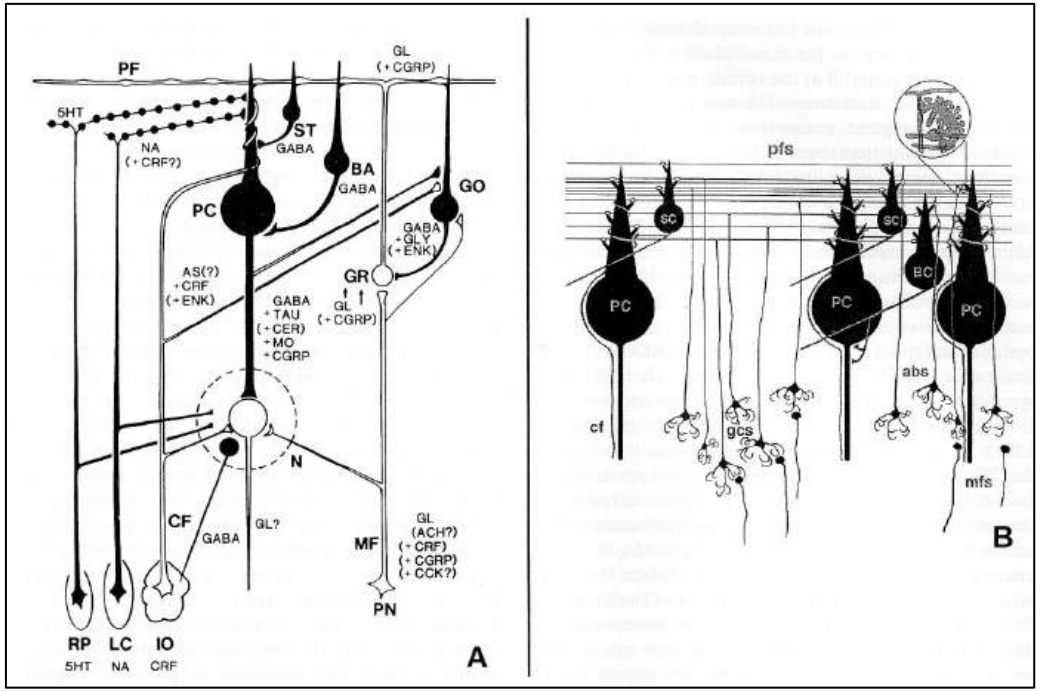
BRAINBOW PCs; Tamily Weisman

Photos by Jinny Sagorin

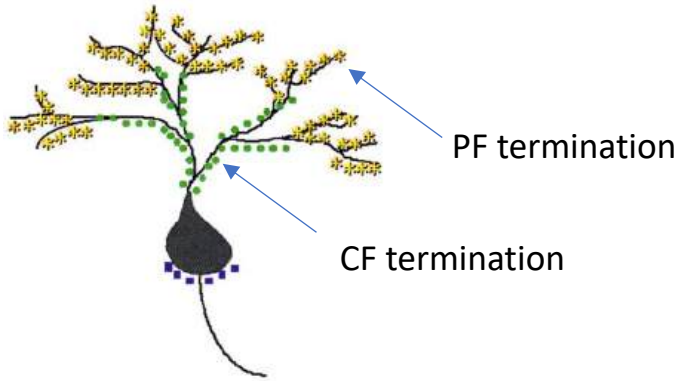
Schematics of cerebellar circuitry



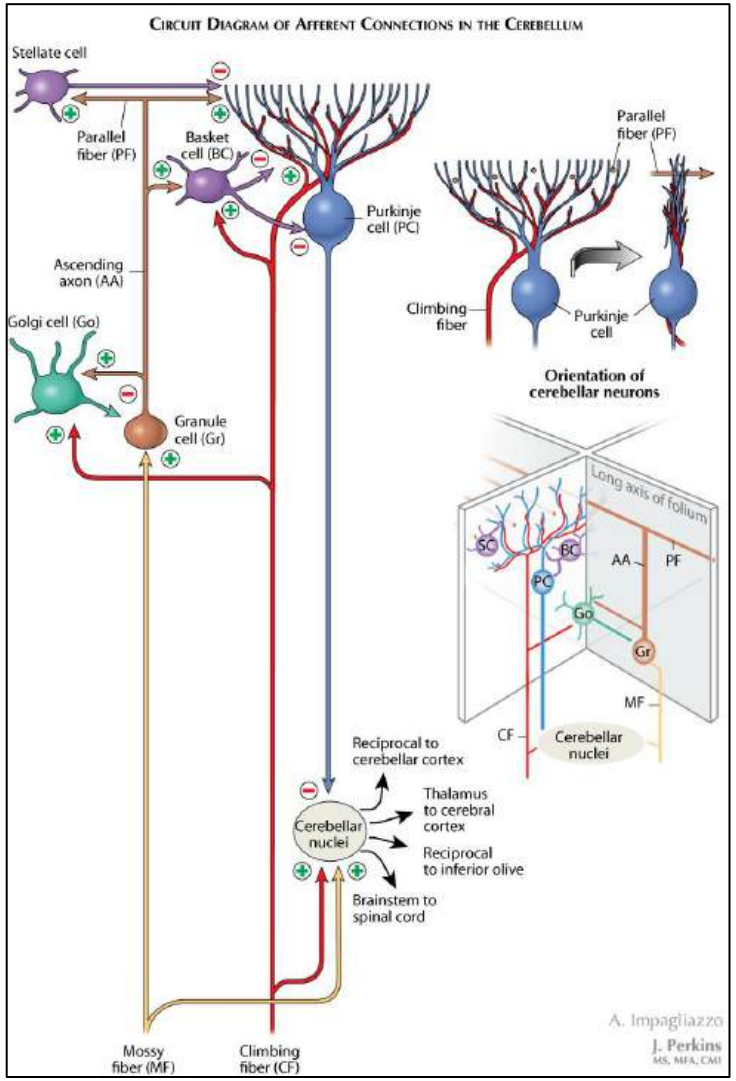
Eccles, Ito, Szentágothai, 1967



Ito, 1984; Bower, 1997

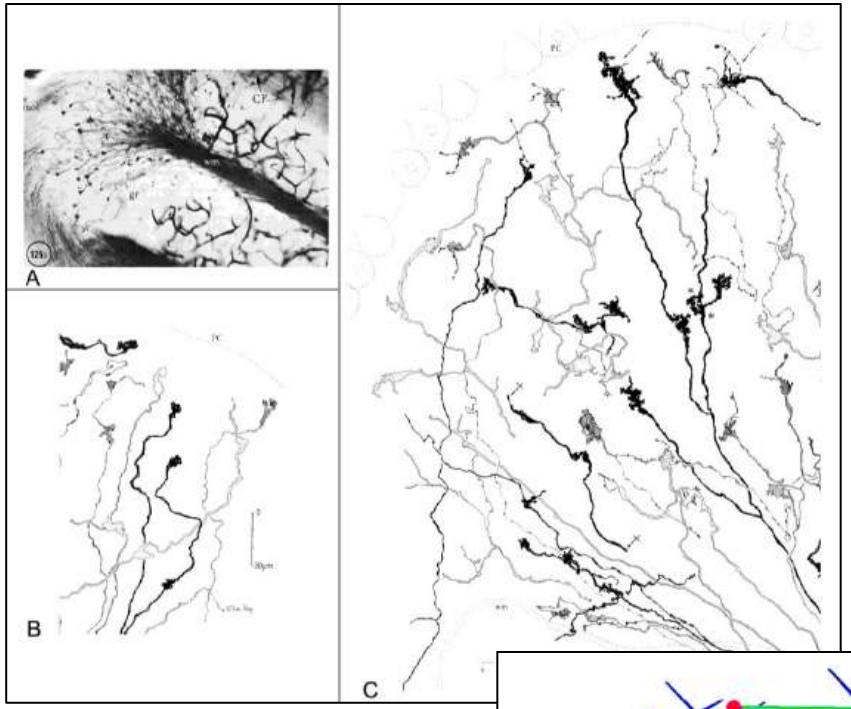


Oberdick et al., 1998



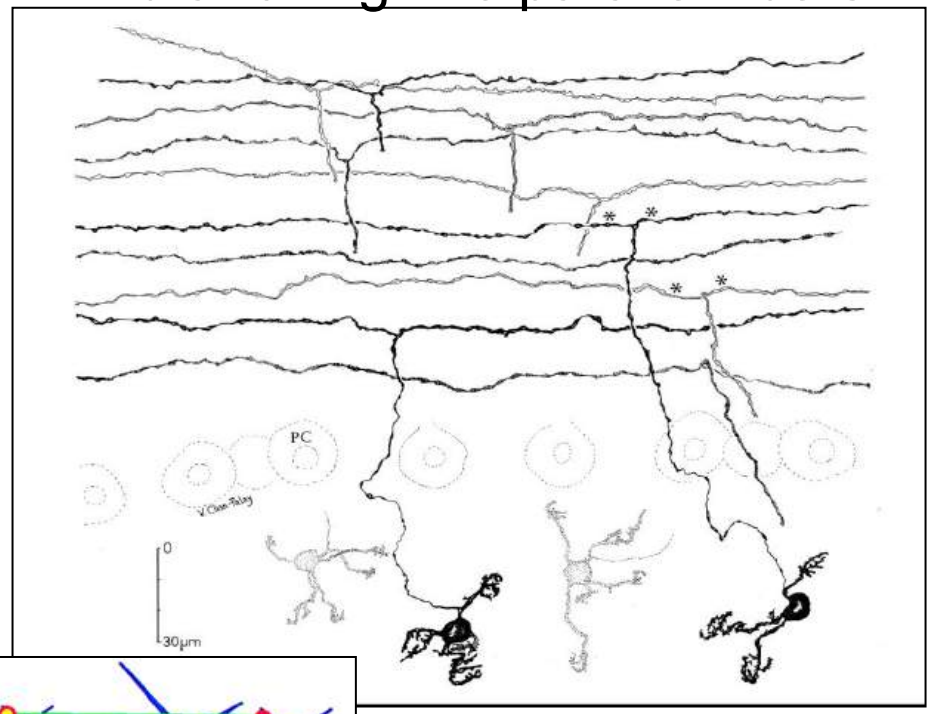
Netter, 2nd edition. Volume 7

Why they are called mossy fibers



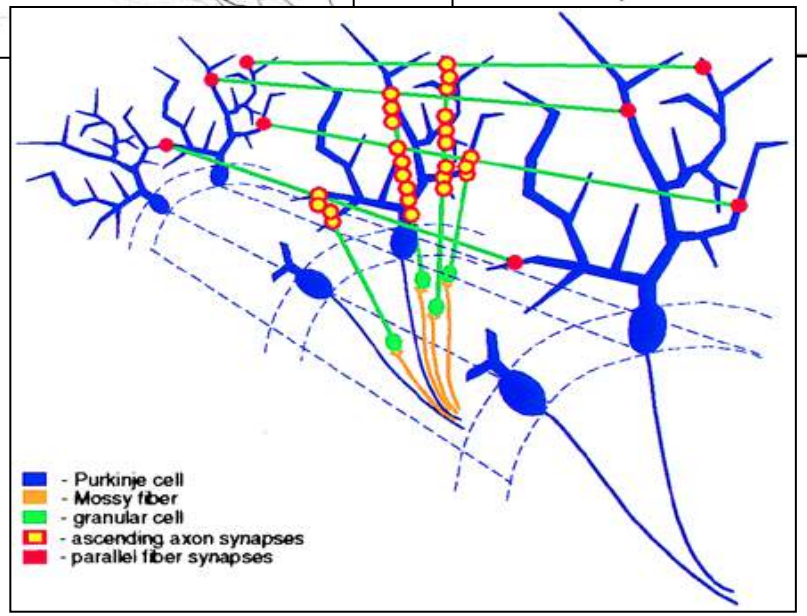
Palay and Chan Palay 1974

Granule cells, ascending axons branching into parallel fibers



Palay and Chan Palay 1974

Ascending granule cell axon

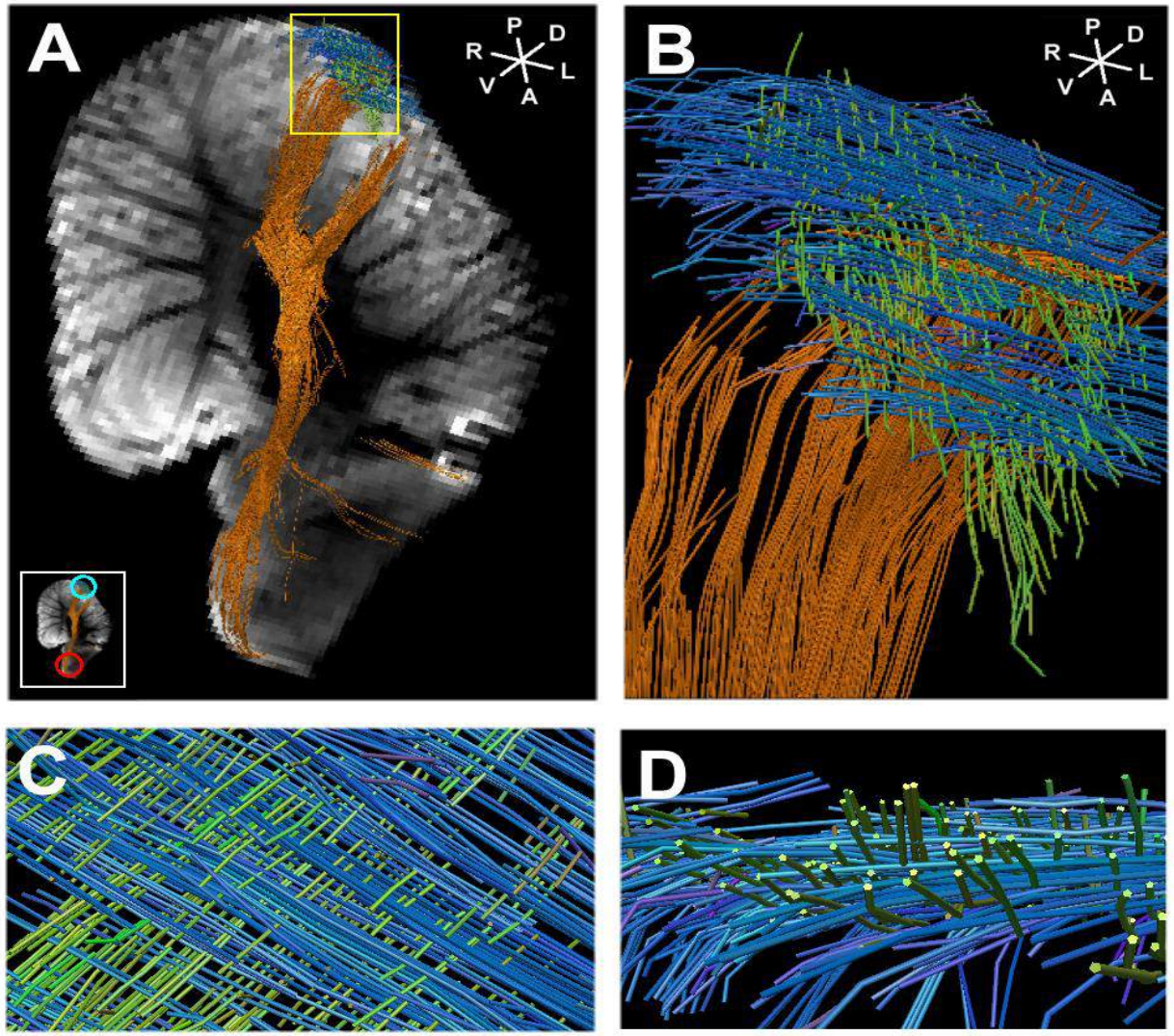


Cohen and Yarom. PNAS 1998

Diffusion spectrum imaging:

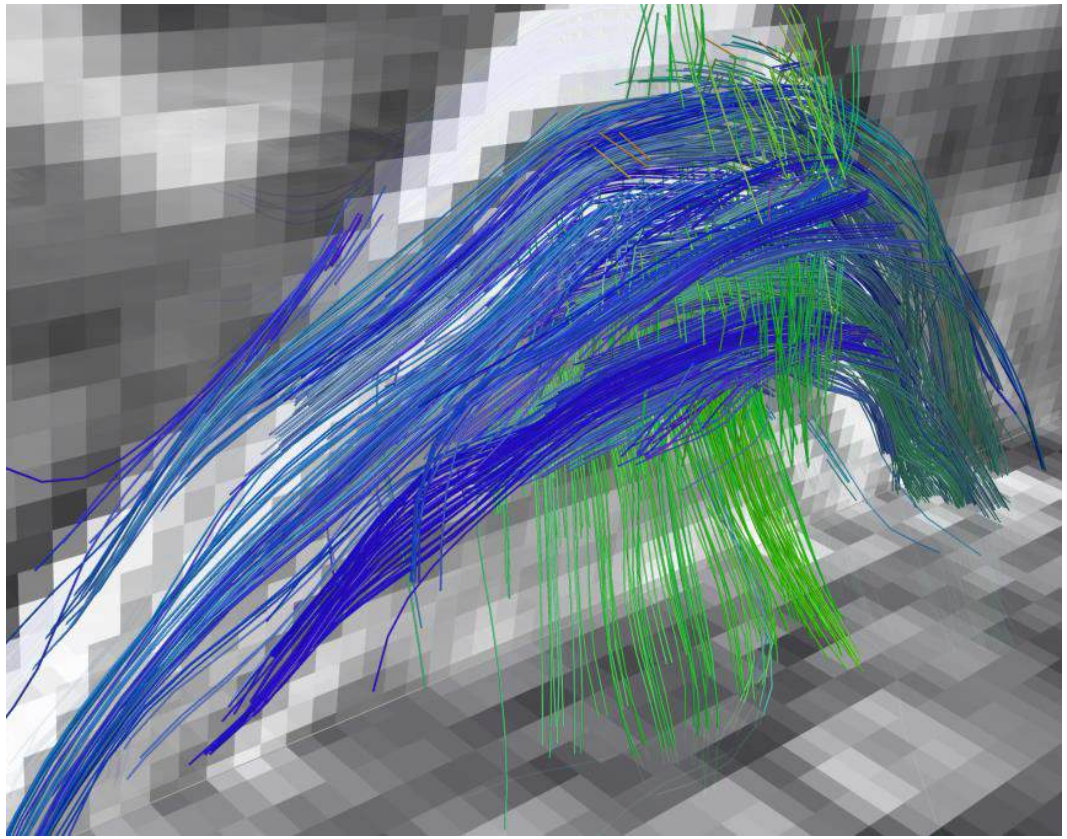
Orientation of parallel fibers and basket and stellate cell interneuron fibers

Human



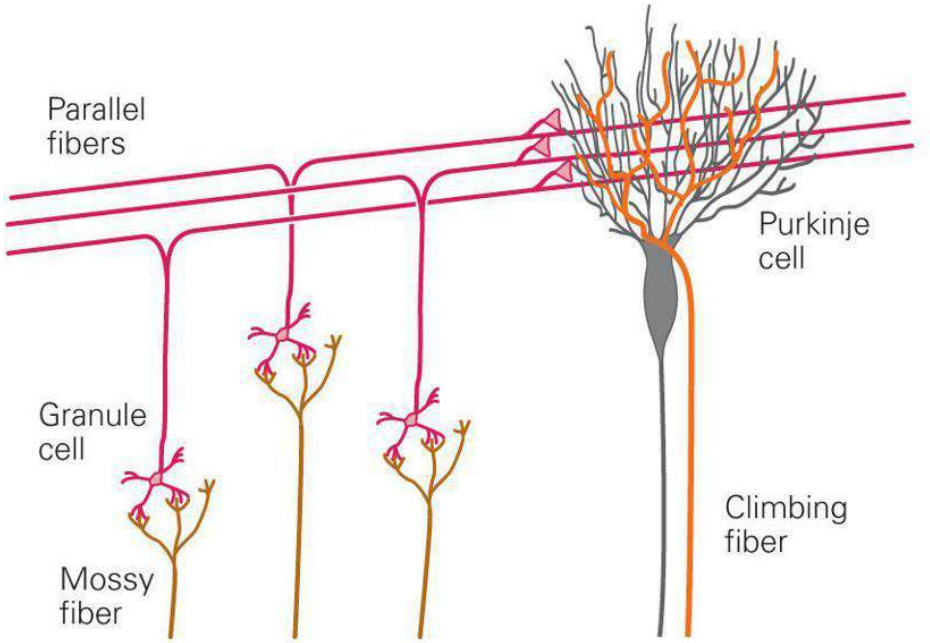
Takahashi E, Song JW, Folkerth RD, Grant PE, Schmahmann JD. 2013

Monkey



Wedeen, Schmahmann, Dai, Wang, Benner, Hagmann

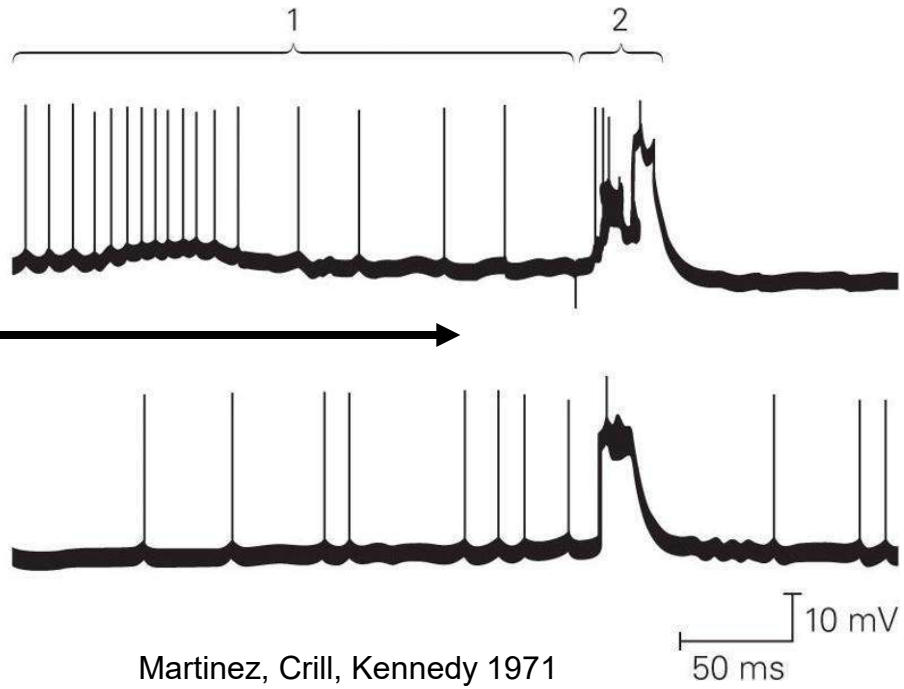
Parallel Fibers (from pons, spinal cord)
Climbing Fibers (from inferior olive)



PC Simples spikes, ~ 50Hz
Evoked by parallel fiber input
= Context

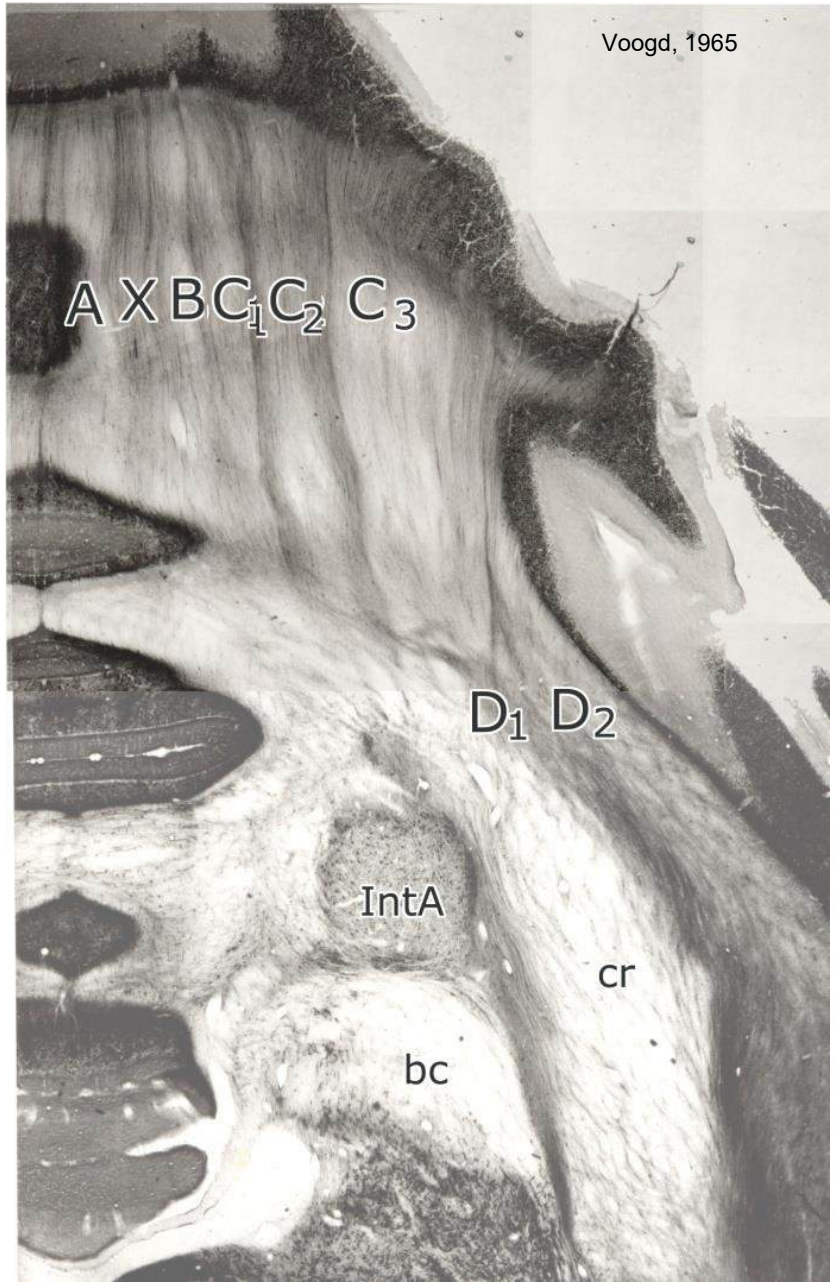
PC Complex spikes ~ 1 Hz
Evoked by climbing fiber input
= Error signal

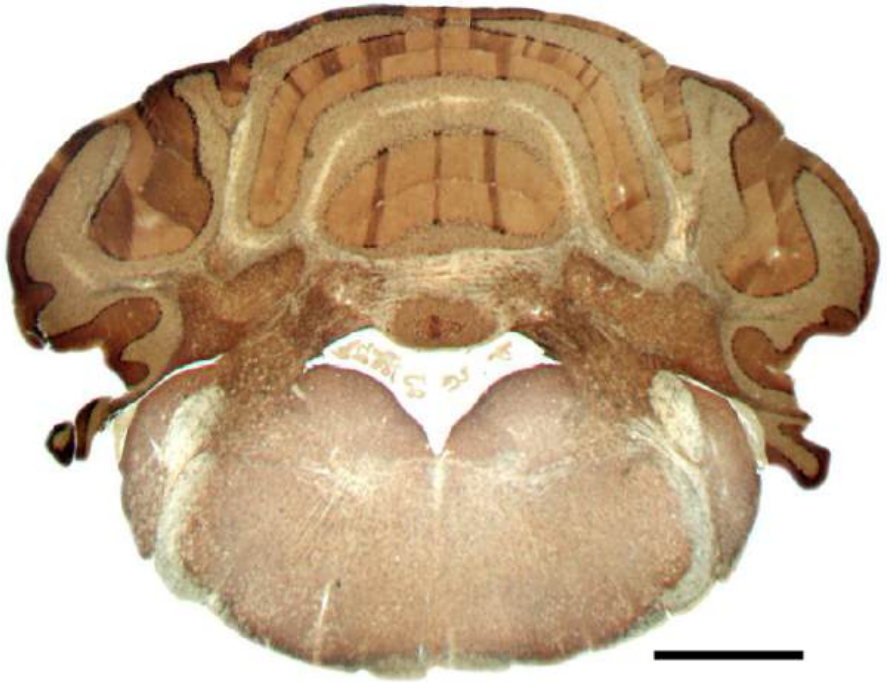
Interaction between these underlies cerebellar cortical information processing



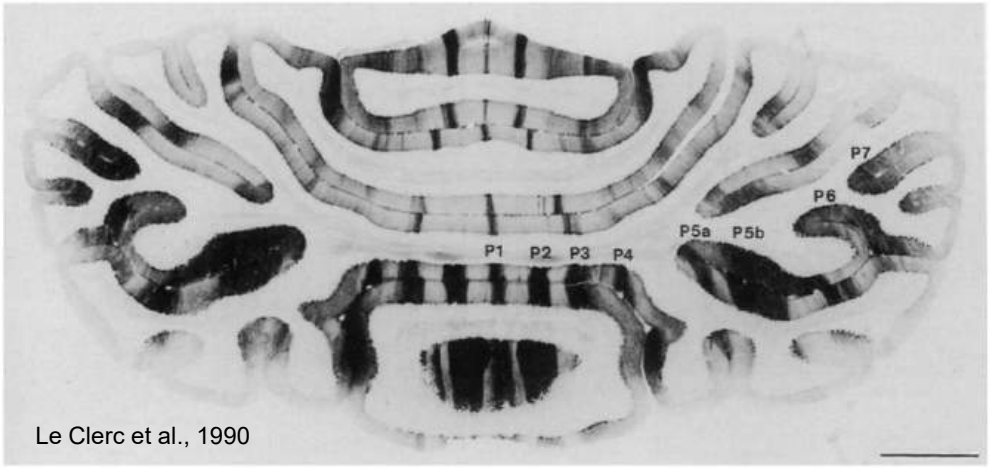
Martinez, Crill, Kennedy 1971

Parasagittal zonation in the cerebellum (zebrin bands)



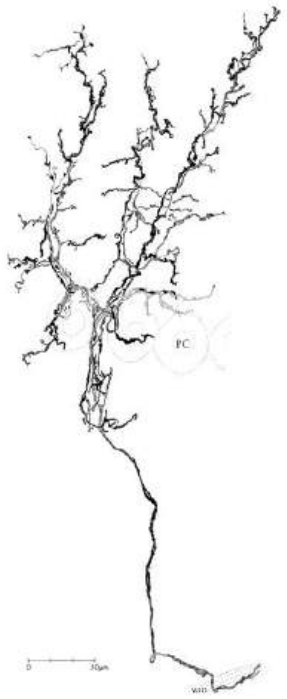


Courtesy of Richard Hawkes, 1999



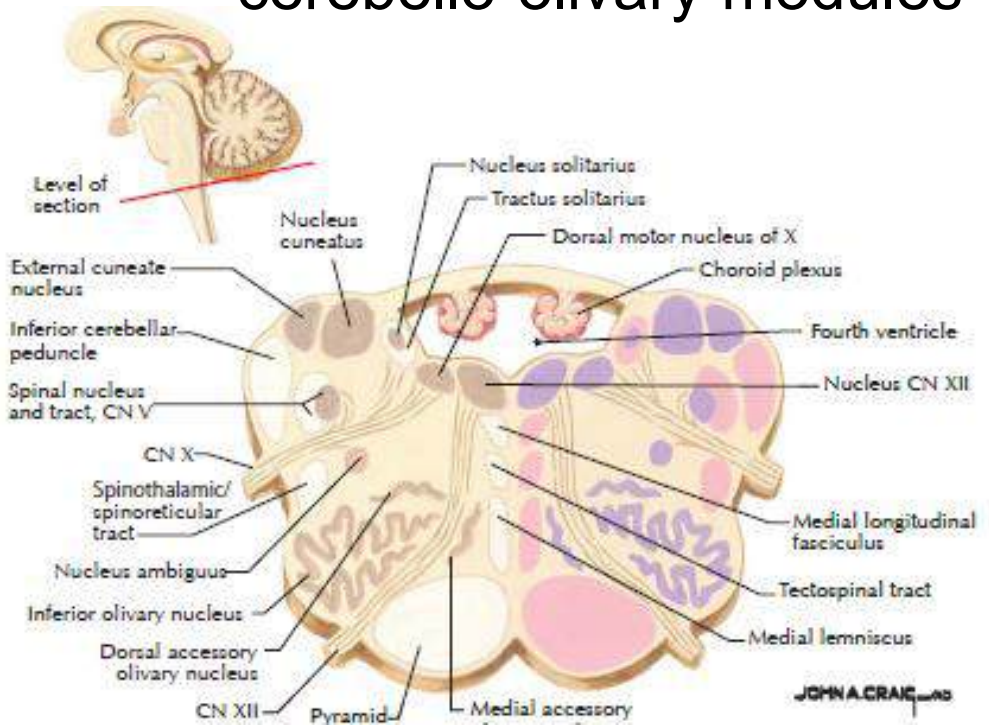
Le Clerc et al., 1990

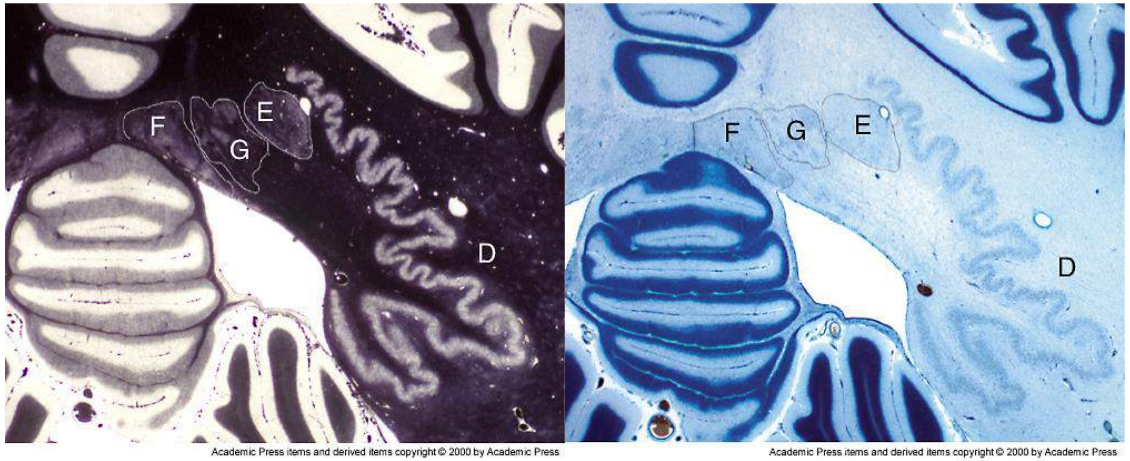
Climbing fiber

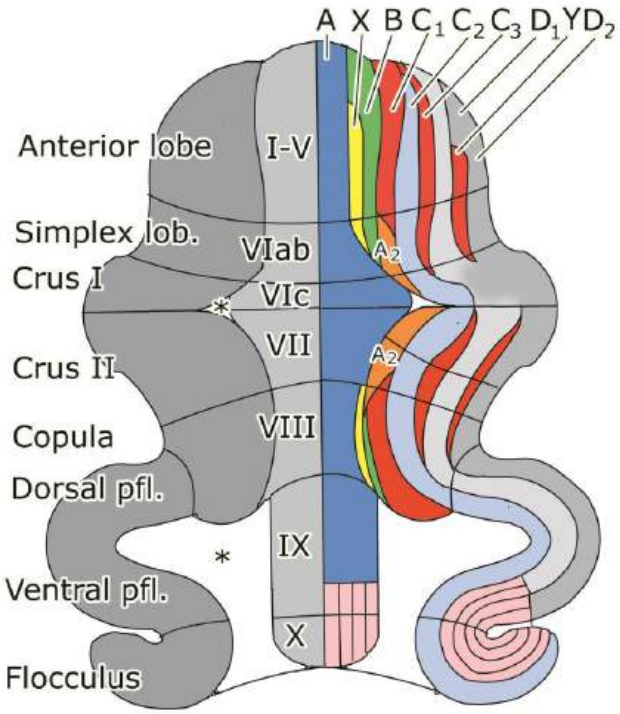


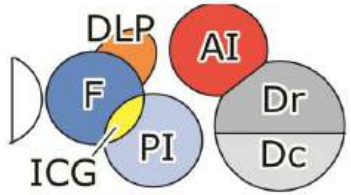
Palay and
Chan Palay 1974

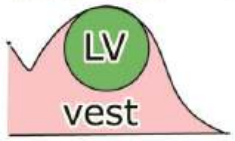
Corticonuclear microcomplexes; cerebello-olivary modules

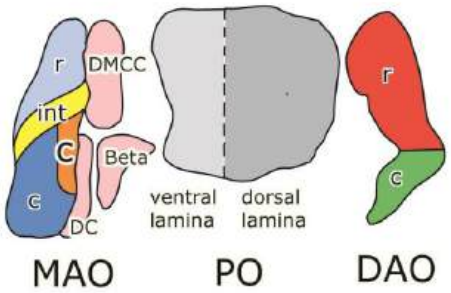






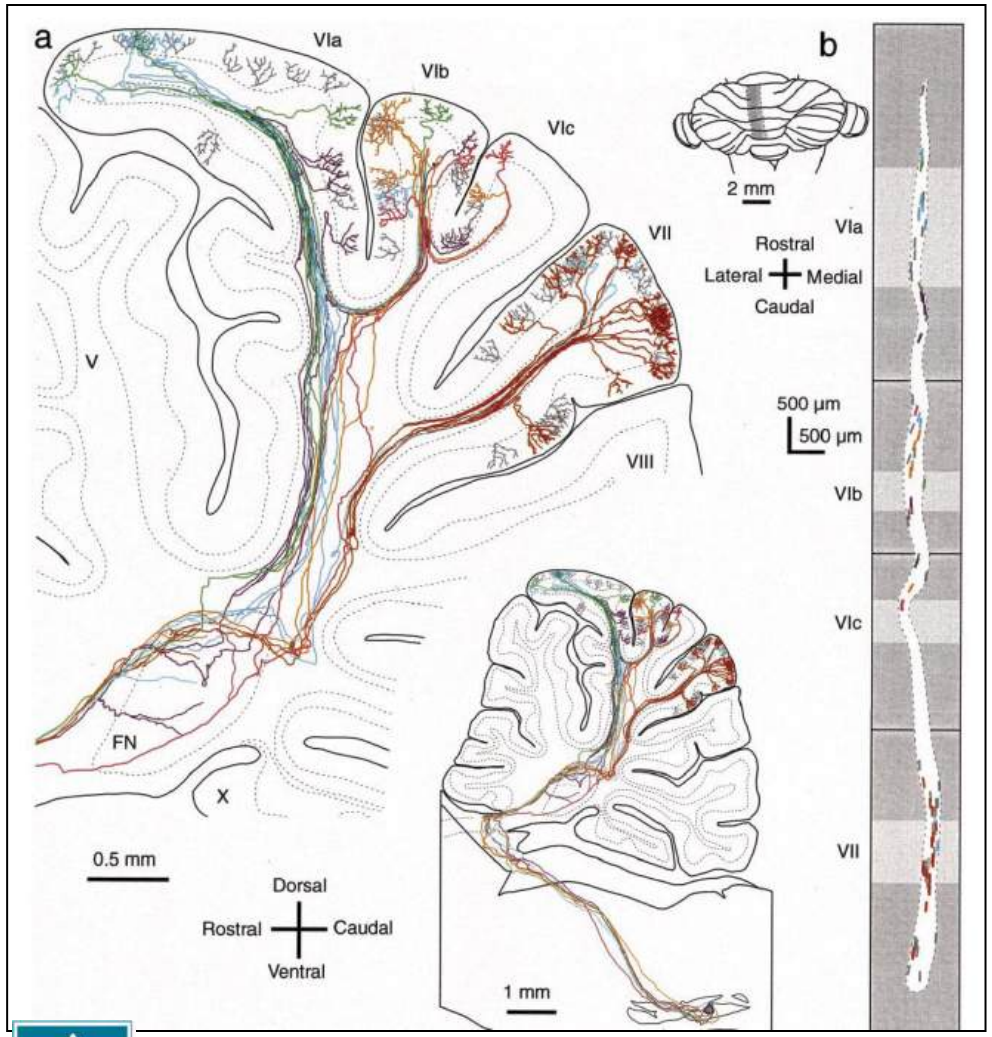


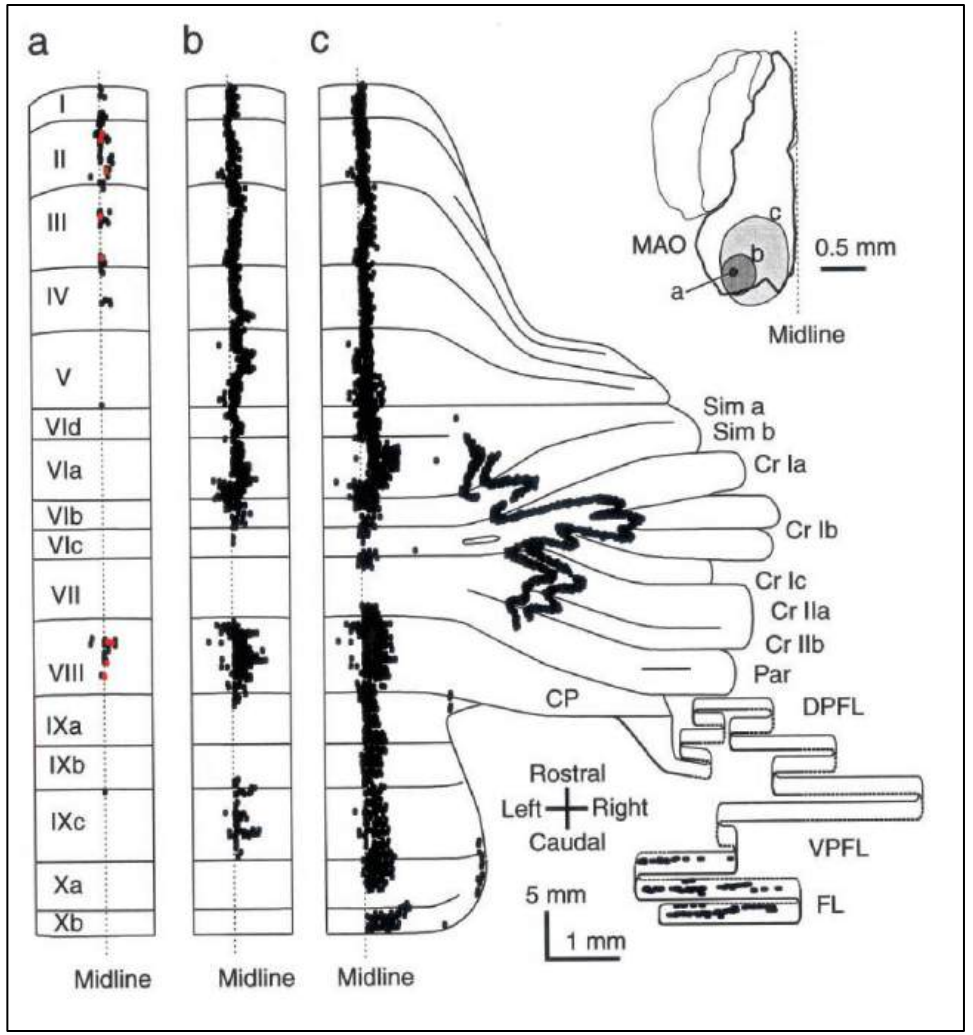


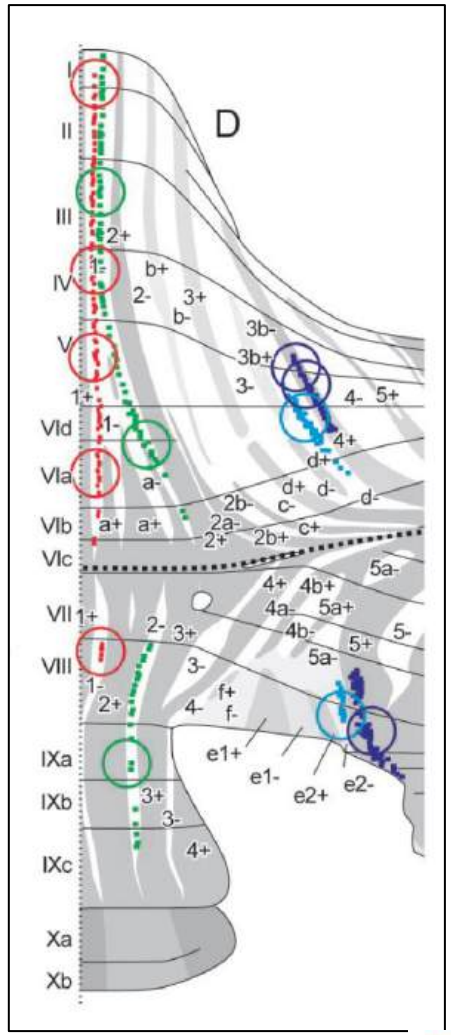


Schmahmann et al., 2000; Voogd, 1965; Voogd and Glickstein, 1998;

Olivocerebellar axons branch to ~7 climbing fibers, terminations clustered in a single narrow longitudinal band / parasagittal zone across one or multiple lobules, respecting zebrin band architecture. Transverse branching between vermis compartments.

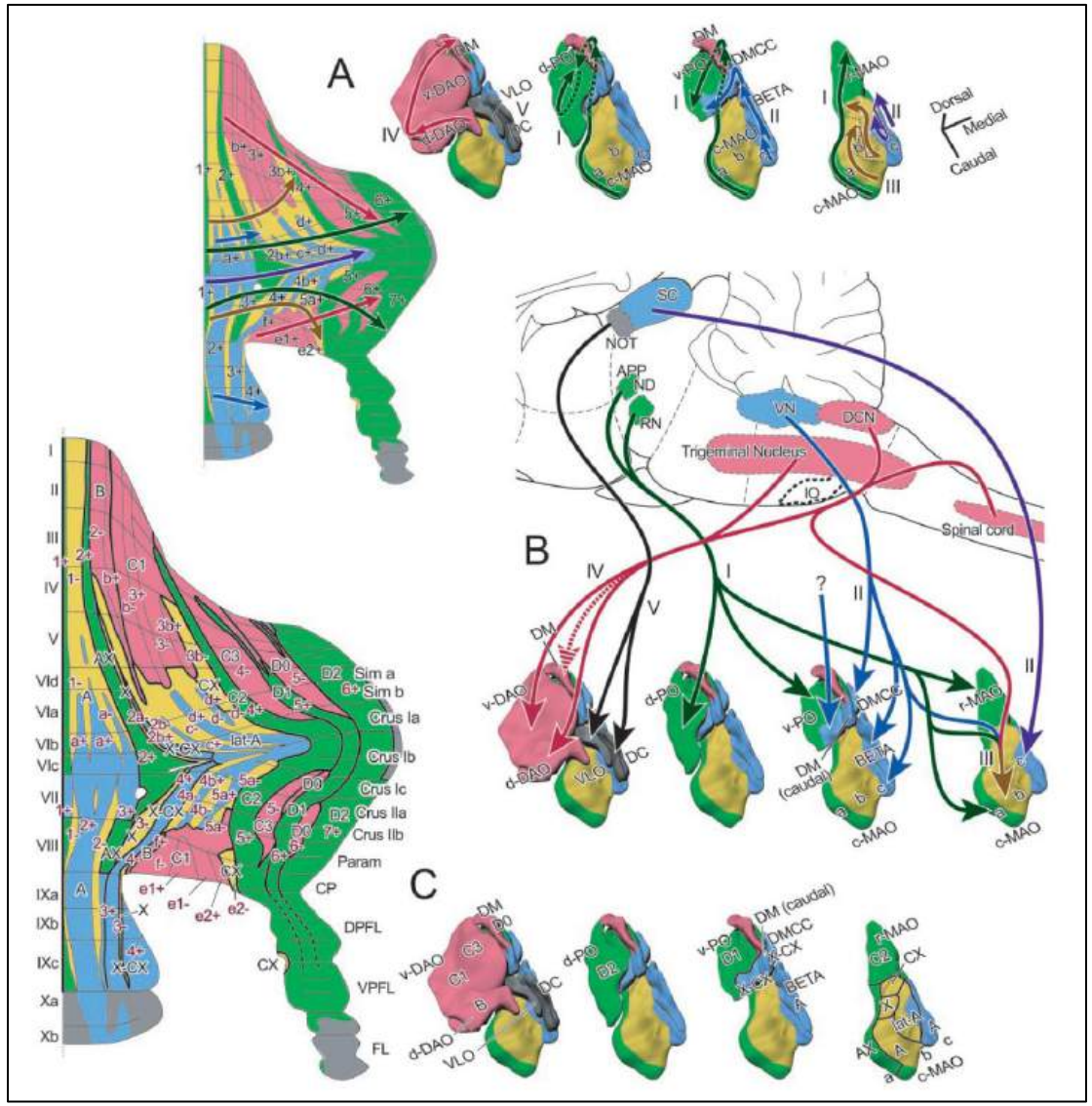




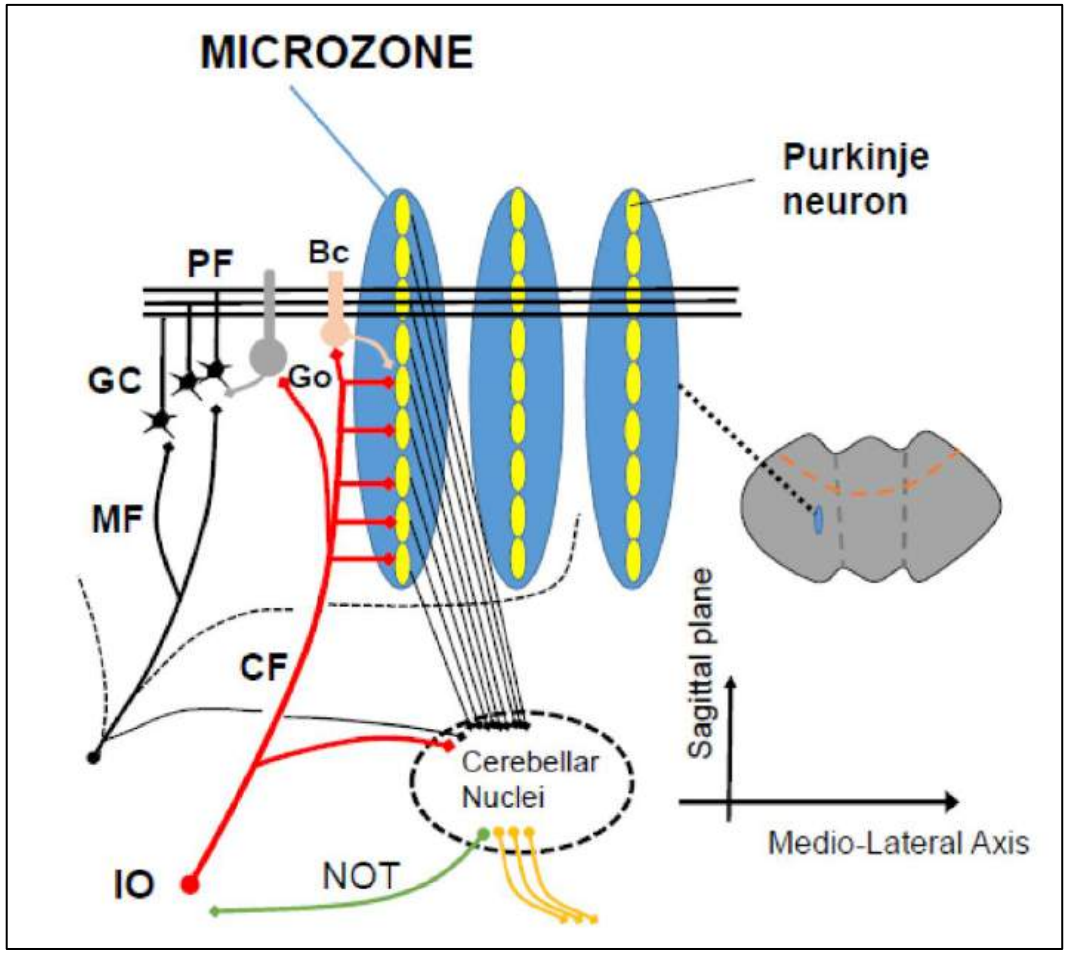


Sugihara I, Wu HS, Shinoda Y. J Neurosci. 2001 Oct 1;21(19):7715-23.
Sugihara I, Shinoda Y. J Neurosci. 2004 Oct 6;24(40):8771-85. Fujita and Sugihara, 2013

Olivocerebellar connections; microzones in cerebellar cortex

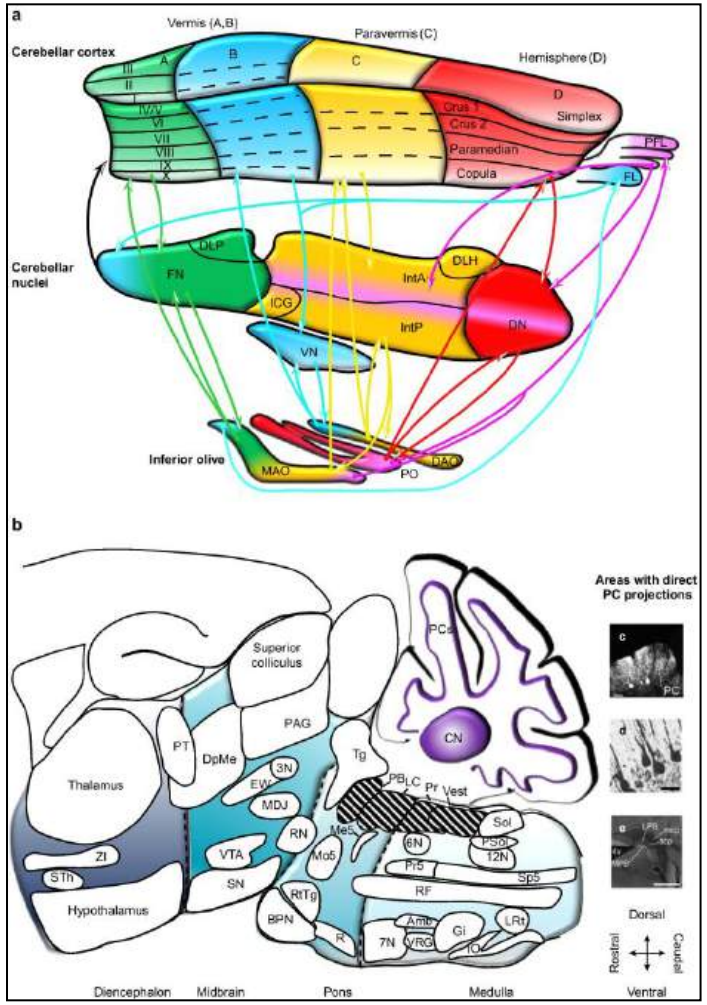


Sugihara I, Wu HS, Shinoda Y. J Neurosci. 2001 Oct 1;21(19):7715-23.
Sugihara I, Shinoda Y. J Neurosci. 2004 Oct 6;24(40):8771-85. Fujita and Sugihara, 2013

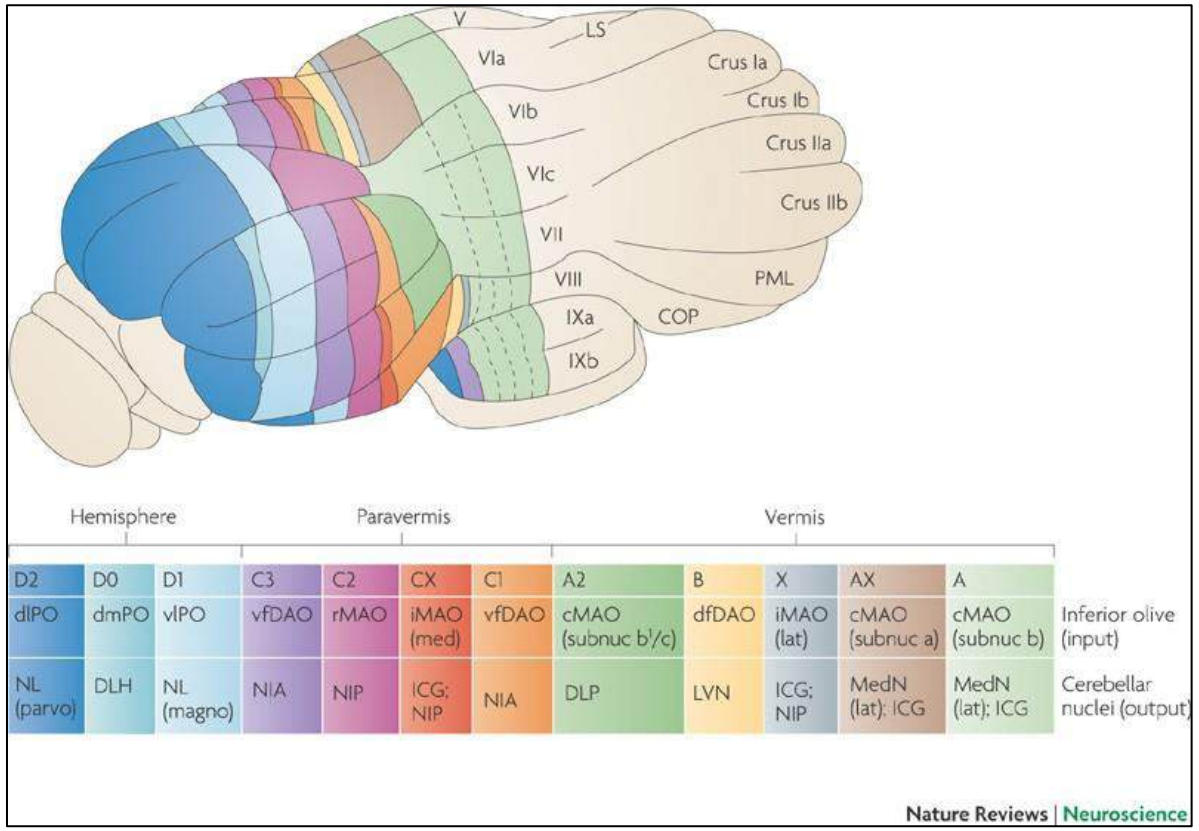


Mitoma H, Kakei S, Yamaguchi K, Manto M. Physiology of Cerebellar Reserve: Redundancy and Plasticity of a Modular Machine. Int J Mol Sci. 2021 Apr 30;22(9):4777.

Climbing fibers organized in parasagittal microzones tracking zebrin stripes, enables cerebellar modular organization for error signaling, motor learning, domain-specific processing - motor, cognitive, emotional.
Z− higher simple spike rates, greater plasticity (e.g., LTD), phasic
Z+ lower baseline firing, tonic/modulatory



Novello M, Bosman LWJ, De Zeeuw CI. CA Cerebellum. 2024 Feb;23(1):210-239.

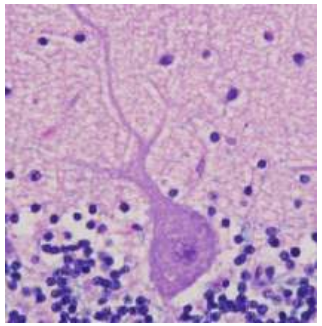


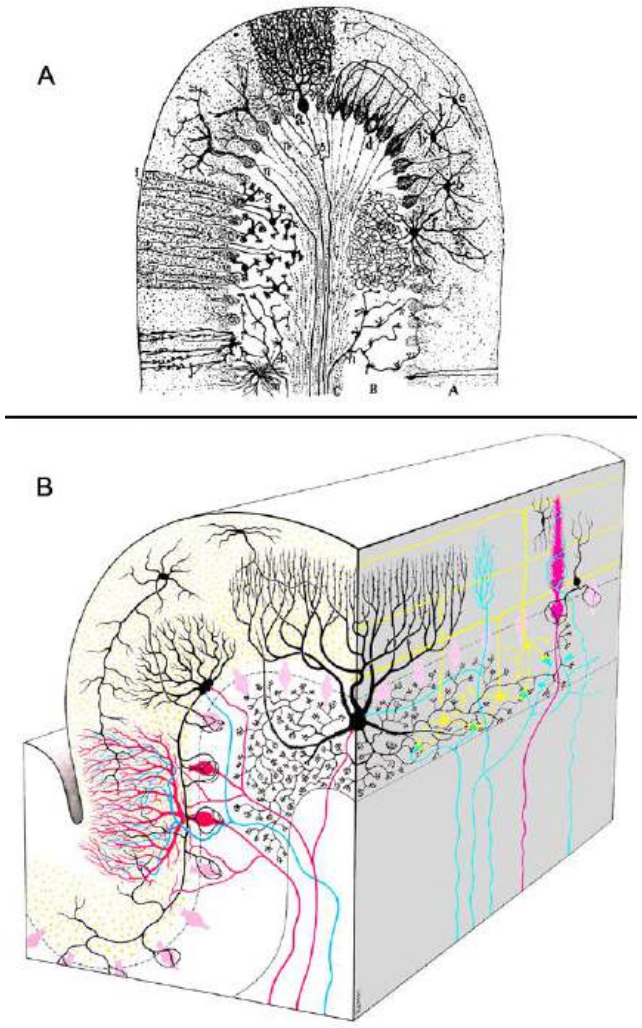
Apps R, Hawkes R. Cerebellar cortical organization: a one-map hypothesis. Nat Rev Neurosci. 2009 Sep;10(9):670-81.

Cerebellar histology is essentially consistent throughout

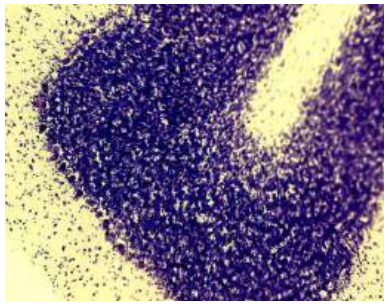
The computing power of the cerebellum which contains 70 - 80% of the brain's neurons is applied to almost every domain of neurological function.

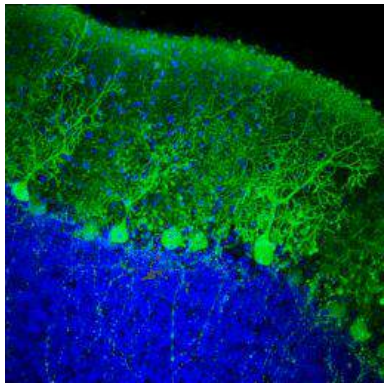
Santiago Ramon y Cajal,1911
vocesdelaciencia.com.ar





Eccles, Ito, Szentágothai, 1967

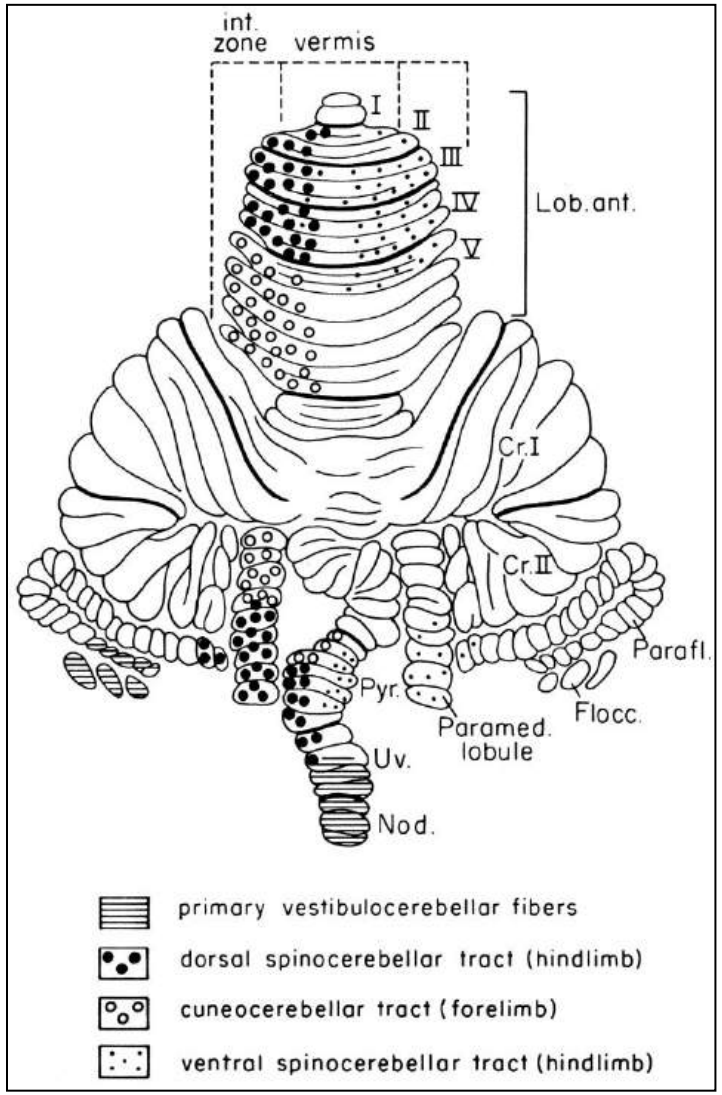


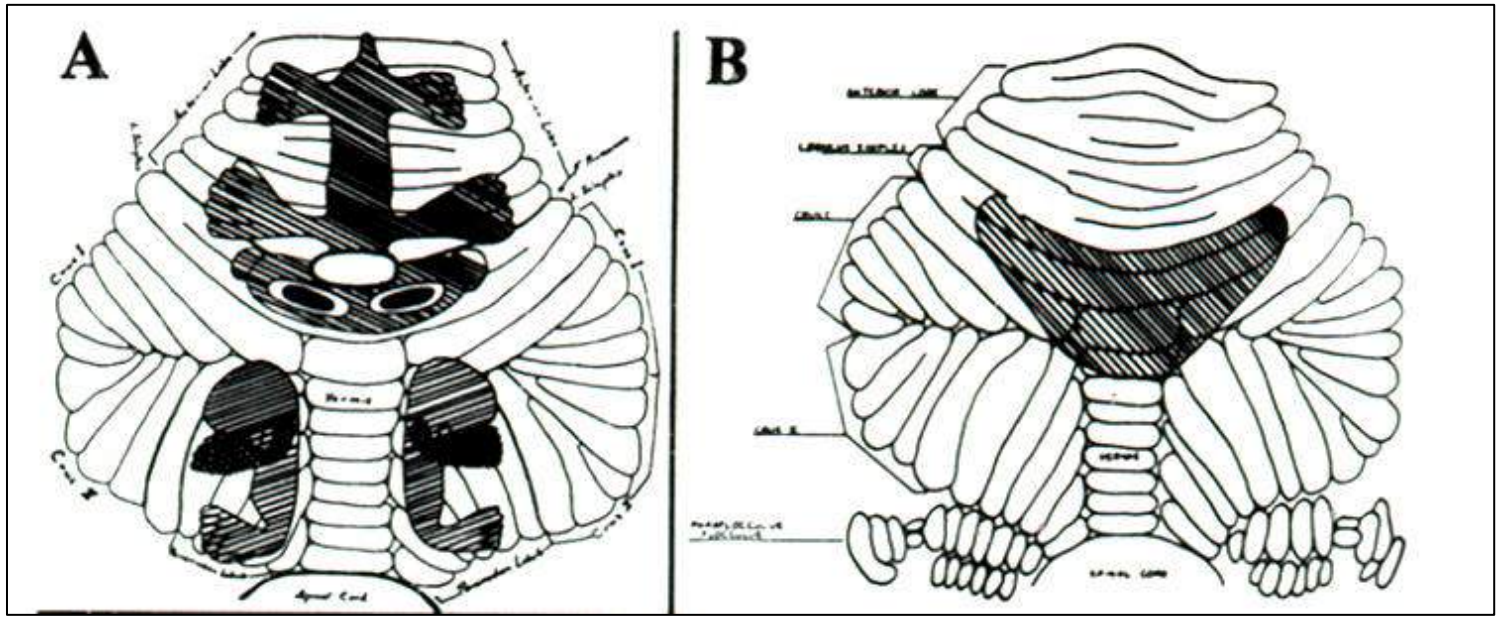


The mostly invariant architecture of the cerebellar cortex contrasts with the heterogeneity of cerebellar connections with extracerebellar structures

Schmahmann et al., 2019

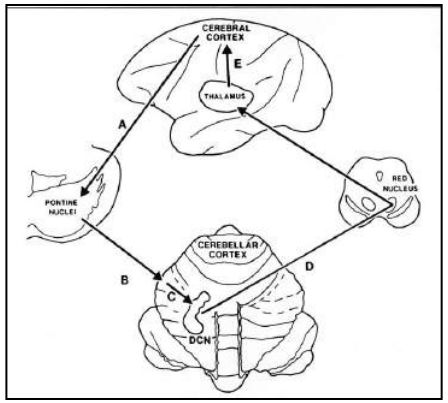
Functional topography shapes the understanding of cerebellar neurobiology and disease



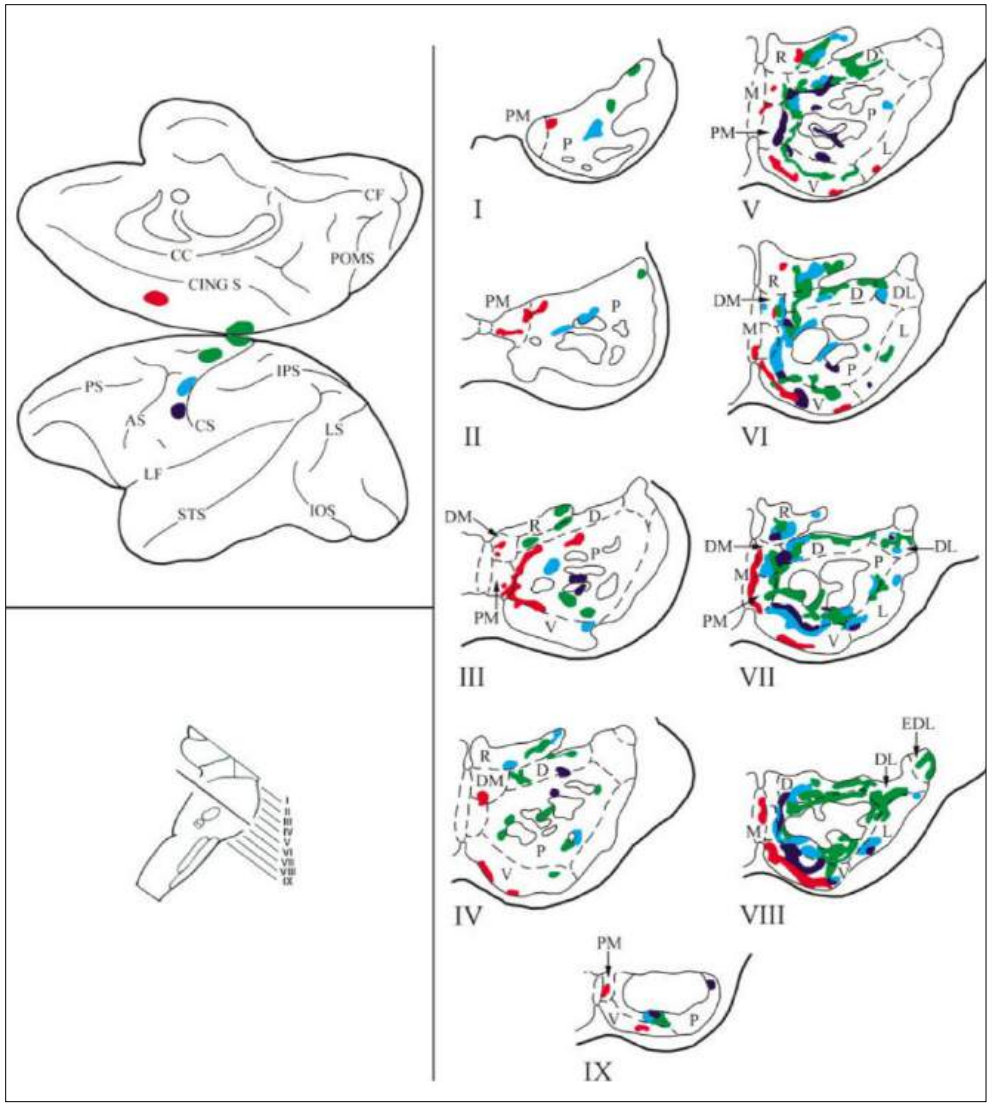


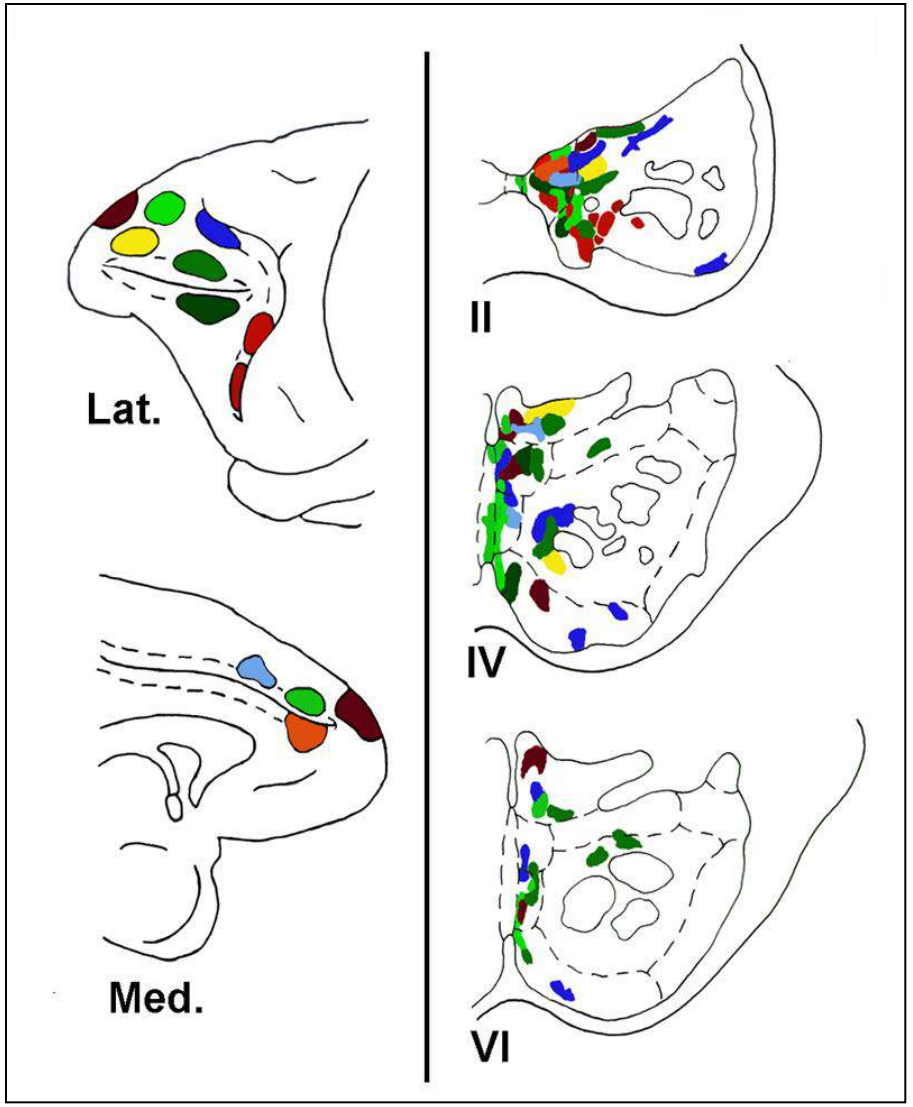
Snider and Stowell, 1946
Snider, 1950
Snider and Eldred, 1951

Corticopontine projections in rhesus monkey



Deepak Pandya





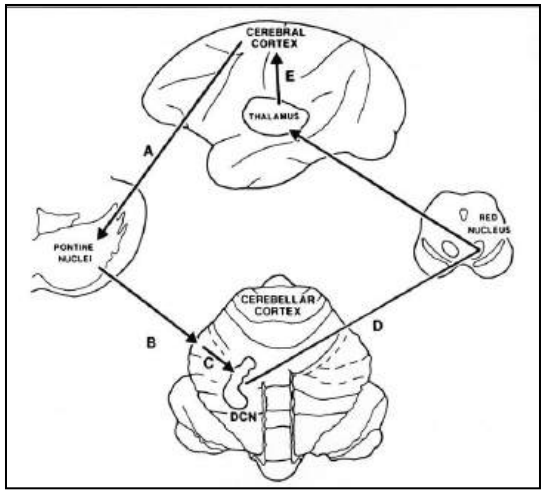
Motor projections

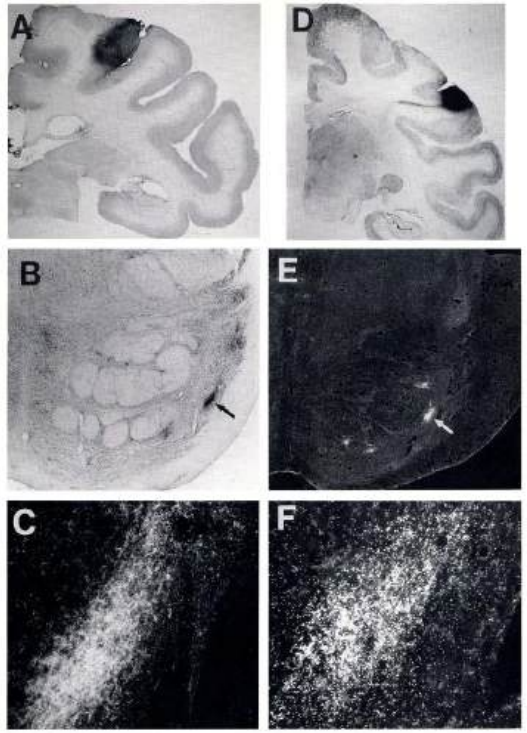
Schmahmann, Rosene, Pandya. J Comp Neurol, 2004

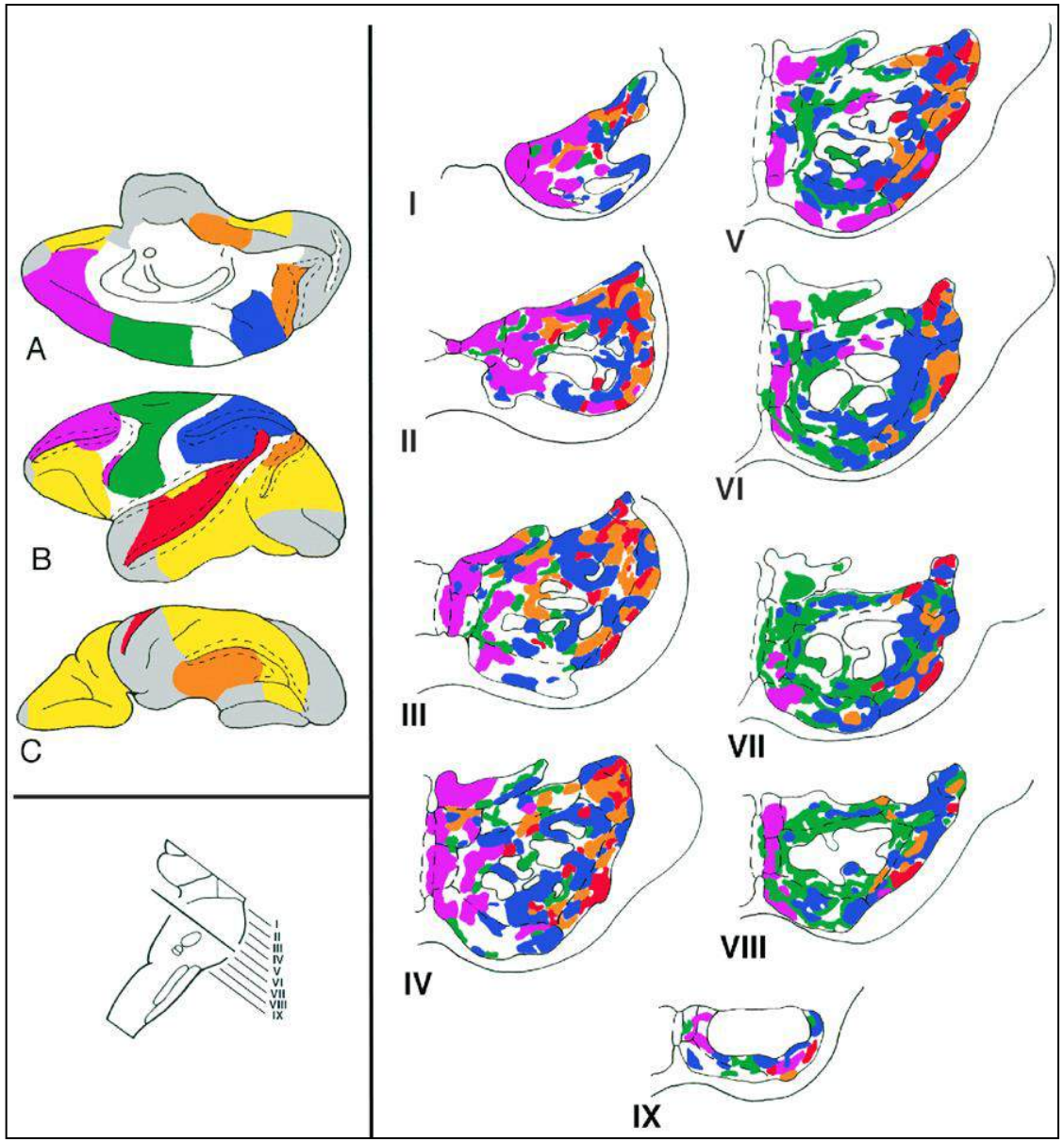
Prefrontal projections

Schmahmann and Pandya, Neurosci Let, 1995; J Neurosci 1997

Cerebro-cerebellar circuits: Feedforward limb





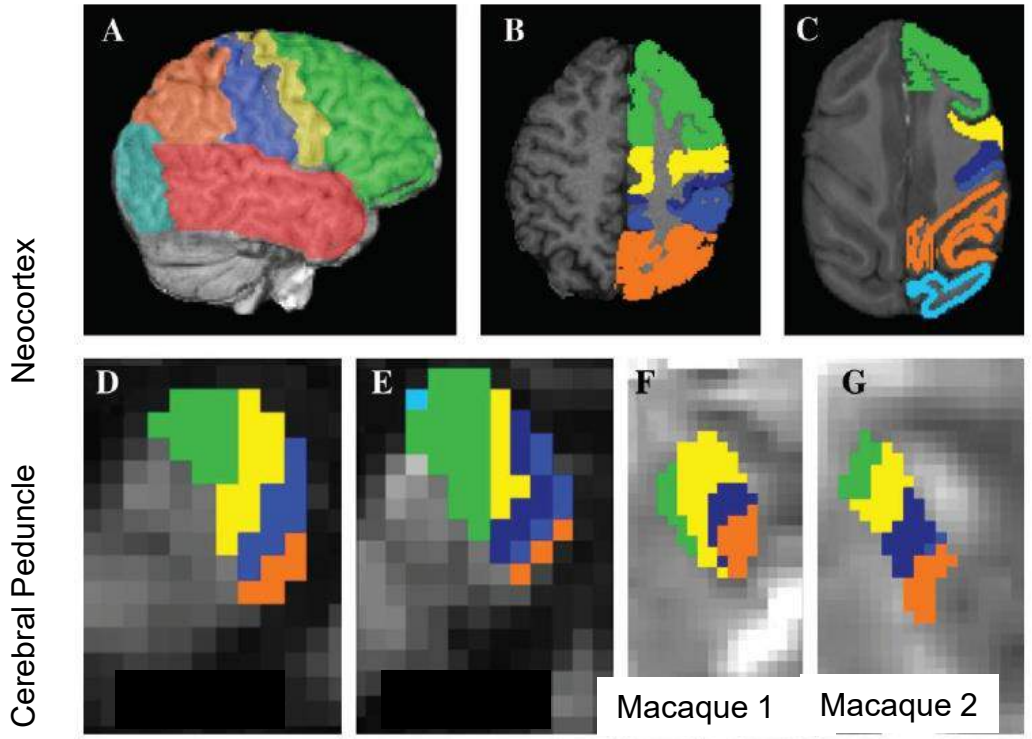


Schmahmann and Pandya. Neurology, 1987. Int Rev Neurobiol, 1997, based on J Comp Neurol 1989, 1991, 1992, 1993, 1997, 2004; Schmahmann, Hum Brain Mapp, 1996

Evolution of corticopontine inputs

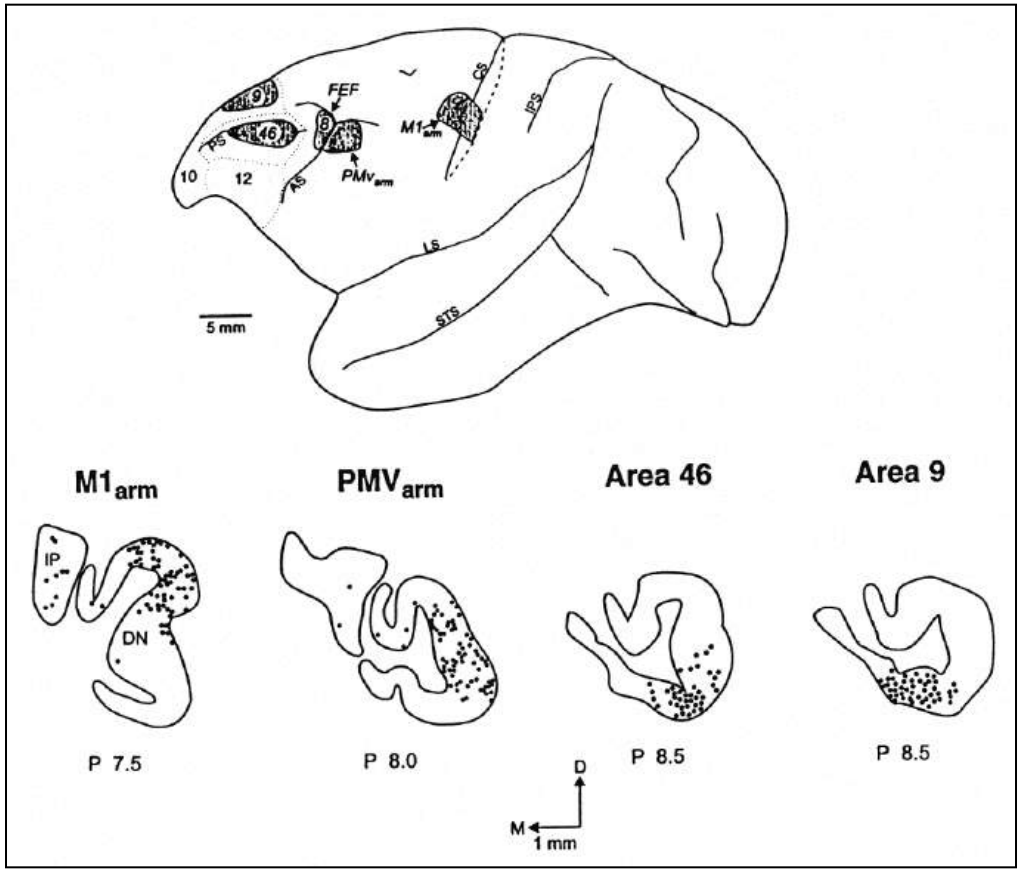
Fiber tracking (Diffusion MRI): Segmenting the **cerebral peduncle**
on the basis of fibers of origin

Prefrontal cortex Premotor cortex Primary motor cortex	Largest segment in <u>human</u> Largest segment in <u>macaque</u>

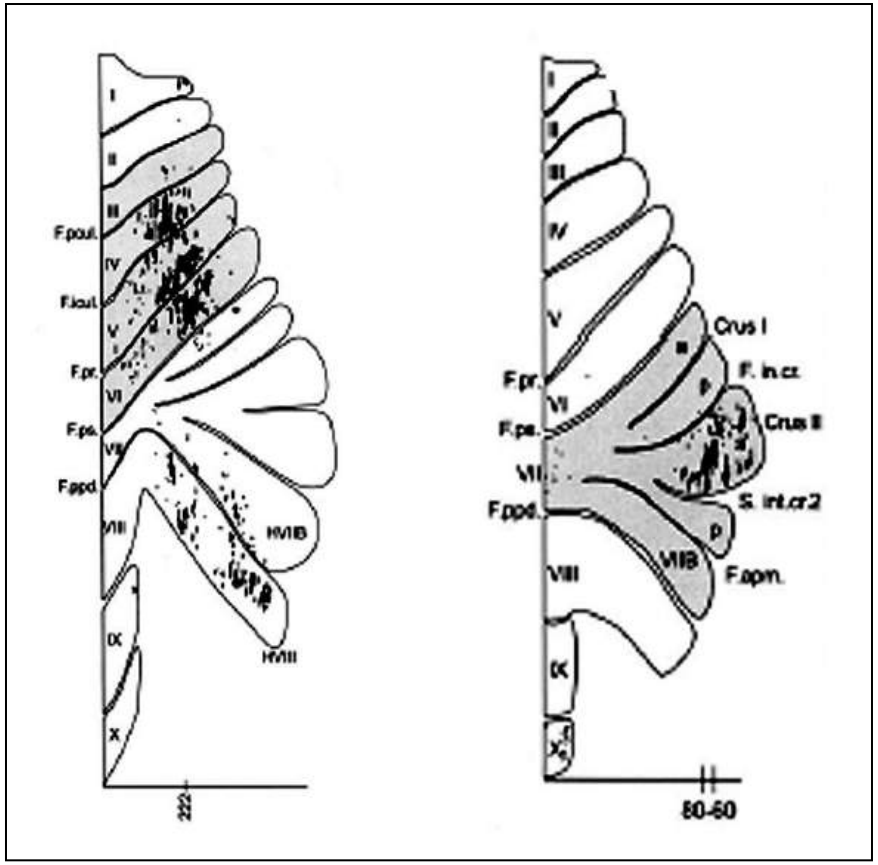


Ramnani et al. Cerebral Cortex 2004;16:811-818

Cerebro-cerebellar circuits: Feedback limb



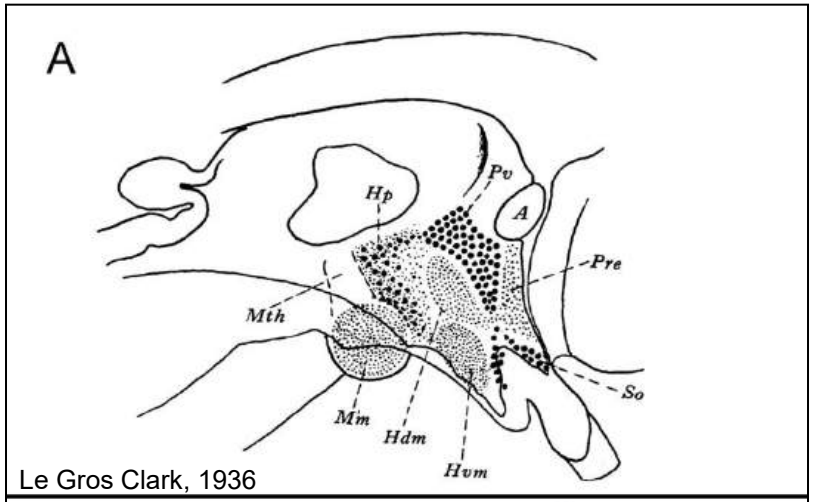
M1 **Area 46**



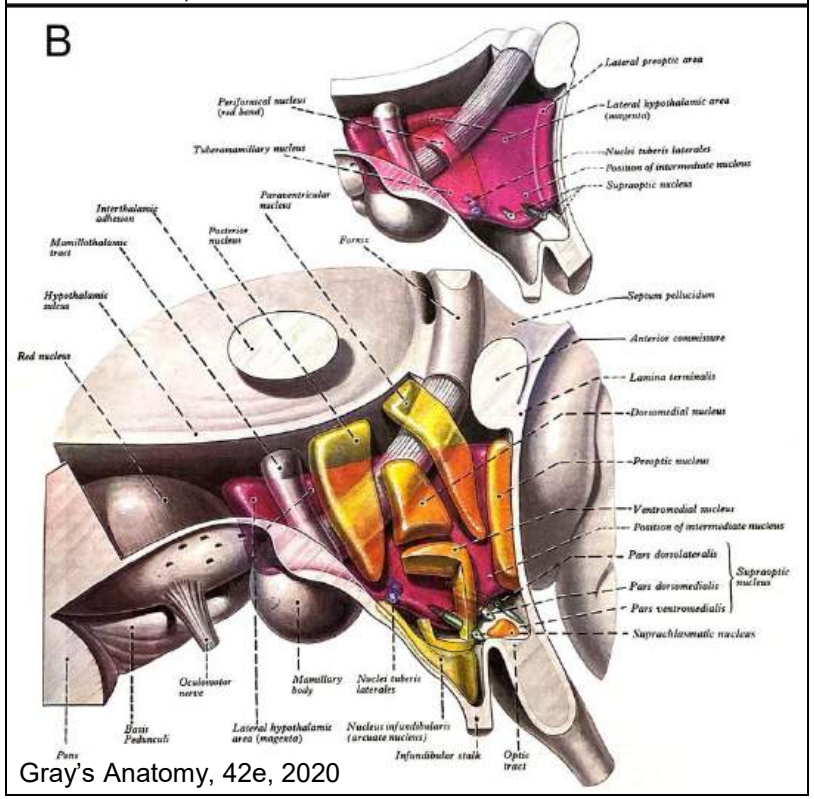
Middleton and Strick. Science, 1994

Kelly and Strick. J Neurosci, 2003

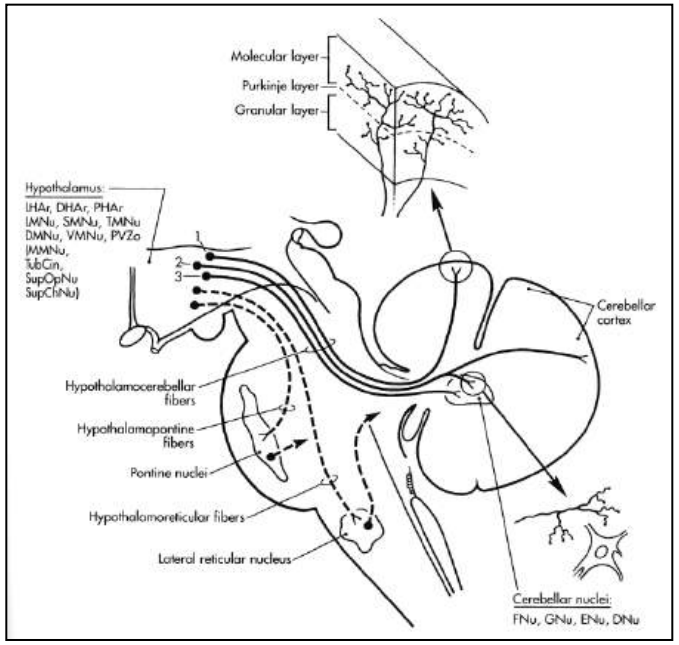
Hypothalamocerebellar connections

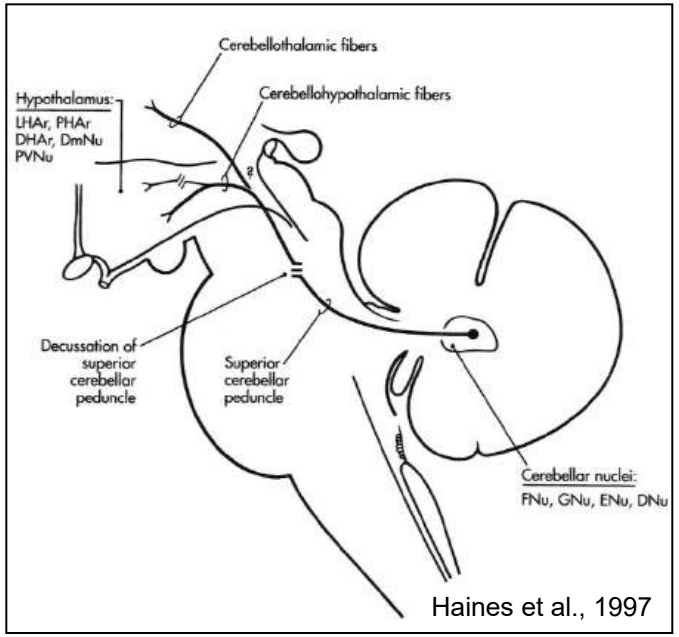


Le Gros Clark, 1936



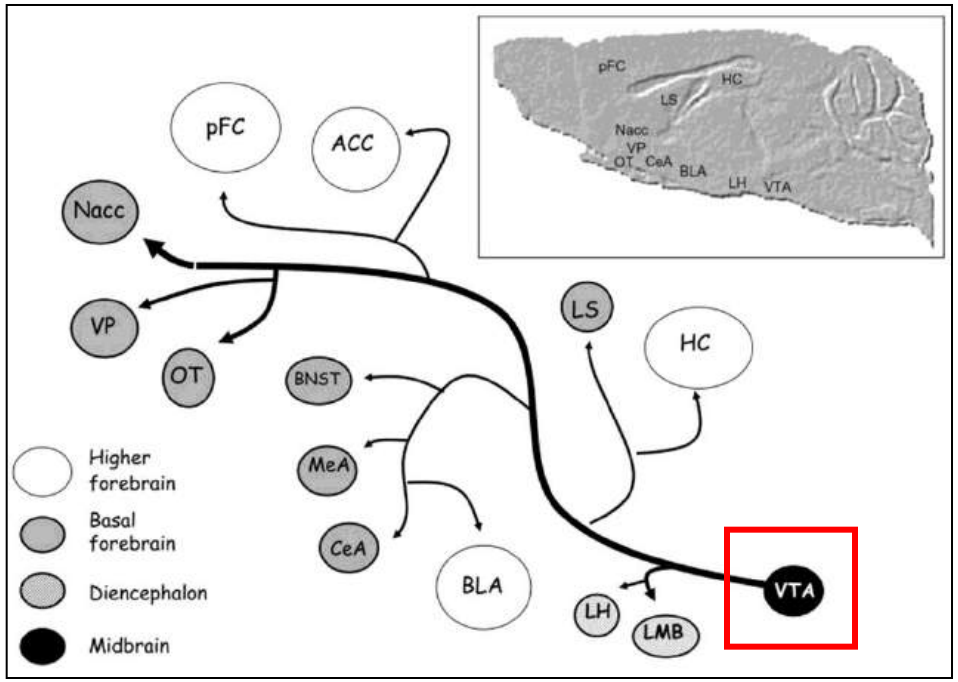
Gray's Anatomy, 42e, 2020





Haines et al., 1997

Ventral tegmental area: mesolimbic dopaminergic system



From Alcaro et al., 2007

Cerebellar modulation of the reward circuitry and social behavior

Ilaria Carta[1*], Christopher H. Chen[1*], Amanda L. Schott[1], Schnaude Dorizan[1], Kamran Khodakhah[1,2,3†]

The cerebellum has been implicated in a number of nonmotor mental disorders such as autism spectrum disorder, schizophrenia, and addiction. However, its contribution to these disorders is not well understood. In mice, we found that the cerebellum sends direct excitatory projections to the ventral tegmental area (VTA), one of the brain regions that processes and encodes reward. Optogenetic activation of the cerebello-VTA projections was rewarding and, in a three-chamber social task, these projections were more active when the animal explored the social chamber. Intriguingly, activity in the cerebello-VTA pathway was required for the mice to show social preference in this task. Our data delineate a major, previously unappreciated role for the cerebellum in controlling the reward circuitry and social behavior.

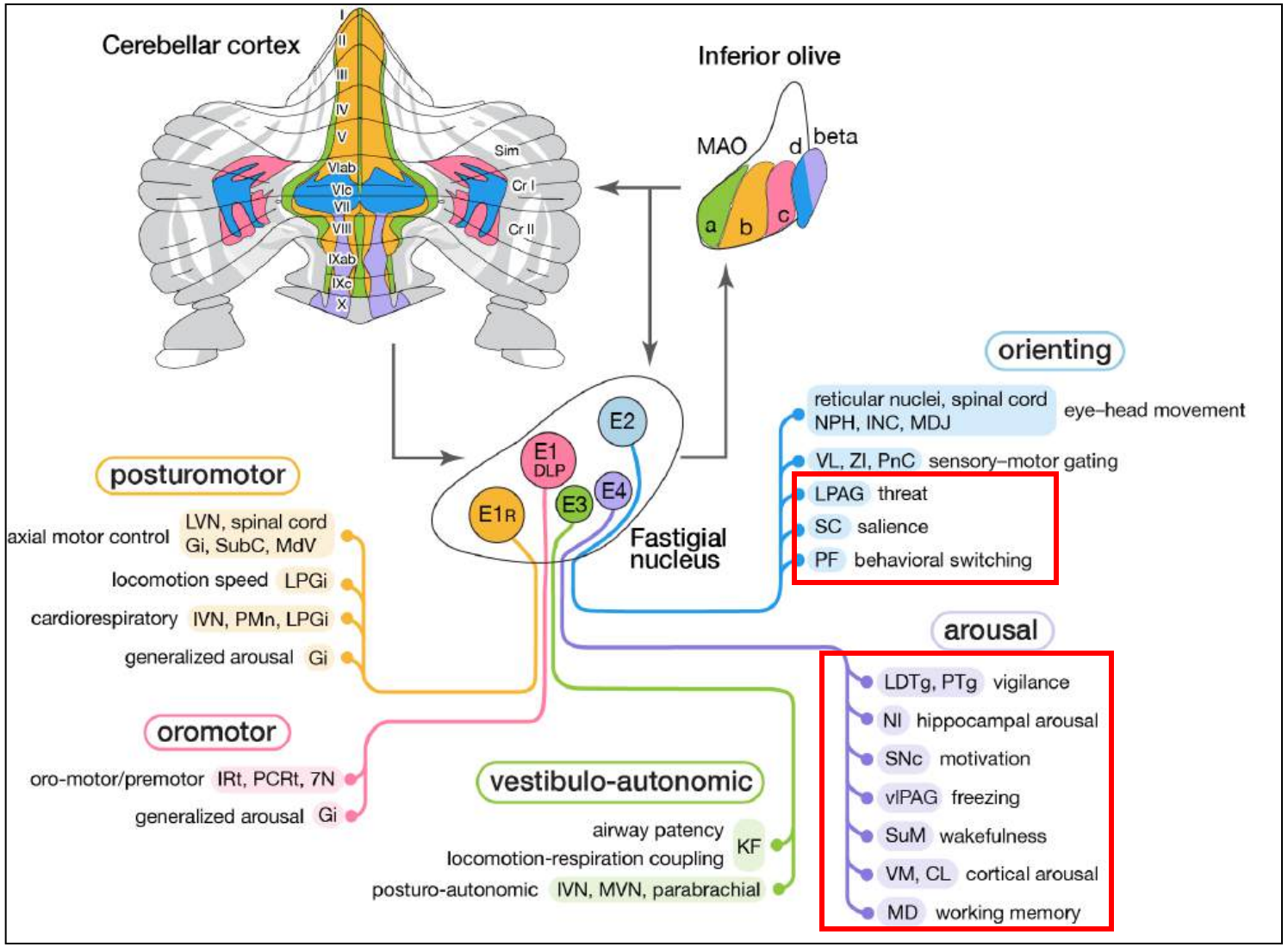
Science. 2019;363(6424):eaav0581

Cerebellar granule cells encode the expectation of reward

Wagner MJ, Kim TH, Savall J, Schnitzer MJ, Luo L. Cerebellar granule cells encode the expectation of reward. Nature. 2017 Apr 6;544(7648):96-100.

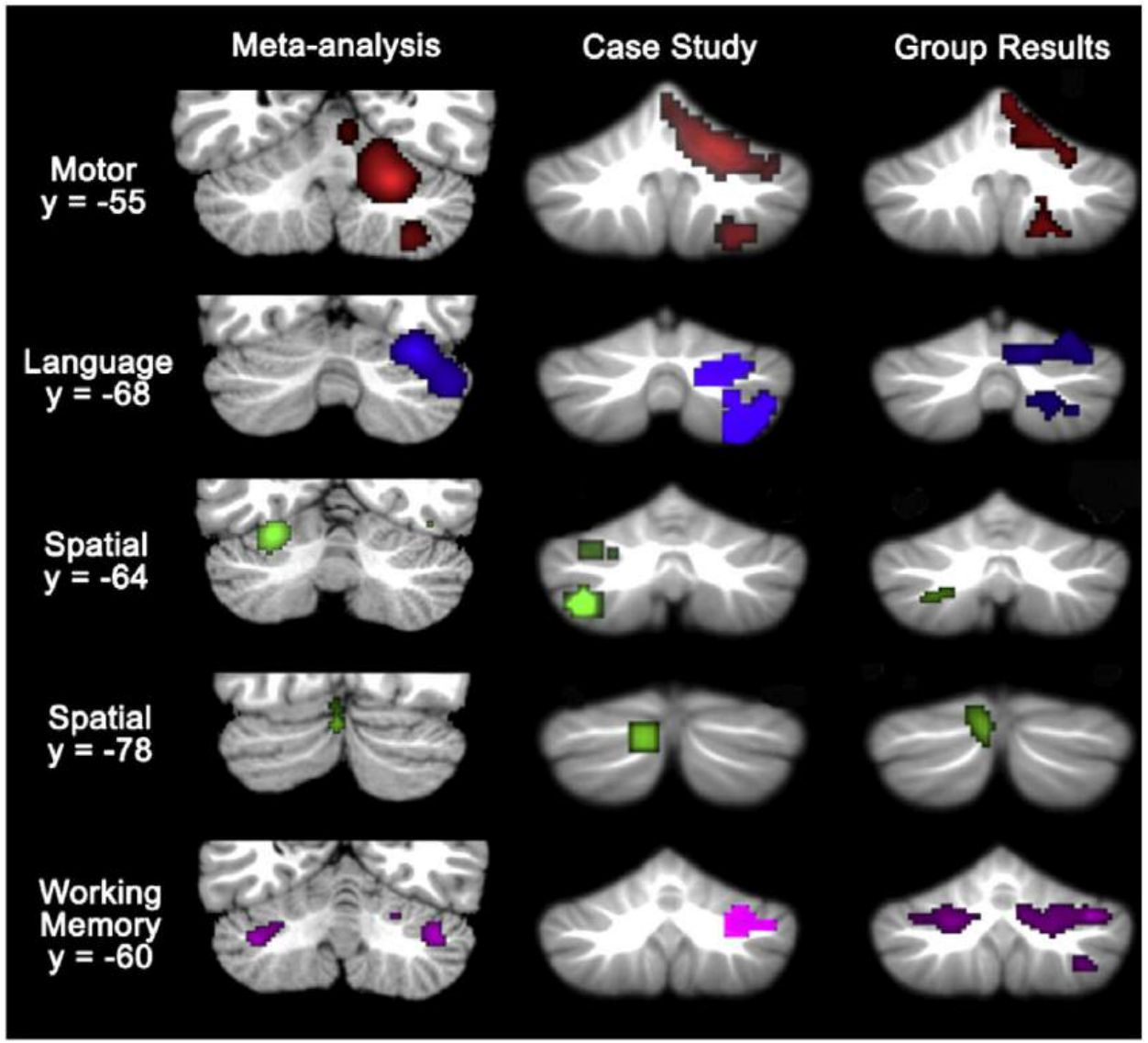
Fastigial nucleus – VTA
Snider et al., 1976;
Snider and Maiti, 1976

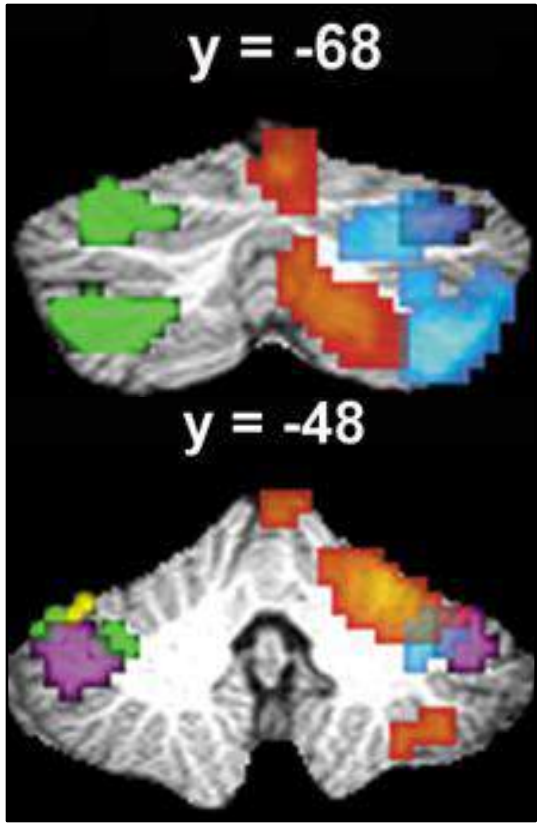
Modular output circuits of the fastigial nucleus for diverse motor and nonmotor functions of the cerebellar vermis



Fujita H, Kodama T, du Lac S. Elife. 2020 Jul 8;9:e58613

Human cerebellar functional topography. Task-based fMRI



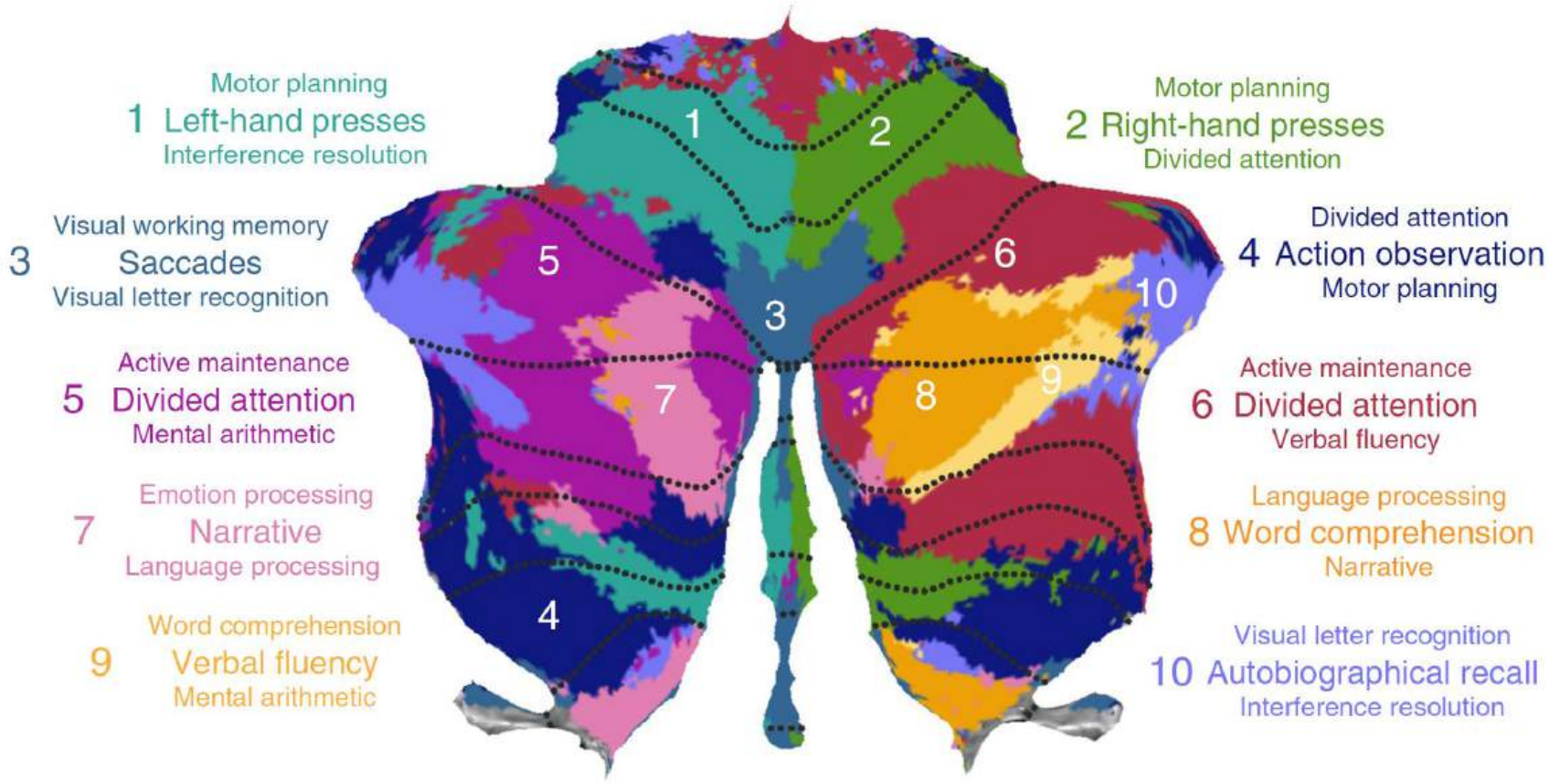


Stoodley and Schmahmann, NeuroImage 2009
Stoodley, Valera, Schmahmann. Behav Neurol. 2010, NeuroImage 2012

Catherine Stoodley

Eve Valera

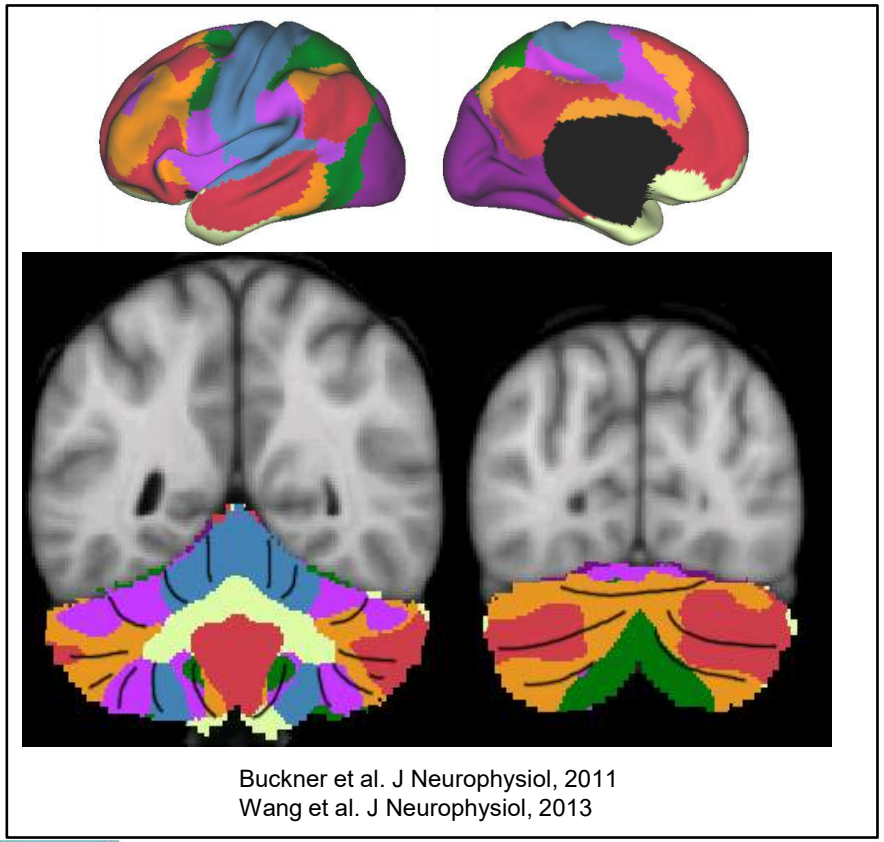
Functional boundaries in the human cerebellum revealed by a multi-domain task battery



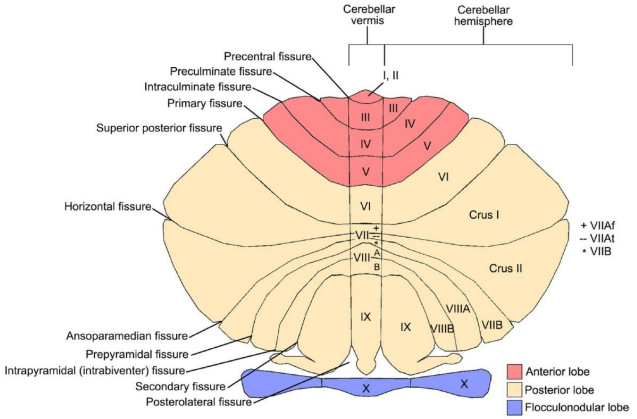
King M, Hernandez-Castillo CR, Poldrack RA, Ivry RB, Diedrichsen J.
Nat Neurosci. 2019; 22: 1371-1378.

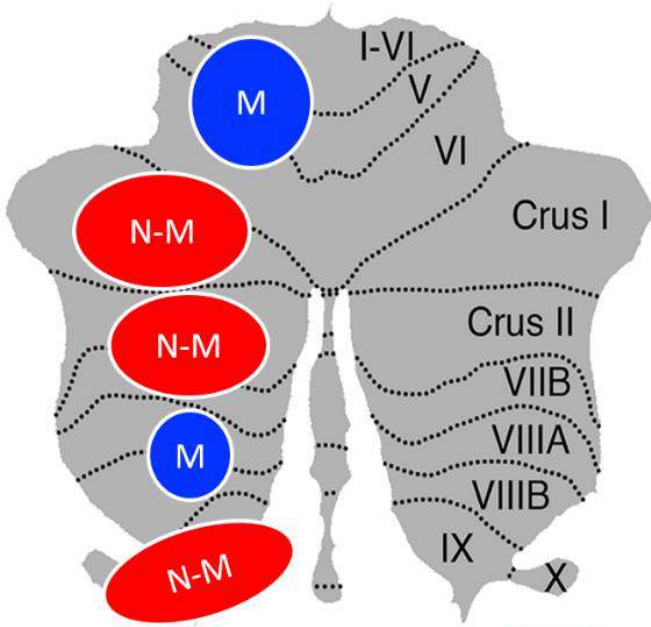
Cerebellum has primary and secondary sensorimotor representations; and primary, secondary, and tertiary cognitive representations

Xavier Guell



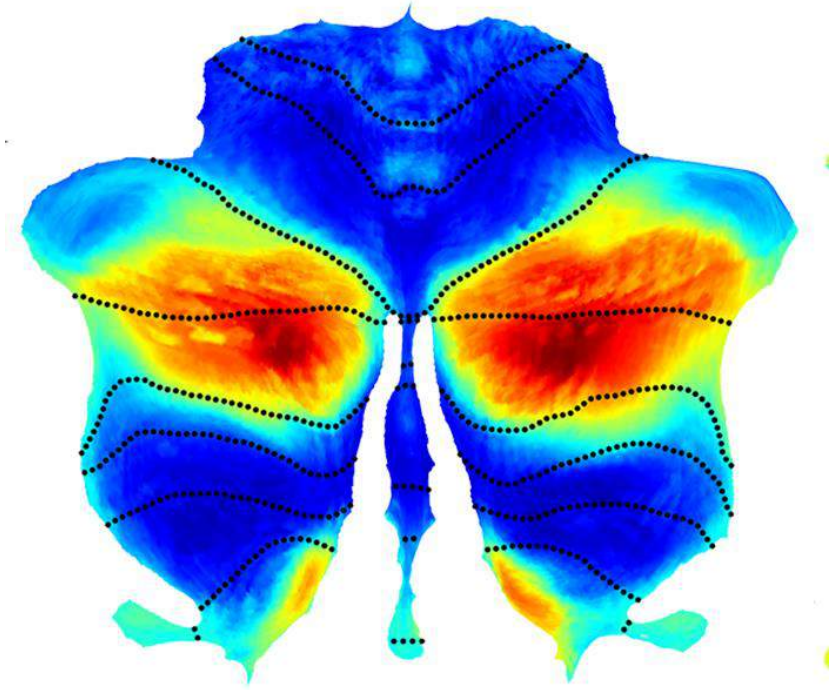
Buckner et al. J Neurophysiol, 2011
Wang et al. J Neurophysiol, 2013





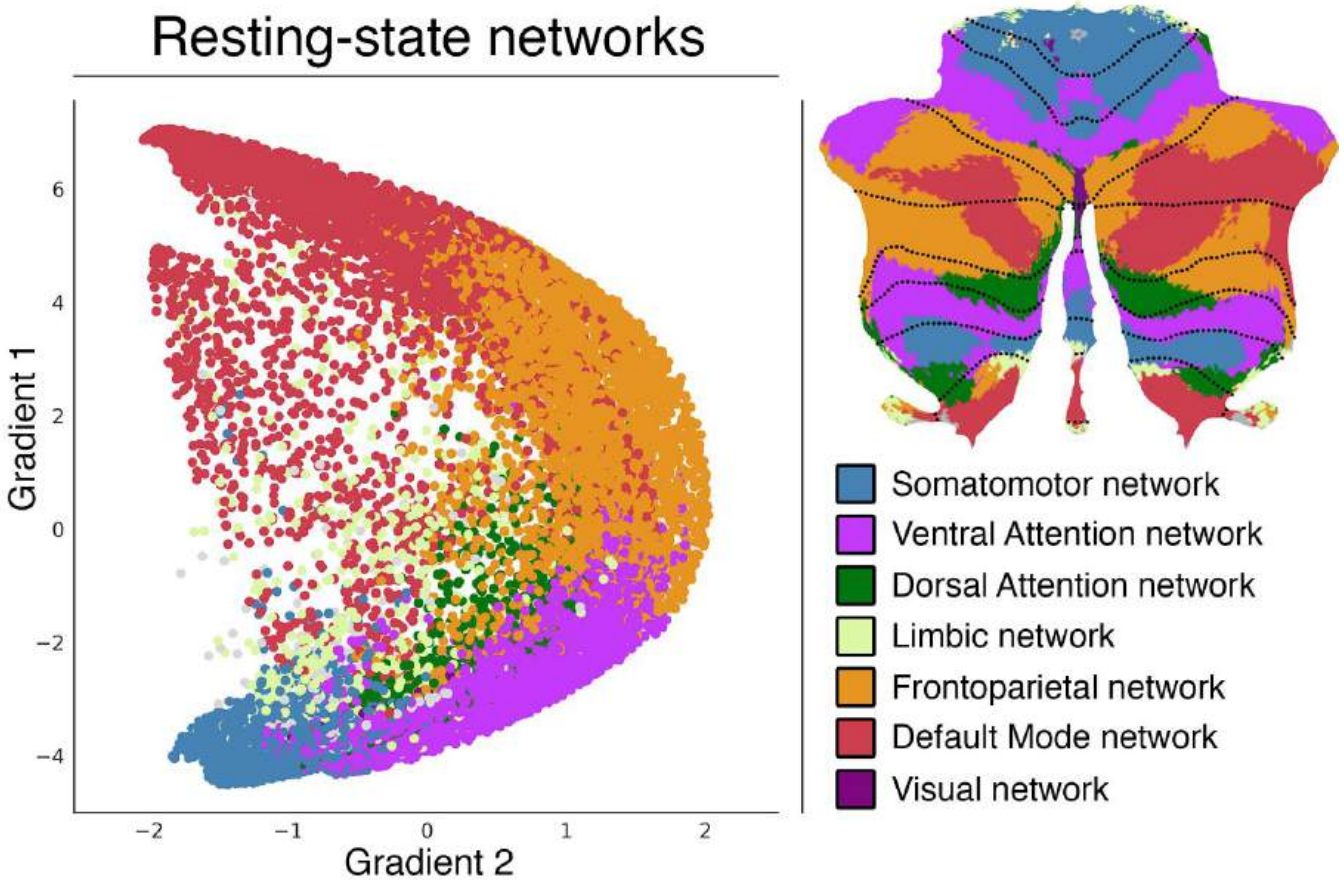
Guell, Gabrieli, Schmahmann. NeuroImage 2018

Principal gradient of cerebellar organization: from motor to default-mode network areas



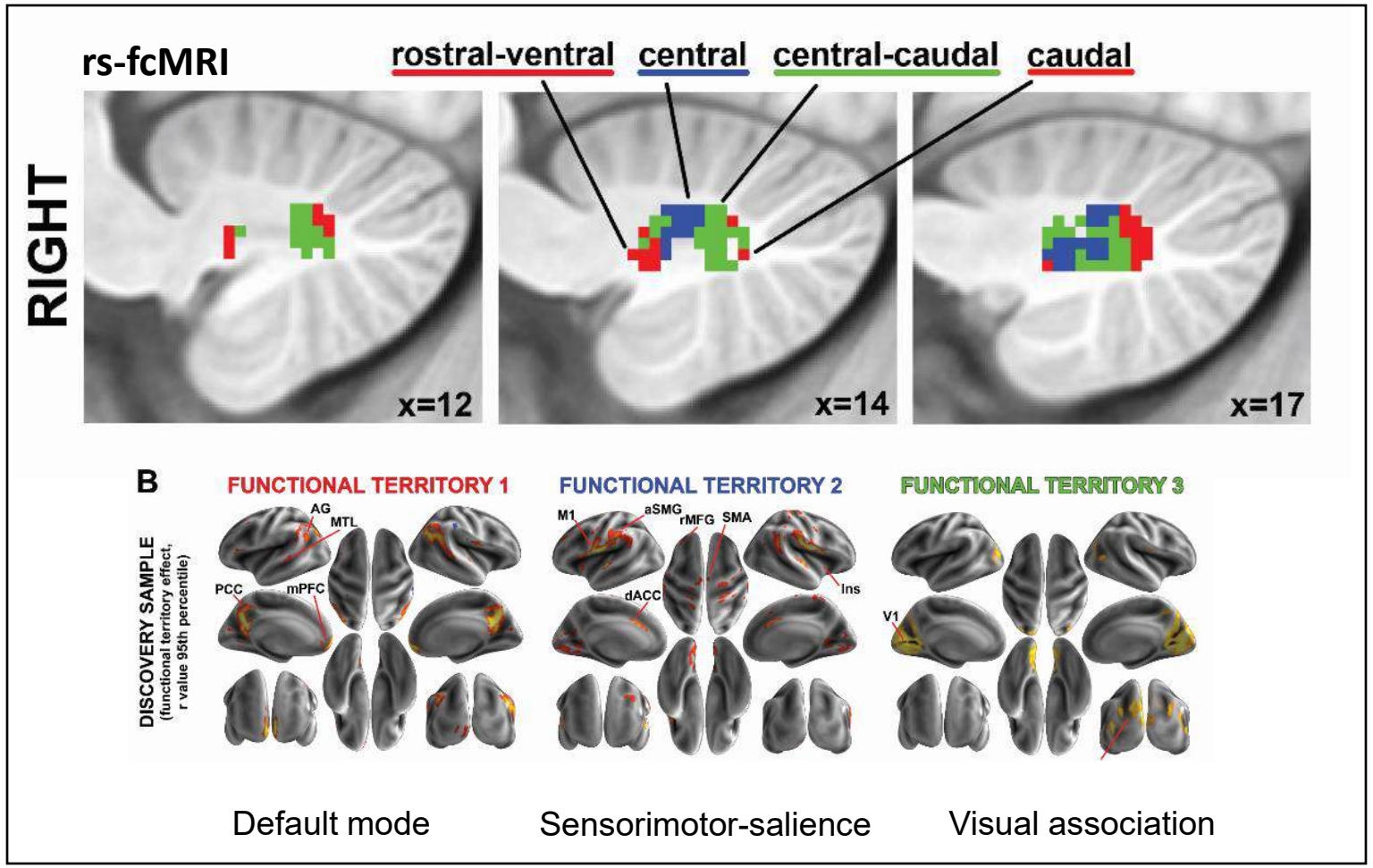
Gradient 1

Gradient 1: From motor (blue) to default-mode (red)



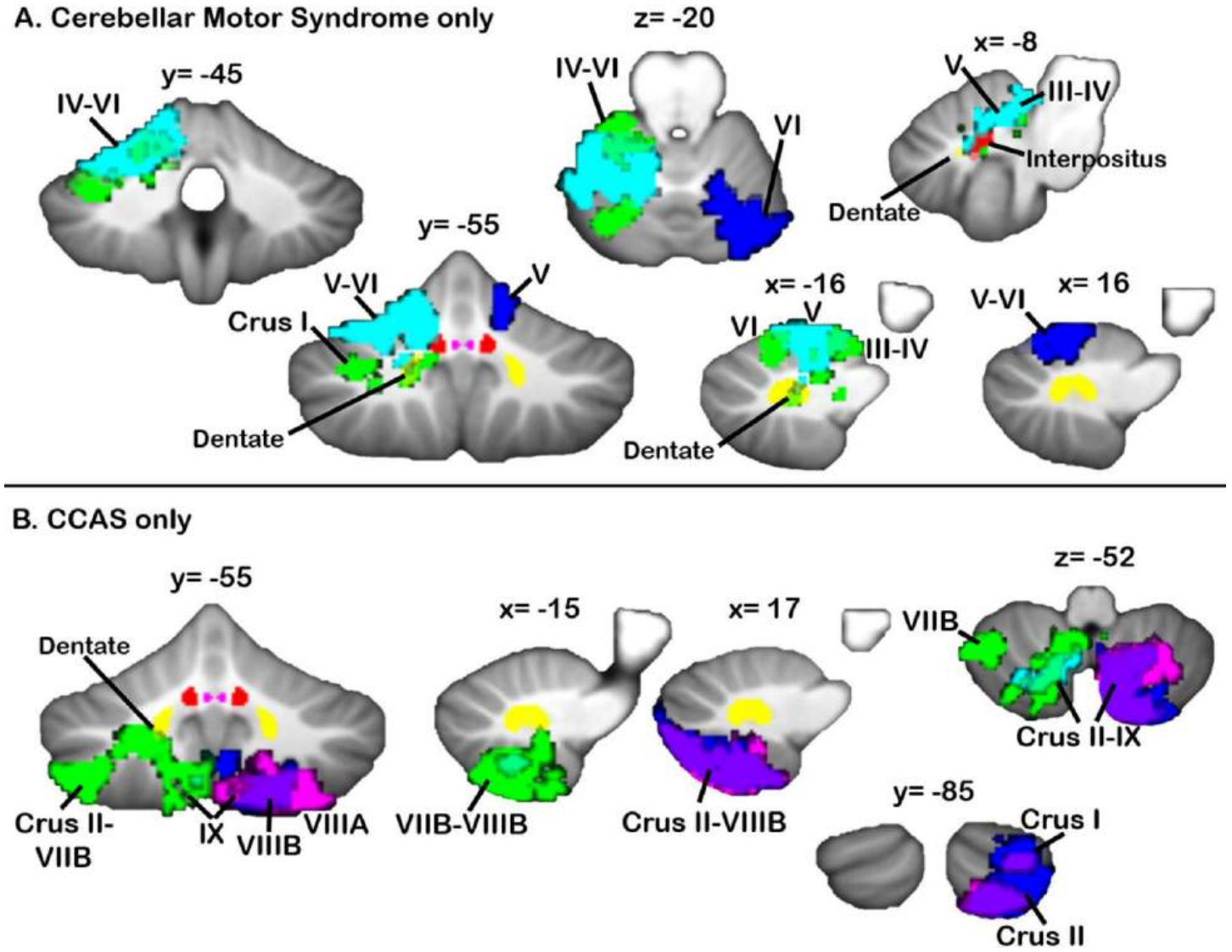
Guell X, Schmahmann JD, Gabrieli J, Ghosh SS. Functional gradients of the cerebellum. Elife. 2018 Aug 14;7. pii: e36652.

Human Dentate Nucleus functional territories



Guell X, D'Mello AM, Hubbard NA, Romeo RR, Gabrieli JDE, Whitfield-Gabrieli S, Schmahmann JD, Anteraper SA. Cerebral Cortex, 2020; 30:2401-2417.

Location of lesion determines motor vs. cognitive consequences in patients with cerebellar stroke



Stoodley, MacMore. Makris, Sherman, Schmahmann. NeuroImage Clinical, 2016
Also – Schmahmann, MacMore, Vangel. Neuroscience 2009; Schmahmann and Sherman, 1998

Cerebellar Cognitive Affective Syndrome (CCAS)

- Executive Function

  Planning, set-shifting, verbal fluency, abstract reasoning, working memory

- Spatial Cognition

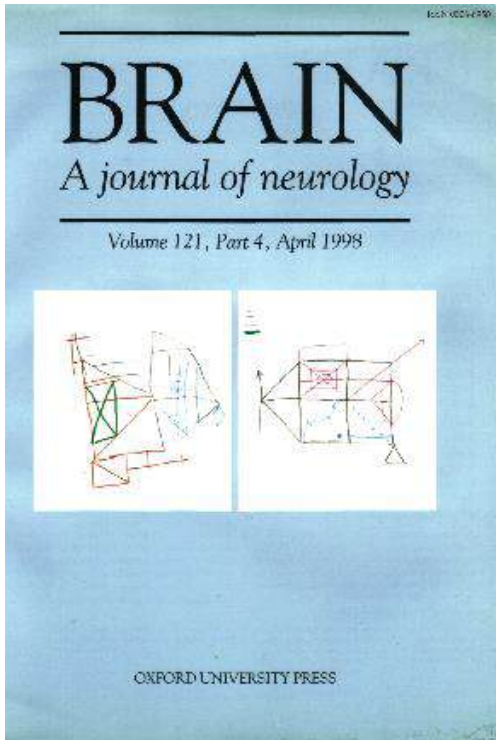
  Visual spatial organization and memory

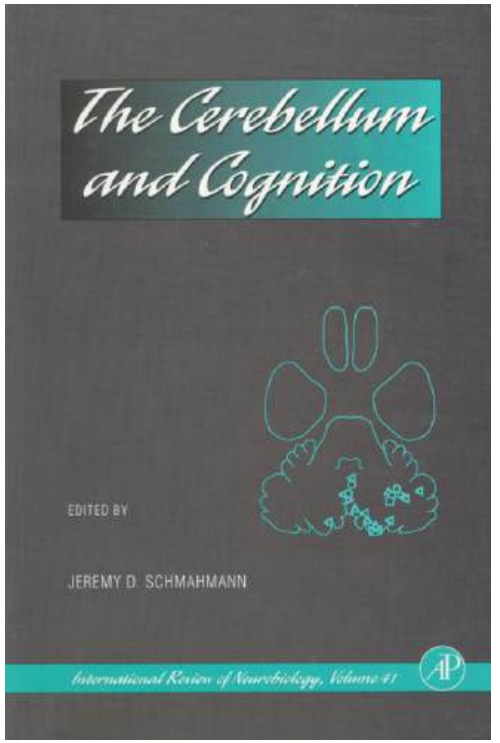
- Language Deficits

  Agrammatism, aprosodia, anomia

- Personality Change

  Blunting of affect, disinhibited and inappropriate behavior





Schmahmann and Sherman. Brain, 1998

Schmahmann's syndrome - identification of the third cornerstone of clinical ataxiology

Mario Manto and Peter Mariën. Cerebellum and Ataxias 2015;2:2

Cerebellar Motor Syndrome

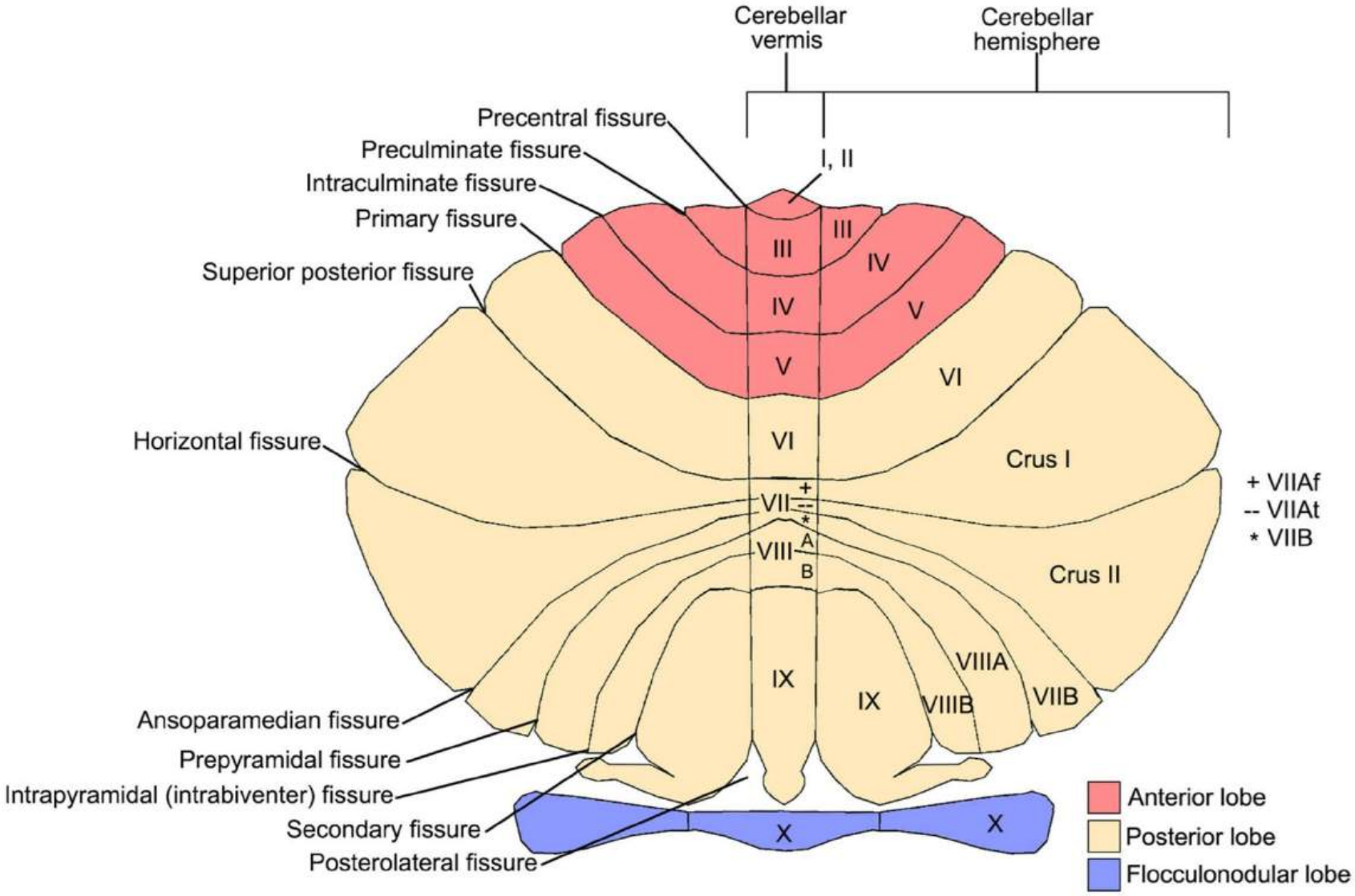
The clinical syndrome that follows lesions of the sensorimotor regions of the cerebellum.

Cerebellar Cognitive Affective Syndrome

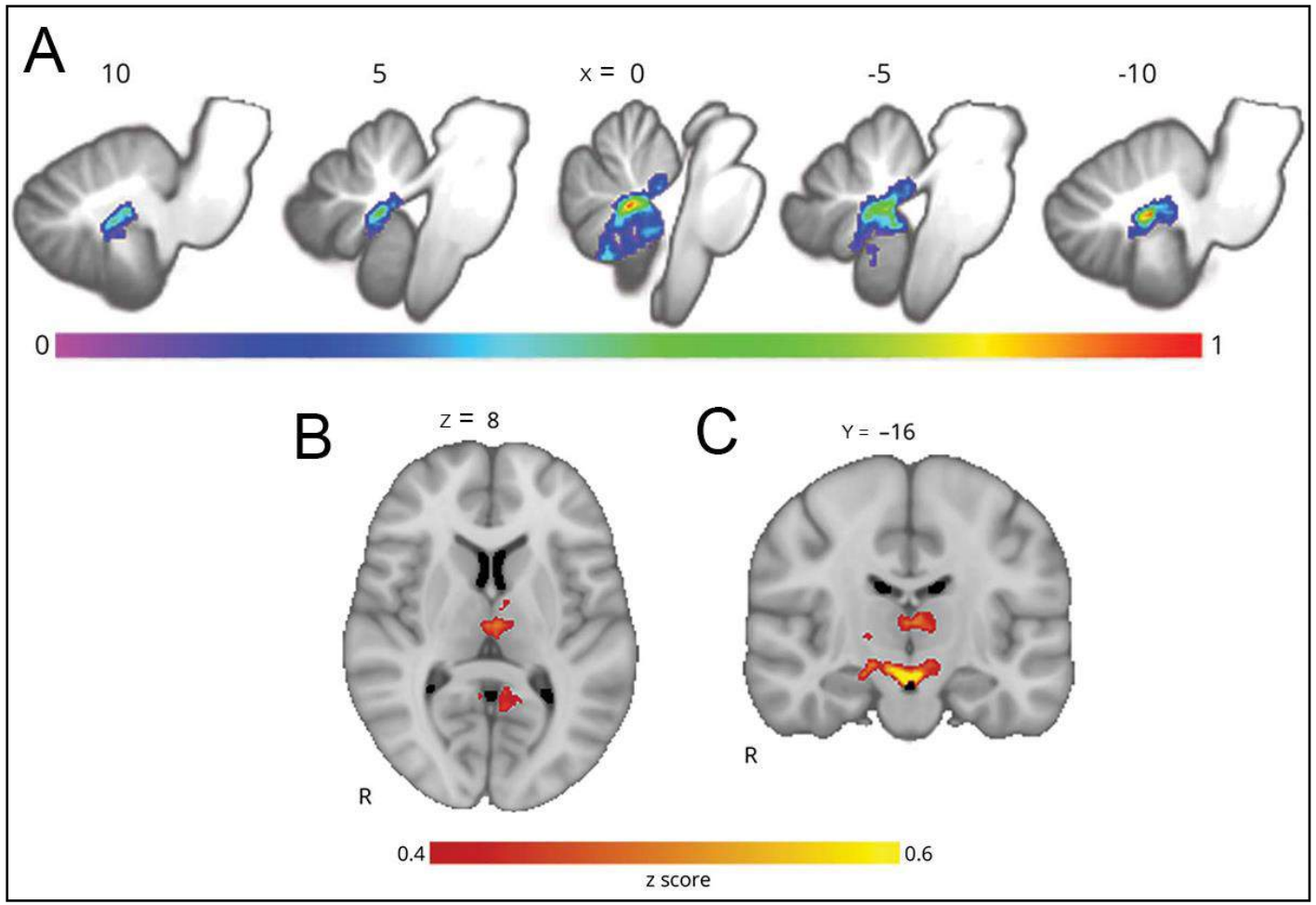
The clinical syndrome that follows lesions of the cognitive and limbic regions of the cerebellum.

Cerebellar Vestibular Syndrome

The clinical syndrome that follows lesions of the vestibular regions of the cerebellum.



Pediatric postoperative cerebellar cognitive affective syndrome follows outflow pathway lesions



POSTERIOR FOSSA SYNDROME

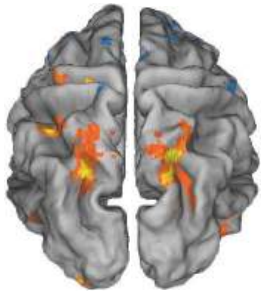
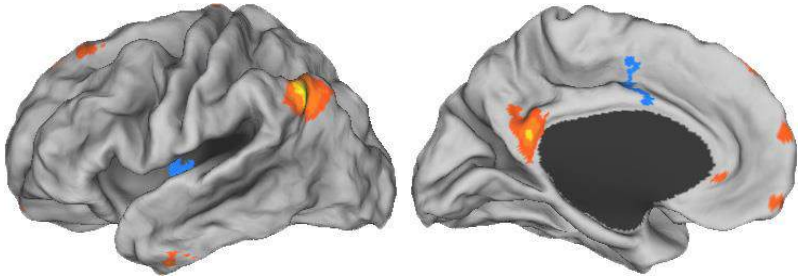
1. CCAS +/- mutism
2. Cerebellar motor ataxia
3. Brainstem syndromes

Albazron FM, Bruss J, Jones RM, Yock TI, Pulsifer MB, Cohen AL, Nopoulos PC, Abrams AN, Sato M, Boes AD. 2019 Oct 15;93(16):e1561-e1571.

Cerebral networks modified by Cerebellar TMS

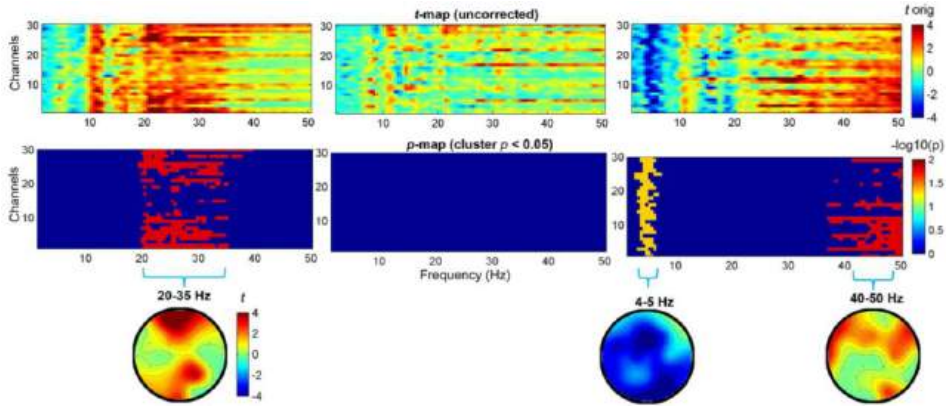
rs-fcMRI affected in a network specific manner

Halko et al.
J Neurosci,
2014

Dorsal attention network	Default mode network
	
Vermis stimulation	Crus I / II stimulation

Cerebellar subregions control the temporal dynamics of cerebral networks with which they are interconnected

Farzan et al.
Sci Rep, 2016



Vermis stimulation Sham Crus I / II stimulation

Schizophrenia Research 124 (2010) 91–100

Contents lists available at ScienceDirect

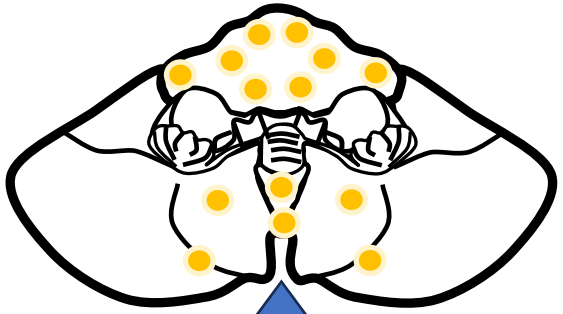
Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Safety and proof of principle study of cerebellar vermal theta burst stimulation in refractory schizophrenia

Asli Demirtas-Tatlidede [a,b], Catarina Freitas [a,b], Jennifer R. Cromer [a,c], Laura Safar [a,c], Dost Ongur [a,d], William S. Stone [a,e], Larry J. Seidman [a,e], Jeremy D. Schmahmann [a,f], Alvaro Pascual-Leone [a,b,*]

The vestibulocerebellar syndrome disrupts gait because the vestibular gyroscope is damaged



Cerebellar Motor Syndrome

SARA

BARS / ICARS

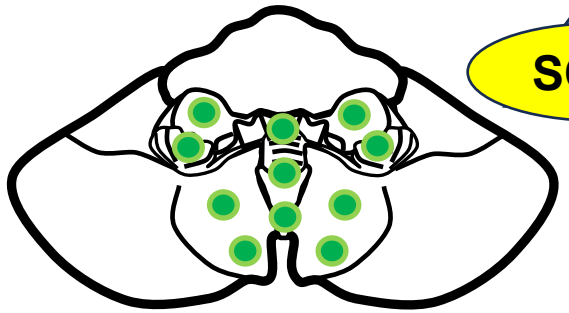
DYSMETRIA

PROM-Ataxia

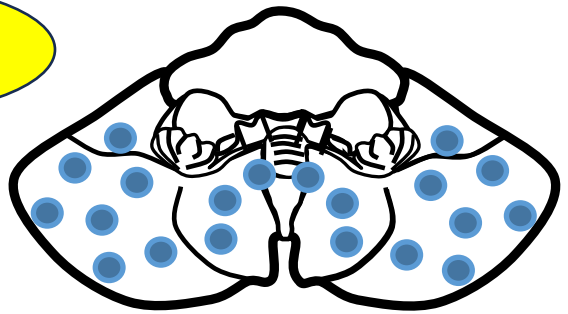
SODA

CCAS/SS CNRS-2

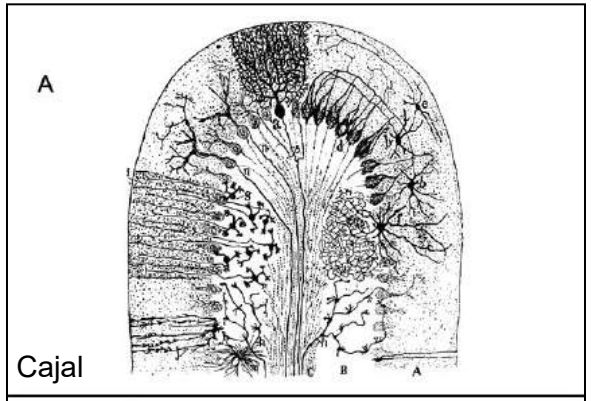
Cerebellar Vestibular Syndrome



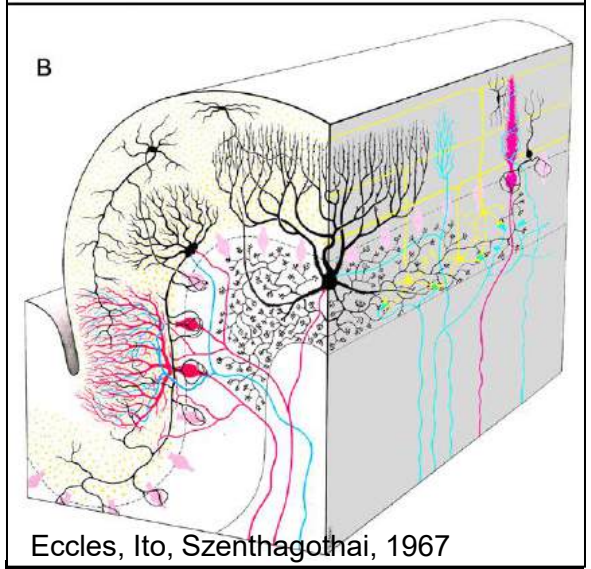
Cerebellar Cognitive Affective / Schmahmann Syndrome



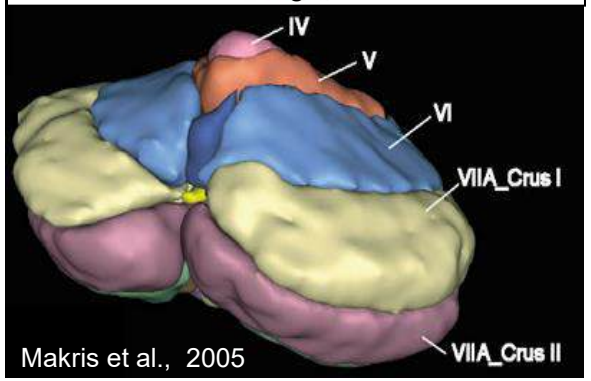
Manto MM, Mitoma H, Burt AL, Schmahmann JD.
Cerebellar clinical syndromes: The triad and rating scales. J Neurol, in press.



Cajal



Eccles, Ito, Szenthagothai, 1967



Makris et al., 2005

Dysmetria of Thought Theory

Cerebellum is an integral node in the distributed neural circuits subserving sensorimotor, vestibular, cognitive, limbic and autonomic function.

Predicated on two complementary anatomical realities:

- Invariant architecture of cerebellar cortex
- Topographic arrangement of connections

An Emerging Concept

The Cerebellar Contribution to Higher Function

Schmahmann. Arch Neurol,1991; 48:1178-87

Human Brain Mapp 1996; J Neurolinguistics 2000; J Neuropsychiatry Clin Neurosci 2004

Dysmetria of Thought

Universal Cerebellar Transform Theory

Cerebellum optimizes performance by
modulating behavior
around a homeostatic baseline
automatically, implicitly, and according to context

Schmahmann. Archiv Neurol 1991; Human Brain Mapp 1996;
J Neurolinguistics 2000; J Neuropsychiatry Clin Neurosci 2004

Dysmetria of Thought

Universal Cerebellar Impairment

= Dysmetria

Lesions of sensorimotor cerebellum

Dysmetria of movement

The cerebellar motor syndrome

Lesions of cognitive – limbic cerebellum

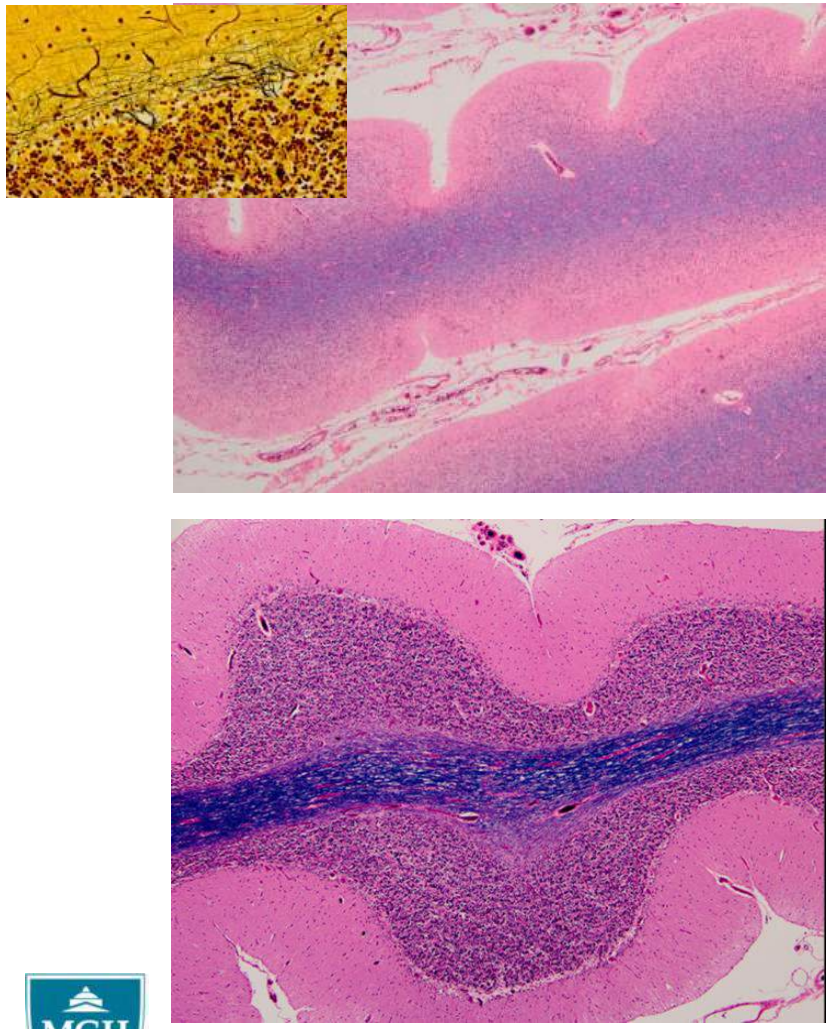
Dysmetria of thought and emotion

The *cerebellar cognitive affective syndrome*

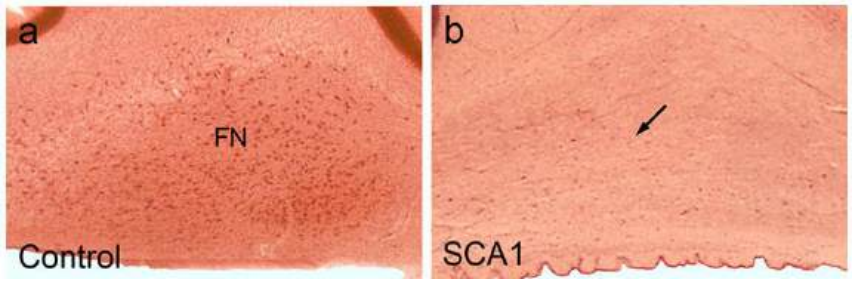
Schmahmann. Archiv Neurol 1991; Human Brain Mapp 1996;
J Neurolinguistics 2000; J Neuropsychiatry Clin Neurosci 2004

Neuropathology in ataxias / SCA = spinal cord

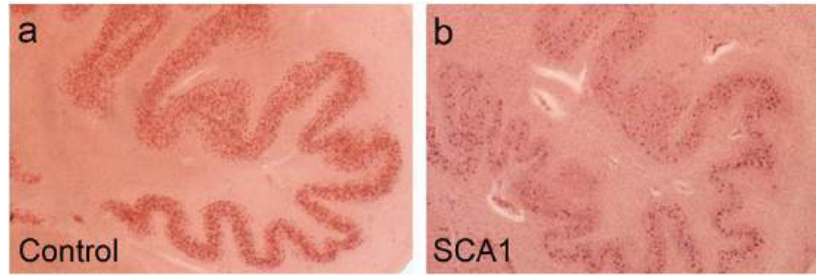
Cerebellar folium; empty baskets



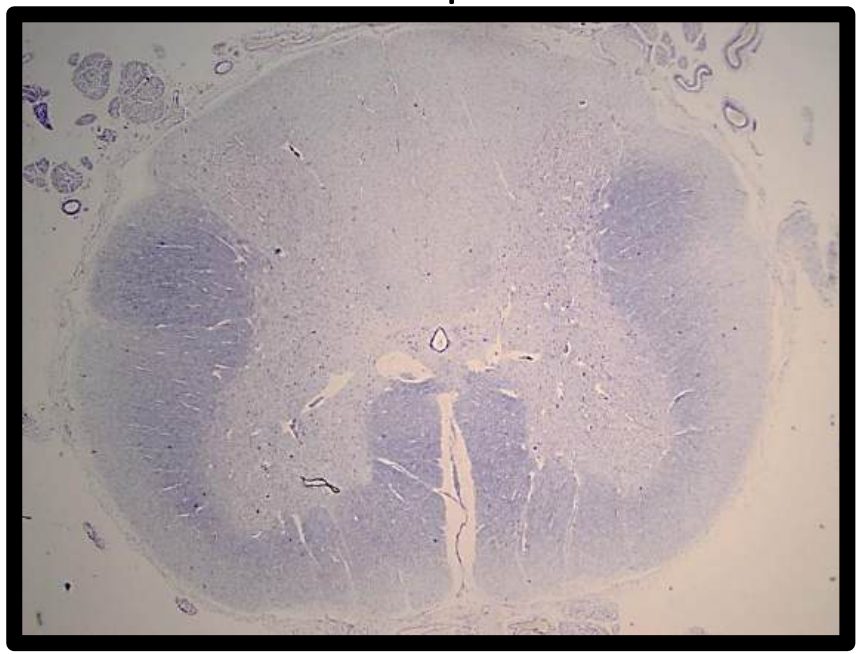
Fastigial nucleus



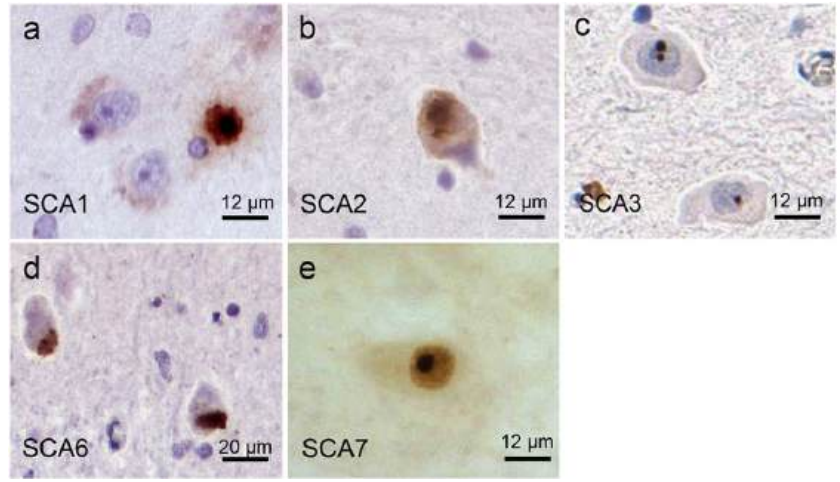
Inferior olivary nucleus



Cervical spinal cord



Neuronal intranuclear inclusions



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Horton LC, Frosch MP, Vangel MG, Weigel-DiFranco C, Berson EL, Schmahmann JD. Cerebellum. 2013 Apr;12(2):176-93.

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Photo by Jinny Sagorin

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