

# Cognitive and Emotional Aspects of Cerebellar Function and Dysfunction: 1. Anatomical Substrates

Annual Meeting, Pacific Northwest Neuropsychological Society  
University of Washington Faculty Club  
Seattle, WA  
March 6<sup>th</sup>, 2010

**Jeremy D. Schmahmann, M.D.**

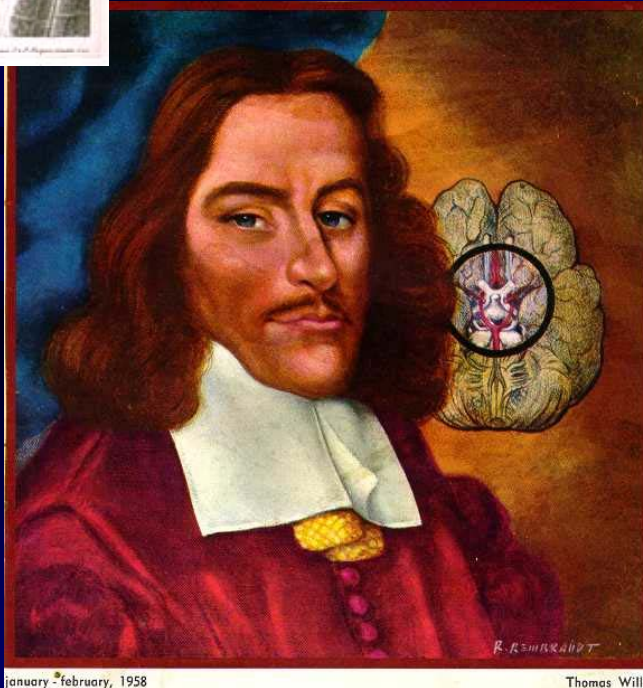
Professor of Neurology, Harvard Medical School  
Director, Ataxia Unit; Cognitive/Behavioral Neurology Unit  
Laboratory for Neuroanatomy and Cerebellar Neurobiology

Department of Neurology  
Massachusetts General Hospital



Nicolas Steno  
(Niels Steensen, Niels Stensen,  
Nicolaus Stenonis,  
1638 – 1686)

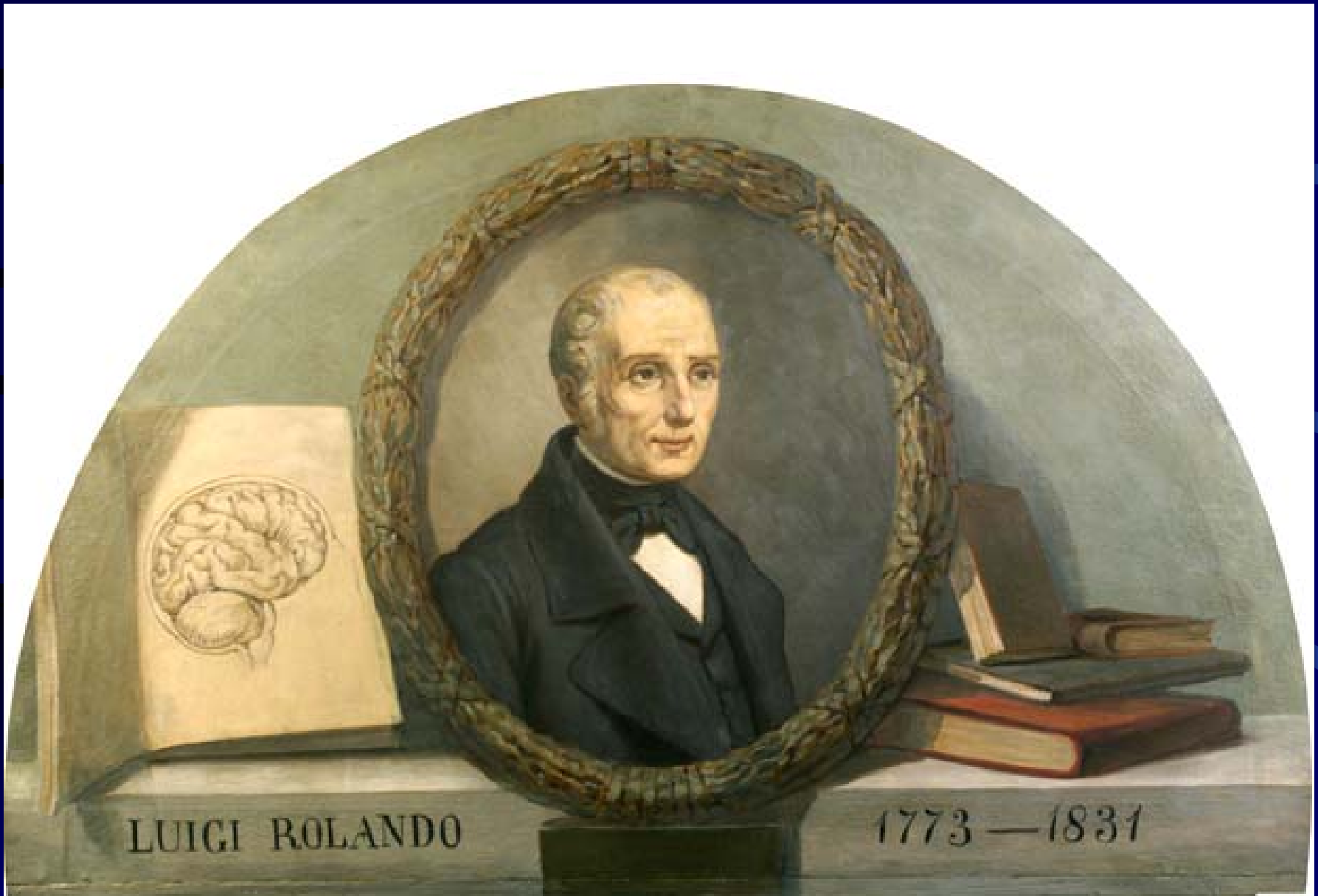
Thomas Willis  
1621-1675

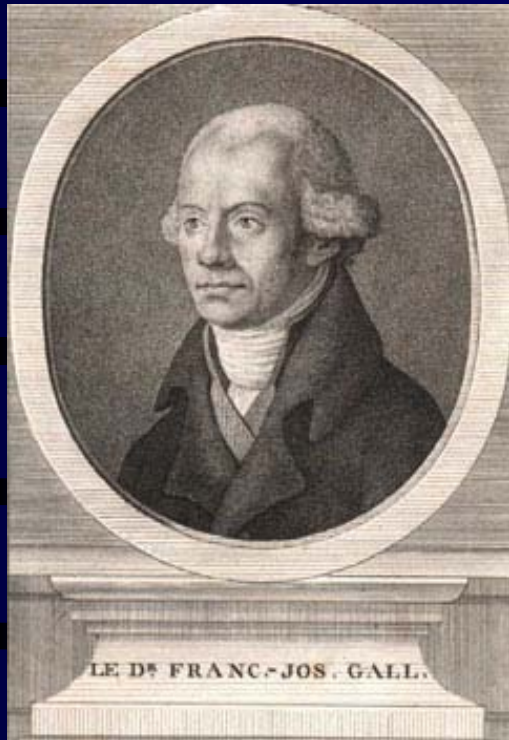


Vincenzo Malacarne  
(1744-1816)

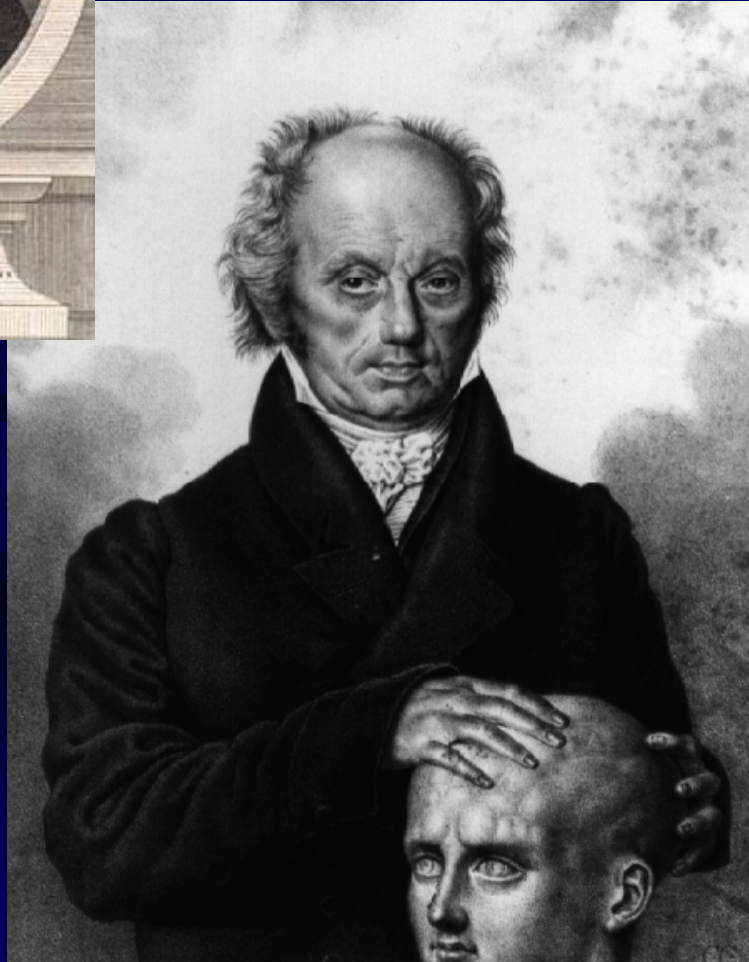


Luigi Rolando 1773-1831

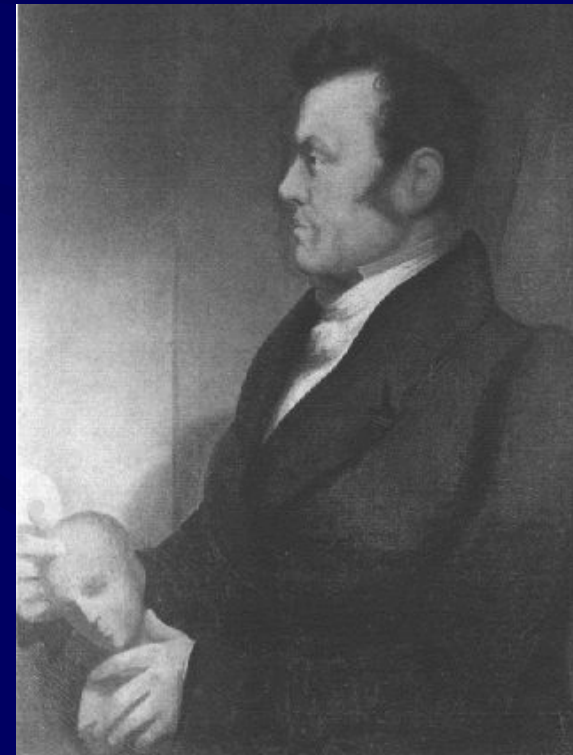




Franz Josef Gall  
(1758- 1828)

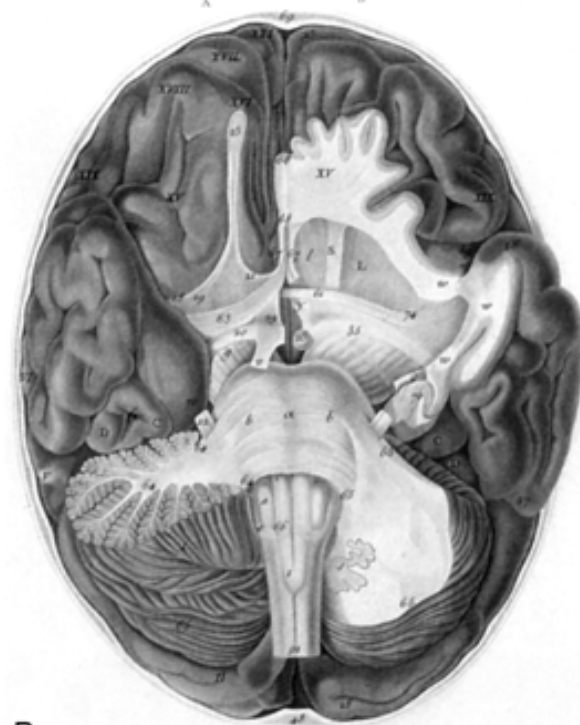


Johann Gaspar  
Spurzheim  
(1776-1832)





A



B



C

Gall and Spurzheim. 1810

Marie Jean-Pierre Flourens  
(1794 - 1867)



Lodewijk ('Louis') Bolk  
(1866-1930)

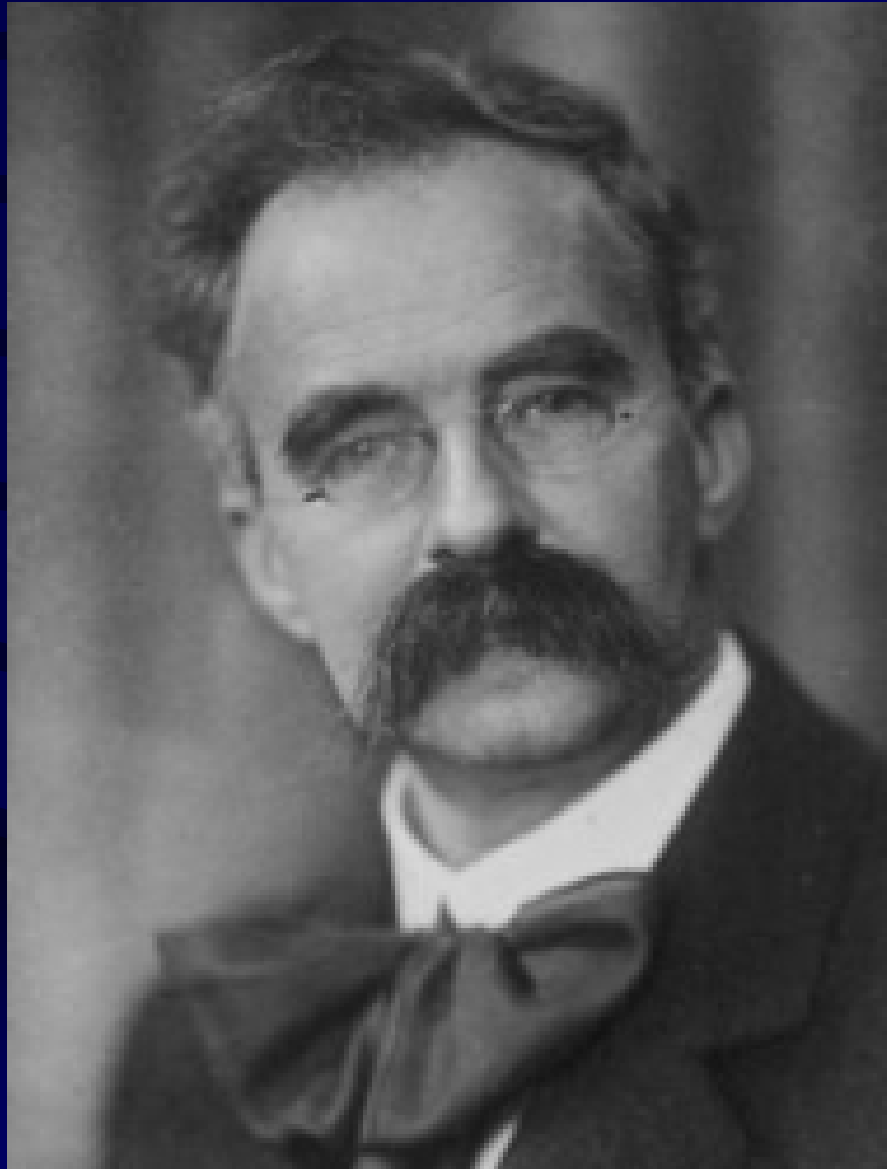
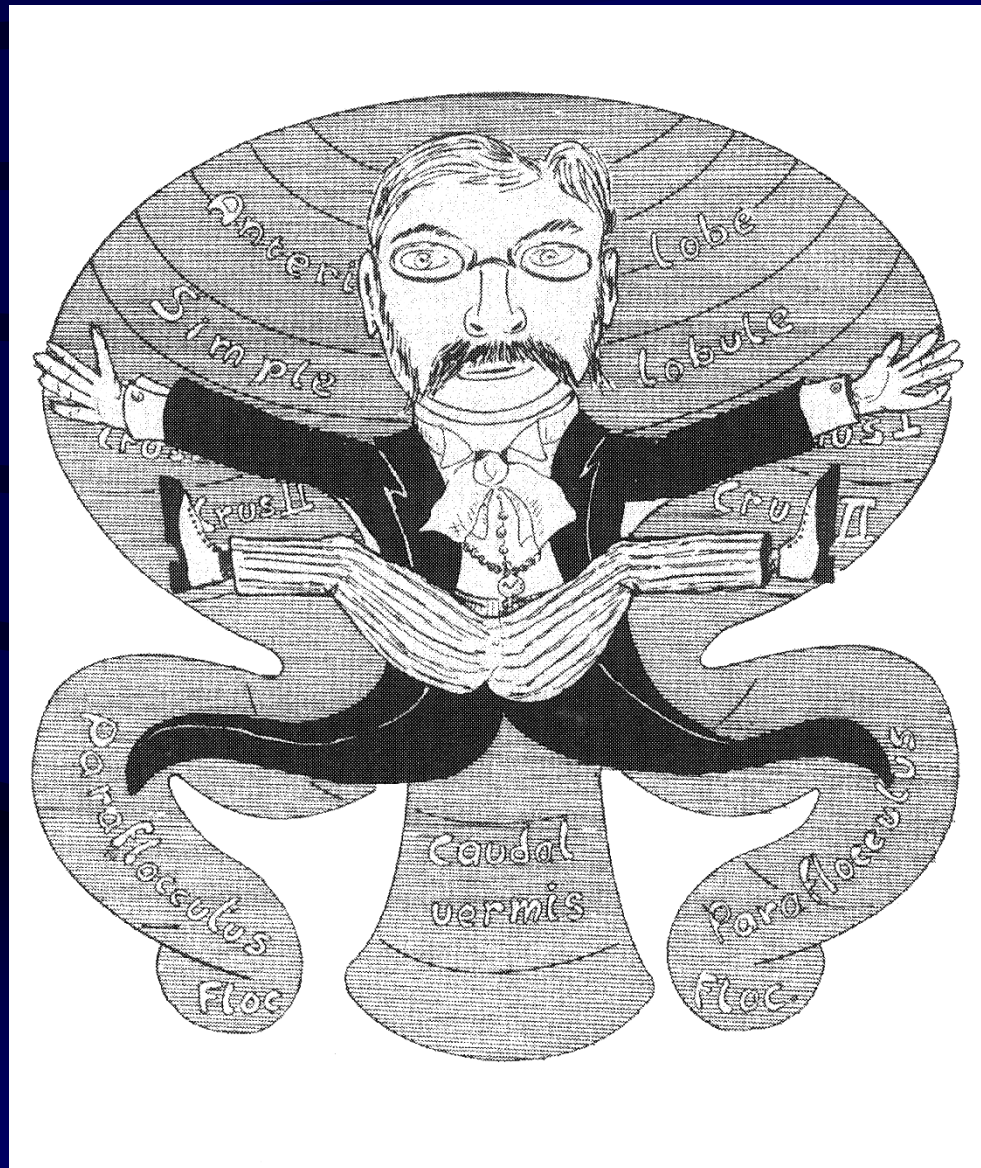




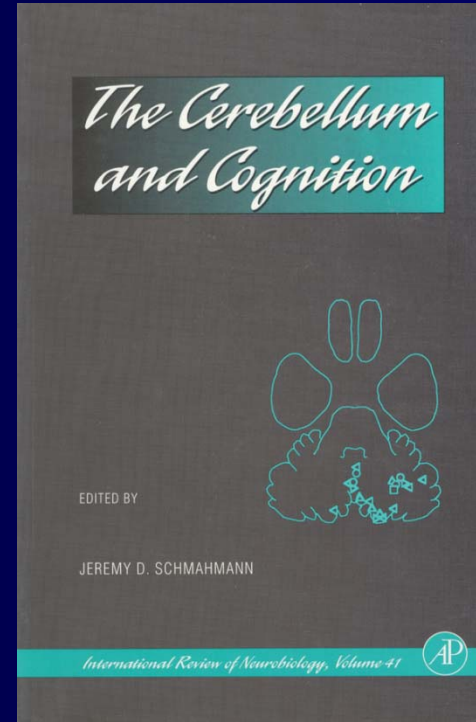
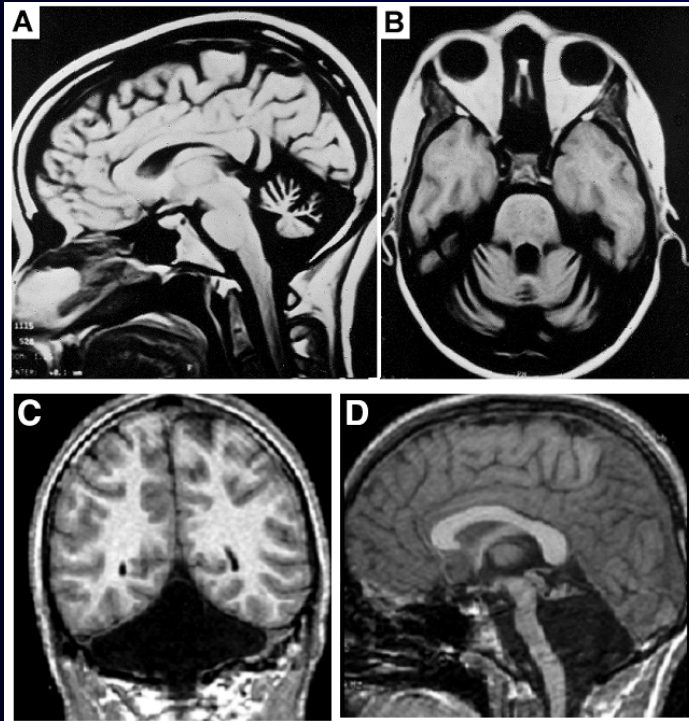
Diagram by Jan Voogd representing Bolk's notion of functional localization in the cerebellum.



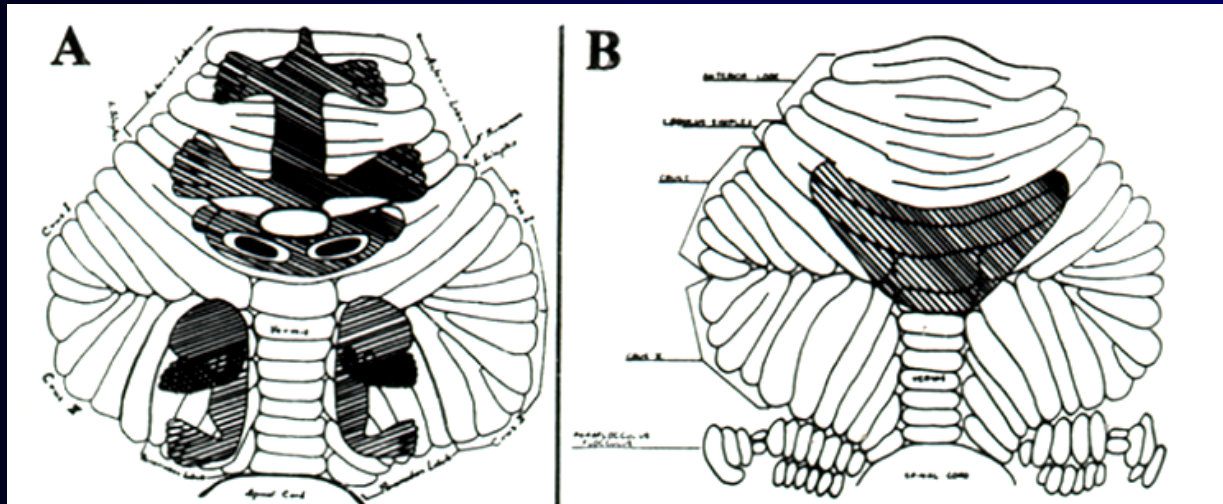
# Cerebellar clinical features – the cerebellar “motor” syndrome

- Gait ataxia
- Dysmetria of extremities
- Eye movement abnormalities
- Dysarthria

# Cerebellum and Cognition



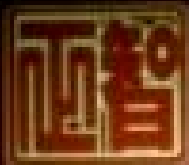
Schmahmann, 1997



Snider, 1950

# Cerebellum - Essential anatomy





纯中药制剂 国家基本药物

国药准字Z61020095

# 补脑丸

主治

记忆减退

心烦失眠



18 वीं अन्तर्राष्ट्रीय एपिलेप्सी कांग्रेस

तथा XIV वीं विश्व न्यूरोलॉजी कांग्रेस



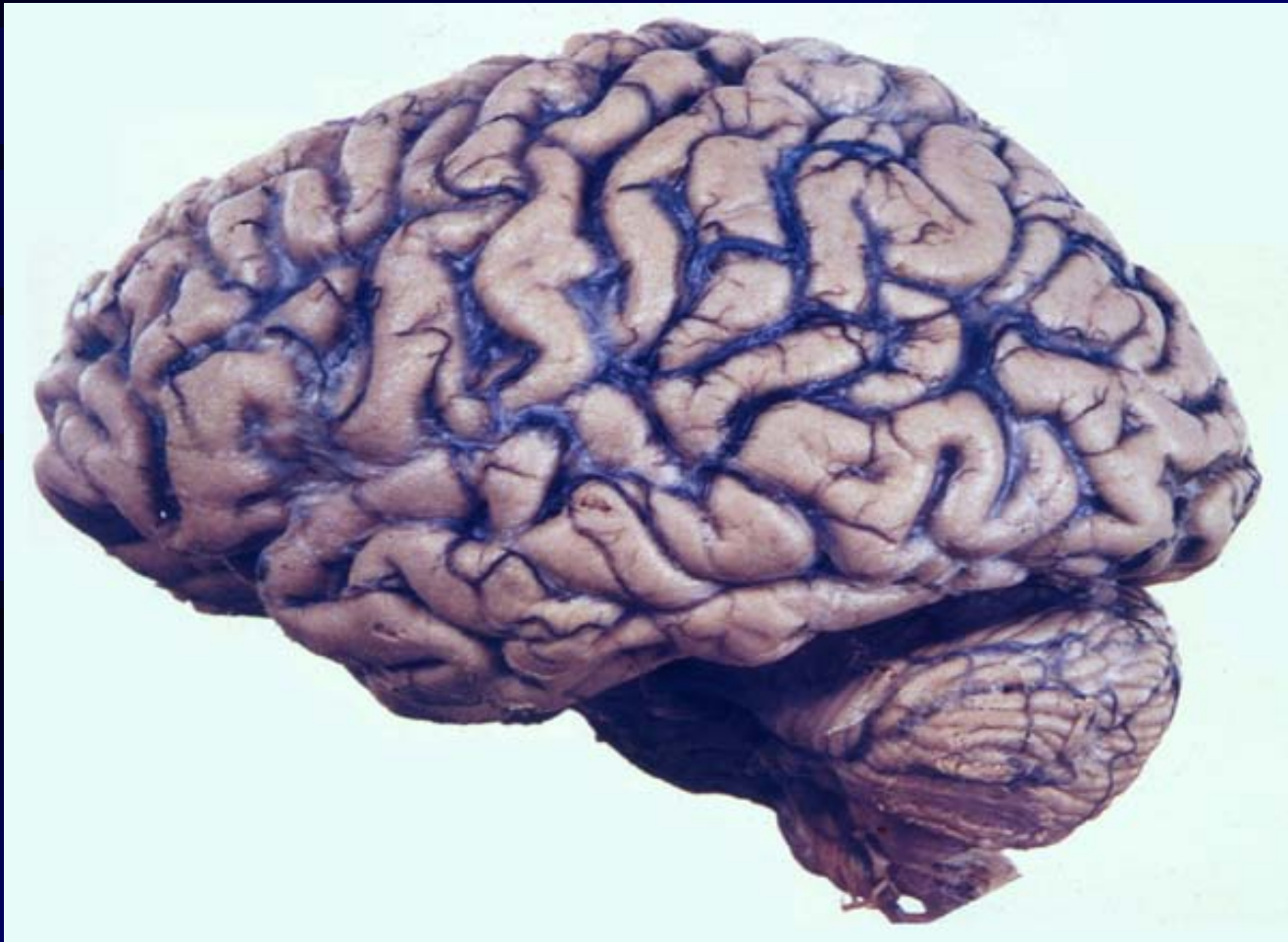
650

भारत  
INDIA

1989

18TH INTERNATIONAL EPILEPSY CONGRESS AND  
XIV WORLD CONGRESS ON NEUROLOGY 1989

# Anatomic Organization of the Cerebrocerebellar System

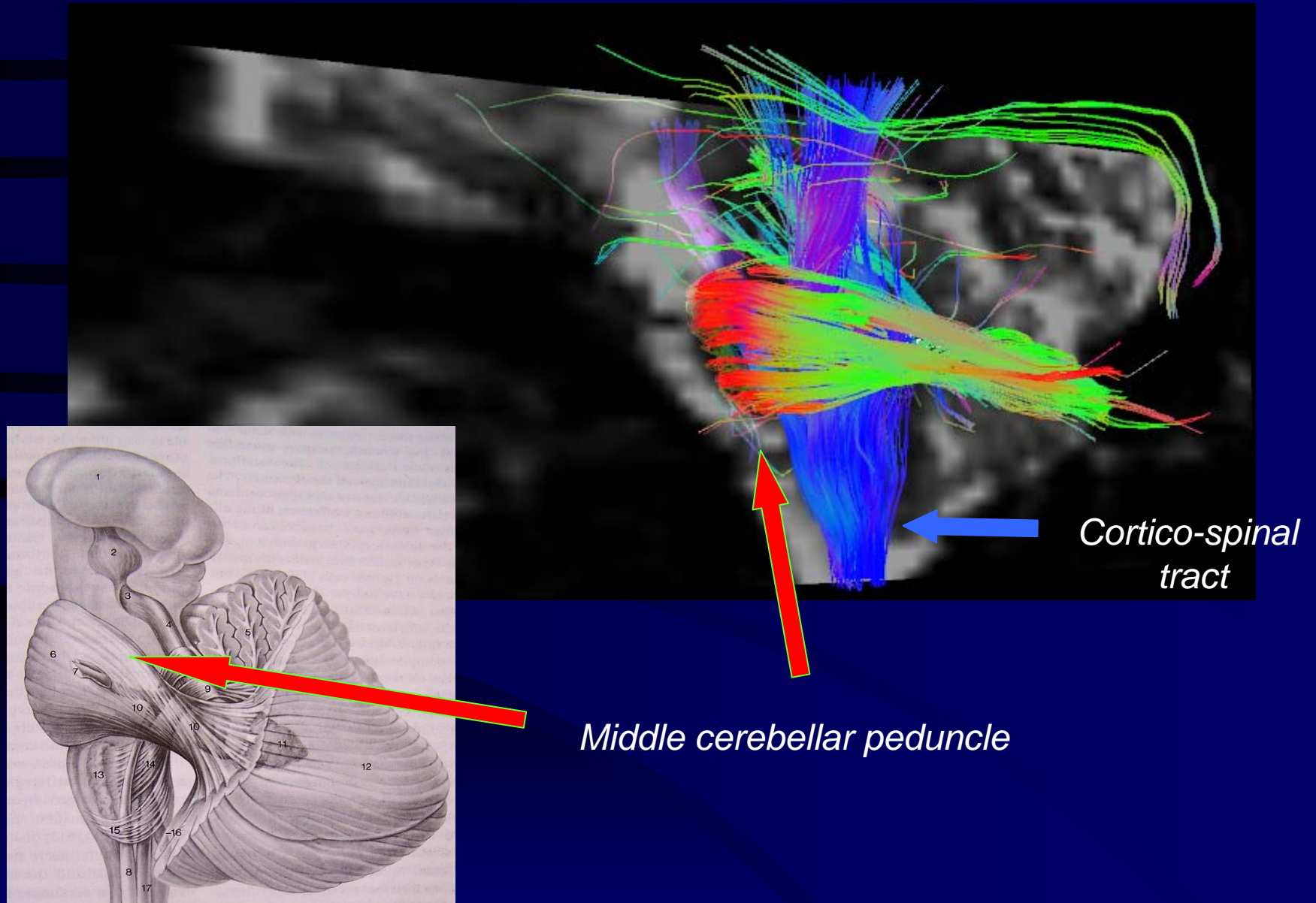




Harvard Magazine, 1999

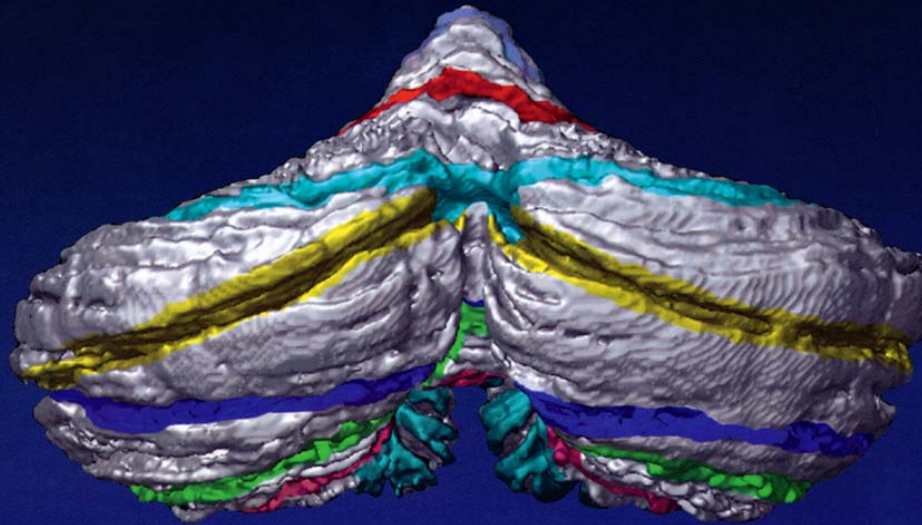


# Human cerebellar peduncles - DSI





MRI ATLAS  
*of the*  
**HUMAN CEREBELLUM**



Jeremy D. Schmahmann

Julien Doyon

Arthur W. Toga

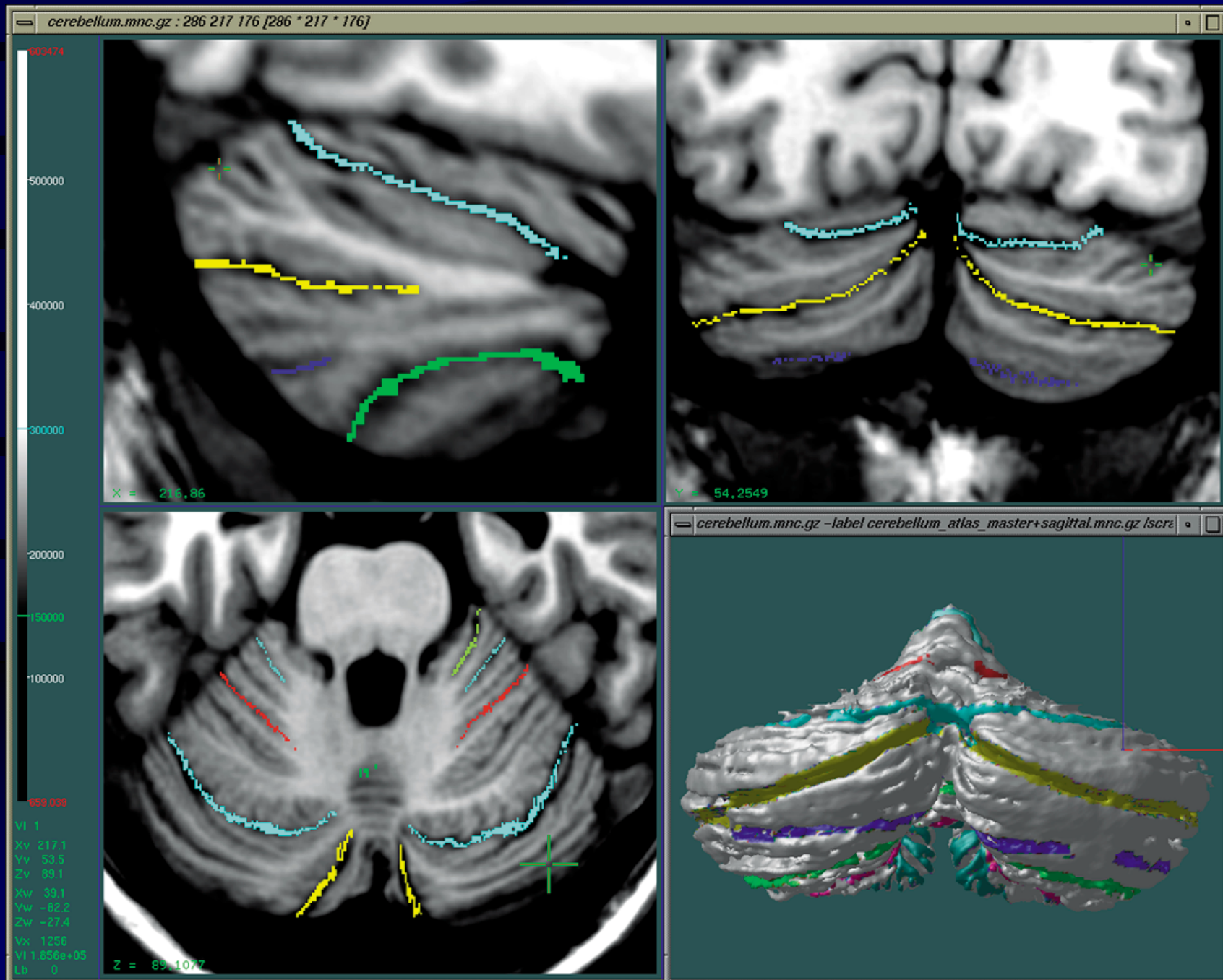
Michael Petrides

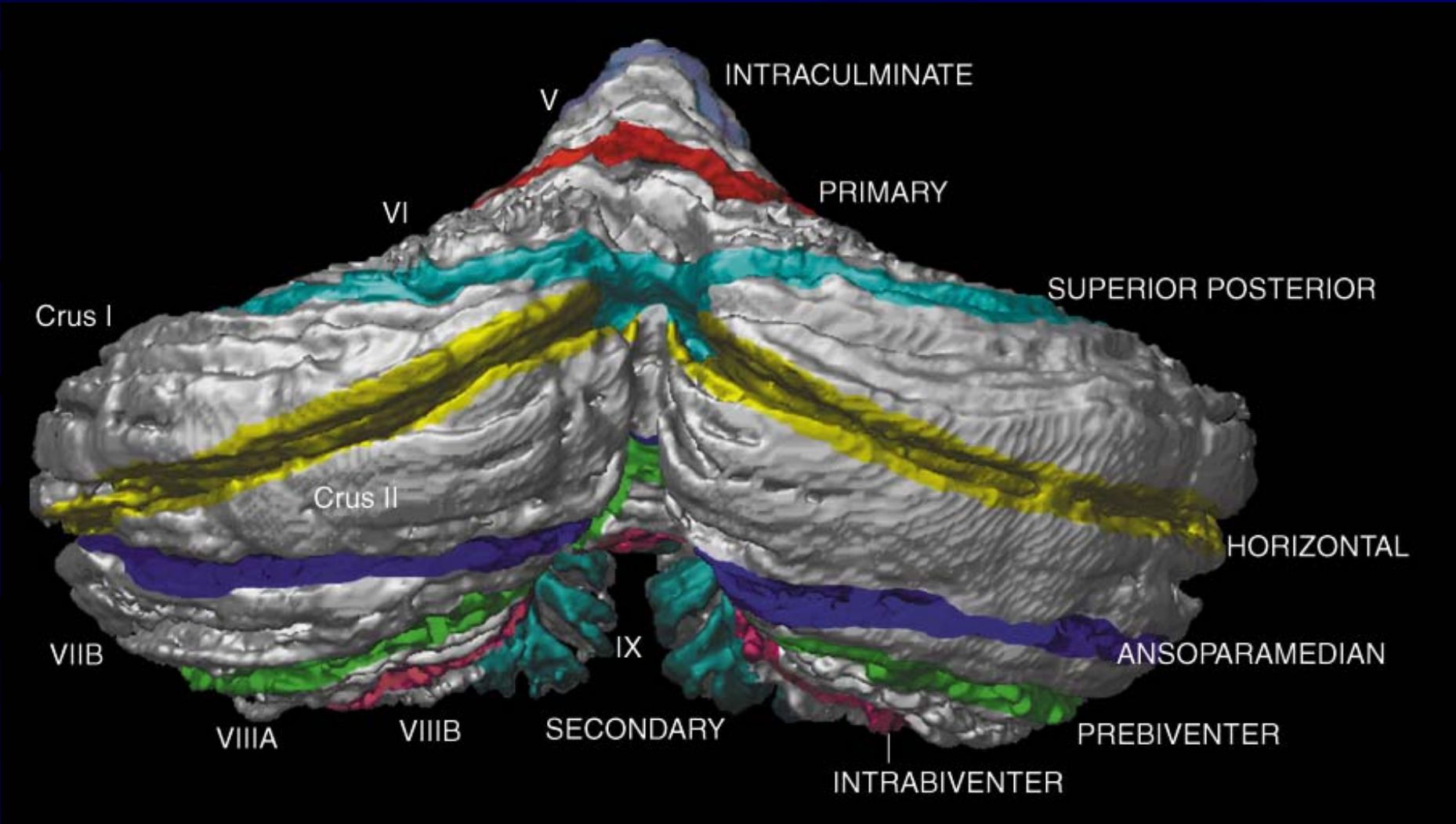
Alan C. Evans

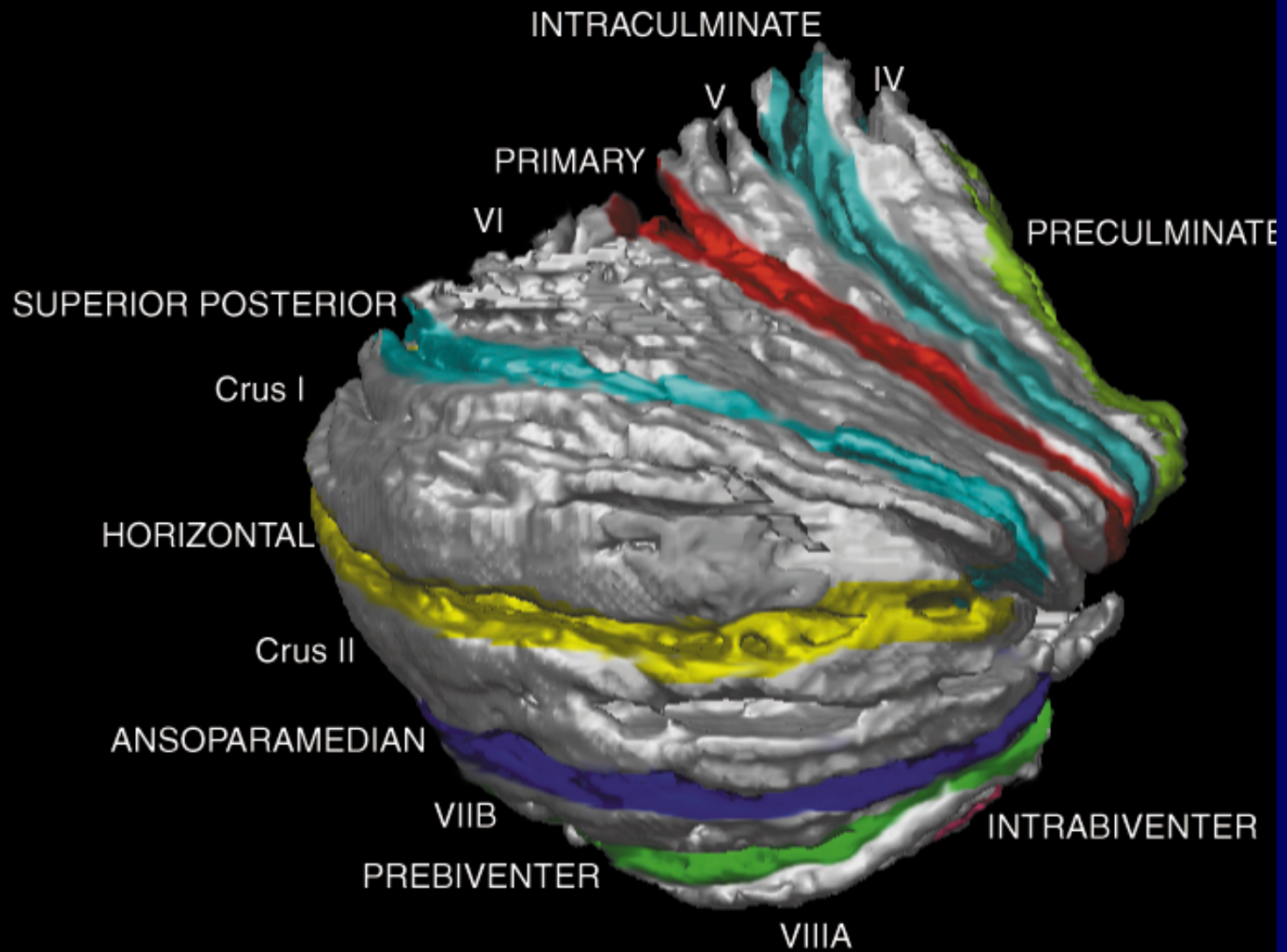


Free Software Included

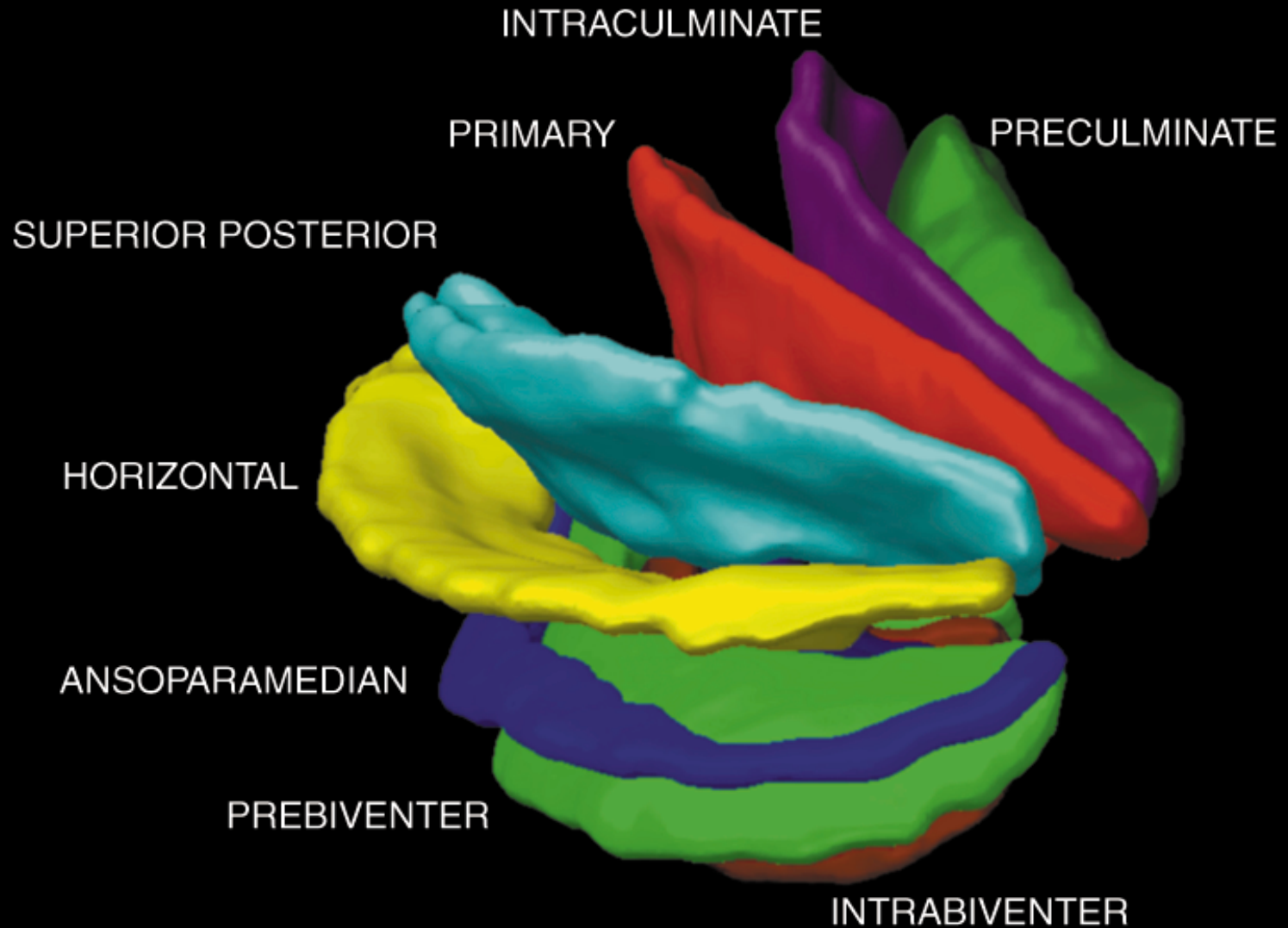








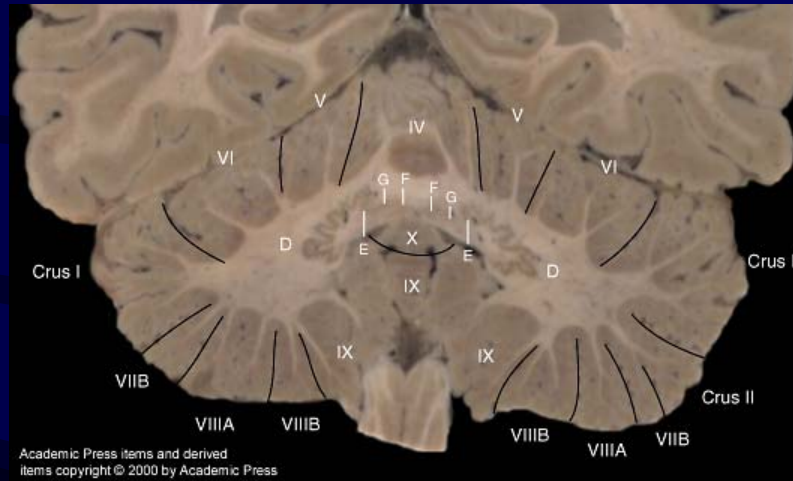
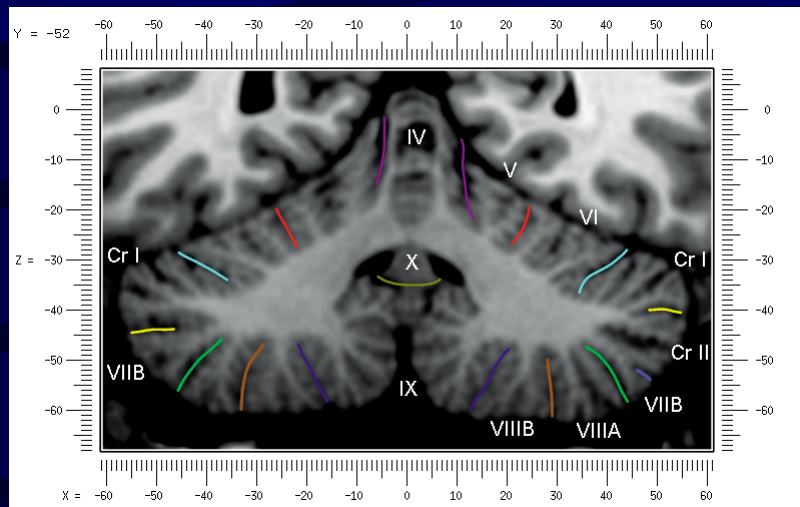
Schmahmann et al., 2000



Cerebellar fissures in 3-D space  
Right lateral view

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

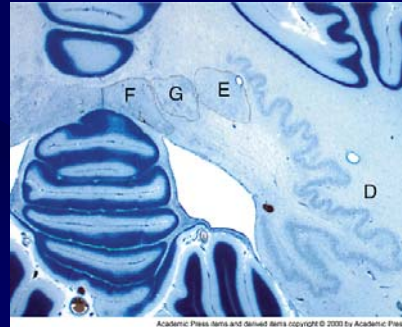




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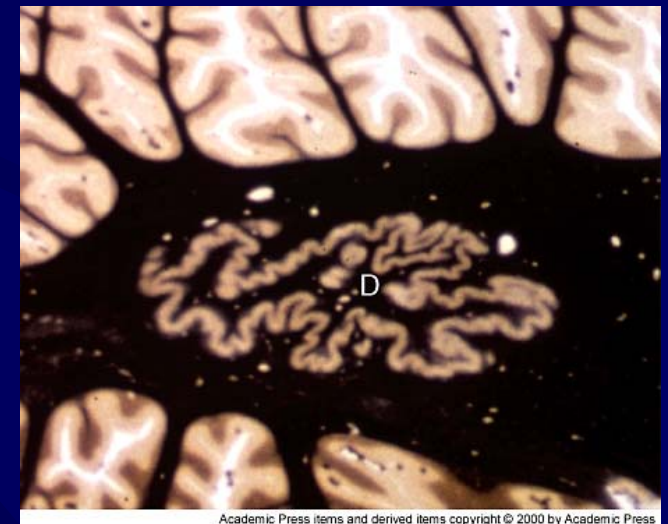
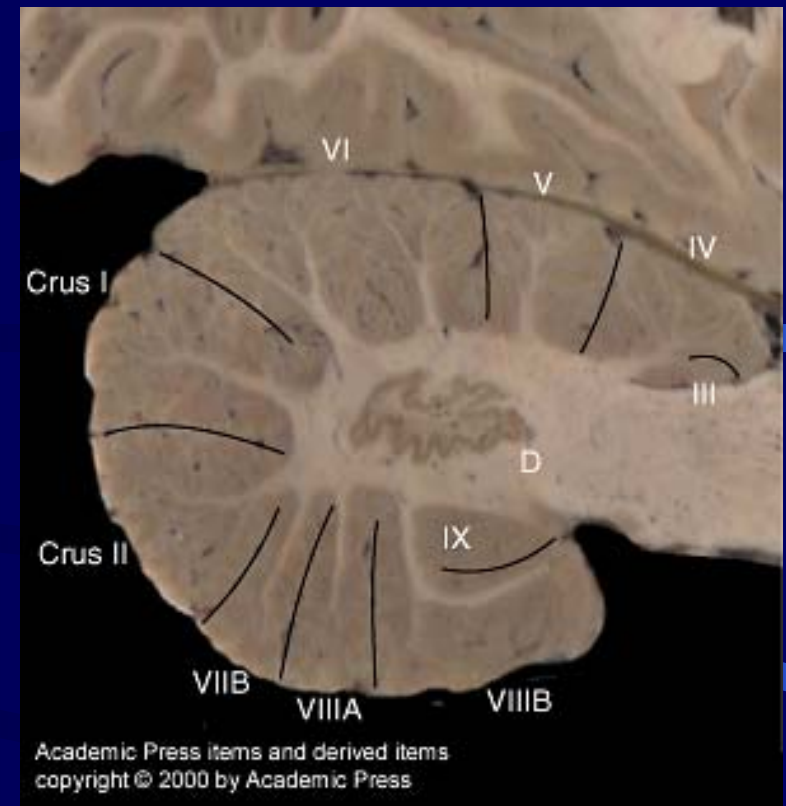
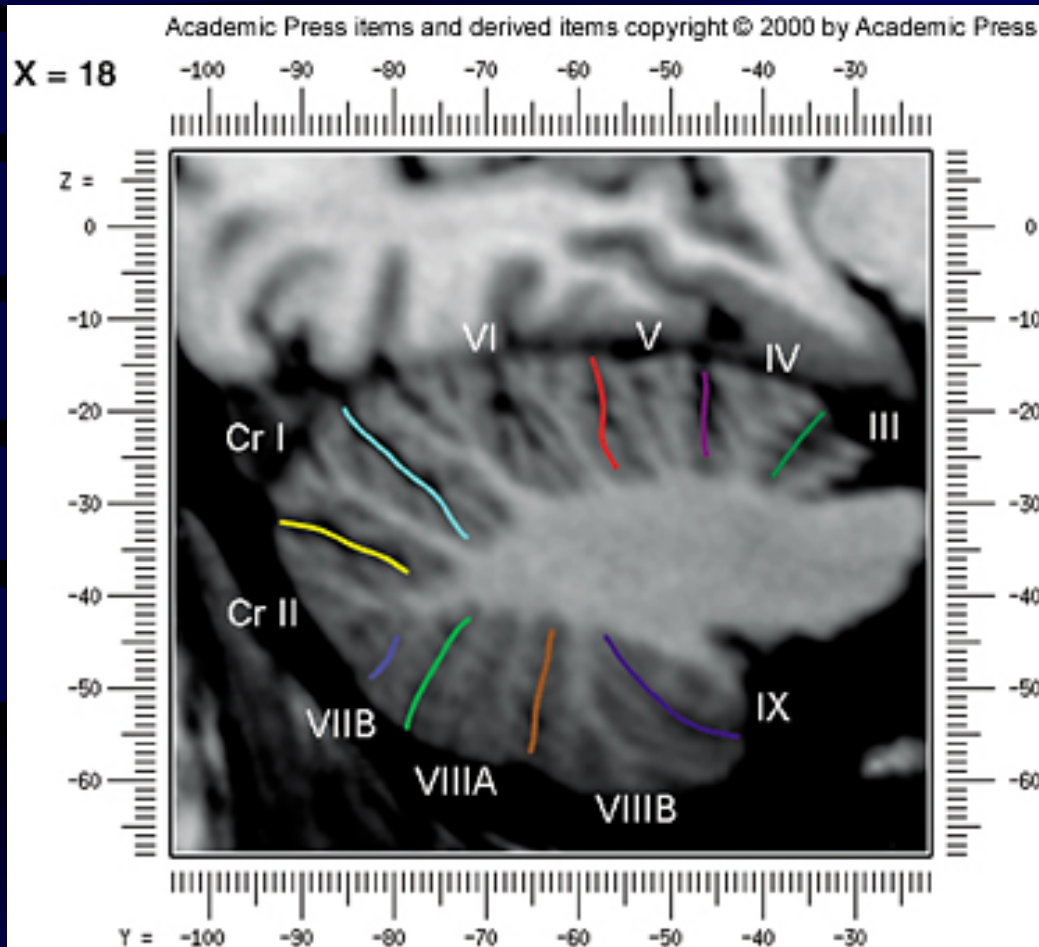


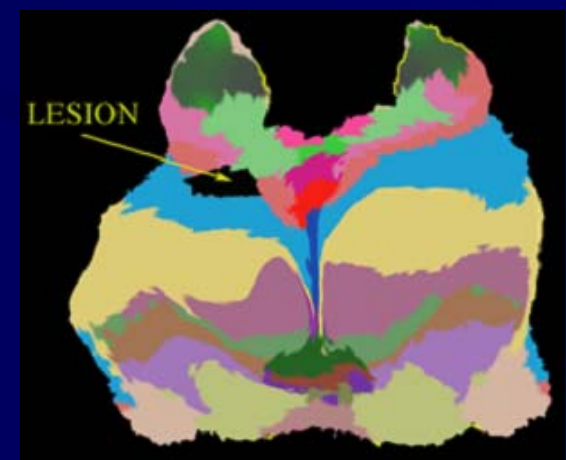
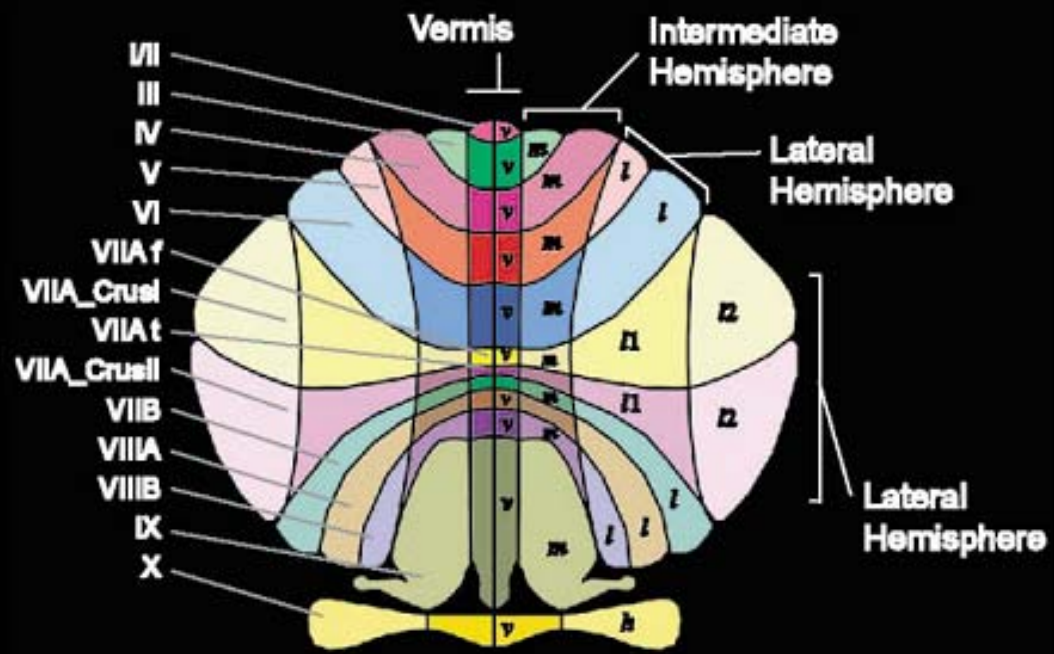
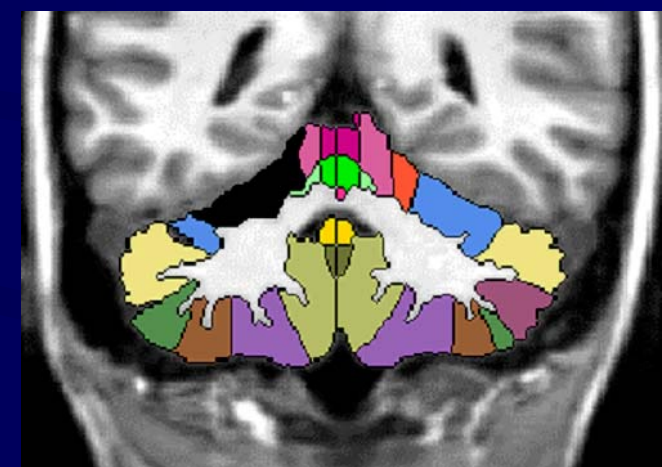
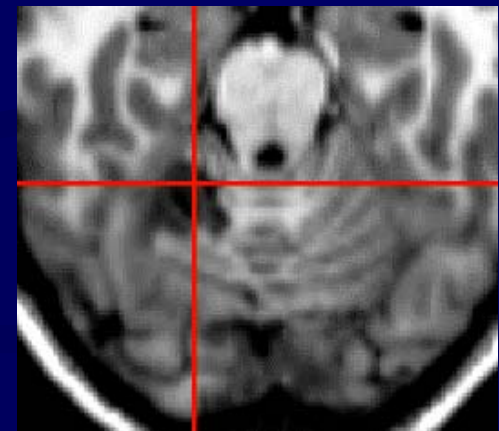
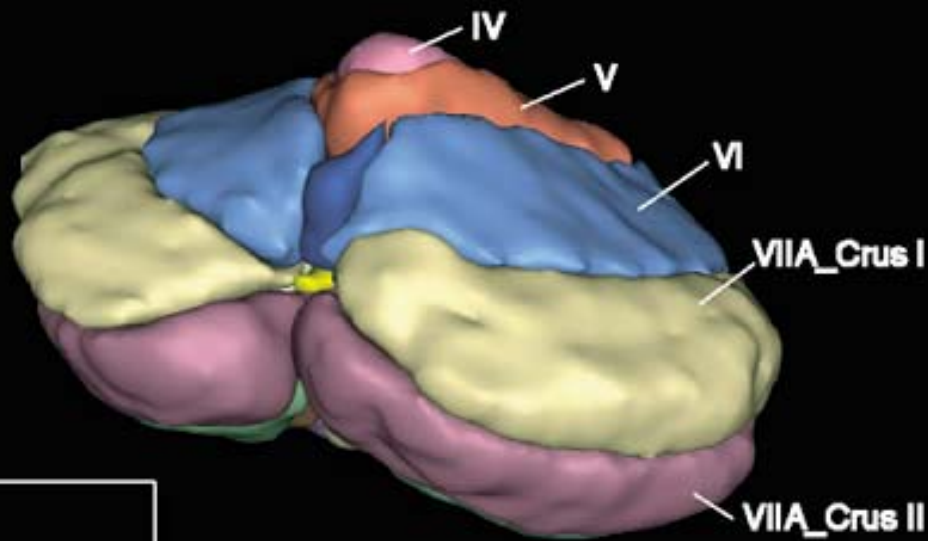
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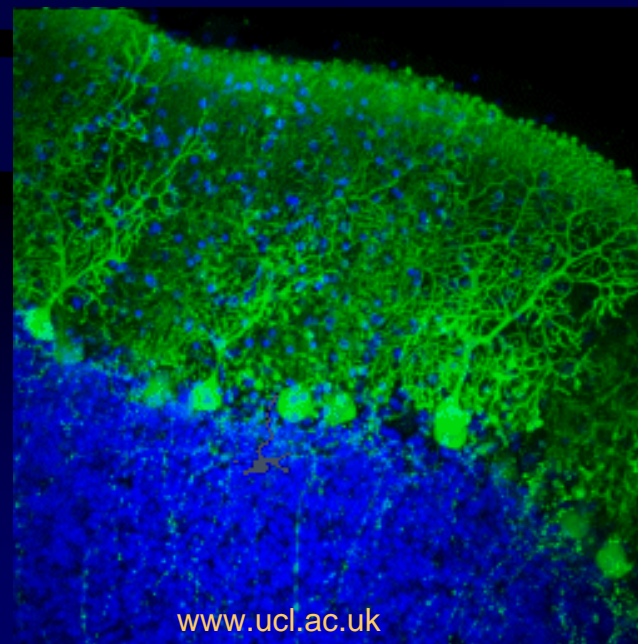
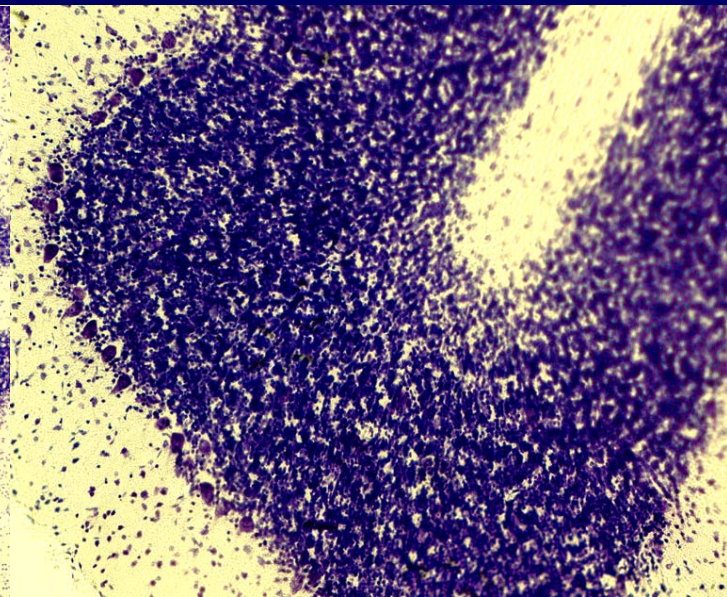
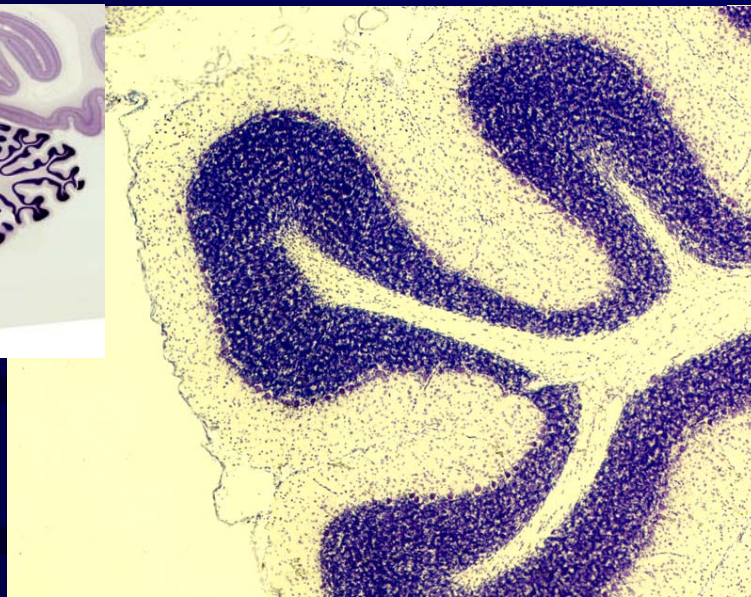
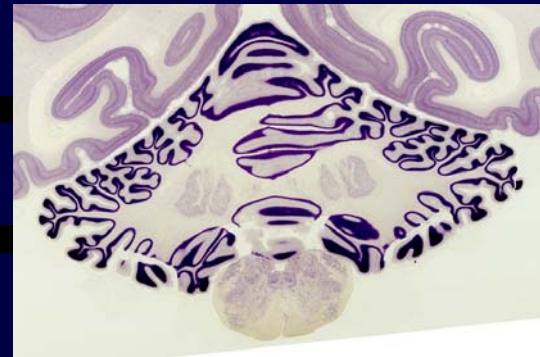
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# Sagittal +18

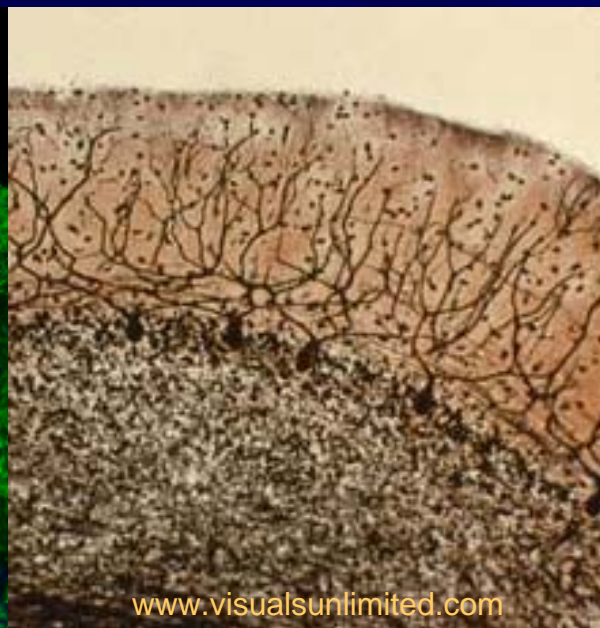




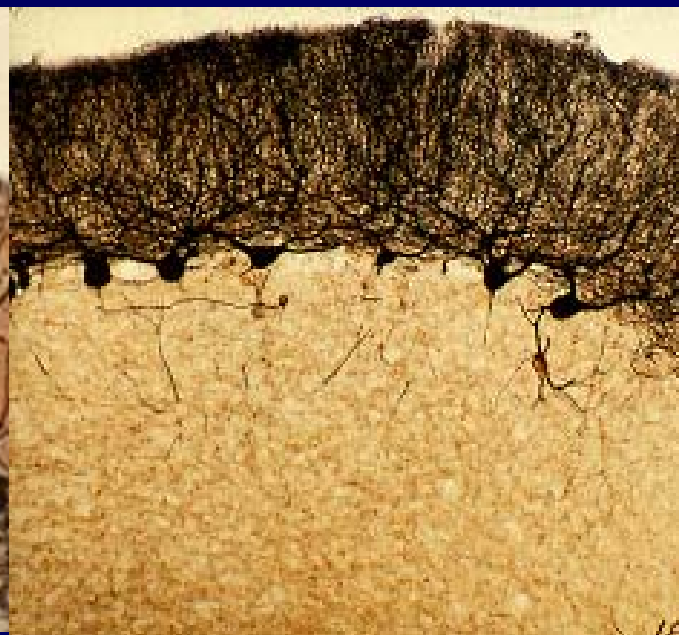
Makris et al., 2005



[www.ucl.ac.uk](http://www.ucl.ac.uk)



[www.visualsunlimited.com](http://www.visualsunlimited.com)





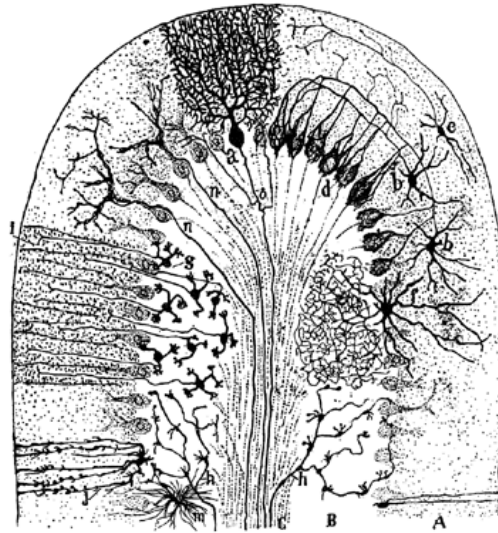
“Purkinje cell tree”



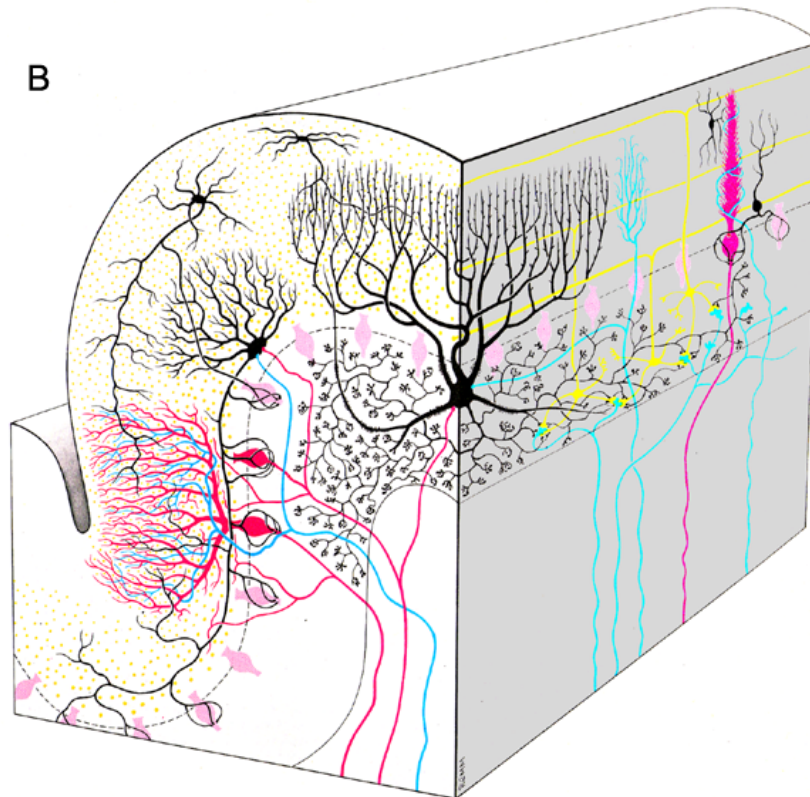


Santiago Ramon y Cajal  
[www.vocesdelaciencia.com.ar](http://www.vocesdelaciencia.com.ar)

A

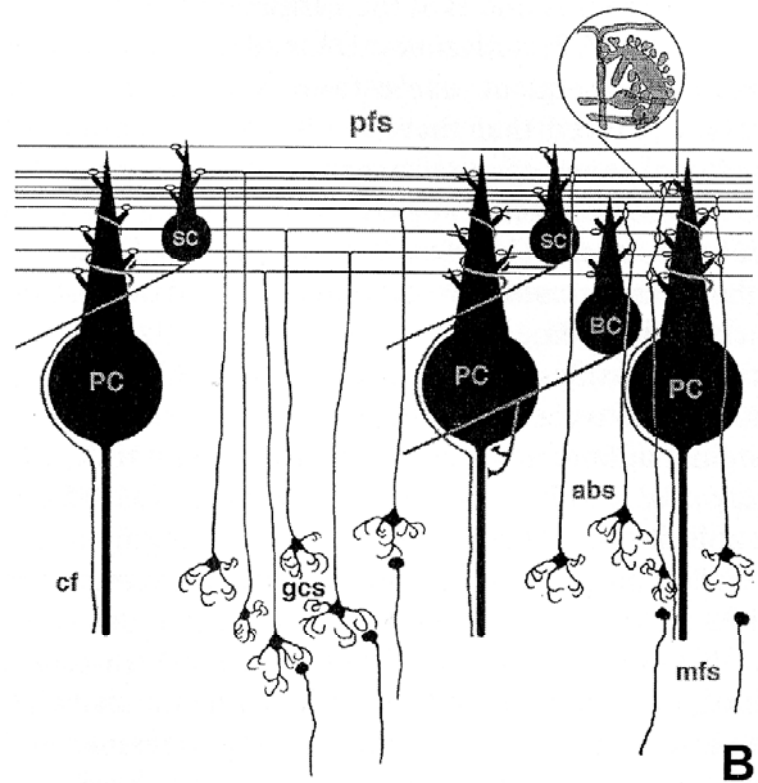
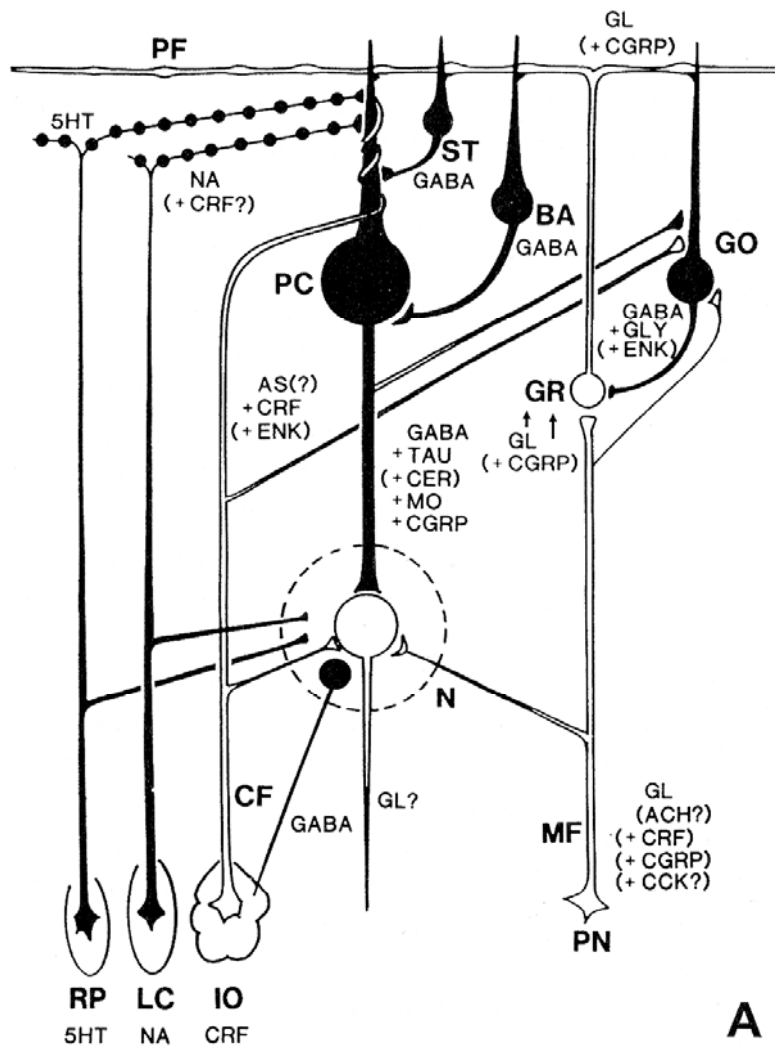


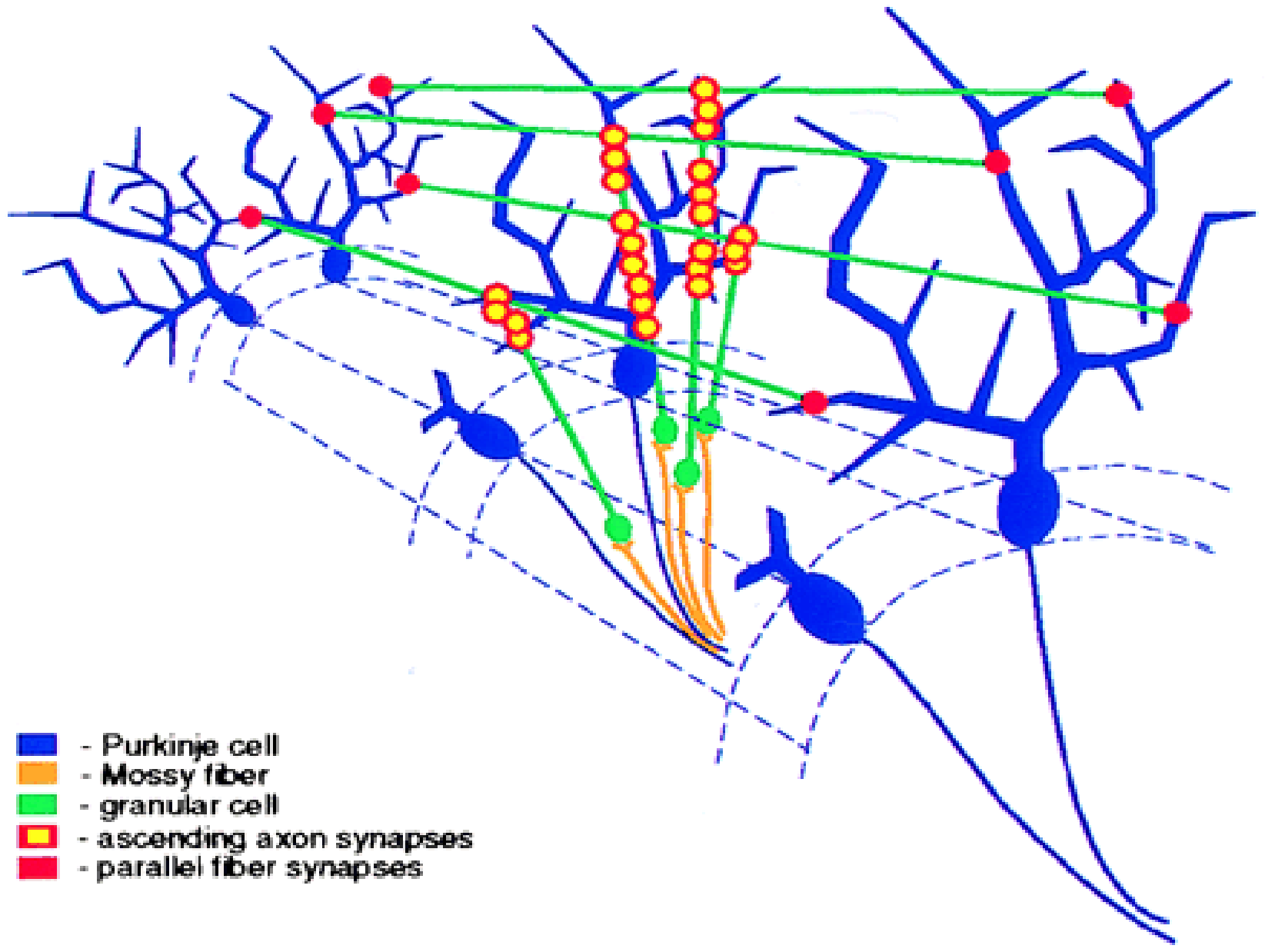
B



Cajal, 1911

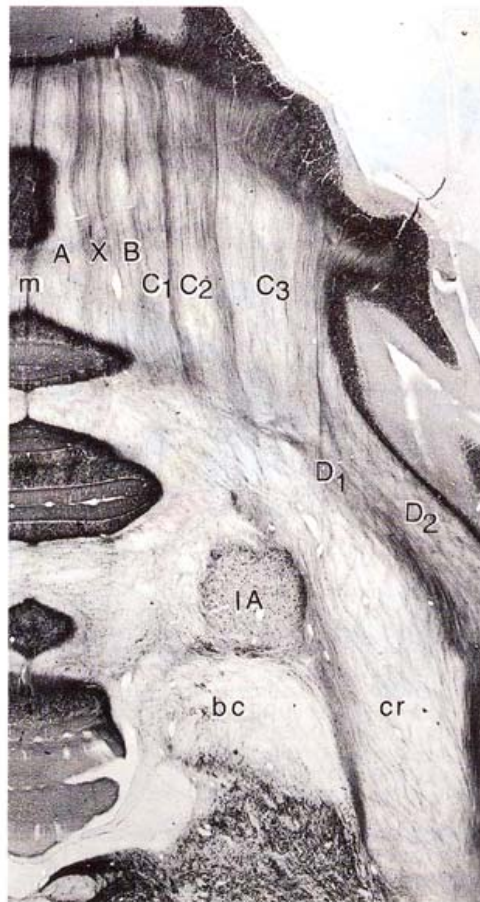
Eccles, Ito, Szentagothai,  
1967



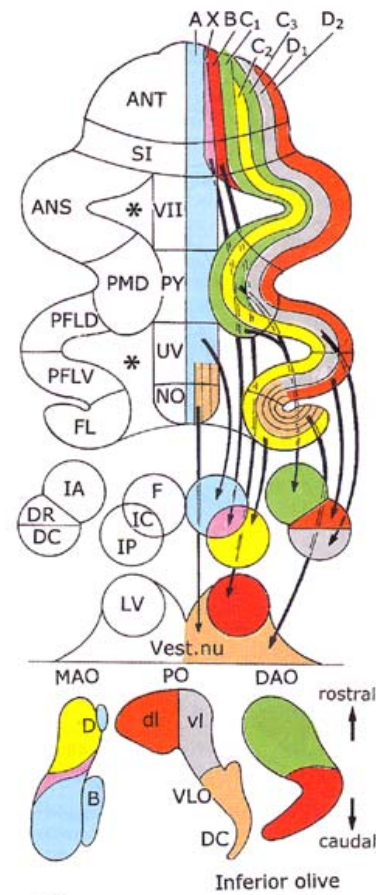


Cohen and Yarom. PNAS 1998; 95:15032-6.

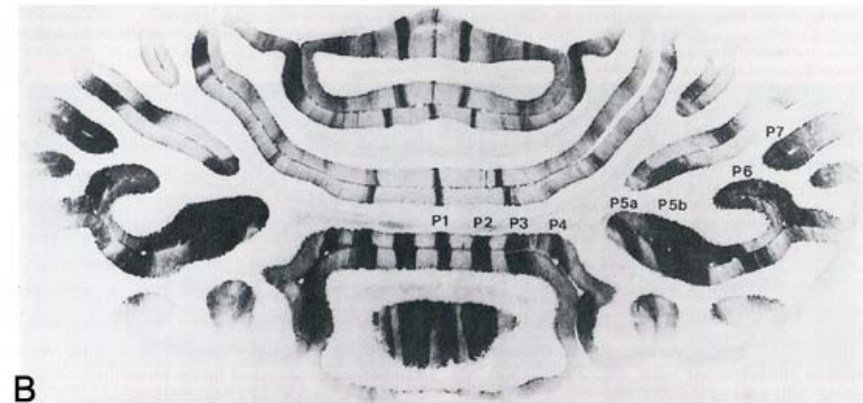




A



C

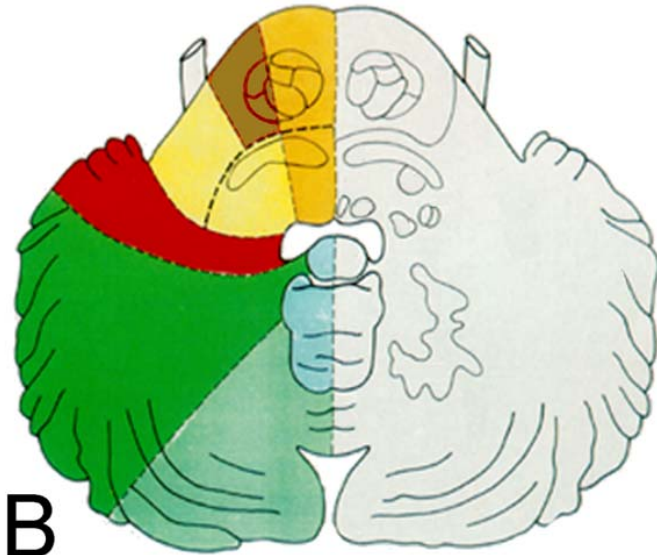


B

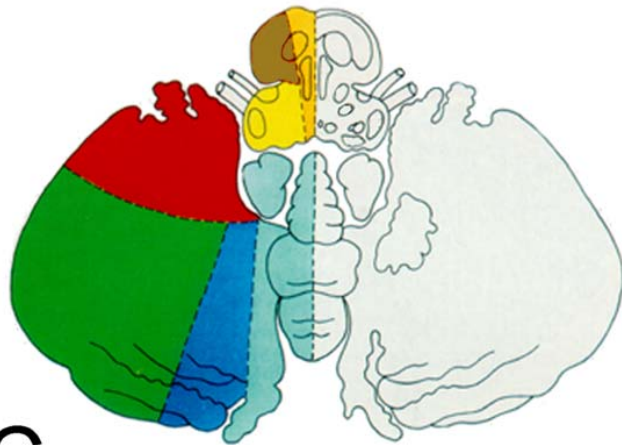
Voogd and Glickstein, 1998  
 Leclerc et al., 1990



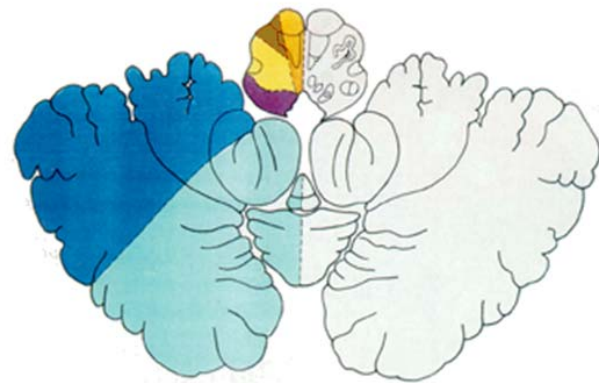
A



B



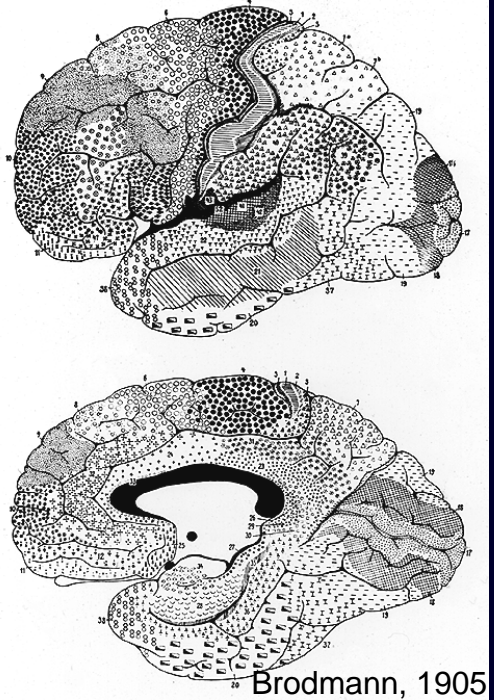
C



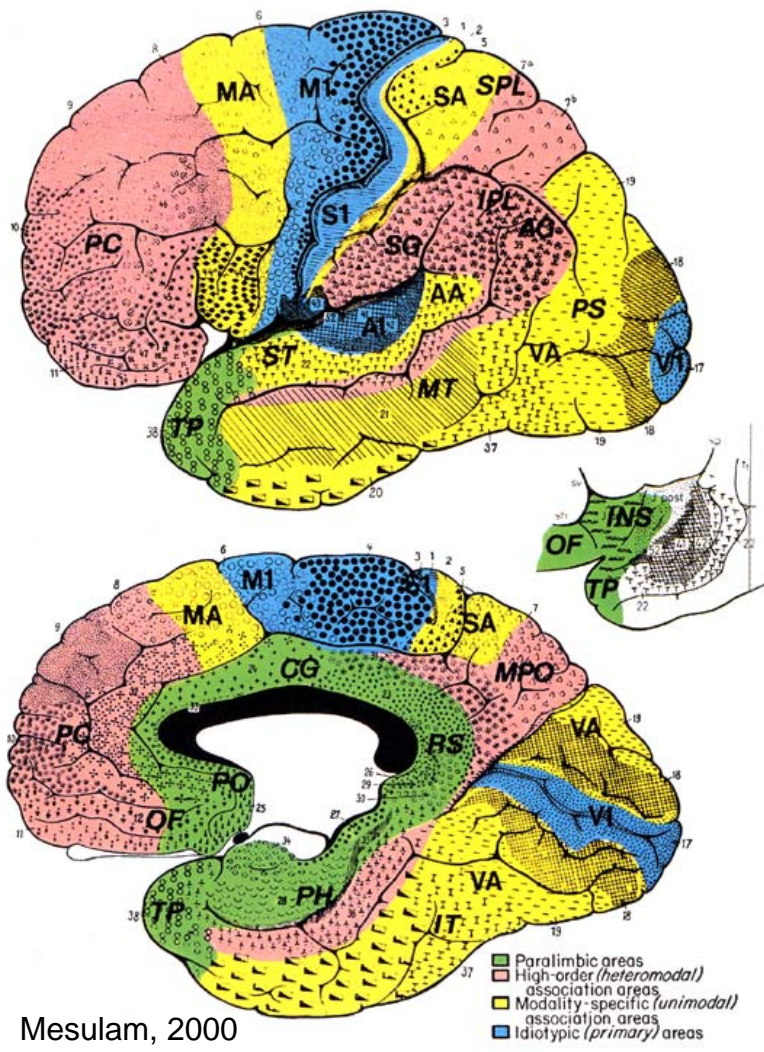
D

Blood supply of human cerebellum.

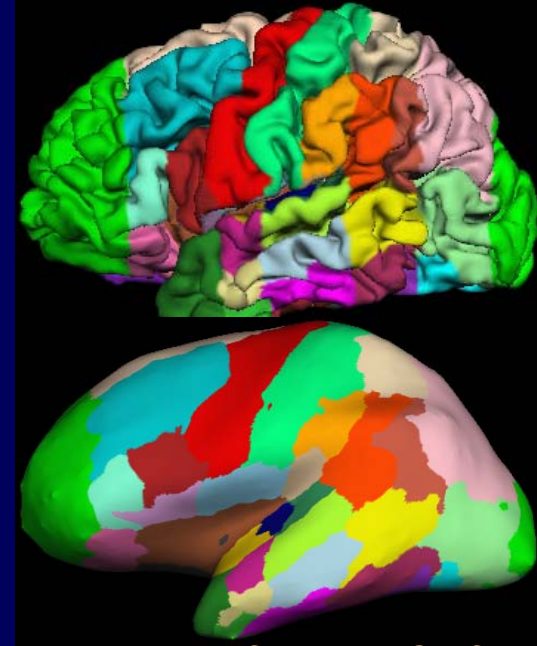
Adapted from Tatu et al., 1996



Brodman, 1905

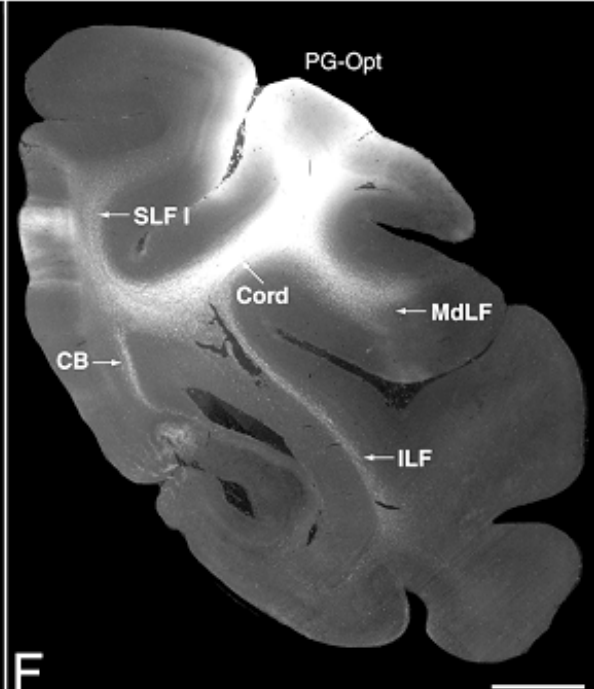
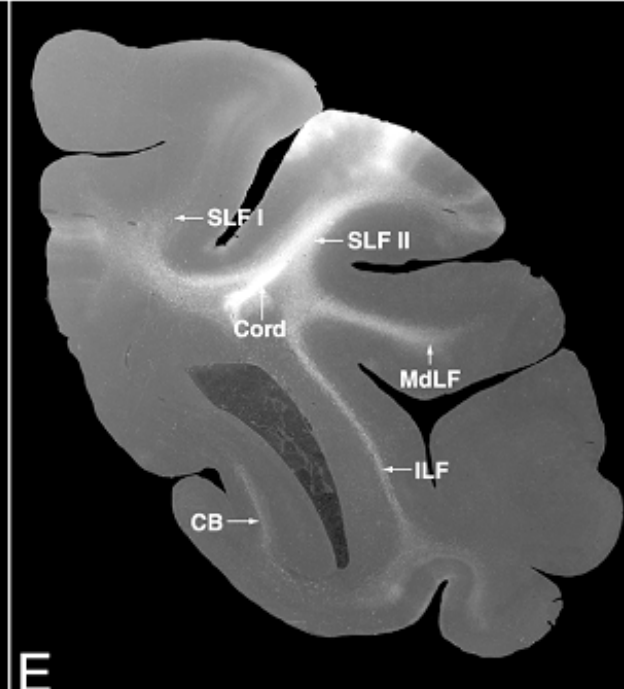
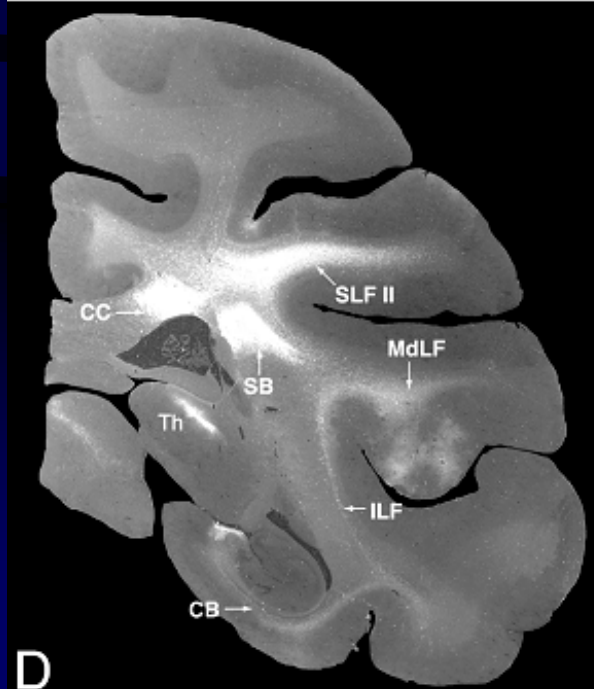
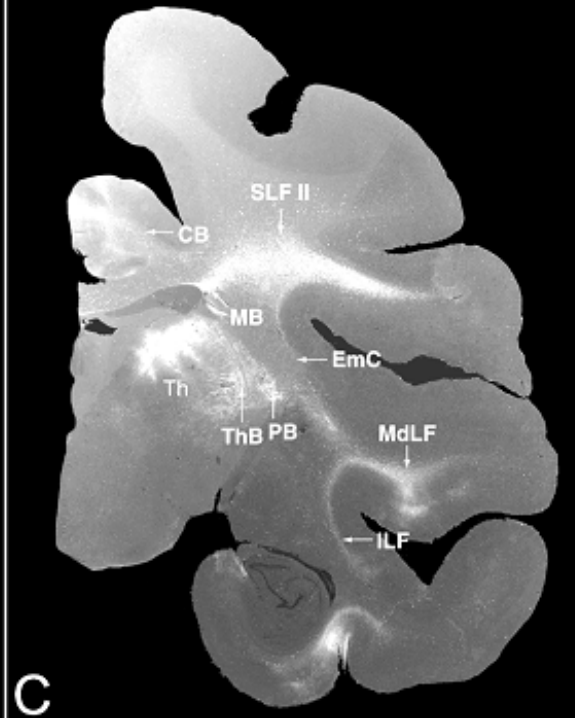
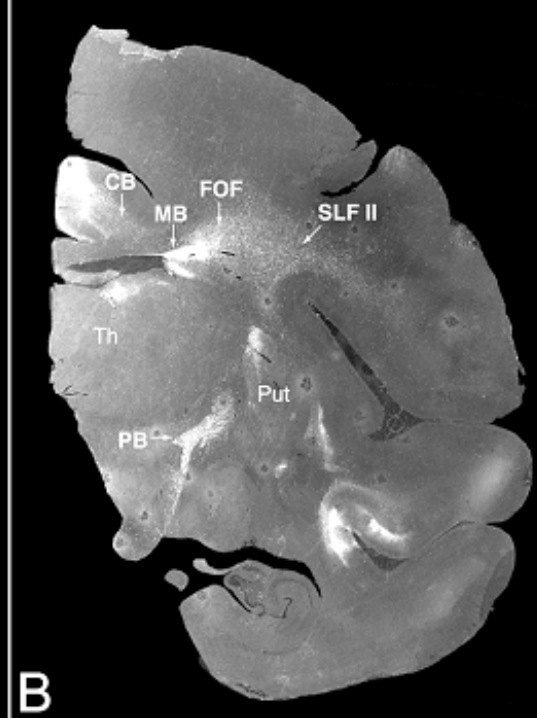
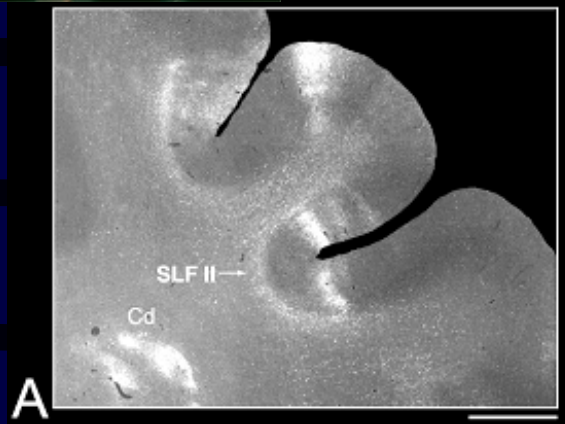


Mesulam, 2000

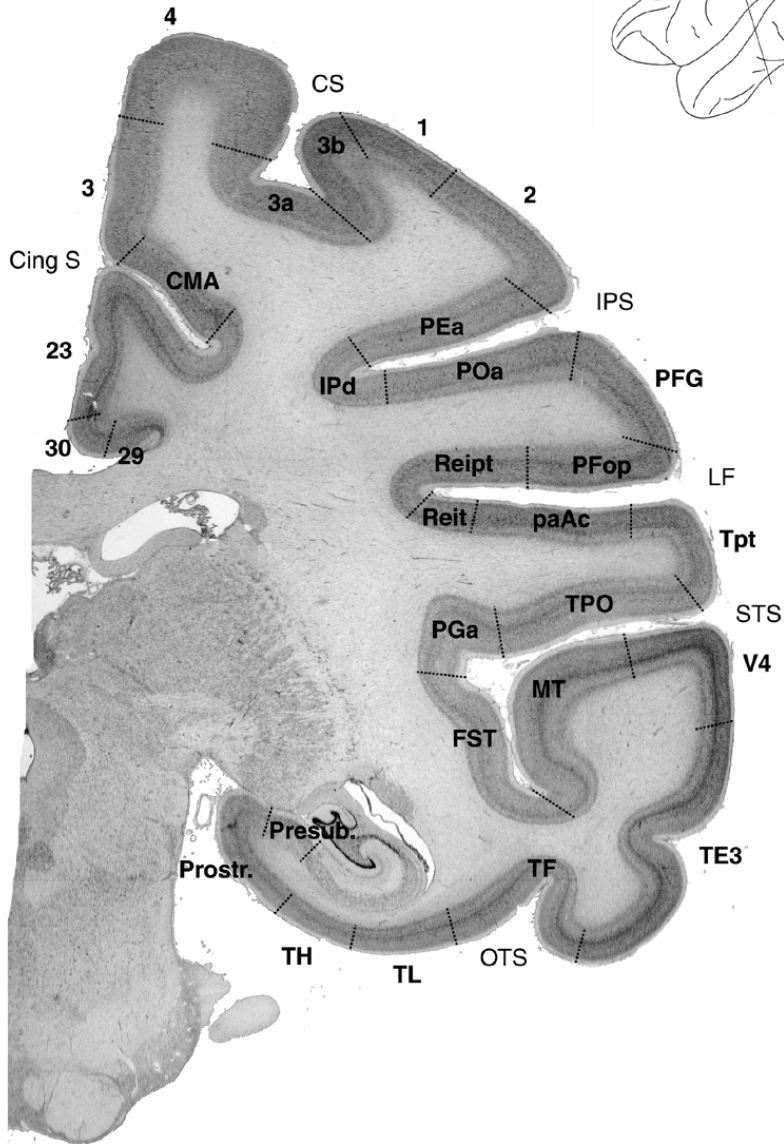
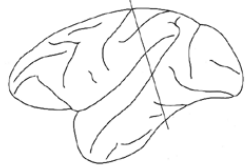


Courtesy MGH-CMA

Distributed neural systems comprise anatomic regions, or nodes  
 Unique architectural properties  
 Geographically arranged throughout cortical and subcortical areas  
 Linked anatomically in a precise and unique manner



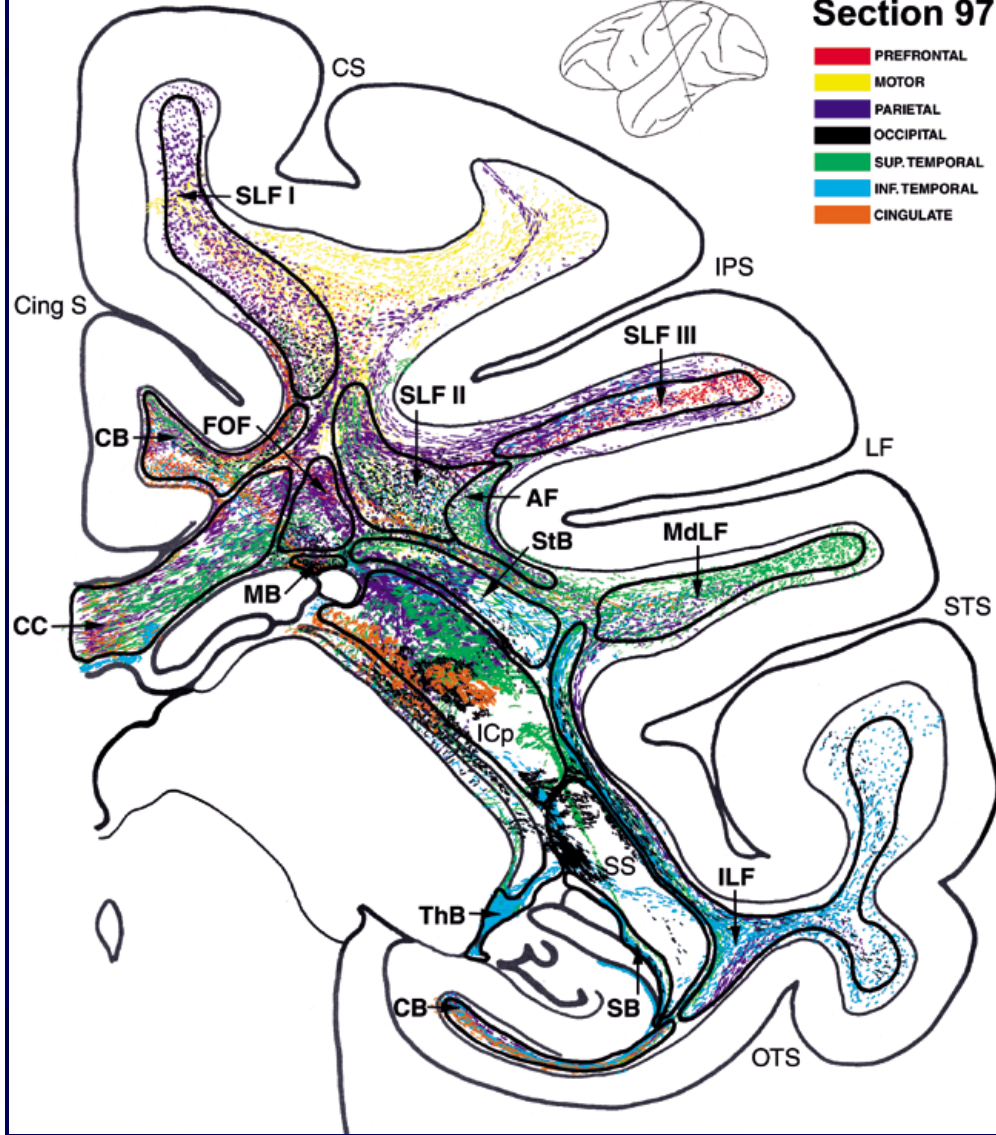
### Section 97



### Section 97



- PREFRONTAL
- MOTOR
- PARIETAL
- OCCIPITAL
- SUP. TEMPORAL
- INF. TEMPORAL
- CINGULATE



# General principle of organization of cerebral connections: 5 major pathways

Association fibers

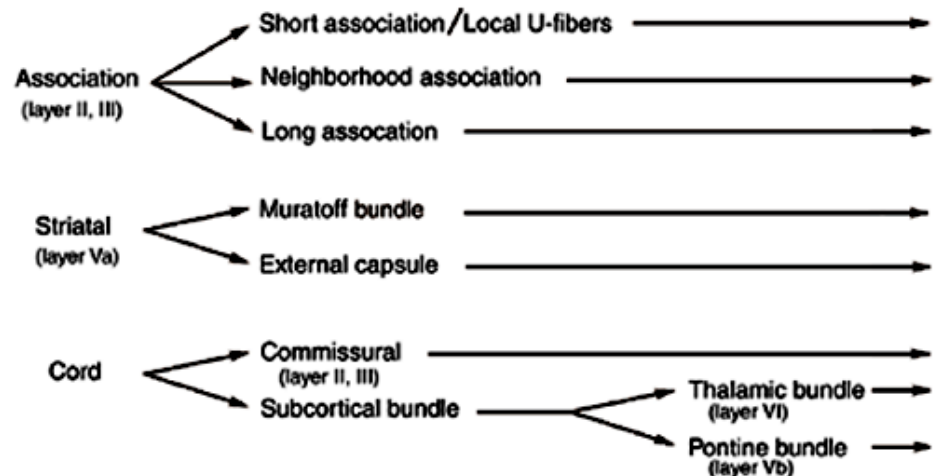
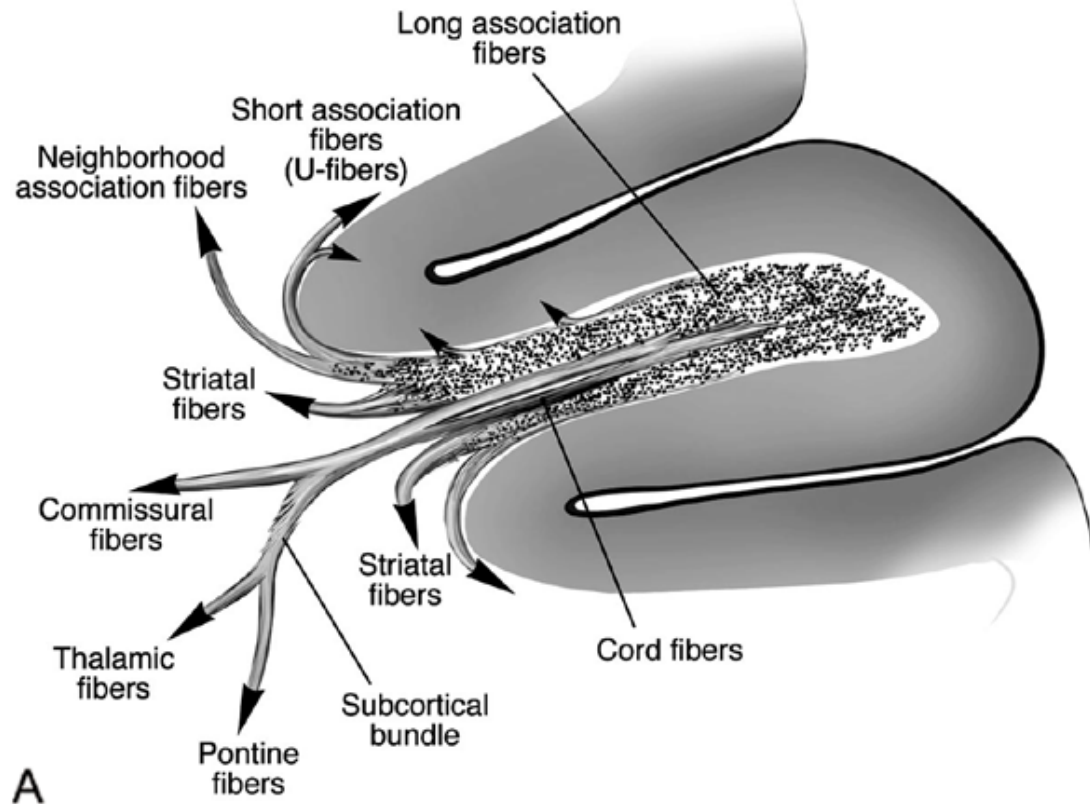
Striatal fibers

Commissural fibers

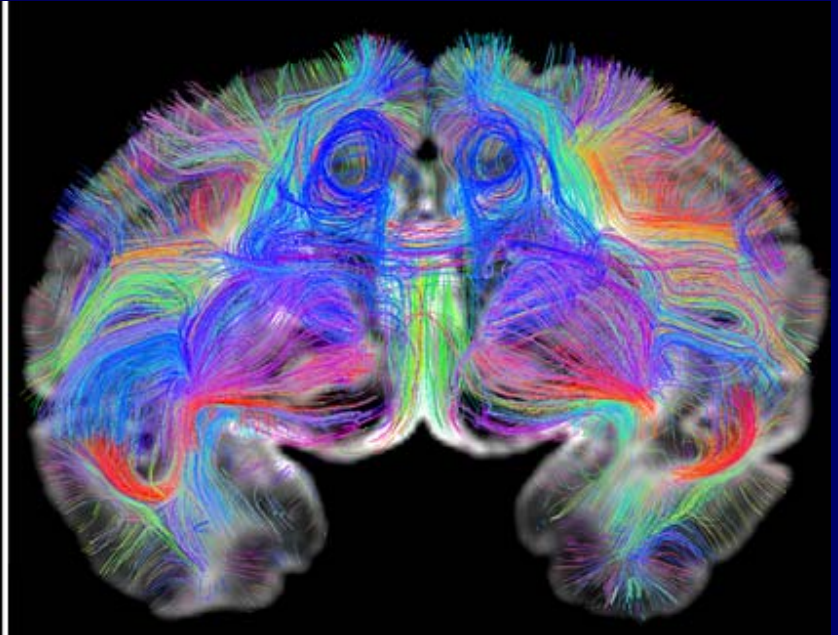
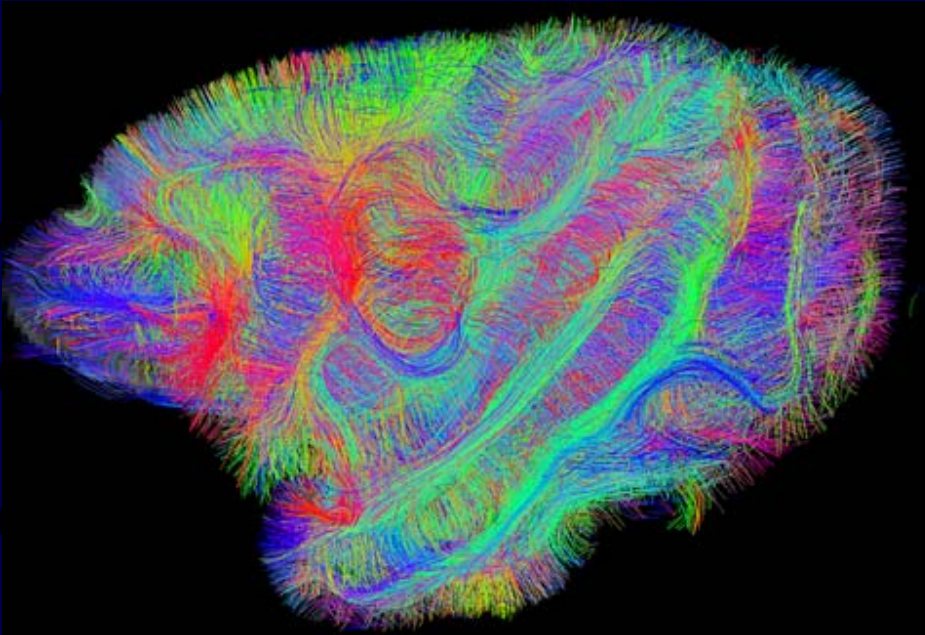
Projection fibers

–Thalamic bundle

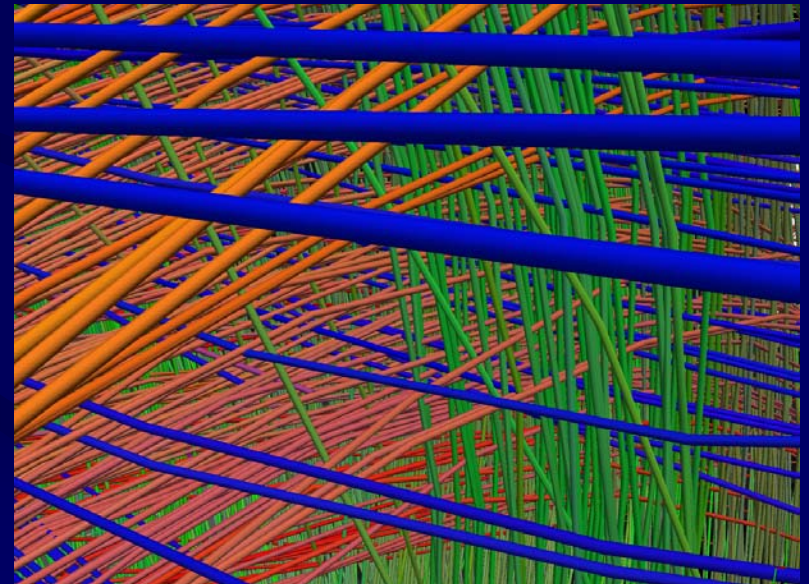
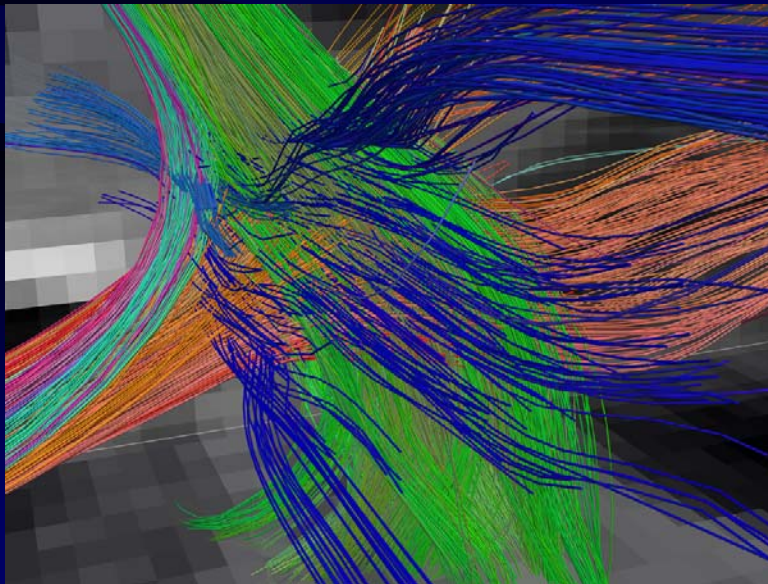
–Pontine bundle



# Diffusion spectrum imaging (DSI) - monkey

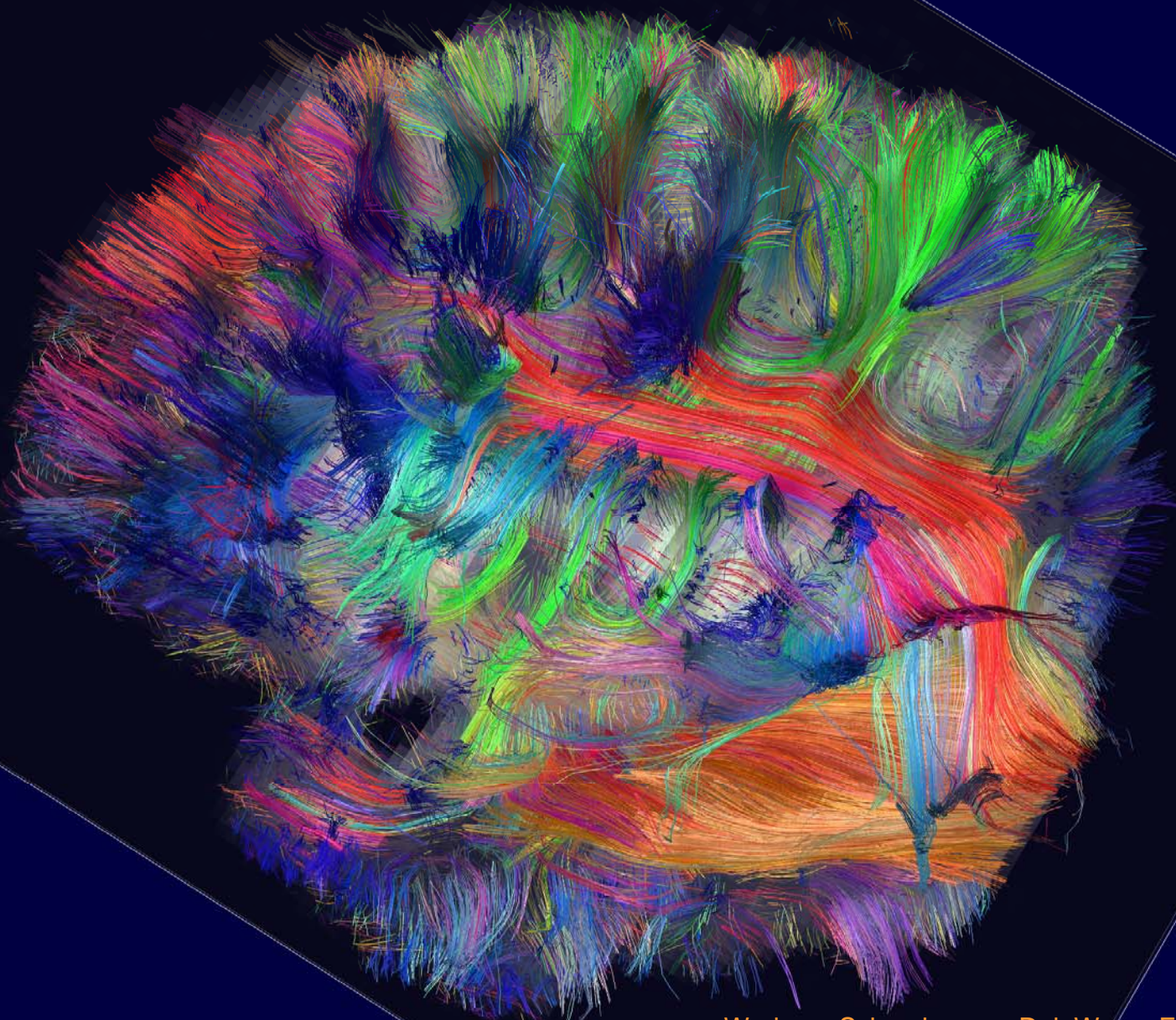


Schmahmann, Pandya, Wang, Dai, D'Arceuil, de Crespigny, Wedeen, Brain, 2007



Wedeen, Wang, Schmahmann et al., NeuroImage 2008

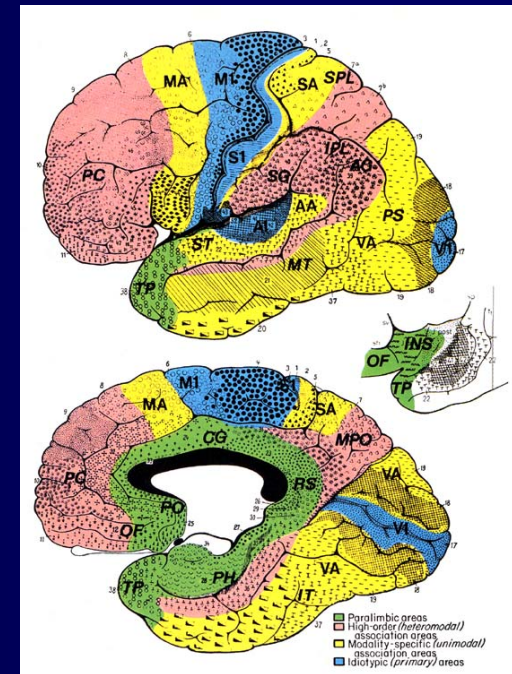
# Ex-vivo DSI Tractography of 80-90% of a Human Cerebral Left Hemisphere



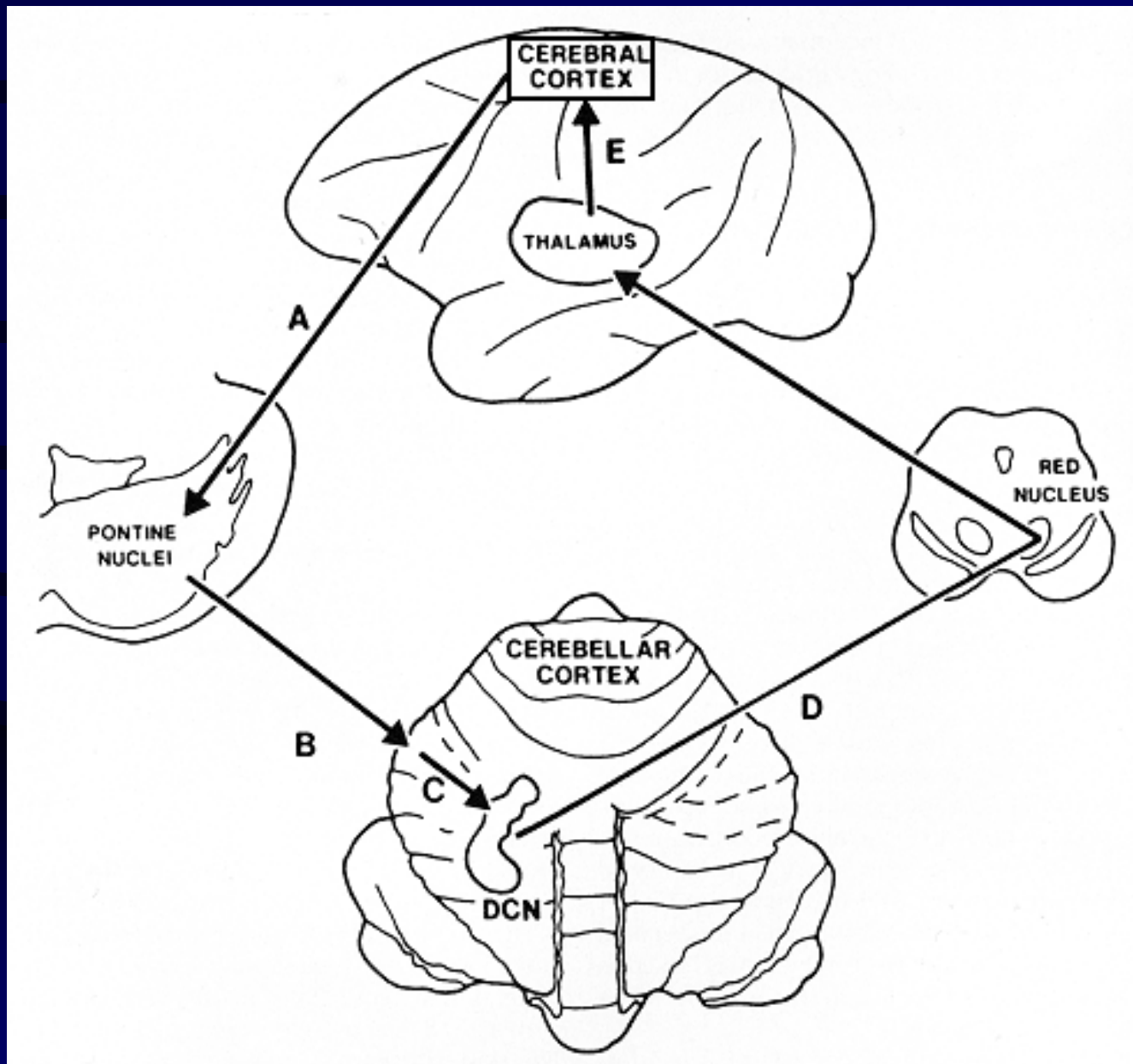


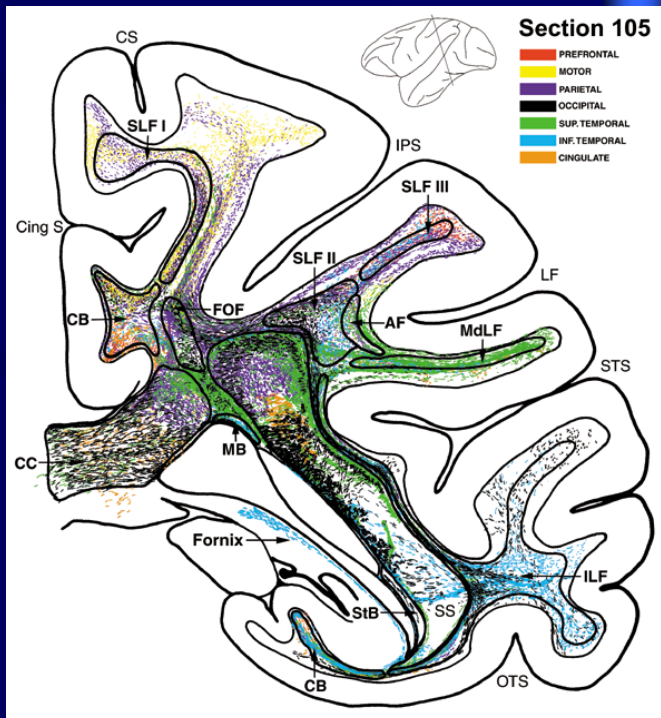
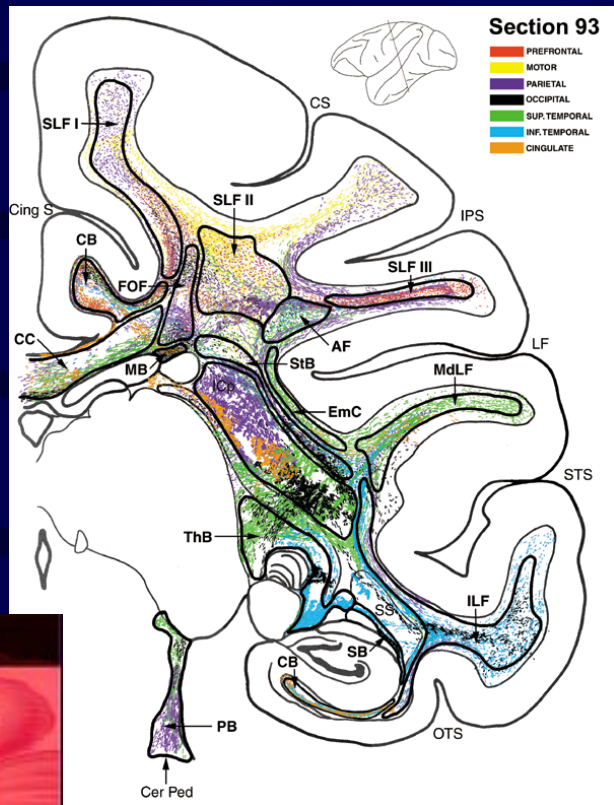
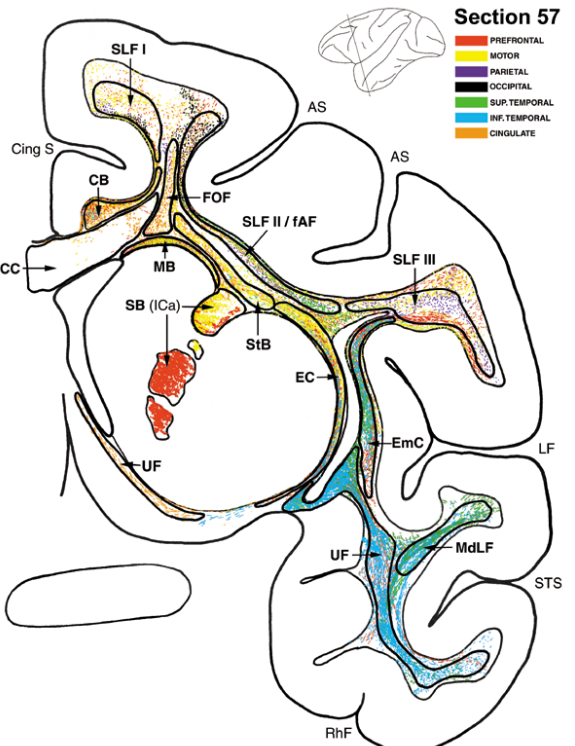
# Subcortical Nodes in Distributed Neural Circuits

- Basal Ganglia
- Thalamus
- Cerebellum
- Cerebral White Matter



# The cerebrocerebellar circuit



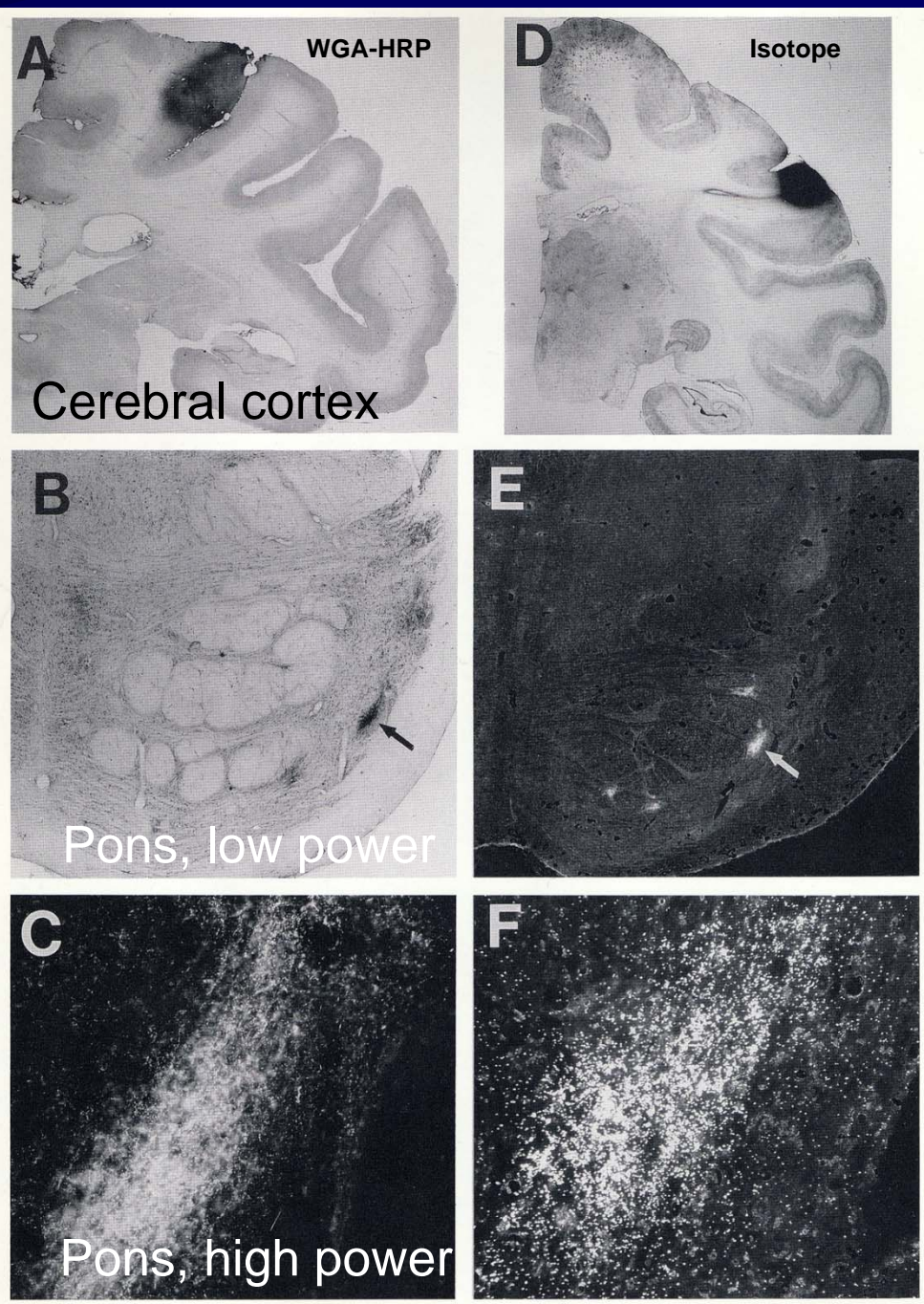
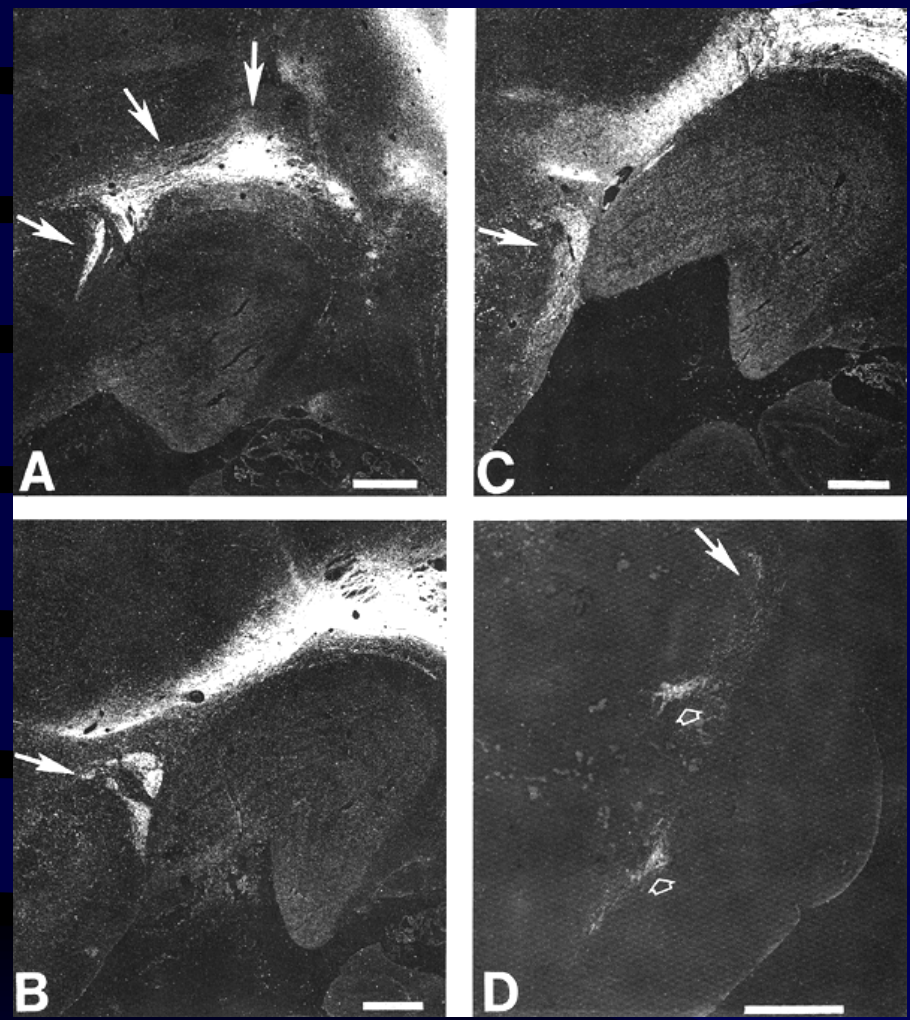


SCHMAHMANN  
PANDYA

Fiber Pathways of the Brain

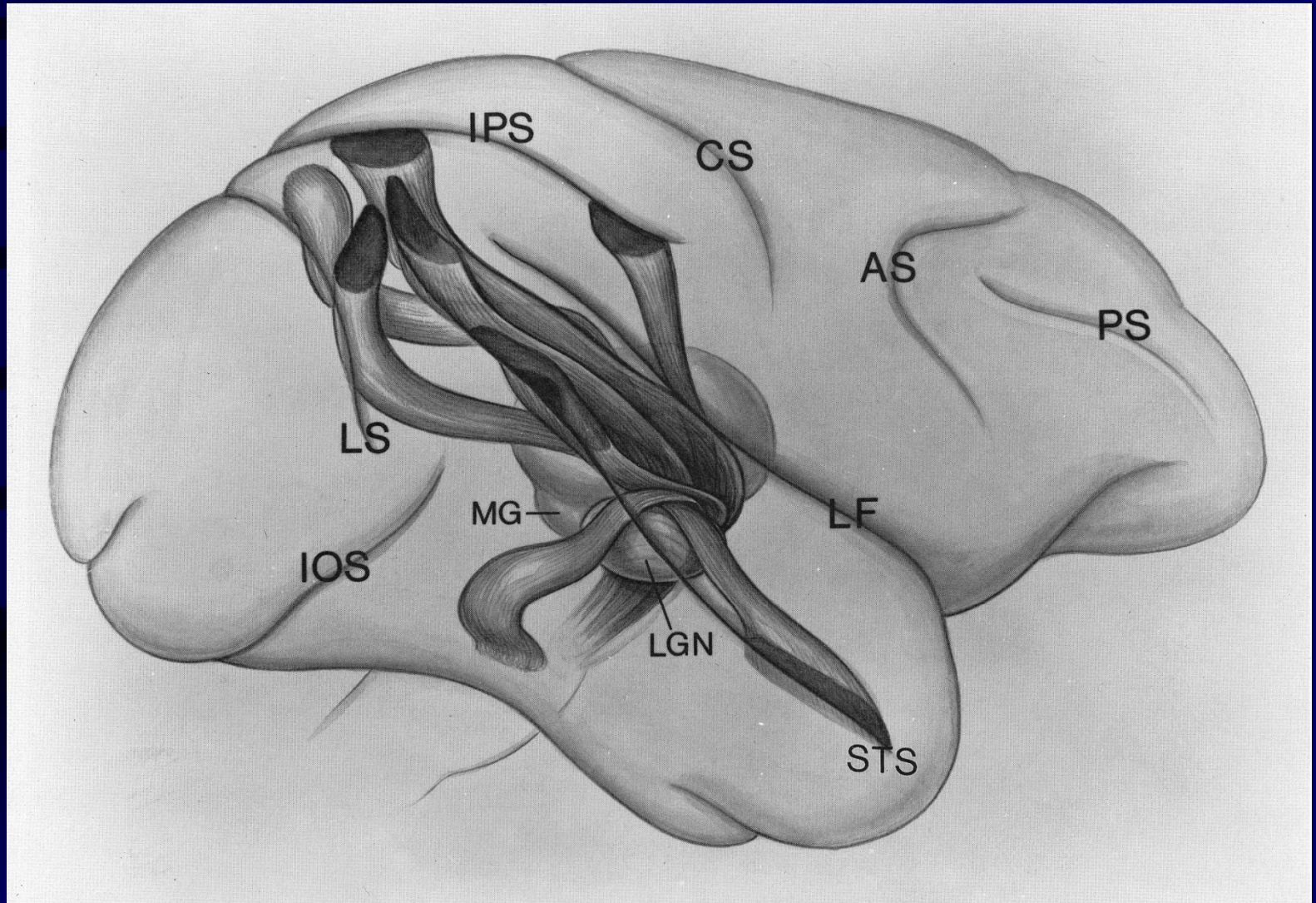
JEREMY D. SCHMAHMANN  
DEEPAK N. PANDYA

OXFORD

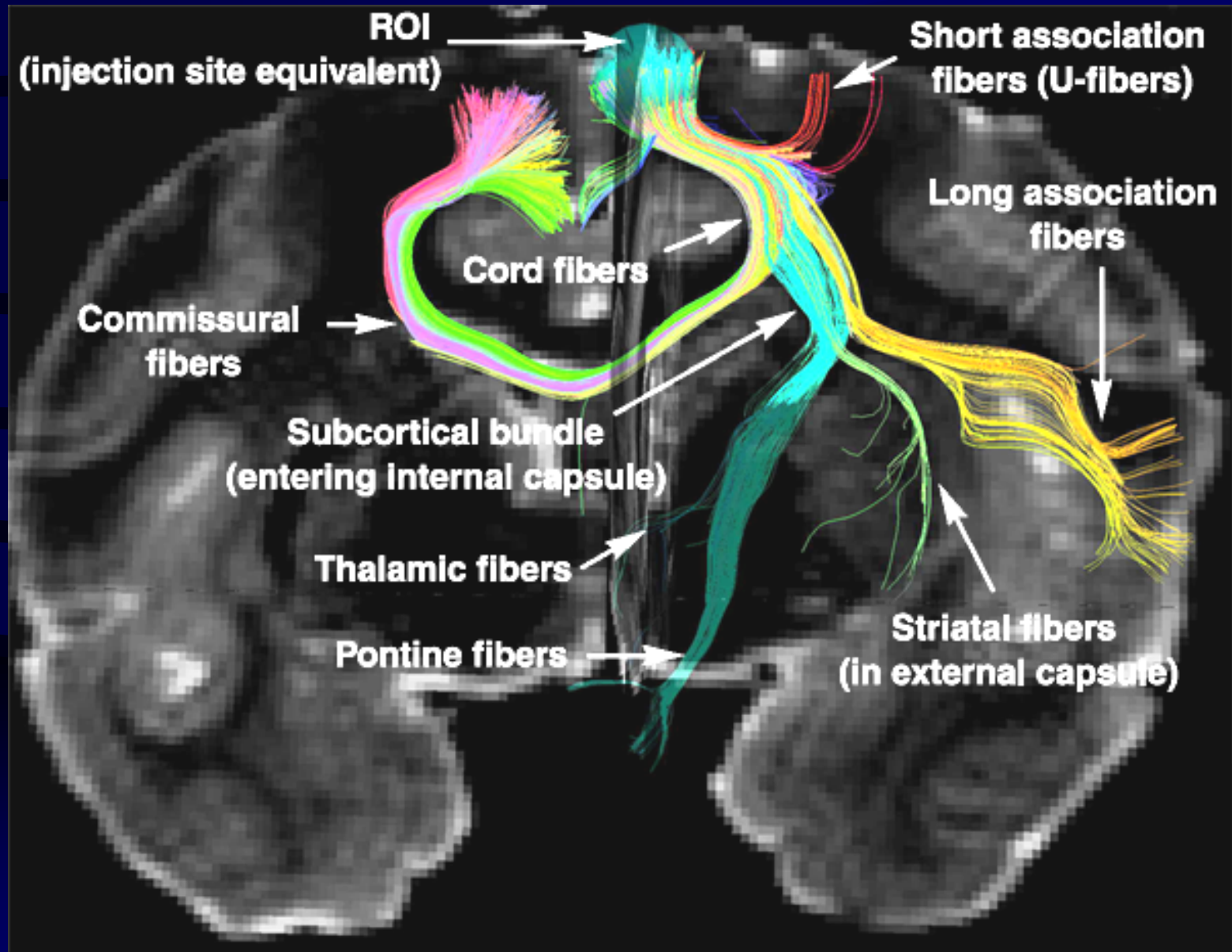


Schmahmann and Pandya, 1989, 1992

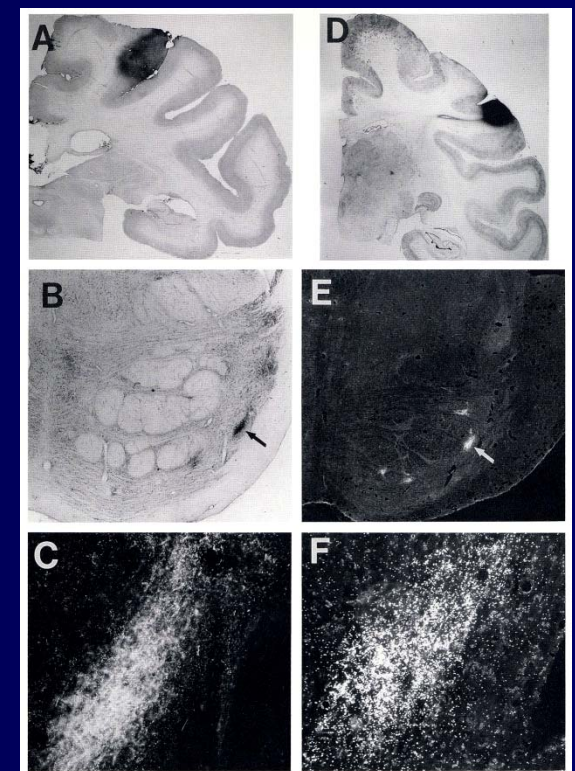
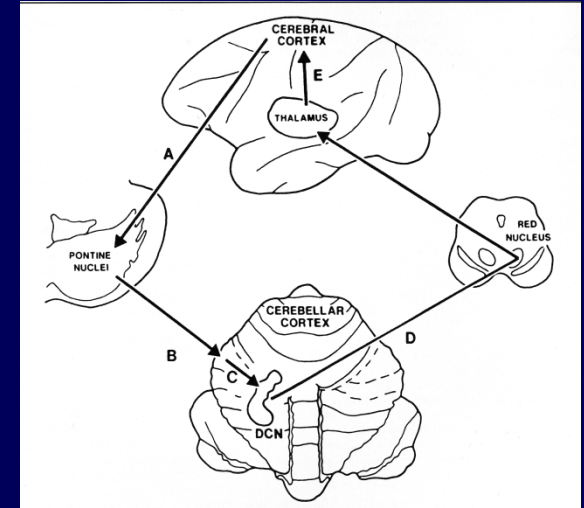
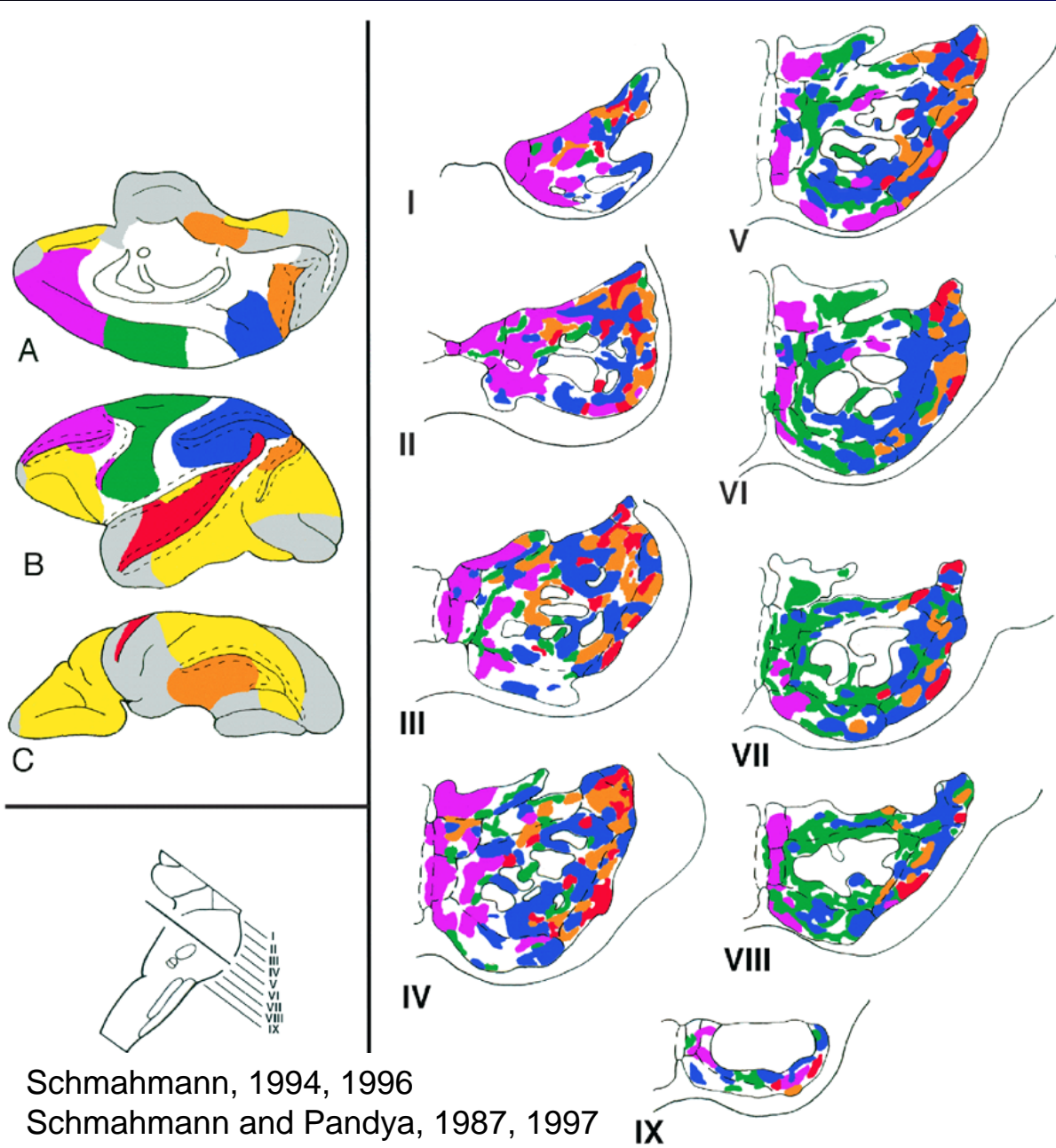
# Trajectory of corticopontine fibers in monkey.



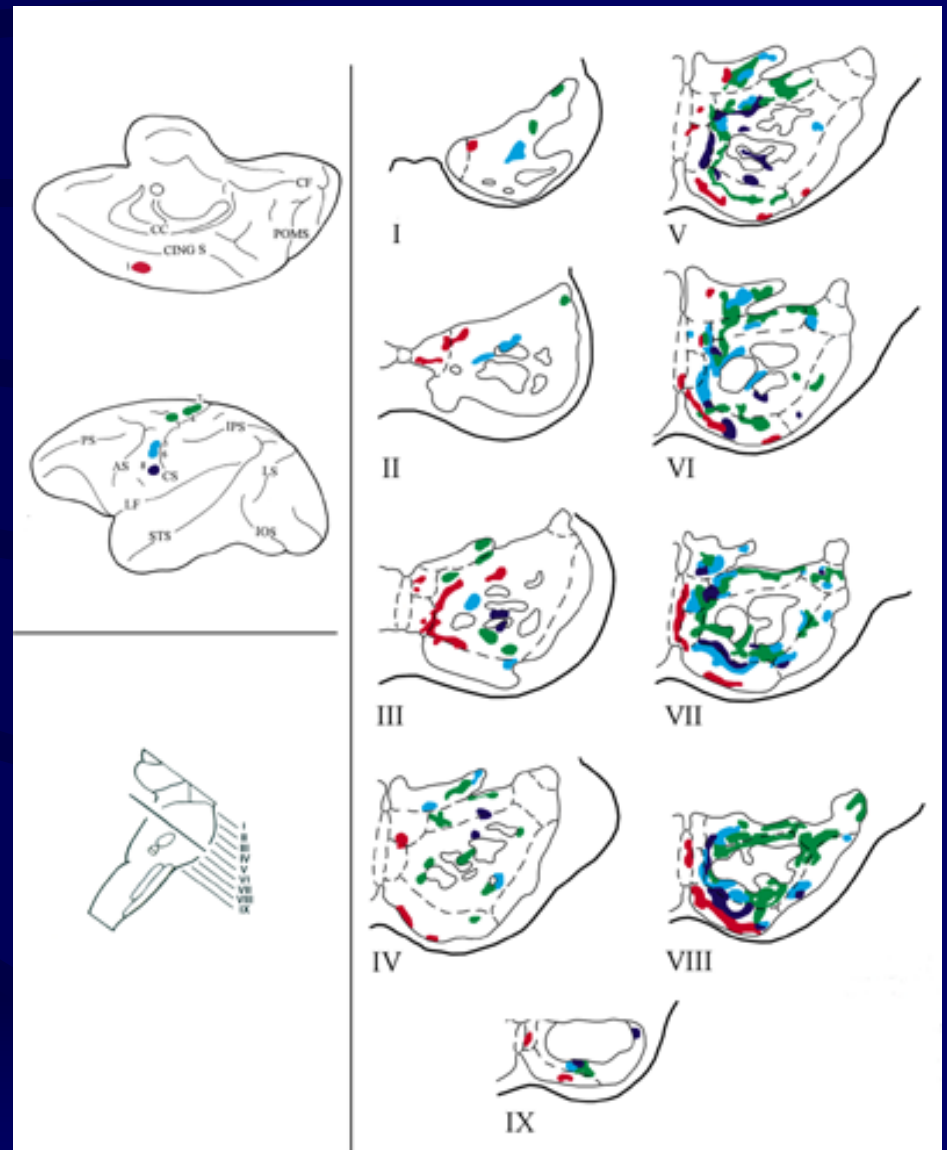
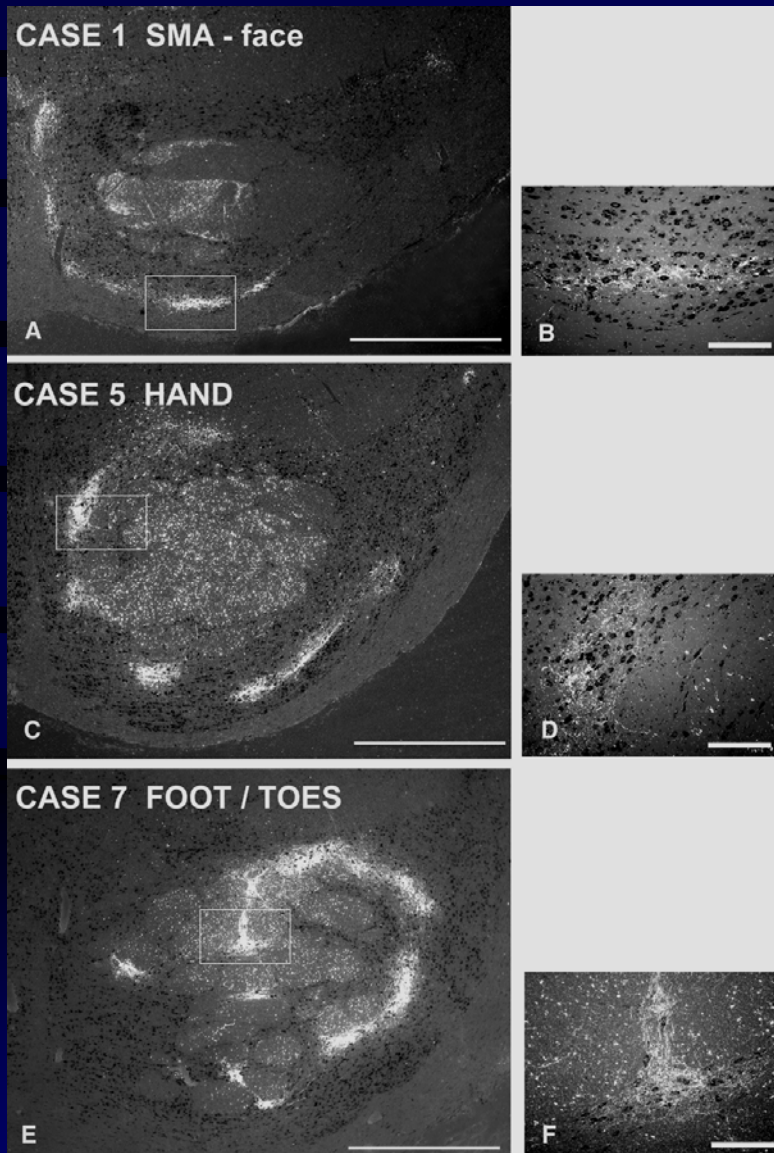
# Connectional neuroanatomy with diffusion spectrum imaging



# Cerebro-cerebellar loops: Feedforward limb

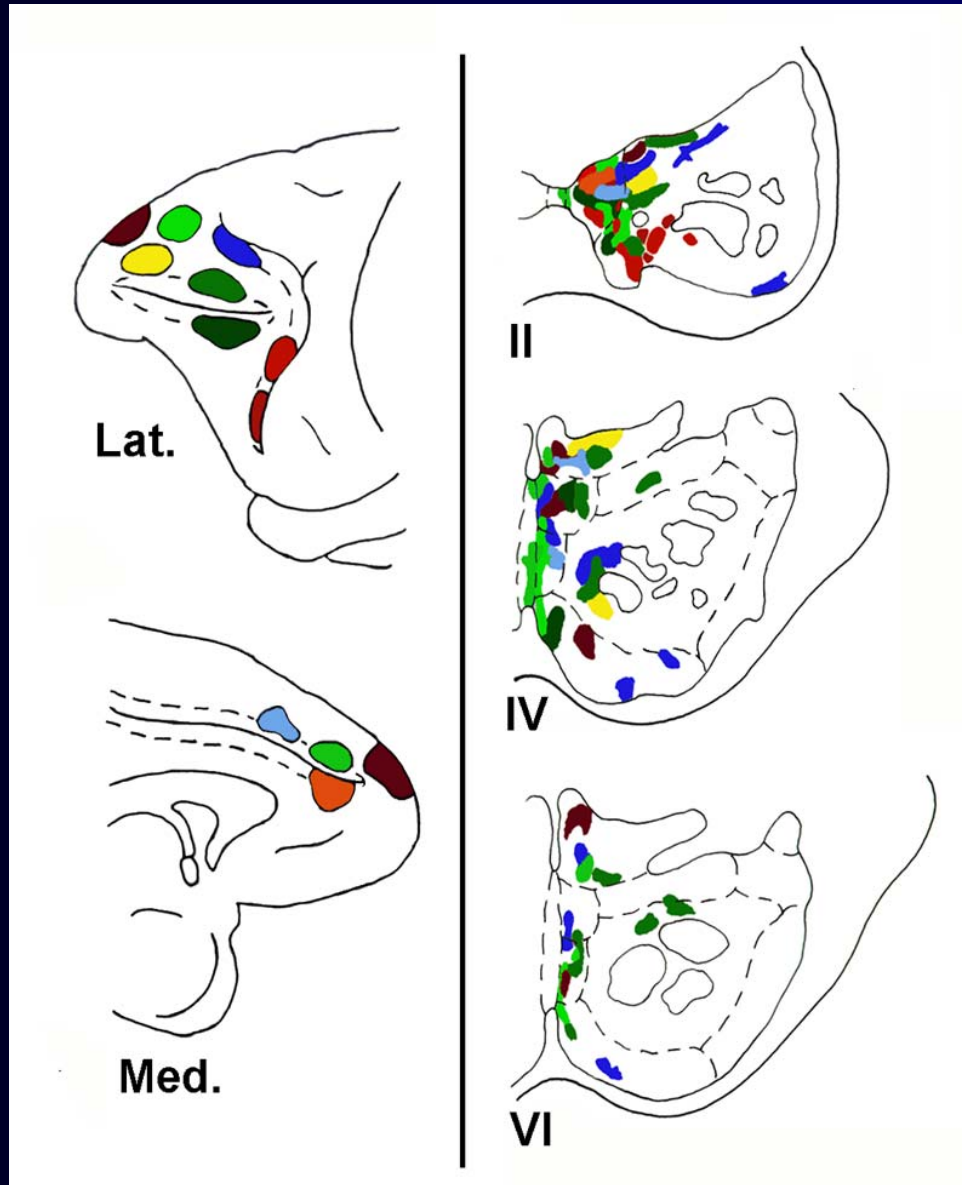


# Motor corticopontine projections in rhesus monkey

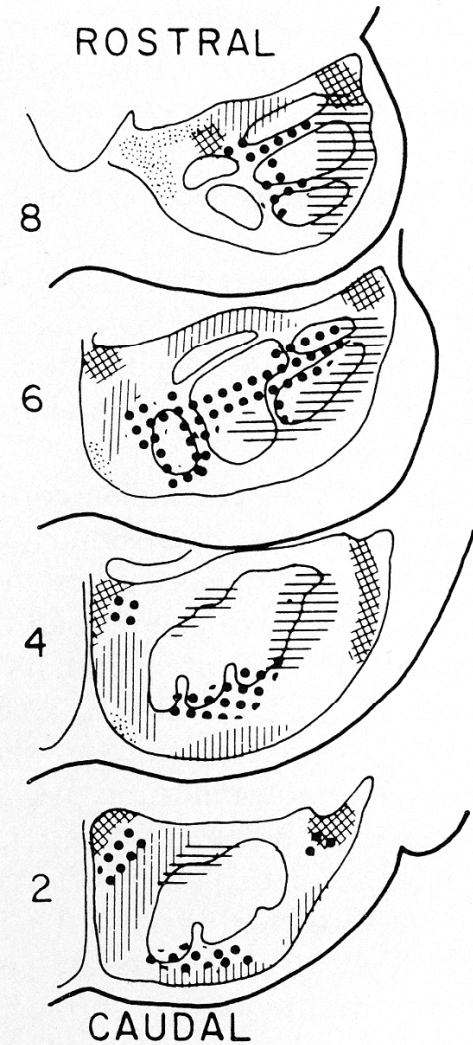
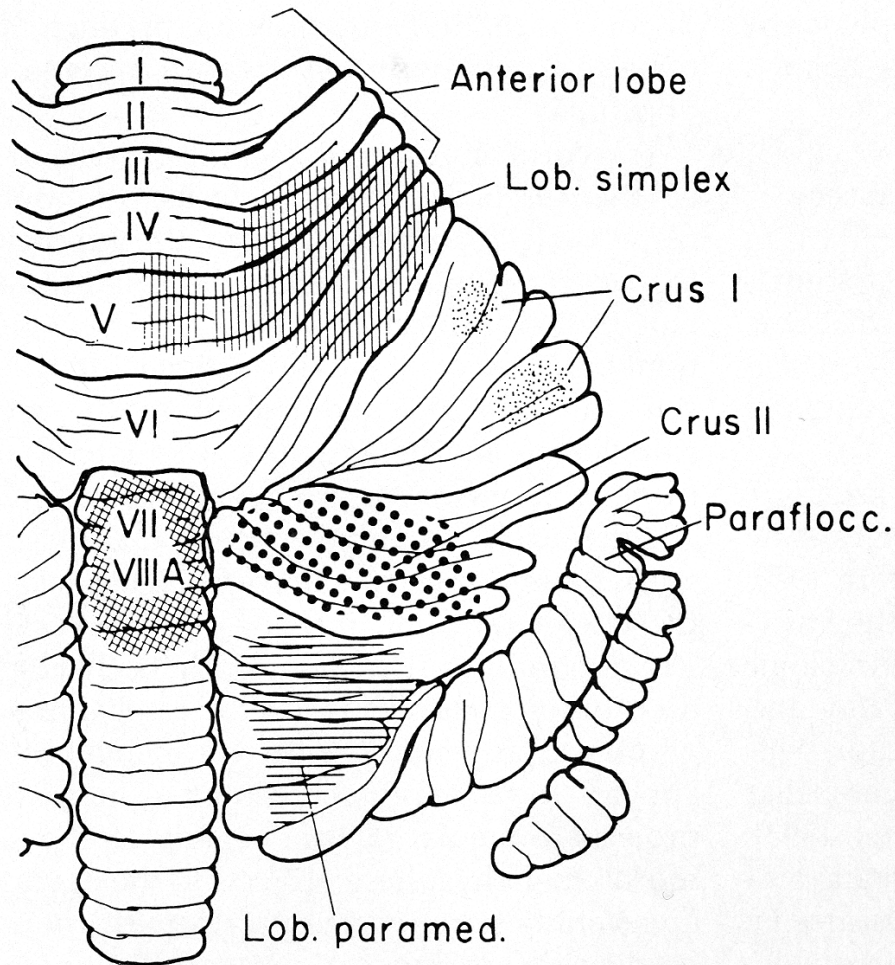




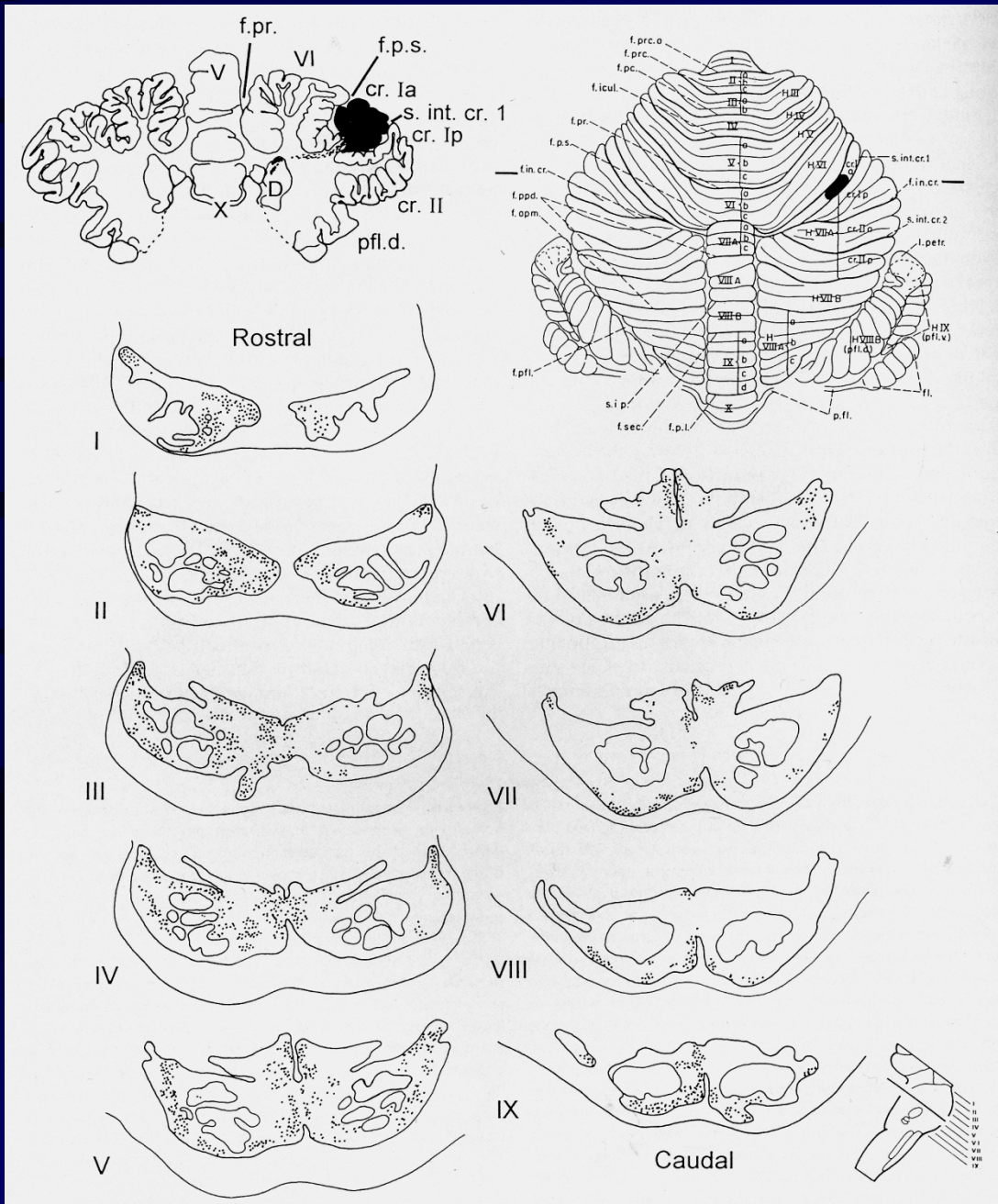
# Prefrontopontine projections in rhesus monkey



# Pontocerebellar projection in monkey

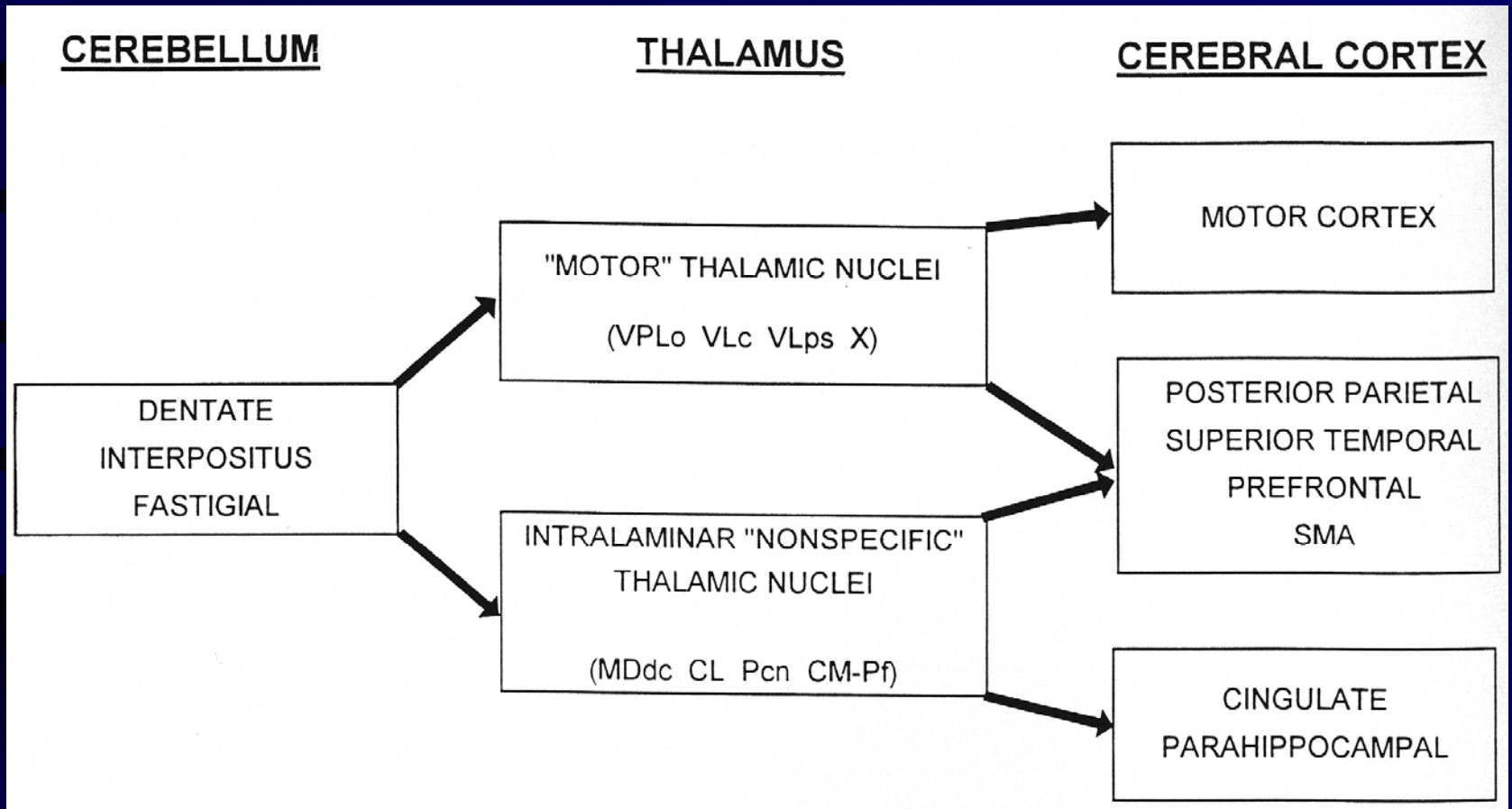


# Pontine projections to cerebellar crus I



Schmahmann and Pandya,  
(from Schmahmann 1996)

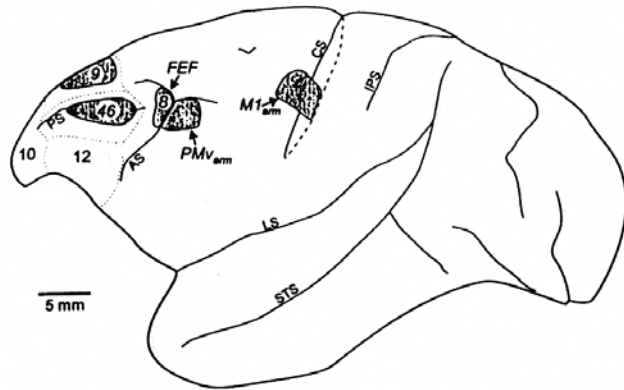
# Cerebello-cerebral feedback circuit



# Cerebellar projections to frontal lobe

M1

Area 46

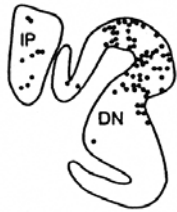


M1<sub>arm</sub>

PMV<sub>arm</sub>

Area 46

Area 9



P 7.5



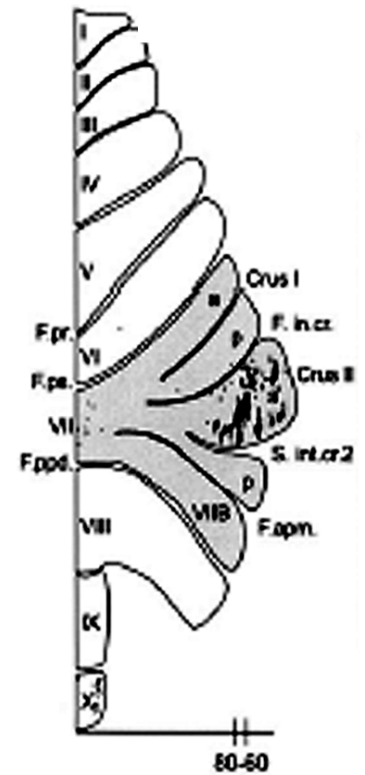
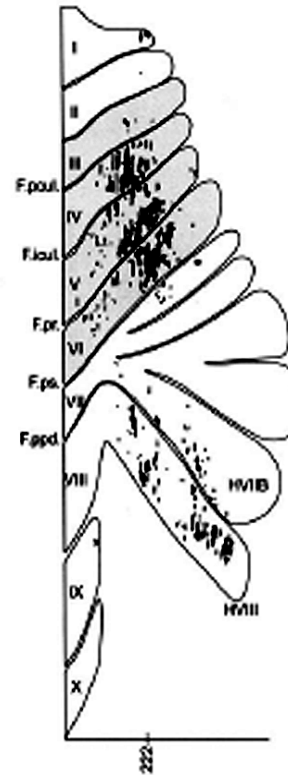
P 8.0



P 8.5



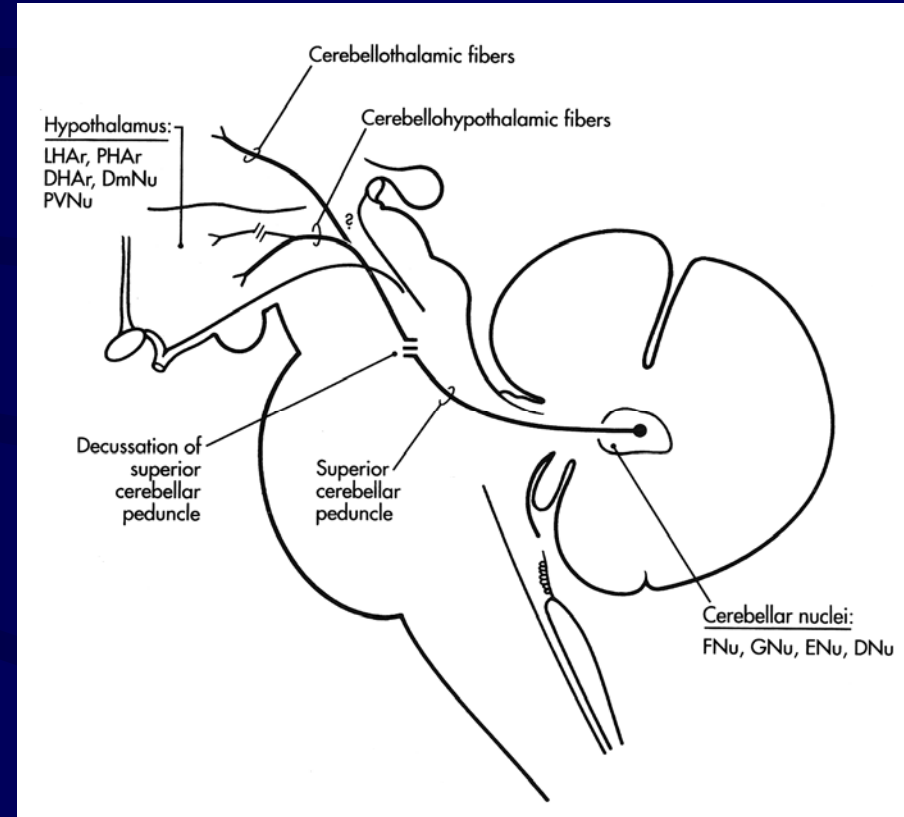
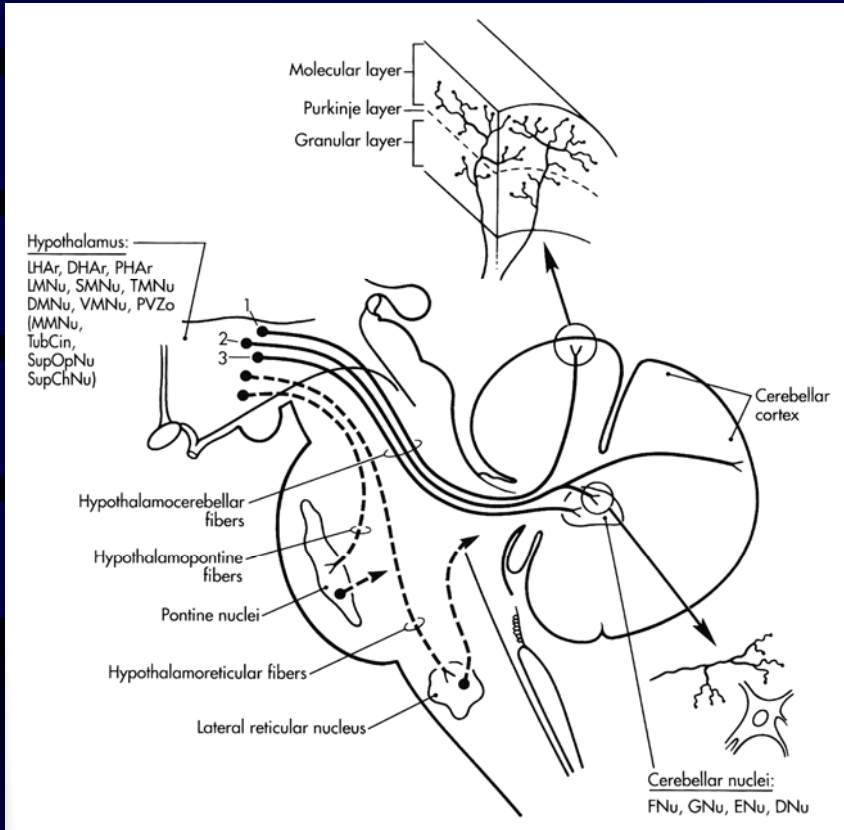
P 8.5



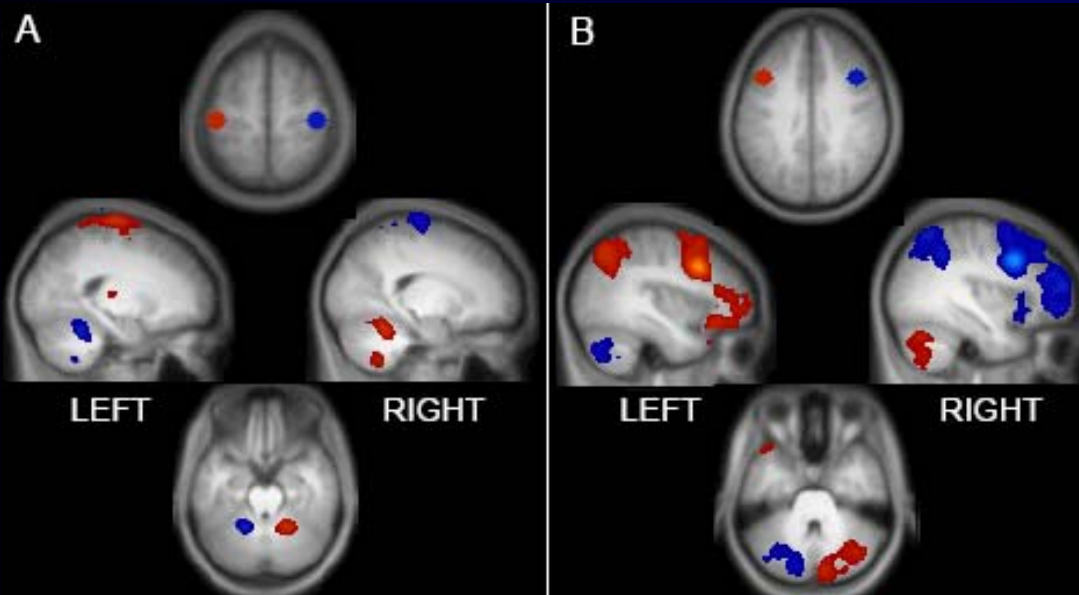
Middleton and Strick, 1997

Kelly and Strick, 2003

# Reciprocal hypothalamocerebellar projections

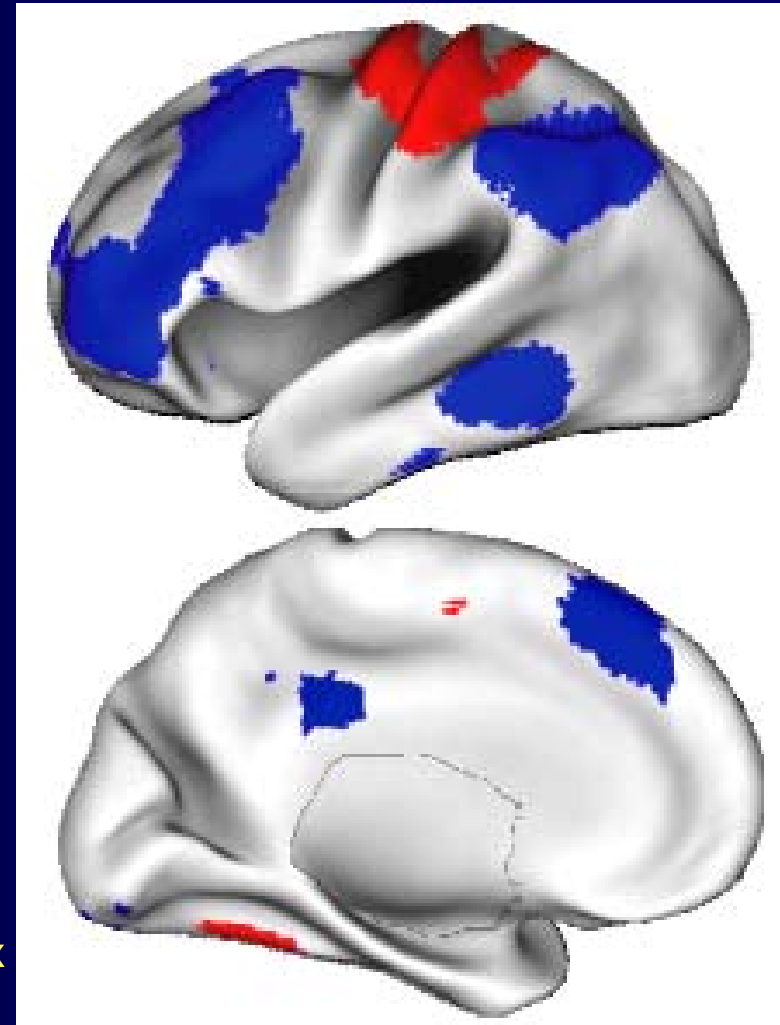


# Sensorimotor vs. prefrontal and association area dichotomy in cerebrocerebellar interactions (fcMRI)

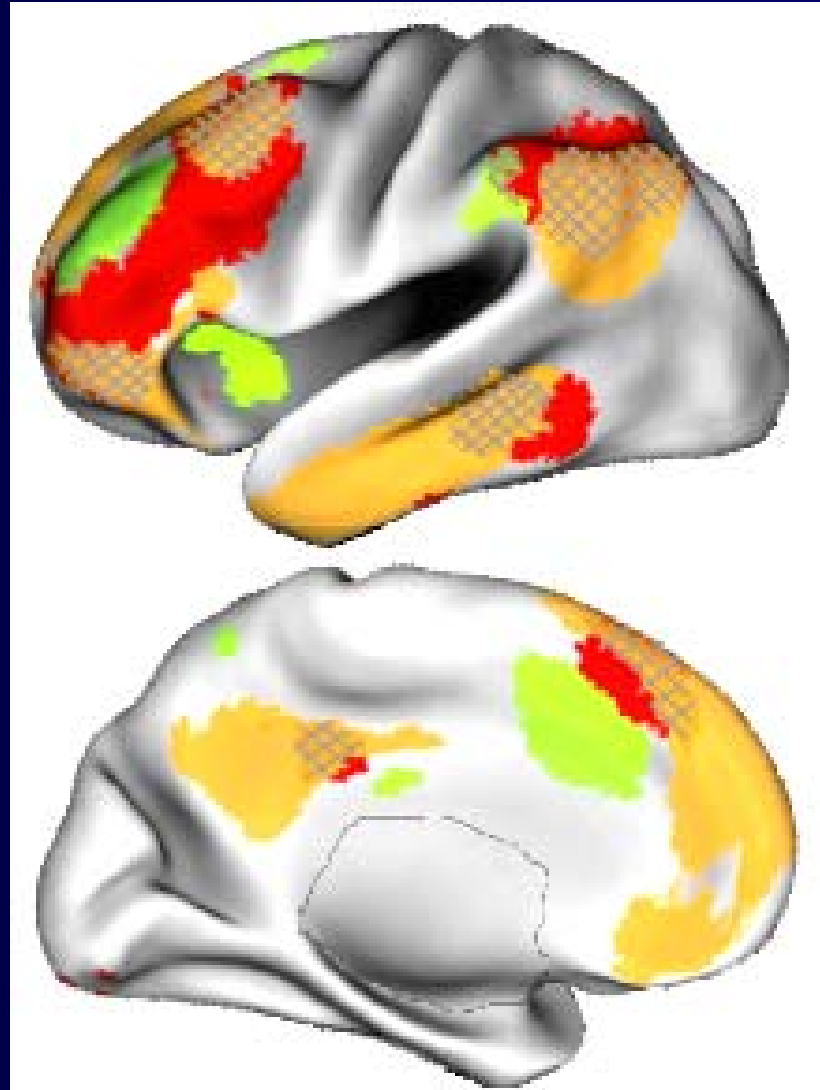
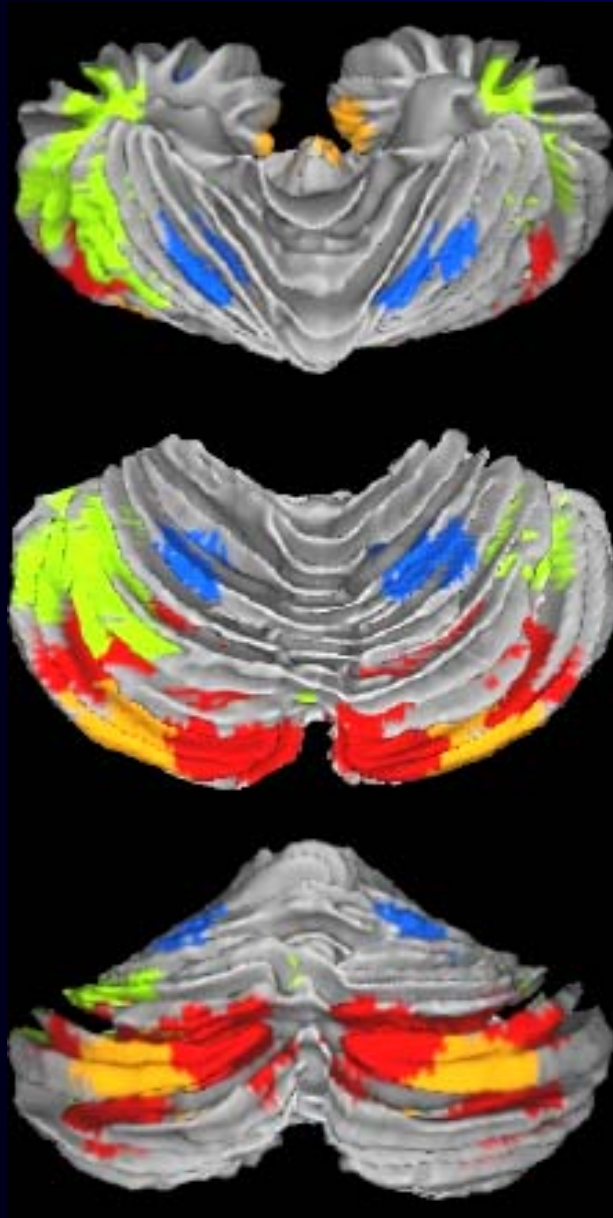


A. Motor cortex seeds label cerebellar anterior lobe  
B. DLPFC seeds lobes cerebellar posterior lobe

Cerebellar anterior lobe seeds label sensorimotor cortex  
Cerebellar posterior lobe seeds label association areas



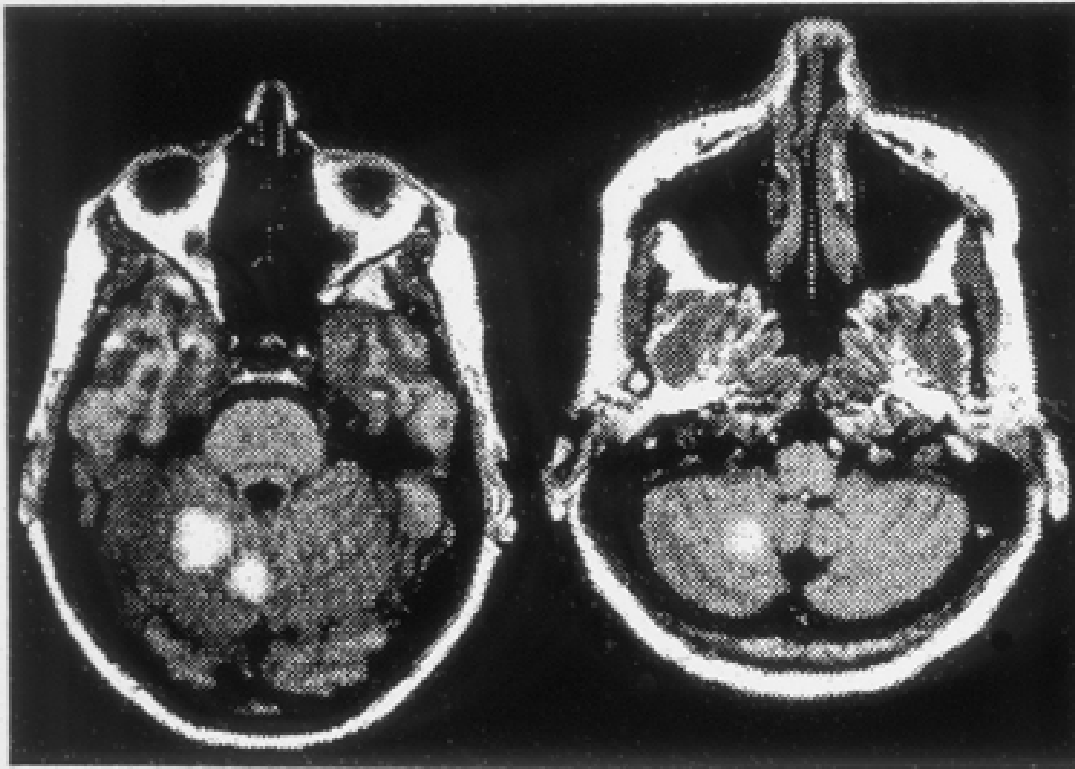
# Functional topography of human cerebrocerebellar connections as determined by fcMRI



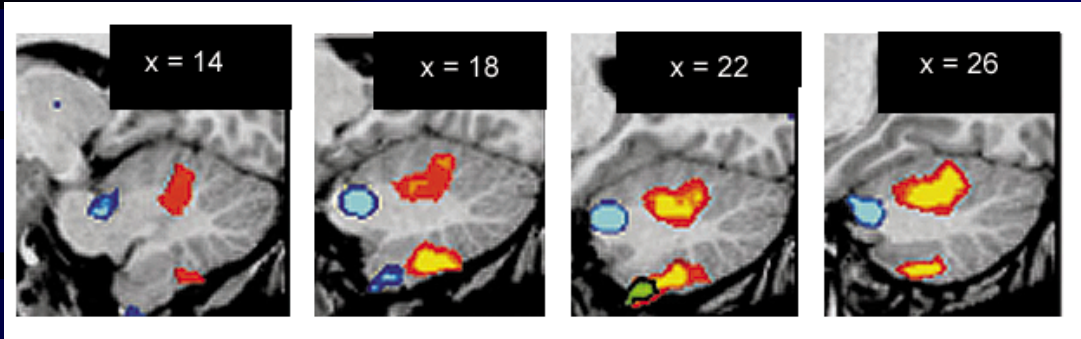


right hand

right foot



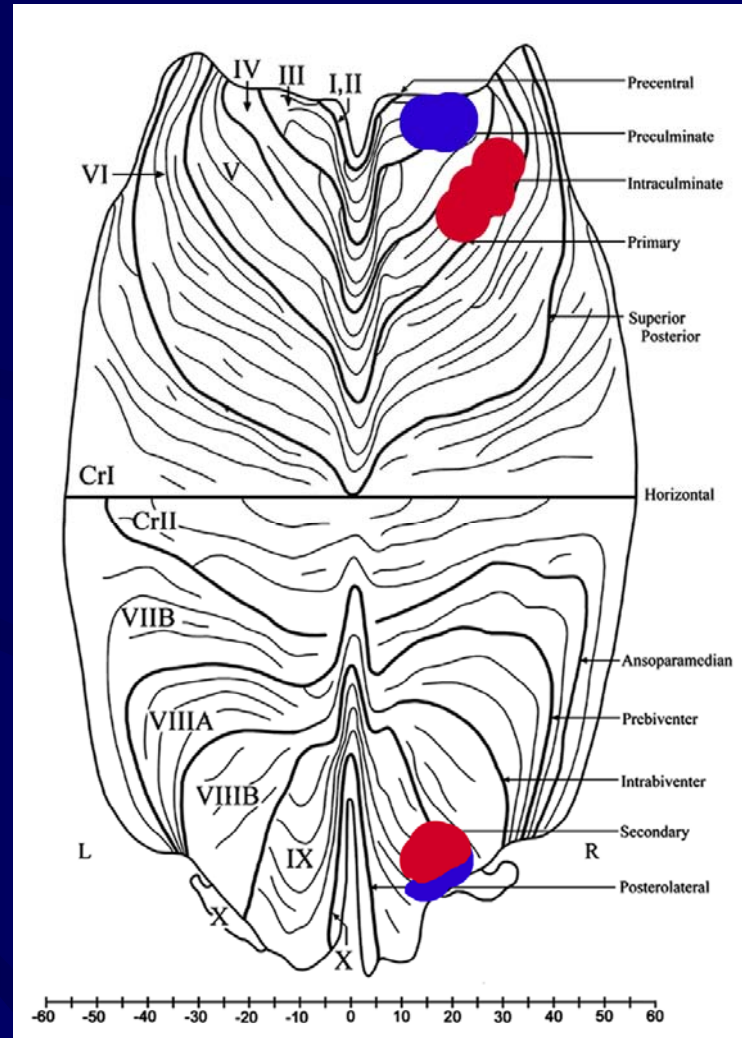
# Multiple tactile maps in the human cerebellum



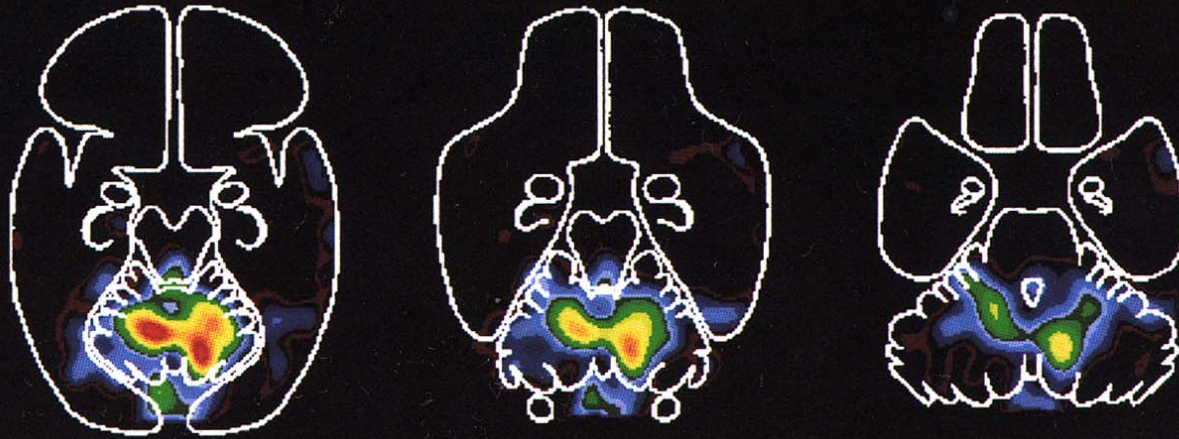
Red - Hand  
Blue - Foot

Bushara et al., NeuroReport 2001;12:2483-86

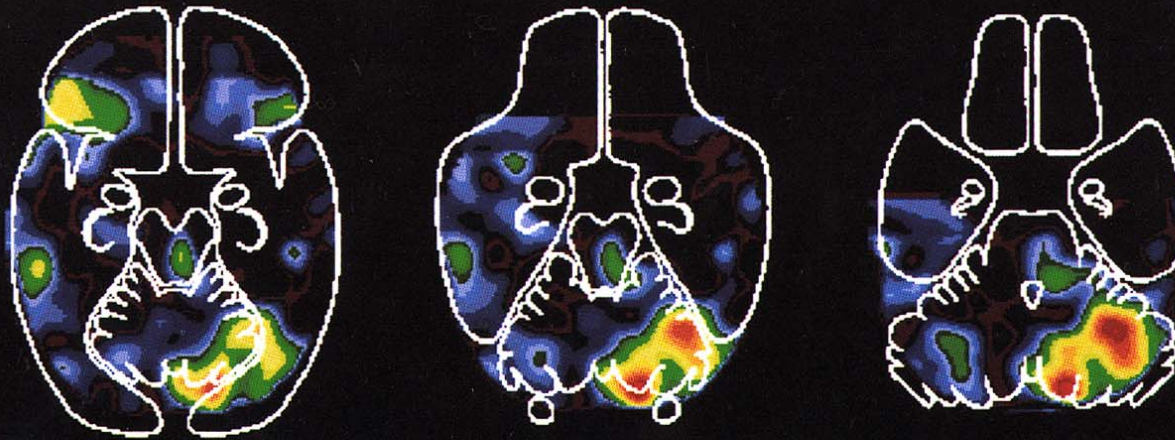
Representation of tactile maps for hand (red) and foot (blue) on semi-flattened map of cerebellum



# Speaking Aloud Visual Nouns minus Passively Viewing Nouns



# Generating Verbs minus Speaking Aloud Visual Nouns



Z = -12

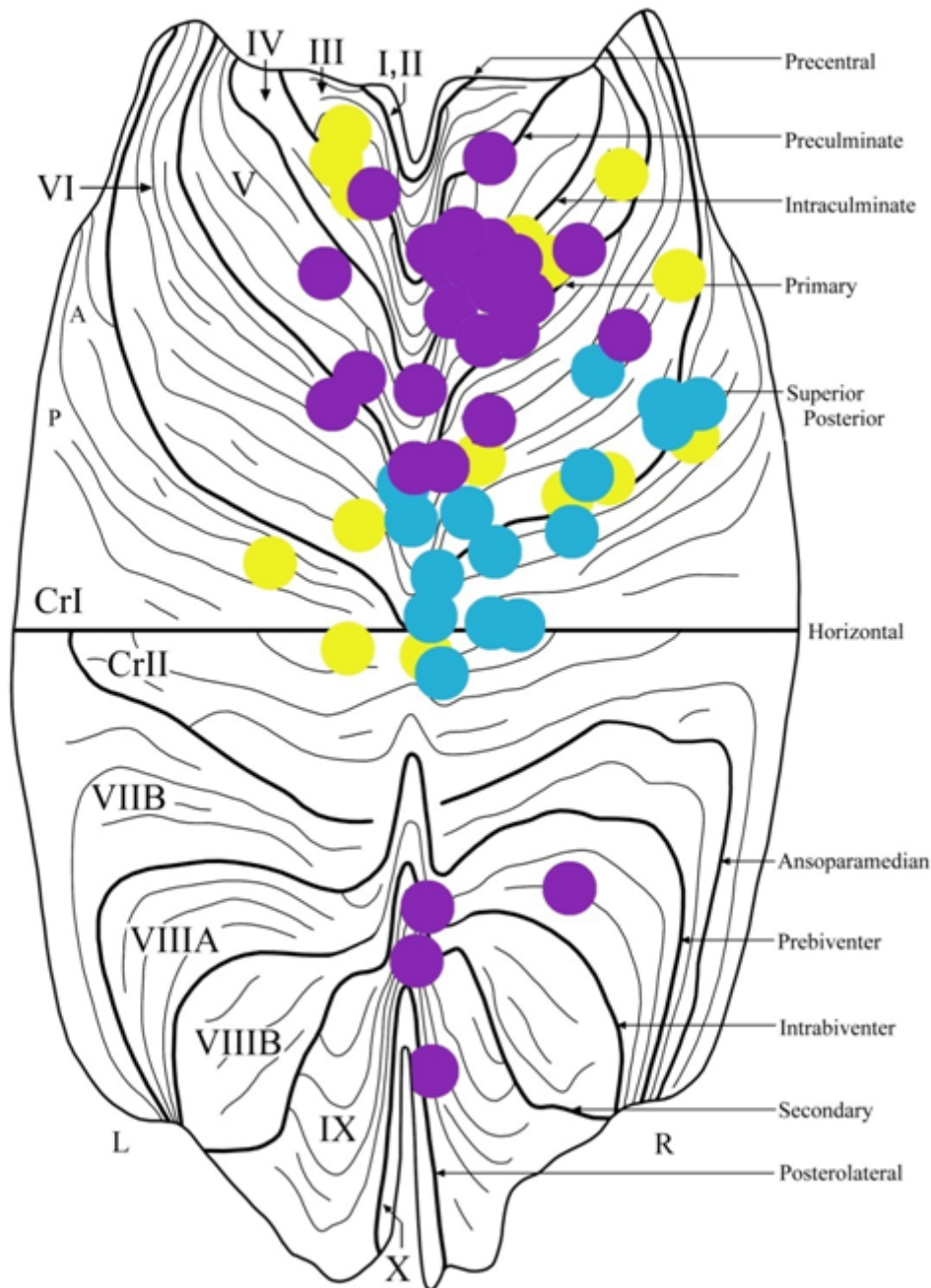
Z = -16

Z = -20

min

max

# Functional topography in the human cerebellum.



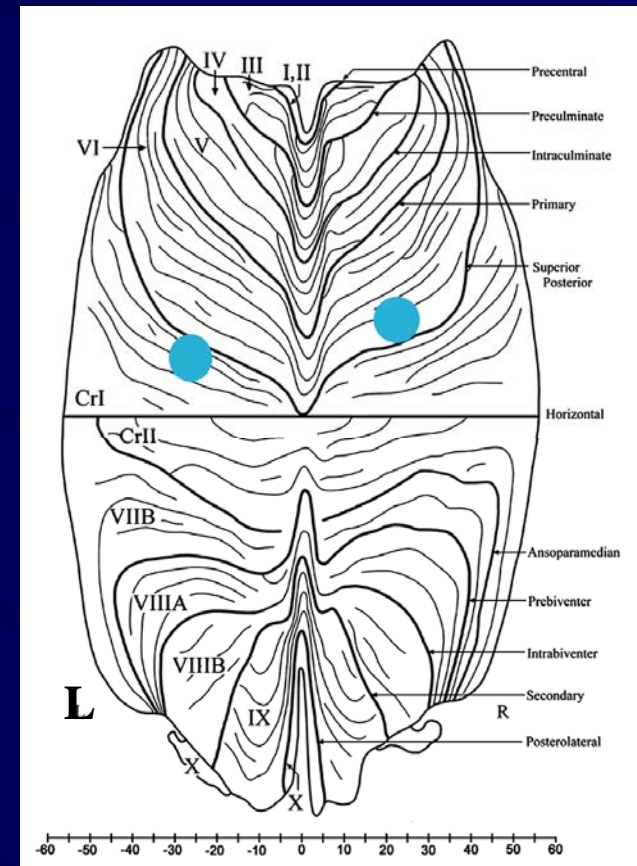
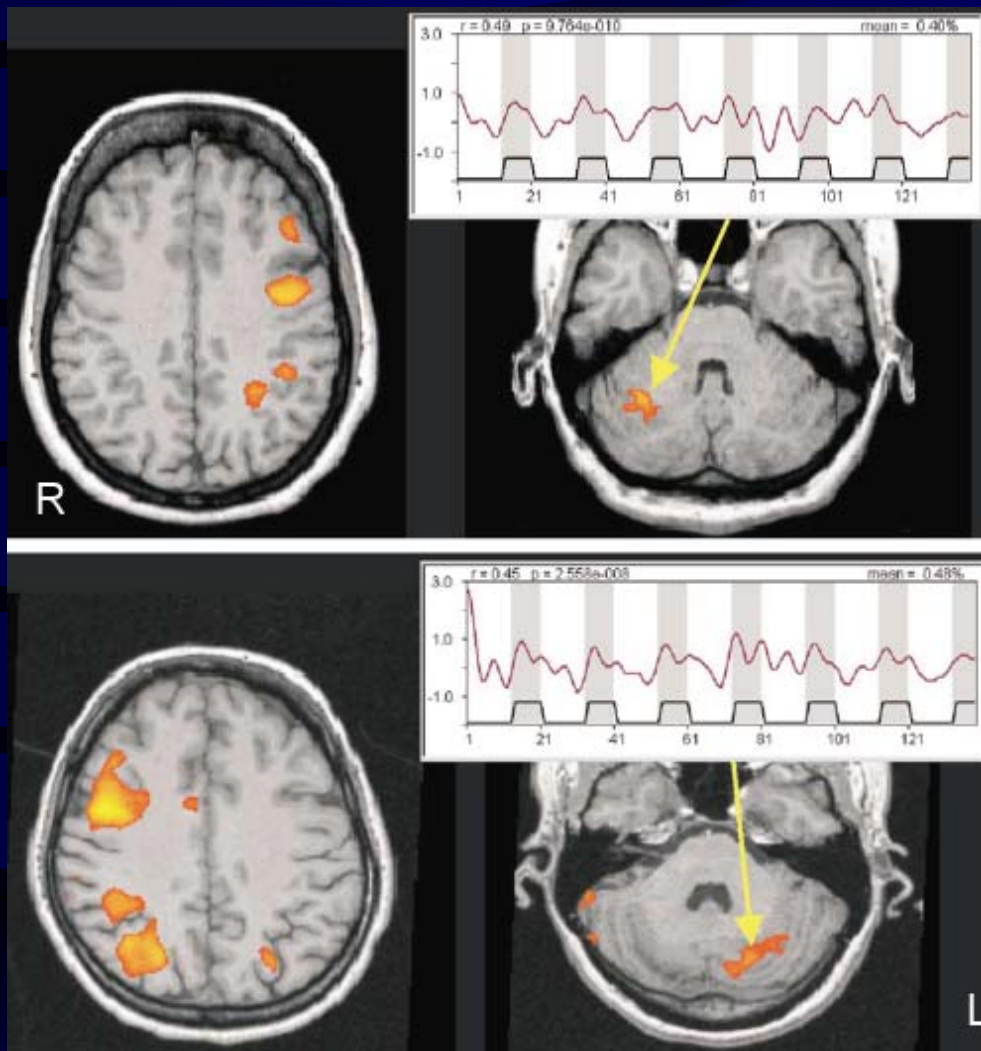
Motor



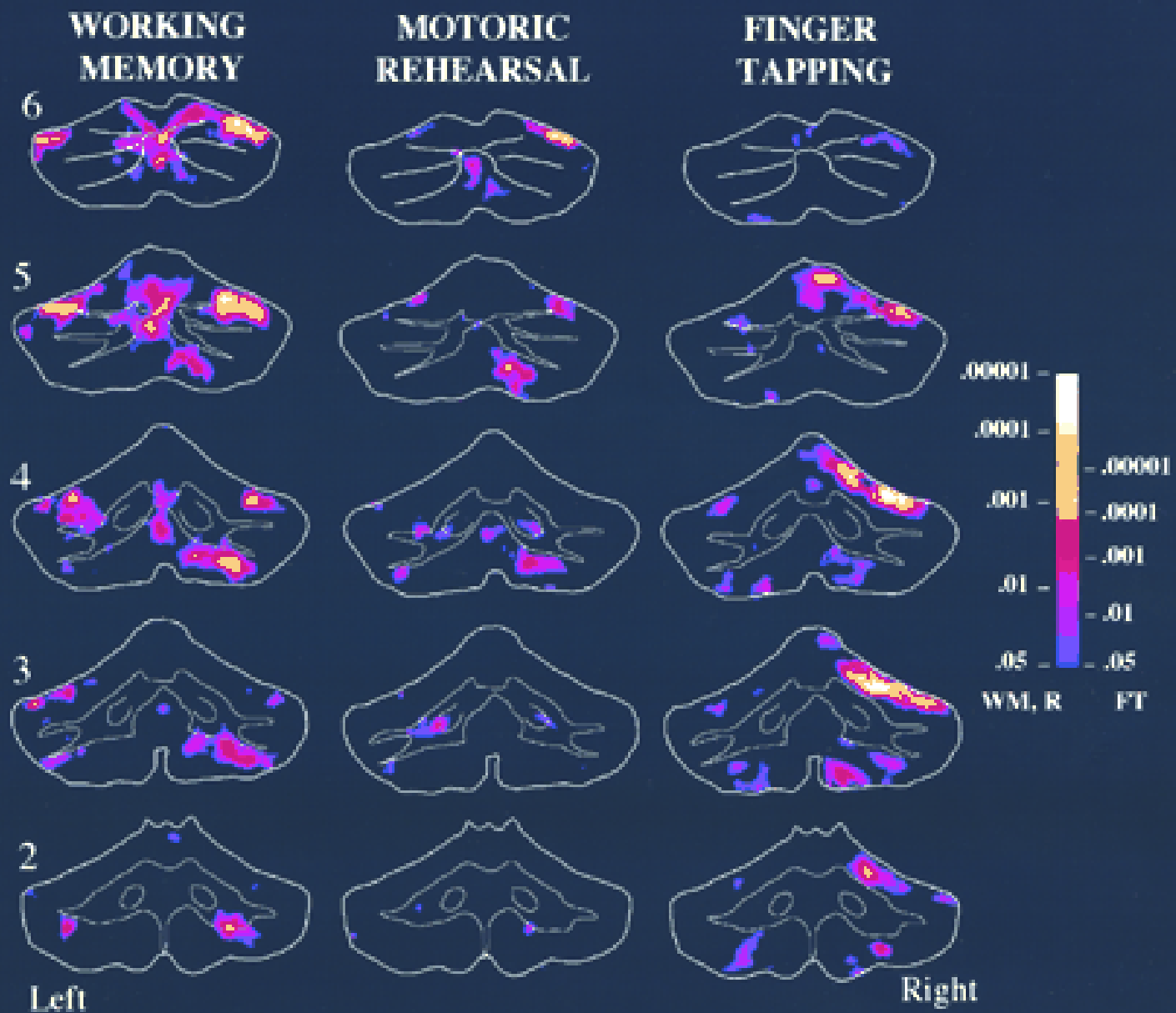
Mental Imagery



Language

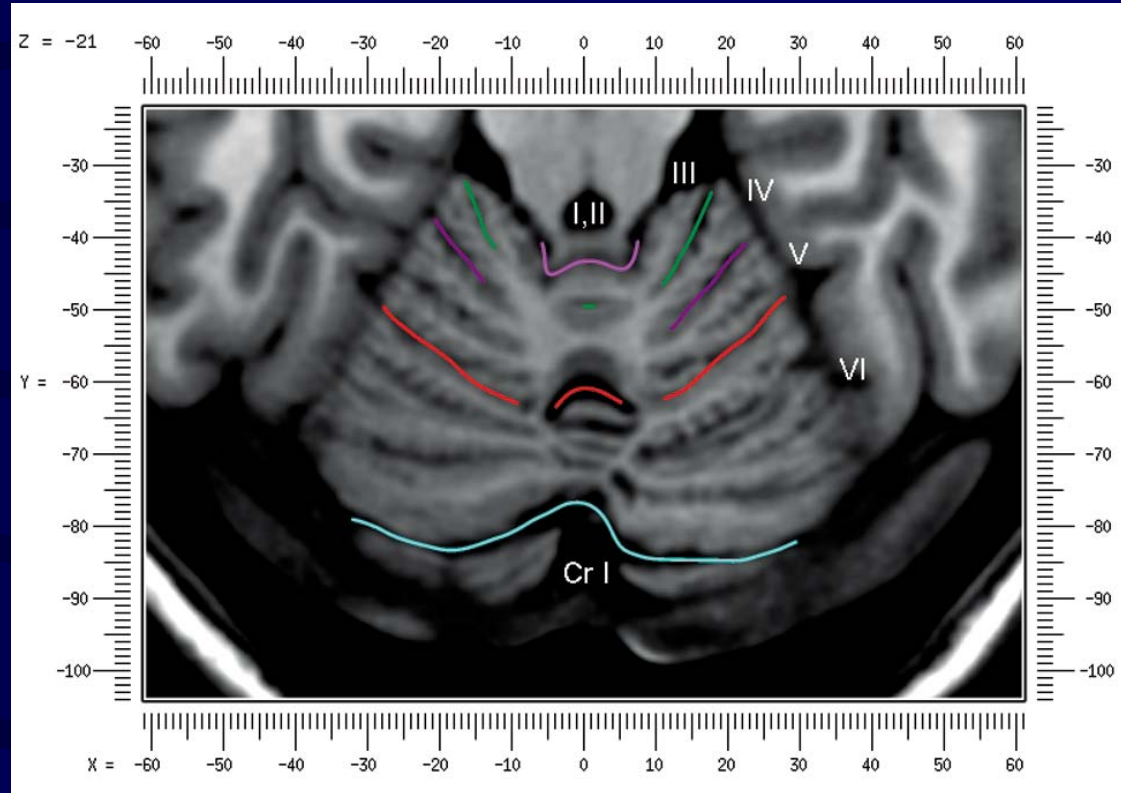
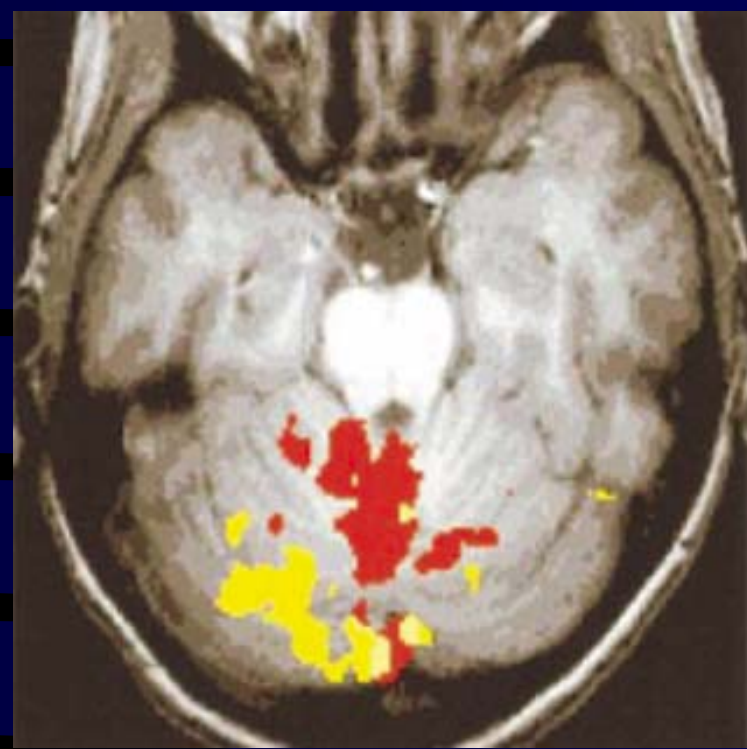


**Activation in cerebral hemispheres and cerebellum in a silent verbal fluency task.**  
**A: Right handed person with left cerebral and right cerebellar activation (Lobule VI).**  
**B: Left handed person with right cerebral and left cerebellar activation (Crus I).**  
 Hubrich-Ungureanu et al., Neuroscience Letters 2002; 319: 91-94.



Desmond et al., J. Neurosci. 1997;17:9675-85.

## Horizontal section from MRI Atlas at z = -21



**PAIN (Red) - vermal lobules III, IV, and V.**

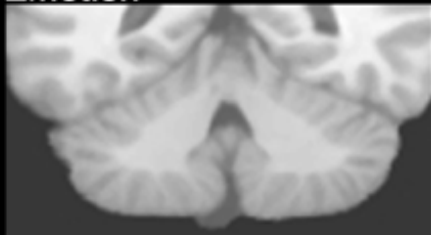
**ANTICIPATION OF PAIN (Yellow) - lobule VI (vermis, paravermian).**

**Ploghaus et al. Science 1999;284:1979-81**

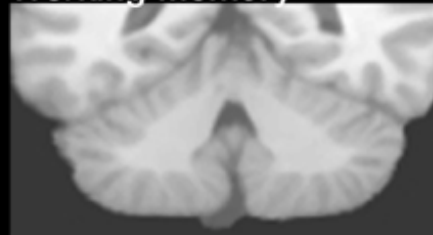
# Separate locations for sensorimotor and neurobehavioral functions

$y = -48$

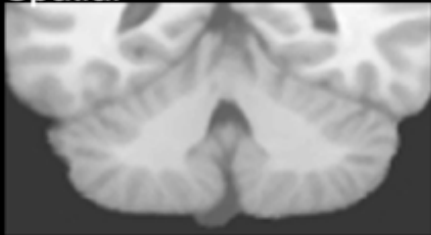
Emotion



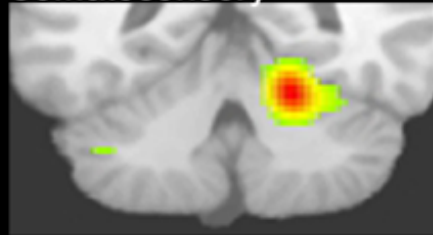
Working Memory



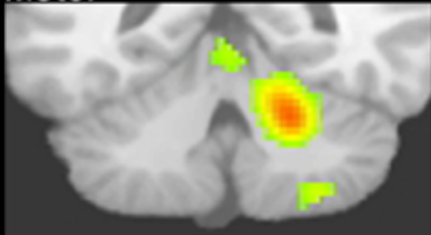
Spatial



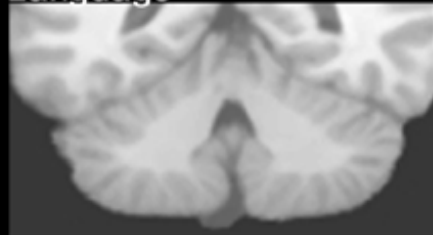
Somatosensory



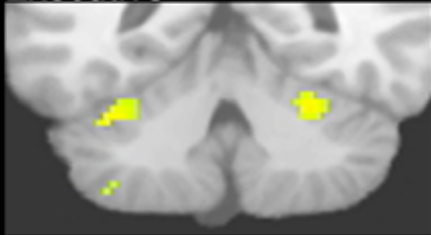
Motor



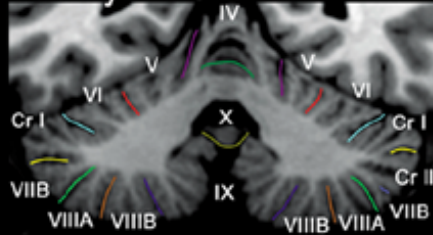
Language



Executive

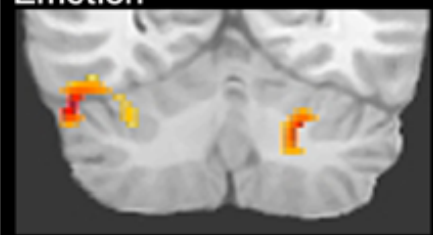


Atlas  $y = -48$

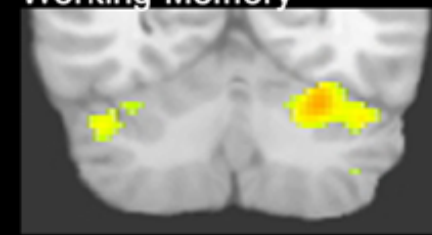


$y = -60$

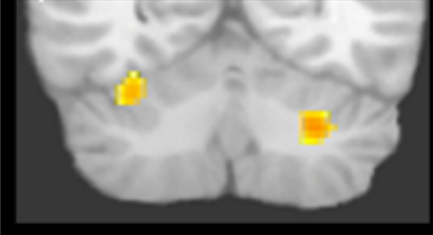
Emotion



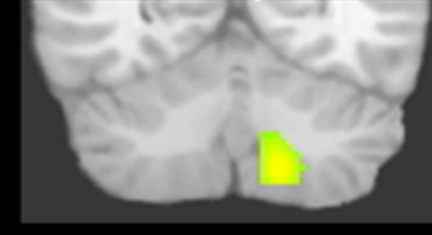
Working Memory



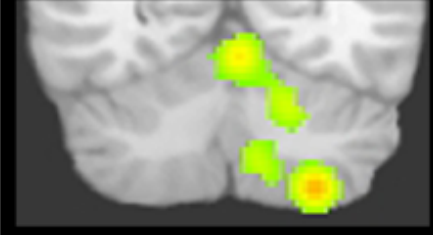
Spatial



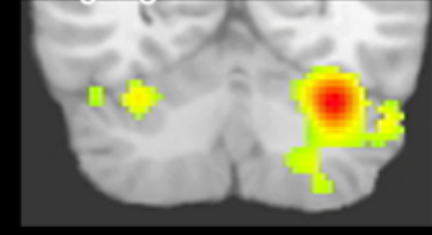
Somatosensory



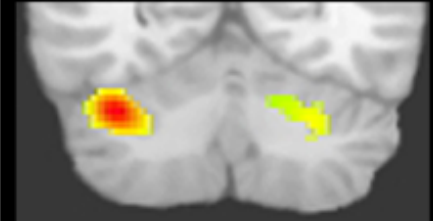
Motor



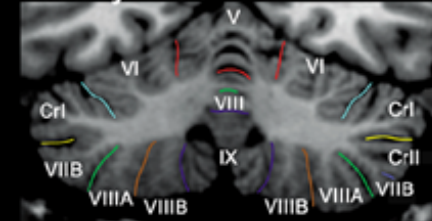
Language



Executive

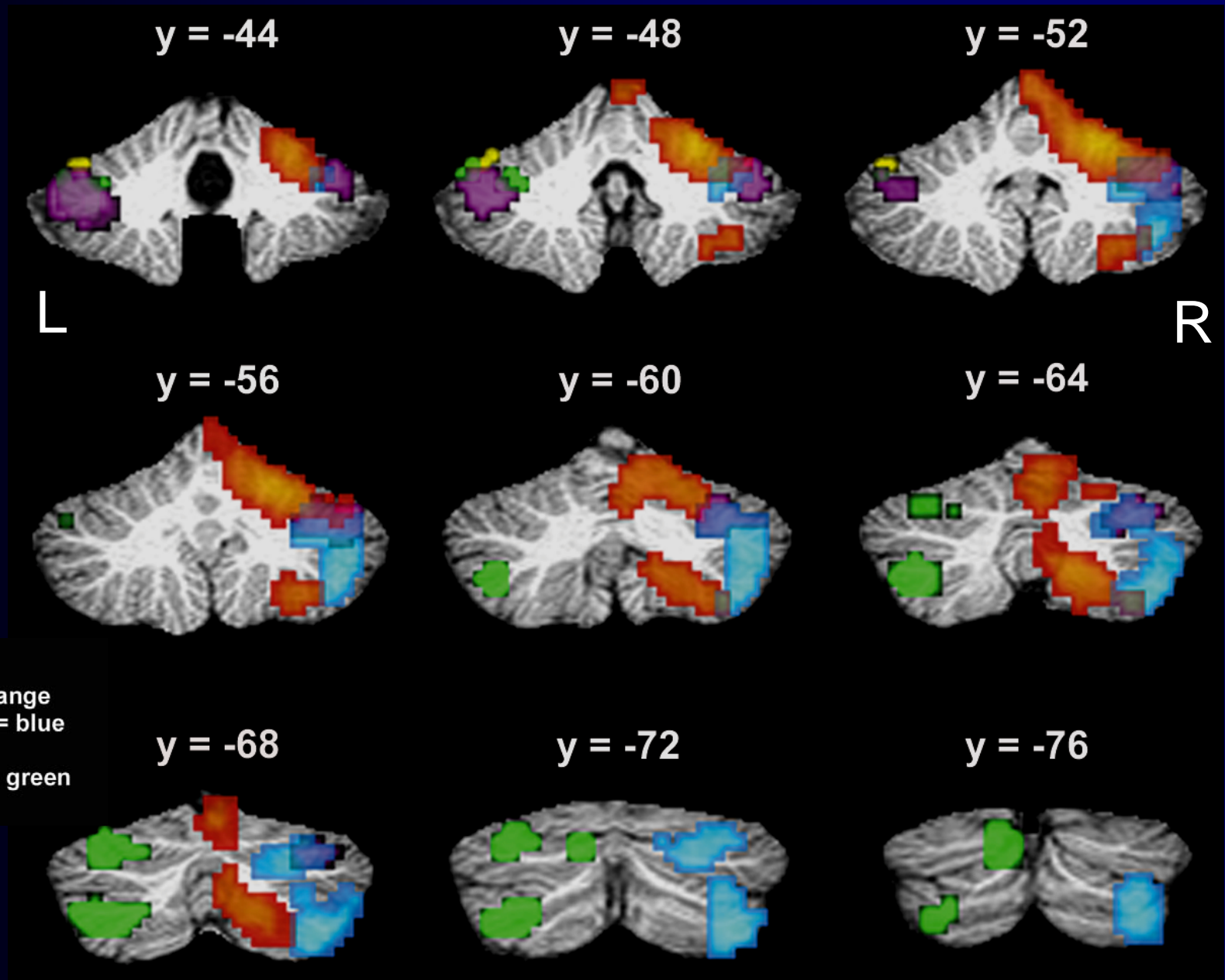


Atlas  $y = -60$





# Cerebellar functional topography. Single case fMRI



# Cerebellum and Cognition

## Cerebro-cerebellar circuits

The associative and paralimbic incorporation into the cerebrocerebellar circuit is the anatomic underpinning of the cerebellar contribution to cognition, emotion and autonomic function.

Discretely organized anatomic sub-units subserve functional sub-systems (loops) within the cerebrocerebellar circuit.