Magnetic resonance imaging in the diagnostic assessment of cerebellar ataxias

Jennifer Faber
Department of Neurology, University Hospital Bonn
German Center for Neurodegenerative Diseases (DZNE), Bonn

Outline

- Anatomy of the cerebellum & brainstem
- Why MRI?
- Which sequence?
- Examples of typical findings

Outline

Learning objectives:

- Define why MRI is included in a diagnostic work-up
- State the recommended sequences
- Identify common imaging features

Diagnostic MRI

What is your background?

Single choice

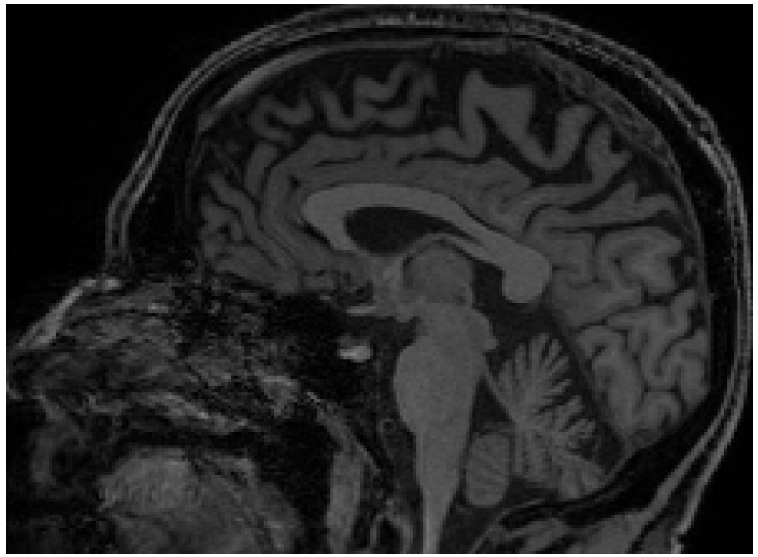
Clinical care

Research

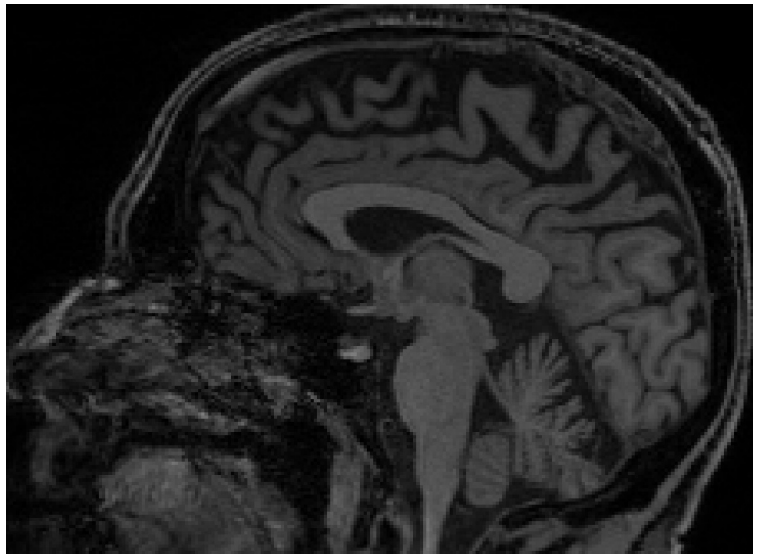
other

Diagnostic MRI

Diagnostic MRI



Diagnostic MRI



Diagnostic MRI

How often is MRI part of your clinical diagnostic work up?

Single choice

0 - 25%

25 – 50%

50 – 75%

75 – 100 %

Diagnostic MRI

How often is MRI essential to confirm a diagnosis?

Single choice

0 - 25%

25 – 50%

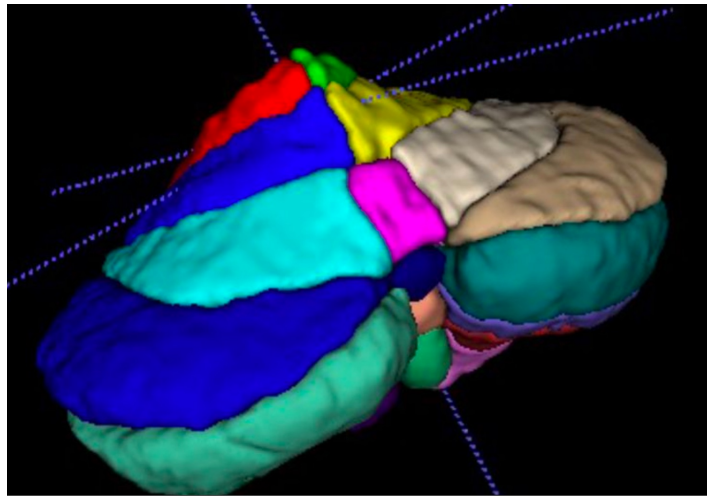
50 – 75%

75 – 100 %

Diagnostic MRI

Cerebellar gray matter			
Lobe	*Fissures*	*Hemispheric lobules**	*Subdivisions of the vermis*
Anterior lobe		I-IV	
	Fissura intraculminalis		
		V	
	Fissura prima		
Superior posterior lobe		VI	VI
	Fissura superior posterior		
		Crus I	VII
	Fissura horizontalis		
		Crus II	
	Fissura ansoparamediana		
		VIIB	
	Fissura prebiventer		
Inferior posterior lobe		VIIIA	VIII
	Fissura intrabiventer		
		VIIIB	
	Fissura secunda		
		IX	IX
	Fissura posterolaterialis		
Flocculonodular lobe		X	X

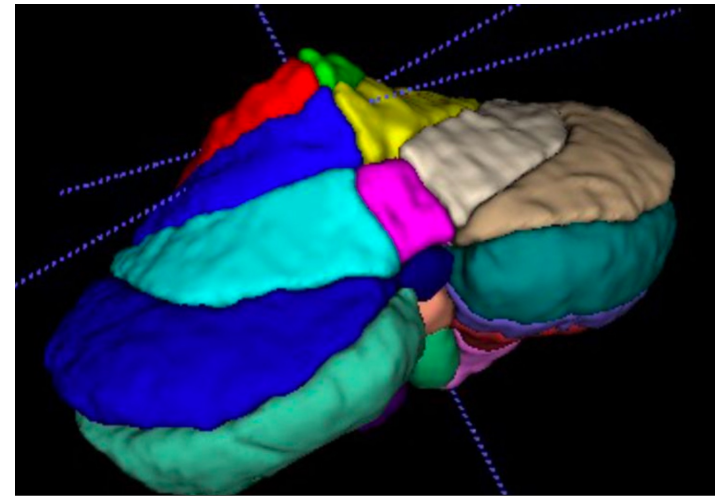
** Left and right*



Diagnostic MRI

Cerebellar gray matter			
Lobe	*Fissures*	*Hemispheric lobules**	*Subdivisions of the vermis*
Anterior lobe		I-IV	
	Fissura intraculminalis		
		V	
	Fissura prima		
Superior posterior lobe		VI	VI
	Fissura superior posterior		
		Crus I	VII
	Fissura horizontalis		
		Crus II	
	Fissura ansoparamediana		
		VIIB	
	Fissura prebiventer		
Inferior posterior lobe		VIIIA	VIII
	Fissura intrabiventer		
		VIIIB	
	Fissura secunda		
		IX	IX
	Fissura posterolaterialis		
Flocculonodular lobe		X	X

** Left and right*



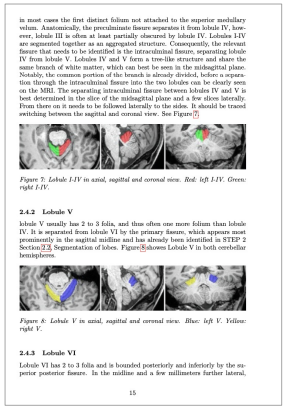
Anterior lobe
Superior posterior lobe
Inferior posterior lobe

Manual sub-segmentation of the cererbellum

Jennifer Faber[1,2], Lea-Sophie Heinz[1], Dagmar Timmann[3], Thomas M. Ernst[3], Katerina Deike-Hofmann[1,4], and Thomas Klockgether[1,2]

[1]German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany
[2]Department of Neurology, University Hospital Bonn, Germany
[3]Department of Neurology, Center for Translational Neuro, and Behavioral Sciences (C-TNBS), University Hospital Essen, University of Duisburg-Essen, Essen, Germany
[4]Department of Neuroradiology, University Hospital Bonn, Germany

Version 1 - April 2022



in most cases the first distinct folium not attached to the superior medullary velum. Anatomically, the precentralmiste fissure separates it from lobule IV, however, lobule III is often at least partially obscured by lobule IV. Lobules I-IV are segmented together as an aggregated structure. Consequently, the relevant fissure that needs to be identified is the intraculminal fissure, separating lobule IV from lobule V. Lobules IV and V form a tree-like structure and share the same branch of white matter, which can best be seen in the midsagittal plane. Notably, the common portion of the branch is already divided, before a separation through the intraculminal fissure into the two lobules can be clearly seen on the MRI. The separating intraculminal fissure between lobules IV and V is best determined in the slice of the midsagittal plane and a few slices laterally. From there on it needs to be followed laterally to the sides. It should be traced switching between the sagittal and coronal view. See Figure 7.

Figure 7: Lobule I-IV in axial, sagittal and coronal view. Red: left I-IV. Green: right I-IV.

2.4.2 Lobule V

lobule V usually has 2 to 3 folia, and thus often one more folium than lobule IV. It is separated from lobule VI by the primary fissure, which appears most prominently in the sagittal midline and has already been identified in STEP 2 Section 2.3. Segmentation of lobes. Figure 8 shows Lobule V in both cerebellar hemispheres.

Figure 8: Lobule V in axial, sagittal and coronal view. Blue: left V. Yellow: right V.

2.4.3 Lobule VI

Lobule VI has 2 to 3 folia and is bounded posteriorly and inferiorly by the superior posterior fissure. In the midline and a few millimeters further lateral,

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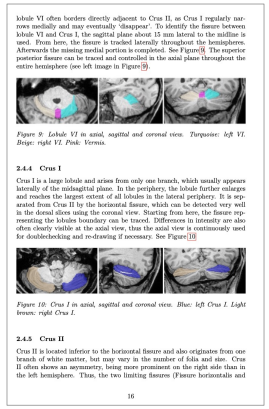

lobule VI often borders directly adjacent to Crus II, as Crus I regularly narrows medially and may eventually 'disappear'. To identify the fissure between lobule VI and Crus I, the sagittal plane about 15 mm lateral to the midline is used. From here, the fissure is tracked laterally throughout the hemispheres. Afterwards the missing medial portion is completed. See Figure 9. The superior posterior fissure can be traced and controlled in the axial plane throughout the entire hemisphere (see left image in Figure 9).

Figure 9: Lobule VI in axial, sagittal and coronal view. Turquoise: left VI. Beige: right VI. Pink: Vermis.

2.4.4 Crus I

Crus I is a large lobule and arises from only one branch, which usually appears laterally of the midsagittal plane. In the periphery, the lobule further enlarges and reaches the largest extent of all lobules in the lateral periphery. It is separated from Crus II by the horizontal fissure, which can be detected very well in the dorsal slices using the coronal view. Starting from here, the fissure representing the lobules boundary can be traced. Differences in intensity are also often clearly visible at the axial view, thus the axial view is continuously used for doublechecking and re-drawing if necessary. See Figure 10.

Figure 10: Crus I in axial, sagittal and coronal view. Blue: left Crus I. Light brown: right Crus I.

2.4.5 Crus II

Crus II is located inferior to the horizontal fissure and also originates from one branch of white matter, but may vary in the number of folia and size. Crus II often shows an asymmetry, being more prominent on the right side than in the left hemisphere. Thus, the two limiting fissures (Fissure horizontalis and

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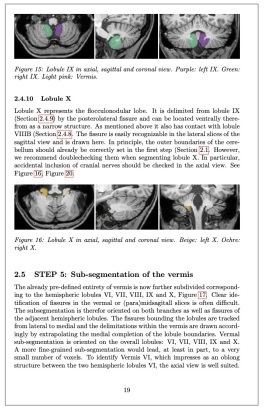


Figure 15: Lobule IX in axial, sagittal and coronal view. Purple: left IX. Green: right IX. Light pink: Vermis.

2.4.10 Lobule X

Lobule X represents the flocculonodular lobe. It is delimited from lobule IX (Section 2.4.9) by the posterolateral fissure and can be located ventrally therefrom as a narrow structure. As mentioned above it also has contact with lobule VIIIB (Section 2.4.8). The fissure is easily recognizable in the lateral slices of the sagittal view and is drawn here. In principle, the outer boundaries of the cerebellum should already be correctly set in the first step (Section 2.1). However, we recommend doublechecking them when segmenting lobule X. In particular, accidental inclusion of cranial nerves should be checked in the axial view. See Figure 16, Figure 20.

Figure 16: Lobule X in axial, sagittal and coronal view. Beige: left X. Ochre: right X.

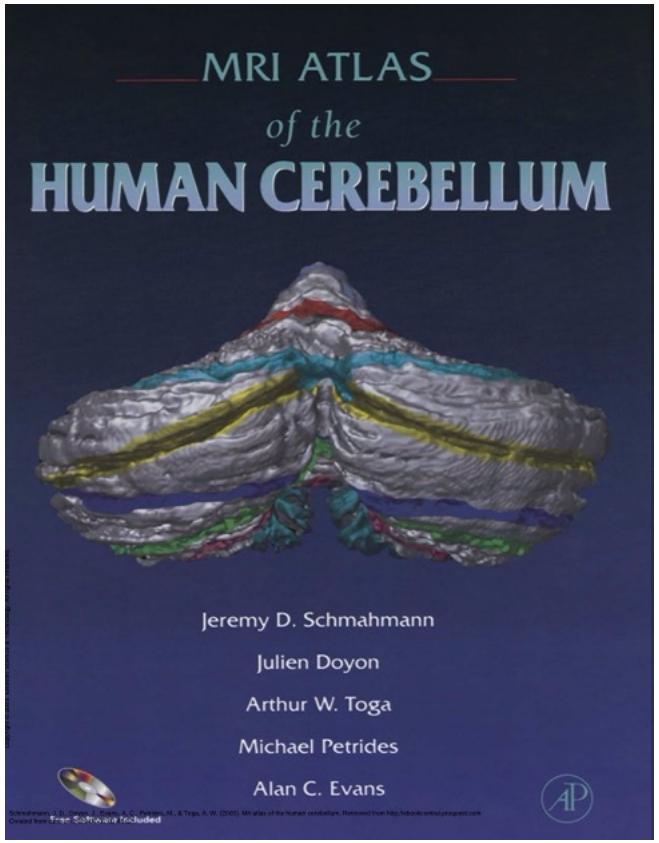
2.5 STEP 5: Sub-segmentation of the vermis

The already pre-defined entirety of vermis is now further subdivided corresponding to the hemispheric lobules VI, VII, VIII, IX and X, Figure 17. Clear identification of fissures in the vermal or (para)midsagittal slices is often difficult. The subsegmentation is therefor oriented on both branches as well as fissures of the adjacent hemispheric lobules. The fissures bounding the lobules are tracked from lateral to medial and the delimitations within the vermis are drawn accordingly by extrapolating the medial completion of the lobule boundaries. Vermal sub-segmentation is oriented on the overall lobules: VI, VII, VIII, IX and X. A more fine-grained sub-segmentation would lead, at least in part, to a very small number of voxels. To identify Vermis VI, which impresses as an oblong structure between the two hemispheric lobules VI, the axial view is well suited.

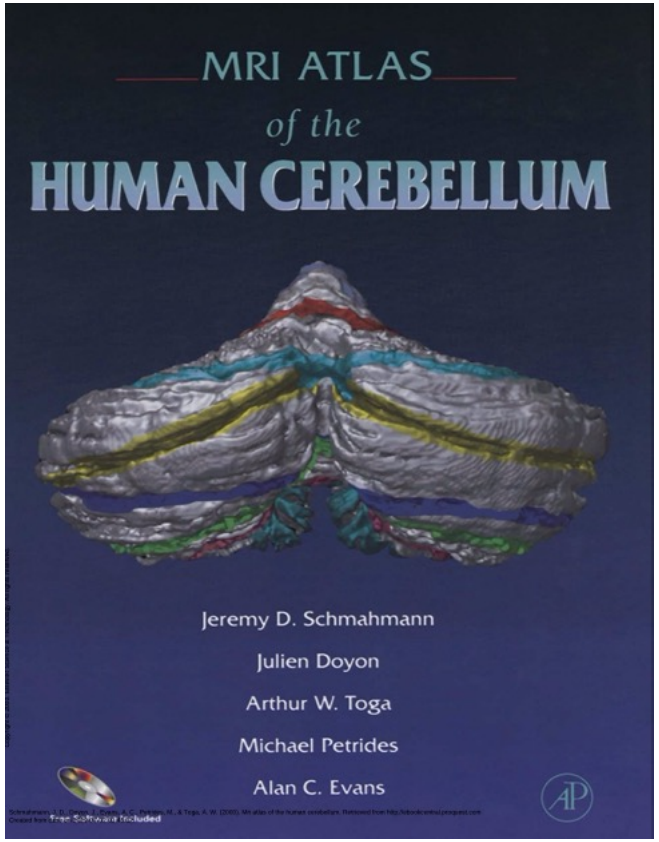
19

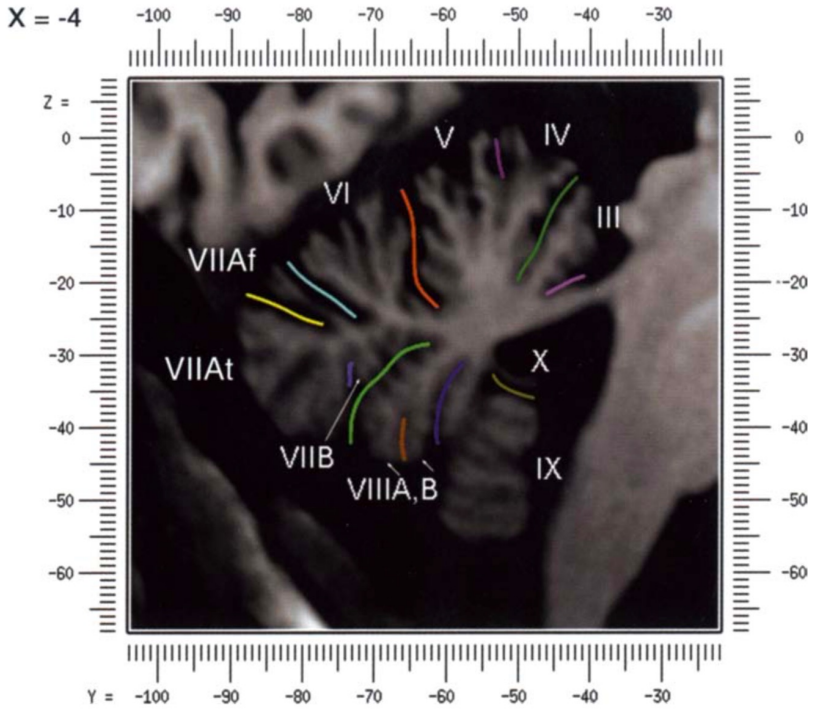
Faber et al., Manual sub-segmentation of the cererbellum. medRxiv 2022. doi: https://doi.org/10.1101/2022.05.09.22274814

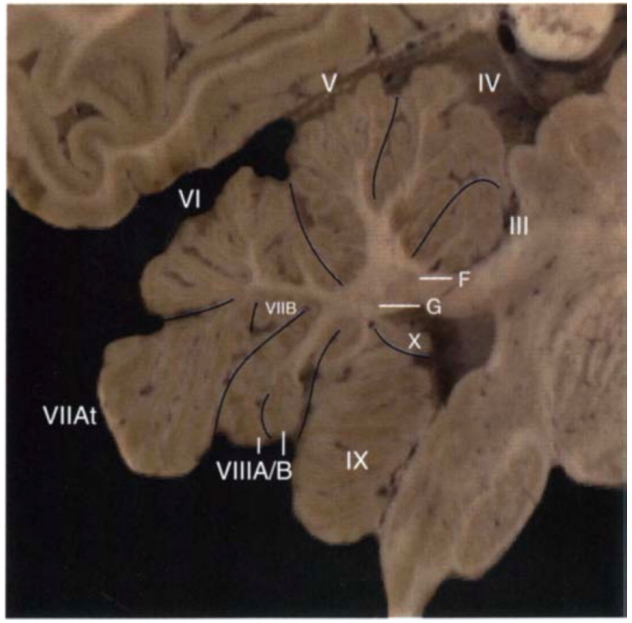
Diagnostic MRI



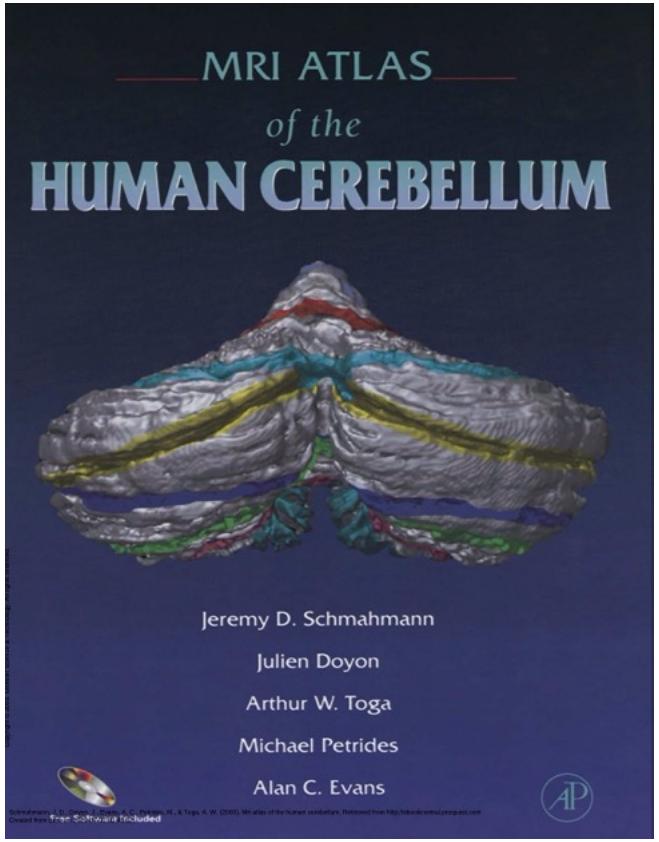
Diagnostic MRI

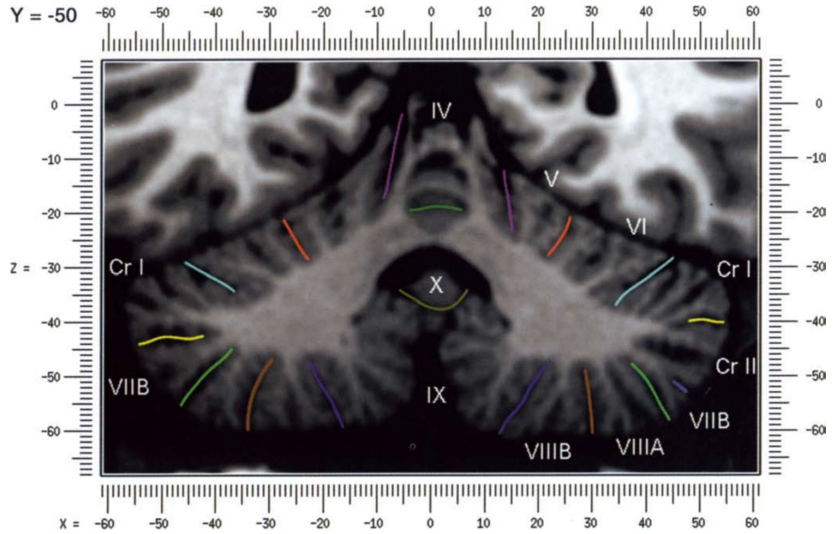


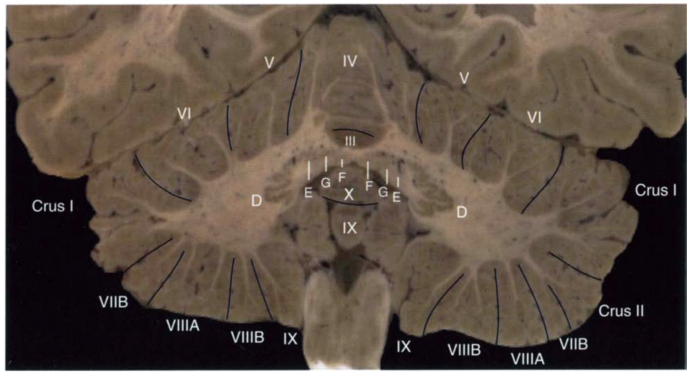




Diagnostic MRI





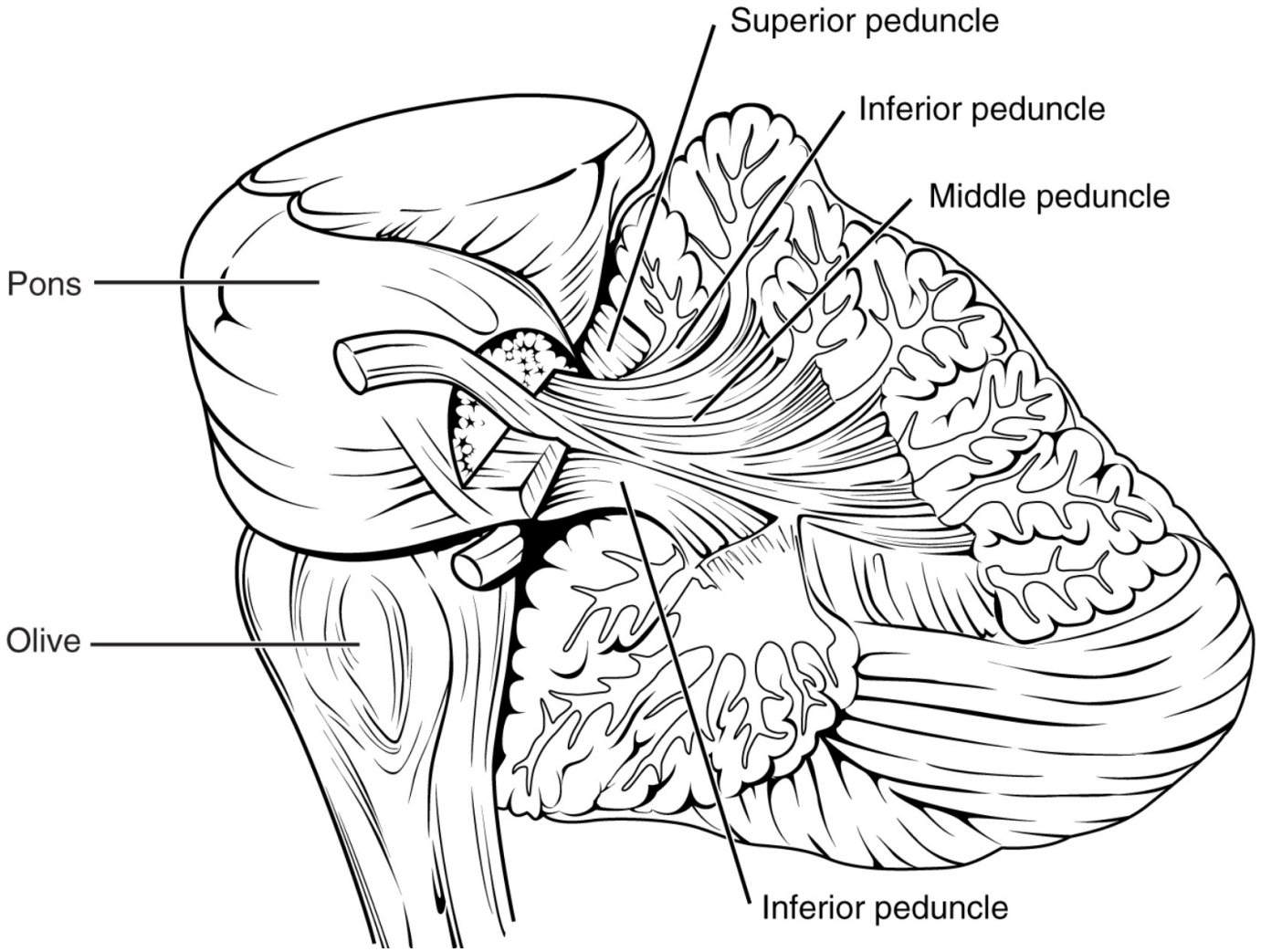


Deep cerebellar nuclei:

Nucleus fastigii (F)
Nucleus globosus (G)
Nucleus emboliformis (E)
Nucleus dentatus (D)

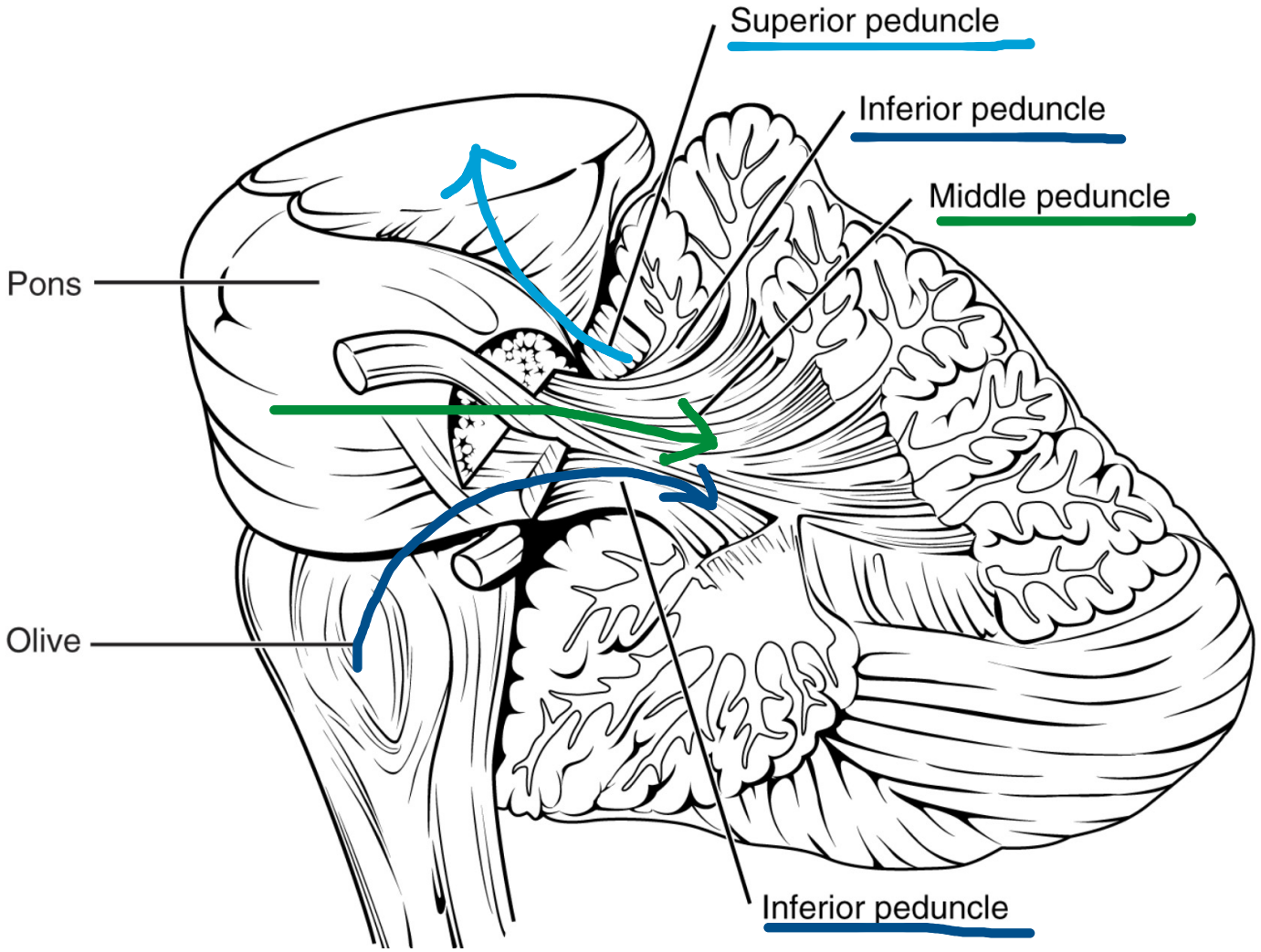
} Ncl. interpositus

Diagnostic MRI



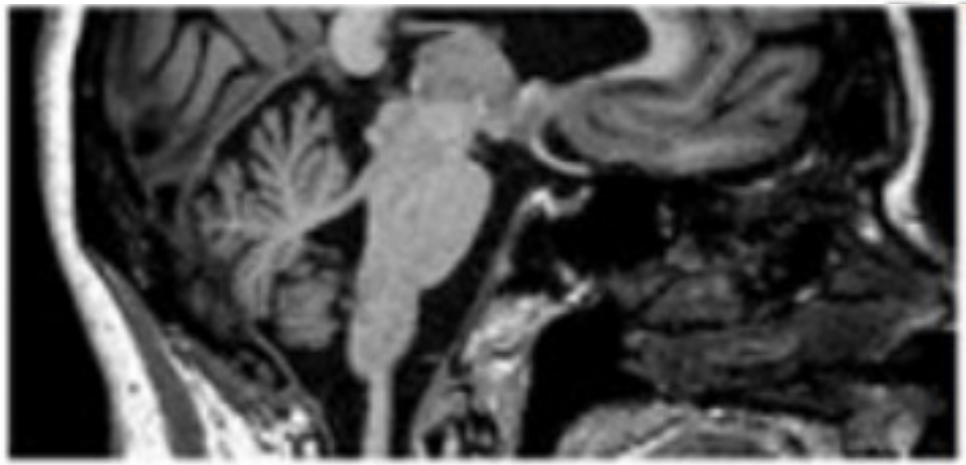
Wikipedia.org
Illustration from Anatomy & Physiology, Connexions Web site. http://cnx.org/content/col11496/1.6/, Jun 19, 2013.

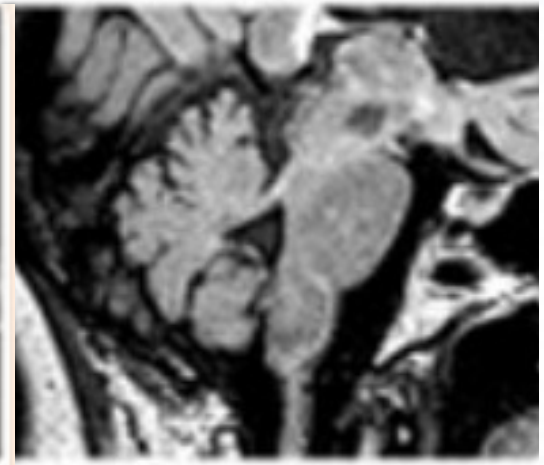
Diagnostic MRI

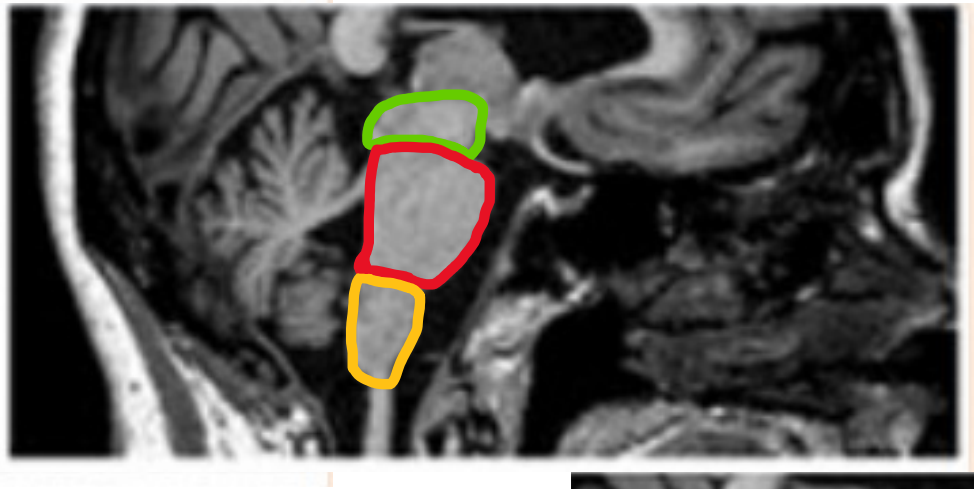


Wikipedia.org
Illustration from Anatomy & Physiology, Connexions Web site. http://cnx.org/content/col11496/1.6/, Jun 19, 2013.

Diagnostic MRI

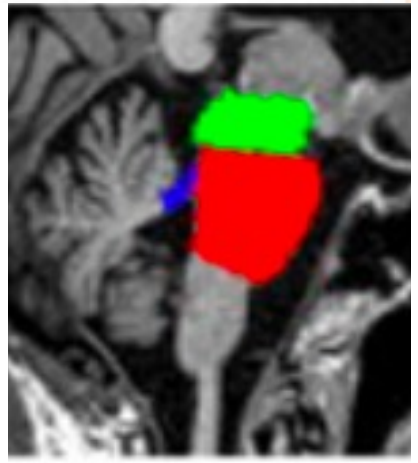






Midbrain (green)
Pons (red)
Medulla oblongata (yellow)

Superior cerebellar peduncle (blue)



Iglesias JE, et al. Neuroimage. 2015
doi: 10.1016/j.neuroimage.2015.02.065.

Diagnostic MRI

Sequences:

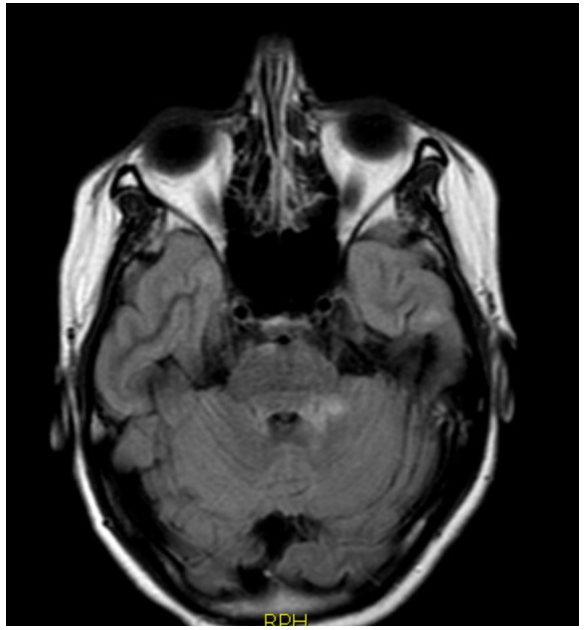
- T1 weigthed
- T2 weighted
- FLAIR
- Diffusion weighted
- Iron sensitive sequences
- Gadolinium

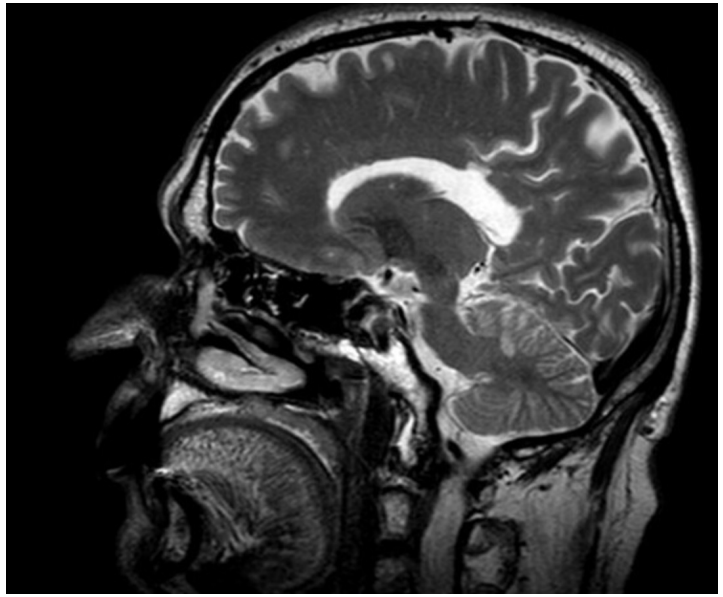
Diagnostic MRI

Hämosiderosis

Chiari malformation

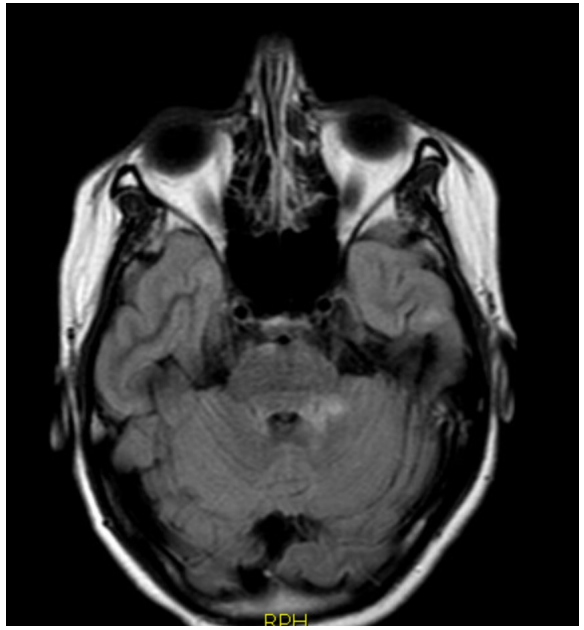
Diagnostic MRI - Examples

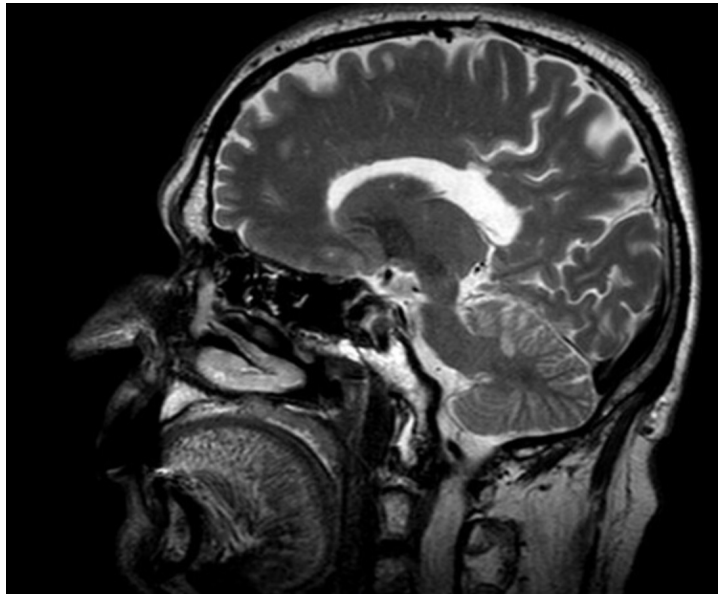




Diagnostic MRI - Examples

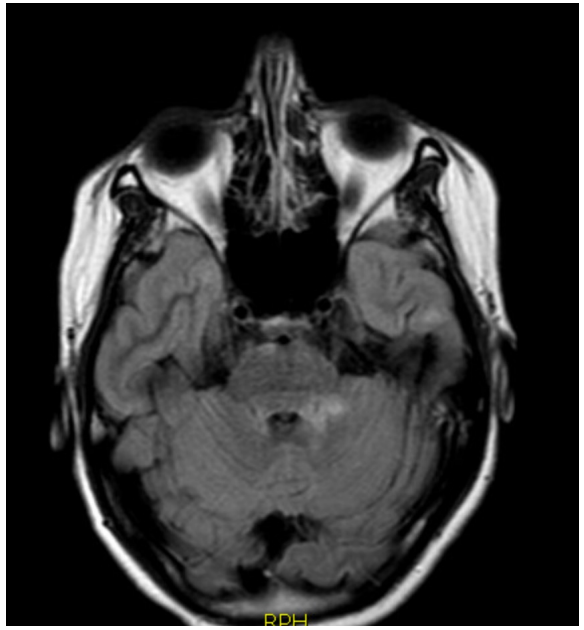
MS lesions

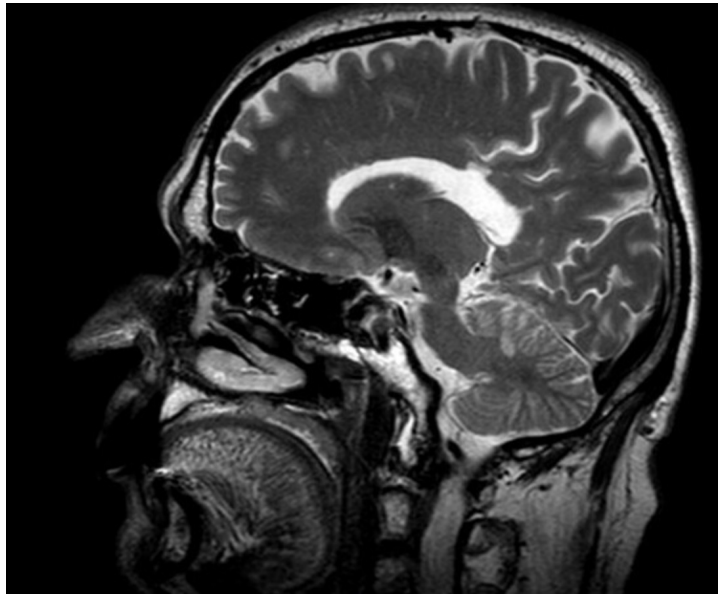




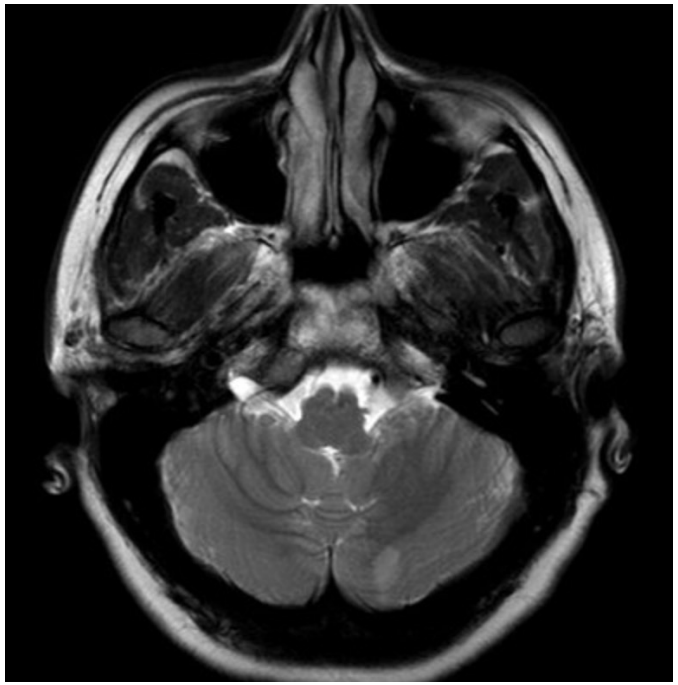
Diagnostic MRI - Examples

MS lesions



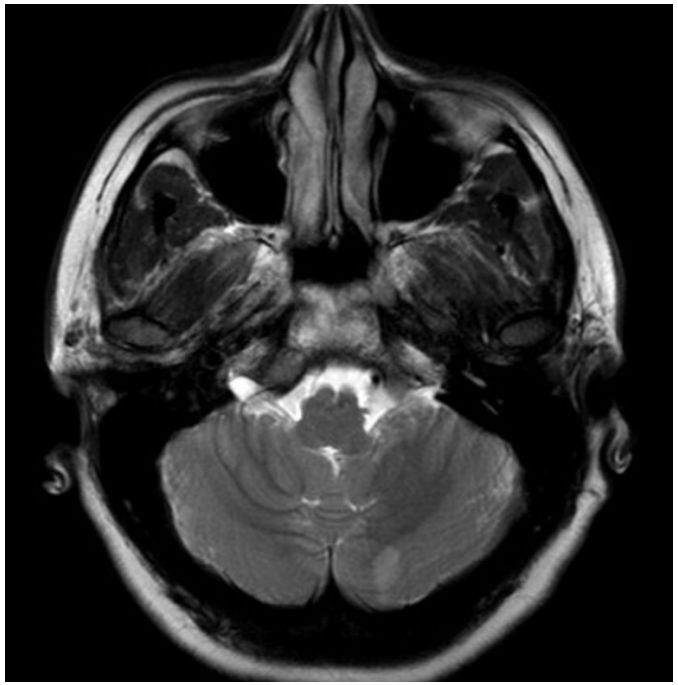


Diagnostic MRI - Examples



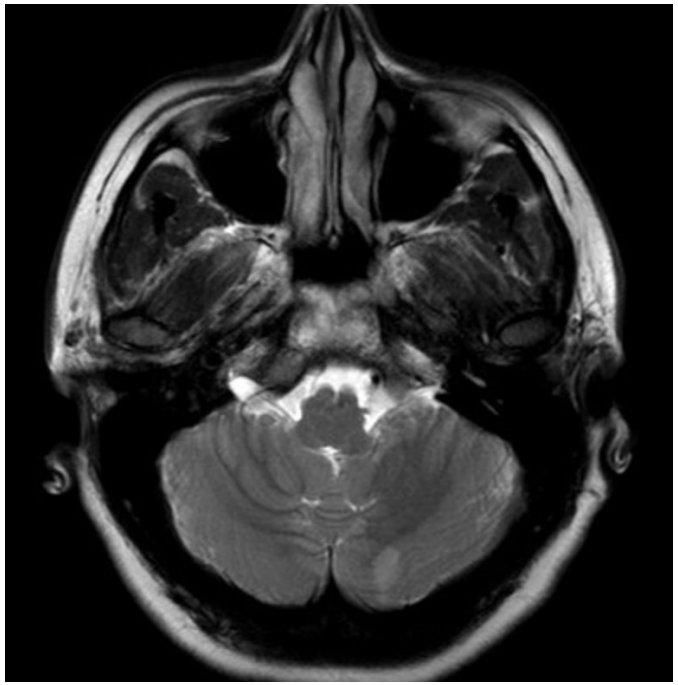
Diagnostic MRI - Examples

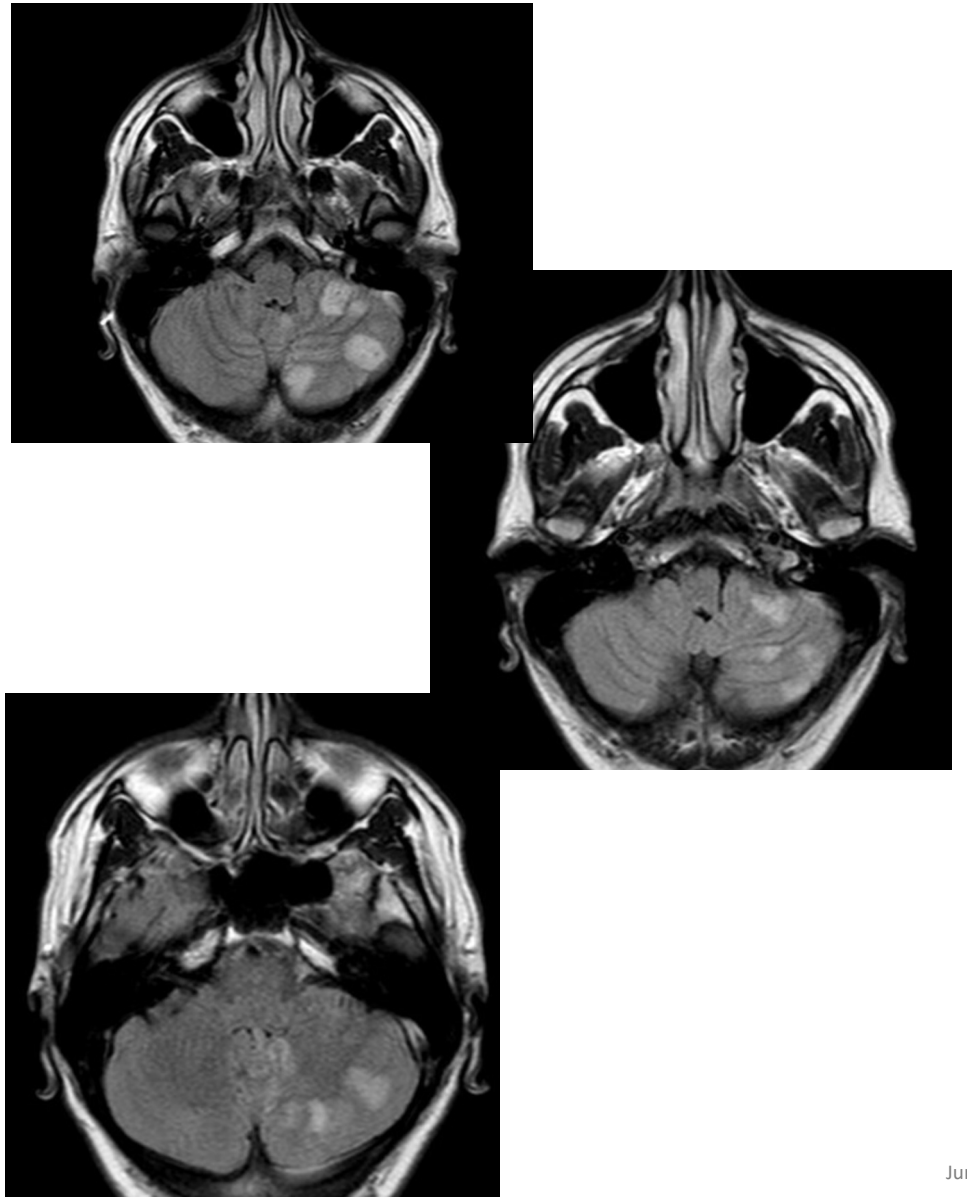
Stroke:

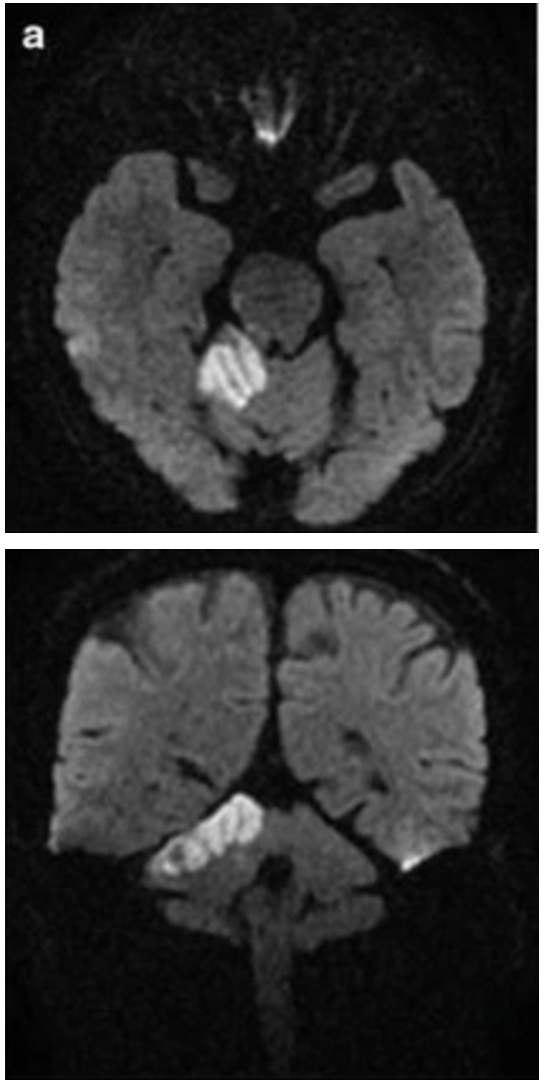


Diagnostic MRI - Examples

Stroke:







Jung, KH., et al. (2013), Handbook of the Cerebellum and Cerebellar Disorders.
https://doi.org/10.1007/978-94-007-1333-8_90

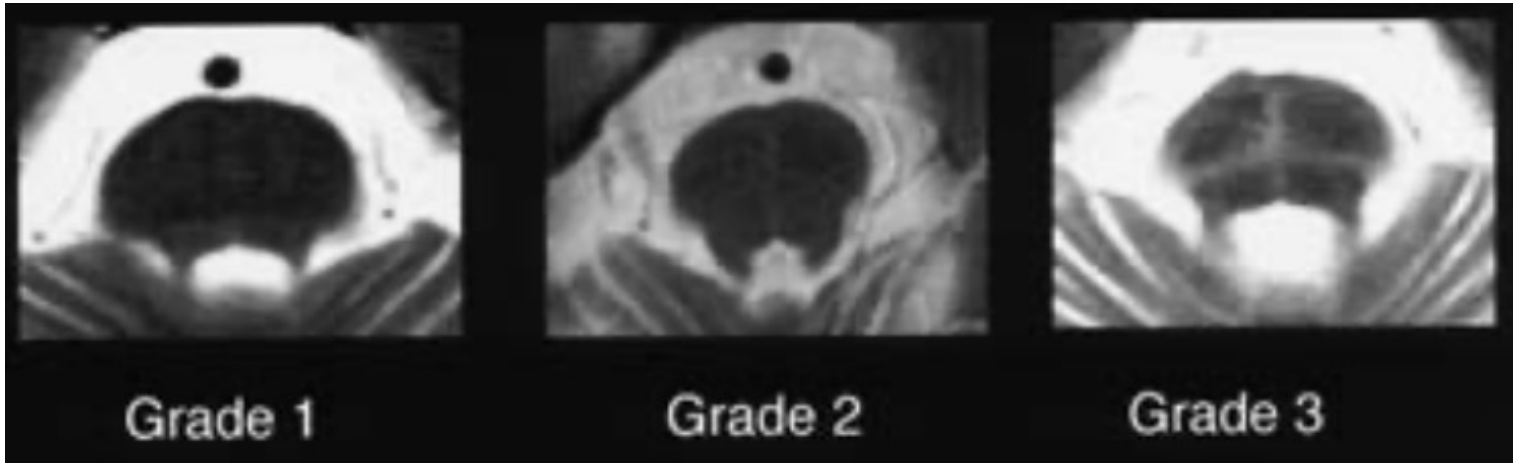
Diagnostic MRI

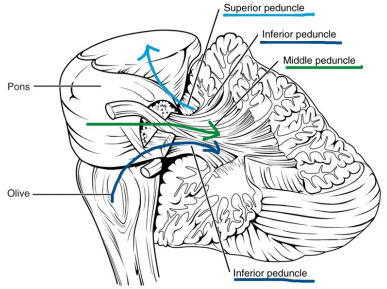
MSA

Abe et al., J Neuroimaging 2006;
doi: 10.1177/1051228405279988

Diagnostic MRI

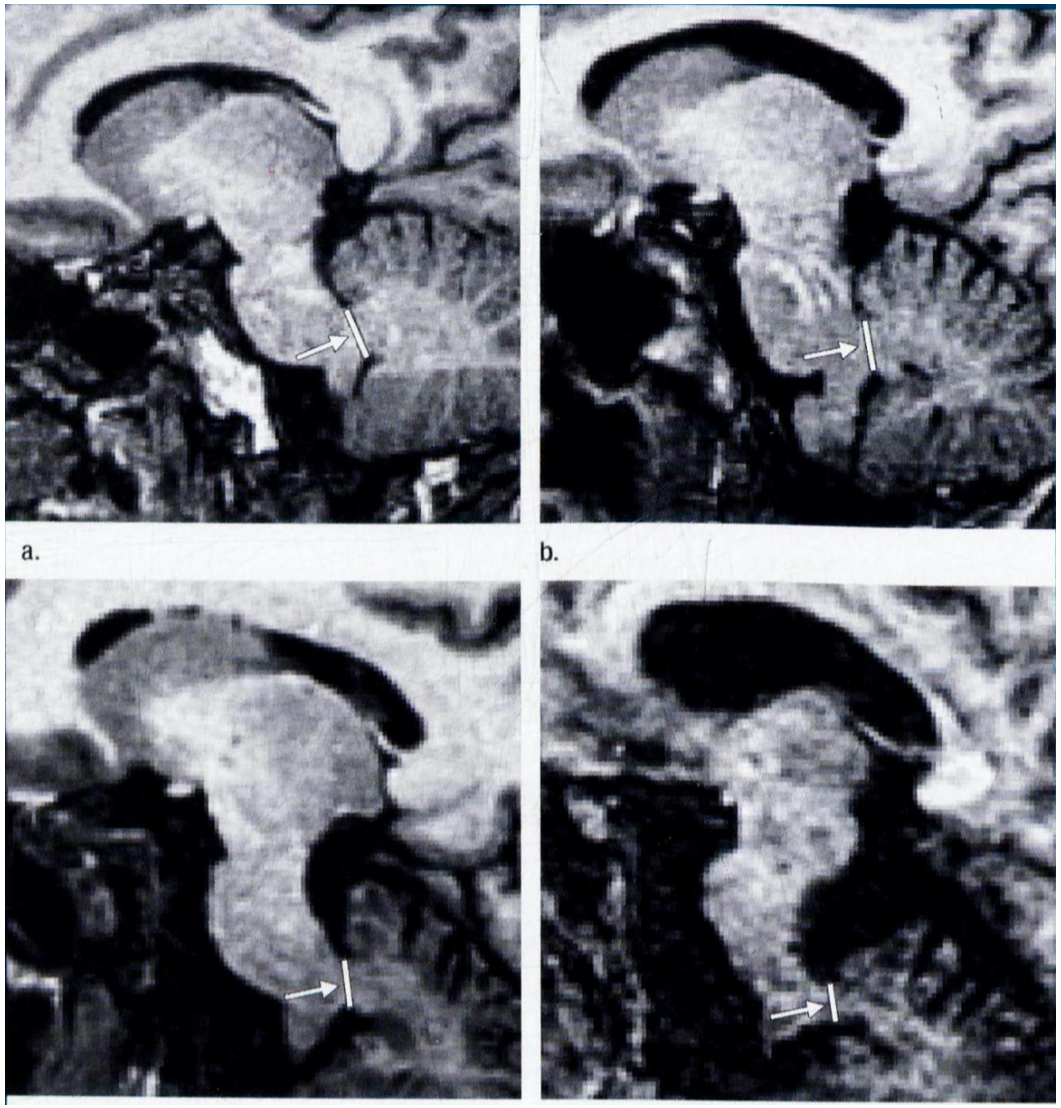
MSA



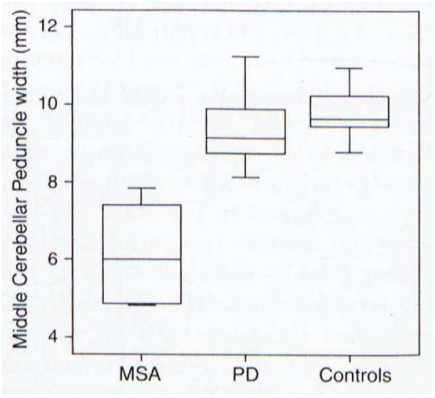


Abe et al., J Neuroimaging 2006;
doi: 10.1177/1051228405279988

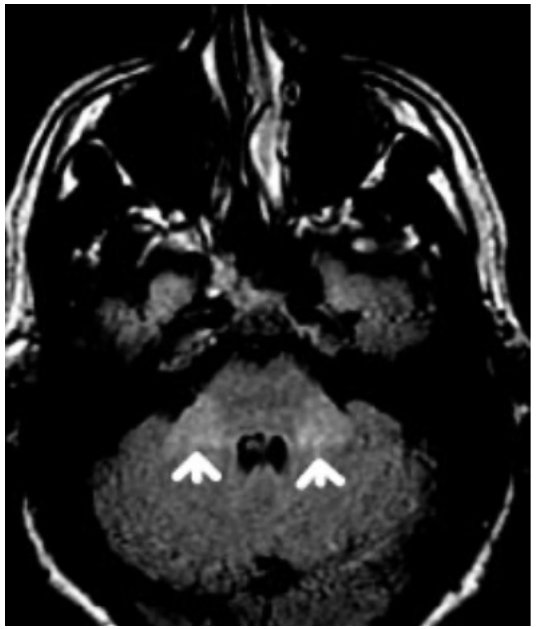
Diagnostic MRI



Width of the middle cerebellar peduncle (MCP) in MSA



Nicoletti G, et al. Radiology. 2006
doi: 10.1148/radiol.2393050459



Hyperintensities of the MCP in MSA

Diagnostic MRI

Is this a hot cross bun sign?

Single choice

Yes

No

Cocozza S, et al. Neuroradiology. 2021
doi: 10.1007/s00234-021-02682-2

Diagnostic MRI

69-year old female with ataxia. What diagnosis do you think is probable?

Single choice

MSA-C

Other

Cocozza S, et al. Neuroradiology. 2021
doi: 10.1007/s00234-021-02682-2

Diagnostic MRI

SCA1

Cocozza S, et al. Neuroradiology. 2021
doi: 10.1007/s00234-021-02682-2

Diagnostic MRI

Stroke

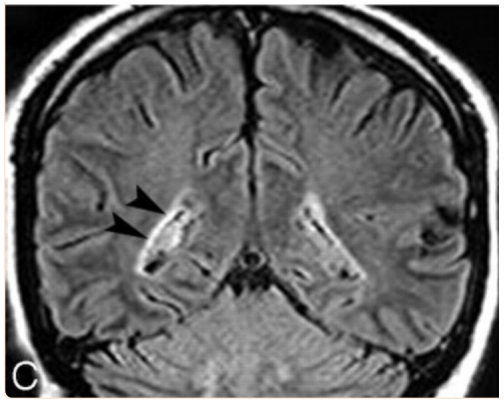
MS lesions

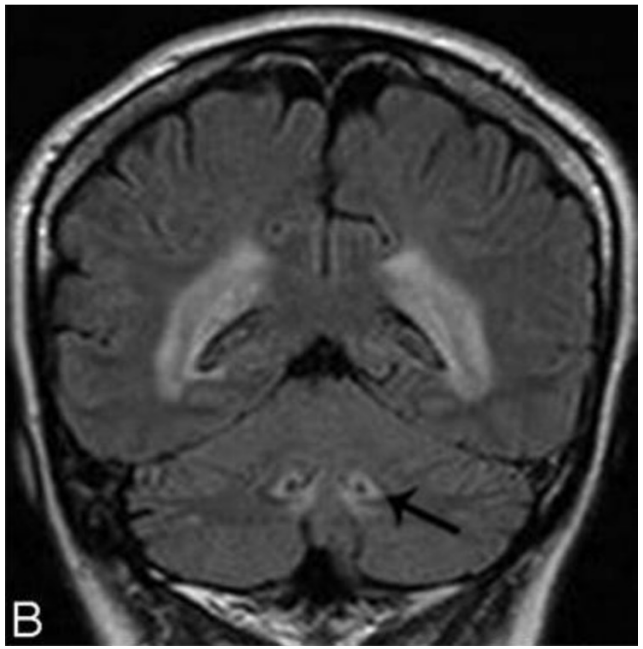
Chiari malformation

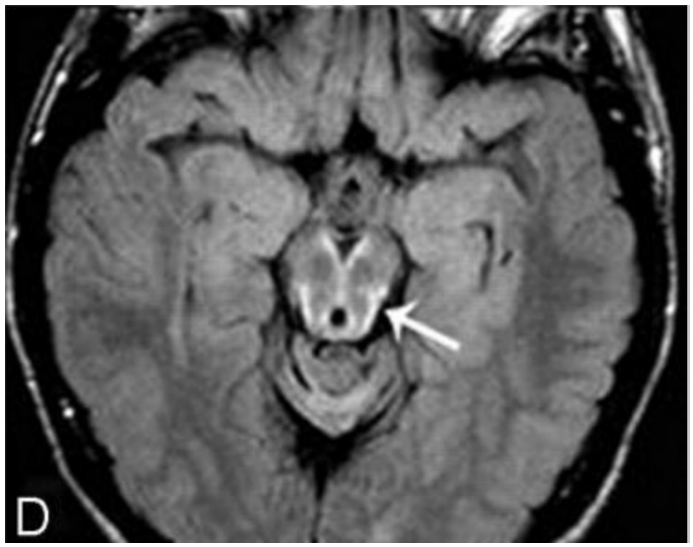
Superficial siderosis

….

Diagnostic MRI







Morbus Alexander

Farina L, et al. AJNR Am J Neuroradiol.
doi: 10.3174/ajnr.A1060.

Diagnostic MRI

AOA2

SCA6

SCA3

Cocozza S, et al. Neuroradiology. 2021
doi: 10.1007/s00234-021-02682-2

Diagnostic MRI

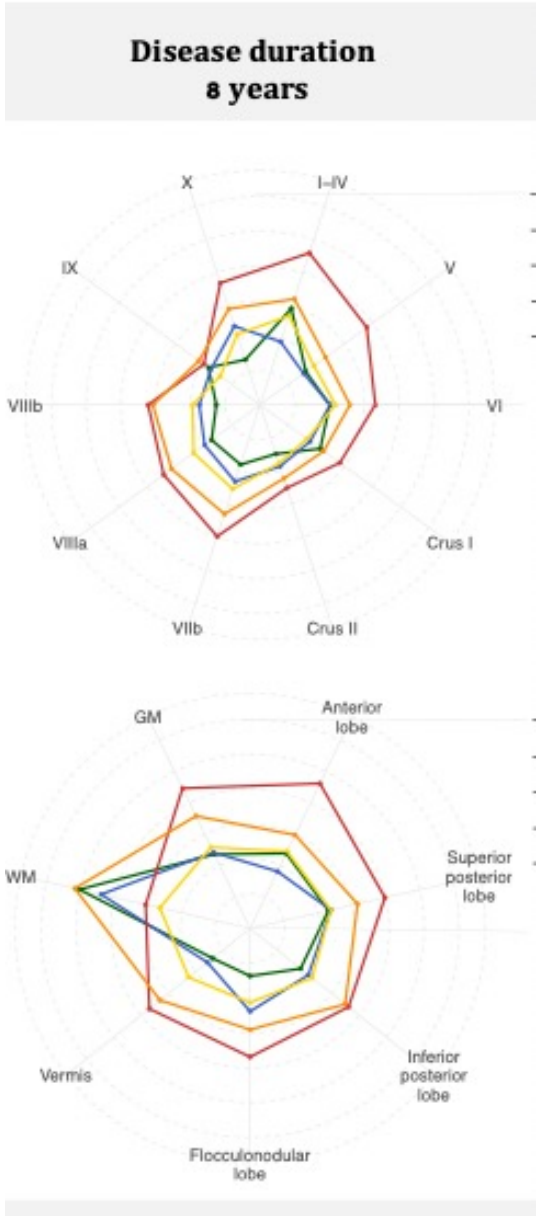
SCA6

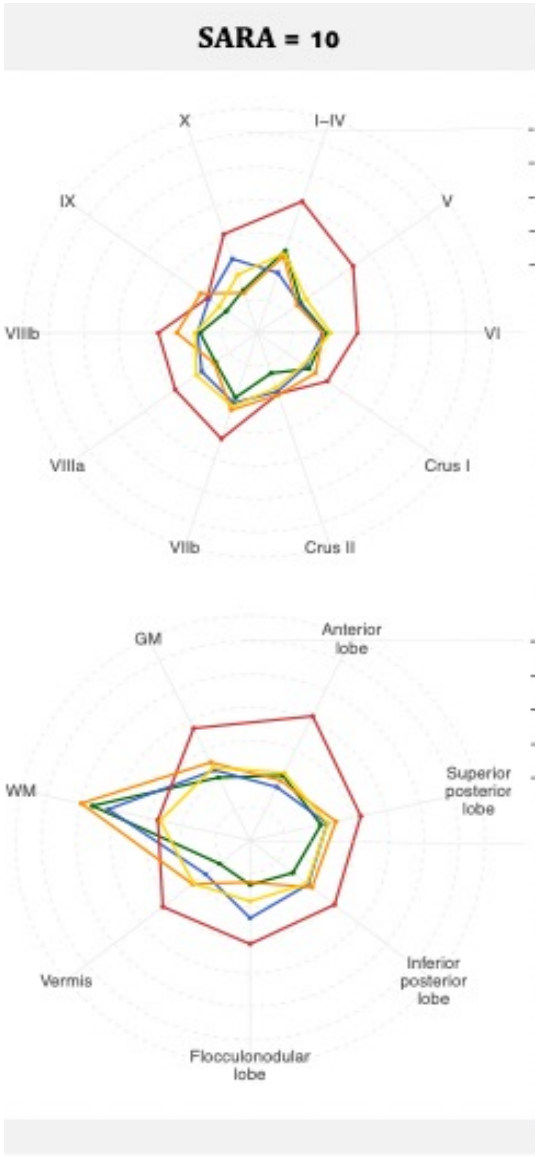
AOA2

SCA3

Faber, UKB
Cocozza S, et al. Neuroradiology. 2021
doi: 10.1007/s00234-021-02682-2

Diagnostic MRI





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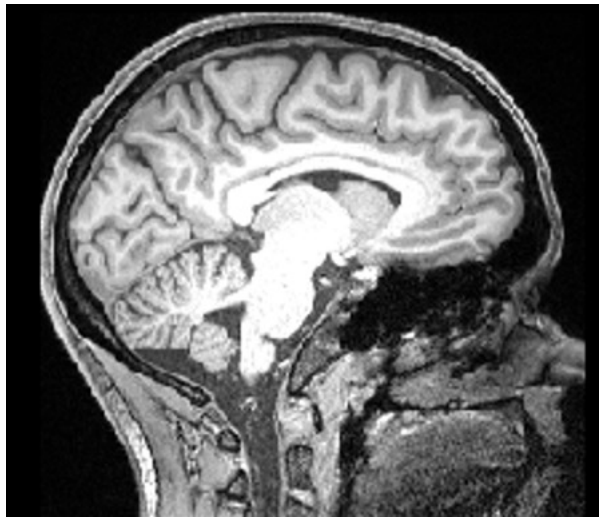

HC

FRDA

Diagnostic MRI

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- Essential in the diagnostic work-up
- **High relevance for identifying acquired causes**
- Limited relevance for identifying disease specific patters
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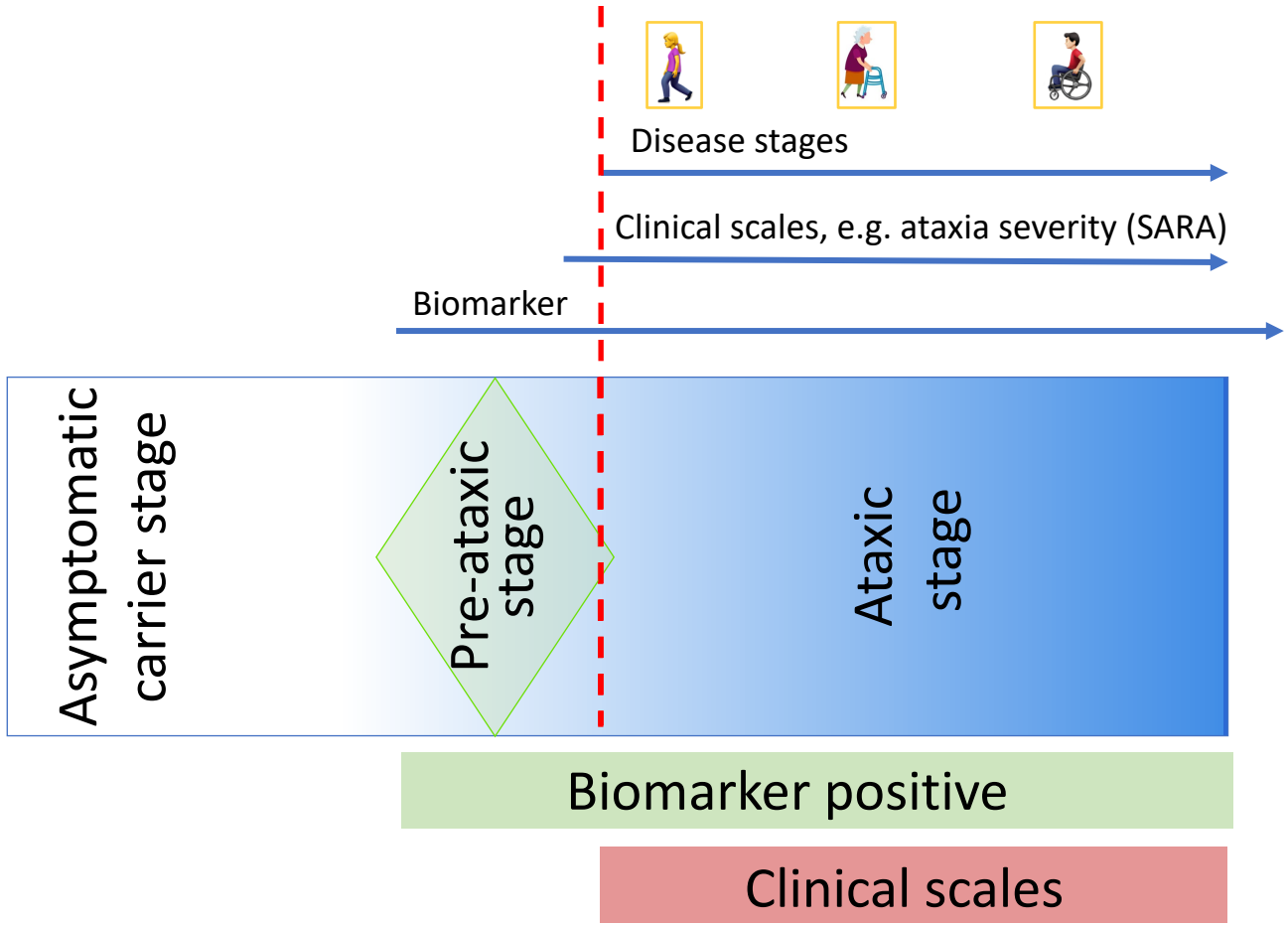
- Take brainstem into consideration

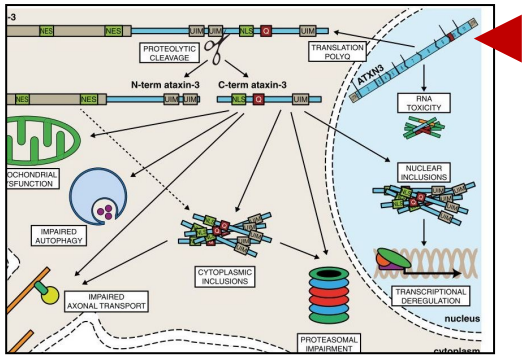
Cerbellar volumetry as a potential imaging biomarker
For spinocerebellar ataxia type 3/Machado-Joseph Disease (SCA3/MJD)

CAG repeat expansion

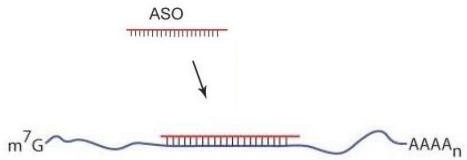
Cerbellar volumetry as a potential imaging biomarker For spinocerebellar ataxia type 3/Machado-Joseph Disease (SCA3/MJD)



CAG repeat expansion

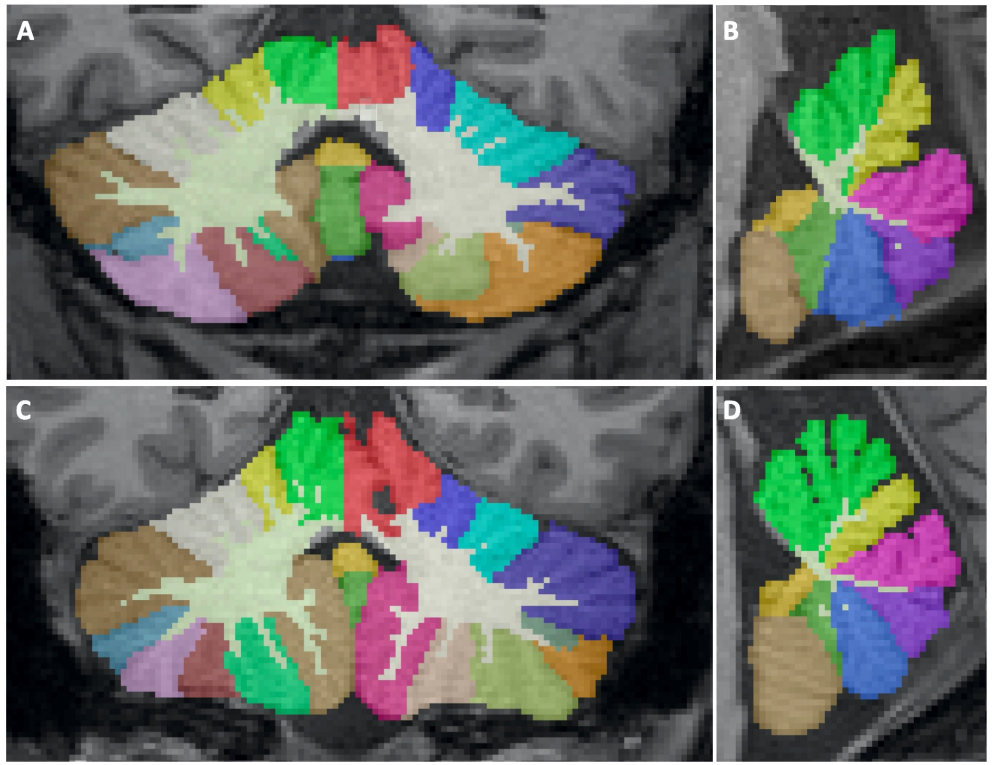


Antisense Oligonucleotides



Evers et al., Mol Neurobiol 2014

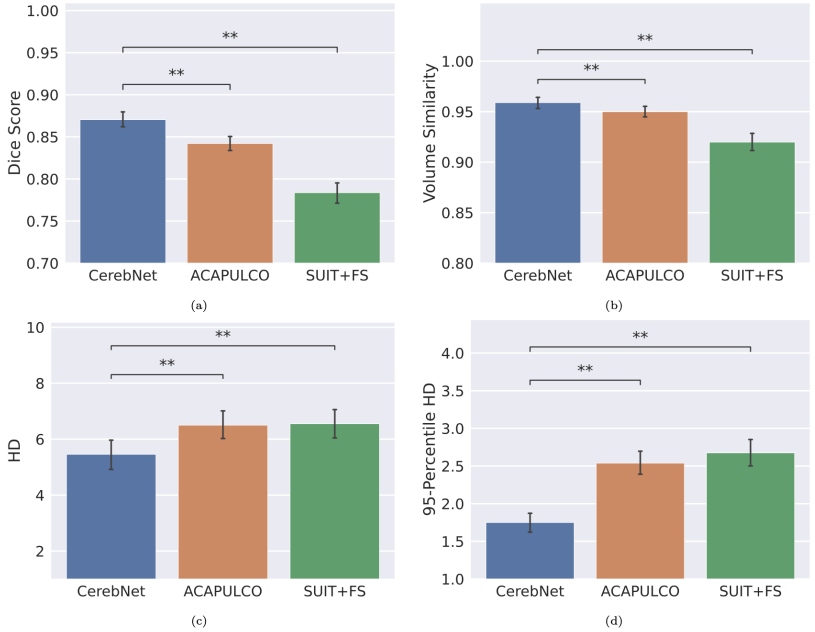
Diagnostic MRI <> MRI in research



- Fully automated segmentation of the cerebellum
- No preprocessing
- 12 sec per subject
- High accuracy outperforming state-of-the-art methods

CerebNet

A fast and reliable deep-learning pipeline for detailed cerebellum sub-segmentation



Faber, Bahrami, Kuegler, et al., submitted 2022

in co-operation with AI in Medical Imaging, DZNE, Bonn

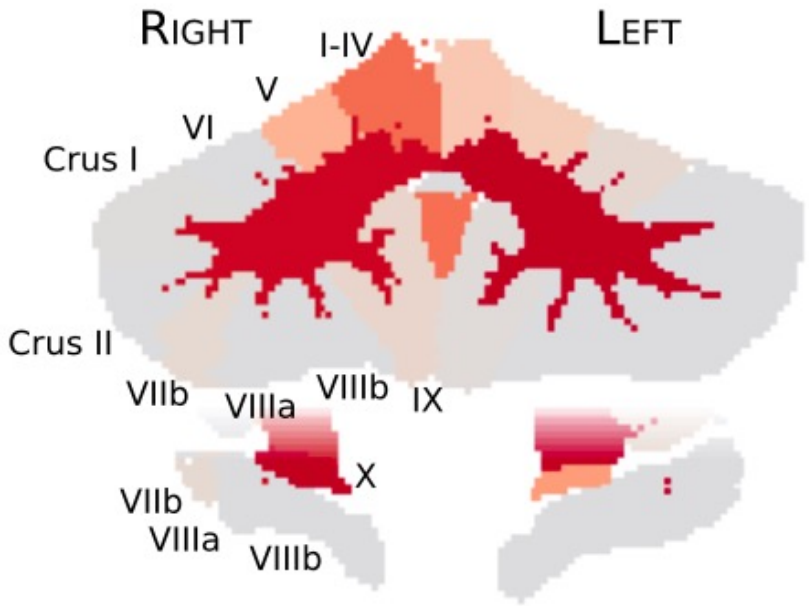
Martin Reuter
David Kuegler
Ehmad Bahrami

Artificial Intellegence in Medical Imaging

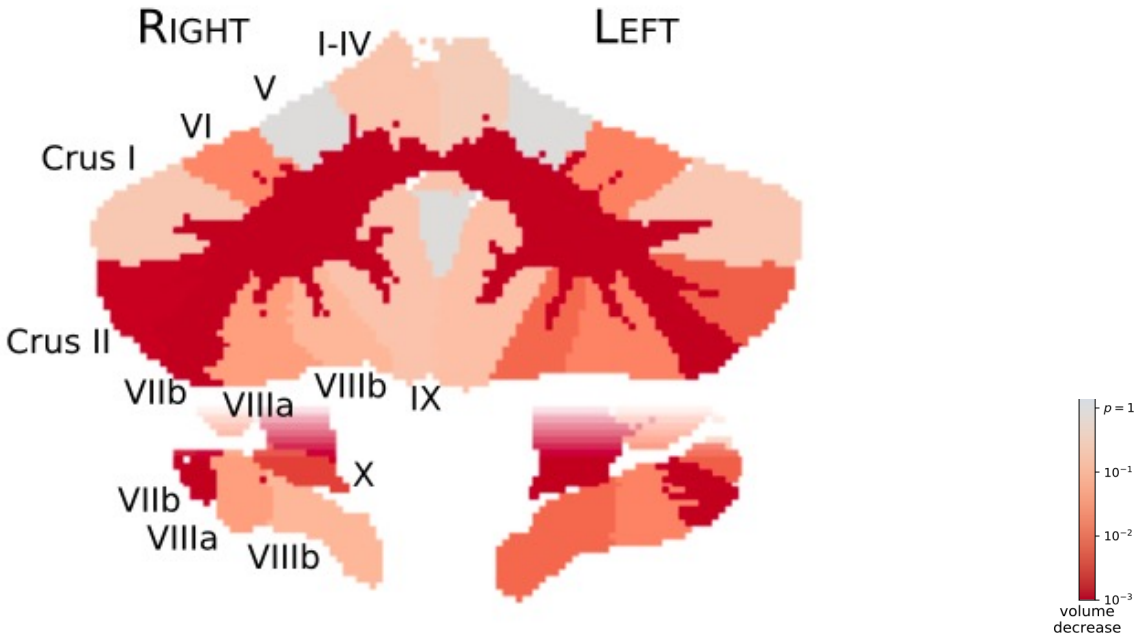
SCA Young Investigator Research Grant

Diagnostic MRI <> MRI in research

Pre-ataxic SCA3 vs. HC

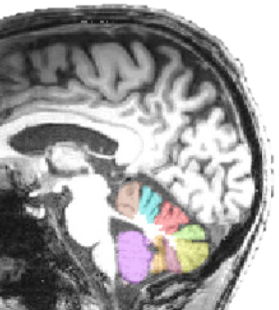


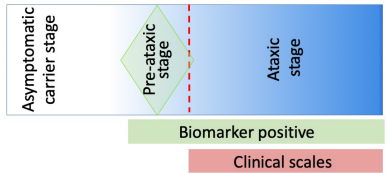
Ataxic SCA3 vs. Pre-ataxic SCA3



Pre-ataxic SCA3 N=42 | Ataxic SCA3 N=67 | HC N=41

Faber, Bahrami, Kuegler, et al., submitted 2022





Thank you for your attention!

Thomas Klockgether
Dept. of Neurology, University Hospital Bonn
Clinical Research, DZNE

Marcus Grobe-Einsler
Demet Önder
Berkan Koyak

Ekaterina Lejber

Tim Elter

Mónica Ferreira

Philipp Wegner

SCAmingo

UNIVERSITÄT BONN

ukb universitäts klinikum bonn

DZNE

JPND research

ESMI
European Spinocerebellar Ataxia Type 3/Machado-Joseph Disease Initiative

SCAIFIELD

European Reference Network
for rare or low prevalence complex diseases
Network Neurological Diseases (ERN-RND)

ean european academy of neurology

NAF National Ataxia Foundation
Connecting Ataxia families, researchers, clinicians and the community

Martin Reuter
Artificial Intellegence in Medical Imaging, DZNE Bonn
David Kuegler
Ehmad Bahrami

Tony Stöcker
MR Physics, DZNE Bonn
Eberhard Pracht
Rüdiger Stirnberg
Yannik Voelzke

Alexander Radbruch
Neuroradiologie, UKB
DZNE Bonn

Tamara Schaprian
Statistician
DZNE Bonn

Matthias Schmid
Institute of Medical Biometry, Informatics and Epidemiology, University Hospital Bonn

Dagmar Timmann
Experimental Neurology, University Hospital Essen

https://ataxia-global-initiative.net/about-the-young-investigator-initiative/

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