ROMA
17-18 marzo 2026

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5th edition

Il contributo dell'imaging avanzato nello studio dei parkinsonismi

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IMAGING e DISTURBI DEL MOVIMENTO

- ✓ Despite well-established Parkinson's disease (PD) diagnostic criteria, diagnosis can still be challenging, with a high rate of misdiagnosis in atypical cases (APDs), especially in **early disease stages**.
- ✓ The extensive development of **neuroimaging** in recent years has profoundly changed the study of PD.
- ✓ Imaging now plays a pivotal role in **aiding diagnosis** in PD early or pre-manifest stages and in **enabling a differential diagnosis** with APDs.

Reimao S., et Al.: *A standardized MR Imaging protocol for Parkinsonism.* Mov Disorders 2020

IMAGING e DISTURBI DEL MOVIMENTO

The heterogeneity of MR scanners and parameters (eg, field strength, gradient system, manufacturer, sequences) may lead to different results

Without a dedicated protocol, information loss and inability to value pathological findings may increase the number of false-negatives because of missing or disregarded data.

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Reimao S., et Al.: *A standardized MR Imaging protocol for Parkinsonism.* Mov Disorders 2020

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Techniques	Measures	Information
CONVENTIONAL MRI		
T1-w,	Shape, volume	Atrophy
T2-w, FLAIR, PD-w	Signal changes	Signal abnormalities (gliosis and demyelination of white matter)
T2*-w, SWI	Iron load	Iron deposition Nigral dorsolateral hyperintensity
Neuromelanin-sensitive sequence	Signal and volume	Content of catecholaminergic neurons in the SNpc and the locus
T2 -weighted multiecho Magnitude image	Relaxation times R2 = 1/T2	Iron load
Magnitude and phase images	Quantitative susceptibility mapping	Iron load
DIFFUSION IMAGING		
Diffusion-weighted imaging (DWI)	Apparent diffusion coefficient (ADC), Trace (D)	Magnitude of water diffusion

The clinical application of advanced imaging technologies is still limited, and their standardization will take time given the multidimensionality of these diseases.

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Chougar L., et Al.: *The Role of Magnetic Resonance Imaging for the Diagnosis of Atypical Parkinsonism.* Front Neurology 2020

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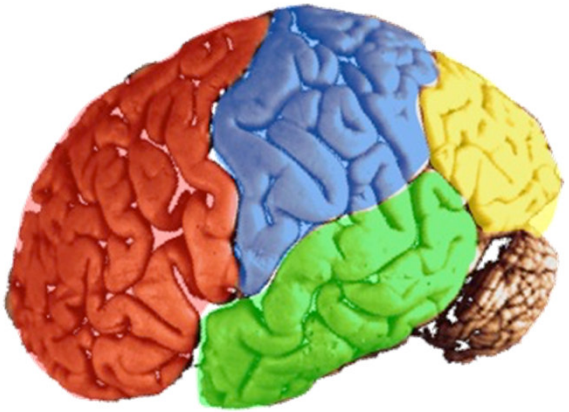
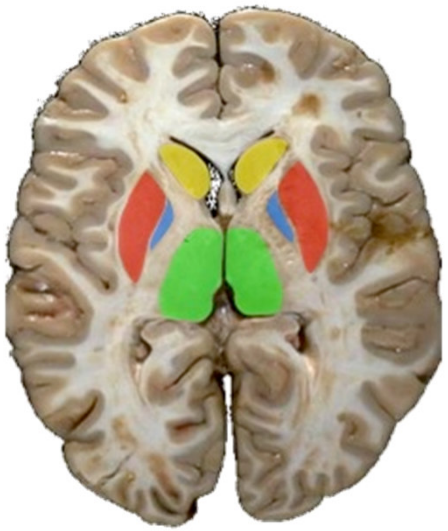
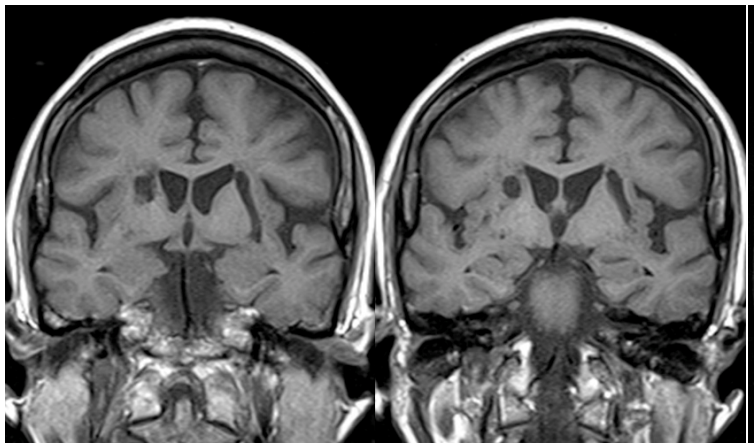


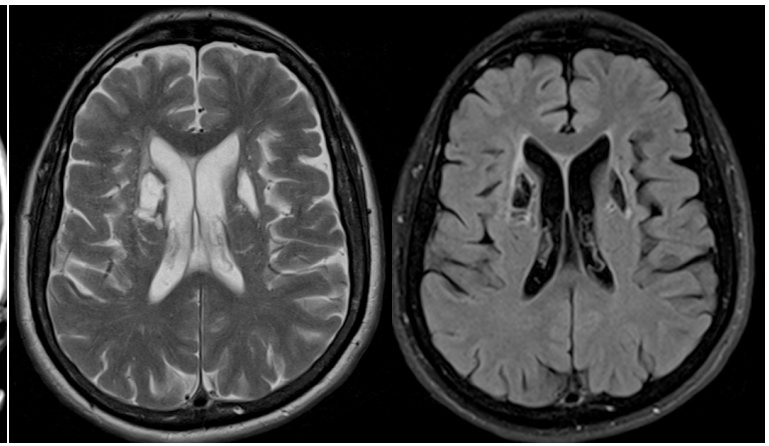


IMAGING e DISTURBI DEL MOVIMENTO

✓ *Escludere cause secondarie*

STATO LACUNARE
Putamino-pallido-thalamic pathways





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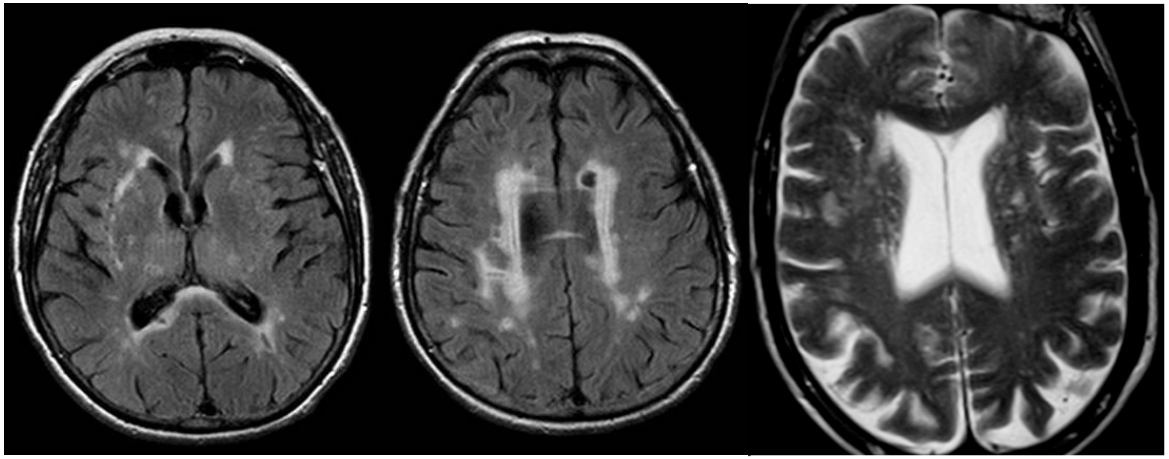

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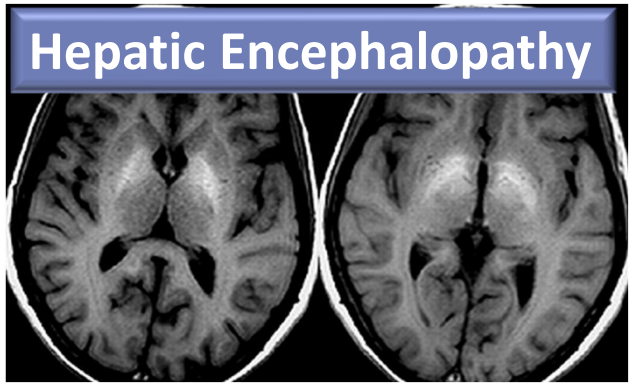
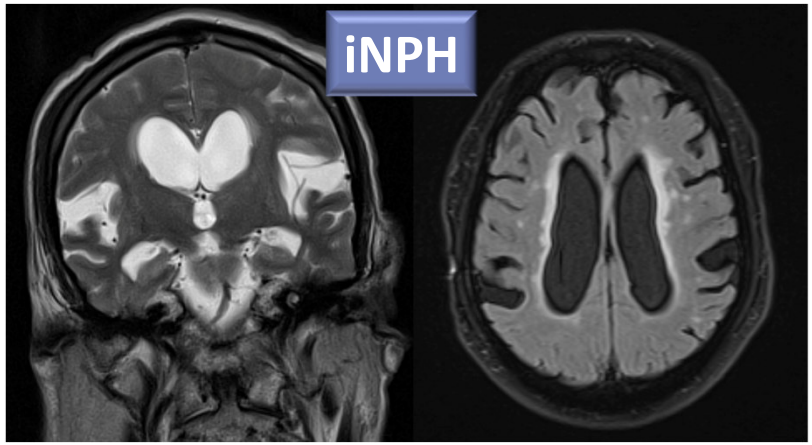
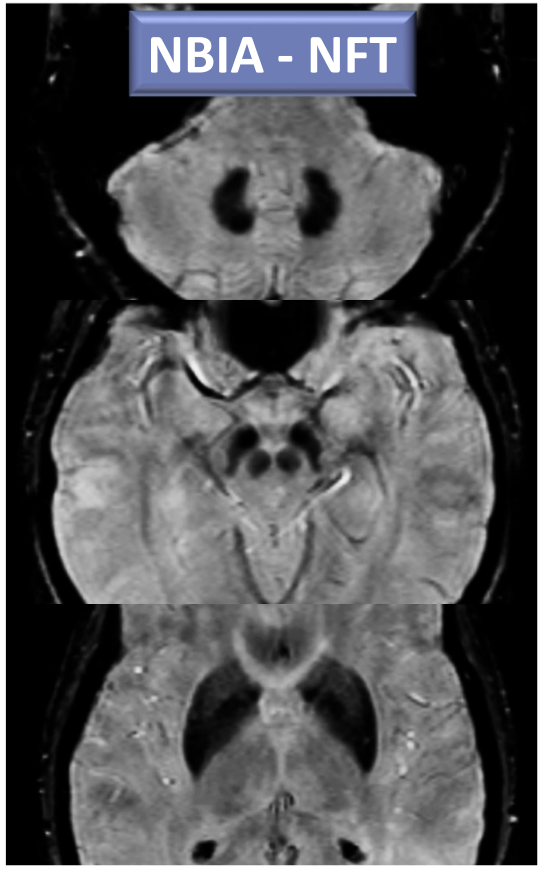
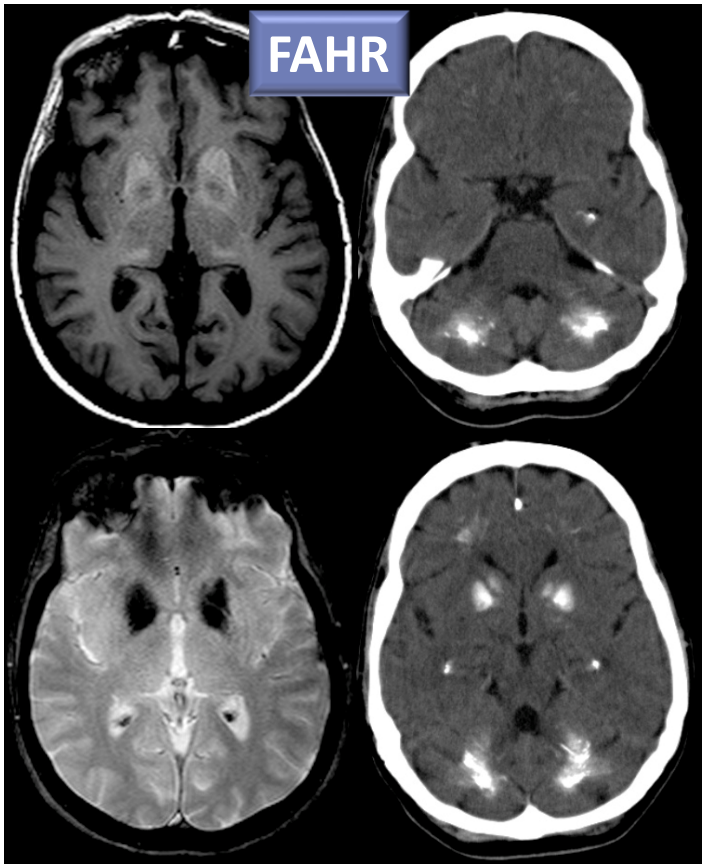
✓ *Escludere cause secondarie*









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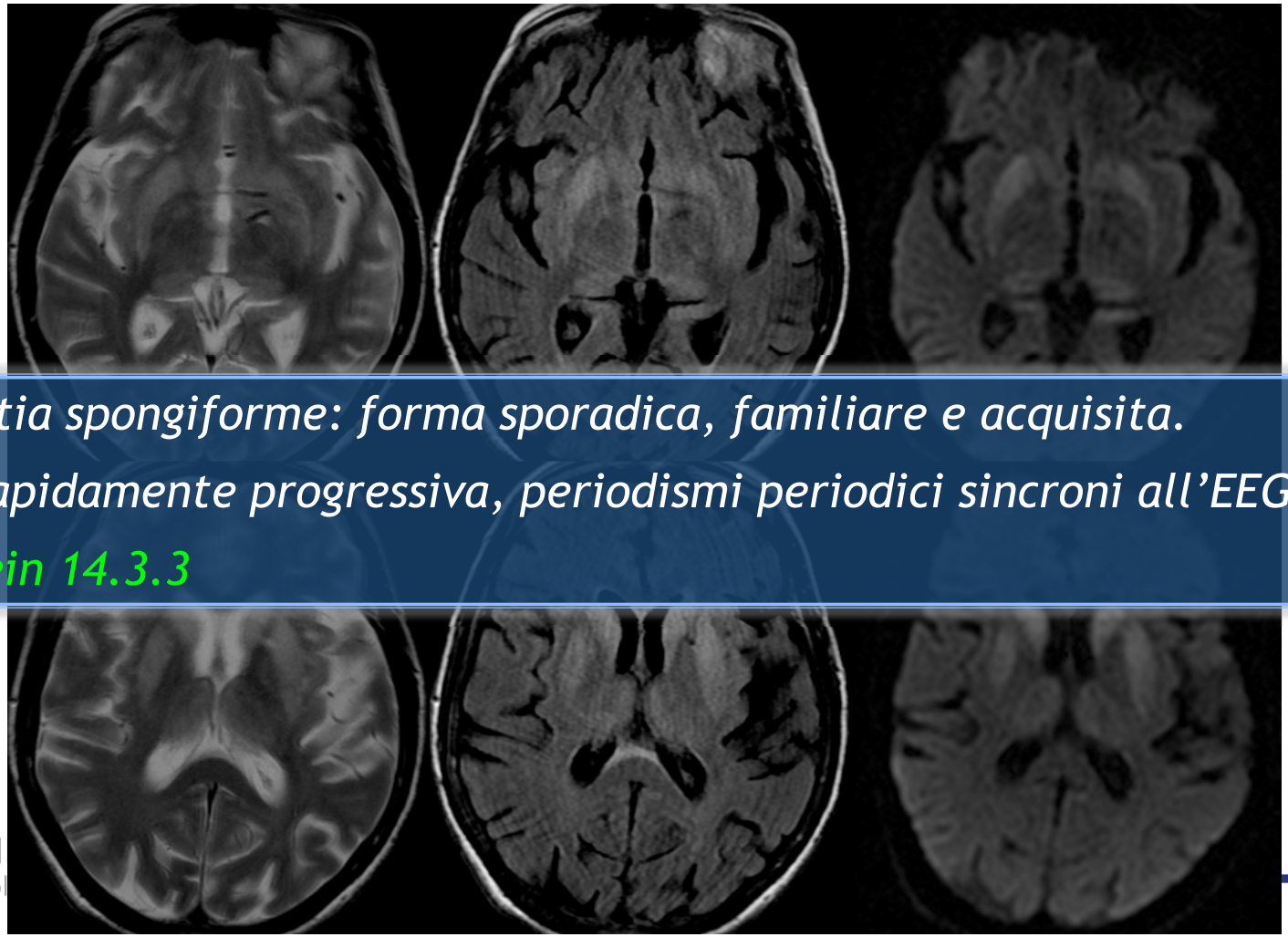
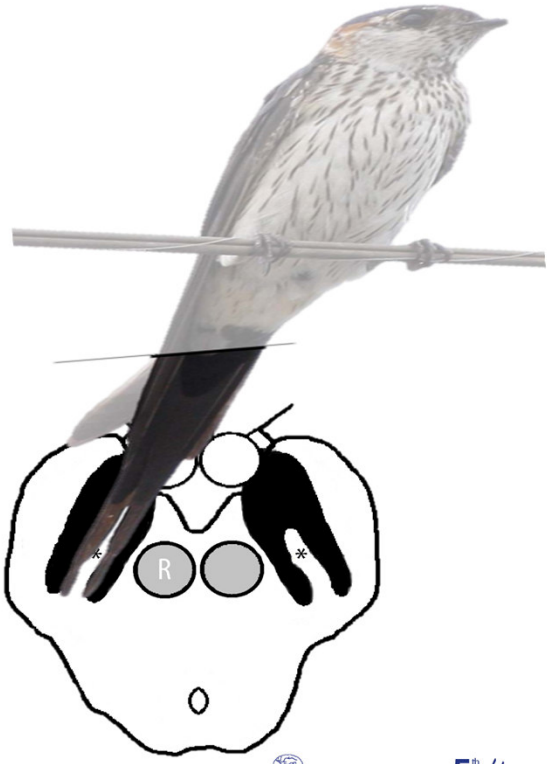
✓ *Escludere cause secondarie*



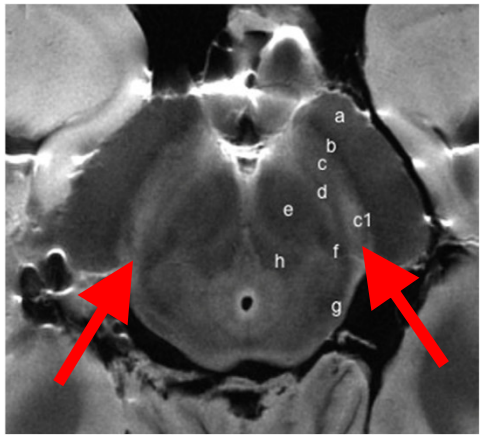
- ✓ *Encefalopatia spongiforme: forma sporadica, familiare e acquisita.*
- ✓ *Demenza rapidamente progressiva, periodismi periodici sincroni all'EEG, mioclonie.*
- ✓ *+ CSF protein 14.3.3*

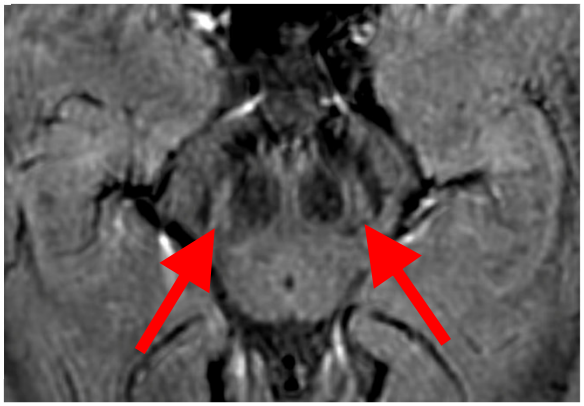
IMAGING e DISTURBI DEL MOVIMENTO

Imaging del NIGROSOMA



✓ Parkinson





- ✓ Nigrosome-1, the largest of the **dopaminergic cell clusters** lying dorsolateral in the substantia nigra pars compacta (SNc), is the most prominently affected dopaminergic region in PD.
- ✓ STS loss/absence has been well-described in individuals with PD.
- ✓ **Low signal on iron- sensitive MRI** sequences (eg, SWI, T2*) is thought to be related to decreased neuromelanin content and accumulation of free iron, as a result of degeneration of presynaptic dopaminergic neurons, making the detection of STS abnormalities a specific cellular marker.

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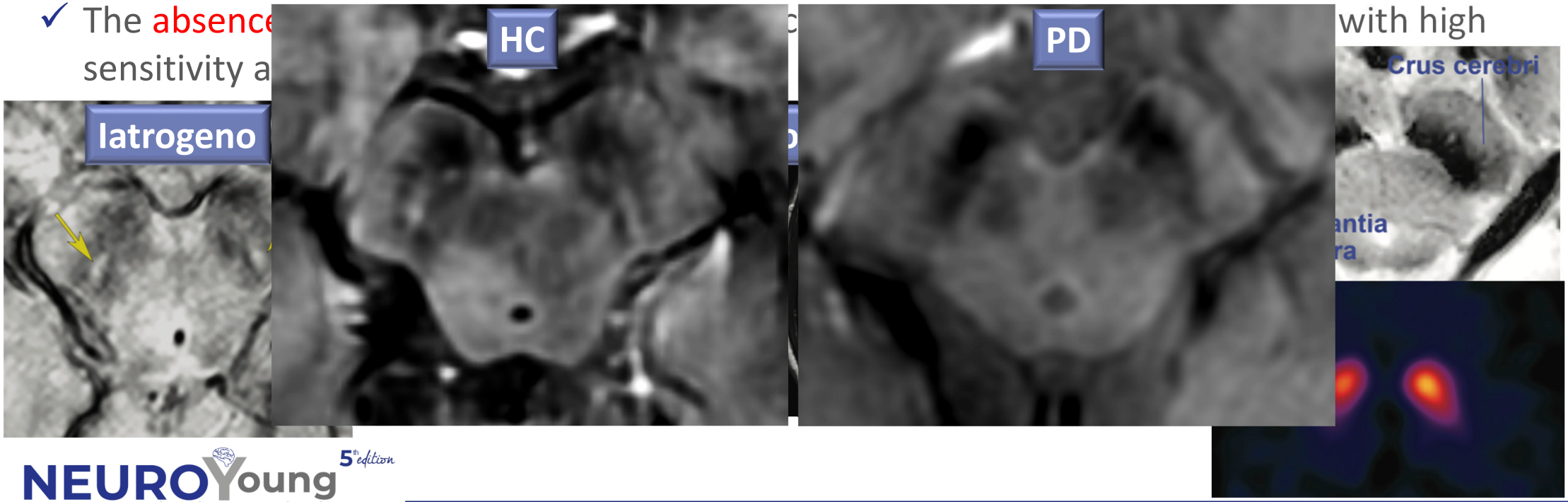
Pavese N, et Al.: *Nigrosome Imaging and Neuromelanin Sensitive MRI in Diagnostic Evaluation of Parkinsonism.* Mov Disorders 2018

IMAGING e DISTURBI DEL MOVIMENTO

✓ Parkinson

- ✓ Using 3 T MRI the absence of the DNH signal have **100% sensitivity** and **95% specificity** in **distinguishing PD from HCs**. It may become a potential biomarker for **premotor stages** of PD.
- ✓ The absence … with high sensitivity a…

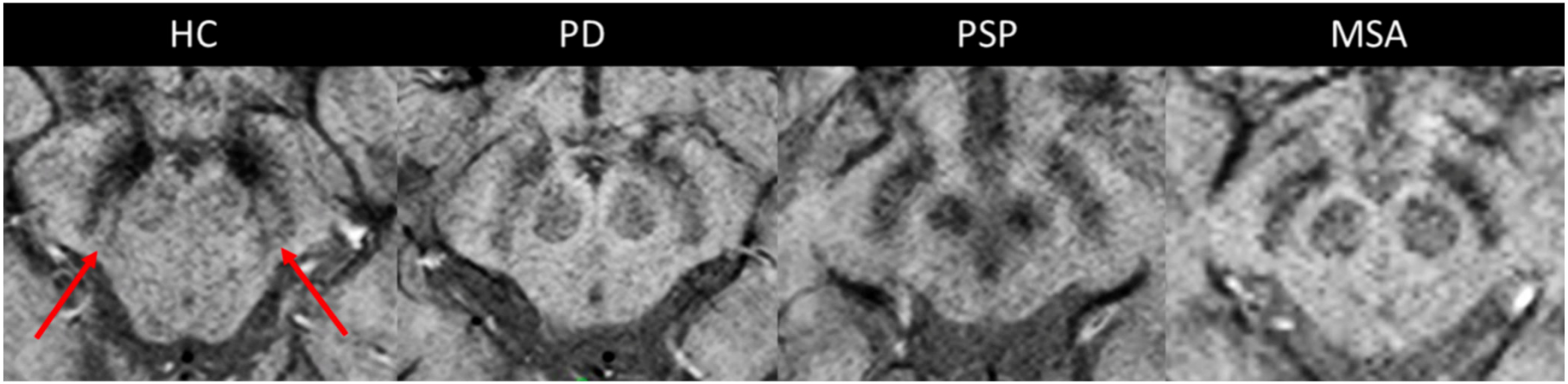


Pavese N, et Al.: *Nigrosome Imaging and Neuromelanin Sensitive MRI in Diagnostic Evaluation of Parkinsonism.* Mov Disorders 2018

IMAGING e DISTURBI DEL MOVIMENTO

✓ *Parkinson*

- ✓ DNH signal it is unable to **differentiate PD from APDs** because the DNH signal loss is also seen in patients with APDs.



- ✓ DNH imaging may be considered in the **differential diagnosis** of degenerative from nondegenerative parkinsonisms or from ET, and in this context its use may be comparable to DAT- SPECT.

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Pavese N, et Al.: *Nigrosome Imaging and Neuromelanin Sensitive MRI in Diagnostic Evaluation of Parkinsonism.* Mov Disorders 2018

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Imaging del NIGROSOMA

✓ Parkinson

Movement Disorders
CLINICAL PRACTICE
RESEARCH ARTICLE

Dorsolateral Nigral Hyperintensity on 1.5 T Versus 3 T Susceptibility-Weighted Magnetic Resonance Imaging in Neurodegenerative Parkinsonism

Anna Grossauer, MD,[1] Christoph Müller, MD,[1] Anna Hussl, MD,[1] Florian Krismer, MD, PhD,[1] Michael Schocke, MD,[2,3] Elke Gizewski, MD,[2,3] Philipp Mahlknecht, MD, PhD,[1] Christoph Scherfler, MD,[1,3] Gregor K. Wenning, MD, PhD,[1] Werner Poewe, MD,[1,3] Klaus Seppi, MD,[1,3,*] and Beatrice Heim, MD, PhD[1,*]

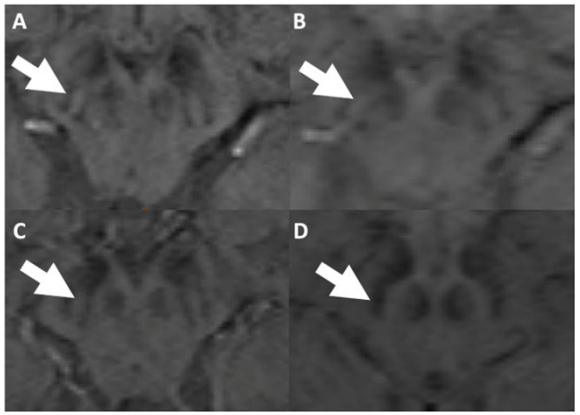


TABLE 2 *Diagnostic accuracy of absent DNH for the differentiation of patients with PD, MSA or PSP from HC using 3.0 T MRI*

At least unilateral absence of DNH				
PD	**MSA**	**PSP**	**All PS**	**HC**
30/33	18/18	20/20	68/71	1[b]/22
Diagnostic accuracy of at least unilateral absence of DNH				
	PD vs. HC	**MSA vs. HC**	**PSP vs. HC**	**All PS vs. HC**
p-value[a]	< 0.001	< 0.001	< 0.001	< 0.001
Sensiti				9.7)
Specifi				4.9)
PPV				9.7)
NPV				7.2)
Likelih				
Overa				8.4)

TABLE 3 *Diagnostic accuracy of absent DNH for the differentiation of patients with PD, MSA or PSP from HC using 1.5 T MRI*

At least unilateral absence of DNH				
PD	**MSA**	**PSP**	**All PS**	**HC**
31/33	18/18	20/20	69/71	**15/22**
Diagnostic accuracy of at least unilateral absence of DNH				
	PD vs. HC	**MSA vs. HC**	**PSP vs. HC**	**All PS vs. HC**
P-value[a]	0.022	0.011	0.009	< 0.001

✓ While visual assessment of **DNH using high field** routine SWI sequences serves as a simple diagnostic imaging marker for neurodegenerative parkinsonism, its use at 1.5T cannot be recommended.

IMAGING e DISTURBI DEL MOVIMENTO

Imaging del NIGROSOMA

✓ *Parkinson*


Movement Disorders
CLINICAL PRACTICE
REVIEW
Check for updates

Is the Swallow Tail Sign a Useful Imaging Biomarker in Clinical Neurology? A Systematic Review

Vasilis-Spyridon Tseriotis, MD, MSc,[1,2,*] Kyriaki Eleftheriadou, MD, MSc,[1] Theodoros Mavridis, MD, MSc, PhD,[3] Georgios Konstantis, MD, MSc,[2] Bjoern Falkenburger, MD, PhD,[4] and Marianthi Arnaoutoglou, MD, PhD[5]

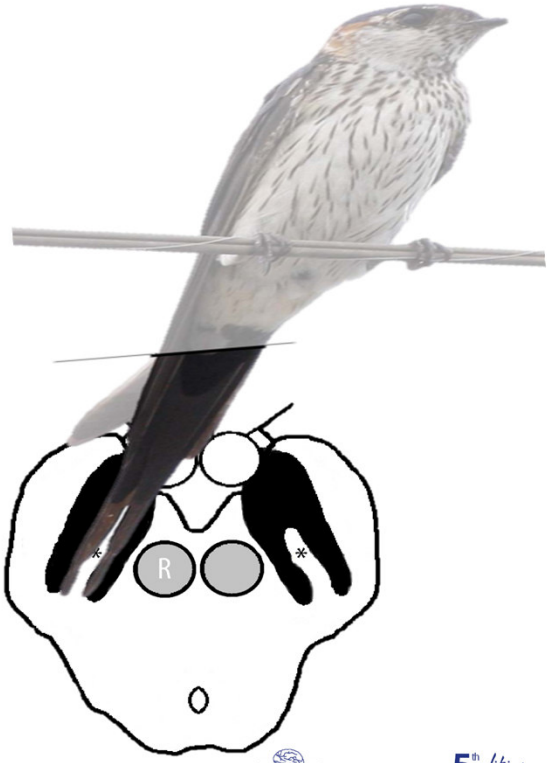
- ✓ Discrepancies to differences in **MRI parameters**, **experimental groups** (disease duration/staging), **neuroradiologists' experience** and **study design**. For instance, degenerative parkinsonism groups included APS in some studies, while others only included PD. Comparator groups consisted of HCs, DCs, non-degenerative movement disorder patients, or were mixed.
- ✓ We herein underscore the **lack of a standardized MRI protocol** as a source of heterogeneity, with MRI field strength and raters' experience comprising crucial factors for good STS performance.
- ✓ We thus highlight the **need for multicenter future studies**, with optimized MRI interpretation between different centers.

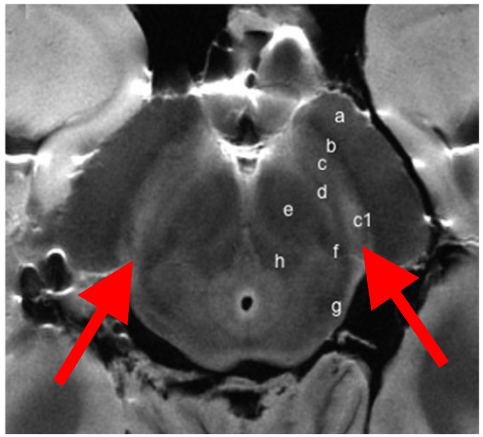
IMAGING e DISTURBI DEL MOVIMENTO

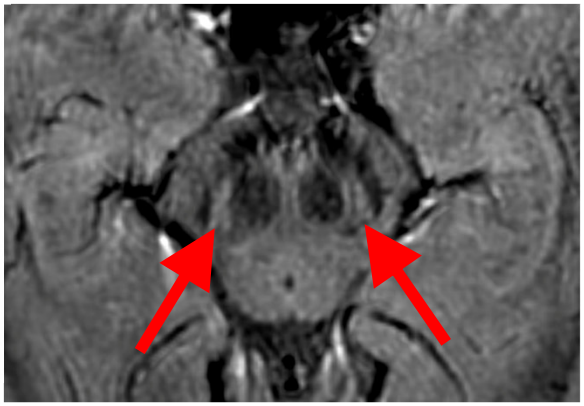
Imaging del NIGROSOMA

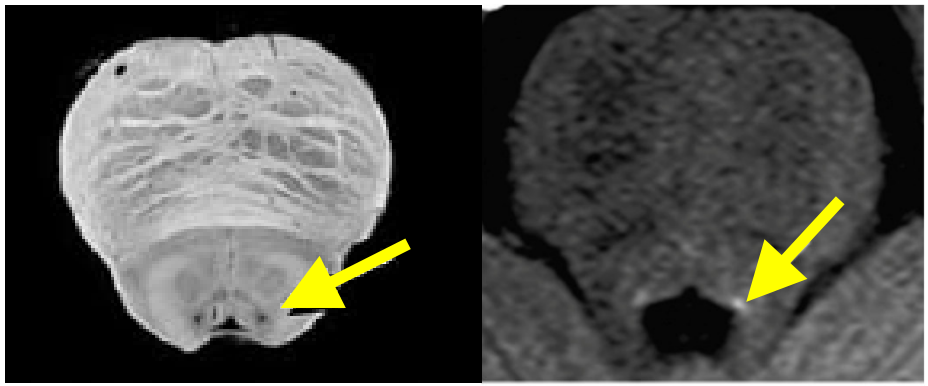
✓ *Parkinson*

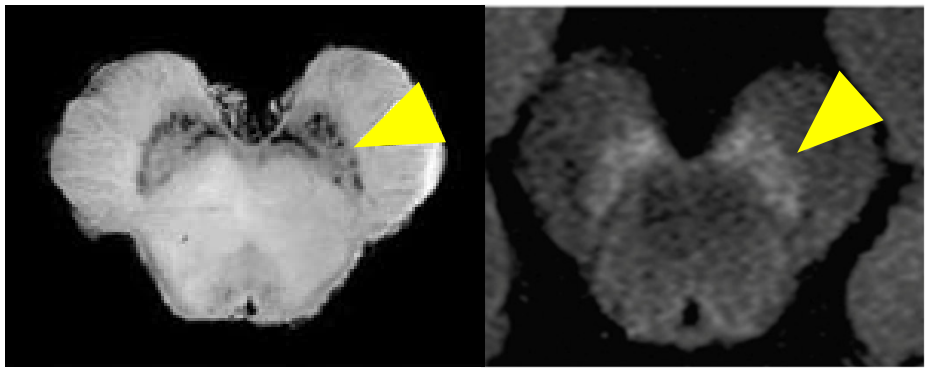
Imaging della NEUROMELANINA











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Pavese N, et Al.: *Nigrosome Imaging and Neuromelanin Sensitive MRI in Diagnostic Evaluation of Parkinsonism.* Mov Disorders 2018

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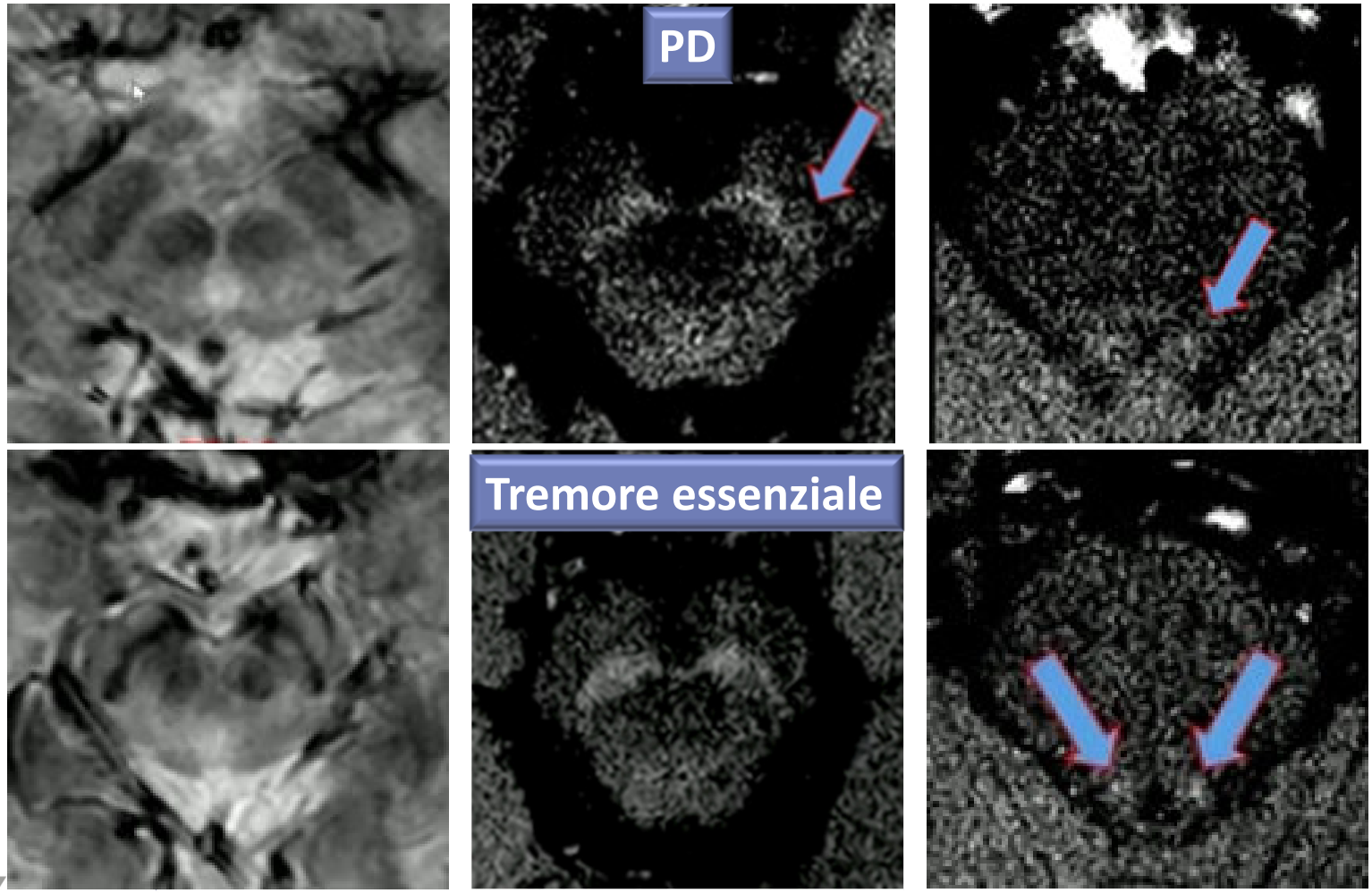
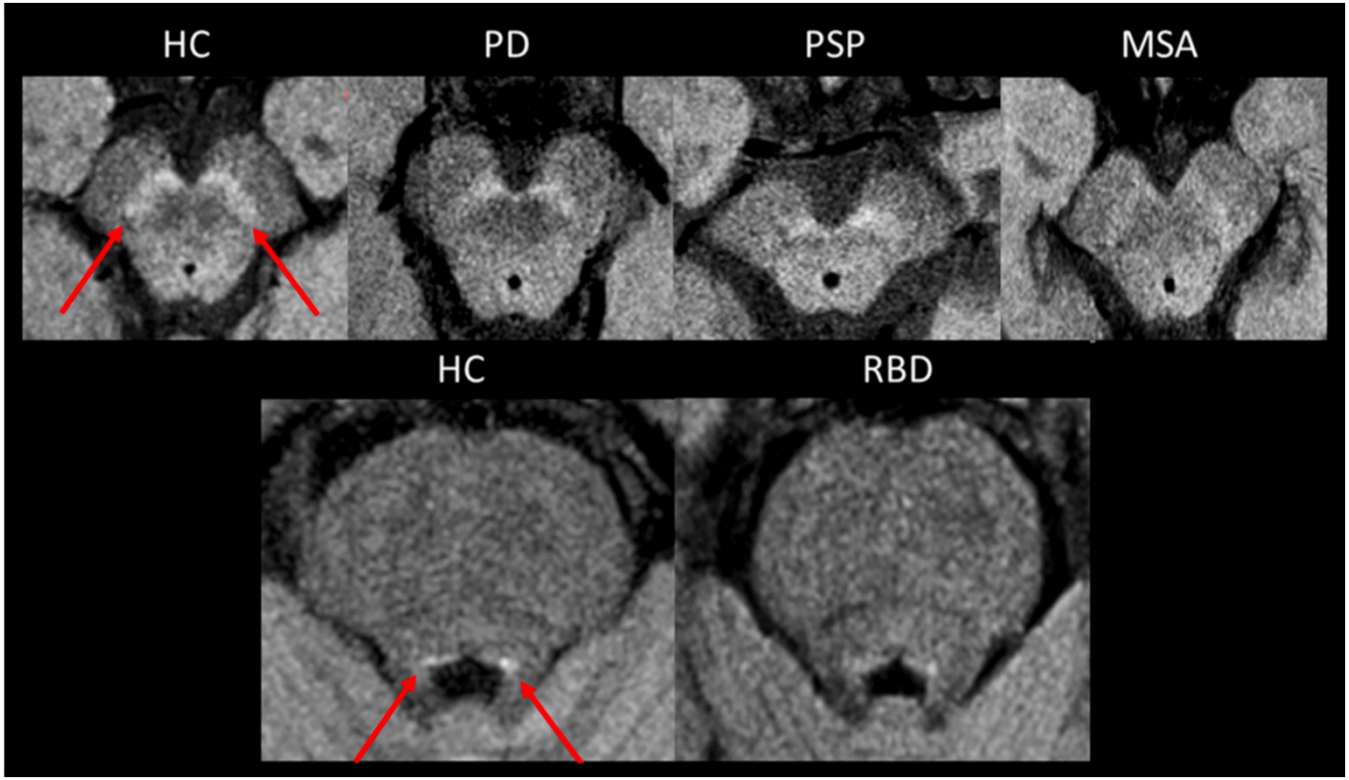


IMAGING e DISTURBI DEL MOVIMENTO

✓ Parkinson

- ✓ Patients with degenerative Parkinsonian syndromes show a reduction in the size and signal intensity of the SNpc.
- ✓ The sensitivity and specificity of this technique are above 80%.
- ✓ A neuromelanin signal decrease has also been observed in patients with idiopathic RBD



Chougar L., et Al.: *The Role of Magnetic Resonance Imaging for the Diagnosis of Atypical Parkinsonism.* Front Neurology 2020

IMAGING e DISTURBI DEL MOVIMENTO

✓ *Parkinsonismi atipici*

✓ APSs, are a heterogeneous group of movement disorders presenting with early dementia, ataxia, dysautonomia, frequent falls, and ocular dysmotility in addition to parkinsonism.

✓ Patients with these syndromes, which include:

- ✓ Progressive supranuclear palsy (PSP);
- ✓ Multisystem atrophy (MSA);
- ✓ Corticobasal degeneration (CBD);
- ✓ Dementia with Lewy bodies (DLB)

Often unresponsive to traditional PD treatments and may even experience harm from such treatments.

Keir G., et Al.: *Atypical Parkinsonian Syndromes: Structural, Functional, and Molecular Imaging Features..* AJNR 2024

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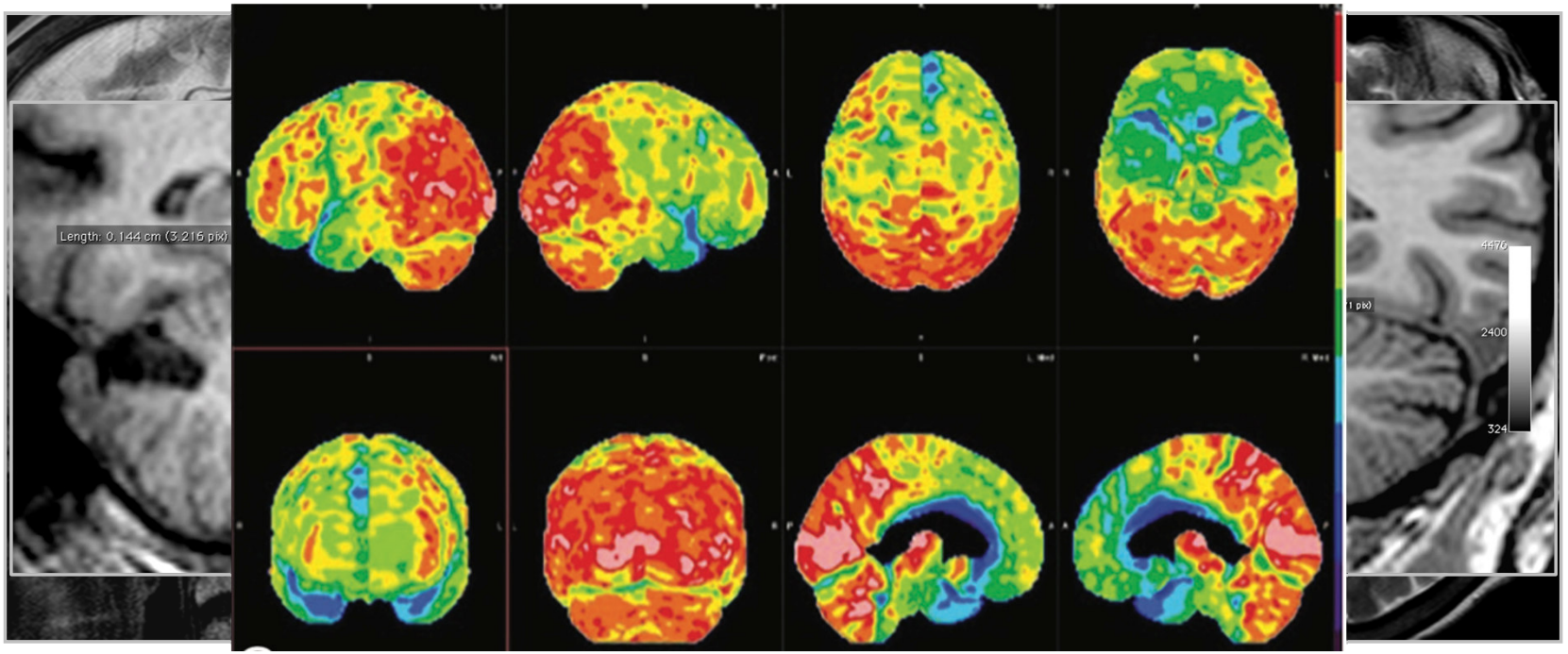
✓ *Parkinsonismi atipici*



✓ *Atrofia mesencefalica, prevalente del tegmento.*

✓ *Atrofia diencefalica.*

✓ *Atrofia peduncoli cerebellari superiori*

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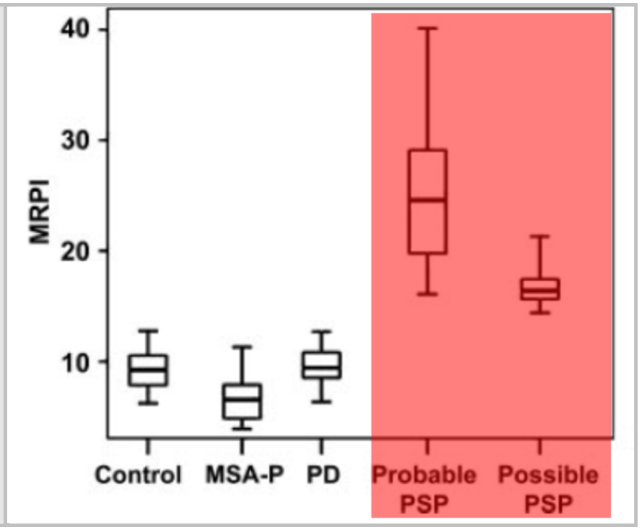
Pavese N, et Al.: *Nigrosome Imaging and Neuromelanin Sensitive MRI in Diagnostic Evaluation of Parkinsonism.* Mov Disorders 2018

IMAGING e DISTURBI DEL MOVIMENTO

✓ *Parkinsonismi atipici - PSP*

MR Parkinsonism Index for Differentiation of Patients with PSP from Patients with PD and MSA-P and Control Participants

Cutoff and Statistical Values	MR Parkinsonism Index Value	MCP/SCP Value	P/M Value
PSP patients vs PD patients			
Cutoff value	≥13.55	≥2.69	≥4.88
Sensitivity (%)	100	78.8	90.9
Specificity (%)	100	88.9	93.5
PPV (%)	100	68.4	81.1
PSP patients vs MSA-P patients			
Cutoff value	≥12.85	≥2.43	≥4.62
Sensitivity (%)	100	93.9	97.0
Specificity (%)	100	89.5	94.7
PPV (%)	100	93.9	97.0
PSP patients vs control participants			
Cutoff value	≥13.58	≥2.69	≥4.65
Sensitivity (%)	100	78.8	97.0
Specificity (%)	100	88.0	94.0
PPV (%)	100	81.2	91.4



(P/M) x (MCP/SCP)

The **MR parkinsonism index** can help distinguish patients with PSP from those with PD and MSA-P on an individual basis.

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Quattrone A, et Al.: *MR Imaging Index for differentiation of PSP from PD and the Parkinson Variant of MSA.* Radiology 2008

IMAGING e DISTURBI DEL MOVIMENTO

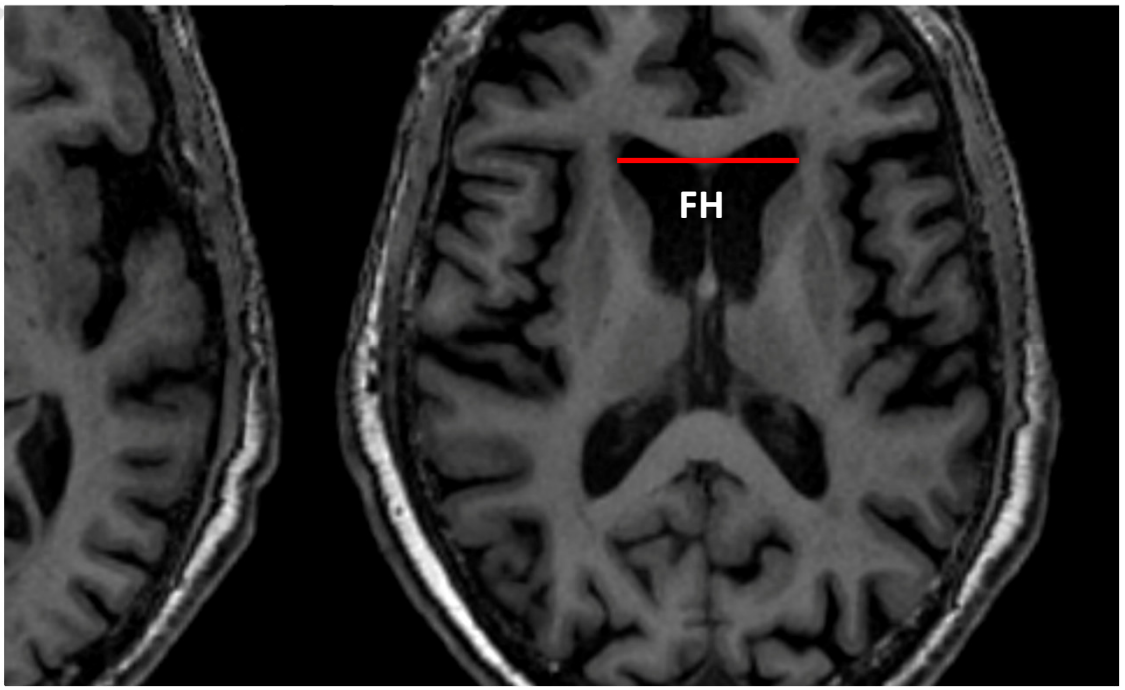
CLINICAL SUBTYPES OF PROGRESSIVE SUPRANUCLEAR PALSY PATHOLOGY

Main phenotype	Key Features
Classic: PSP-Richardson (PSP-R, Richardson syndrome or Steele-Richardson-Olswewski syndrome)	Tremorless, symmetric parkinsonism with axial-predominant rigidity, supranuclear vertical gaze palsy, with backward falls within one year from symptom onset
PSP-Parkinsonism (PSP-P)	Early features indistinguishable from PD. Postural impairment and oculomotor abnormalities occur after two years or later (often, five).
PSP-pure akinesia with gait freezing (PSP-PAGF)	Akinesia but without appendicular rigidity, associated with micrographia, speech disturbances and gait freezing of gait
Primary progressive freezing of gait	Isolated freezing of gait during the first 3 years and subsequent occurrence of postural instability and mild akinesia
PSP-corticobasal syndrome (PSP-CBS)*	Asymmetric parkinsonism with an asymmetric dystonic and apraxic limb
PSP-frontotemporal dementia (PSP-FTLD)*	Frontal-predominant dementia predating or developing concurrently with an otherwise classic motor phenotype

IMAGING e DISTURBI DEL MOVIMENTO

rkinsonismi atipici - PSP

Cutoff and statistical values	MRPI	MRPI 2.0
PSP-P patients vs. PD patients		
Cutoff value	≥ 12.38[a]	≥ 2.18[a]
Sensitivity (%)	73.5	100
Specificity (%)	98.1	94.3
PPV (%)	96.2	91.9
NPV (%)	85.2	100
Accuracy (%)	88.5	96.6
PSP-P patients vs. control subjects		
Cutoff value	≥ 11.34[a]	≥ 2.18[a]
Sensitivity (%)	85.3	100
Specificity (%)	98.1	98.1
PPV (%)	96.7	97.1
NPV (%)	91.2	100
Accuracy (%)	93.1	98.9
PSP-RS patients vs. PD patients		
Cutoff value	≥ 13.88[a]	≥ 2.50[a]
Sensitivity (%)	100	100
Specificity (%)	100	100
PPV (%)	100	100
NPV (%)	100	100
Accuracy (%)	100	100
PSP-RS patients vs. control subjects		
Cutoff value	≥ 13.88[a]	≥ 2.50[a]
Sensitivity (%)	100	100
Specificity (%)	100	100
PPV (%)	100	100
NPV (%)	100	100
Accuracy (%)	100	100



RPI2.0 = MRPI x V3/FH

- ✓ PSP-parkinsonian vs Parkinson disease or control: ≥2.18
- ✓ PSP-Richardson's syndrome vs Parkinson disease or control: ≥2.50

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Quattrone A, et Al.: *A new MR imaging index for differentiation of PSP-parkinsonism from PD.* Parkinsonism&related disorders 2018

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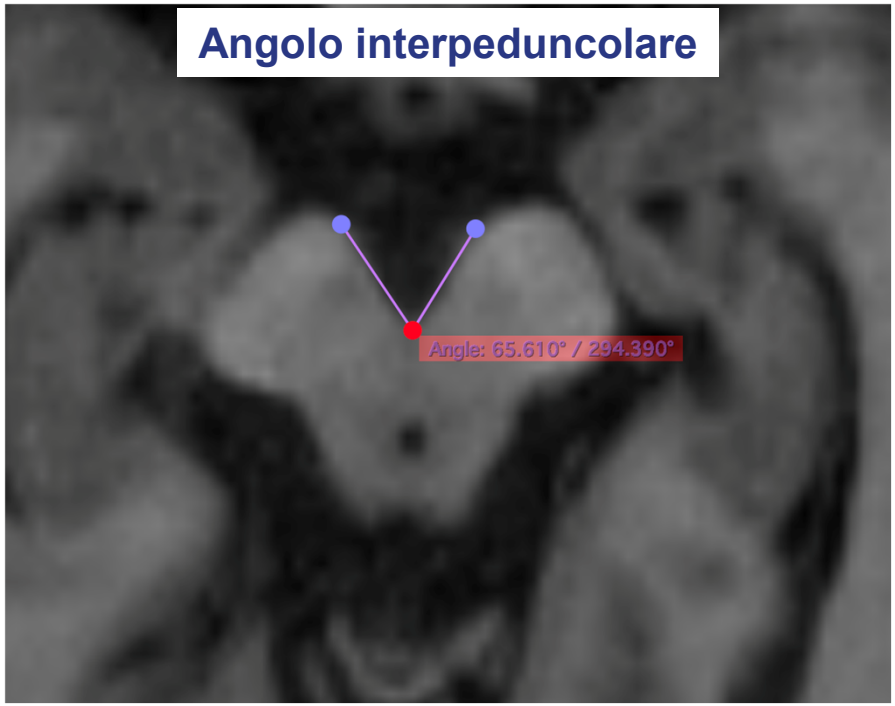
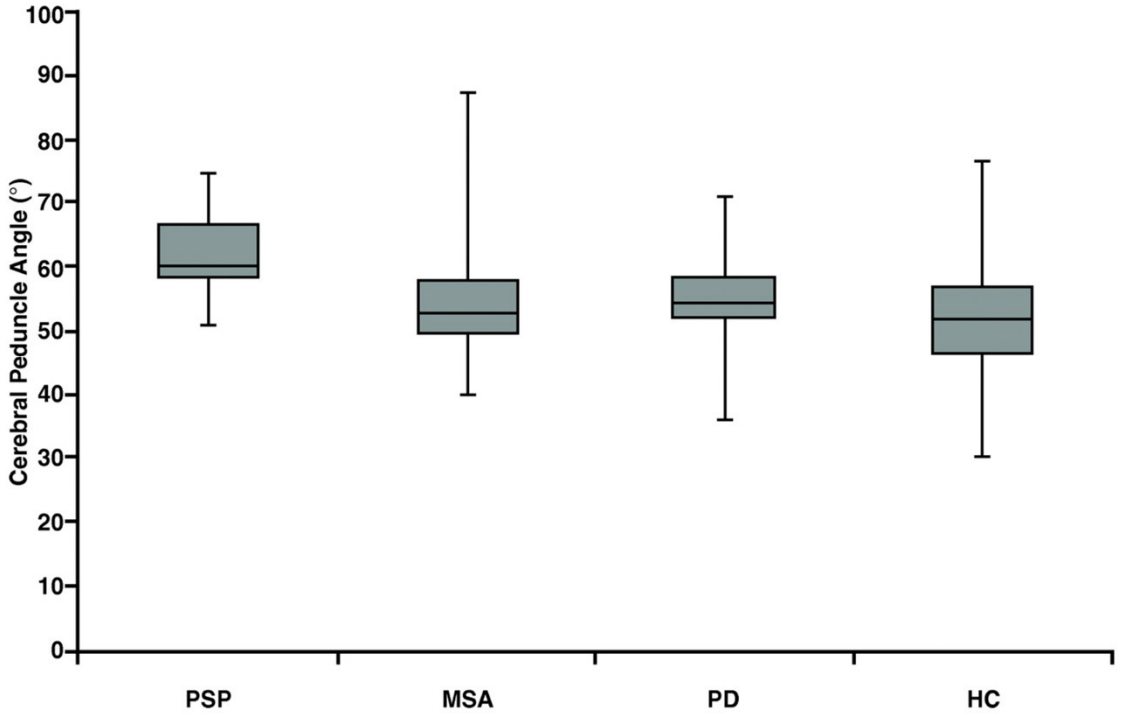
✓ *Parkinsonismi atipici - PSP*





- ✓ In the setting of **PSP**, a threshold of 57° yielded a sensitivity of 100% and specificity of 90% in distinguishing these patients from those with **PD and MSA-P**
- ✓ In **iNPH**, the angle is typically larger, while in PSP, it is smaller.

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Fatterpekar GM, et Al.: *Cerebral Peduncle Angle: An Objective Criterion for Assessing Progressive Supranuclear Palsy Richardson Syndrome.* AJR 2015

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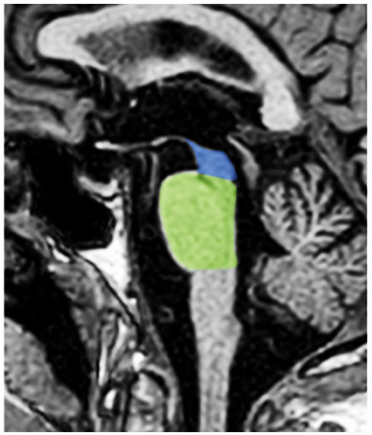
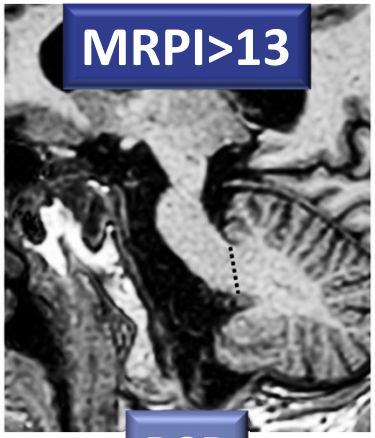
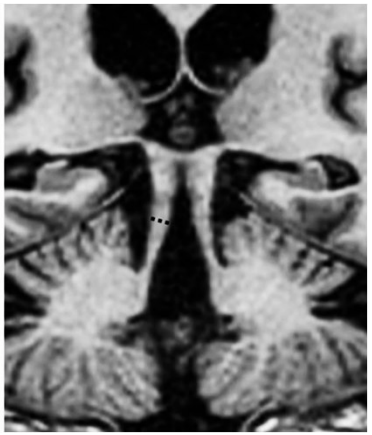
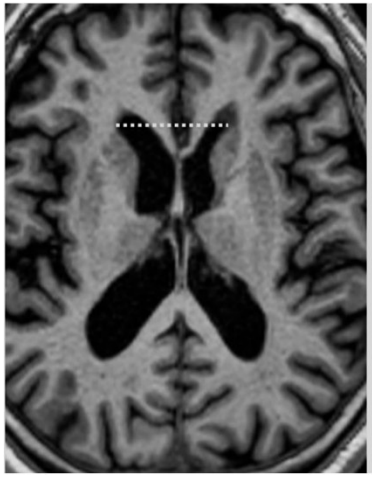
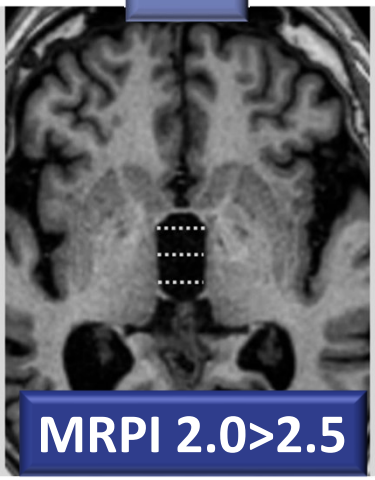


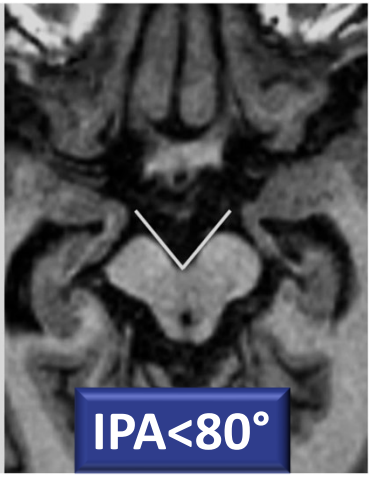


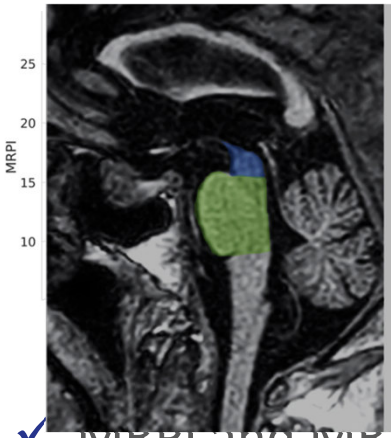


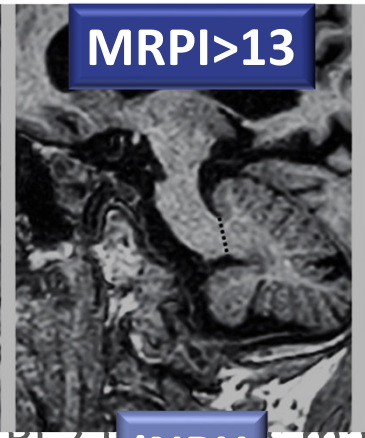
PSP

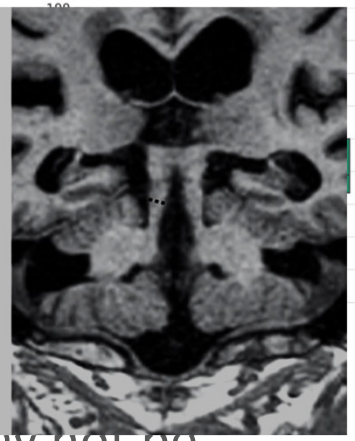






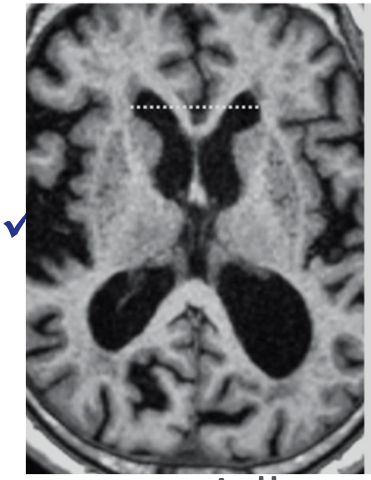


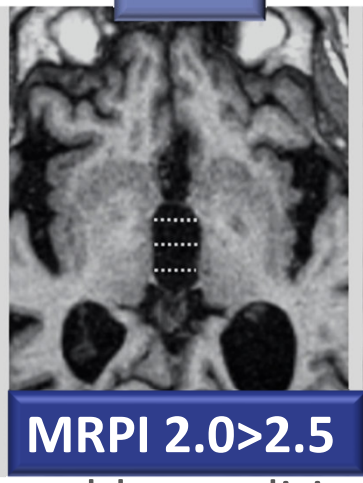


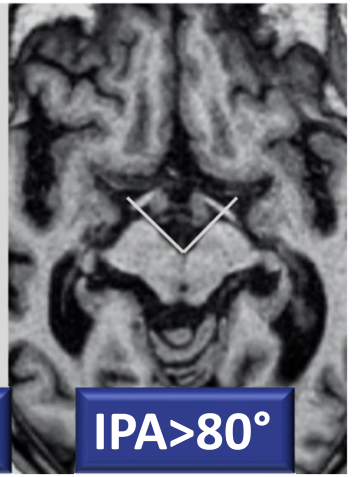


✓ MRPI and MRPI 2.0 s may not be

iNPH







potentially treatable condition.

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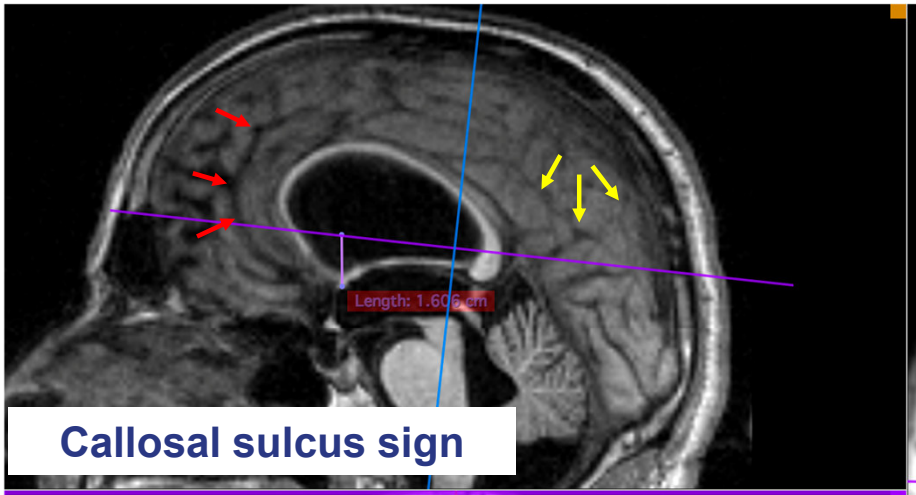
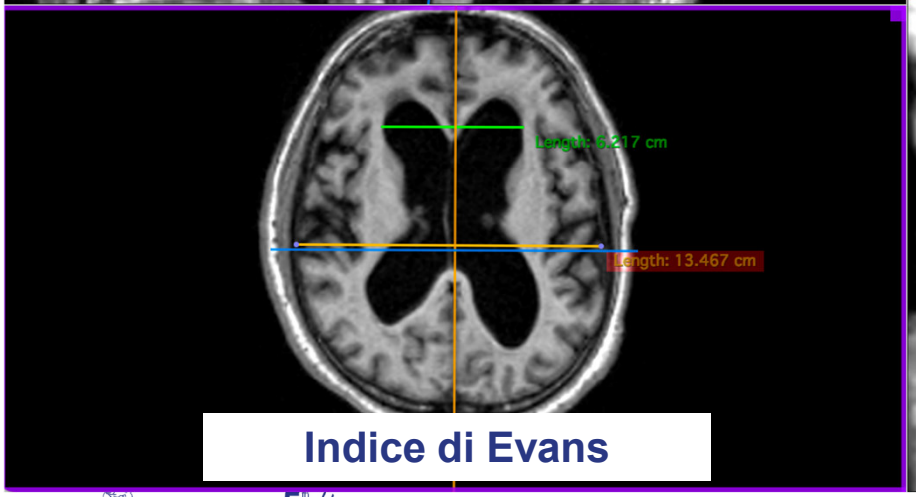
Ugga L, et Al.: *MR parkinsonism indices and interpeduncular angle in iNPH and progressive supranuclear palsy* Neuroradiology 2020

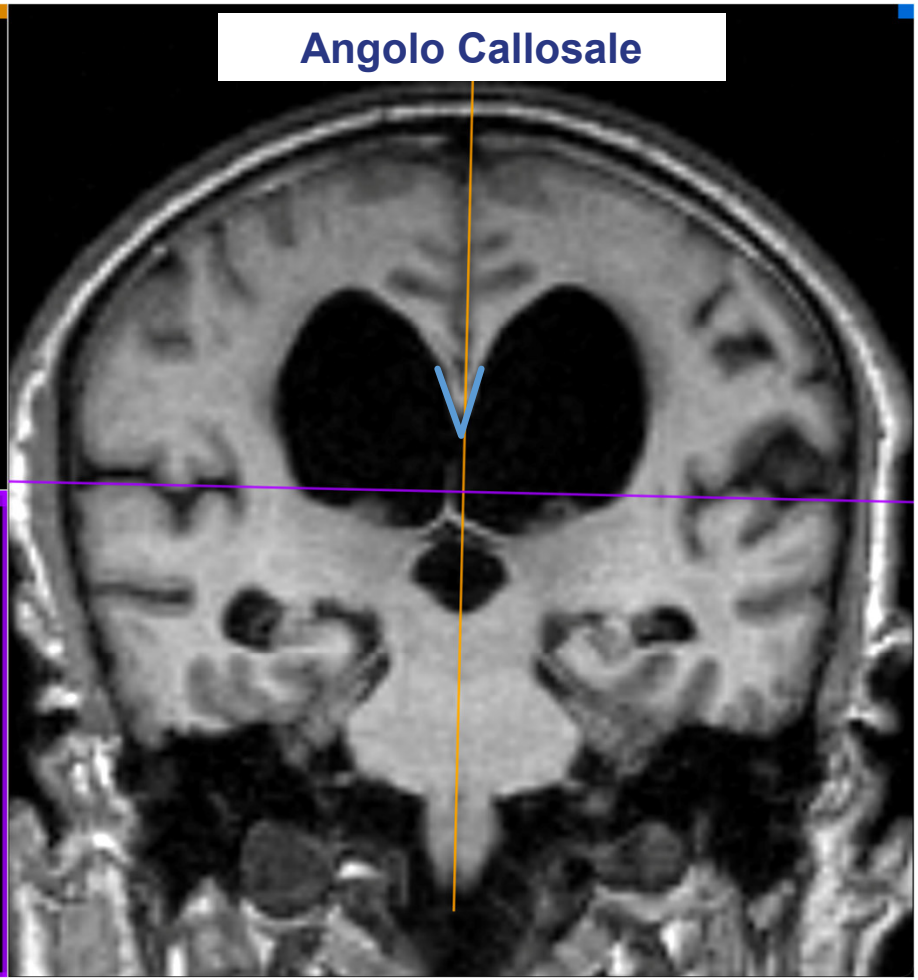
IMAGING e DISTURBI DEL MOVIMENTO



Callosal sulcus sign

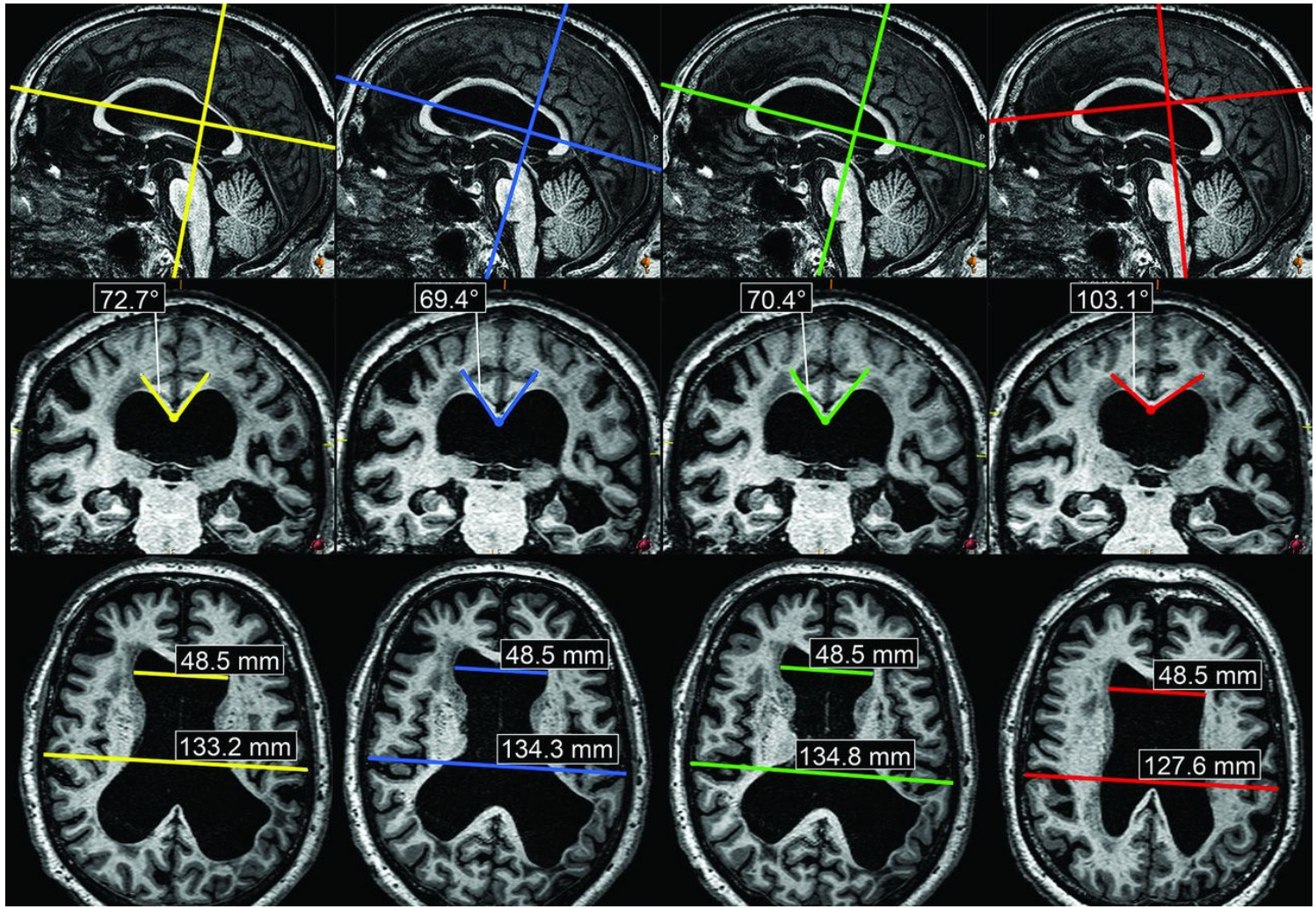


Indice di Evans



Angolo Callosale

IMAGING e DISTURBI DEL MOVIMENTO



NEUROYoung 5th edition
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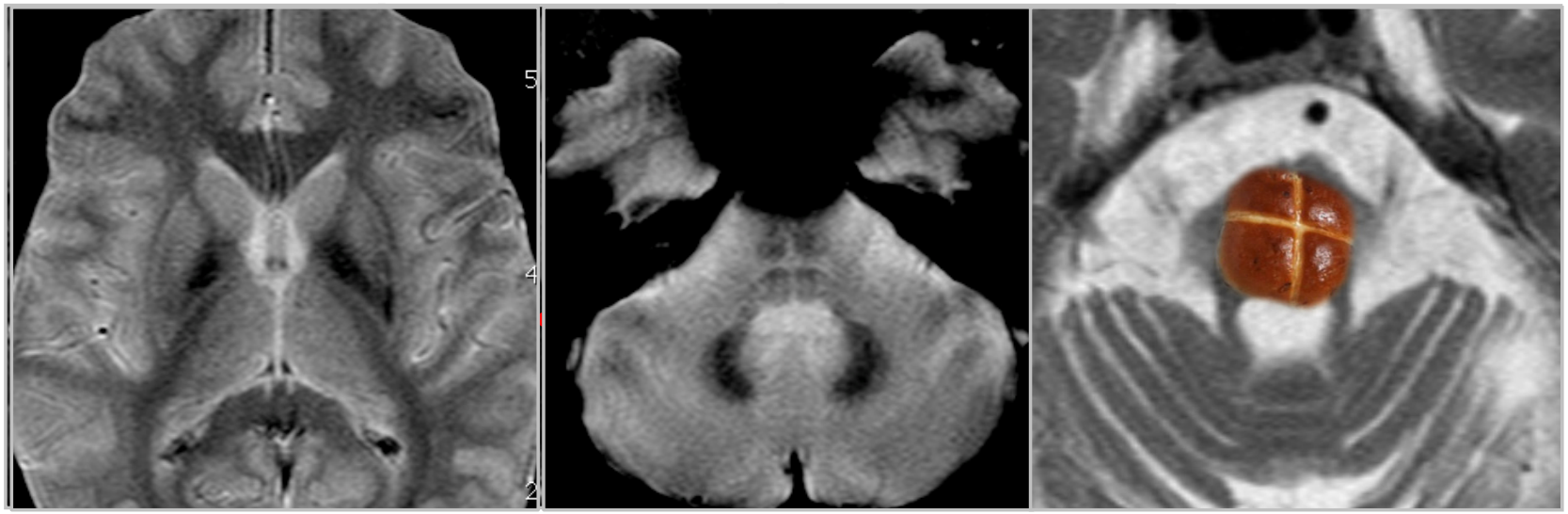
Ryska R., et Al.: *Variability of NPH Imaging Biomarkers with Respect to Section Plane Angulation: How Wrong a Radiologist Can Be?.* AJNR 2021

IMAGING e DISTURBI DEL MOVIMENTO

✓ *Parkinsonismi atipici*

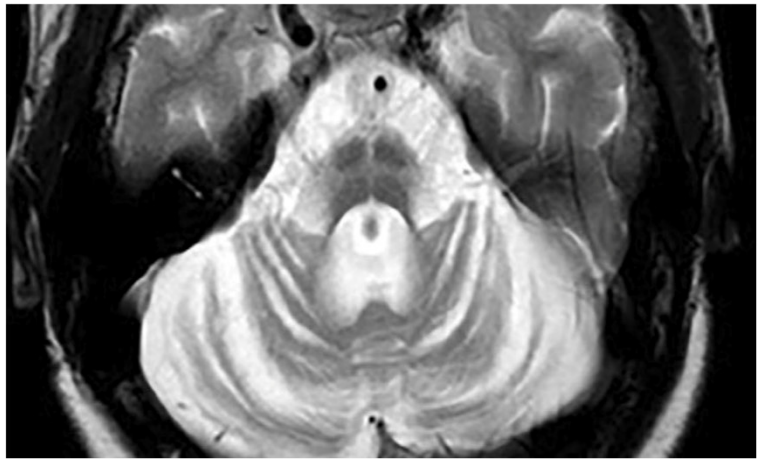


- ✓ Degenerazione nuclei pontini, fibre trasverse, corteccia cerebellare laterale, verme superiore.
- ✓ Degenerazione delle olive bulbari attraverso il peduncolo cerebellare inferiore.

IMAGING e DISTURBI DEL MOVIMENTO

Causes of HCBS Described in the Scoping Review

Reported Aetiologies	Number of Retrieved Reports	Reported SCAS with HCBS	Number of Retrieved Reports
Parkinsonian Syndromes		SCA Type	
Multiple System Atrophy – C	40[20,40,42–44,46,48–51,53–55,61–82]	SCA 1	6[5,7,83–86]
Multiple System Atrophy–P Multiple System Atrophy- A	2[50,51]	SCA 2	11[6–8,18,44,52,84–87]
Probable Dementia with Lewy Body	1[15]	SCA 3	9[6,12,44,3,5,84,86,88,89]
Corticobasal Degeneration (olivopontocerebellar type)	1[14]	SCA 6, 7, 8	17[4,6,44,47,84,86,90,91]
Parkinsonism Related Vasculitis	1[16]	SCA 10	1[84]
Infection		SCA 17	1[10]
Rabies Encepaltiis	1[2]	SCA 23	1[92]
HIV related Progressive Multifocal Leukoencephalopathy	4[22,23,25,58]	SCA 31	1[47]
Natalizumab associated Progressive Multifocal Leukoencephalopathy	1[29]	SCA 34	4[13,86,93,94]
HIV related JCV granule cell neuronopathy	1[60]	SCA 42	1[95]
HIV	2[27,28]		
Brainstem encephalitis	2[19,20]		
Neoplastic			
Paraneoplastic Rhombencephalitis	2[29,30]		
Leptomeningeal malignant involvement in Breast Cancer and Melanoma	2[31,32]		
Lung Cancer Undefined Cause	1[20]		
Kelch-like protein 11-associated paraneoplastic neurological syndrome associated seminoma	2[29,33]		
Vascular			
Bilateral middle cerebral peduncle infarction	1[17]		
cerebellar hemorrhage (n=1). 16-18 (n=1). 16-18(n=1). 16-18	1[18]		
Neurodegenerative			
Variant Creutzfeldt Jakob Disease	1[26]		
Fragile X tremor ataxia syndrome	1[39]		
Cerebrotendinous xanthomatosis	1[37]		
Non infective Inflammatory			
Neurosarcoidosis	1[36]		
Autoimmune cerebellar ataxia—Homer-3 antibodies.	1[34]		
ADEM, NMO. MS,	1[20]		
Toxin			
Toxic Encephalopathy with Phenytoin Sodium	1[20]		
Other			



- ✓ **HCB sign** has been reported in various **other disorders**, including **SCA**, malignancies, infections, autoimmune disorders, and some vascular and ischemic changes;
- ✓ The widened differential of the **HCB sign** suggests this is a radiological indistinct entity with an **underlying pathological process of wallerian degeneration** of the pontocerebellar fibers rather than a disease specific pathological process.

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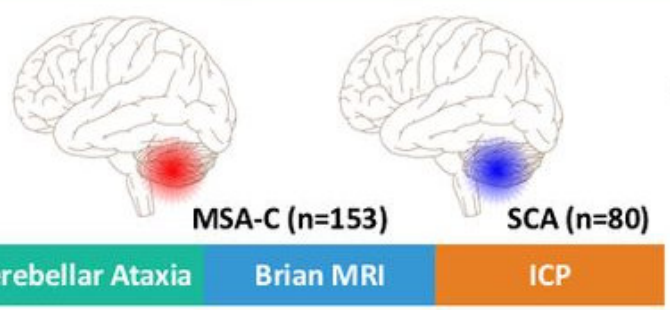
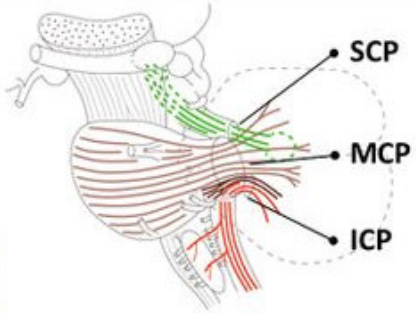
Naidoo AK, et Al.: *The "Hot Cross Bun Sign" in Spinocerebellar Ataxia Types 2 and 7–Case Reports and Review of Literature.* Mov Disorders 2022

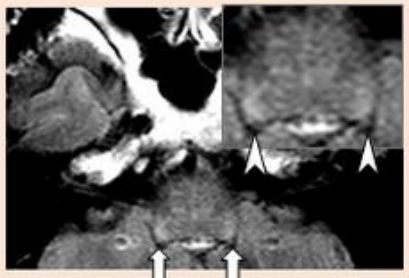
IMAGING e DISTURBI DEL MOVIMENTO

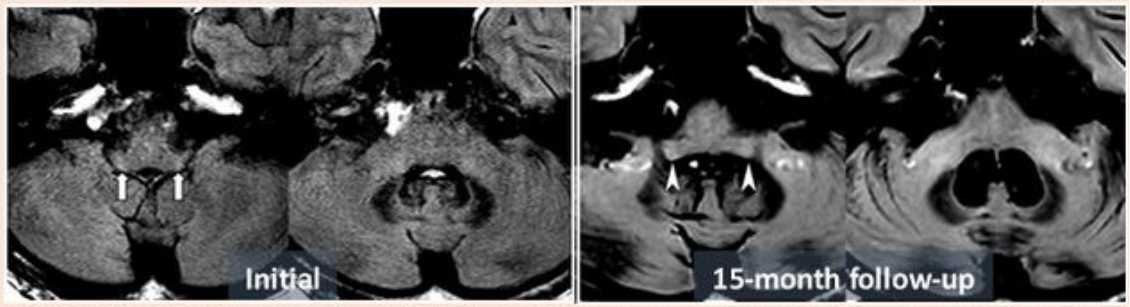
✓ *Parkinsonismi atipici - MSA*

Can ICP sign distinguish MSA-C from SCA in patients with cerebellar ataxia?

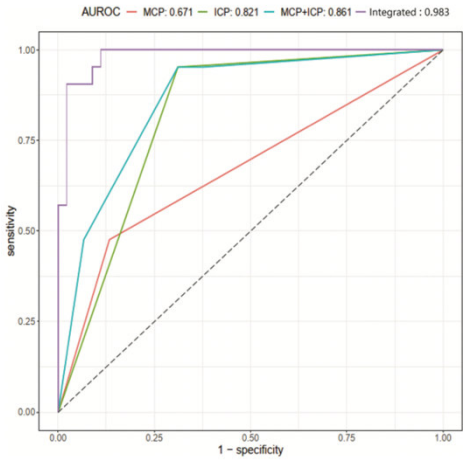








The ICP sign in a 53-year-old male with cerebellar ataxia on initial imaging (left). Follow-up imaging (right) reveals the MCP sign and cerebellar atrophy, confirming MSA-C.



✓ The **inferior cerebellar peduncle** is pathologically affected in MSA-C

✓ FLAIR hyperintensity of the ICP shows **high specificity** (95%) in differentiating MSA-C fron SCA.

✓Combining the **ICP sign with clincal and imaging features** further improves diagnostic accuracy to an AUC of 0.98

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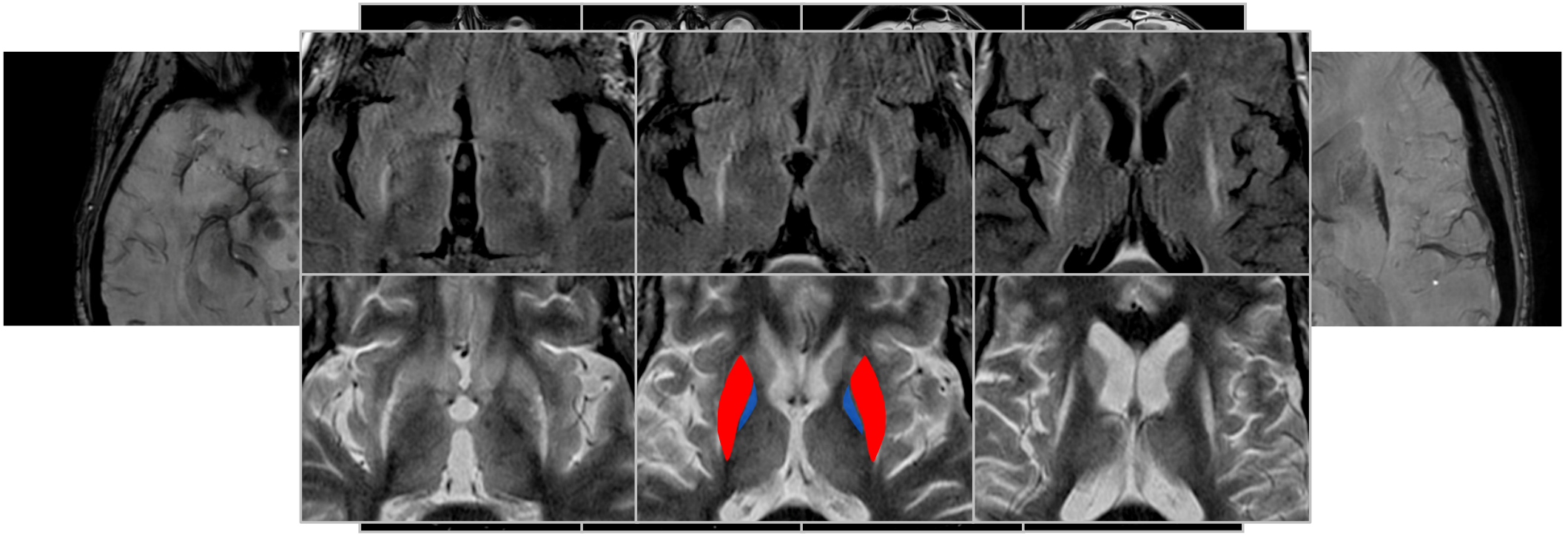
Chae YL, et Al.: *The Inferior Cerebellar Peduncle Sign: A Novel Imaging Marker for Differentiating MSA Cerebellar Type from SCA.* AJNR 2024

IMAGING e DISTURBI DEL MOVIMENTO

✓ *Parkinsonismi atipici*

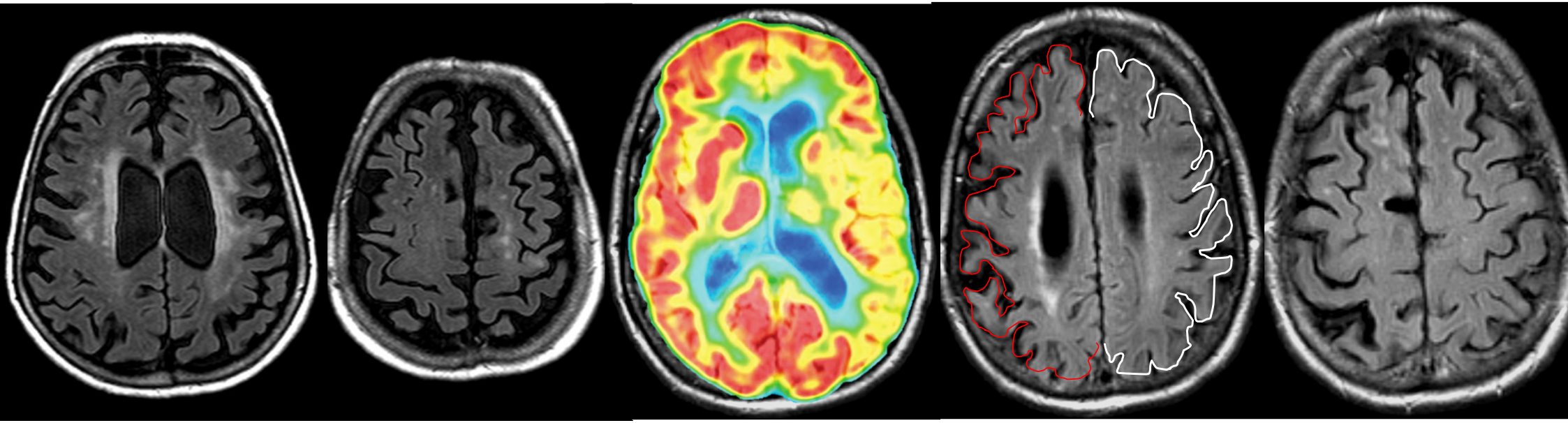


✓ Atrofia selettiva dello striato (putamen > caudato).

✓ Degenerazione della substantia nigra.

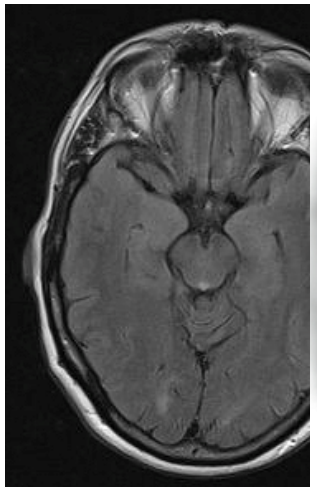
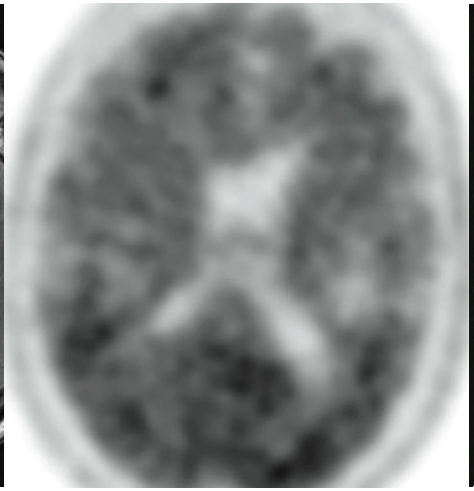
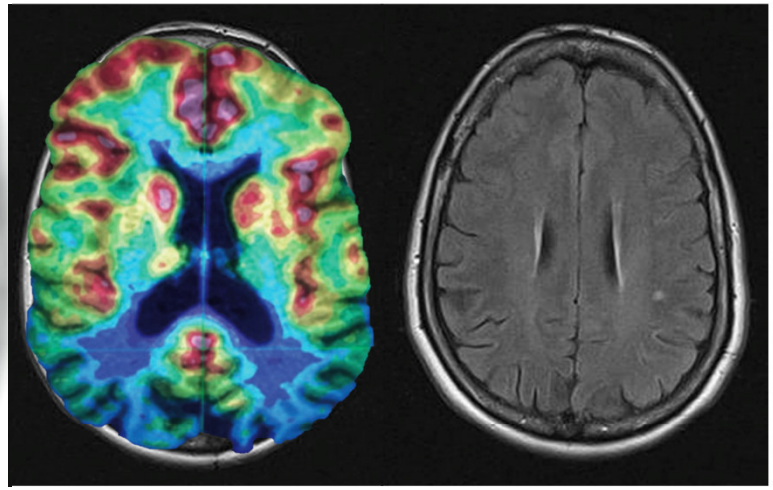
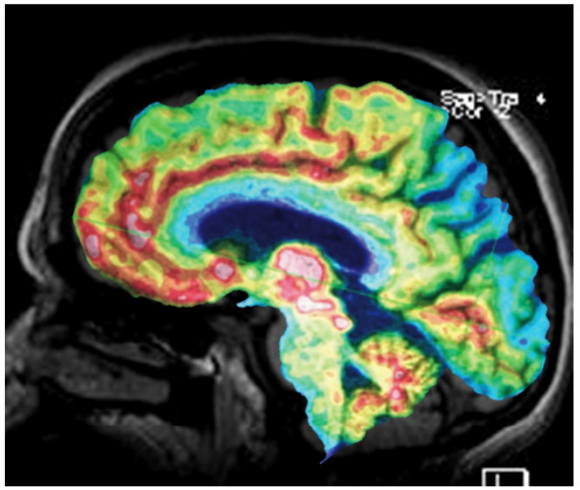
IMAGING e DISTURBI DEL MOVIMENTO

✓ *Parkinsonismi atipici*

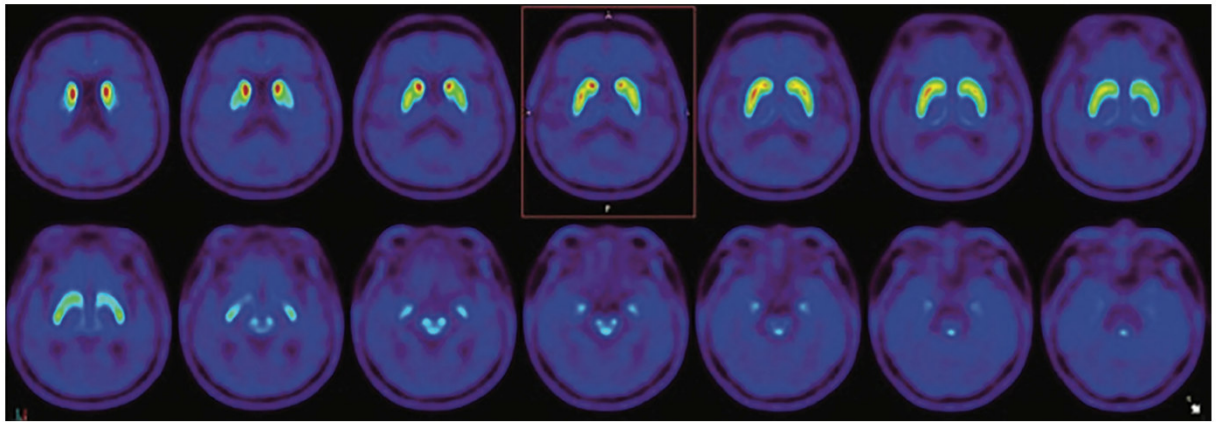


IMAGING e DISTURBI DEL MOVIMENTO

✓ Parkinsonismi atipici

- ✓ The **cingulate island sign** has been highlighted as a specific imaging biomarker in DLB, representing sparing of the posterior cingulate gyrus compared with the precuneus and cuneus on FDG-PET or SPECT.



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Keir G., et Al.: *Atypical Parkinsonian Syndromes: Structural, Functional, and Molecular Imaging Features..* AJNR 2024

IMAGING e DISTURBI DEL MOVIMENTO

- ✓ The role of imaging biomarkers has progressed from merely excluding secondary causes of parkinsonisms to aiding in the differential diagnosis of PD from APDs based on changes in brainstem structures and the BG.

Peralta C, et Al.: *Pragmatic approach on neuroimaging techniques for the differential diagnosis of Parkinsonism.* Mov Disorders 2020

- ✓ New consensus criteria for the diagnosis of Parkinsonian syndromes incorporating MRI biomarkers should be considered in the future.

Chougar L., et Al.: *The Role of Magnetic Resonance Imaging for the Diagnosis of Atypical Parkinsonism.* Front Neurology 2020

- ✓ We suggest that brain MRI be performed in all patients presenting with parkinsonism when there is clinical doubt about the diagnosis, preferably in a 3.0T scanner when available, with a protocol designed to provide the highest amount of information possible in a routine clinical setting.

Reimao S., et Al.: *A standardized MR Imaging protocol for Parkinsonism.* Mov Disorders 2020

SINTESI ANAMNESTICA

Uomo, 60 anni

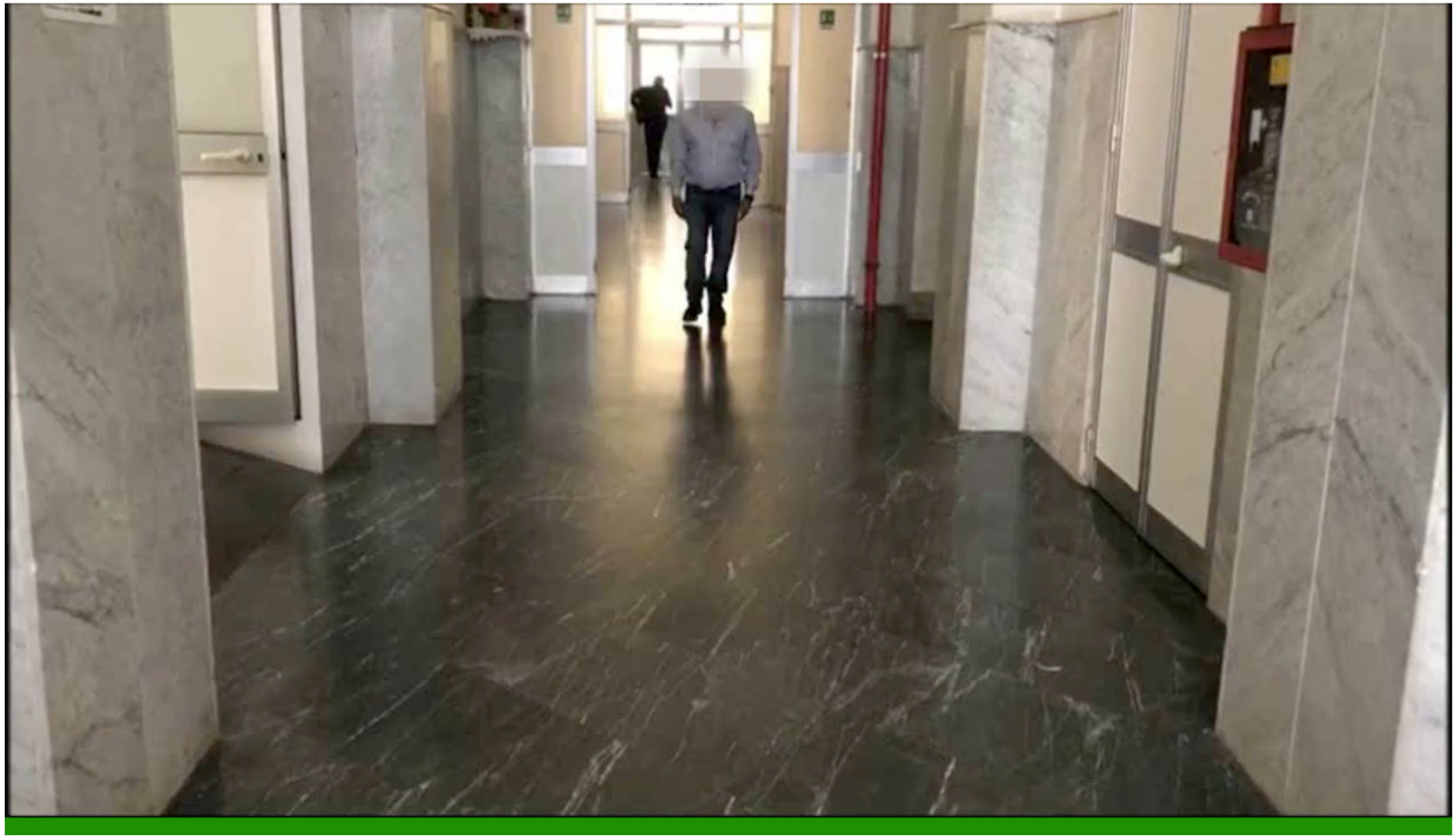
- Esordio insidioso circa un anno orsono di tremore all'AS dx progressivamente ingravescente

- **Anamnesi familiare**
- La madre avrebbe presentato tremore e disturbo cognitivo dall'età di 70 anni

- **Anamnesi fisiologica**
- Urgenza minzionale
- Insonnia lacunare
- Stipsi

- **Anamnesi patologica remota:**
- Ipertensione arteriosa in trattamento farmacologico
- Ipercolesterolemia
- Pregressa cardiopatia ischemica pregressa.

ESAME OBIETTIVO NEUROLOGICO

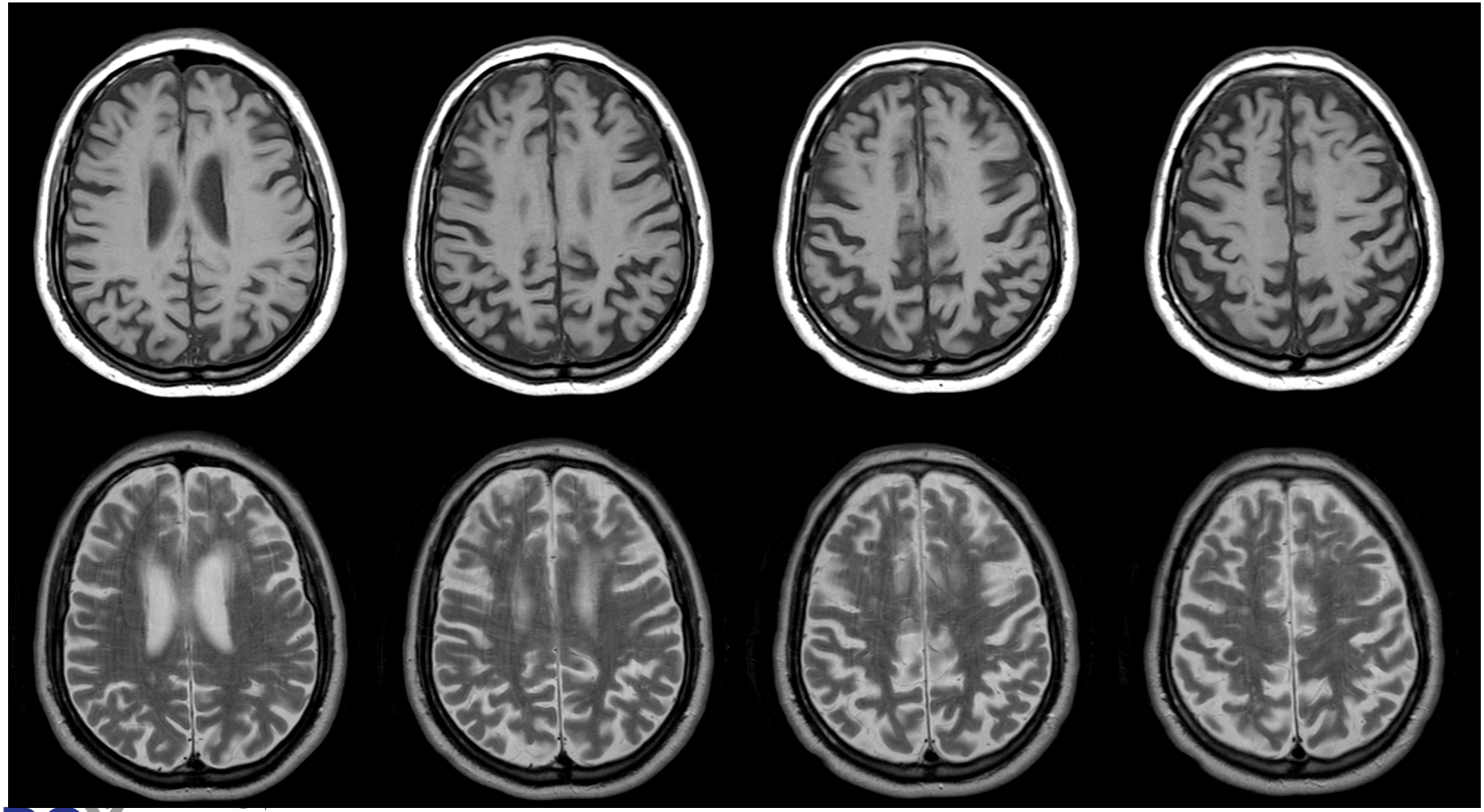


- Tremore a riposo ASdx
- Tremore posturale intenzionale AASS dx>sn

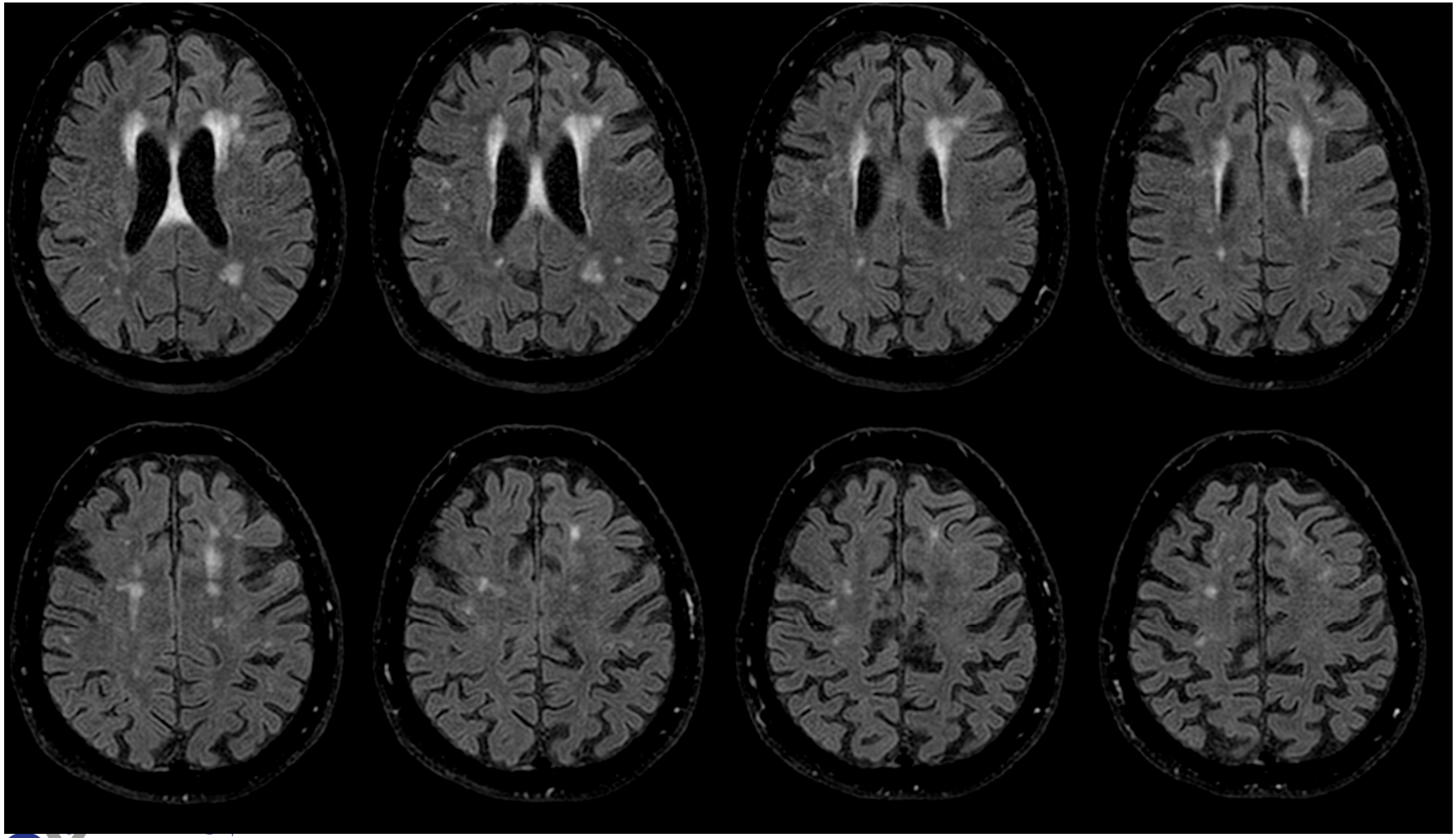
ESAME OBIETTIVO NEUROLOGICO

- Facies ipomimica
- Pull-test negativo
- Tono muscolare nella norma ai 4 arti
- Assenza di bradicinesia alle prove di agilità ai 4 arti

CASO CLINICO 2 - RM



CASO CLINICO 2 - RM



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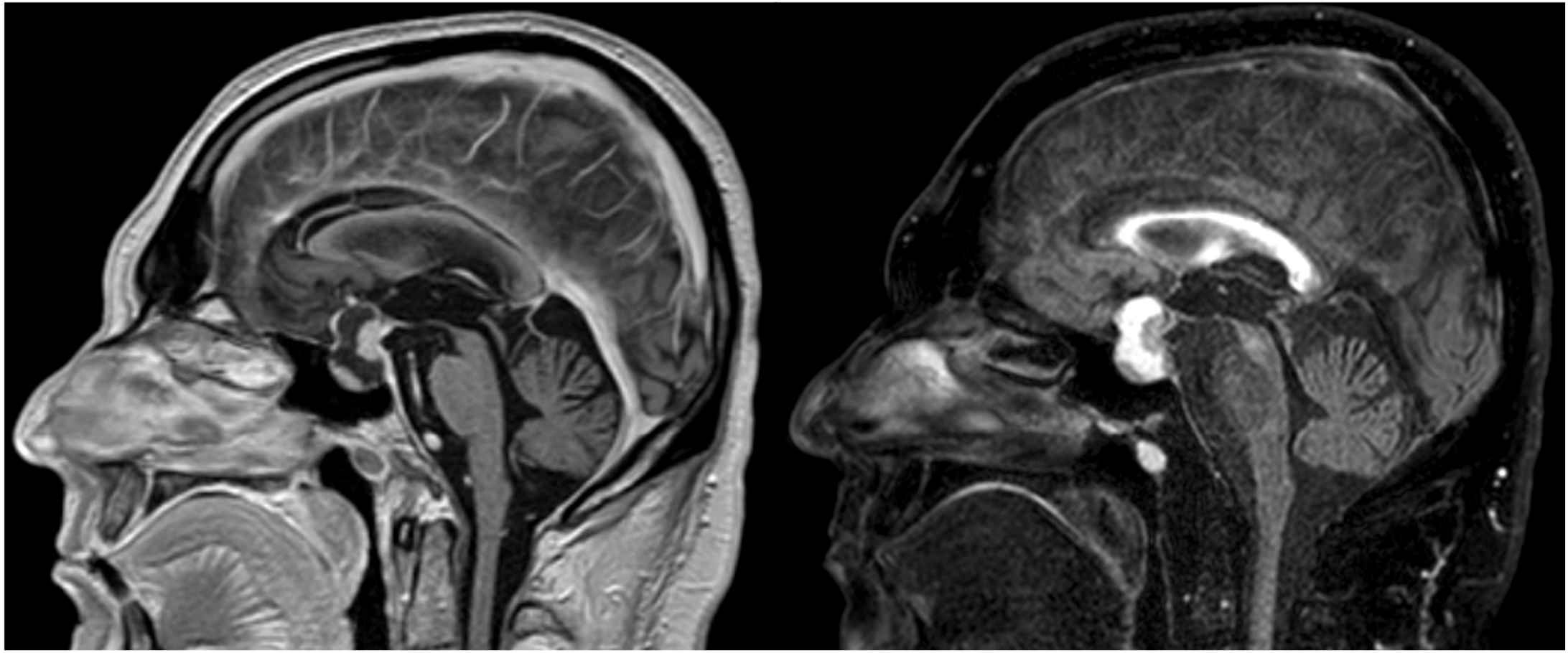

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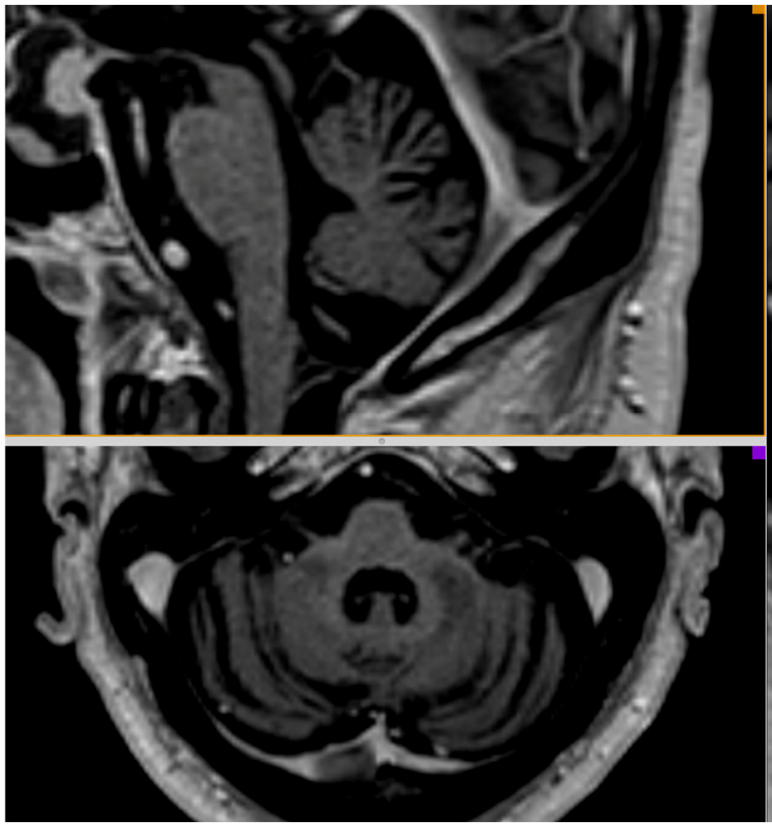

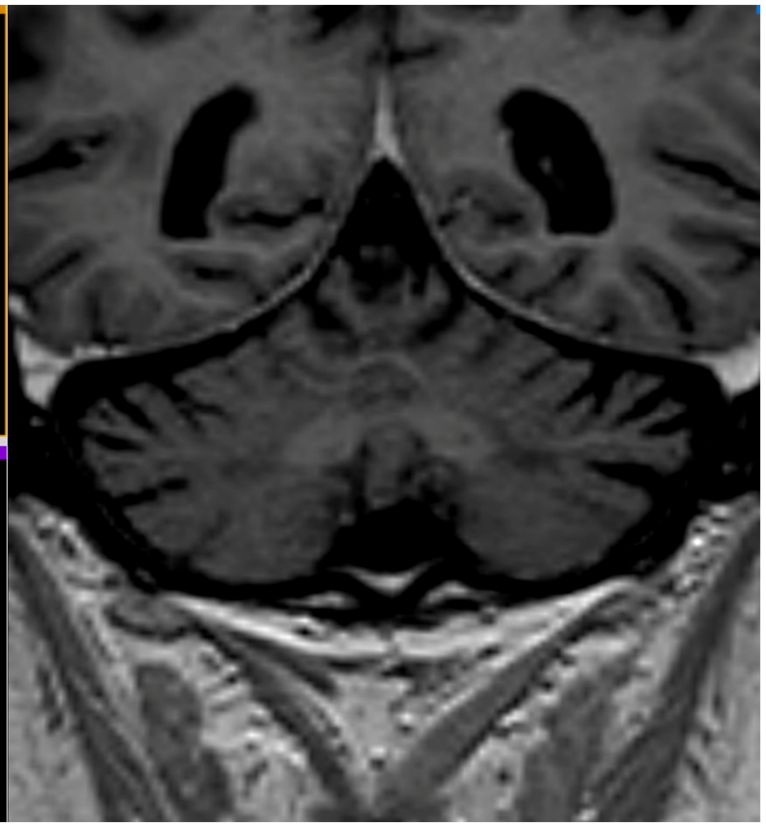

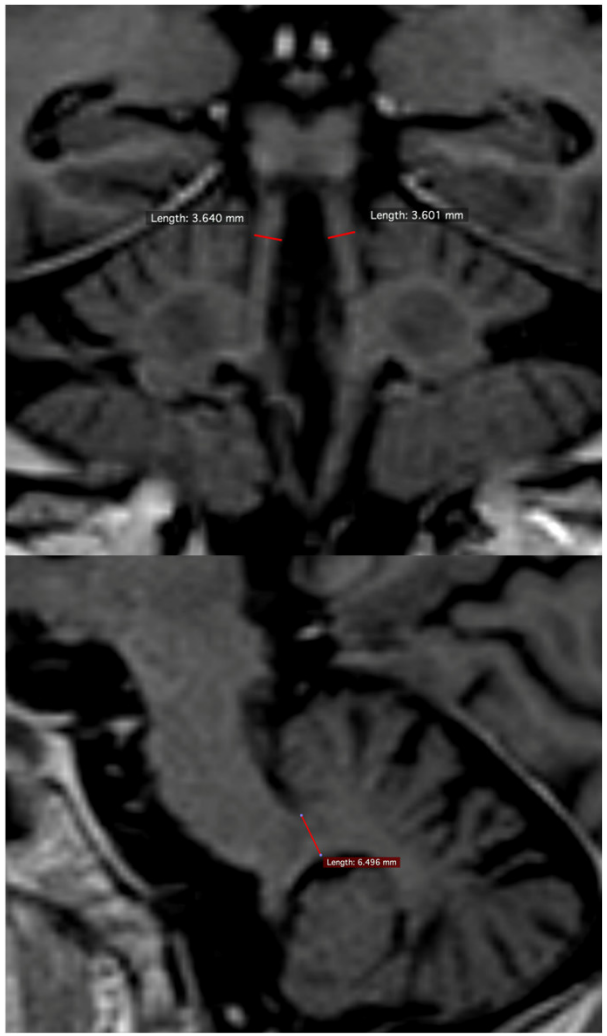

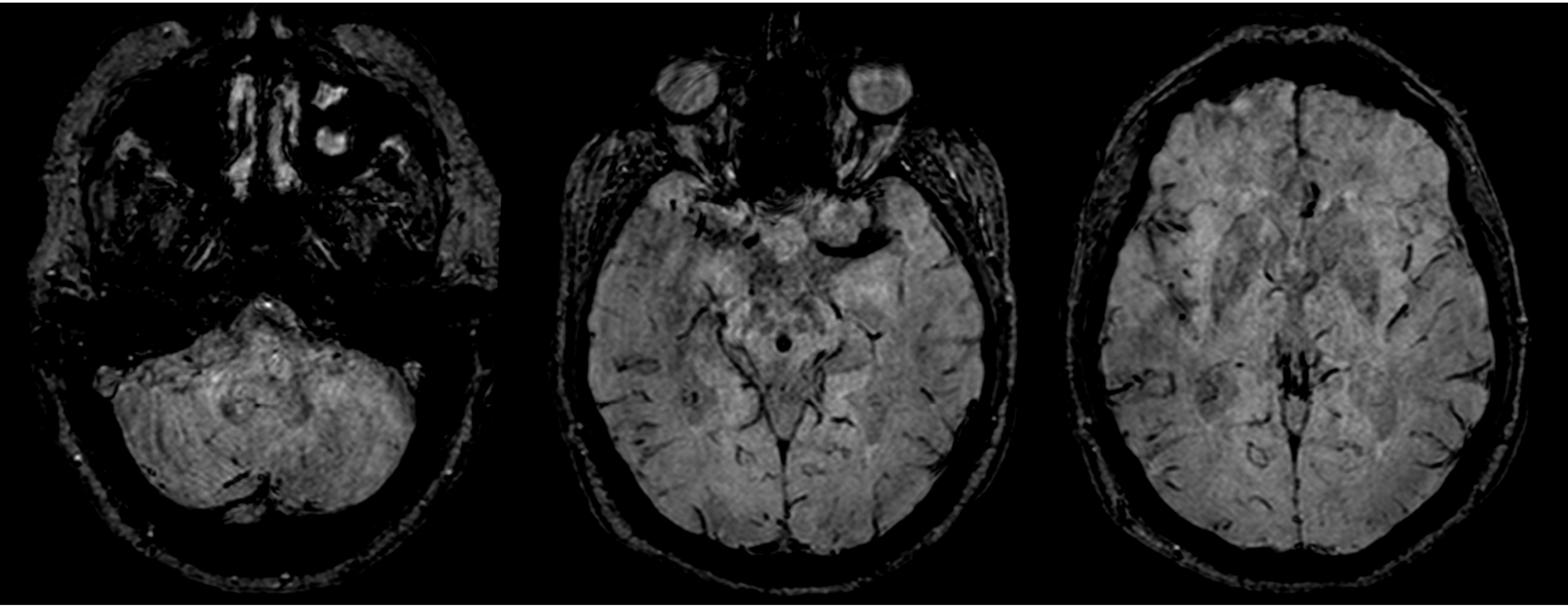

I reperti riconoscibili in fossa cranica posteriore orientano verso quale delle seguenti entità patologiche?

1) MSA-C
2) PSP
3) Alterazione transitoria tossico-metabolica
4) Vasculopatia con degenerazione walleriana e associati segni di atrofia sopra e sotto-tentoriali.
5) Altro

In considerazione dei reperti patologici sopra e sotto-tentoriali quale delle seguenti ipotesi diagnostiche seguireste?

1) Xantomatosi cerebrotendinea
2) FXTAS
3) SCA2-SCA3
4) AQP4-IgG+ NMO
5) Altro

Indagine genetica

- ✓ Analisi genetica per *FMR1*: premutazione (95 triplette CGG)

The revised FXTAS diagnostic criteria include two major radiological features :

- ✓ The ‘‘**MCP sign**”, (60% of affected males, 13% of affected females). The presence of the MCP sign is **correlated with more severe cognitive deficits and a longer history of symptoms**;
- ✓ **Hyperintensity of corpus callosum splenium** (CCS) has been recently reported and this sign has become a major radiological criterion in the diagnosis of FXTAS. CCS hyperintensity is encountered as frequently as the MCP sign, occurs more commonly in males and is a **marker of disease progression**.

Revised Fragile X-associated tremor/ataxia syndrome diagnostic criteria [3]

Diagnostic	Definite	One major clinical plus one major radiological; or one major clinical plus intranuclear inclusions
	Probable	Two major clinical; or one minor clinical plus one major radiological
	Possible	One major clinical plus one minor radiological
Clinical	Major	Intention tremor
		Gait ataxia
	Minor	Parkinsonism
		Moderate to severe short-term memory deficiency
		Executive function deficit
		Neuropathy
Radiological	Major	MRI white matter lesions in middle cerebellar peduncle
		MRI white matter lesions in splenium of the corpus callosum
	Minor	MRI white matter lesions in cerebrum
		Moderate to severe generalised atrophy

Inclusion criterion for all categories: *FMR1* gray zone, premutation or full mutation

Hall DA, et Al.: *The Corpus Callosum Splenium Sign in Fragile X-Associated Tremor Ataxia Syndrome.* Mov Disorders, 2016

FXTAS Diagnostic criteria		
Molecular	Required	*FMR1* Premutation excluding gray zone and FM with mosaicism.
Clínic	Major	Intention tremor
		Cerebellar gait ataxia
	Minor	Parkinsonism
		Neuropathy
		Memory and executive function deficits
Neuroradiological	Major	White matter disease in the middle cerebellar peduncles (MCP)
	Minor	White matter disease in splenium of the corpus callosum (CCS)
		Cerebral white matter lesions
		Moderate-to-severe generalized brain atrophy
Neuropathological	Major	FXTAS Ubiquitin-positive intranuclear inclusions in central and peripheral nervous system

Level of confidence	
Definite	Presence of 1 major radiological sign plus 1 major clinical symptom
Probable	Presence of either 1 major radiological sign plus 1 minor clinical symptom or has the 2 major clinical symptoms.
Possible	Presence of 1 minor radiological sign plus 1 major clinical symptom

The **middle cerebellar peduncle (MCP) sign** is a feature of a number of conditions, particularly neurodegenerative diseases, and most commonly associated with fragile X-associated tremor/ataxia syndrome (FXTAS) although many other conditions are recognized.

It represents high T2 signal in the middle cerebellar peduncles, which contain the frontocerebellar tracts (connecting to orbitofrontal and dorsolateral prefrontal cortex) [1].

The MCP sign is seen in a number of conditions including [1,2]:

- chronic liver disease
  - acquired non-wilsonian hepatocerebral degeneration
  - Wilson disease
- adrenoleukodystrophy
- Behcet disease
- chasing the dragon (heroin inhalation toxic leukoencephalopathy)
- cyclosporin-A encephalopathy
- demyelination
  - multiple sclerosis
  - acute disseminated encephalomyelitis
- infective
  - HIV encephalopathy
  - JC virus granule cell neuronopathy
  - Zika virus encephalitis in adults
- neurodegenerative
  - CARASIL: with involvement of pons; known as the arc sign [3]
  - recessive ataxia
  - spinocerebellar ataxia
  - multiple system atrophy - cerebellar (MSA-C): atrophy is usually the striking abnormality
  - fragile X-associated tremor/ataxia syndrome (FXTAS)
- vascular
  - bilateral anterior inferior cerebellar artery infarction
  - posterior reversible encephalopathy syndrome (PRES)
  - Wallerian degeneration secondary to pontine stroke

PET/TC con 18F DOPA