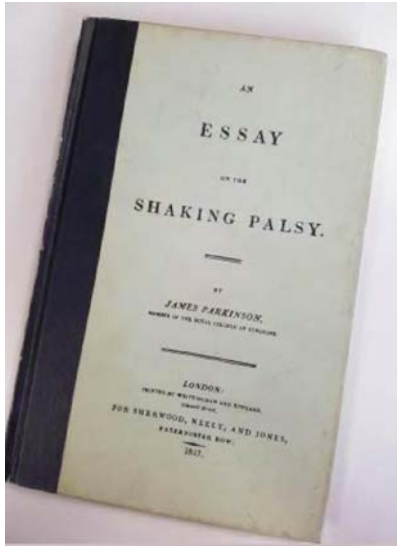
14-16 Novembre 2022
San Benedetto del Tronto

La Malattia di Parkinson e i Parkinsonismi

Dott.ssa Claudia Frau
Università degli Studi di Sassari

Parkinson’s Disease

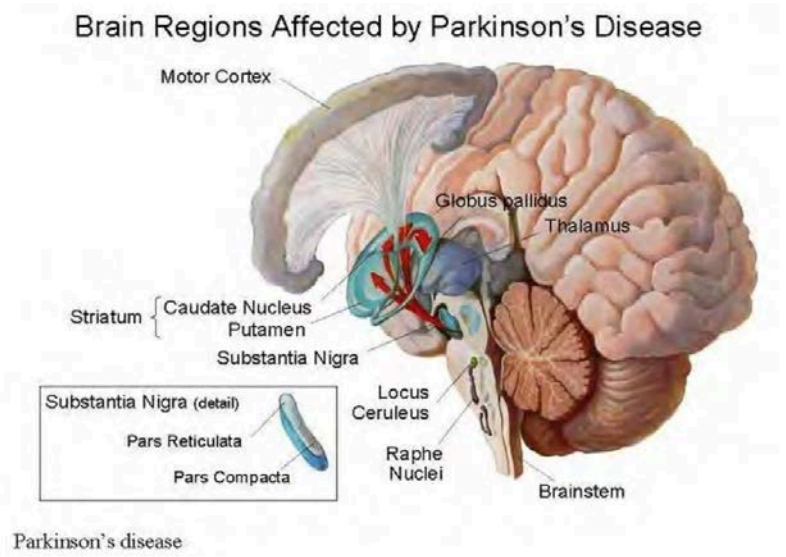
- The second most common neurodegenerative disorder *(Poewe, W., Seppi, K., Tanner, C. et al. Parkinson disease. Nat Rev Dis Primers 3, 2017)*
- 2-3% of the population > 65 years of age
- 6.1 million people who had been affected worldwide in 2016 *(GBD 2016 Neurology Collaborators. Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2019)*
- 3-5% monogenic PD
- PD not exists as a single entity. Every person has their own unique PD. We could say that there are over 6 million different variants of PD in the world *(Bloem BR, Okun MS, Klein C. Parkinson's disease. Lancet. 2021 Jun 12)*

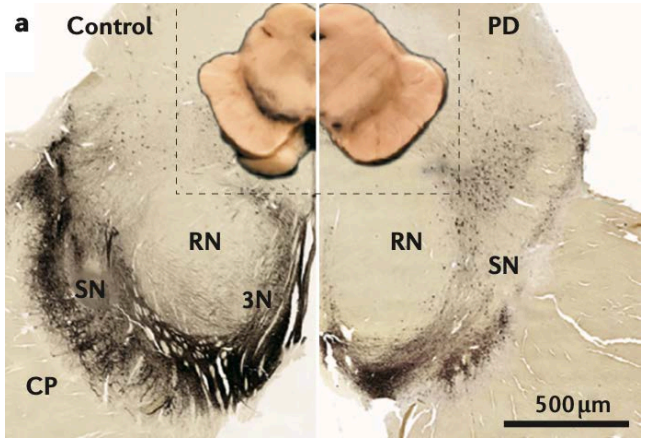


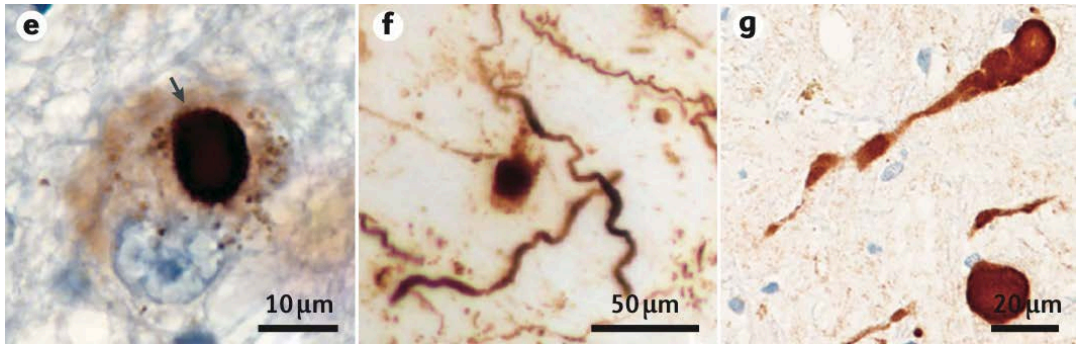
What happens in Parkinson's Disease ?

Loss of pigmented dopaminergic neurons in the Substantia Nigra (SN)

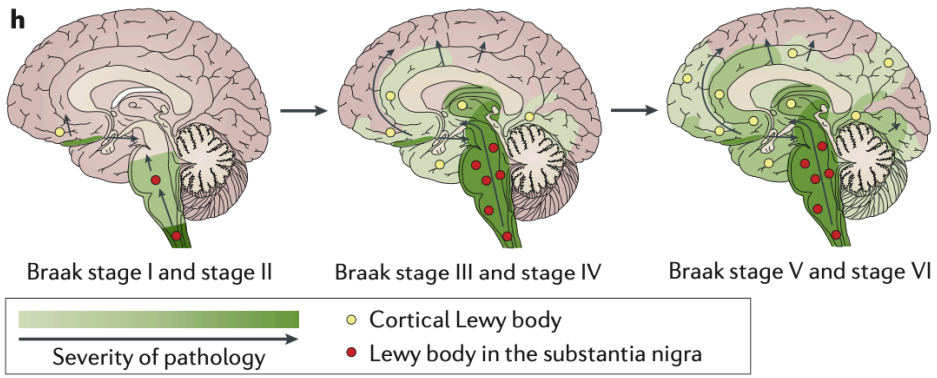
Abnormal deposition of alfa-sinuclein in the cytoplasm of certain neurons in several different brain regions (Lewy Bodies)

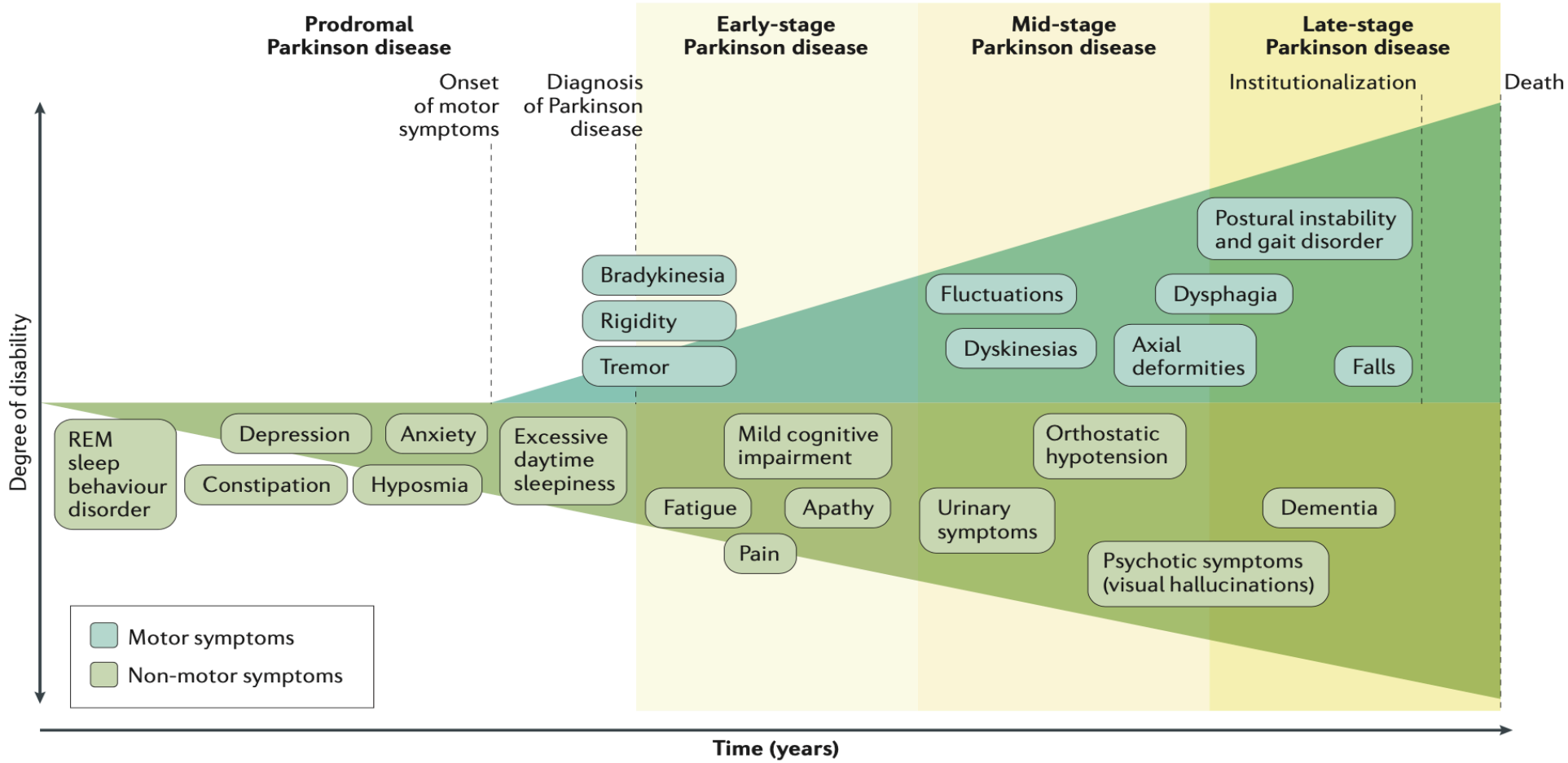




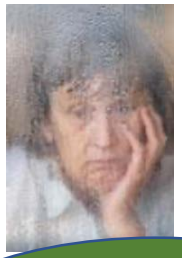


Braak's hypothesis

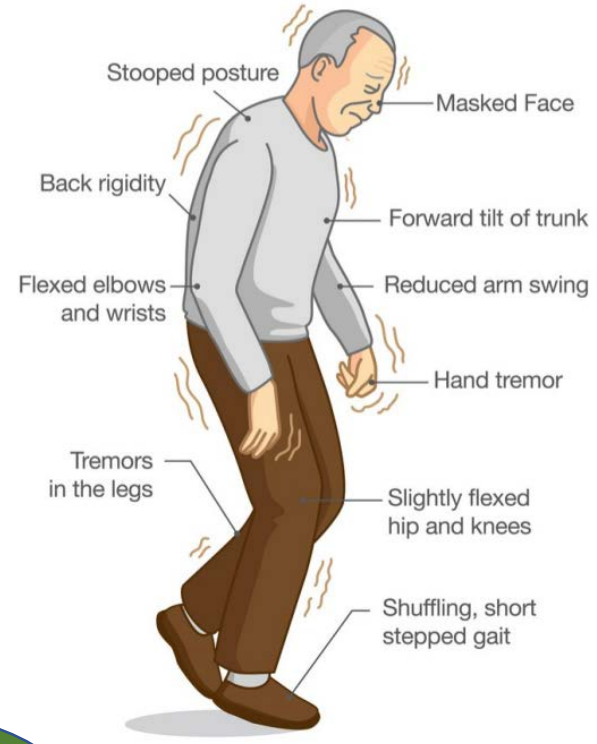


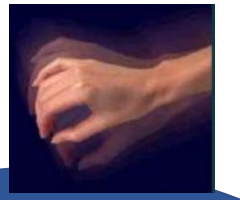


(*Poewe, W., Seppi, K., Tanner, C. et al. Parkinson disease. Nat Rev Dis Primers 3, 2017*)



Neuropsychiatric symptoms





CARDINAL SYMPTOMS

- Bradykinesia
- Resting tremor
- Rigidity

Cognitive dysfunctions

Sleep disorders

Autonomic dysfunctions

REVIEW

CME

MDS Clinical Diagnostic Criteria for Parkinson's Disease

Ronald B. Postuma, MD, MSc,[1†*] Daniela Berg, MD,[2†*] Matthew Stern, MD,[3] Werner Poewe, MD,[4] C. Warren Olanow, MD, FRCPC,[5] Wolfgang Oertel, MD,[6] José Obeso, MD, PhD,[7] Kenneth Marek, MD,[8] Irene Litvan, MD,[9] Anthony E. Lang, OC, MD, FRCPC,[10] Glenda Halliday, PhD,[12] Christopher G. Goetz, MD,[13] Thomas Gasser, MD,[2] Bruno Dubois, MD, PhD,[14] Piu Chan, MD, PhD,[15] Bastiaan R. Bloem, MD, PhD,[16] Charles H. Adler, MD, PhD,[17] and Günther Deuschl, MD[18]

Step 1: diagnosis of parkinsonism (core feature)

- Presence of bradykinesia as a slowness of movement and a decrement in amplitude or speed (or progressive hesitations or halts) as movements are continued
- In combination with at least one of: rigidity and/or rest tremor

Step 2: determining Parkinson disease as the cause of parkinsonism with two levels of diagnostic certainty

Diagnosis of clinically established Parkinson disease requires all three of the below parameters:

- Absence of absolute exclusion criteria. These criteria include clinical or imaging evidence for alternate diagnoses of parkinsonism, such as atypical parkinsonism, drug-induced parkinsonism or essential tremor.
- Two or more supportive criteria. These include L-DOPA responsiveness, the presence of classic rest tremor, the presence of L-DOPA-induced dyskinesias, the presence of either olfactory loss or cardiac sympathetic denervation on metaiodobenzylguanidine (MIBG) scintigraphy.
- No red flags. This refers to features that are unusual but not absolutely exclusionary for Parkinson disease, for example, the rapid progression of gait impairment that requires wheelchair use or the development of severe autonomic failure within 5 years after onset.

Diagnosis of clinically probable Parkinson disease requires:

- Absence of absolute exclusion criteria (mentioned above)
- Presence of red flags (mentioned above) that are counterbalanced by supportive criteria

For a full listing of absolute exclusion criteria, red flags and supportive criteria see REF. 118.

MDS, International Parkinson and Movement Disorder Society.

When typical motor symptoms appear more than 60% of nigro-striatal neurons have been lost

DOI: 10.1093/brain/awh198 *Brain* (2004), **127,** 1693–1705

REVIEW ARTICLE

Biomarkers and Parkinson's disease

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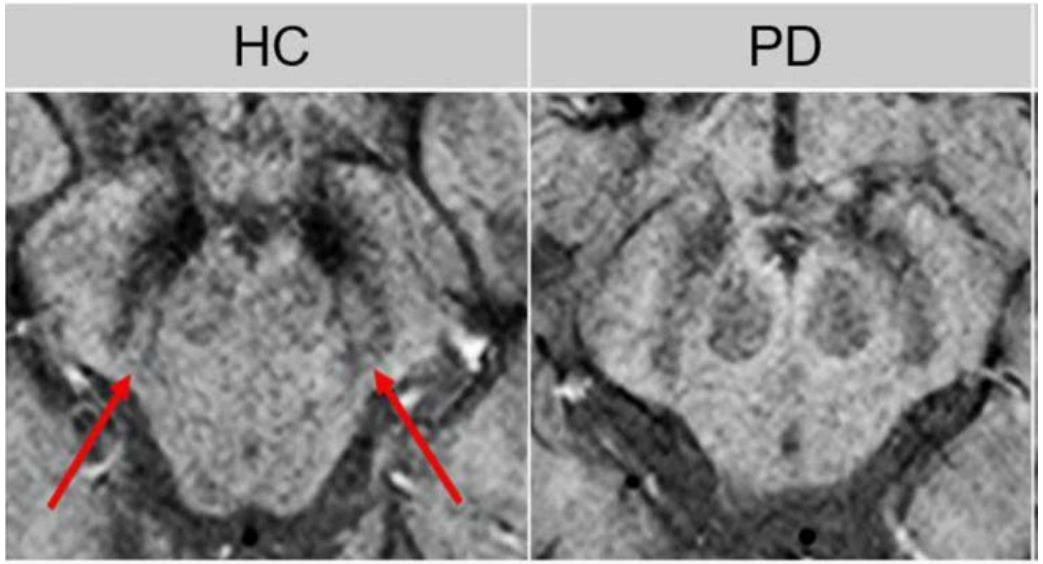
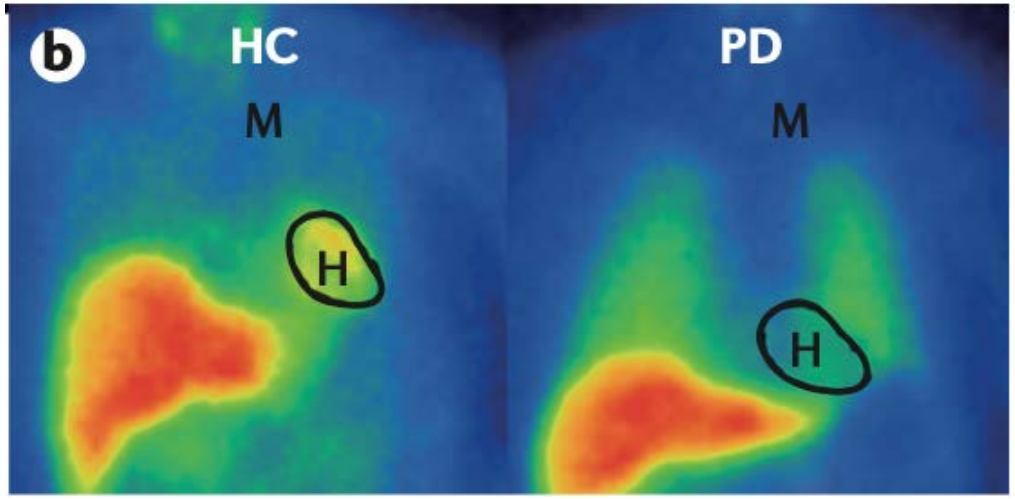
nomic, affective and cognitive deficits. Parkinson's disease can be difficult to diagnose in its early stages, and may be mimicked by other diseases, such as essential tremor, multiple system atrophy (MSA) and progressive supranuclear palsy (see reviews by Galvin *et al.*, 2001; Burn and Lees, 2002; Poewe and Wenning, 2002).

Even in highly specialized centres the sensitivity of the clinical diagnosis of Parkinson's disease in symptomatic patients is only about 91% (Hughes *et al.*, 2002), and it is likely to be far less in other settings (Rajput *et al.*, 1991; Hughes *et al.*,





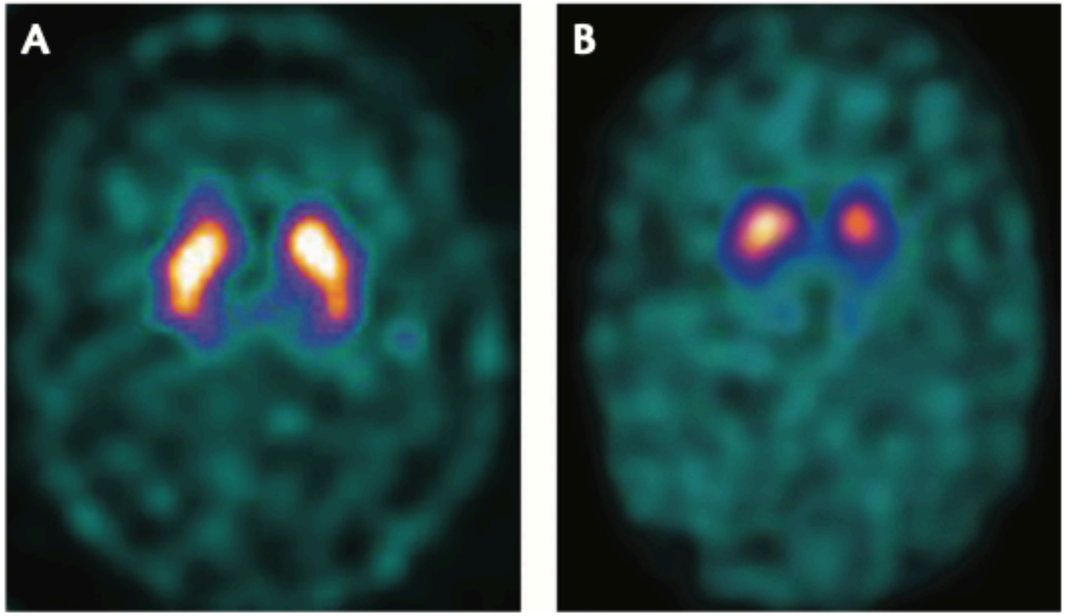
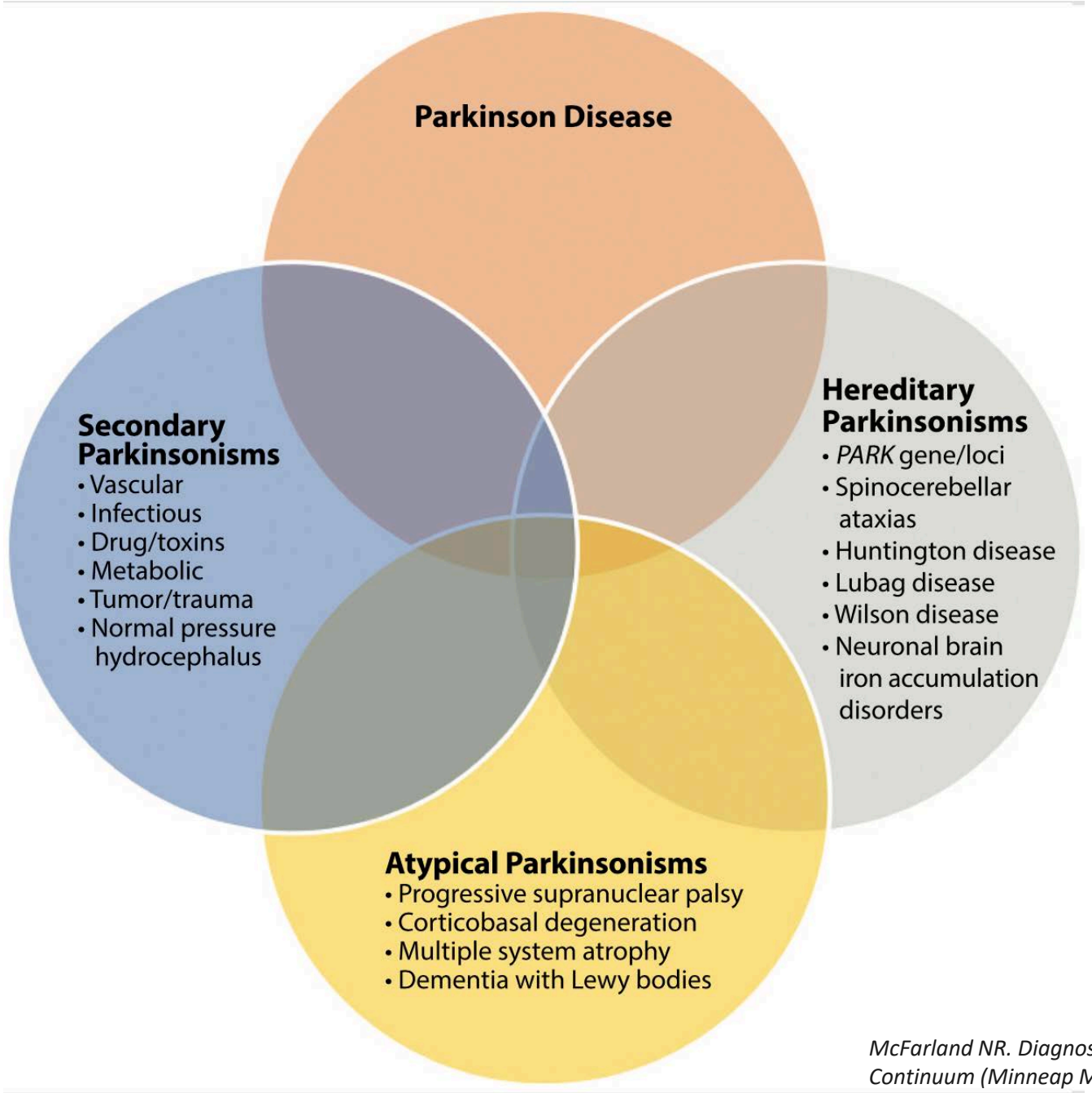


Figure 1. Dopamine Transporter (DaT) Scan Using Single-Photon Emission CT (SPECT). In a person without presynaptic dopamine transporter (DaT) loss, tracer activity appears uniform throughout the bilateral striatum (caudate nucleus and putamen), which has a "comma-shaped" appearance on axial images (A). In a person with Parkinson's disease, activity is asymmetrically reduced in the putamen (posterior portion of the comma) with preserved but lower than normal uptake in the caudate nuclei (B).

Saeed U, Lang AE, Masellis M. Neuroimaging Advances in Parkinson's Disease and Atypical Parkinsonian Syndromes. Front Neurol. 2020



McFarland NR. Diagnostic Approach to Atypical Parkinsonian Syndromes. Continuum (Minneap Minn). 2016 Aug

Progressive Supranuclear Palsy (PSP)

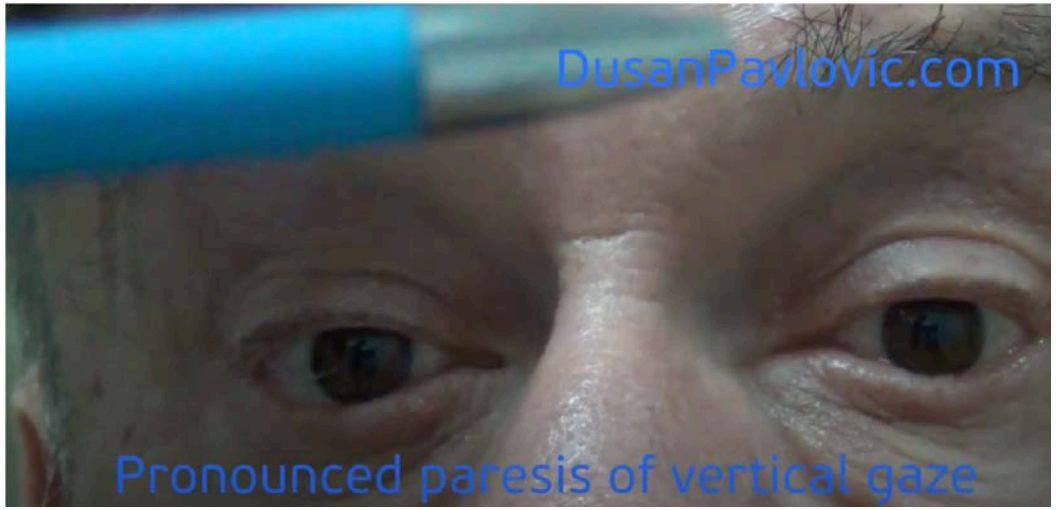
Symptoms	Signs
Cognitive change (apathy, impulsivity)	Akinetic rigidity—neck and axial rigidity >limbs 'sniffing morning breeze sign'
Impaired balance	Slow saccades and 'round the houses' vertical saccades
Early falls (with increased fracture risk)	Vertical supranuclear gaze palsy
Blurry or double vision	Frontalis overactivity, reduced blink, staring expression
Sleep difficulties	Tendency to lose balance spontaneously or on the 'pull test'
Dysphagia (especially liquids)	Uncontrolled decent into a chair
Drooling, sialorrhoea	Dystonia, cervical, axial >limbs
Urinary urgency or incontinence	Apraxia (CBS overlap)
Constipation	Emotional lability (pseudobulbar affect)
Depression or anxiety	Reduced verbal fluency
Hyperphagia and change in food preferences	Dysarthrophonia
Weight loss (with possible malnutrition)	

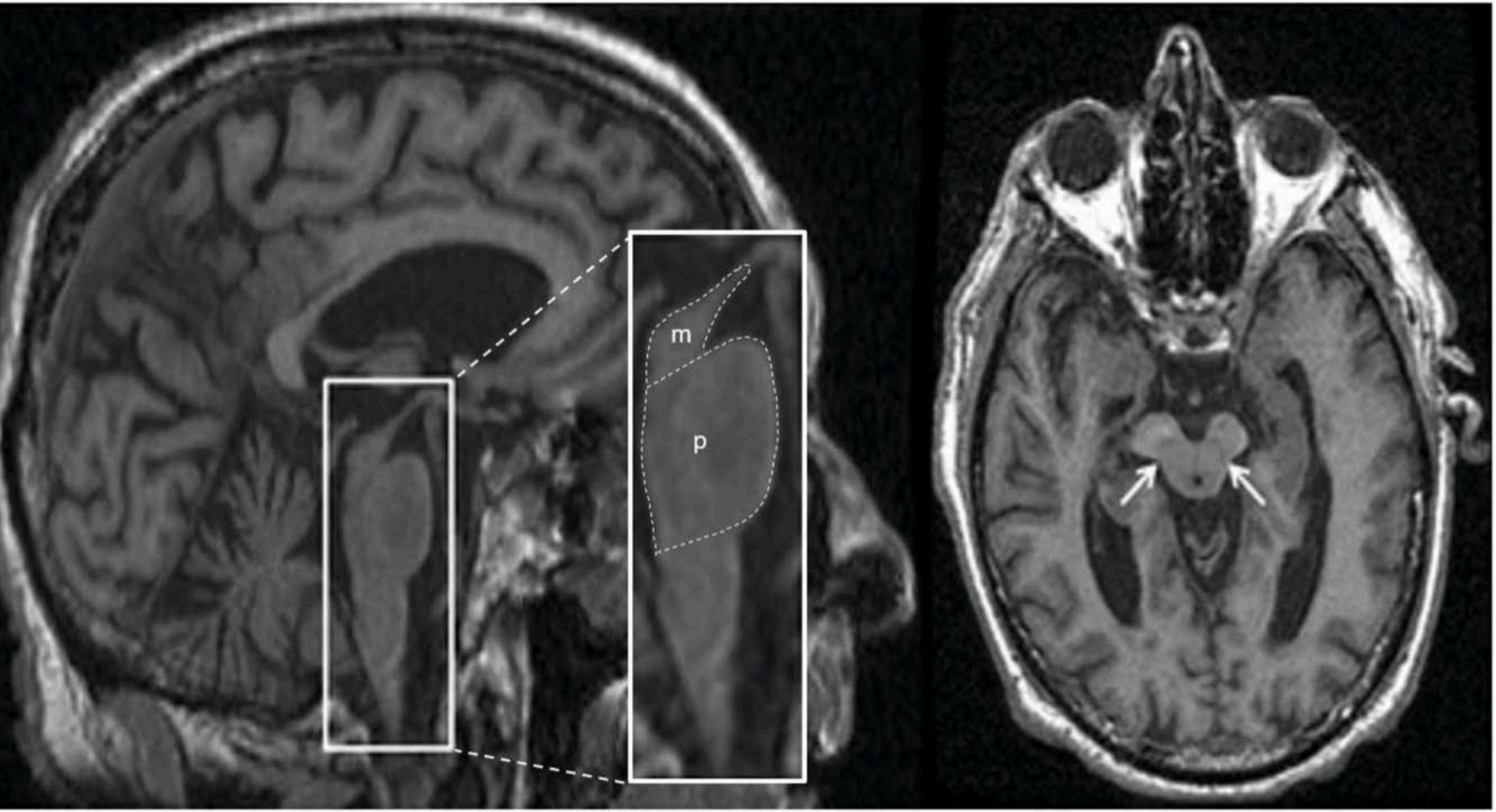
CBS, corticobasal syndrome; PSP, progressive supranuclear palsy.

Published in final edited form as:
Mov Disord. 2017 June ; 32(6): 853–864. doi:10.1002/mds.26987.

Clinical Diagnosis of Progressive Supranuclear Palsy: The Movement Disorder Society Criteria

Gunter U. Hoglinger, MD[1,2,*], Gesine Respondek, MD[1,2], Maria Stamelou, MD[3], Carolin Kurz,




m
p

Multiple System Atrophy (MSA)

TABLE. DIAGNOSTIC CRITERIA FOR DIFFERENT LEVELS OF CERTAINTY OF MULTISYSTEM ATROPHY

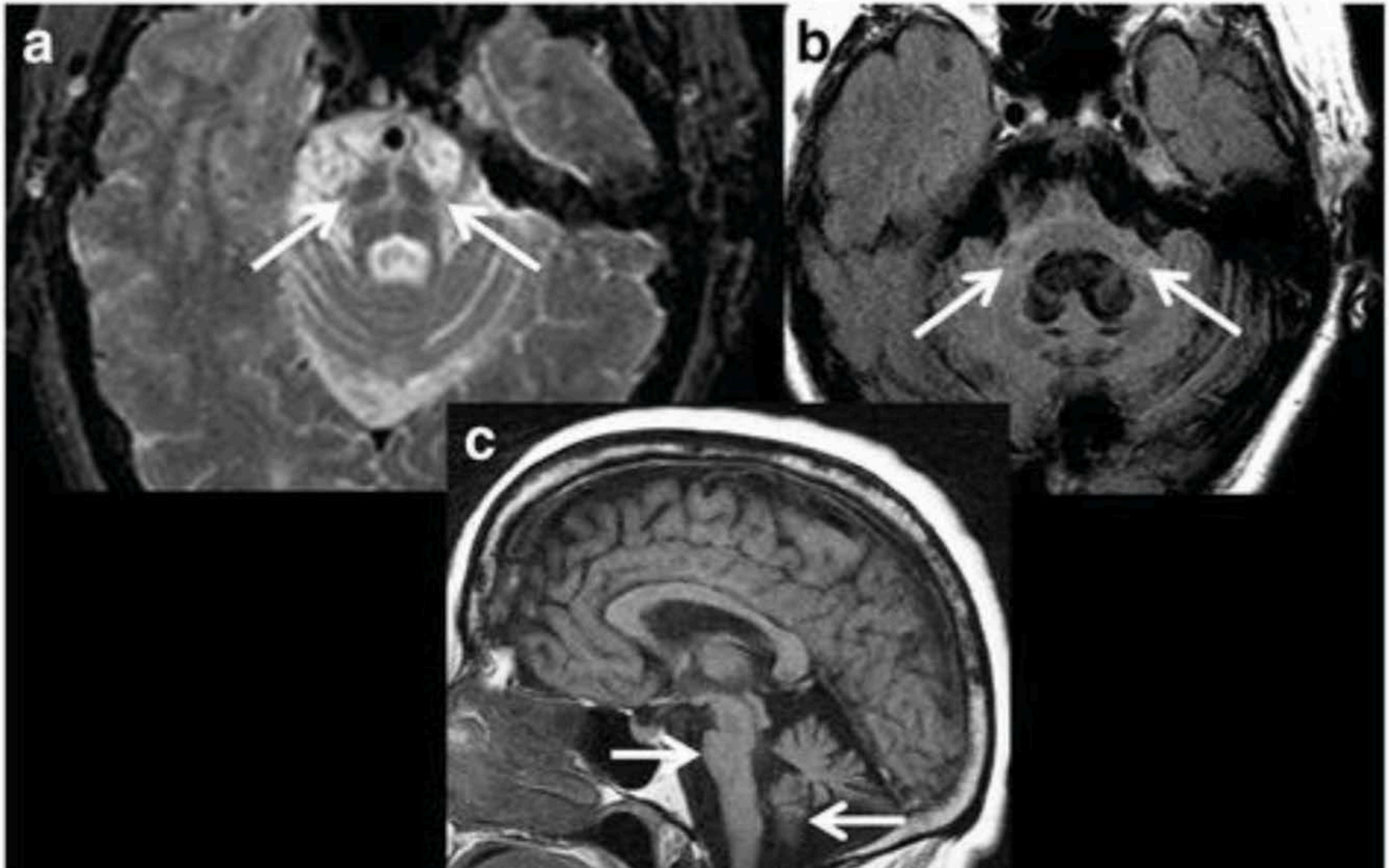
SYMPTOMS AND FINDINGS		POSSIBLE	PROBABLE	DEFINITE
Neuropathologic findings of widespread α-synuclein inclusion in glial cytoplasm in association with neurodegenerative changes in striatonigral or olivopontocerebellar structures				X
Autonomic failure	Urinary incontinence Erectile dysfunction Orthostatic hypotension	One of these AND	X	
Parkinsonian symptoms	Bradykinesia Rigidity Tremor Postural instability	X	X	
Parkinsonian symptoms unresponsive to levodopa therapy			X	
		OR	OR	
Cerebellar syndrome	Gait ataxia Cerebellar dysarthria Limb ataxia Cerebellar oculomotor dysfunction	X	X	
Additional features	Babinski sign with hyperflexia Stridor Rapid progression of symptoms Poor response to levodopa therapy Postural instability within 3 years of diagnosis Ataxia Dysphagia within 5 years of diagnosis	AND one of these		
Imaging findings	Atrophy of putamen, middle cerebellar peduncal, pons, or cerebellum Positive dopamine active transporter scan Hypometabolism in putamen, brainstem, or cerebellum on FDG-PET	OR one of these		

Second consensus statement on the diagnosis of multiple system atrophy

S. Gilman, MD, FRCP
G.K. Wenning, MD, PhD
P.A. Low, MD,

ABSTRACT

Background: A consensus conference on multiple system atrophy (MSA) in 1998 established criteria for diagnosis that have been accepted widely. Since then, clinical, laboratory, neuropathologic, and imaging studies have advanced the field, requiring a fresh evaluation of diagnostic


a
b
c

Lewy Body Disease

Table 1 **Revised[1,2] criteria for the clinical diagnosis of probable and possible dementia with Lewy bodies (DLB)**

Essential for a diagnosis of DLB is dementia, defined as a progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational functions, or with usual daily activities. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention, executive function, and visuoperceptual ability may be especially prominent and occur early.
Core clinical features (*The first 3 typically occur early and may persist throughout the course.*)
Fluctuating cognition with pronounced variations in attention and alertness. Recurrent visual hallucinations that are typically well formed and detailed. REM sleep behavior disorder, *which may precede cognitive decline.* One or more spontaneous cardinal features of parkinsonism: these are bradykinesia (defined as slowness of movement and decrement in amplitude or speed), rest tremor, or rigidity.
Supportive clinical features
Severe sensitivity to antipsychotic agents; postural instability; repeated falls; syncope or other transient episodes of unresponsiveness; severe autonomic dysfunction, e.g., constipation, orthostatic hypotension, urinary incontinence; hypersomnia; hyposmia; hallucinations in other modalities; systematized delusions; apathy, anxiety, and depression.
Indicative biomarkers
Reduced dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET. Abnormal (low uptake) ^{123}iodine-MIBG myocardial scintigraphy. Polysomnographic confirmation of REM sleep without atonia.
Supportive biomarkers
Relative preservation of medial temporal lobe structures on CT/MRI scan. Generalized low uptake on SPECT/PET perfusion/metabolism scan with reduced occipital activity ± the cingulate island sign on FDG-PET imaging. Prominent posterior slow-wave activity on EEG with periodic fluctuations in the pre-alpha/theta range.


VIEWS & REVIEWS

Diagnosis and management of dementia with Lewy bodies

Fourth consensus report of the DLB Consortium

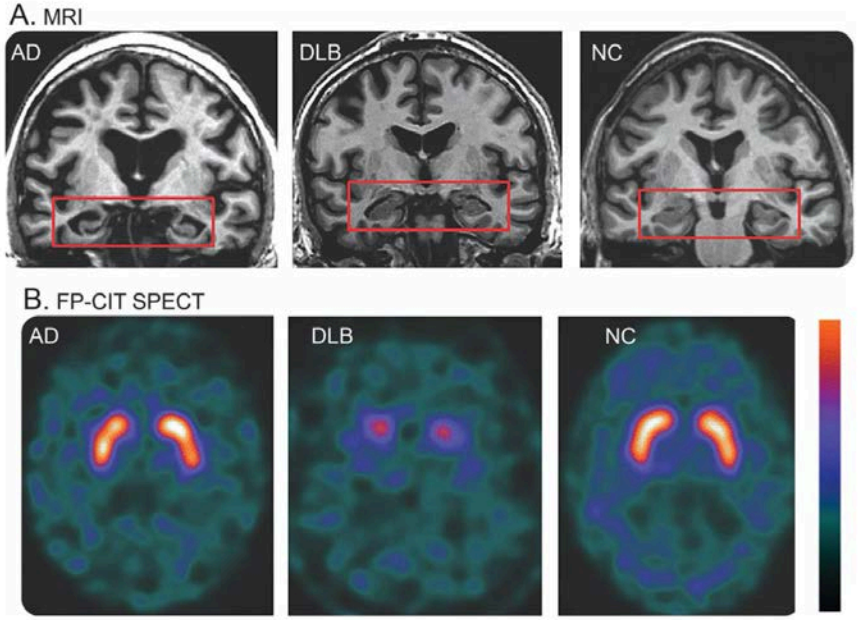
OPEN

Ian G. McKeith, MD, F Med Sci

ABSTRACT

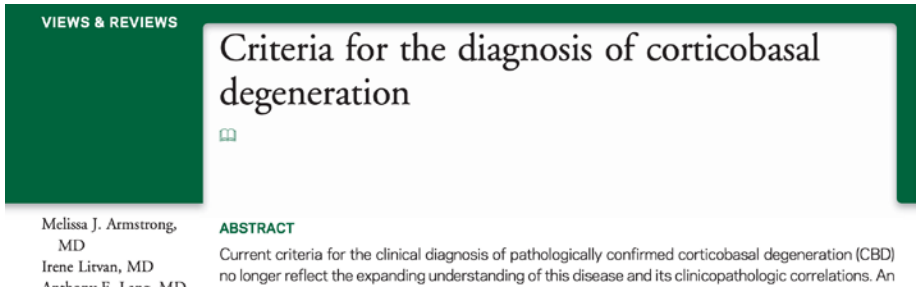
The Dementia with Lewy Bodies (DLB) Consortium has refined its recommendations about the

Figure 1 **Coronal T1-weighted MRI and ^{123}iodine FP-CIT SPECT images in Alzheimer disease (AD), dementia with Lewy bodies (DLB), and normal controls (NC)**



(A) On the MRI, note the relative preservation of medial temporal lobe volume (rectangles) in DLB, which is similar to NC, whereas atrophy is obvious in AD. (B) On the FP-CIT SPECT images, note the minimal uptake in DLB, which is restricted to the caudate (period or full-stop appearance) compared to the robust uptake in the caudate and putamen in AD and NC (comma appearance). Reproduced with permission from Dr. Val Lowe, Mayo Clinic, Rochester, MN.

Corticobasal Degeneration


VIEWS & REVIEWS

Criteria for the diagnosis of corticobasal degeneration

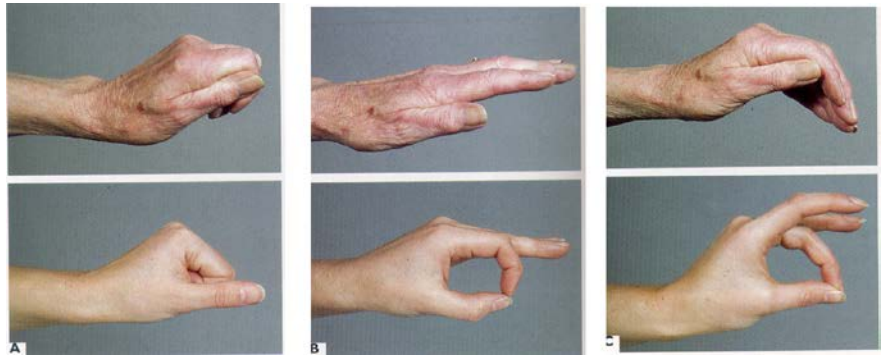
Melissa J. Armstrong, MD
Irene Litvan, MD

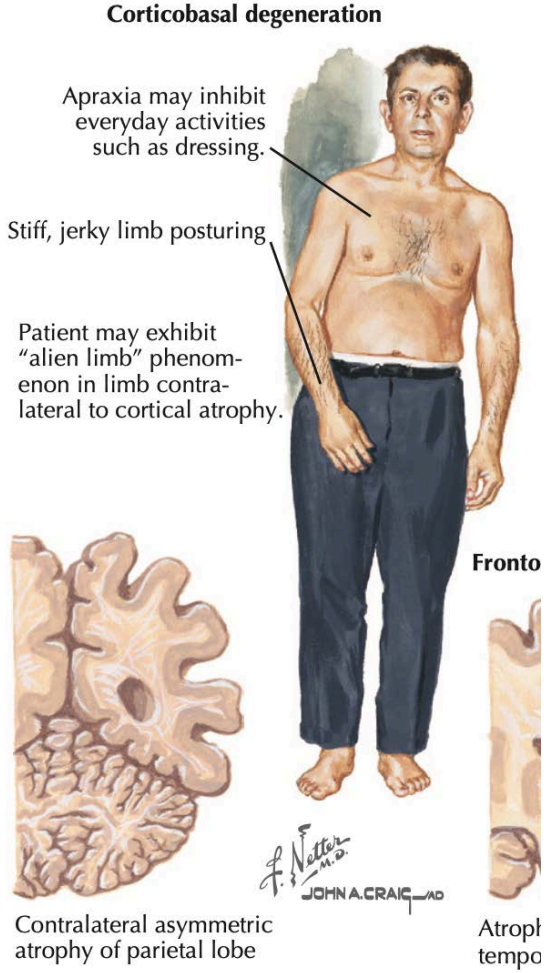
ABSTRACT

Current criteria for the clinical diagnosis of pathologically confirmed corticobasal degeneration (CBD) no longer reflect the expanding understanding of this disease and its clinicopathologic correlations. An

Table 4 Proposed clinical phenotypes (syndromes) associated with the pathology of corticobasal degeneration[a]

Syndrome	Features
Probable corticobasal syndrome	Asymmetric presentation of 2 of: a) limb rigidity or akinesia, b) limb dystonia, c) limb myoclonus plus 2 of: d) orobuccal or limb apraxia, e) cortical sensory deficit, f) alien limb phenomena (more than simple levitation)
Possible corticobasal syndrome	May be symmetric: 1 of: a) limb rigidity or akinesia, b) limb dystonia, c) limb myoclonus plus 1 of: d) orobuccal or limb apraxia, e) cortical sensory deficit, f) alien limb phenomena (more than simple levitation)
Frontal behavioral-spatial syndrome	Two of: a) executive dysfunction, b) behavioral or personality changes, c) visuospatial deficits
Nonfluent/agrammatic variant of primary progressive aphasia	Effortful, agrammatic speech plus at least one of: a) impaired grammar/sentence comprehension with relatively preserved single word comprehension, or b) groping, distorted speech production (apraxia of speech)
Progressive supranuclear palsy syndrome	Three of: a) axial or symmetric limb rigidity or akinesia, b) postural instability or falls, c) urinary incontinence, d) behavioral changes, e) supranuclear vertical gaze palsy or decreased velocity of vertical saccades





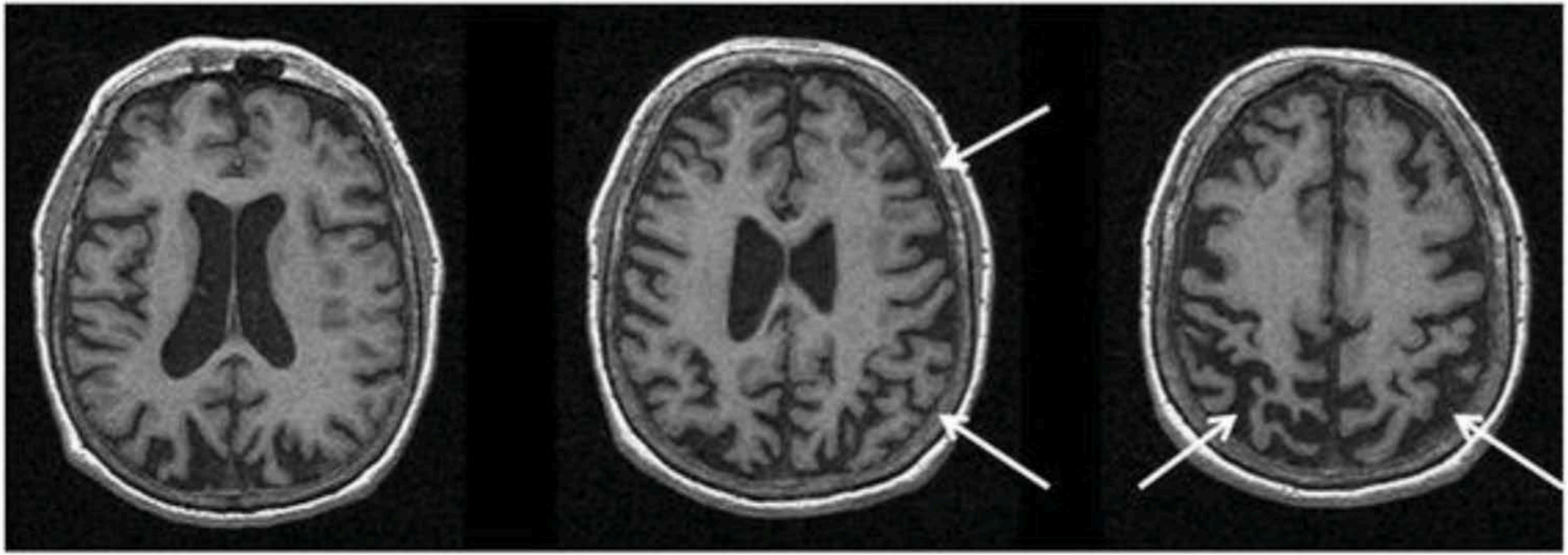
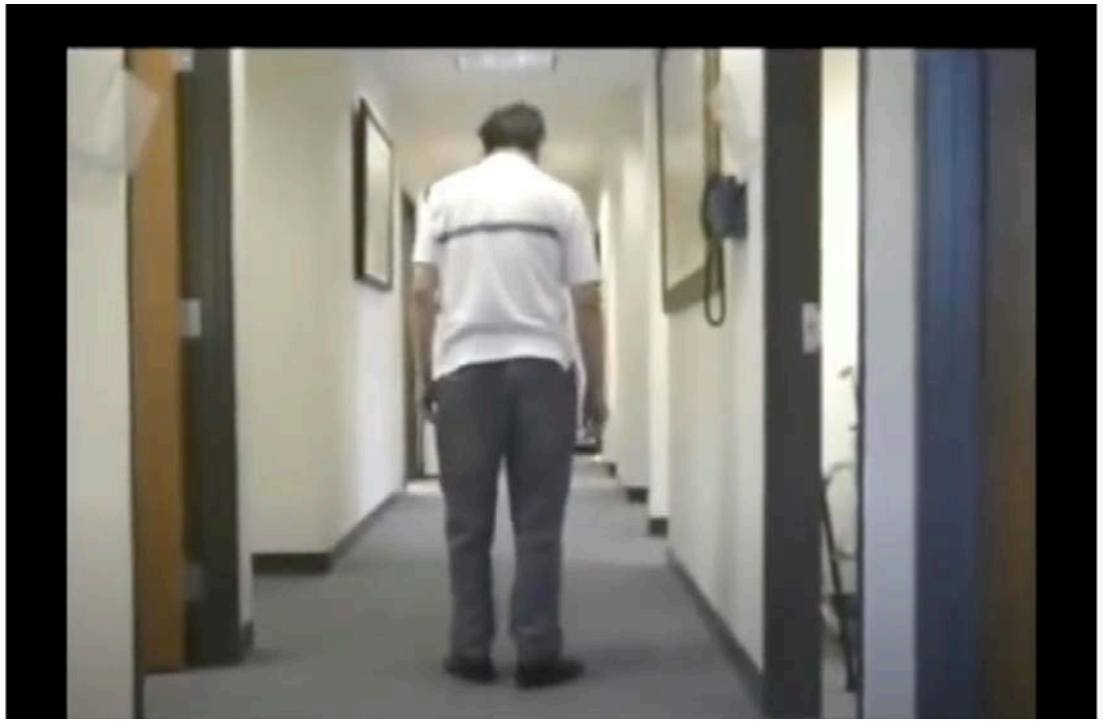


FIGURE 6 | Magnetic resonance imaging of a patient with a pathology-proven diagnosis of corticobasal degeneration. Serial axial T1-weighted sequences are presented showing right greater than left parietofrontal atrophy commonly seen in corticobasal syndrome. Figure reproduced from Saeed et al. (10), under the Creative Commons Attribution License 4.0 (https://creativecommons.org/licenses/by/4.0/).

Vascular parkinsonism

- ✓ Lower body parkinsonism (less narrow base of gait compared to PD)
- ✓ Posture is instable
- ✓ Spastic legs rather than rigid with brisk tendon reflexes
- ✓ Pseudobulbar palsy
- ✓ Gait ignition failure
- ✓ Cognitive impairment
- ✓ Multiple vascular risk factors
- ✓ History of stroke
- ✓ Poor response to dopaminergic therapy



Korczyn AD. Vascular parkinsonism--characteristics, pathogenesis and treatment. Nat Rev Neurol. 2015 Jun

Drug-induced Parkinsonism

- ✓ Parkinsonian symptoms emerge over the first **2 to 3** months, although they may also develop years after initial exposure and take months to resolve after discontinuation
- ✓ Rigidity is the most common finding.
- ✓ Bradykinesia and resting tremor are more variable

TABLE 2. Drugs potentially responsible for DIP

Potential Risk of DIP	Pharmacological Group	Drug
High	Dopamine D2 receptor antagonists	Typical antipsychotics: phenothiazines (chlorpromazine); butyrophenones (haloperidol); thioxanthene (flupenthioxol)Atypical antipsychotics (at higher doses): benzamides (sulpiride); diphenylbutylpiperazines (pimozide); dibenzyldiazepines (clozapine).
	Dopamine depleters	Tetrabenazine, reserpine
	Dopamine synthesis blockers	Alfa-methyldopa
	Calcium channel antagonists (P-channel)	Flunarizine, cinnarizine
Intermediate	Atypical antipsychotics	Ziprasidone
	Antiemetic and gastric motility agents	Prochlorperazine, metoclopramide, substituted benzamides
	Calcium channel antagonists (L-channel)	Verapamil, diltiazem
	Others	Lithium, valproate, phenytoin
Low	Antidepressants	SSRI (fluoxetine, sertraline), tricyclic (phenetzine), MAO-I (moclobemide)
	Others	Amiodarone, procaine, tacrolimus, ciclosporin

SSRI, selective serotonin reuptake inhibitors; MAO-I, monoamine oxidase inhibitors.

Erro R, Bhatia KP, Tinazzi M. Parkinsonism following neuroleptic exposure: A double-hit hypothesis? Mov Disord. 2015 May

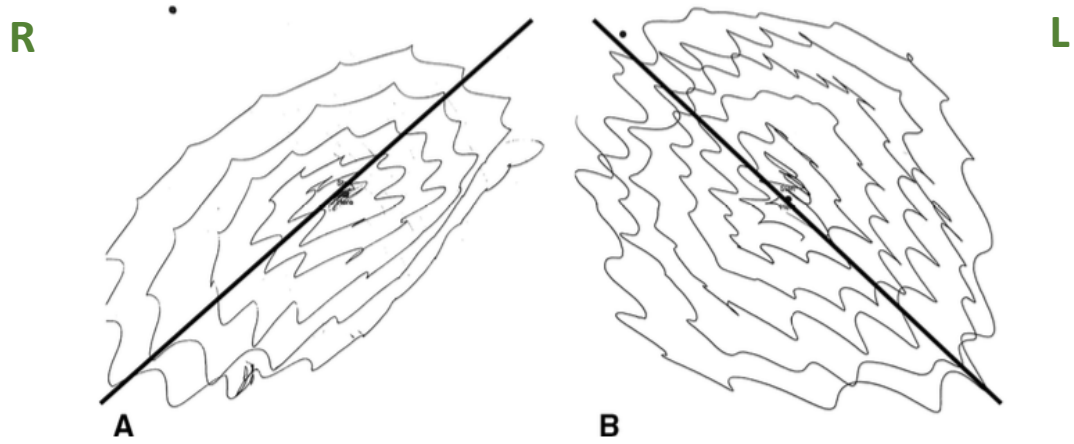
Essential Tremor

Criteria for diagnosis of essential tremor[1,2]

Core criteria	Secondary criteria	Exclusion criteria
▪ Bilateral action tremor of the hands and forearms (but not resting tremor) ▪ Absence of other neurologic signs, with the exception of cogwheel phenomenon ▪ With or without tremor in other locations (head, voice, lower limbs)	▪ Long duration (>3 years) ▪ Positive family history ▪ Beneficial response to alcohol	▪ Isolated focal tremors (voice, head) ▪ Orthostatic tremor with frequency >12 Hz ▪ Task- and position-specific tremors ▪ Sudden onset and stepwise deterioration

References:

1. *Bain P, Brin M, Deuschl G, et al. Criteria for the diagnosis of essential tremor. Neurology 2000; 54(11 Suppl 4):S7.*
2. *Bhatia KP, Bain P, Bajaj N, et al. Consensus Statement on the classification of tremors from the task force on tremor of the International Parkinson and Movement Disorder Society. Mov Disord 2018; 33:75.*



Accuracy of clinical diagnosis of Parkinson disease

A systematic review and meta-analysis

Giovanni Rizzo, MD
Massimiliano Copetti, PhD
Simona Arcuti, PhD
Davide Martino, MD
Andrea Fontana, MSc
Giancarlo Logroscino, MD

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ABSTRACT

Objective: To evaluate the diagnostic accuracy of clinical diagnosis of Parkinson disease (PD) reported in the last 25 years by a systematic review and meta-analysis.

Methods: We searched for articles published between 1988 and August 2014. Studies were included if reporting diagnostic parameters regarding clinical diagnosis of PD or crude data. The selected studies were subclassified based on different study setting, type of test diagnosis, and gold standard. Bayesian meta-analyses of available data were performed.

Results: We selected 20 studies, including 11 using pathologic examination as gold standard. Considering only these 11 studies, the pooled diagnostic accuracy was 80.6% (95% credible interval [CrI] 75.2%–85.3%). Accuracy was 73.8% (95% CrI 67.8%–79.6%) for clinical diagnosis performed mainly by nonexperts. Accuracy of clinical diagnosis performed by movement disorders experts rose from 79.6% (95% CrI 46%–95.1%) of initial assessment to 83.9% (95% CrI 69.7%–92.6%) of refined diagnosis after follow-up. Using UK Parkinson's Disease Society Brain Bank Research Center criteria, the pooled diagnostic accuracy was 82.7% (95% CrI 62.6%–93%).

Conclusion: The overall validity of clinical diagnosis of PD is not satisfying. The accuracy did not significantly improve in the last 25 years, particularly in the early stages of disease, where response to dopaminergic treatment is less defined and hallmarks of alternative diagnoses such as atypical parkinsonism may not have emerged. Misclassification rate should be considered to calculate the sample size both in observational studies and randomized controlled trials. Imaging and biomarkers are urgently needed to improve the accuracy of clinical diagnosis in vivo.

Neurology® 2016;86:1–11

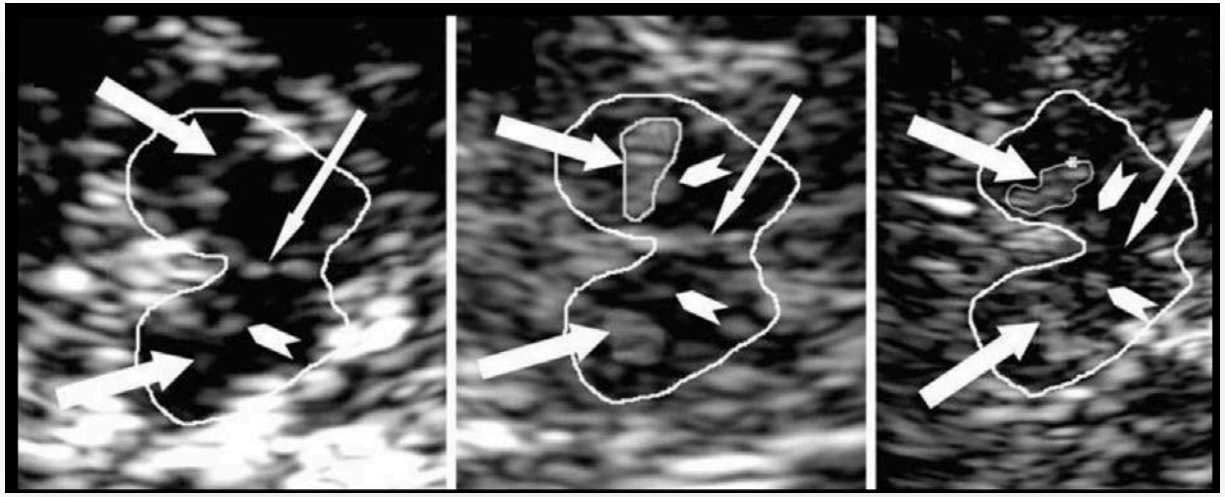
Brain Parenchyma Sonoghraphy

European Journal of Neurology 2013, **20:** 16–34 doi:10.1111/ene.12022

EFNS/MDS-ES GUIDELINES/CME ARTICLE

EFNS/MDS-ES recommendations for the diagnosis of Parkinson's disease

A. Berardelli[a*], G. K. Wenning[b], A. Antonini[c], D. Berg[d], B. R. Bloem[e], V. Bonifati[f], D. Brooks[g], D. J. Burn[h], C. Colosimo[i], A. Fanciulli[b], J. Ferreira[j], T. Gasser[d], F. Grandas[k], P. Kanovsky[l], V. Kostic[m], J. Kulisevsky[n], W. Oertel[o], W. Poewe[b], J.-P. Reese[p], M. Relja[q], E. Ruzicka[r], A. Schrag[s], K. Seppi[b], P. Taba[t] and M. Vidailhet[u]



Recommendations

Transcranial sonography is recommended (Level A) for

I Differential diagnosis of PD from APS and secondary parkinsonian syndromes

II Early diagnosis of PD

III Detection of subjects at risk for PD

The technique is so far not universally used and requires some expertise. Because specificity of TCS for the development of PD is limited, TCS should be used in conjunction with other screening tests.

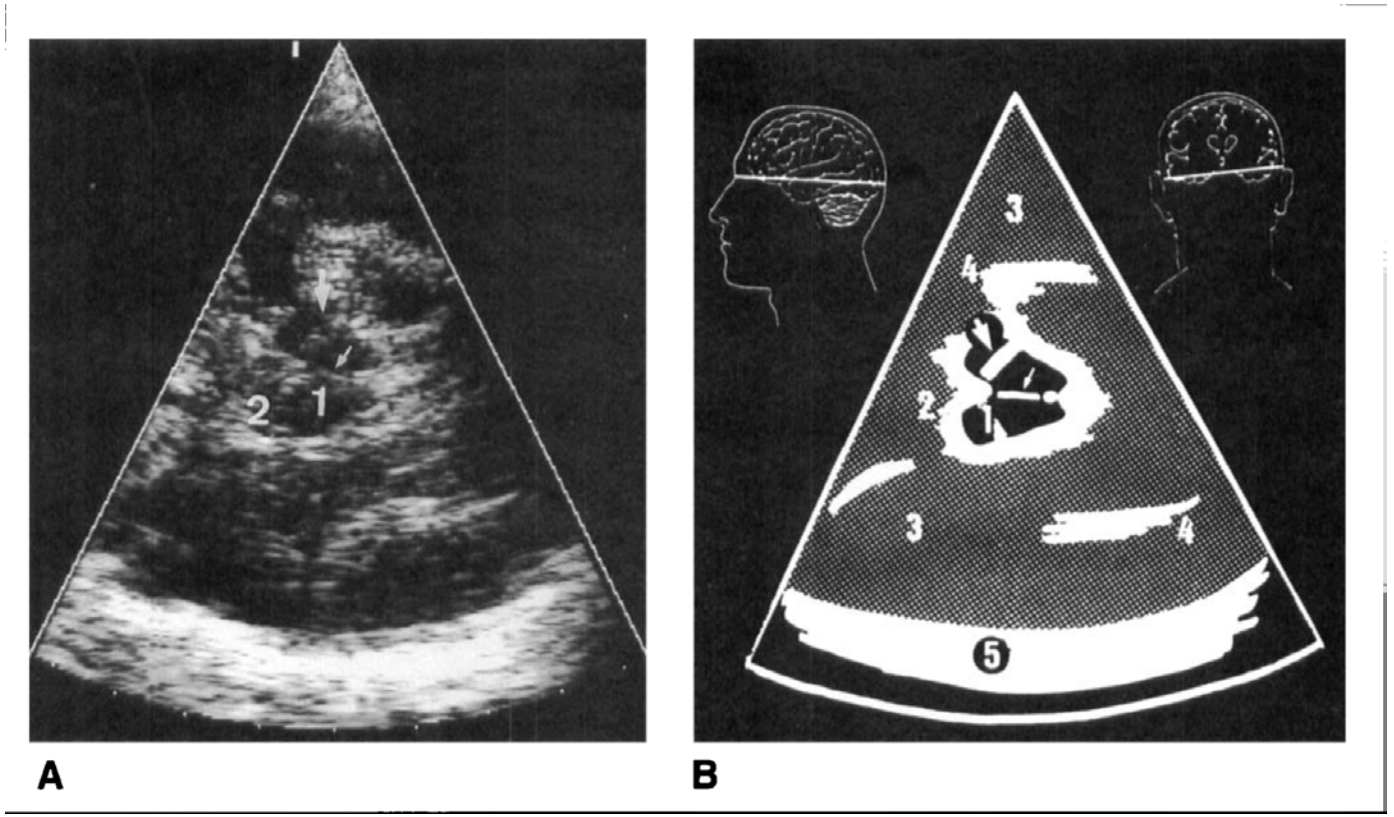
Hyperechogenicity of Substantia nigra

Neurology®

Degeneration of substantia nigra in chronic Parkinson's disease visualized by transcranial color-coded real-time sonography

G. Becker, J. Seufert, U. Bogdahn, et al.

Neurology 1995;45;182-184
DOI 10.1212/WNL.45.1.182

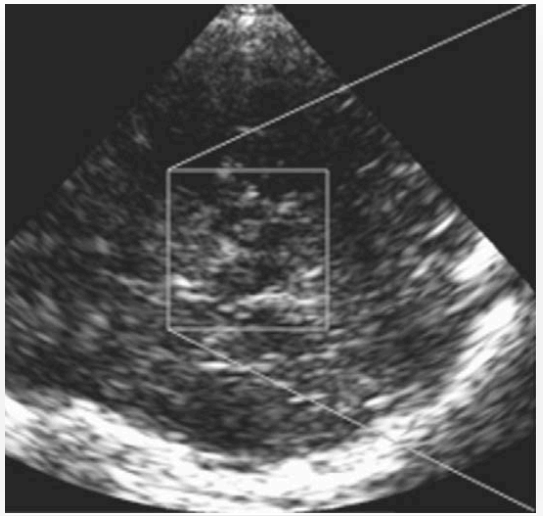


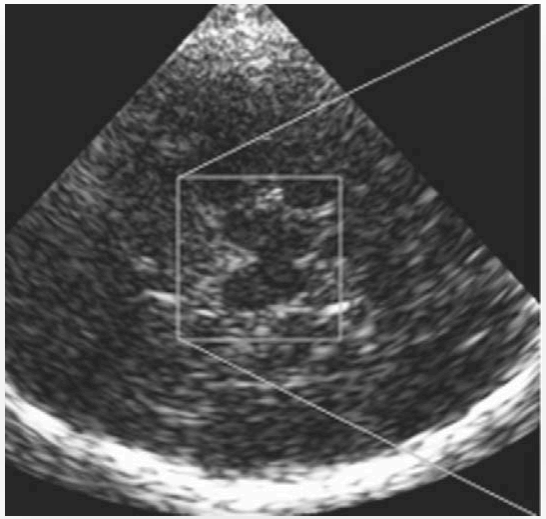
SN hyperechogenicity as a vulnerability marker

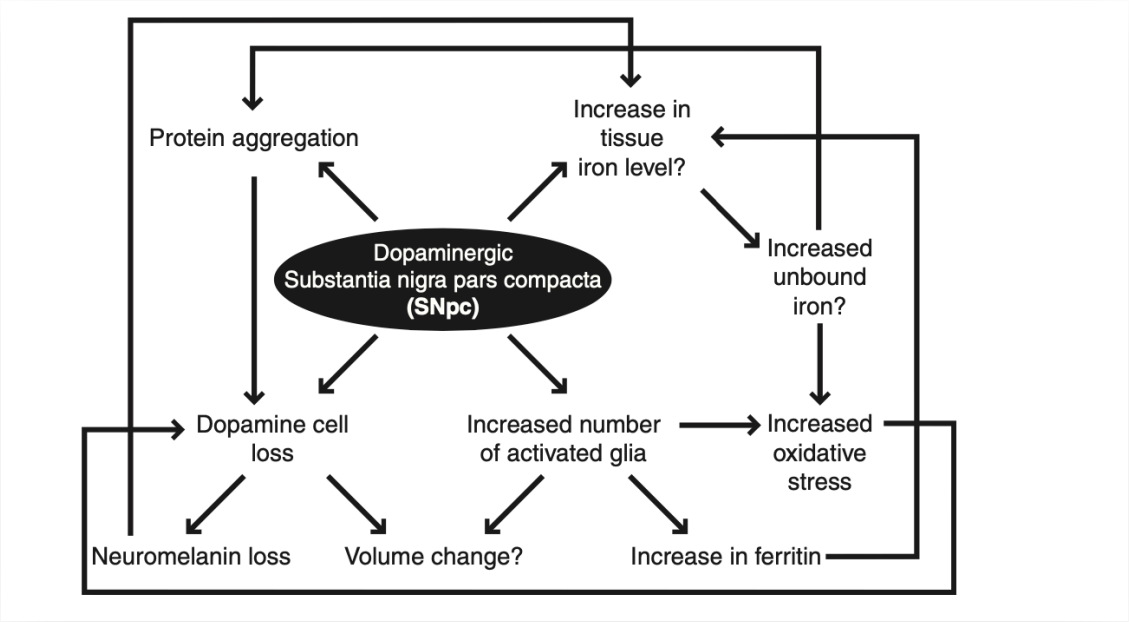
SN hyperechogenicity can be detected in some healthy subjects (2 of 30 subjects):

2 years later 1 of these subjects was diagnosed as having PD *(Becker et al. 1995)*

Physiopathology of the hyperechogenicity of Substantia Nigra







- **Increased iron deposition**
- **Loss of neuromelanin**
- **Increased glial cells**

TECHNIQUE

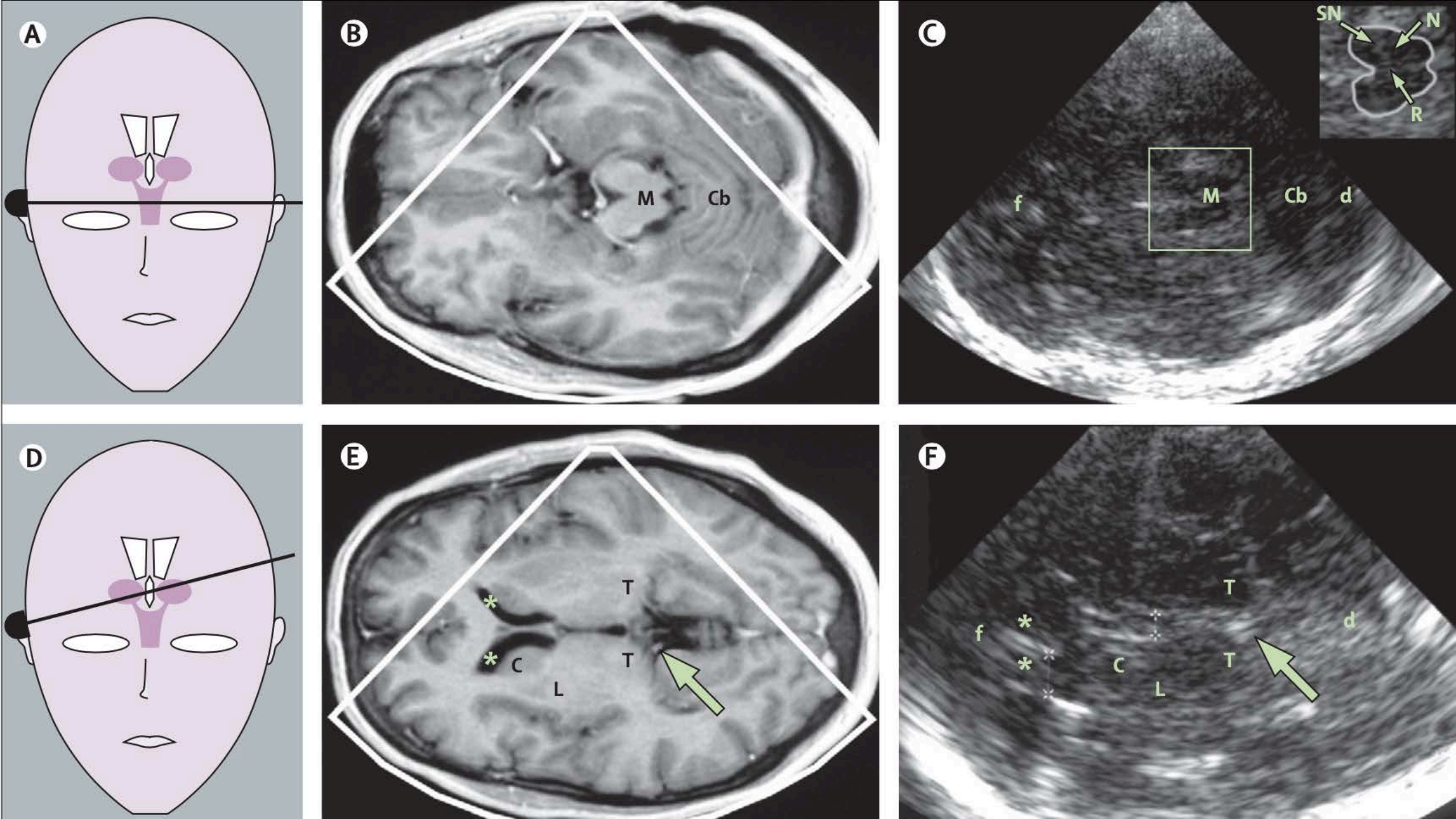
parameter	settings
ultrasound machine	
image depth	start with 14 – 16 cm, adapt as needed
dynamic range	45 – 55 dB
post-processing function	moderate suppression of low echogenic signals
time gain compensation	adapt manually as needed or, if available, apply automated image optimization (i. e., press the referring button on the keyboard, standard with contemporary high-end ultrasound systems)
image brightness	adapt manually as needed or, if available, apply automated image optimization (i. e., press the referring button on the keyboard, standard with contemporary high-end ultrasound systems)
Ultrasound transducer	
density of crystals / channels	as high as possible, ideally “matrix” probe
center frequency of insonation	2.0 – 3.5 MHz, usually 2.5 MHz

Temporal acoustic bone window, axial scanning planes

Orbitomeatal line

2.0- to 3.5-MHz phased-array transducer

Walter U, Školoudík D. Transcranial sonography (TCS) of brain parenchyma in movement disorders: quality standards, diagnostic applications and novel technologies. Ultraschall Med. 2014 Aug


A
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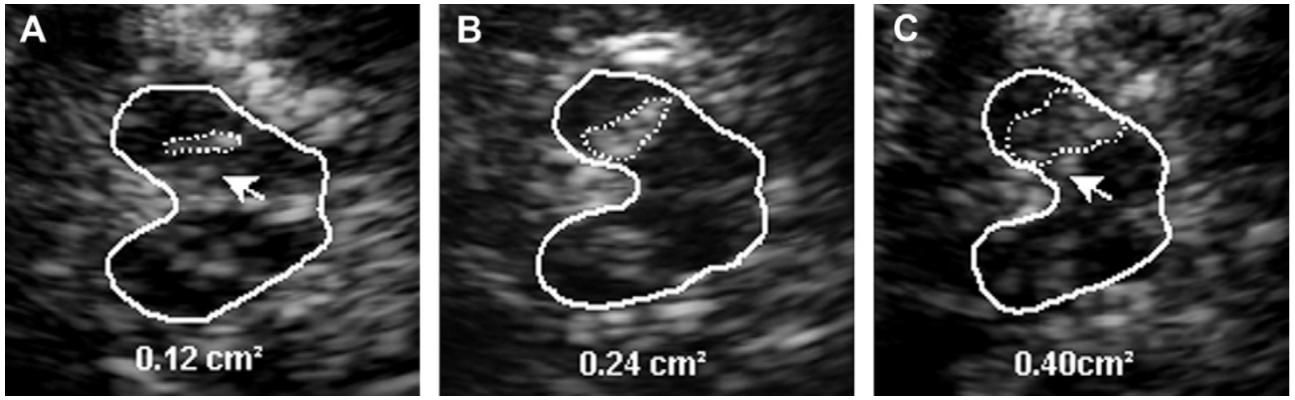
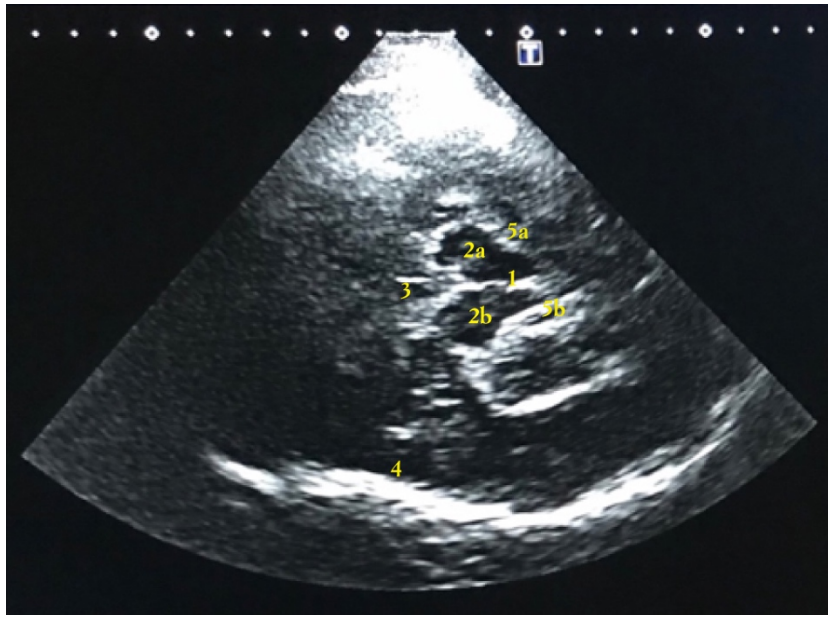
Mesencephalic plane 1

Substantia Nigra





Planimetric assessment

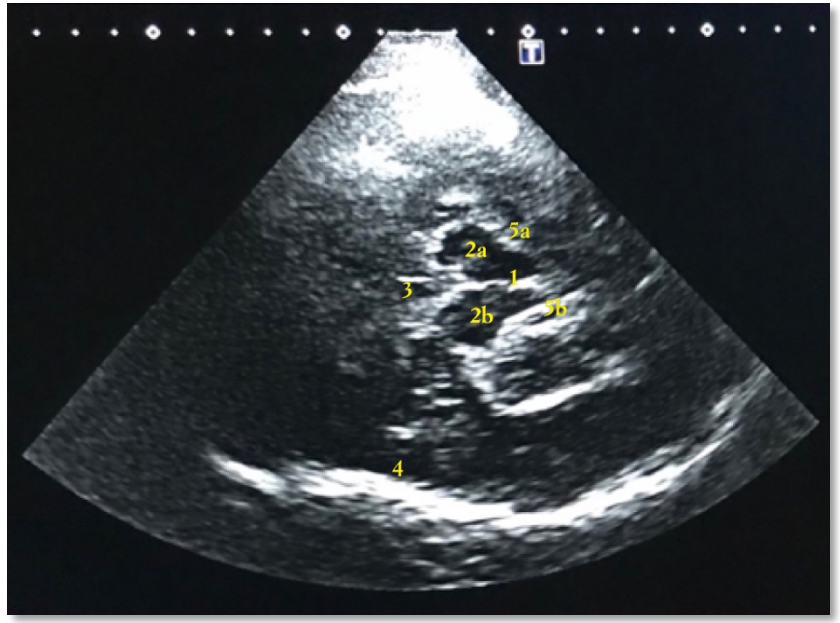
- 0,20 cm^2 - 0,25 cm^2: moderate hyperechogenicity
- > 0,25 cm^2: marked hyperechogenicity
- < 0,20 cm^2: normal

Echogenicity Grading

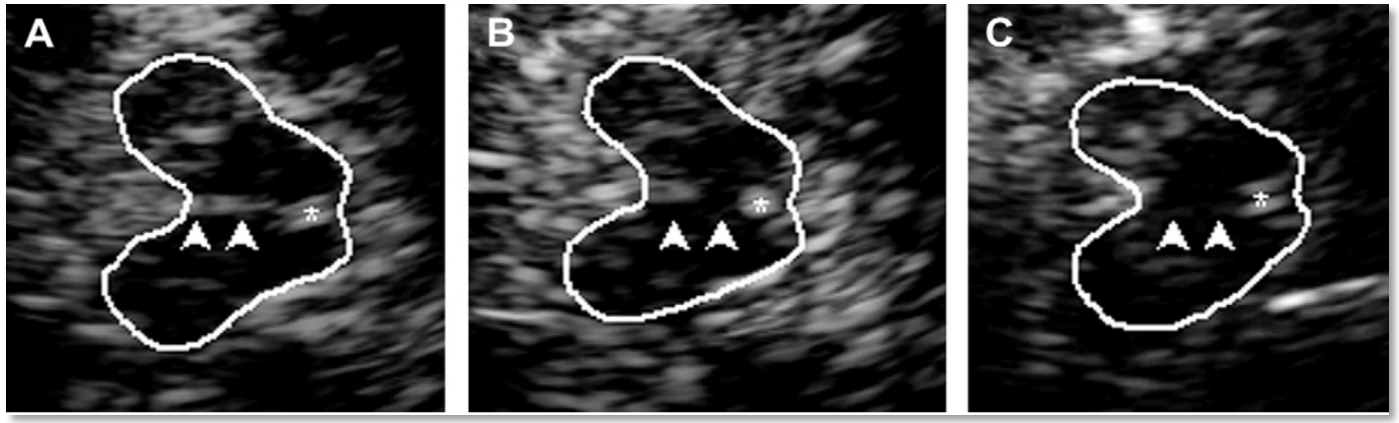
- Moderate
- Marked

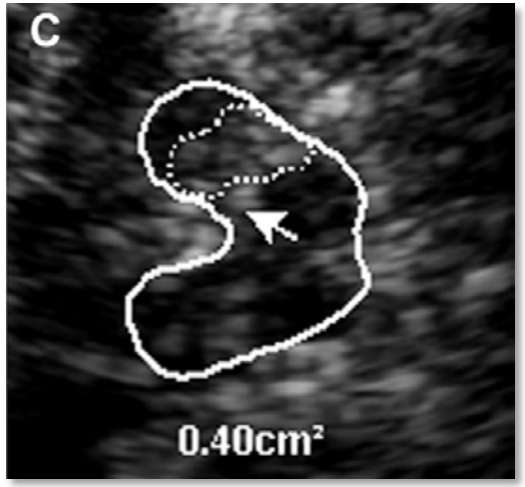
U. Walter *et al.*, «Transcranial brain parenchyma sonography in movement disorders: state of the art», *Ultrasound Med. Biol*

Mesencephalic plane 2



Raphe

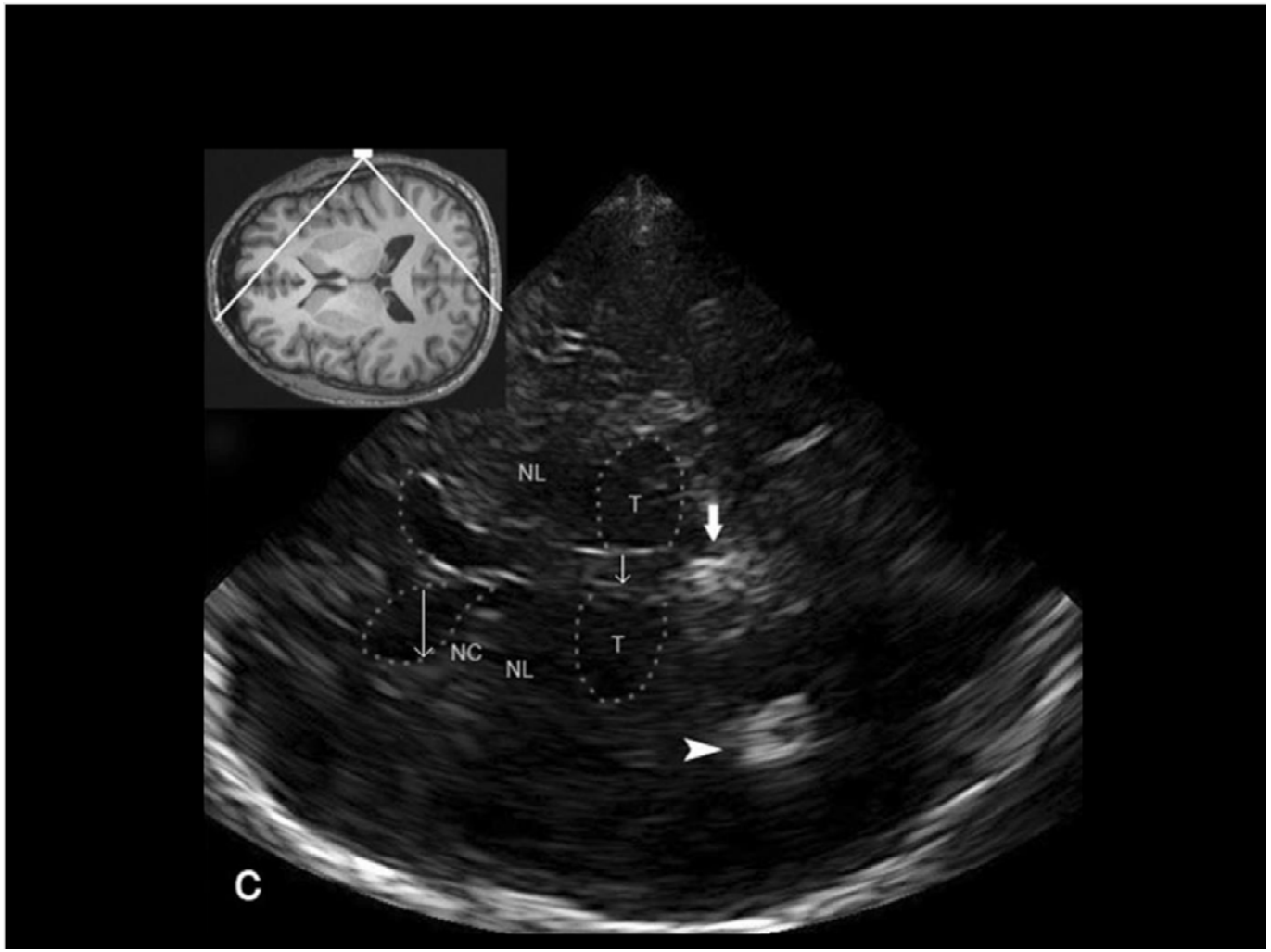




Hypoechogenicity is found in about 50% to 70% of individuals with unipolar depression

Red Nucleus

Diencephalic plane

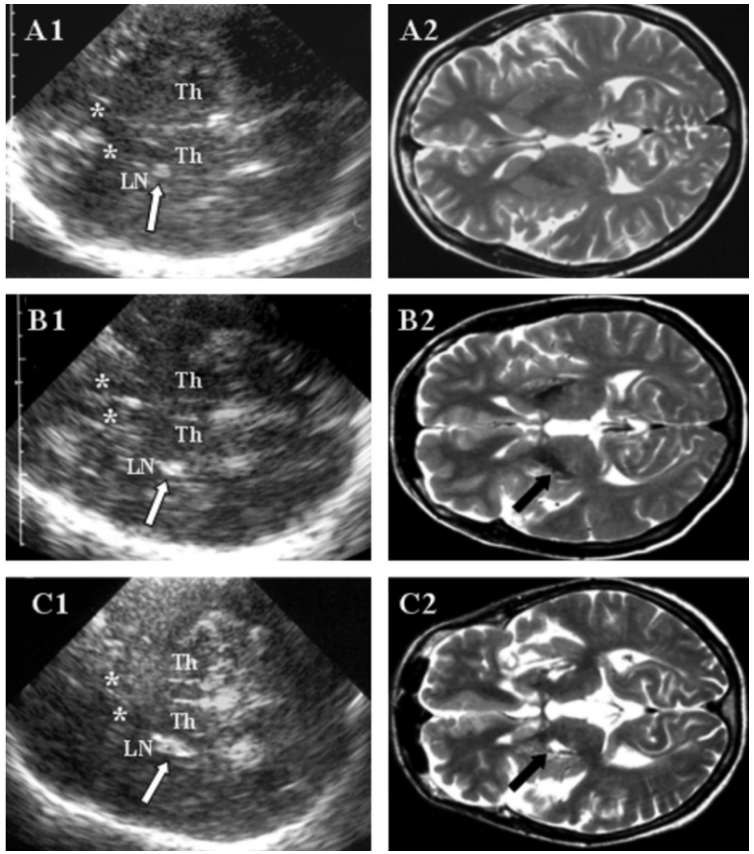


III ventricle

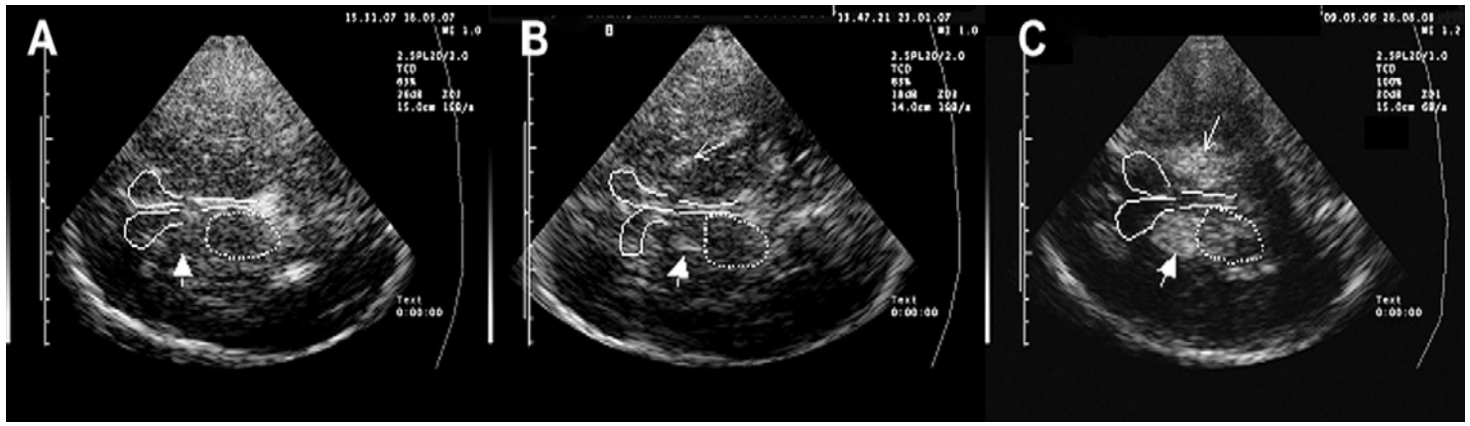
- < 60 years old: < 7 mm
- > 60 years old: < 10 mm

Diencephalic plane 2

Lenticular Nucleus



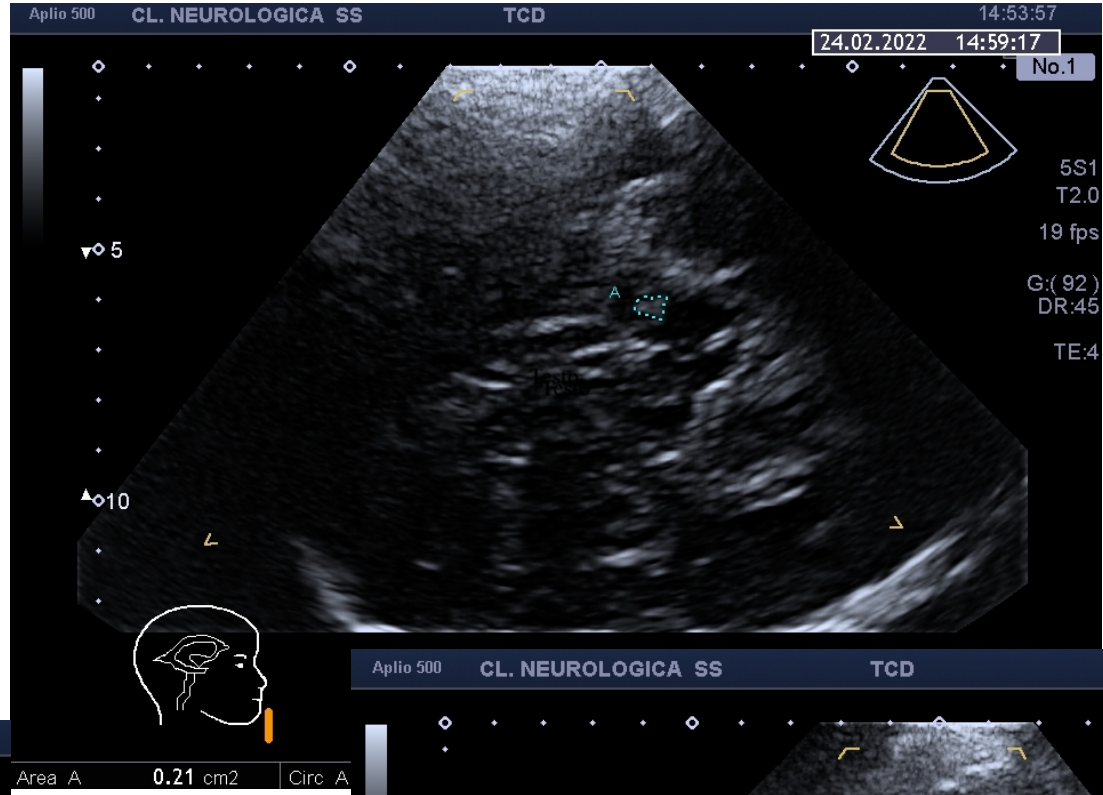
Thalamus

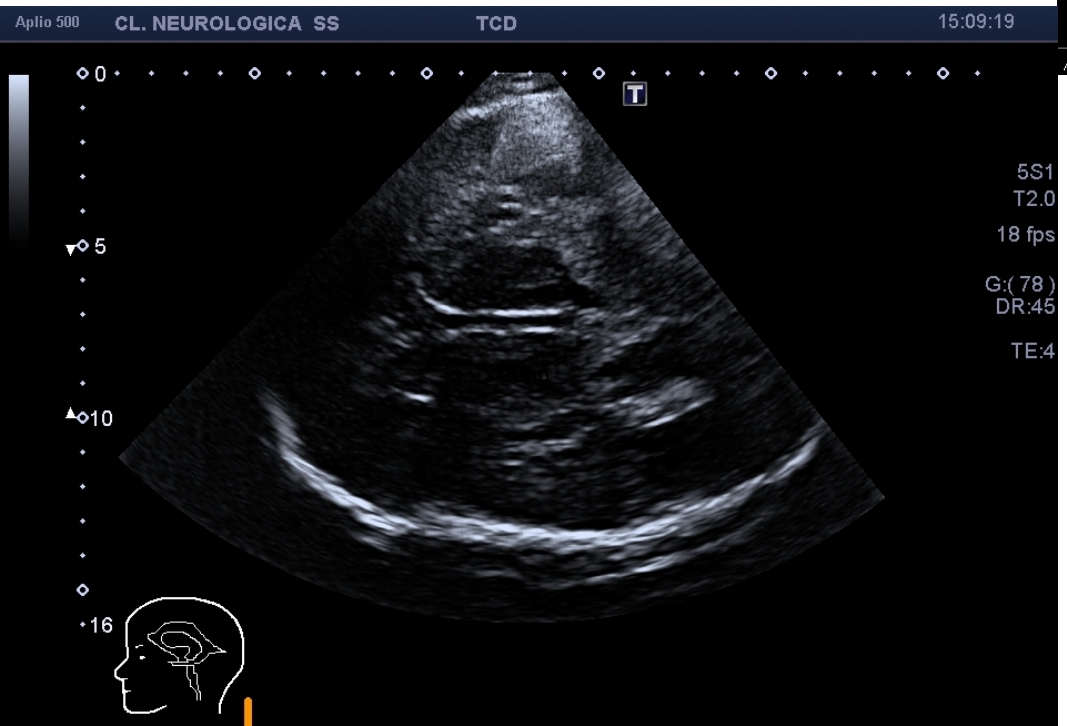


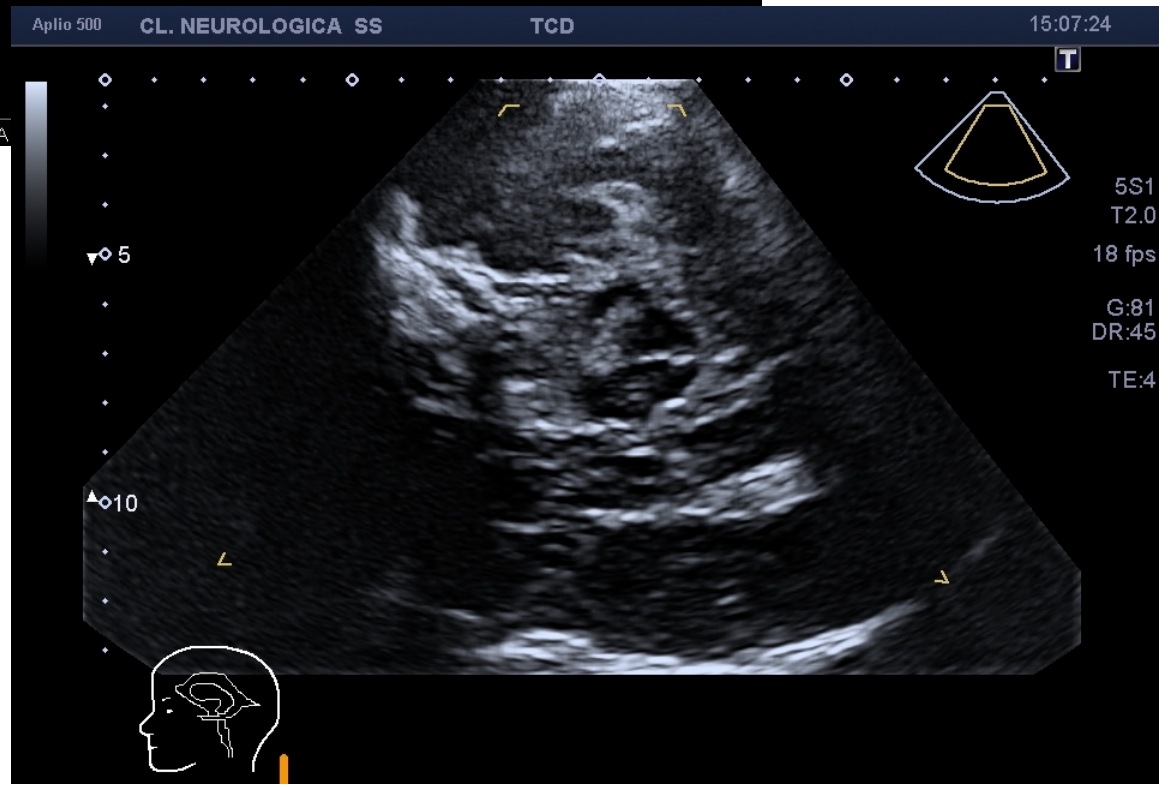
U. Walter, K. Krolikowski, B. Tarnacka, R. Benecke, A. Czlonkowska, e D. Dressler, «Sonographic detection of basal ganglia lesions in asymptomatic and symptomatic Wilson disease», Neurology, vol. 64, n. 10, pagg. 1726–1732, mag. 2005,

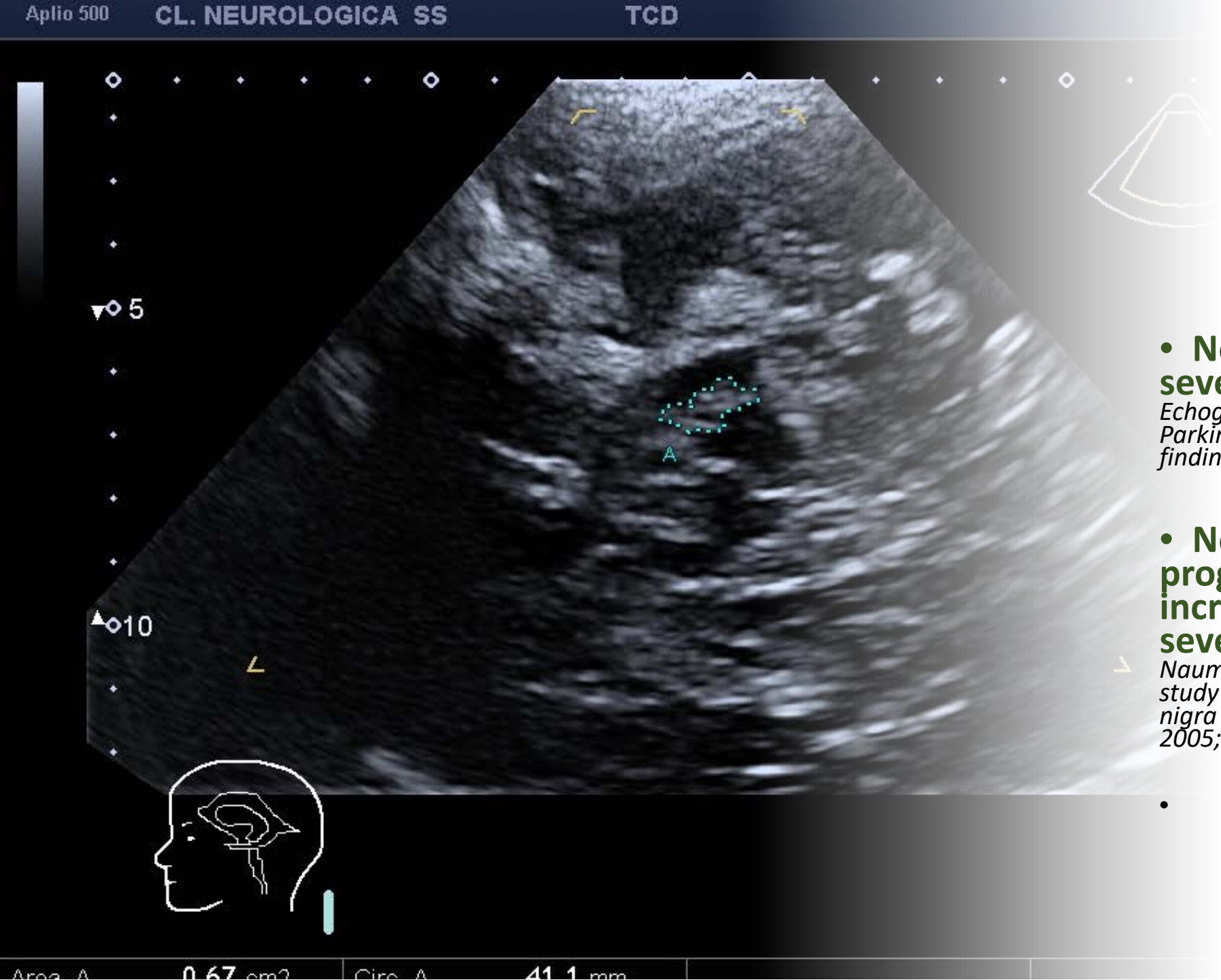
Parkinson’s Disease

- ✓ SN hyperechogenicity
- ✓ Normal raphe
- ✓ Normal III ventricle
- ✓ Normal lenticular nucleus









- **No association with disease severity** *(Berg D, Siefker C, Becker G. Echogenicity of the substantia nigra in Parkinson's disease and its relation to clinical findings. J Neu- rol. 2001)*

- **No modification with progression, although is most increased controlateral to severe side** *(Berg D, Merz B, Reiners K, Naumann M, Becker G. Five-year follow-up study of hyperechogenicity of the substantia nigra in Parkinson's disease. Mov Disord. 2005;20:383–385)*

-

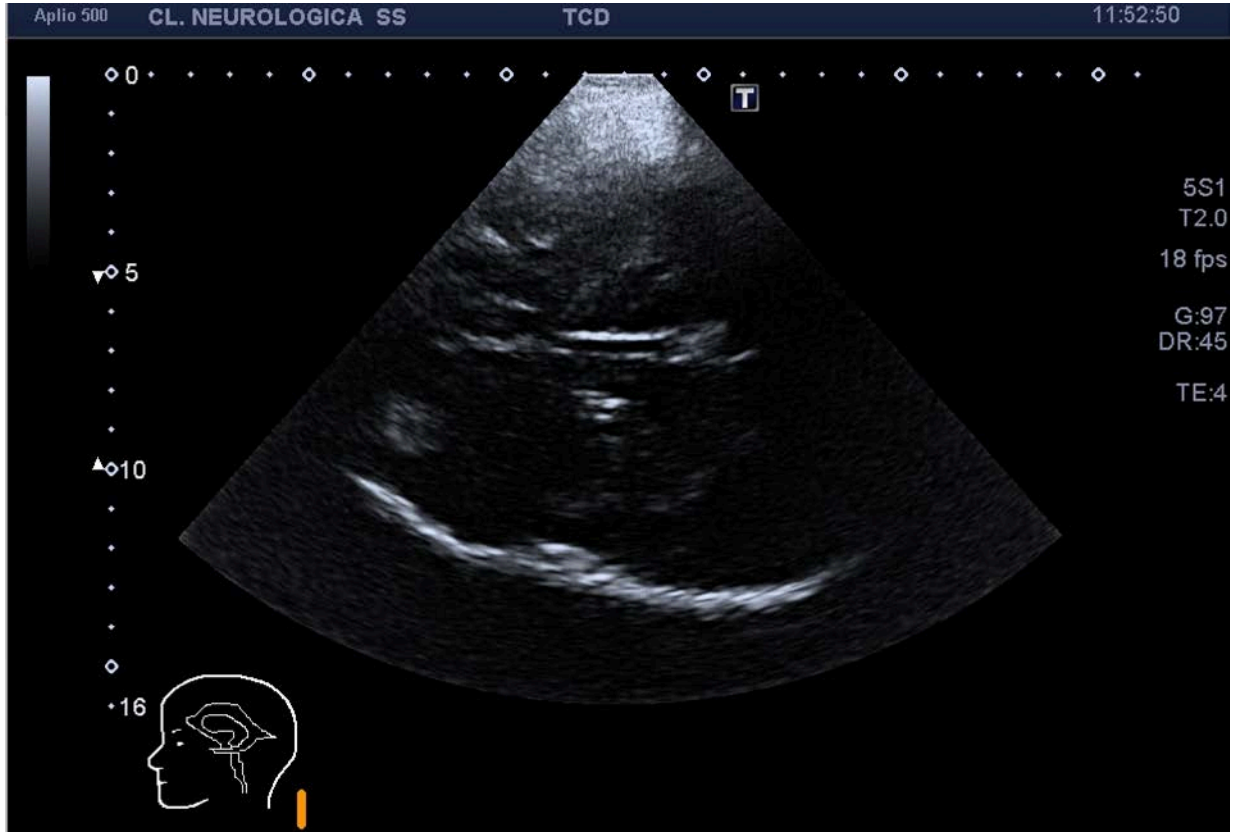
Atypical Parkinsonisms

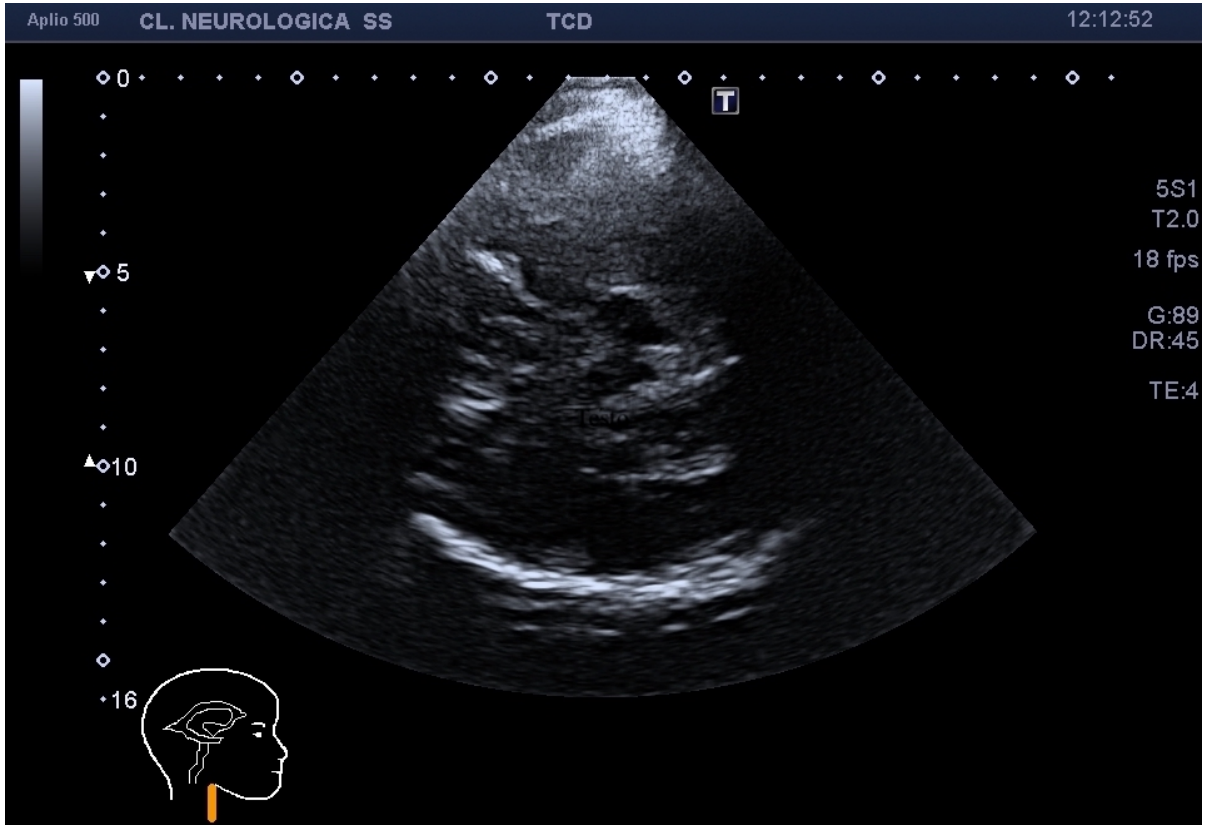
- ✓ SN normally echogenic or only slightly hyperechoic
- ✓ Lenticular nucleus hyperechogenic
- ✓ In PSP increased III ventricle width.

Neurology®

Brain parenchyma sonography discriminates Parkinson's disease and atypical parkinsonian syndromes
U. Walter, L. Niehaus, T. Probst, et al.
Neurology 2003;60;74-77
DOI 10.1212/WNL.60.1.74

This information is current as of January 14, 2003

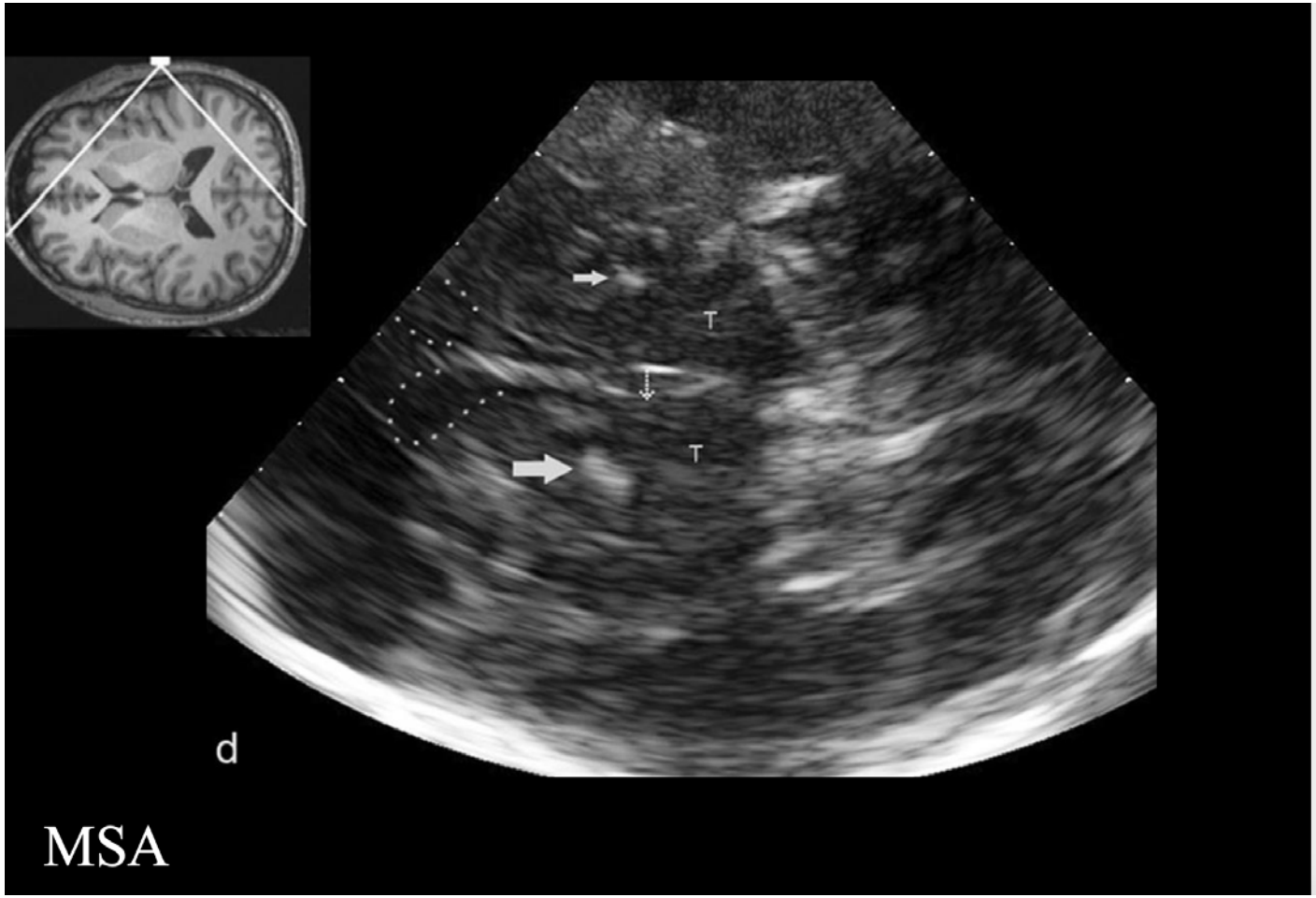




Multiple System Atrophy (MSA)

SN hyperechogenicity 0-25% *(Behnke et al. 2005; Okawa et al. 2007); Walter et al.2007; Gaenslen et al.2008)*

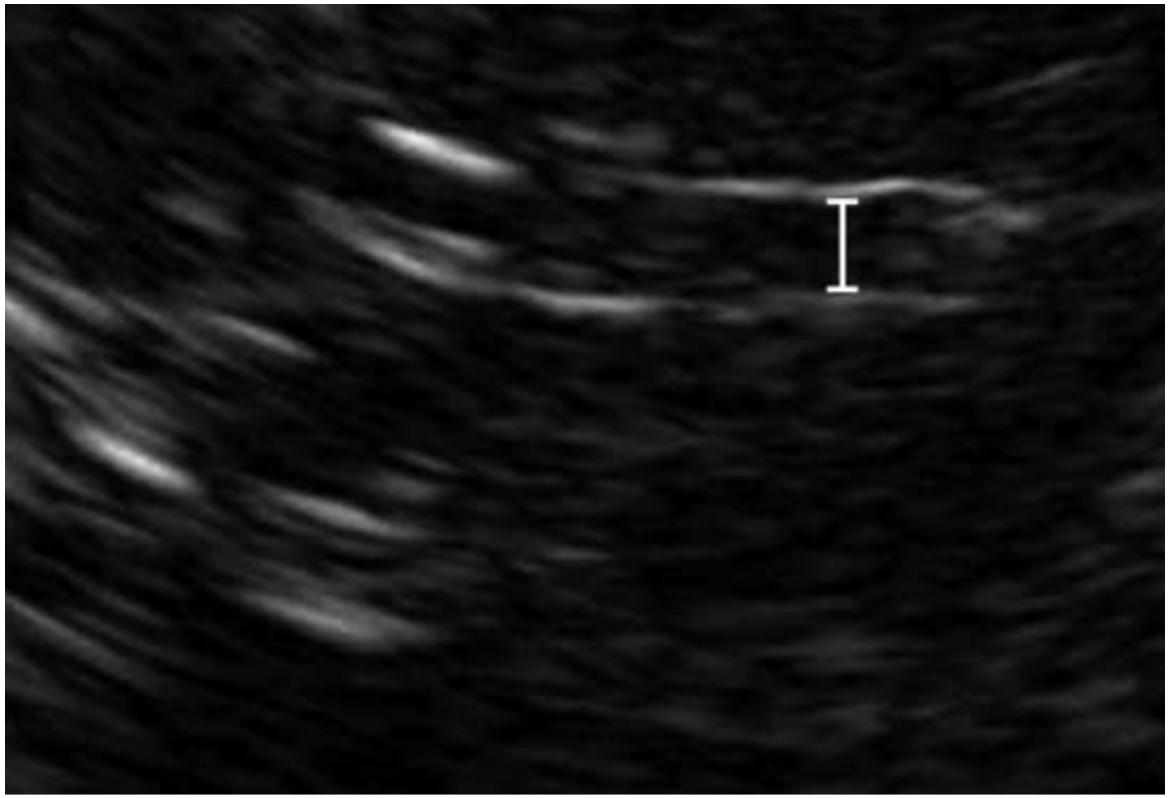
Hyperechogenicity of the lentiform nucleus is found more than 70% of MSA patients

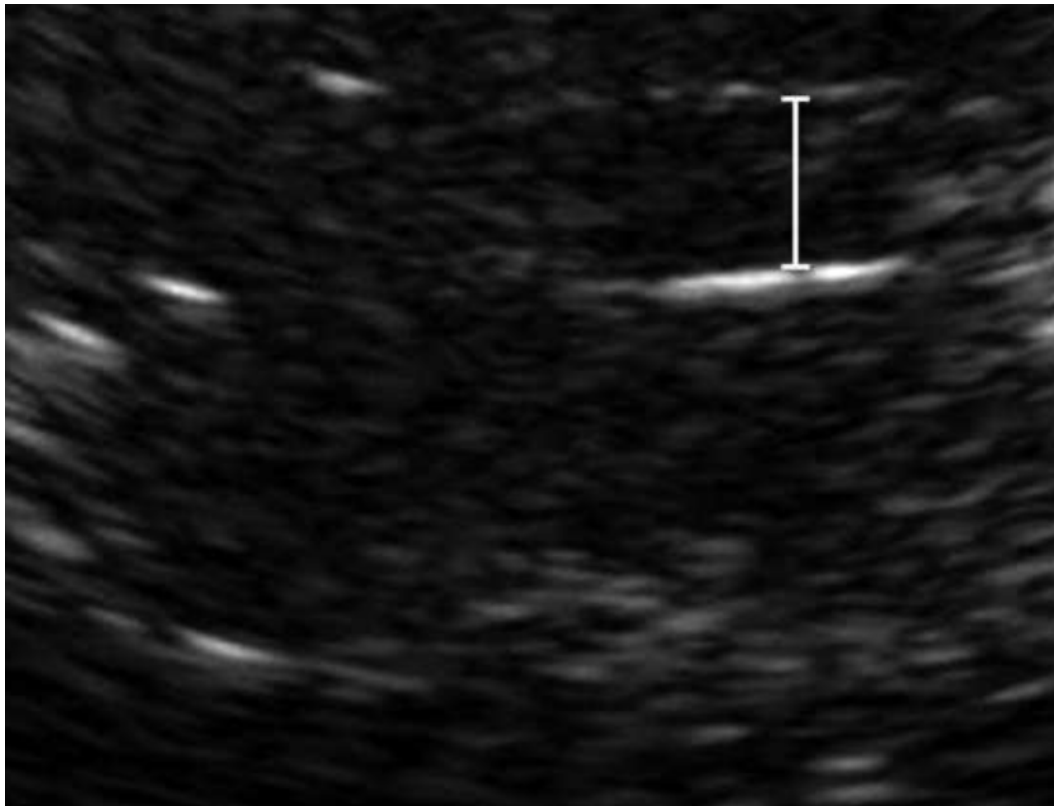


Progressive Supranuclear Palsy (PSP)

SN hyperechogenicity 0-41% *(Behnke et al. 2005; Okawa et al. 2007; Walter et al. 2007; Gaenslen et al. 2008)*

PSP-Parkinsonian subtype of PSP (86%) vs **PSP Richardson type** (1/27 + third ventricle dilatation)





(Bouwmans et al. 2010)

Lewy Body Disease

Uwe Walter
Dirk Dressler
Alexander Wolters
Matthias Wittstock
Brigitte Greim
Reiner Benecke

Sonographic discrimination of dementia with Lewy bodies and Parkinson's disease with dementia

Bilateral marked SN hyperechogenicity compared to PD

Not related to earlier disease onset

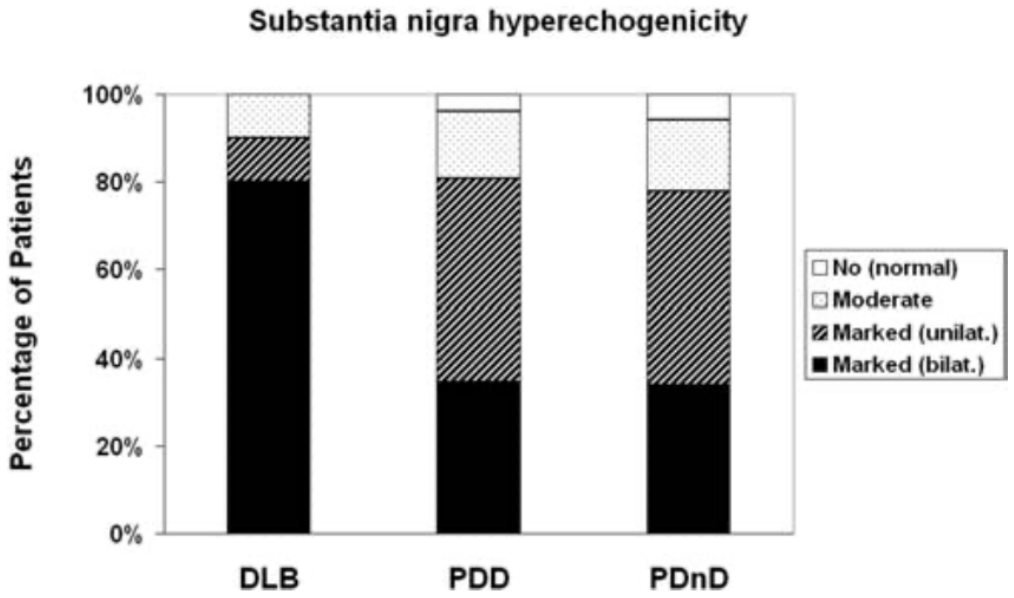


Fig. 1 Diagram showing degree of substantia nigra (SN) hyperechogenicity in patients with dementia with Lewy bodies (DLB), with Parkinson's disease with dementia (PDD), and with Parkinson's disease without dementia (PDnD) in whom SN echogenicity was bilaterally assessable. For both, DLB and PD, SN hyperechogenicity is a characteristic finding. However, in DLB patients SN hyperechogenicity is even more pronounced, with higher frequency of bilateral marked SN hyperechogenicity compared to PDD and PDnD patients

Corticobasal Degeneration

SN hyperechogenicity is frequent (88%)

The co-occurence of hyperechogenicity of lenticular nucleus may help to differentiate

Third-ventricle width < 10 mm

Neurology®

Sonographic discrimination of corticobasal degeneration vs progressive supranuclear palsy

U. Walter, D. Dressler, A. Wolters, et al.

Neurology 2004;63;504-509
DOI 10.1212/01.WNL.0000133006.17909.32

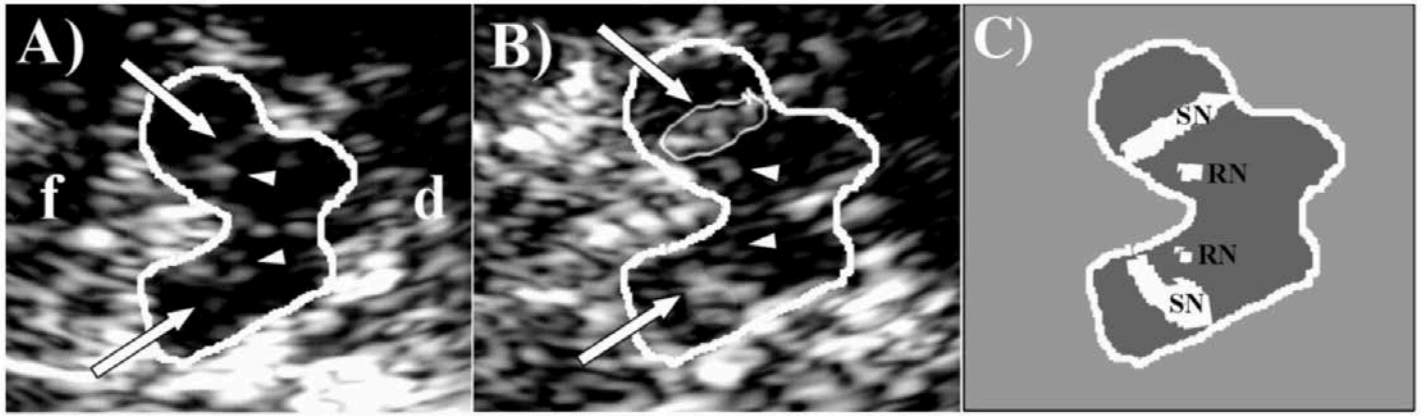
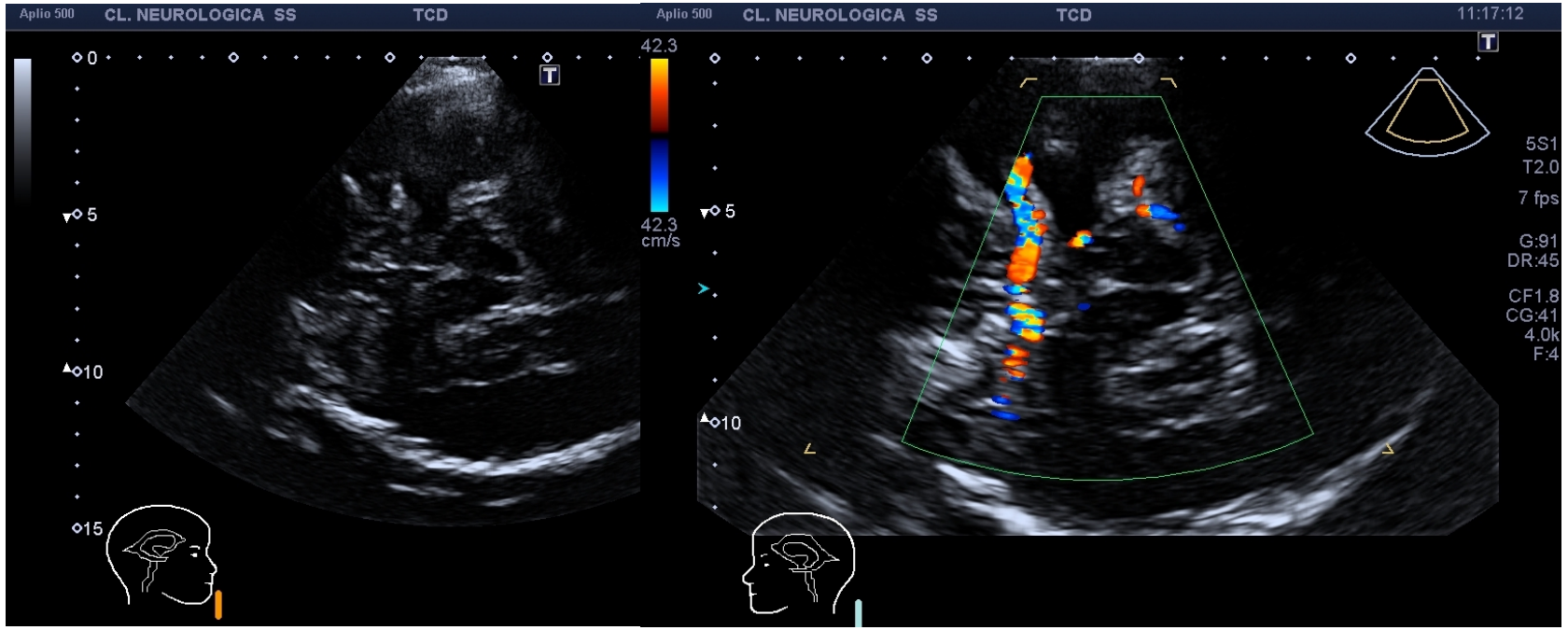


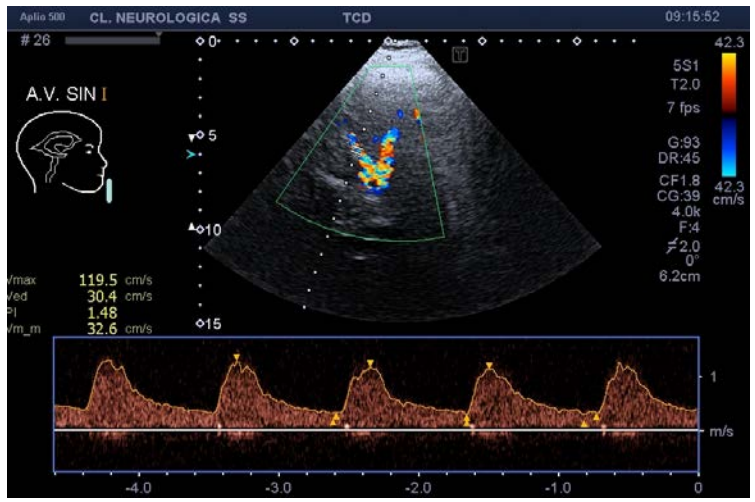
Figure 1. Sonographic images of identical midbrain axial sections in two patients. The butterfly-shaped midbrain is encircled for better visualization; f = frontal, d = dorsal. (A) Patient with progressive supranuclear palsy (PSP) exhibiting normal, nearly invisible substantia nigra (arrows) [red nuclei: arrowheads]. (B) Patient with corticobasal degeneration (CBD). Note the marked bilateral hyperechogenicity of the substantia nigra (arrows) [red nuclei: arrowheads]. Echogenic area of the right substantia nigra was encircled for computerized measurement. (C) Schematic illustration of (B): Within the encircled midbrain axial section, the bilateral substantia nigra (SN) and red nuclei (RN) are highlighted.

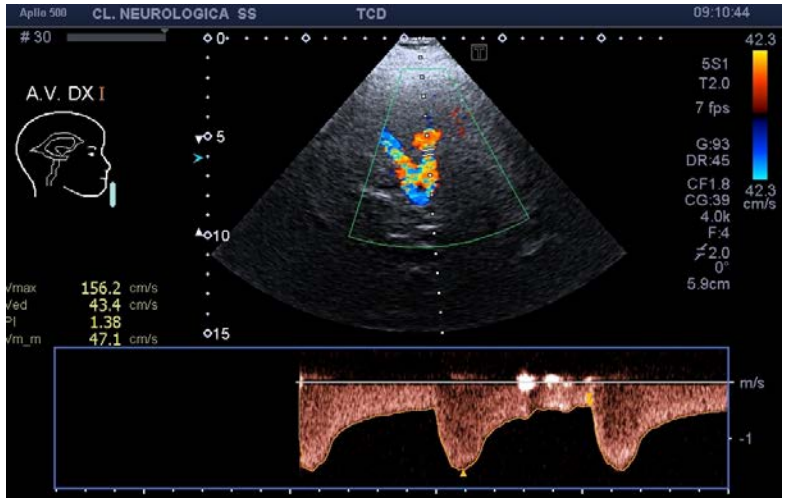
Vascular parkinsonism

(Tsai et al. Transcranial color-coded sonography helps differentiation between idiopathic Parkinson's disease and vascular parkinsonism. 2007)

Donna, 63 anni
AR: stenosi a.succlavia sn, IRC III stadio, ipertensione arteriosa, agenesia seni frontali. Ipertrofisa turbinati. Familiarità per MP.
Da circa sei mesi tremore AS sn.
ENO: Acinesia bilat (>sn), minimo tremore a riposo. Minima instabilità alla tirata. Ridotto pendolamento a sinistra.
RM Encefalo (09/2020): «presenza di puntiformi aree ipointense nelle sequenze GE-T2* nel n.lenticolare bilateralmente, riferibili a minute calcificazioni.
DAT SPECT (08/2020): «non chiaro deficit della distribuzione del trasportatore presinaptico della dopamina»







Essential tremor (ET)

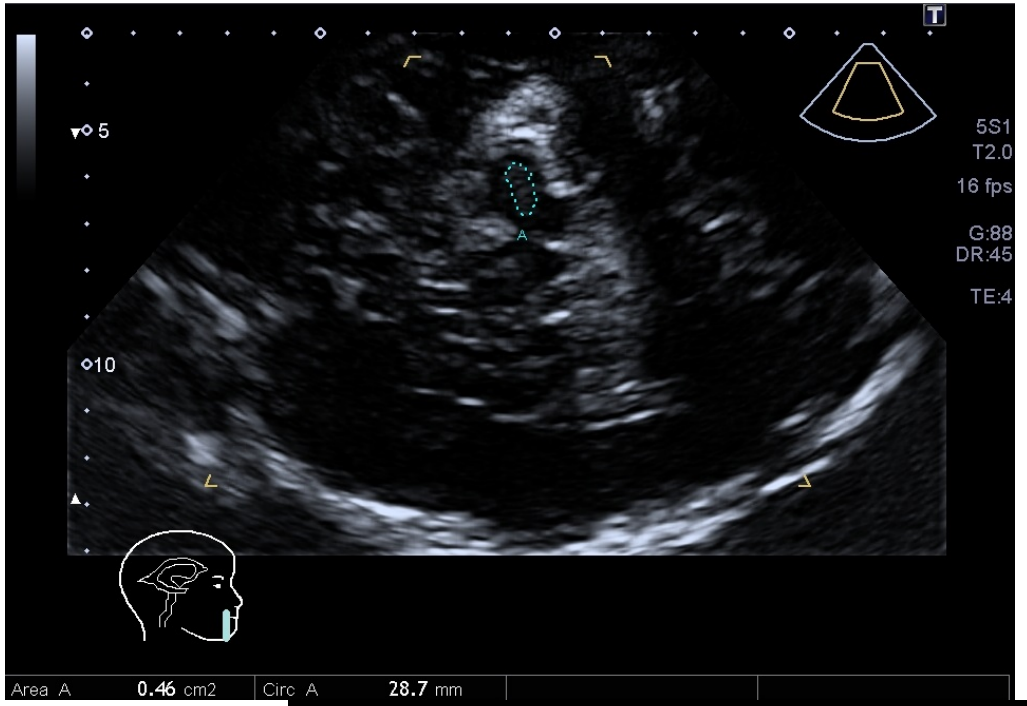
- ✓ ET patients have an increased risk of developing Parkinson's Disease (PD) during their lifetime.
- ✓ Absent SN hyperechogenicity *(Stockner H, Sojer M, K KS, Mueller J, Wenning GK, Schmidauer C, Poewe W. Midbrain sonography in patients with essential tremor. Mov Disord. 2007)*
- ✓ Patients with hyperechogenicity have an increased risk to develop PD

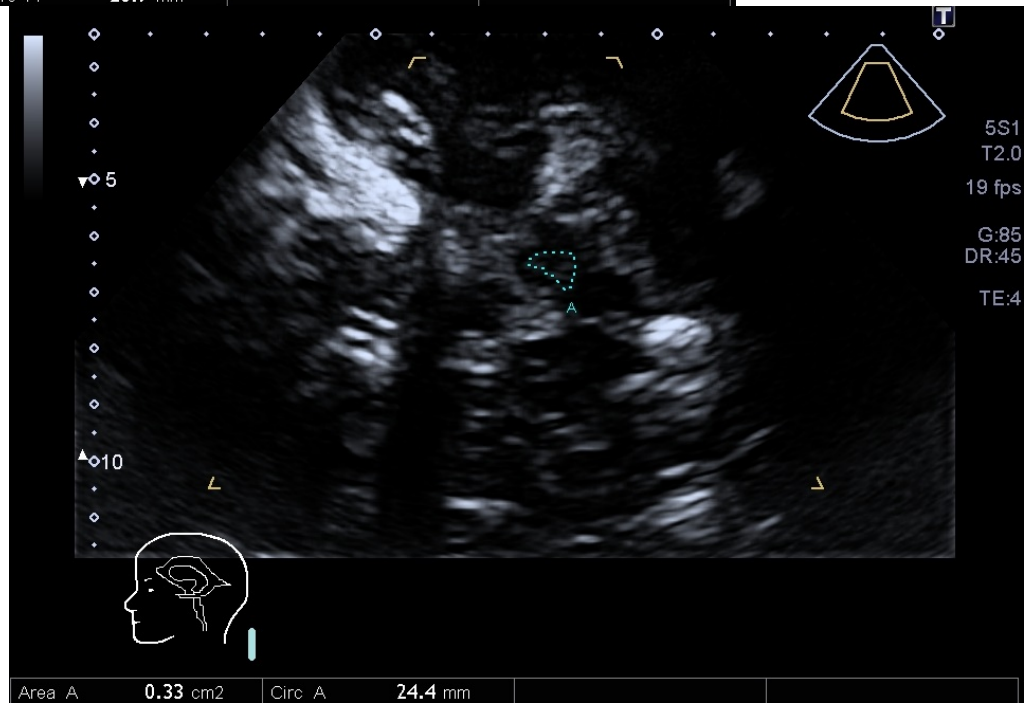
SWEDD *(Stockner et al. Is transcranial sonography useful to distinguish scans without evidence of dopaminergic deficit patients from Parkinson's disease? 2012)*

A female 76-years-old patient, suffering from ET from childhood developed tremor dominant PD, in the last year.

ENO: head and voice tremor, kinetic postural and rest tremor of upper limbs, greater on the left, bilateral bradykinesia and reduction of synkinesis.

Dopaminergic treatment was started with resolution of bradykinesia and improvement of tremor at rest. Brain MRI showed only mild brain atrophy; a DaT SPECT was apparently normal. BPS revealed a bilateral hyperechogenicity of the Substantia Nigra (SN, right 0,46 cm^2, left 0,33 cm^2) (**Figures)**





Advantages and Limits of the method

Advantages

- Broadly available
- Quick to perform in moving patients
- Non-invasive
- Inexpensive

Limits

- Dependency on the temporal acoustic bone window;
- Dependency of the method on the ultrasound system;
- Dependency on the experience and skill of investigator.

Reproducibility and diagnostic accuracy of substantia nigra sonography for the diagnosis of Parkinson's disease

Simone van de Loo,[1] Uwe Walter,[2] Stefanie Behnke,[3] Johann Hagenah,[4] Matthias Lorenz,[1] Matthias Sitzer,[1] Rüdiger Hilker,[1] Daniela Berg[5]

J Neurol Neurosurg Psychiatry 2010;81:1087-1092

Conclusions

- The diagnosis of PD and Parkinsonisms is still largely based on the clinical features

- BPS may have an important role in confirming the diagnosis in clinical practice

Grazie per l'attenzione!