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Association des Aidants
et Malades à Corps de Lewy

Colloque sur la maladie à corps de Lewy

Vendredi 24 novembre Bordeaux

université de BORDEAUX

Module 2

La recherche sur la maladie à corps de Lewy

Module présidé par :

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Neurologue – Bordeaux

CHU Hôpitaux de Bordeaux

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Sommaire : la recherche sur la MCL

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Biomarqueurs scintigraphiques

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VIEWS & REVIEWS

Diagnosis and management of dementia with Lewy bodies

Fourth consensus report of the DLB Consortium

(McKeith et al. Neurology 2017)

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.

Probable DLB can be diagnosed if:

a. Two or more core clinical features of DLB are present, with or without the presence of indicative biomarkers, or

b. Only one core clinical feature is present, but with one or more indicative biomarkers.

Probable DLB should not be diagnosed on the basis of biomarkers alone.

Possible DLB can be diagnosed if:

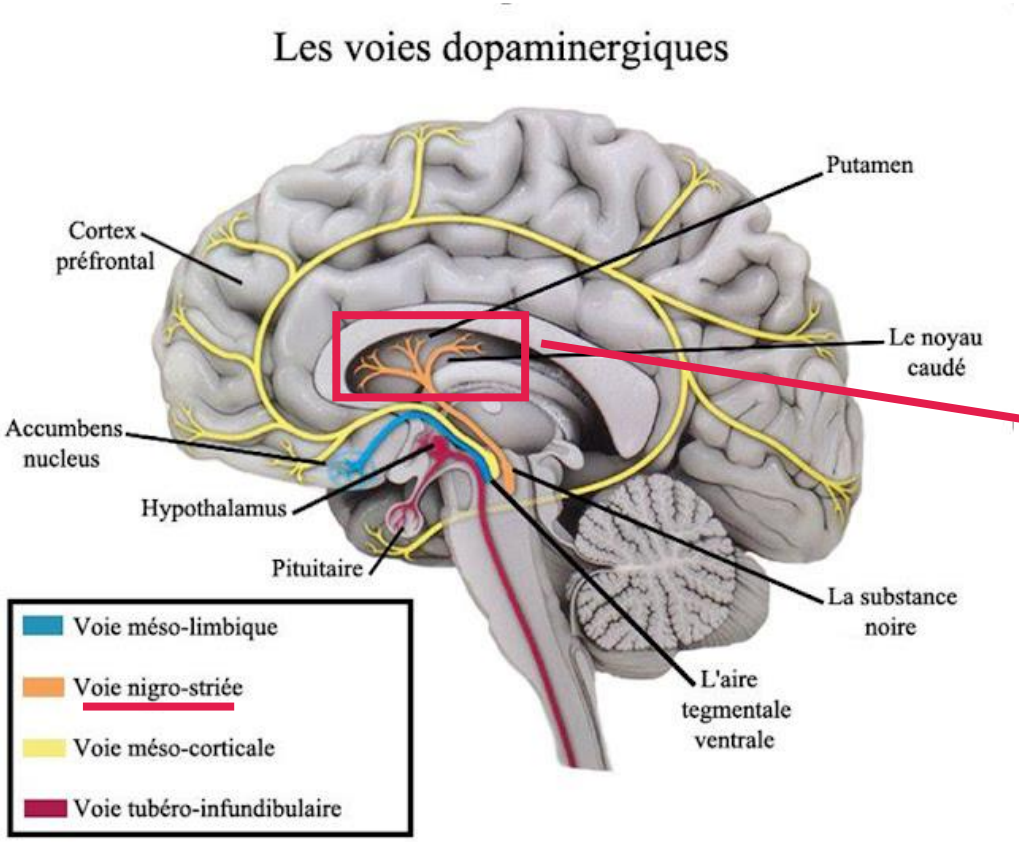
a. Only one core clinical feature of DLB is present, with no indicative biomarker evidence, or

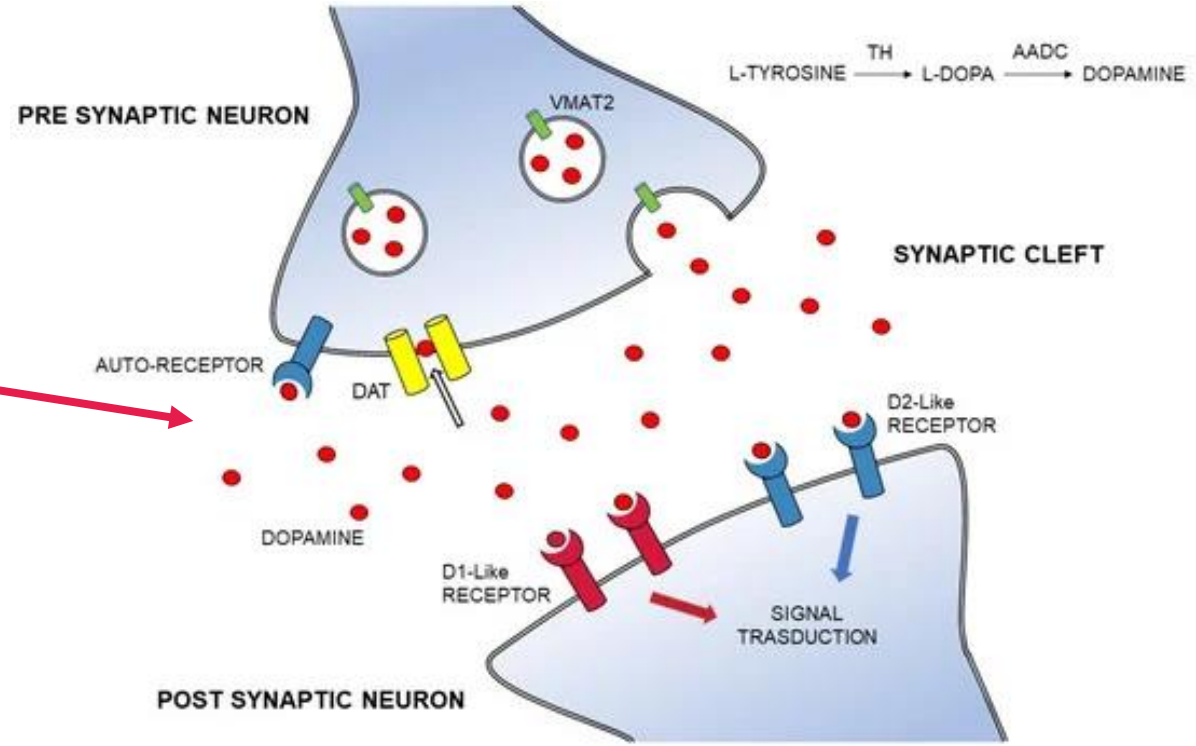
b. One or more indicative biomarkers is present but there are no core clinical features.

Sommaire

La scintigraphie cérébrale DaTSCAN

Dénervation dopaminergique dans les ganglions de la base

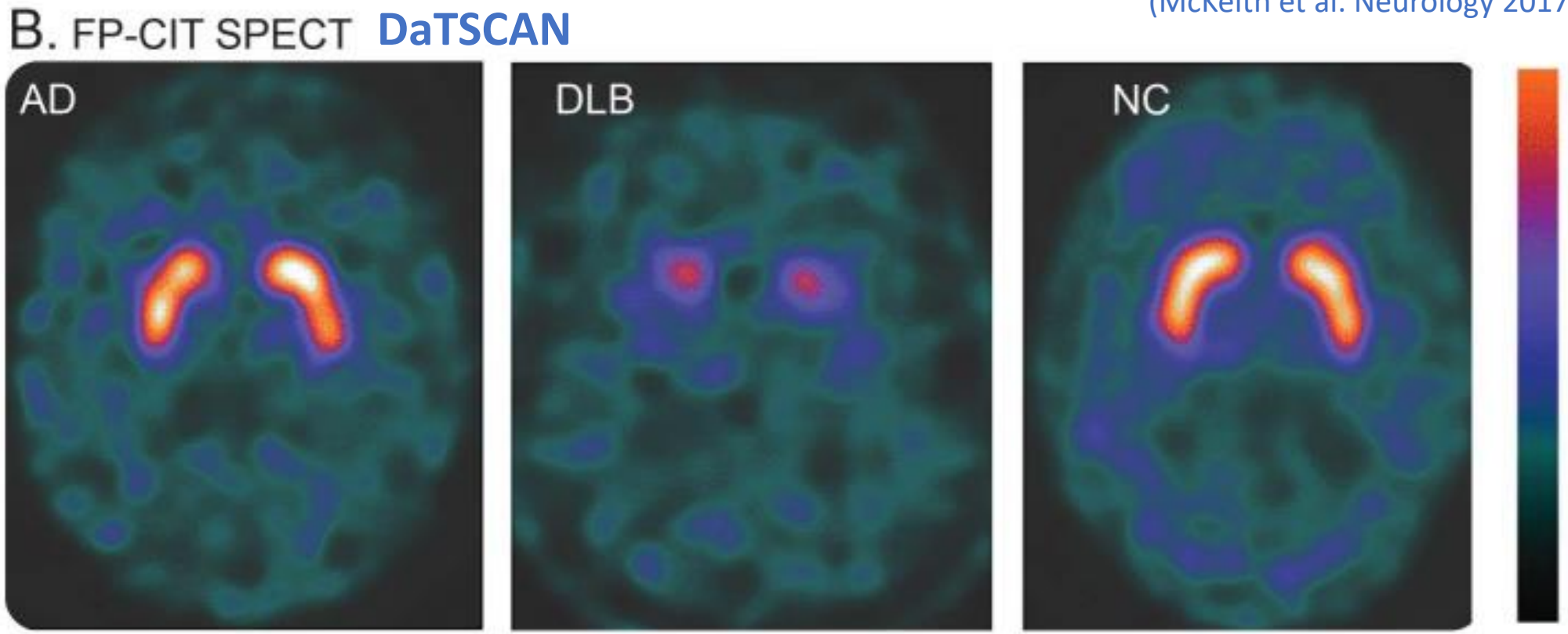




(Palermo et al. Int J. Mol. Sci. 2021)

Dénervation dopaminergique dans les ganglions de la base (SPECT)

(McKeith et al. Neurology 2017)



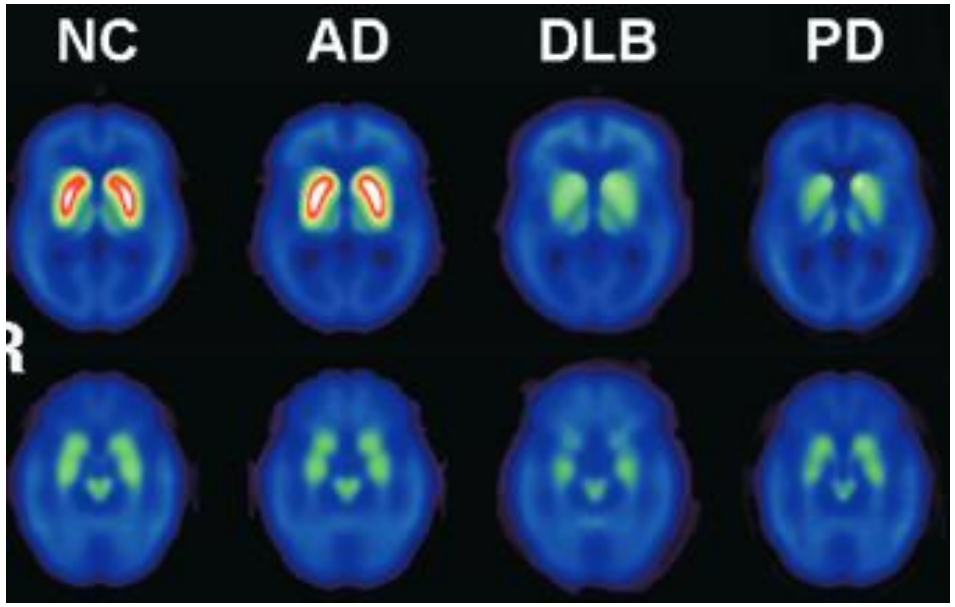
Se 78% - Sp 90%

Dénervation dopaminergique dans les ganglions de la base (PET)

[18F]Fluorodopa → Analogue de la dopamine pré-synaptique

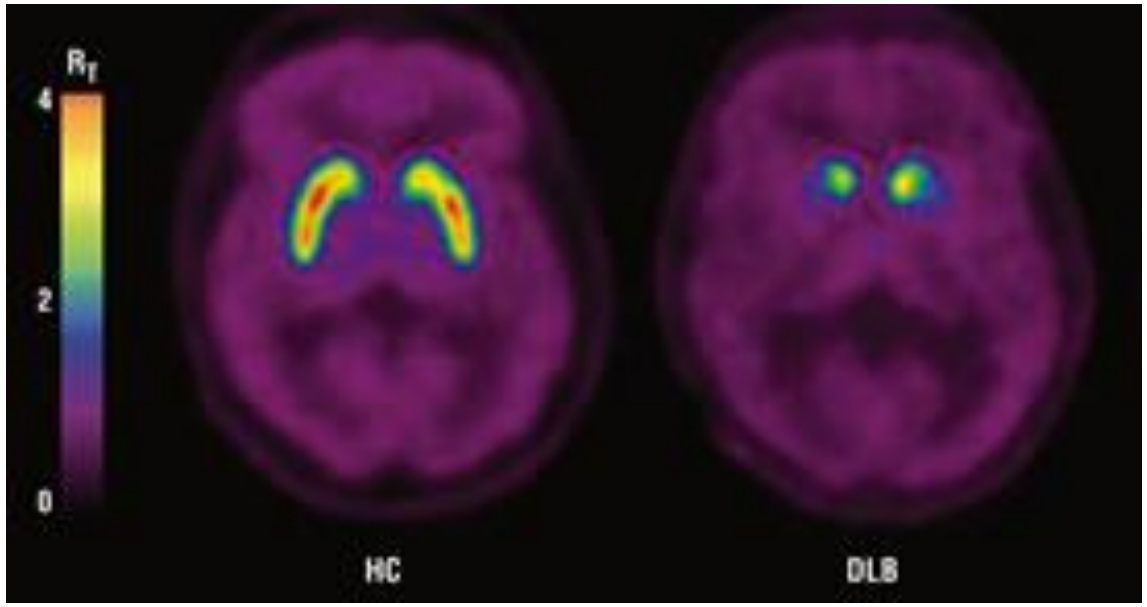
[11C]DTBZ, [18F]F-AV-133 → Cible le VMAT2 (presynaptic Vesicular Mono-Amine Transporter 2)
Moins d'interaction médicamenteuse que le DaTSCAN

[11C]DTBZ



(Koeppe et al. Alzheimers Dement 2018)

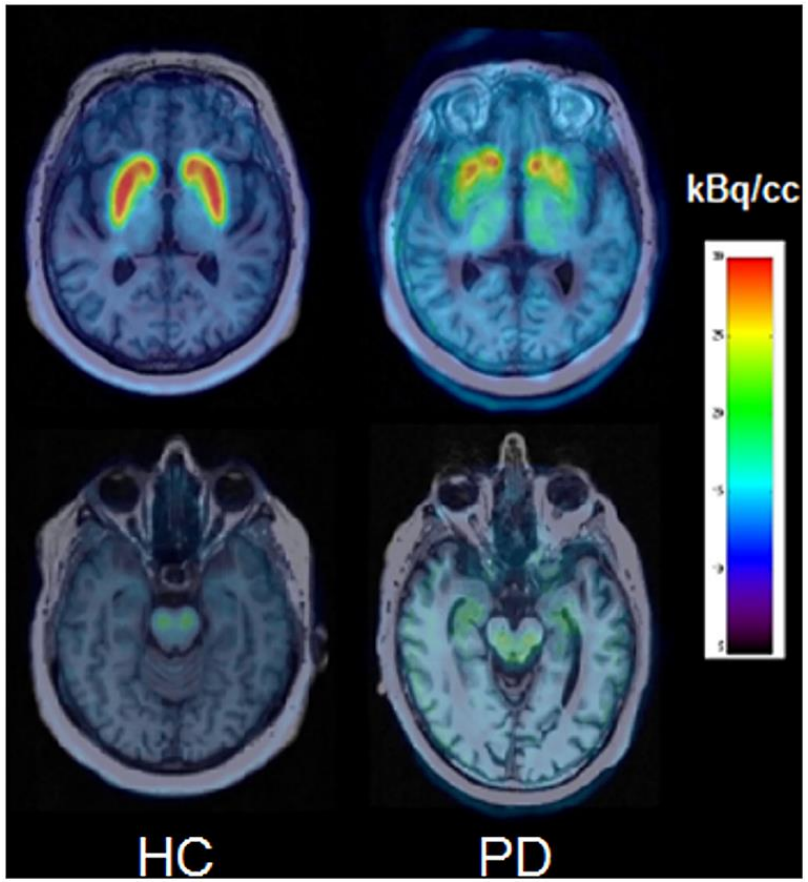
[18F]F-AV-133



(Villemagne et al. Arch Neurol 2011)

Dénervation dopaminergique dans les ganglions de la base (PET)

[18F]LBT-999 → Cible le DAT (comme le DaTSCAN)



(Ribeiro et al. Front Neurol 2020)

RECRUITING

[18F] LBT-999 PET Compared to [123I]-FP/CIT SPECT to Distinguish Between Parkinson's Diseases and Essential Tremor

ClinicalTrials.gov ID NCT04265209

Sponsor Zionexa

Information provided by Zionexa (Responsible Party)

Last Update Posted 2023-01-25

Brief Summary

Clinical study to demonstrate an at least equivalent performance of a new PET molecular Imaging radiopharmaceutical named [18F] LBT-999 in brain imaging compared to the SPECT reference method named [123I]-FP-CIT to establish the differential diagnosis between Parkinson's Disease and Essential Tremor.

Official Title

Non-inferiority Study of the Molecular Imaging of Dopamine Transporters Using [123I]-FP/CIT-SPECT and [18F] LBT-999-PET to Distinguish Between Parkinson's Disease and Essential Tremor.

Prochaine phase : Diagnostic différentiel entre maladie à corps de Lewy et maladie d'Alzheimer

La scintigraphie cardiaque MIBG

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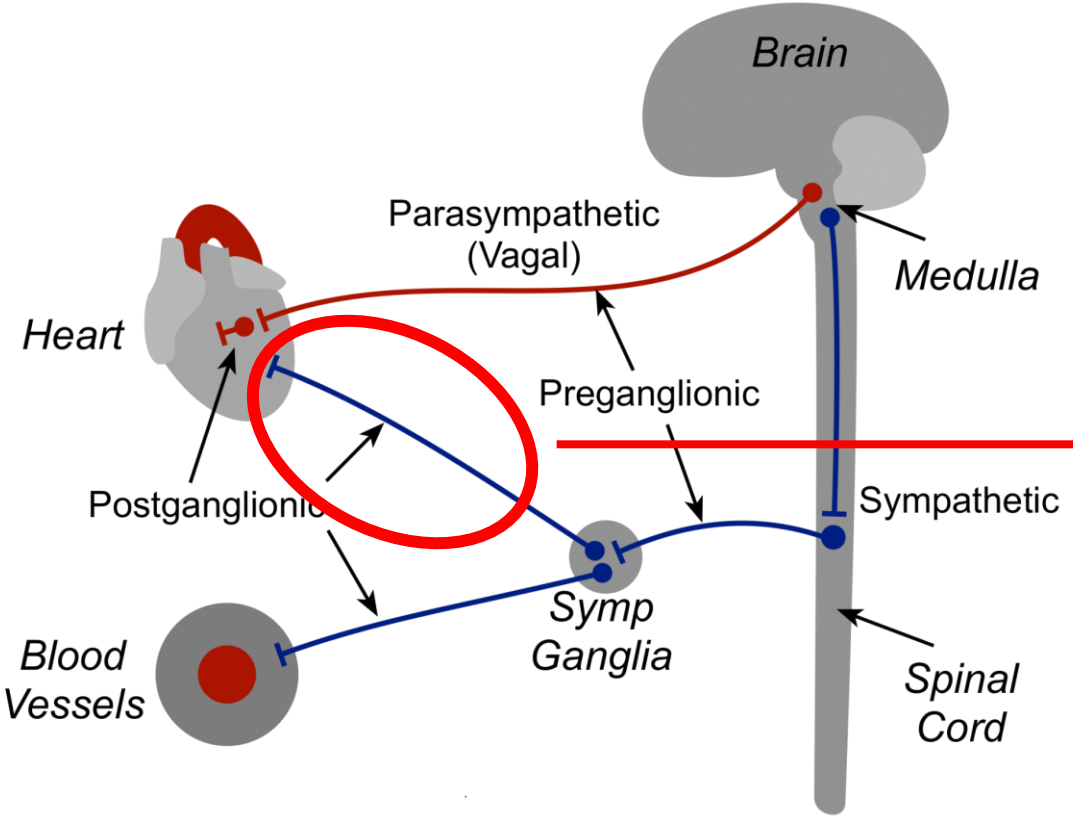
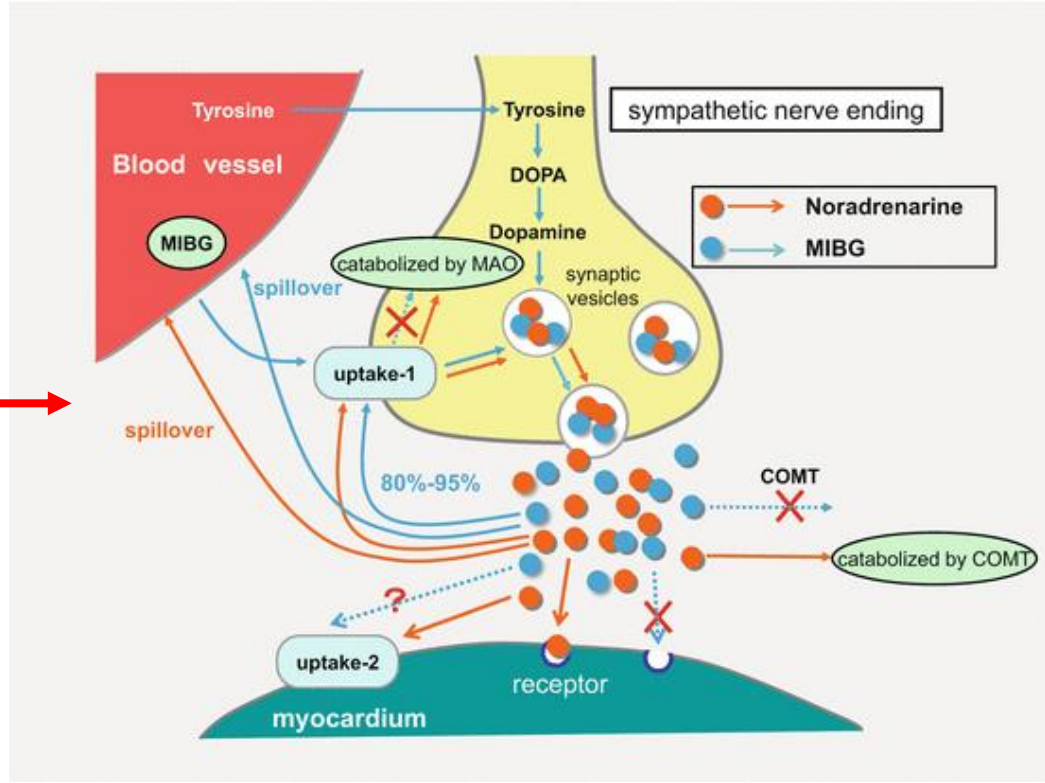
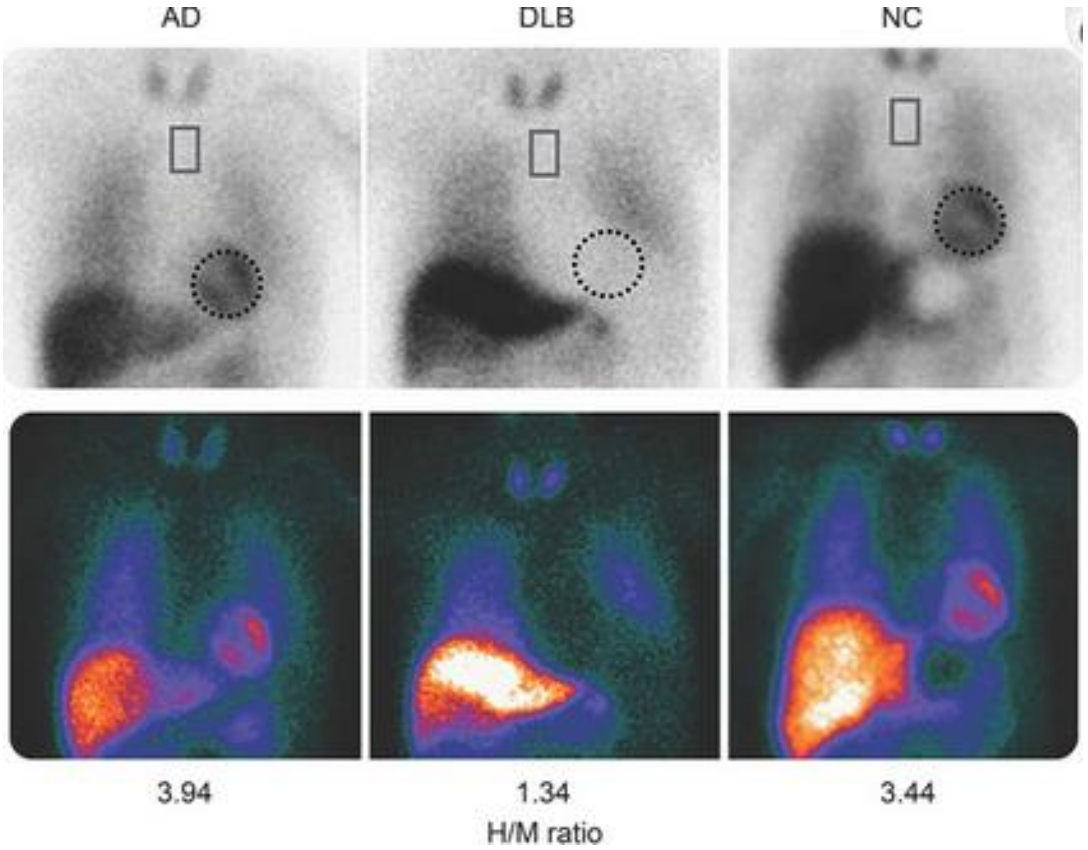
Scintigraphie cardiaque MIBG





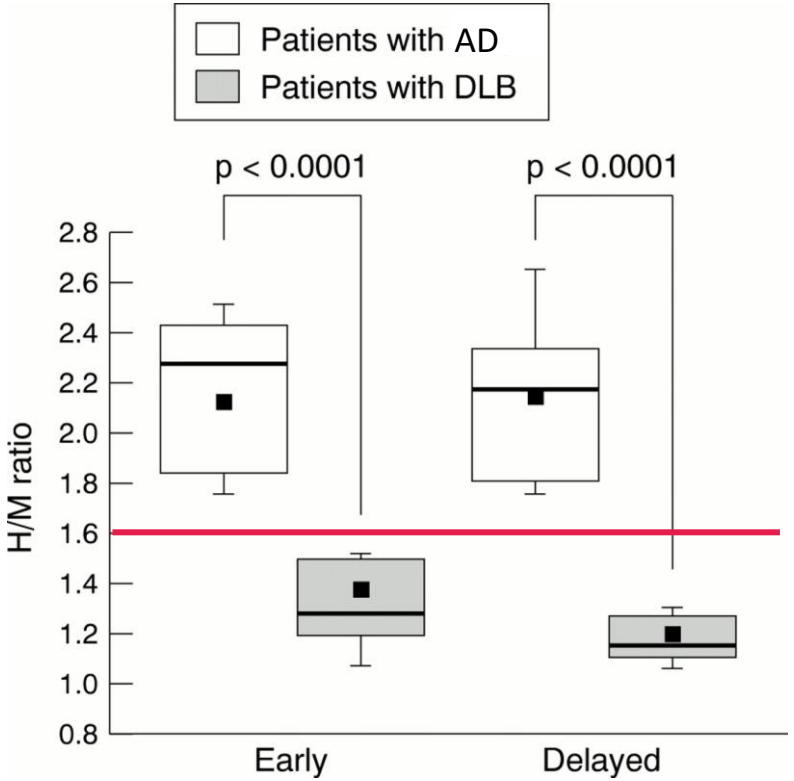
MIBG = Analogue de la noradrénaline

Scintigraphie cardiaque MIBG



Se 69% - Sp 87%

(McKeith et al. Neurology 2017)



(Yoshita et al. Neurol, Neurosurg & Psych 2001)

Scintigraphie cardiaque MIBG

Co-pathologie cardiaque ++
Interactions médicamenteuses ++

Drug group	Approved name	Recommended withdrawal time
Cardiovascular and sympathomimetic drugs		
Antiarrhythmics for ventricular arrhythmias	Amiodarone	Not practical to withdraw
Combined α/β-blocker	Labetalol	72 hours
Adrenergic neurone blockers	Bretylium	48 hours
	Guanethidine	48 hours
	Reserpine	48 hours
α-Blocker	Phenoxybenzamine (intravenous doses only)	15 days
Calcium channel blockers	Amlodipine	48 hours
	Diltiazem	24 hours
	Felodipine	48 hours
	Isradipine	48 hours
	Lacidipine	48 hours
	Lercanidipine	48 hours
	Nicardipine	48 hours
	Nifedipine	24 hours
	Nimodipine	24 hours
	Nisoldipine	48 hours
	Verapamil	48 hours
Inotropic sympathomimetics	Dobutamine	24 hours
	Dopamine	24 hours
	Dopexamine	24 hours
Vasoconstrictor sympathomimetics	Ephedrine	24 hours
	Metaraminol	24 hours
	Norepinephrine	24 hours
	Phenylephrine	24 hours
Opioid analgesics	Tramadol	24 hours
Tricyclic antidepressants	Amitriptyline	48 hours
	Amoxapine	48 hours
	Clomipramine	24 hours
	Dosulepin (dothiepin)	24 hours
	Doxepin	24 hours
	Imipramine	24 hours
	Lofepramine	48 hours
	Nortriptyline	24 hours
	Trimipramine	48 hours
Tricyclic-related antidepressants	Maprotiline	48 hours
	Mianserin	48 hours
	Trazolone	48 hours
	Venlaflaxine	48 hours
	Mirtazepine	8 days
	Reboxetine	3 days

Eur J Nucl Med Mol Imaging (2010) 37:2436–2446
DOI 10.1007/s00259-010-1545-7

GUIDELINES

$^{131}I/^{123}I$-Metaiodobenzylguanidine (mIBG) scintigraphy: procedure guidelines for tumour imaging

Drug group	Approved name	Recommended withdrawal time
β_2 stimulants (sympathomimetics)	Salbutamol	24 hours
	Terbutaline	24 hours
	Eformoterol	24 hours
	Bambuterol	24 hours
	Fenoterol	24 hours
	Salmeterol	24 hours
Other adrenoreceptor stimulants	Orciprenaline	24 hours
Systemic and local nasal decongestants, compound cough and cold preparations	Pseudoephedrine	48 hours
	Phenylephrine	48 hours
	Ephedrine	24 hours
	Xylometazoline	24 hours
	Oxymetazoline	24 hours
Sympathomimetics for glaucoma	Brimonidine	48 hours
	Dipivefrine	48 hours
Neurological drugs		
Antipsychotics (neuroleptics)	Chlorpromazine	24 hours
	Benperidol	48 hours
	Flupentixol	48 hours, or 1 month for depot
	Fluphenazine	24 hours, or 1 month for depot
	Haloperidol	48 or 1 month for depot
	Perphenazine	24 hours
	Pimozide	72 hours
	Pipotiazine	1 month for depot
	Prochlorperazine	24 hours
	Promazine	24 hours
	Sulpiride	48 hours
	Thioridazine	24 hours
	Trifluoperazine	48 hours
	Zuclopenthixol	48 hours, or 1 month for depot
	Amisulpride	72 hours
	Clozapine	7 days
	Olanzapine	7–10 days
	Quetiapine	48 hours
	Risperidone	5 days or 1 month for depot
	Sertindole	15 days
	Zotepine	5 days

La TEP/TDM cérébrale FDG

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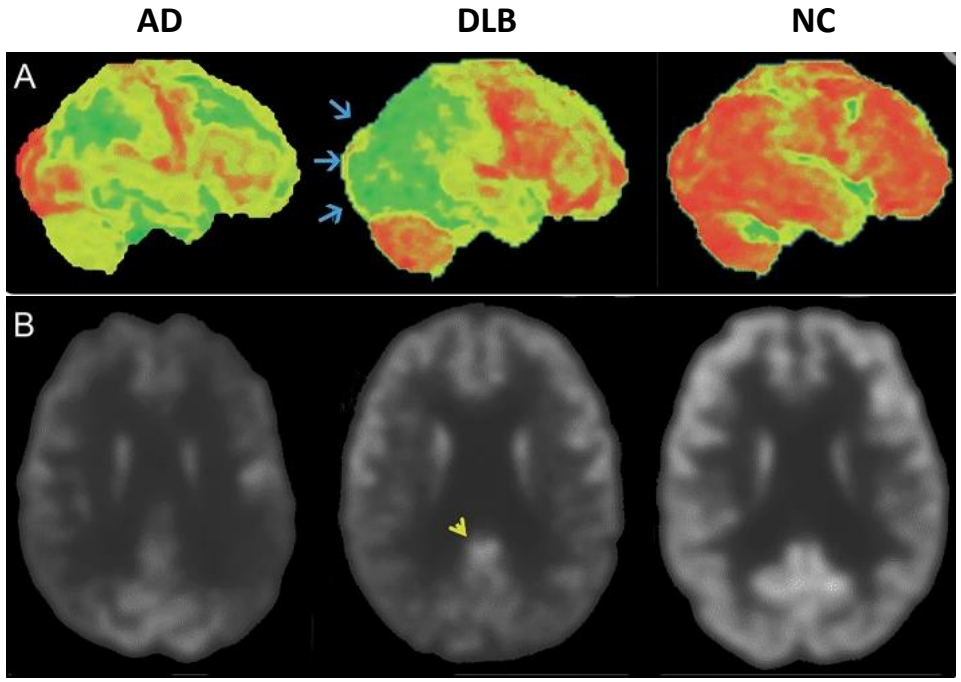
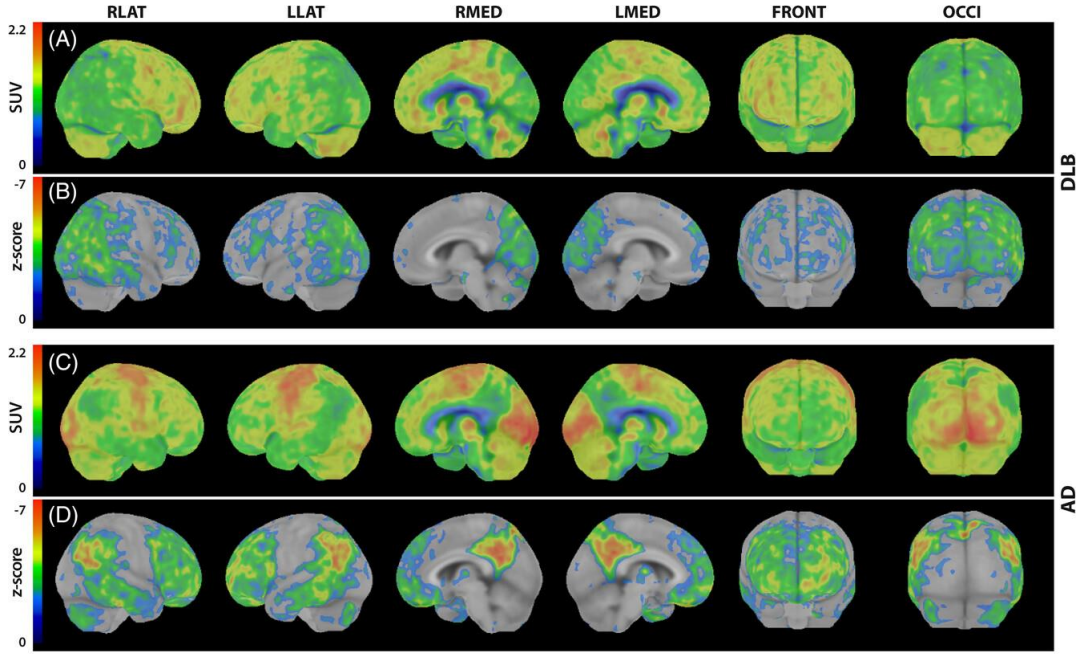
Hypométabolisme occipital et Cingulate Island Sign (CIS)

- FDG = Fluoro-Désoxy-Glucose = Sucre
- Neurone : métabolisme glucidique stricte → Fixation cérébrale physiologique intense du FDG
- Si perte neuronale : ↘ locale de la consommation de sucre : ↘ Fixation FDG



(McKeith et al. Neurology 2017)

Se 70% - Sp 74%

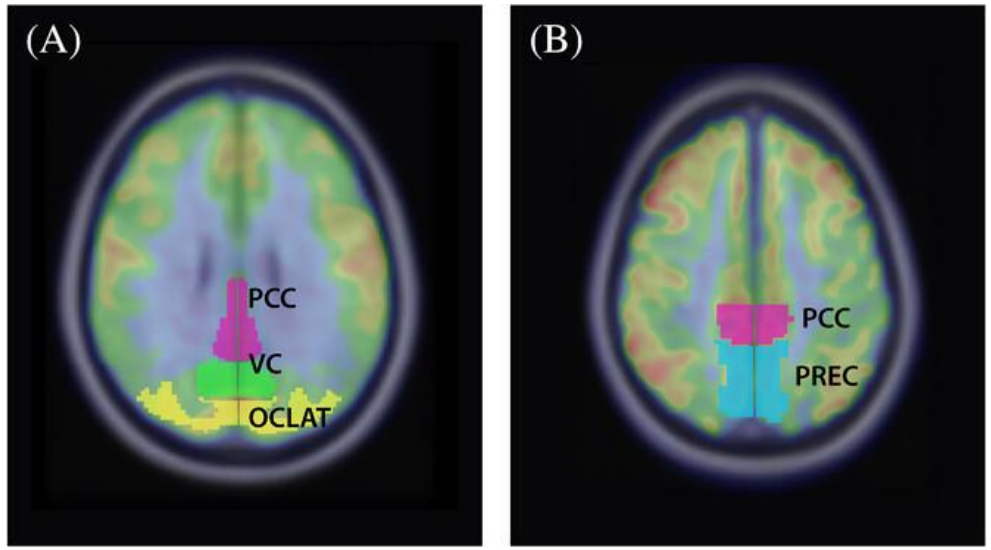


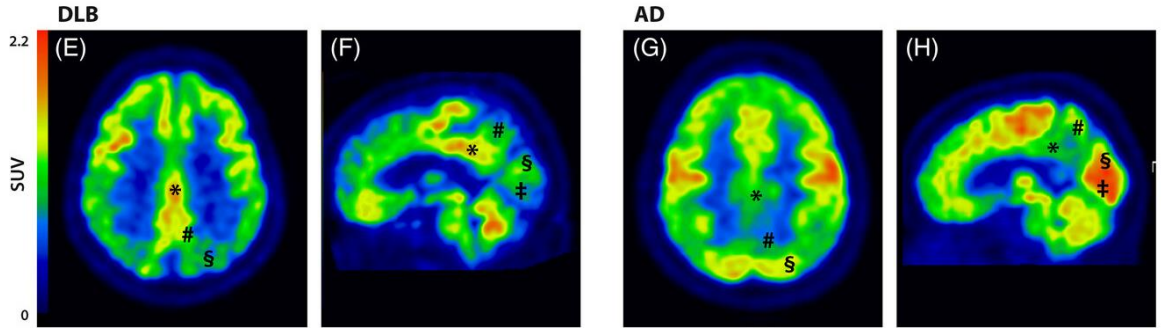
(Woyk et al. Neurology 2022)

Se 64-80% - Sp 60-73%

Hypométabolisme occipital et Cingulate Island Sign (CIS)

(Woyk et al. Neurology 2022)





$$CIS\ RATIO = \frac{PCC}{PREC + VC}$$

(le plus utilisé)

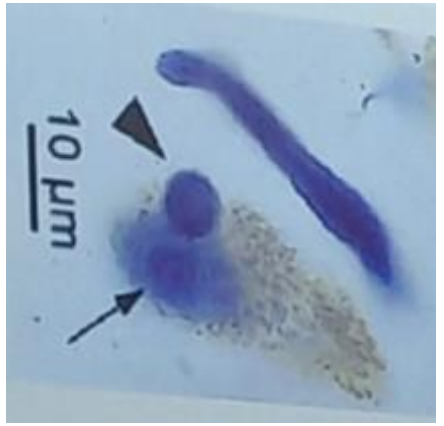
Cut-off = 0,4995
Se 61,1% - Sp 71,1%

$$CIS\ RATIO = \frac{PCC}{VC + OCLAT}$$

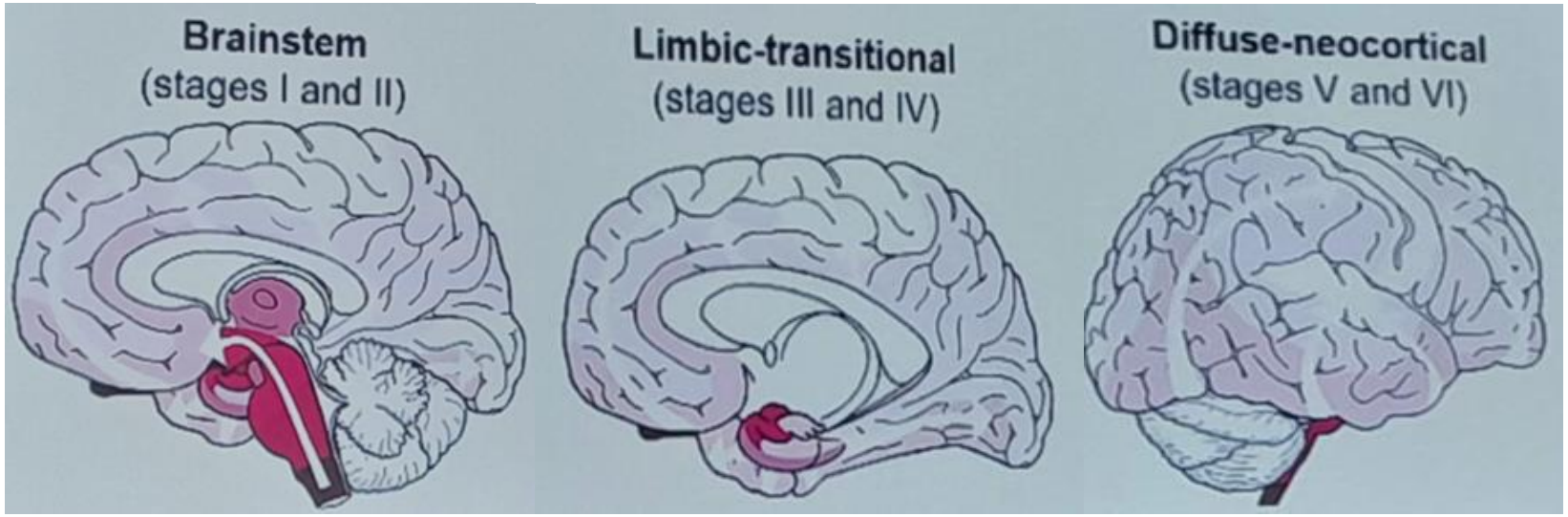
Cut-off = 0,5103
Se 75% - Sp 82,2%

La TEP/TDM cérébrale a-synucléine

PHYSIOATHOLOGIE



- Agrégation pathologique de protéines α-synucléines : Corps de Lewy
- Dysfonction synaptique – Perte neuronale
- Braak staging vs McKeith Staging (non applicable dans 50% des cas)



(Braak et al. Neurobiol Aging 2003)

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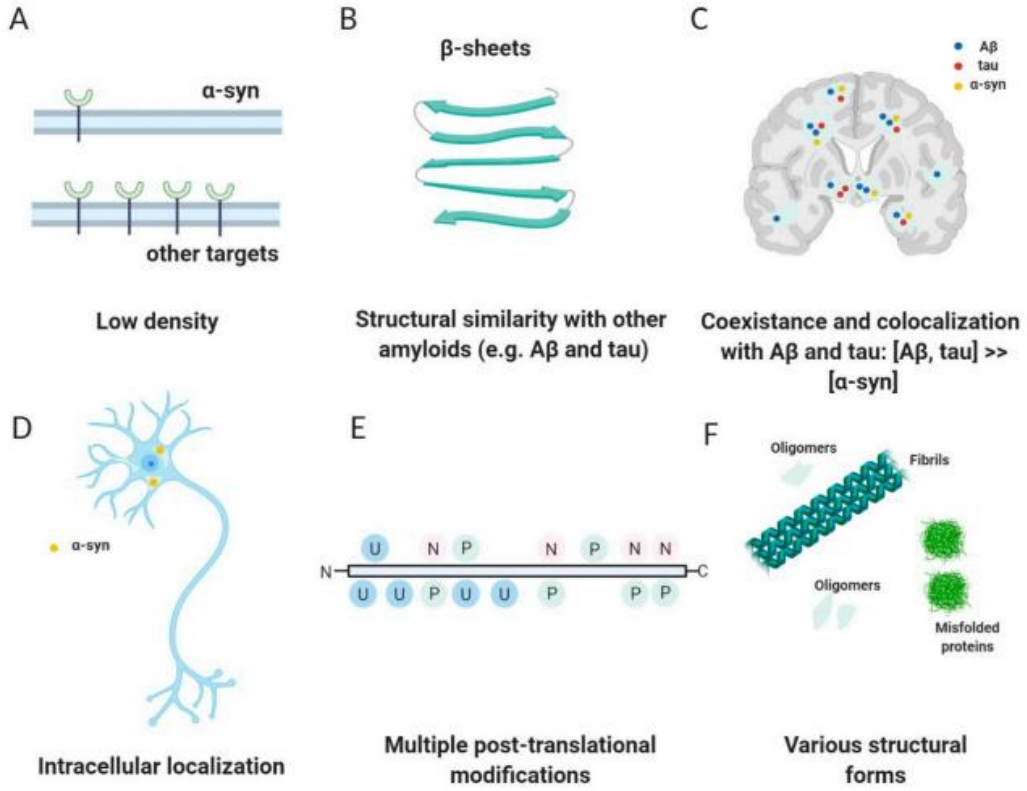
TEP/TDM α-synucléine

- Pas de traceur fiable à l'heure actuelle

- Challenges importants :
  (Korat et al. Pharmaceuticals 2021)



- Milliers de molécules ont été ou sont en cours d'études

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Merci de votre attention

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