Place de l'imagerie dans le diagnostic des démences

Pierre Krolak-Salmon

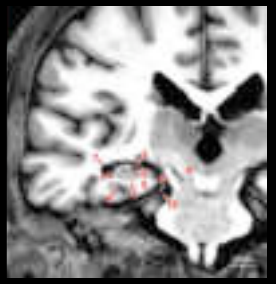
Centre de Mémoire, de Ressource et de Recherche de Lyon

Hôpitaux de Lyon

Institut Fédératif des Neurosciences LYON

Dynamique cérébrale et cognition
INSERM U821

Maladie d'Alzheimer



Lésions protéiques

Lésions

Perte neuronale

Clinique

Plainte mnésique MCI Démence Décès

Diagnostic « actuel » de MA

Traitements symptomatiques

Traitements étio-pathogéniques

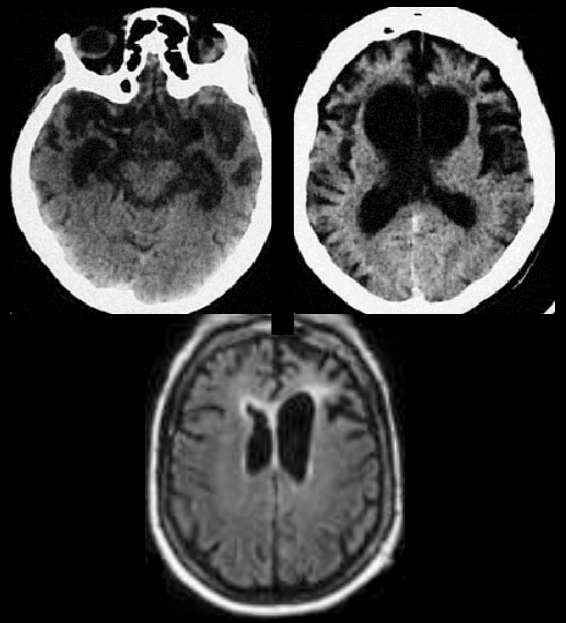
Diagnostic de MA pré-démentielle

Critères diagnostiques révisés de maladie à corps de Lewy

Mc Keith et al, 2005

- Démence attention, F.exécutives et visuo-spatiales, ± amnésie
- Signes cardinaux
  - Fluctuations
  - Hallucinations visuelles
  - Syndrome parkinsonien
- Signes suggestifs
  - Troubles du sommeil (REM)
  - Hypersensibilité aux neuroleptiques
  - Anomalies transporteur de la dopamine (Dat-Scan)
- Signes évocateurs
  - Pertes de connaissance
  - Syndrome dysautonomique
  - Autres hallucinations, délire
  - Dépression
  - Préservation relative lobe temporal médian à l'IRM
  - Hypodébit occipital
  - Scintigraphie myocardique anormale (MIBG)
  - Ondes lentes et pointes temporales

DEMENCE FRONTO-TEMPORALE



I Critères principaux

A - Début insidieux et évolution progressive
B - Inadaptation sociale précoce
C -Troubles précoces du comportement
D - Emoussement émotionnel précoce
E - Perte d'intérêt précoce

II Critères diagnostiques accessoires

A – Troubles du comportement

Négligence corporelle
Réduction de la flexibilité mentale
Distractibilité
Hyperoralité et troubles du comportement alimentaire
Persévérations et stéréotypies
Comportement d'utilisation

B – Parole et langage

Troubles de la parole : aspontanéïté, réduction de la fluence verbale, irrégularité de la parole
Stéréotypies langagières
Echolalie, Persévérations
Mutisme

Neary et al., Neurology, 1998

Diagnostic différentiel DCL/MA

20 patients avec démence
DAT-scan + autopsie

Walker et al. JNNP 2007

Anapath → 8 DCL
9 MA

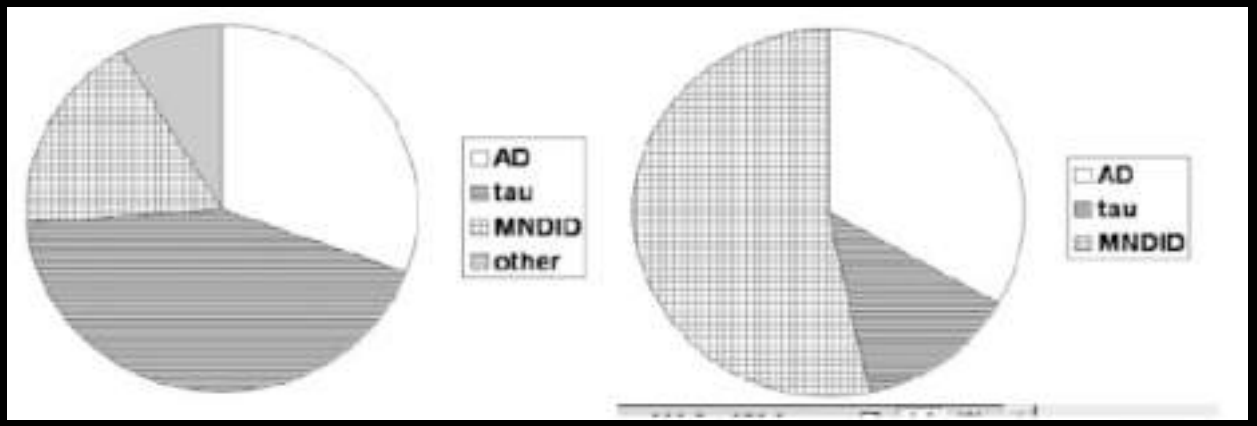
Clinique → Sensibilité : 75%
Spécificité : 42%

Clinical and Pathological Characterization of Progressive Aphasia

Jonathan A. Knibb, MRCP,[1] John H. Xuereb, MD,[2] Karalyn Patterson FMedSci[3] and John R. Hodges, FMedSci[1,3]

Ann Neurol 2006;59:156–165

Non fluente **Fluente**



Démences et syndromes parkinsoniens atypiques

Paralysie Supranucléaire Progressive

Corticobasal ganglionic degeneration
Alien limb syndrome
Severe limb apraxia (inability to use correctly mimed objects, or perform symbolic gestures on command)
Cortical sensory deficits
Markedly asymmetric onset of bradykinesia
Focal frontal or temporoparietal atrophy
Parkinson's disease
Asymmetric onset of bradykinesia symptoms
Tremor-dominant disease
Marked and prolonged levodopa benefit
Dementia with Lewy bodies
Hallucinations or delusions unrelated to dopaminergic therapy
Cortical dementia, especially aphasia
Alzheimer's disease
Cortical dementia (severe amnesia and aphasia, or agnosia, NINCDS-ADRDA criteria)
Multiple system atrophy
Prominent cerebellar symptomatology or unexplained early and prominent incontinence, impotence, or marked postural hypotension*
Multiinfarct parkinsonism
Multiple strokes, one of which involves the brainstem and basal ganglia

iques

ensible

rextension du cou (rétrocolie)

gard

us-cortico-frontal

Critère NINDS-SPSP, Litvan et al , 1996

Institute of Neurology, Londres

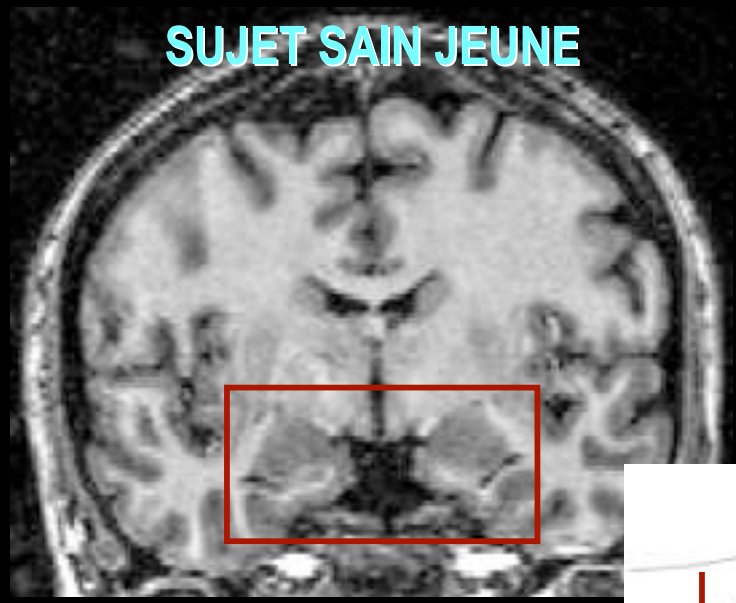
60 cas consécutifs de PSP diagnostiqués cliniquement

	First clinic visit		Last clinic visit	
	Sensitivity (95% CI)	PPV (95% CI)	Sensitivity (95% CI)	PPV (95% CI)
Clinical diagnosis	17 (9–30)	89 (57–98)	100 (92–100)	78 (66–87)
Falls				
NINDS-SPSP falls	36 (24–51)	77 (57–90)	36 (24–51)	77 (57–90)
Down gaze abnormality-Lees	19 (10–33)	100 (70–100)	70 (56–81)	85 (70–93)
Axial rigidity	15 (7–28)	88 (53–98)	49 (35–63)	79 (62–90)
Pseudobulbar palsy	40 (28–55)	76 (57–89)	91 (80–97)	78 (66–87)
Frontal lobe signs-Lees	2 (0–11)	100 (21–100)	30 (19–44)	67 (45–83)
Frontal lobe signs-Tolosa	0	0/0	6 (2–17)	100 (44–100)
Pyramidal signs	9 (3–20)	57 (25–84)	26 (15–40)	75 (51–90)
Bradykinesia	74 (61–85)	78 (64–88)	100 (92–100)	80 (68–87)
Rigidity	74 (61–85)	78 (64–88)	100 (92–100)	78 (66–87)
Bradyphrenia	0	0/0	6 (2–17)	100 (44–100)
Poor levodopa response[a]	87 (73–94)	78 (63–88)	98 (88–100)	79 (66–86)
No tremor	85 (72–93)	83 (70–91)	79 (65–88)	79 (65–88)

L’imagerie anatomique

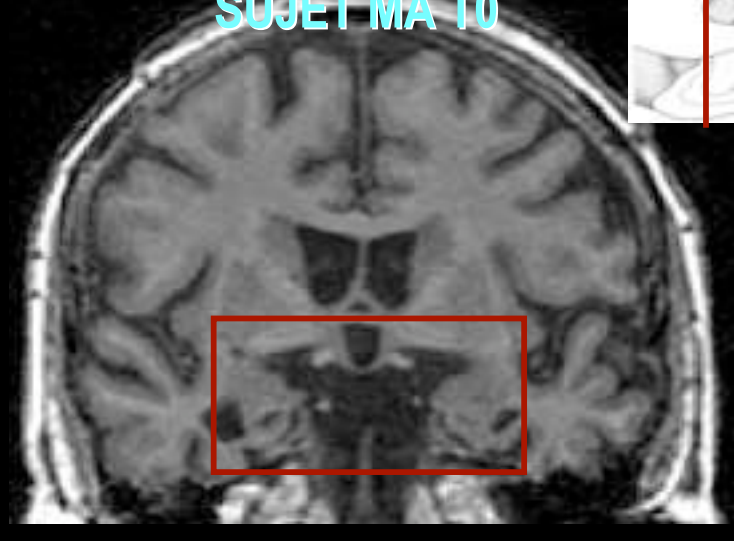
IMAGERIE

SUJET SAIN JEUNE

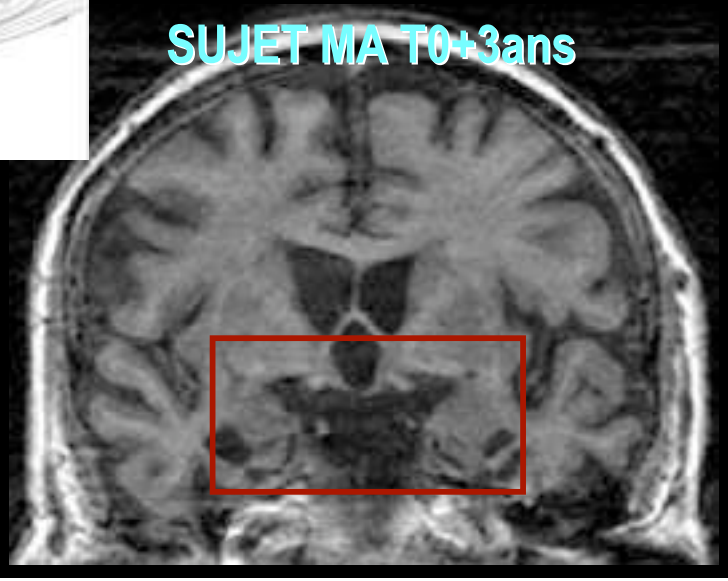


SUJET SAIN ÂGÉ

SUJET MA T0

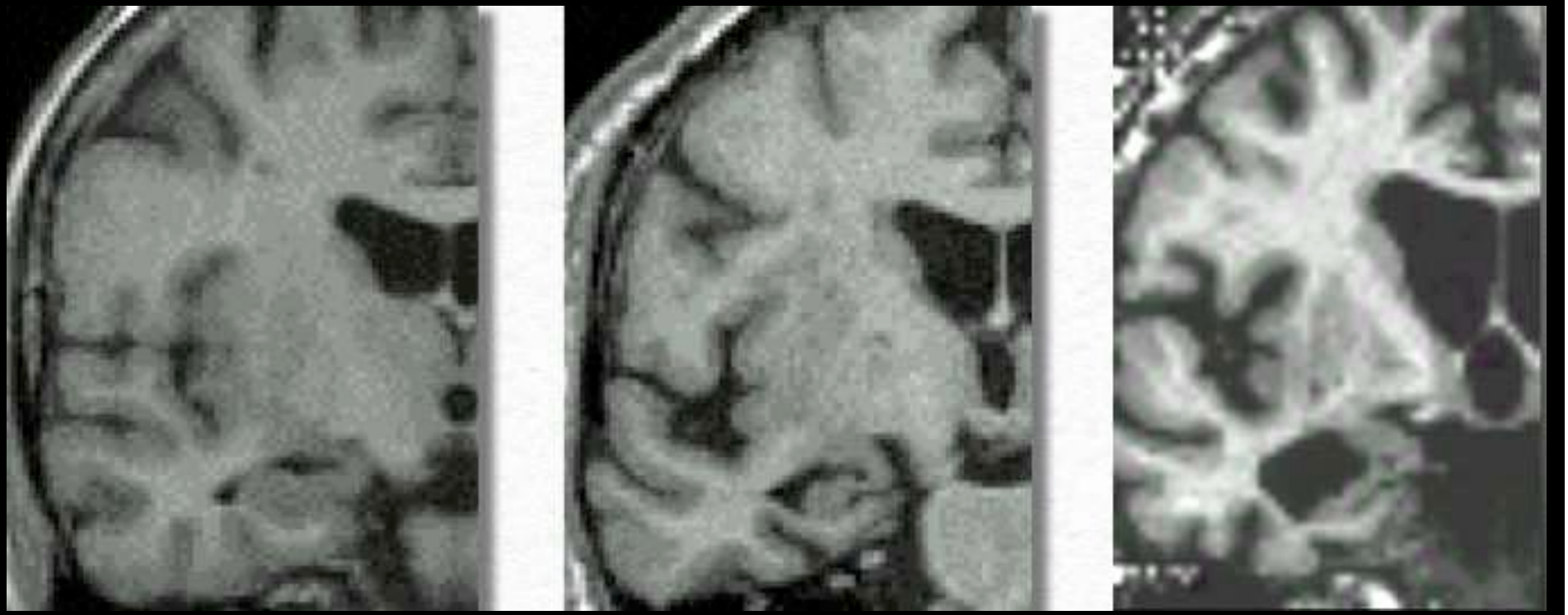


SUJET MA T0+3ans



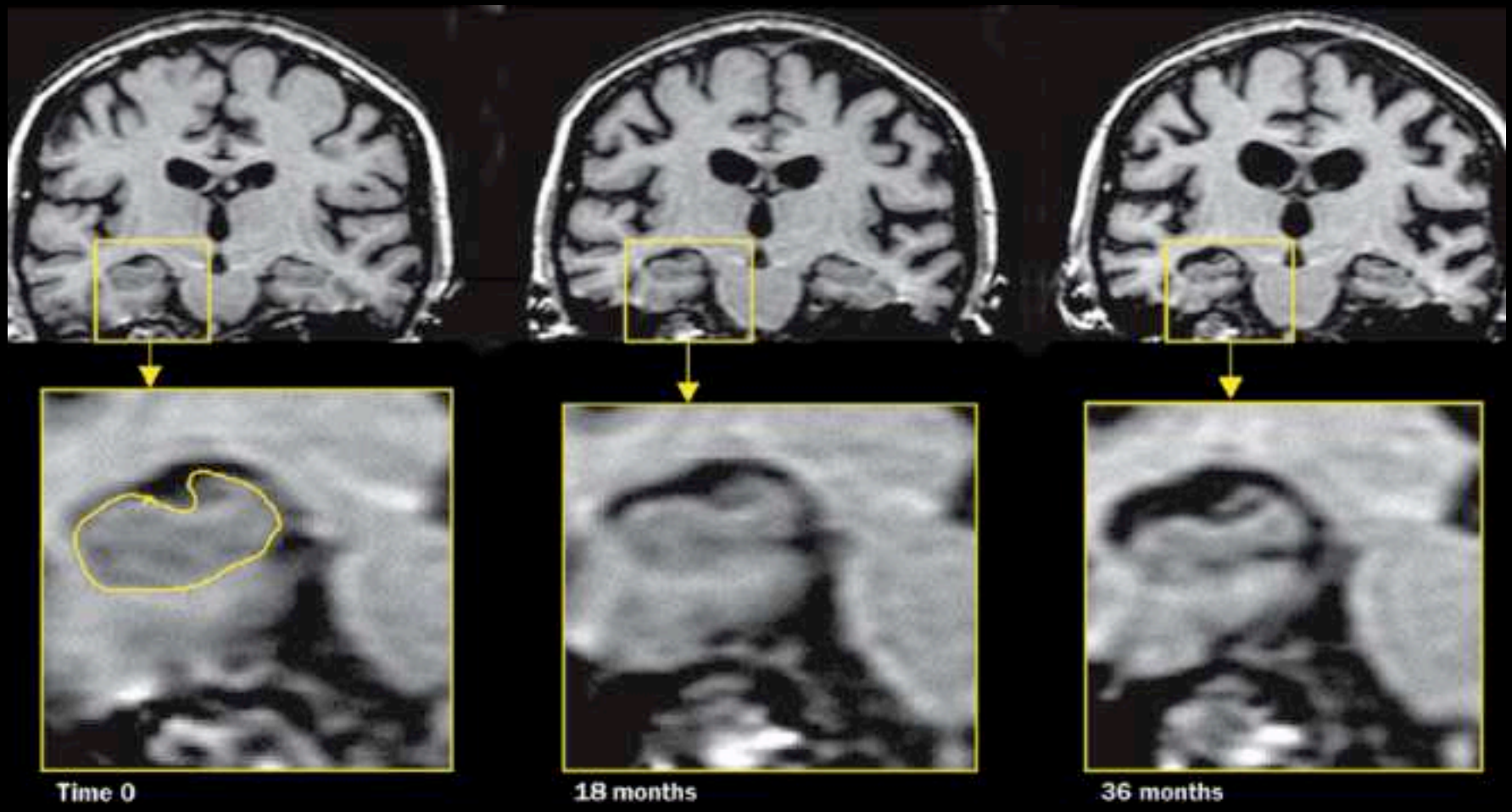
Imagerie anatomique

Maladie d'Alzheimer et atrophie mésio-temporale



Maladie d'Alzheimer et atrophie mésio-temporale

→ Mesures manuelles/automatiques de régions d'intérêt



Scheltens et al. 2002

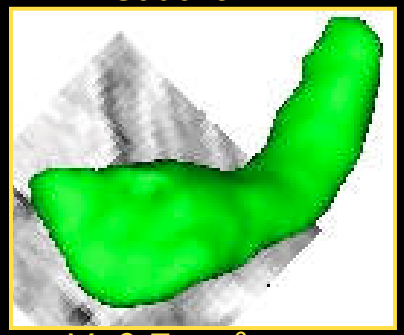
VOLUMÉTRIE : HIPPOCAMPE

SUJET SAIN JEUNE

Droite

$V=2,7\ cm^3$

Gauche



$V=2,7\ cm^3$

SUJET SAIN ÂGÉ

Droite

$V=2,6\ cm^3$

Gauche

$V=2,6\ cm^3$

SUJET MA T0

Droite

$V=1,7\ cm^3$

Gauche

$V=1,5\ cm^3$

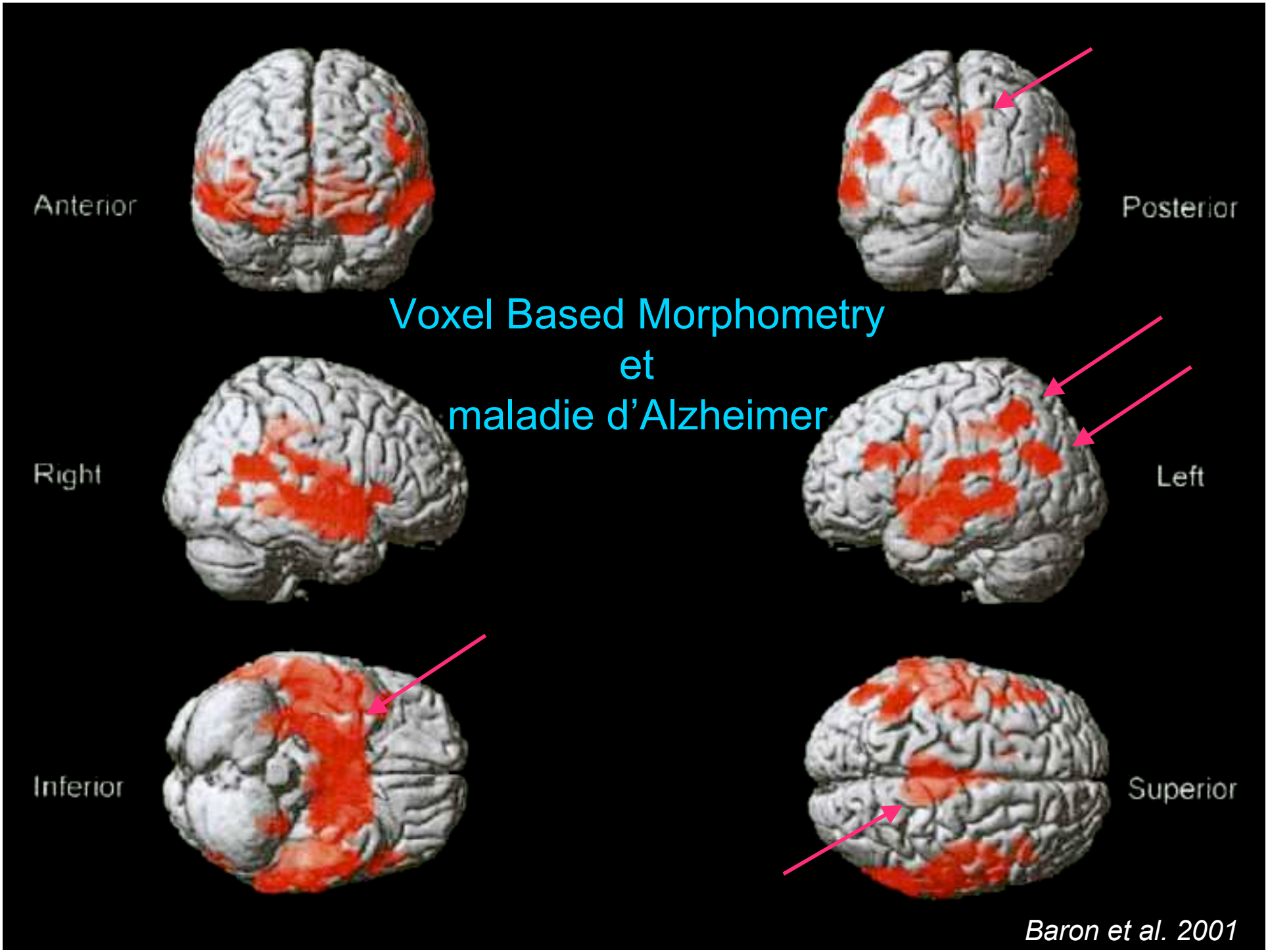
SUJET MA T0+3ans

Droite

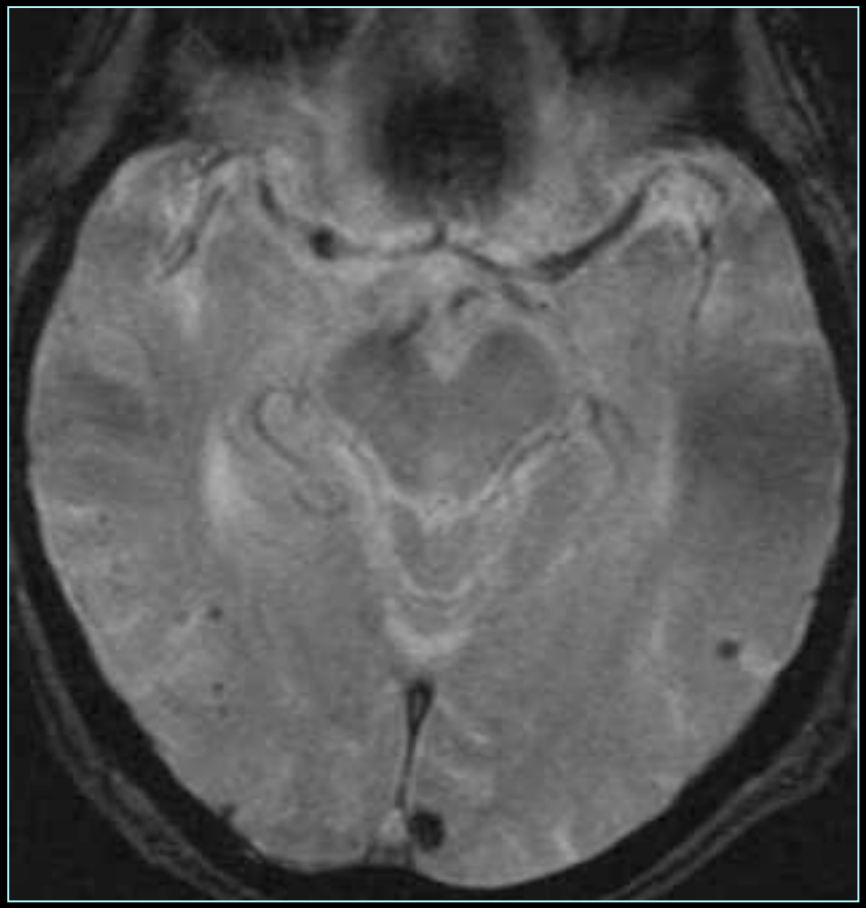
$V=1,3\ cm^3$

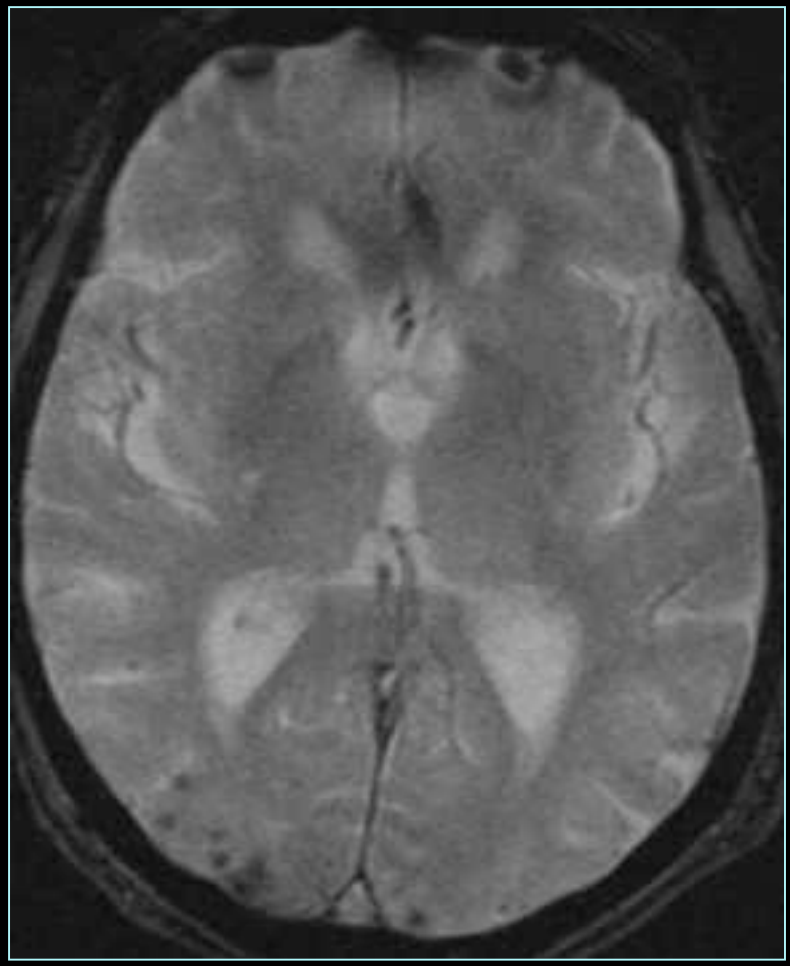
Gauche

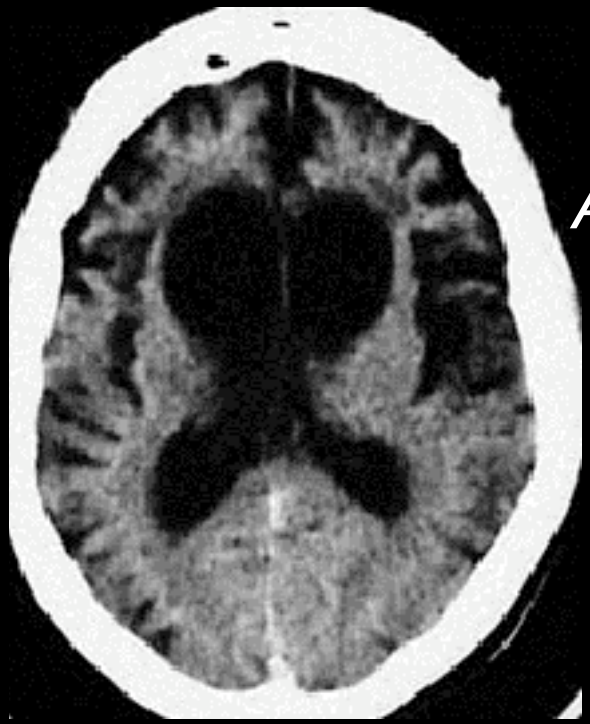
$V=1,3\ cm^3$


Anterior
Posterior
Voxel Based Morphometry
et
maladie d'Alzheimer
Right
Left
Inferior
Superior
Baron et al. 2001

IRM Echo de gradient (T2*)

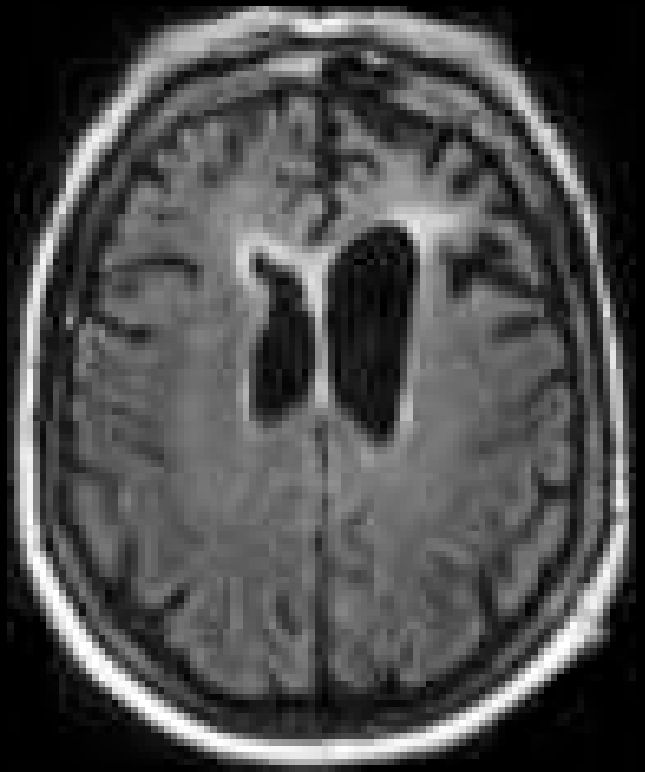




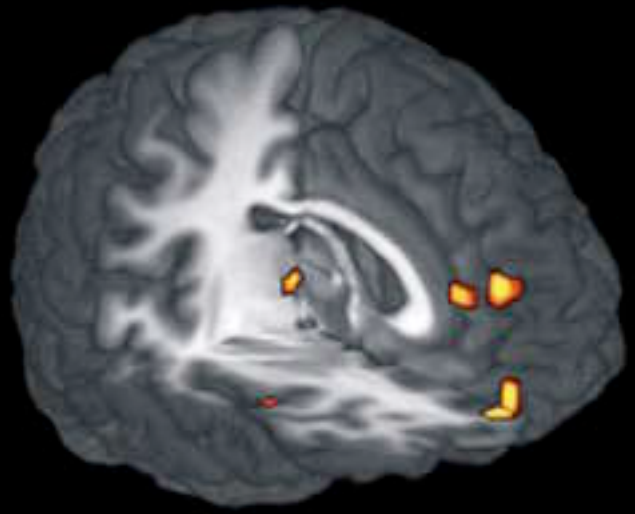


Au-delà de l'exclusion…

Dégénérescences lobaires fronto-temporales



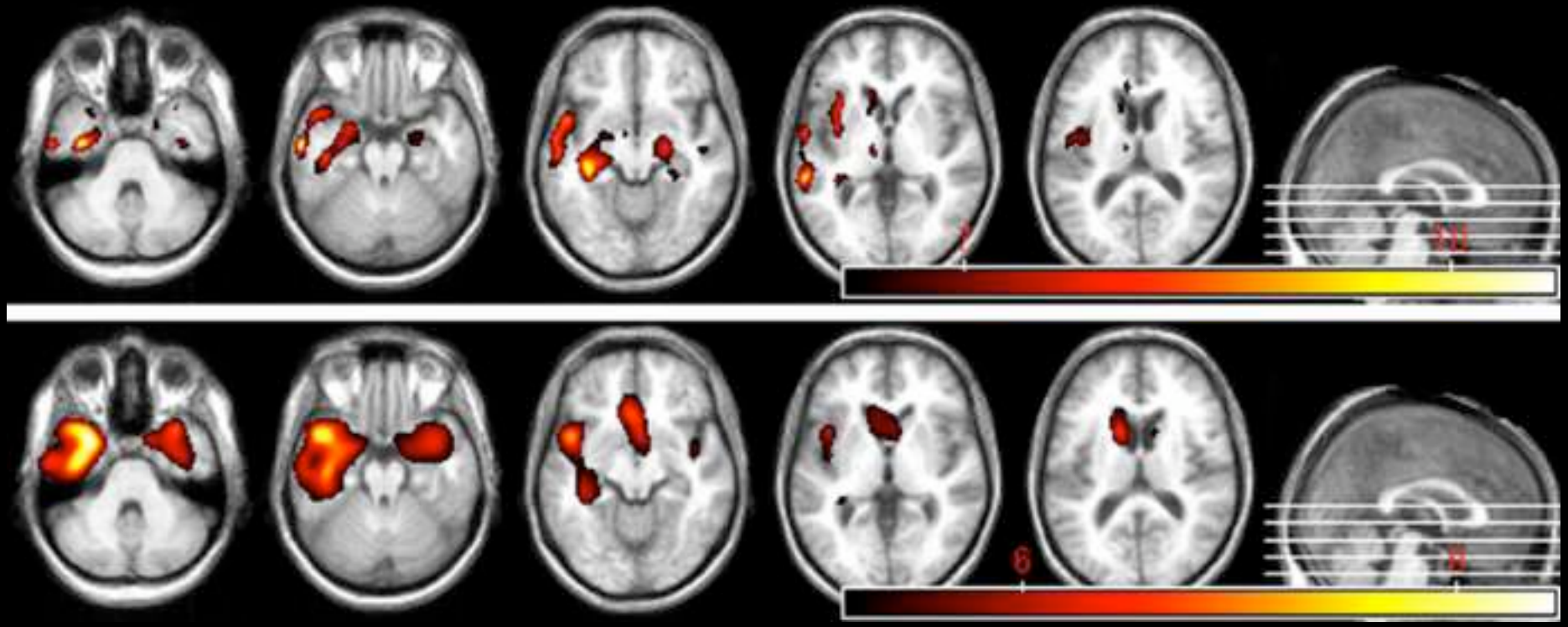
Anomalies structurales et métaboliques dans la DFT



Schroeter et al, , Neurobiol aging, 2008

Démence sémantique

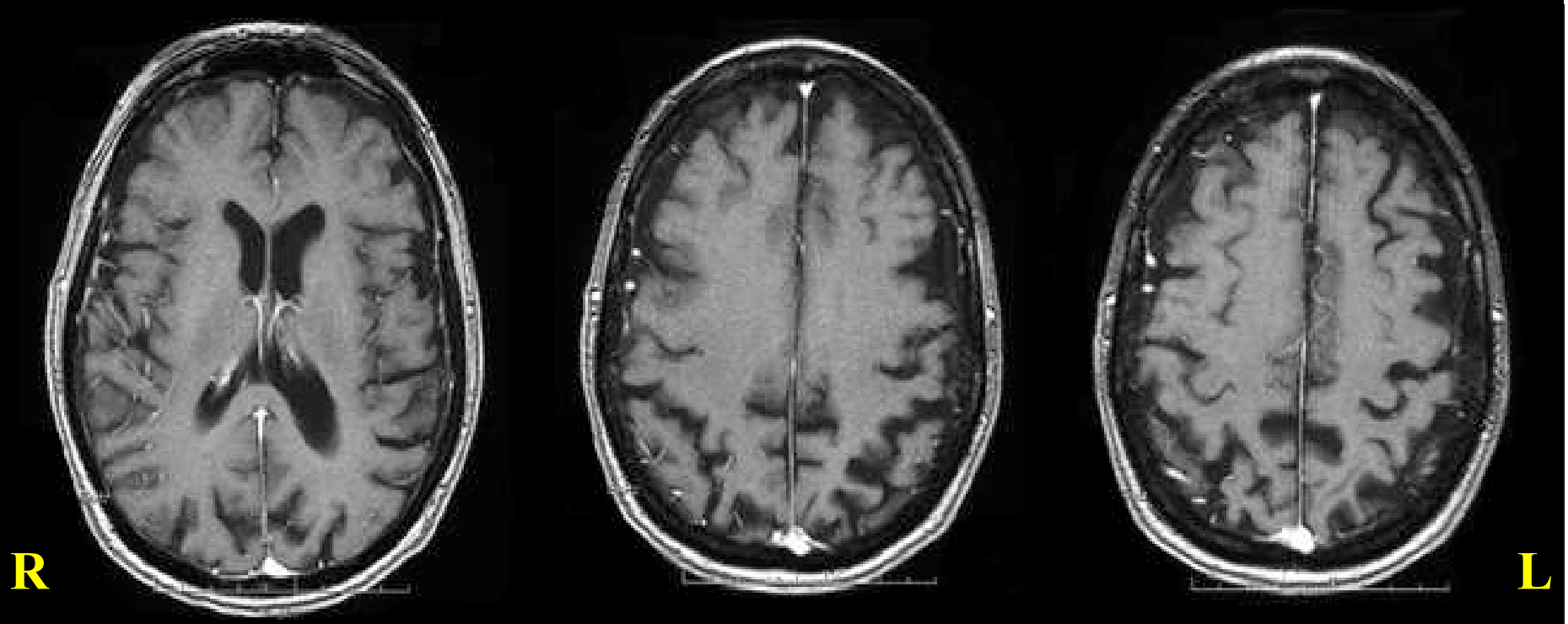
IRM volumétrique



TEP au FDG

L’atrophie corticale postérieure

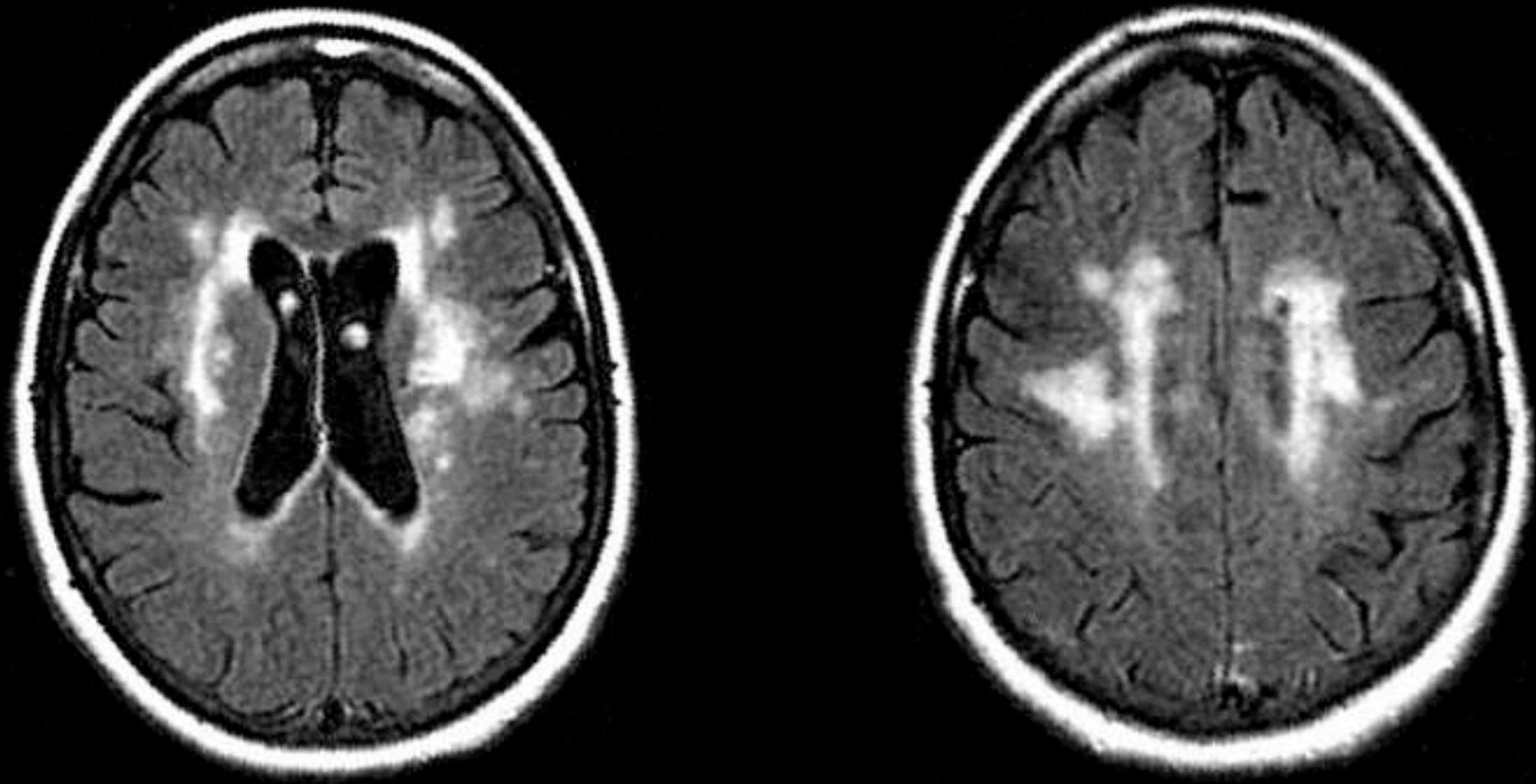
(Syndrome de Benson)



MRI, T1 + Gadolinium

(Patient SA)

Démences vasculaires

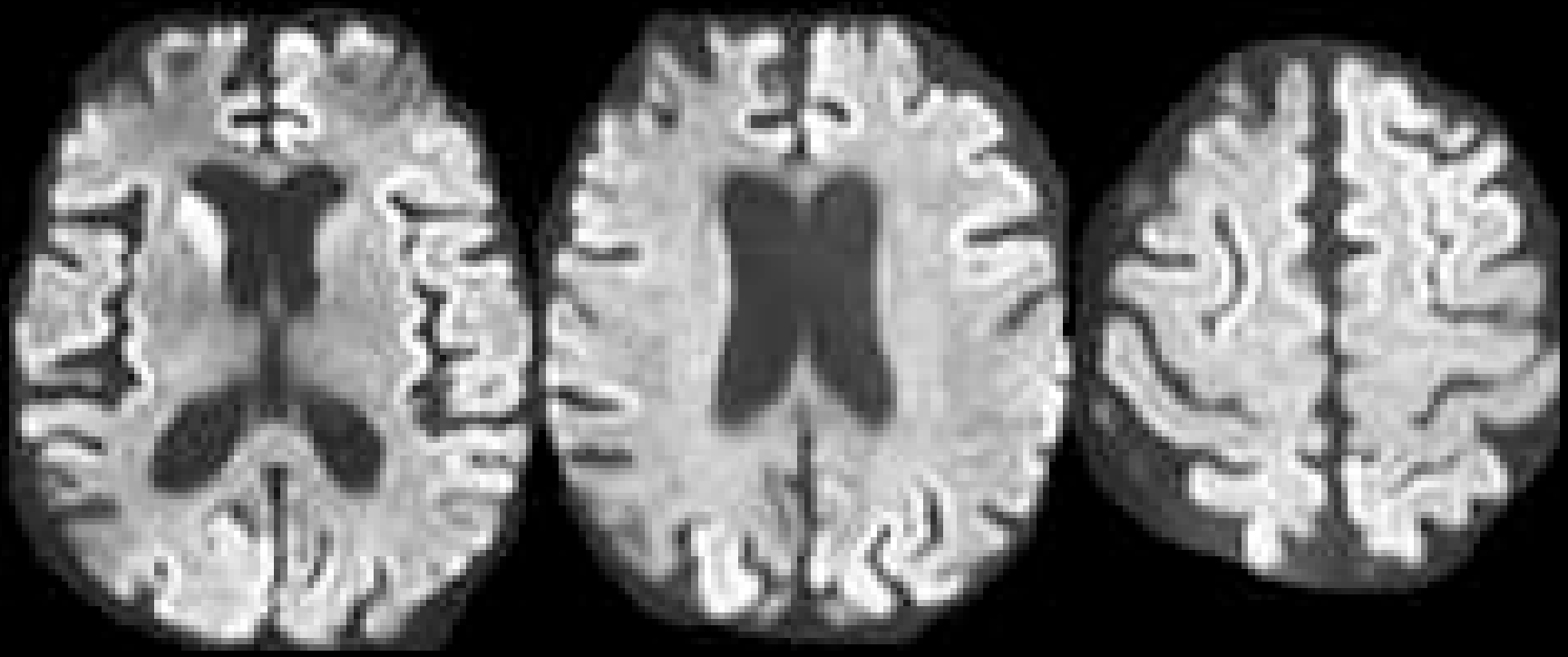


Si : - Anamnèse
- Syndrome sous-cortico-frontal
- Relation clinico-radiologique

La maladie de Creutzfeldt-Jacob

Maladie de Creutzfeldt-Jacob

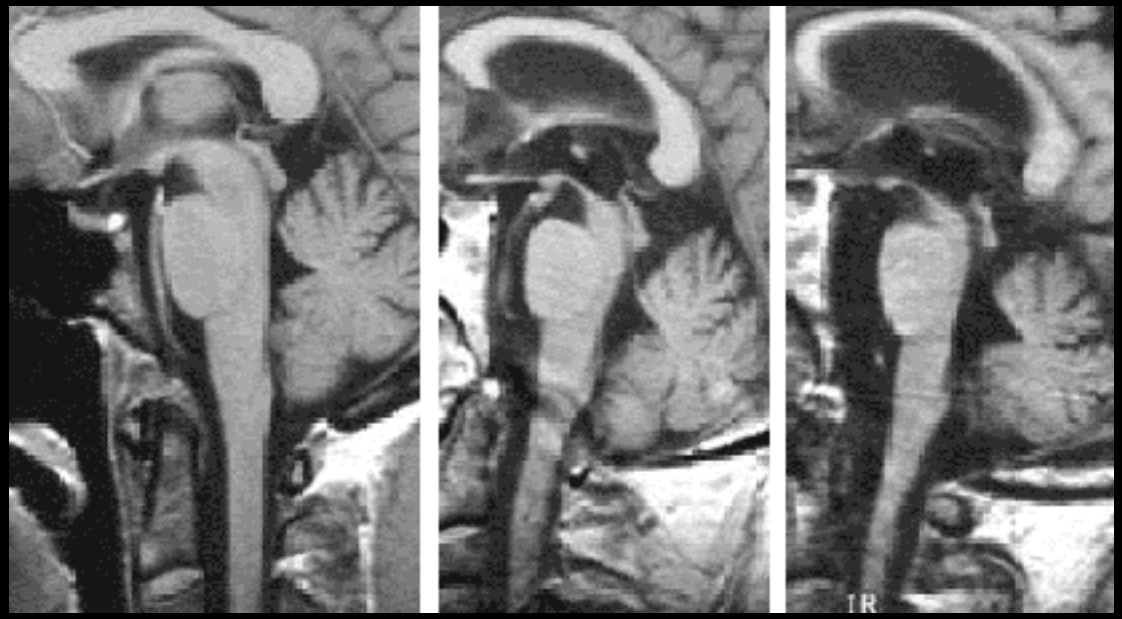
IRM encéphalique (FLAIR, Diffusion)

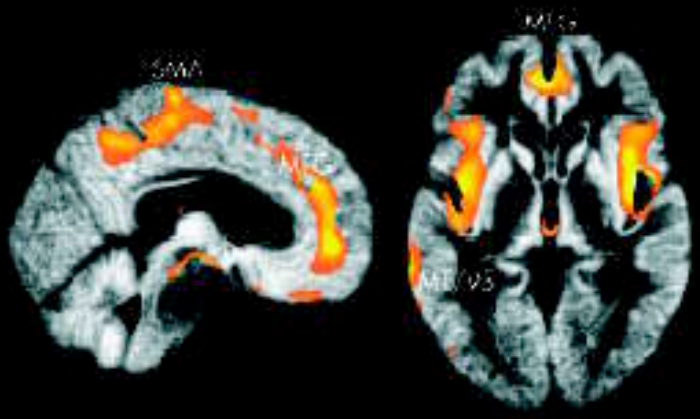


	T2*	FLAIR	Diffusion
Sensibilité	40%	50%	92%
Inter-exam.	68%	82%	100%

Shiga et al. 2004

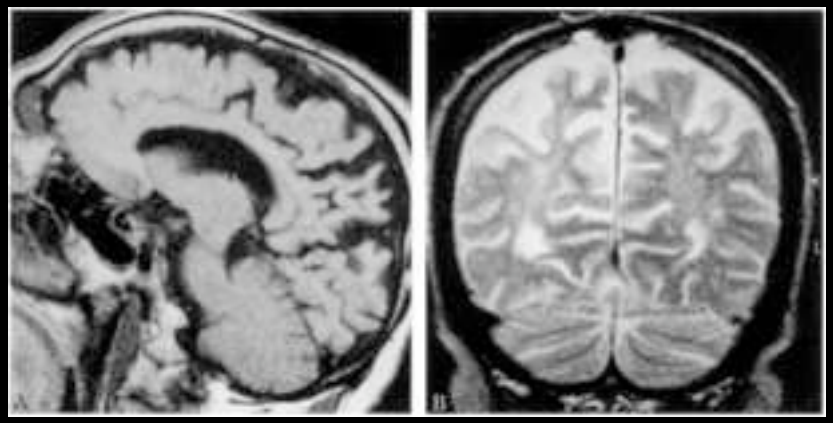
Paralysie Supranucléaire Progressive

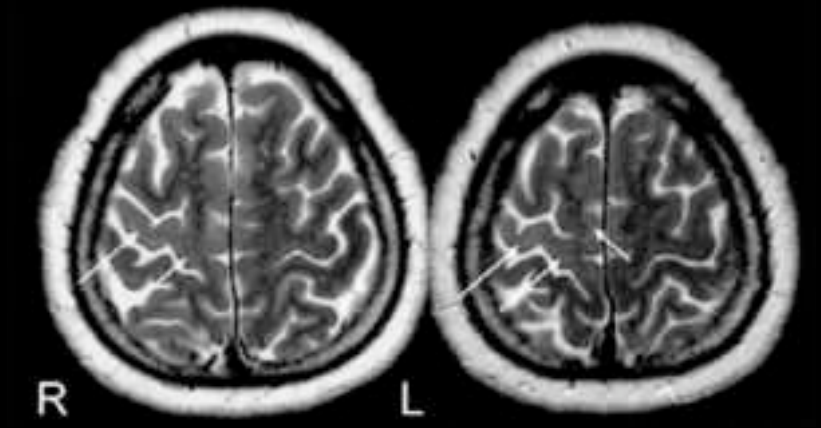




Brenneis et al, 2004; Verin et al, 2005 ; Cordato et al, 2005

Dégénérescence cortico basale et IRM

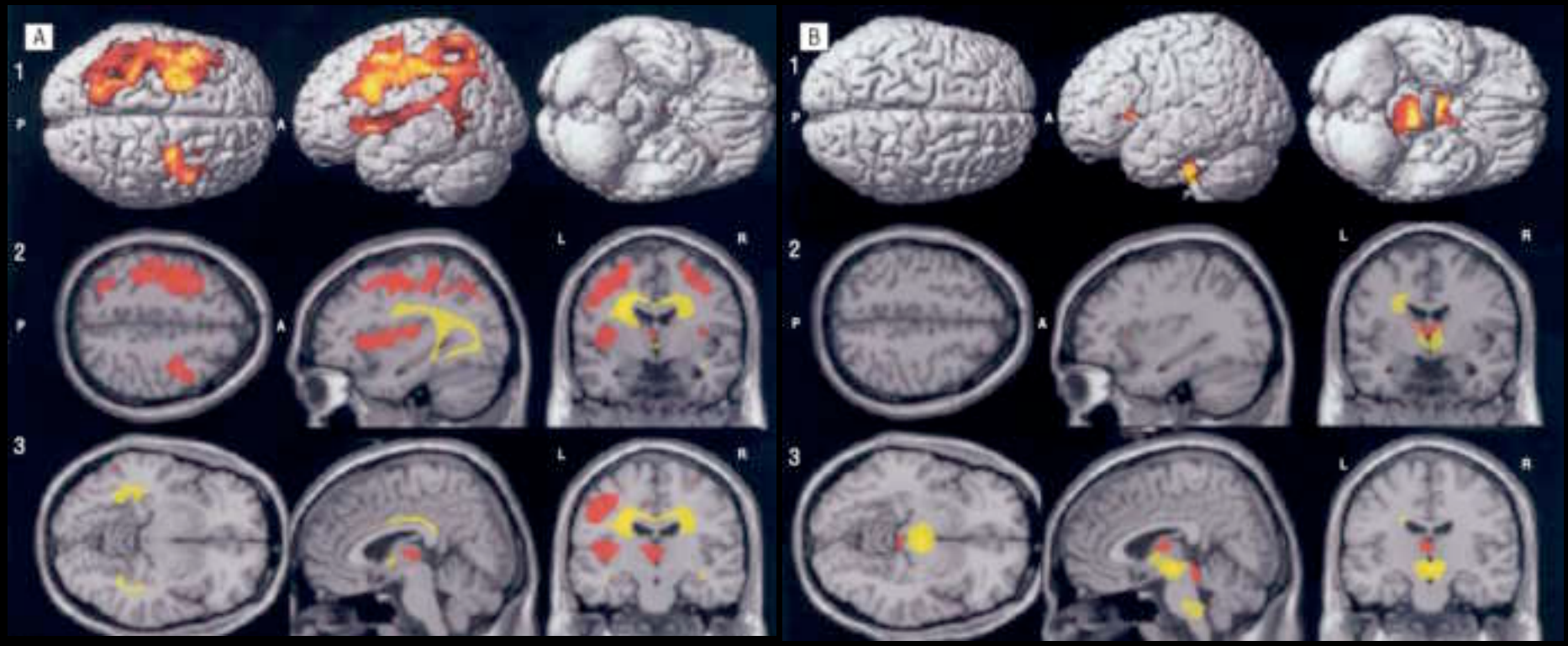




Winkelmann et al, 1999; Soliveri et al, 1999; Groschel et al, 2004

Volume cérébral
« Syndromes DCB / PSP »

Voxel based morphometry



14 syndromes DCB

15 syndromes PSP

% 80 contrôles

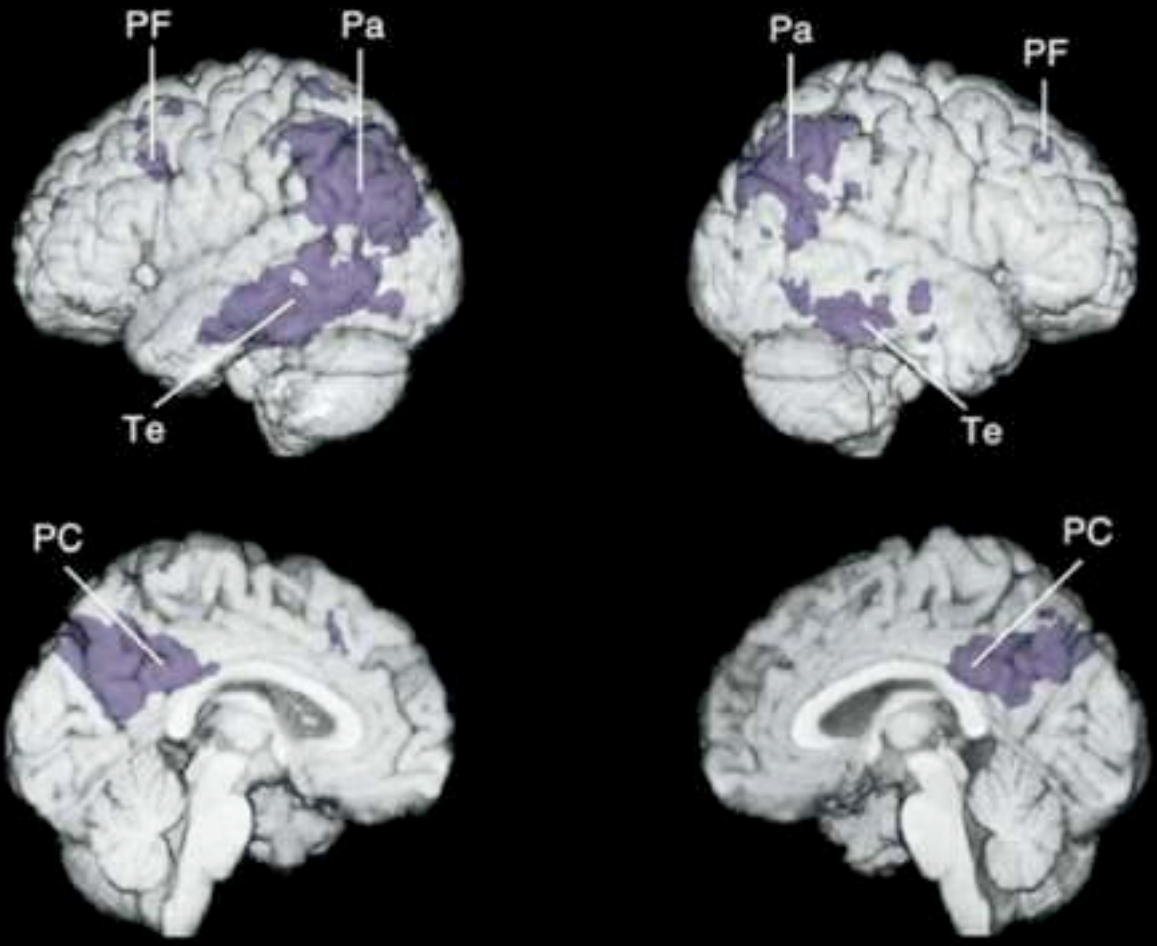
Boxer et al, 2006

L’imagerie métabolique peut-elle aider le diagnostic précoce?

Imagerie métabolique

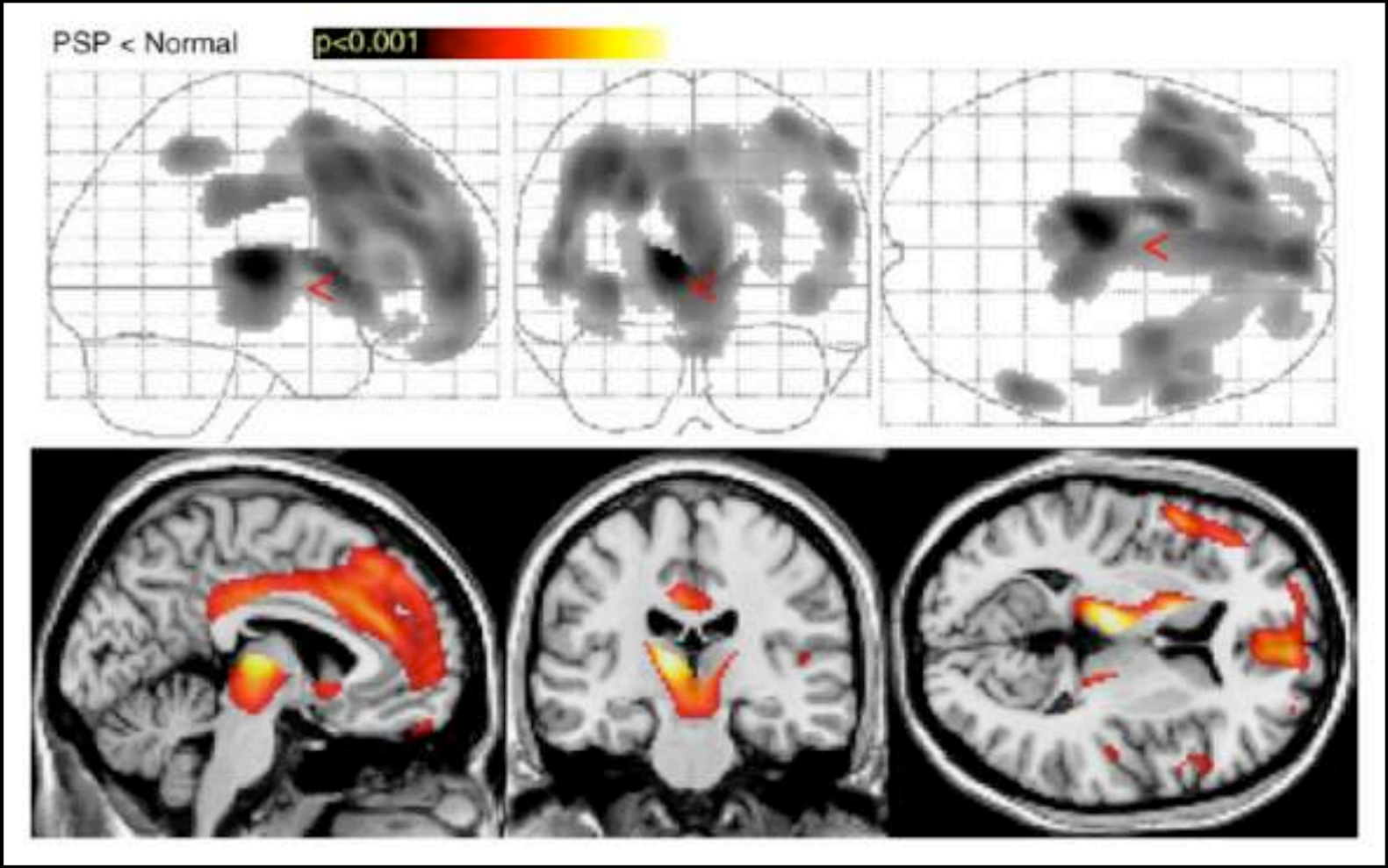
TEP au FD-glucose et MA débutante

Contrôles – MA probable



Reiman et al, NEJM, 1996

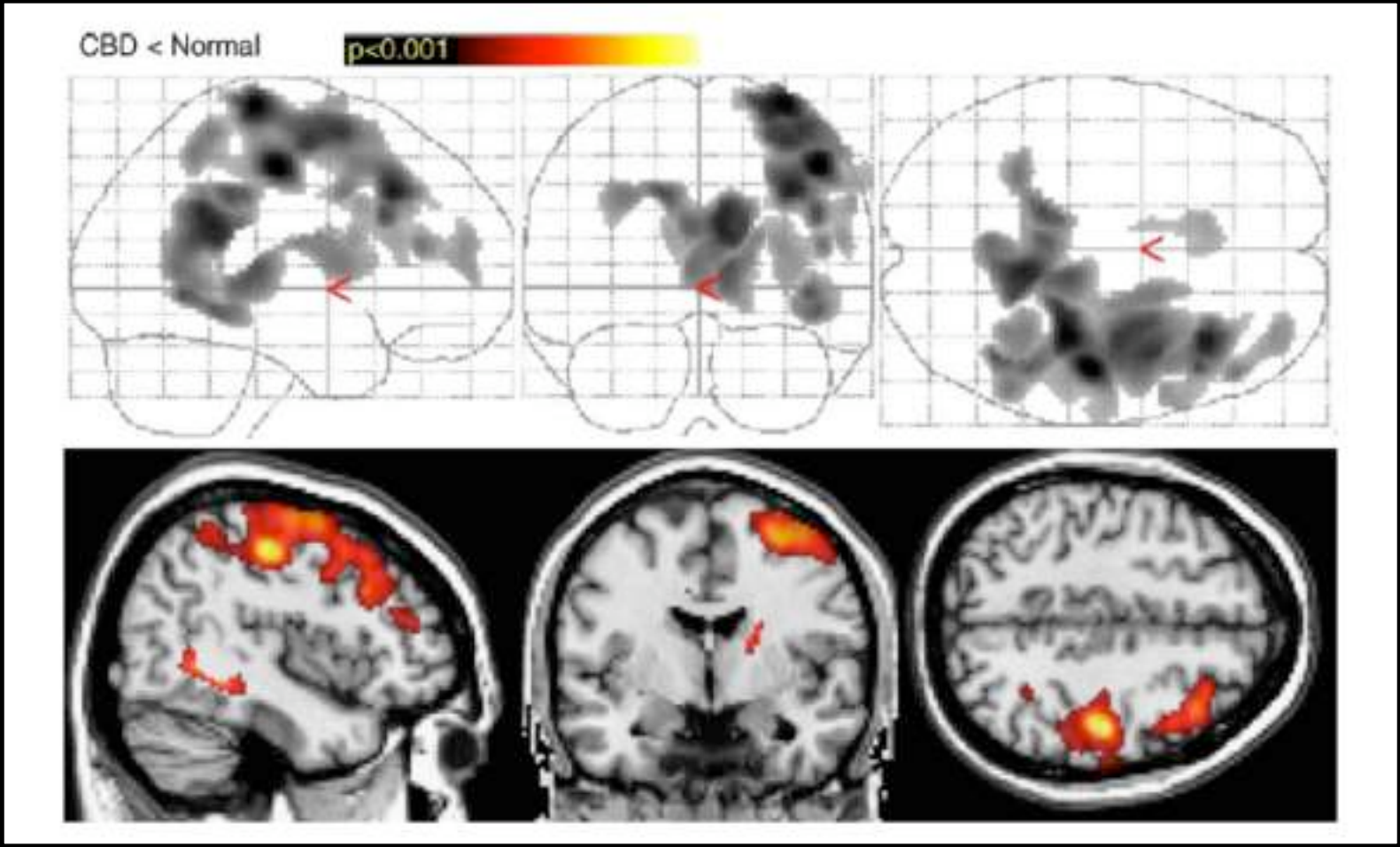
TEP FDG dans la PSP



Hypométabolisme frontal, thalamique, mesencephalique

Thobois et al

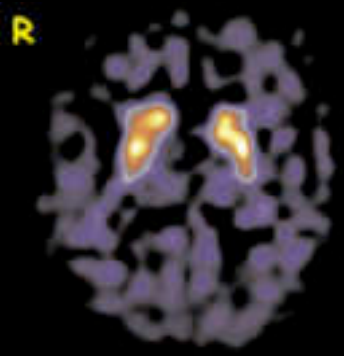
PET FDG DCB

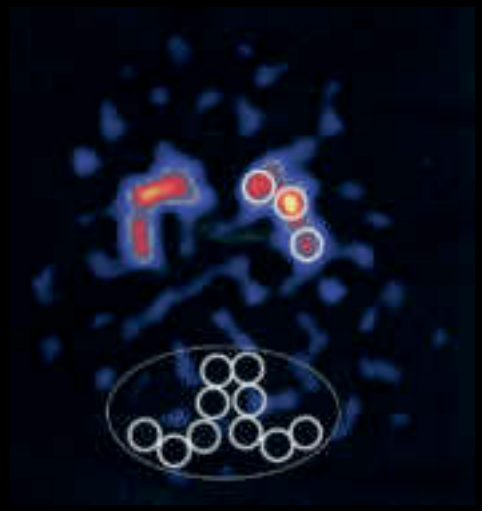


DCB vs Nx : Hypométabolisme asymétrique

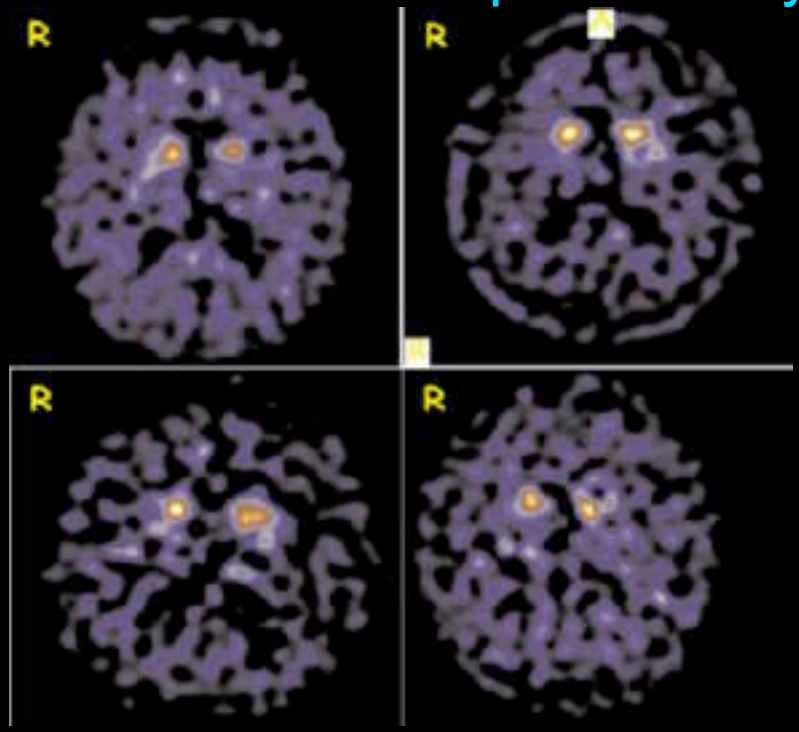
Thobois et al

DAT Scan : SPECT au ioflupane





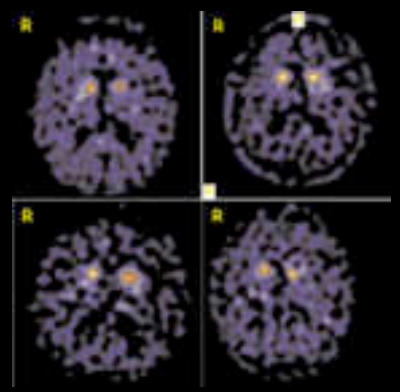
Démence à corps de Lewy



→Critères diagnostiques de consensus

Costa et al. 2003
Walker et al., Neurology 2004
McKeith et al, 2005

DAT scan et diagnostic différentiel DCL/MA

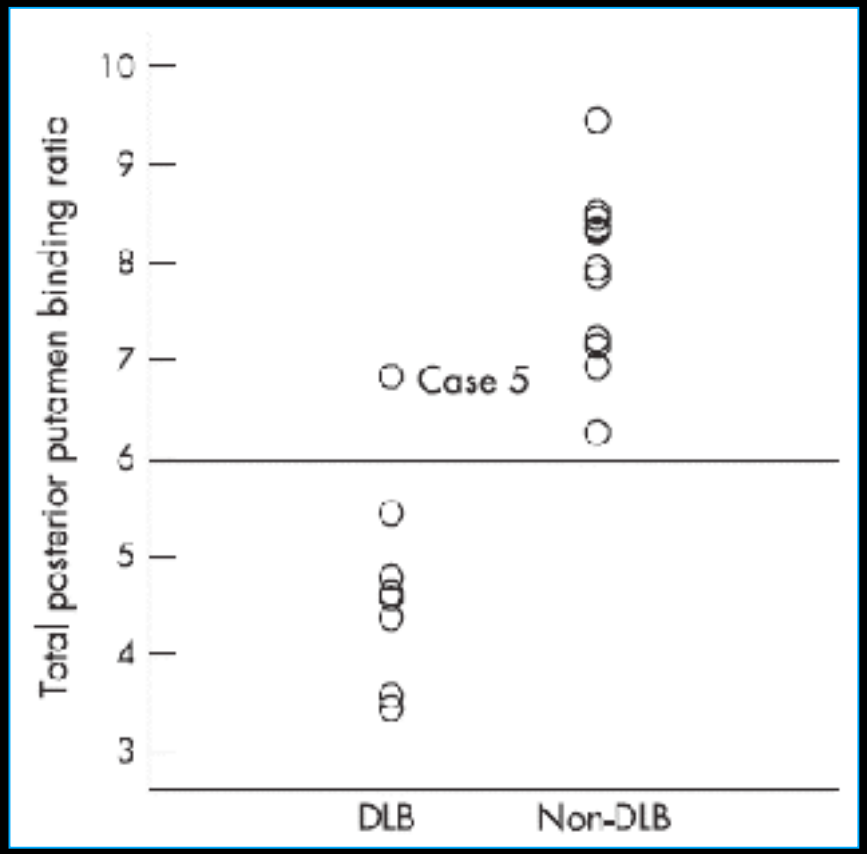


20 patients avec démence
DAT-scan + autopsie

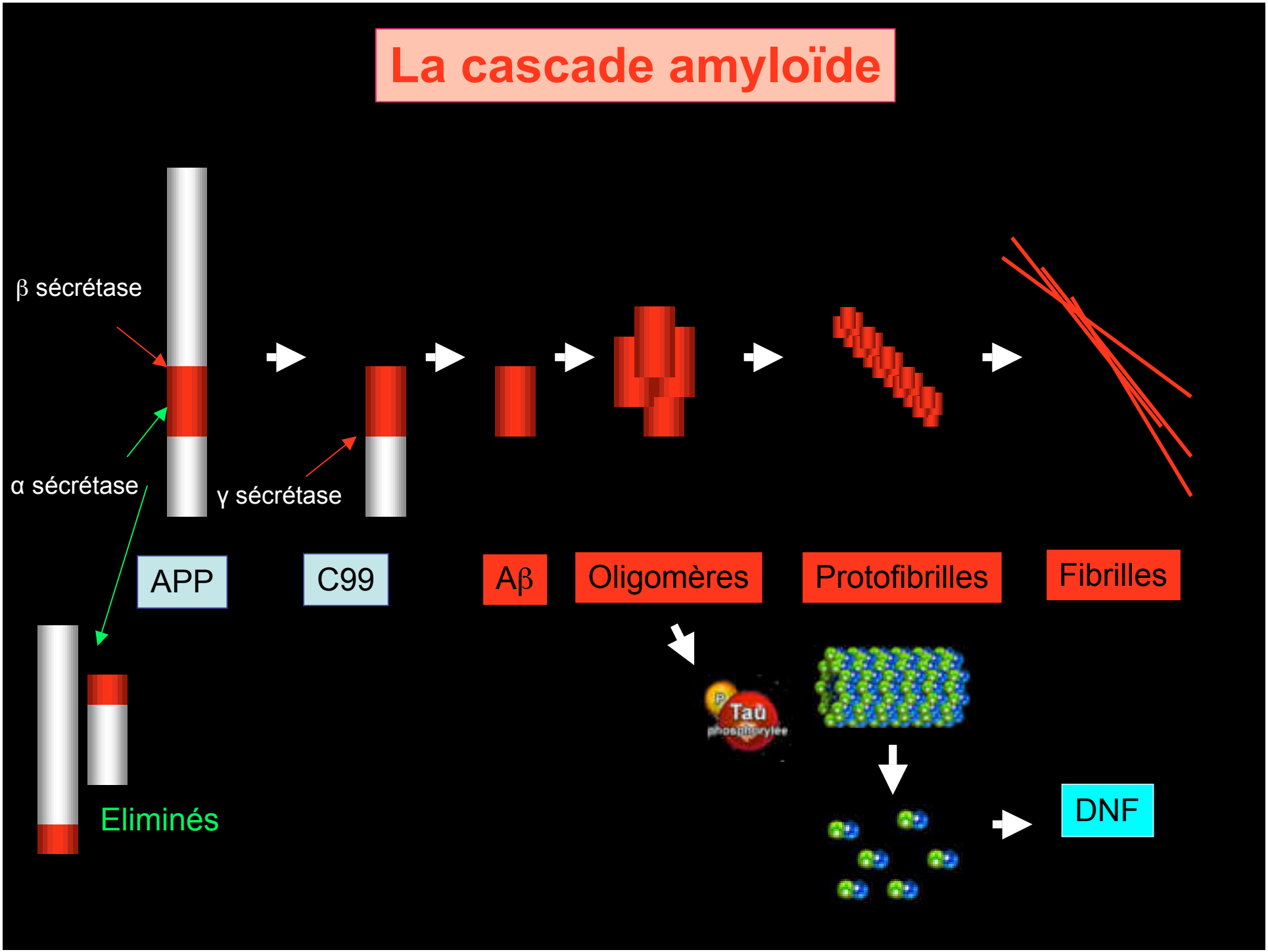
Anapath → 8 DCL
9 MA

Clinique → Sensibilité : 75%
Spécificité : 42%

DAT-Scan → Sensibilité : 88%
Spécificité : 100%

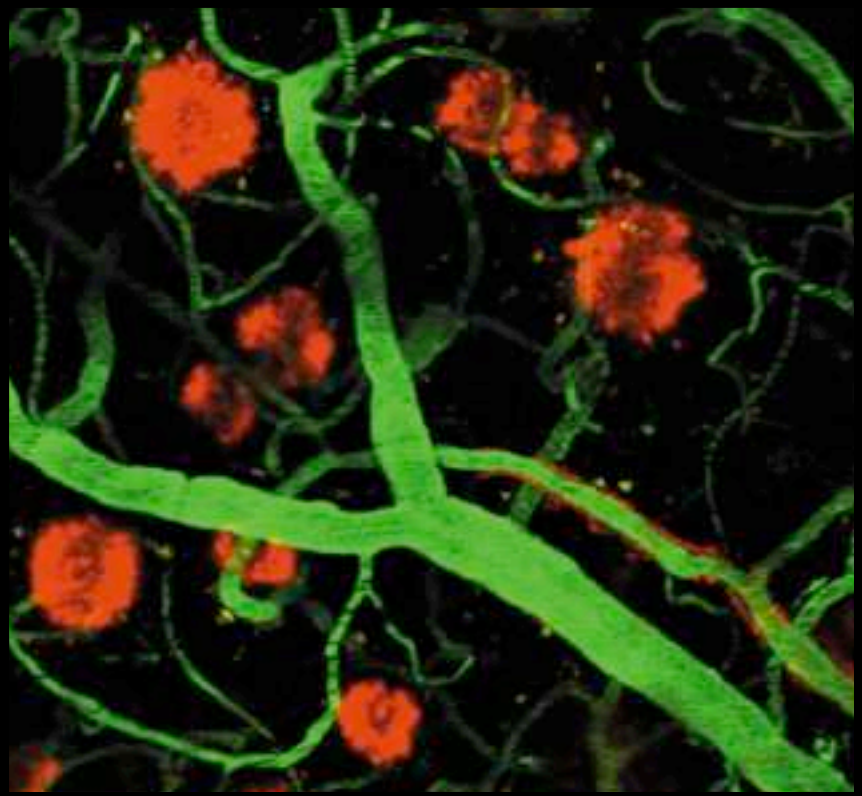


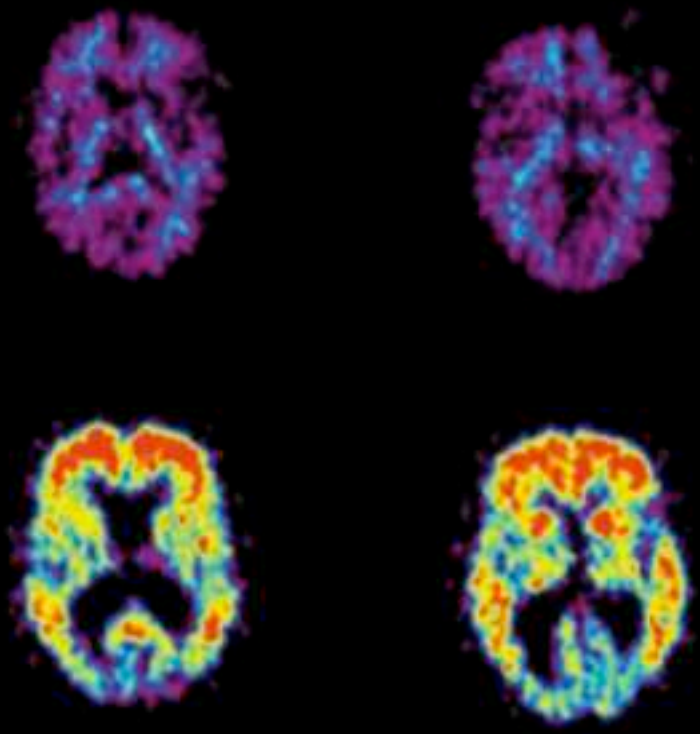
Walker et al. JNNP 2007


La cascade amyloïde
β sécrétase
α sécrétase
γ sécrétase
APP
C99
Aβ
Oligomères
Protofibrilles
Fibrilles
Tau
phosphorylée
Eliminés
DNF

TEP et marqueur amyloïde

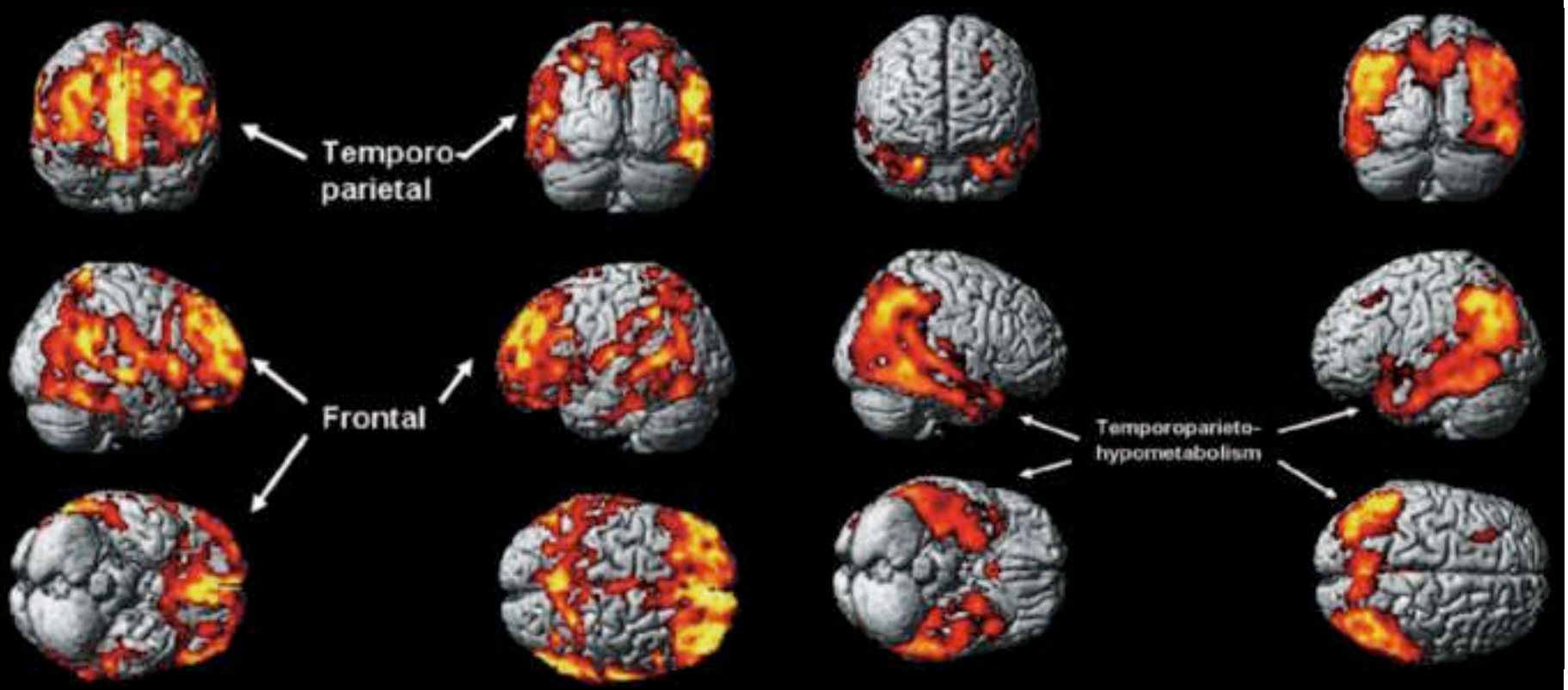
→ Fibrilles amyloïdes insolubles, bonnes corrélations neuropathologiques





Klunk et al, Ann Neurol, 2004
Nordberg et al., Lancet Neurol 2004

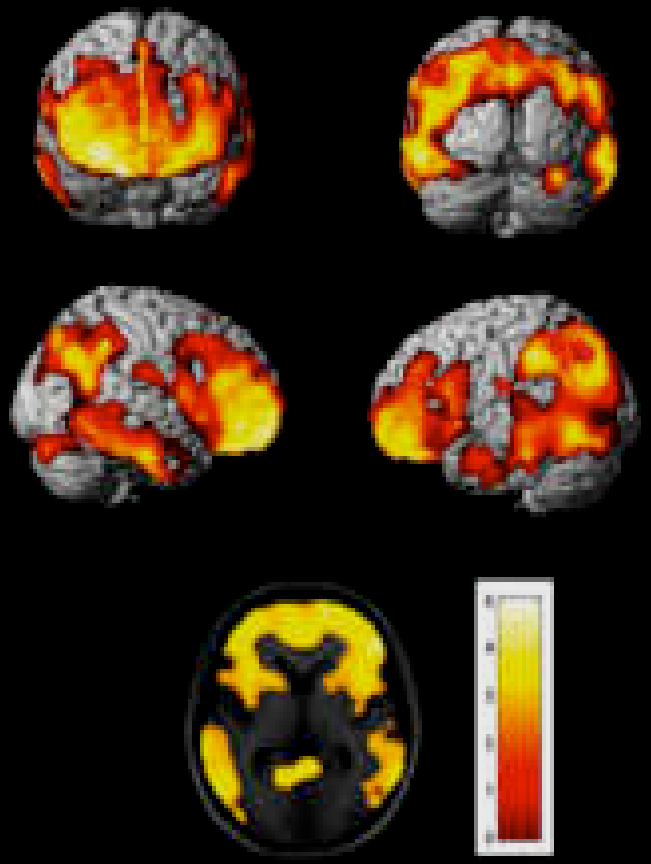
Dépôts amyloïdes et métabolisme du glucose

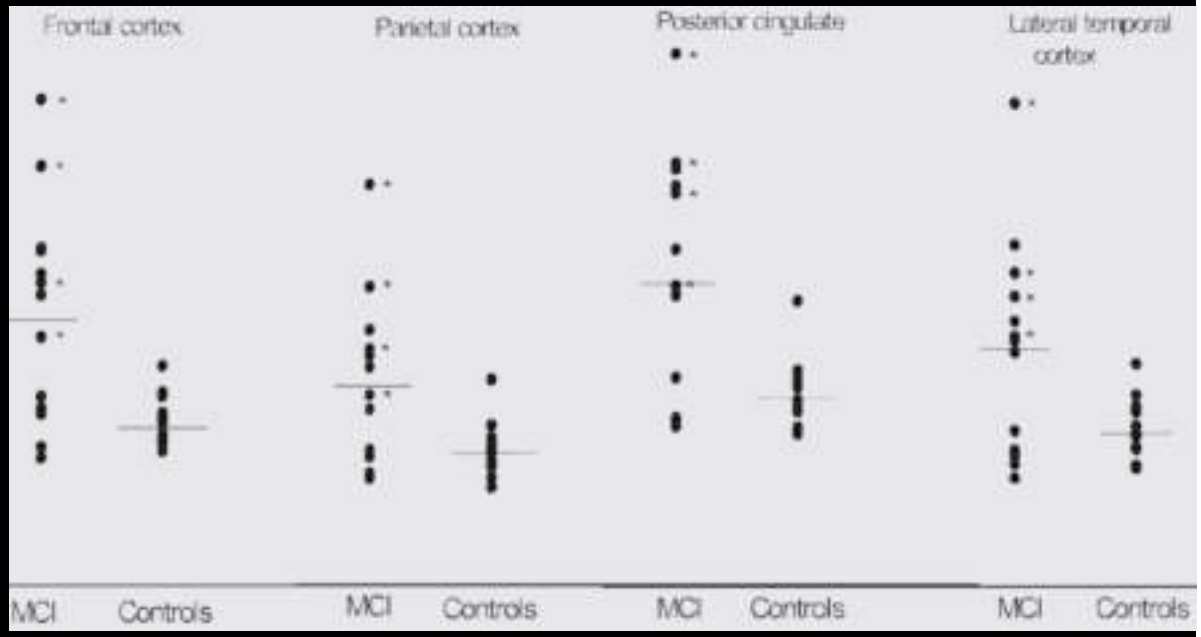


Edison et al, Neurology 2007

PIB et Trouble Cognitif Léger

40-60% des « MCI » évoluent vers une MA

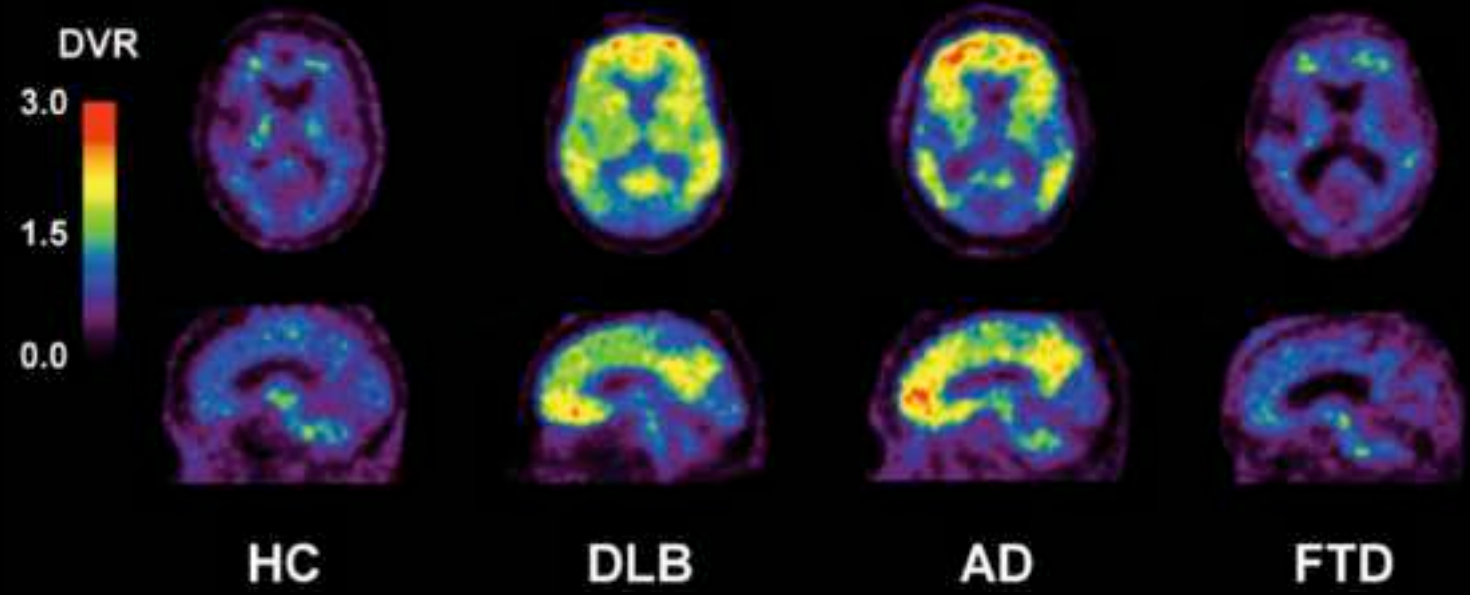


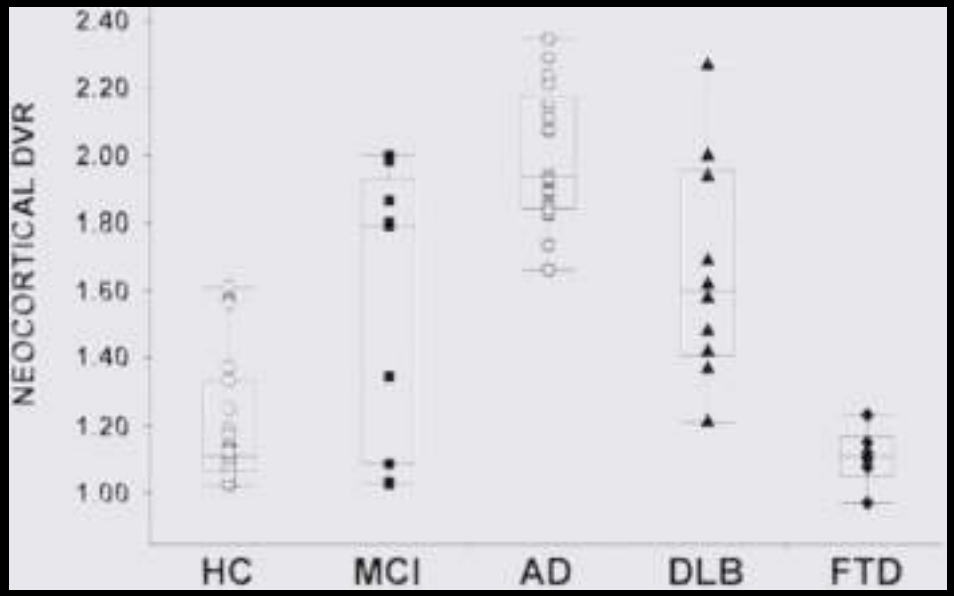


Blennow et al, Nat Med 2006

Kemppainen et al, Neurology 2007

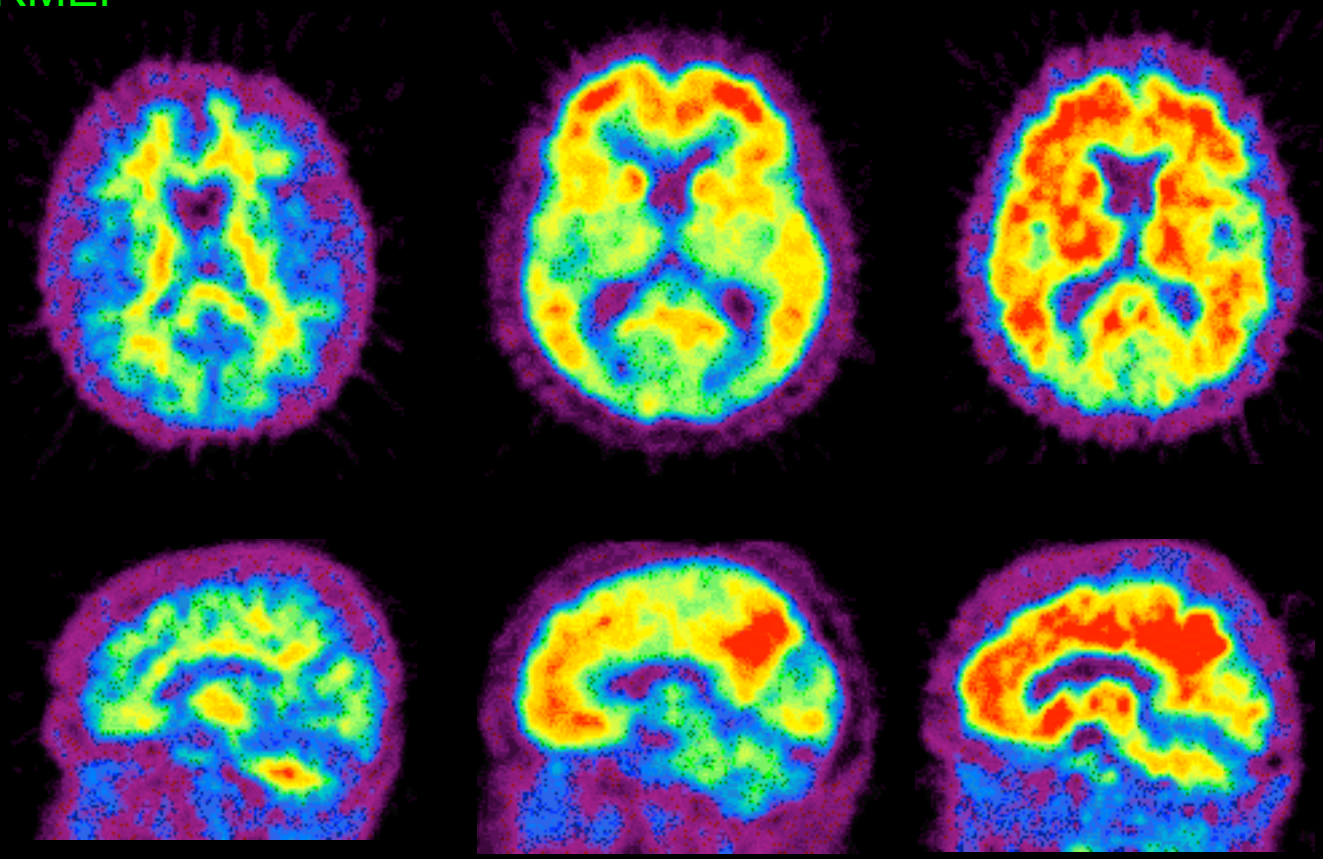
PIB et diagnostic différentiel MA/DCL/DFT





Rowe et al, Neurology 2007

LYON CERMEP



Témoin
66 ans
MMSE= 30
CDR= 0

MA pré-démentielle
80 ans
MMSE= 26
CDR= 0,5

MA démentielle
70 ans
MMSE= 20
CDR= 1

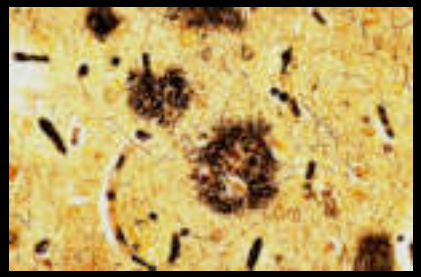
Formaglio et al, 2008

Conclusion

- Traitements anti-amyloïde

→ Optimiser le diagnostic précoce

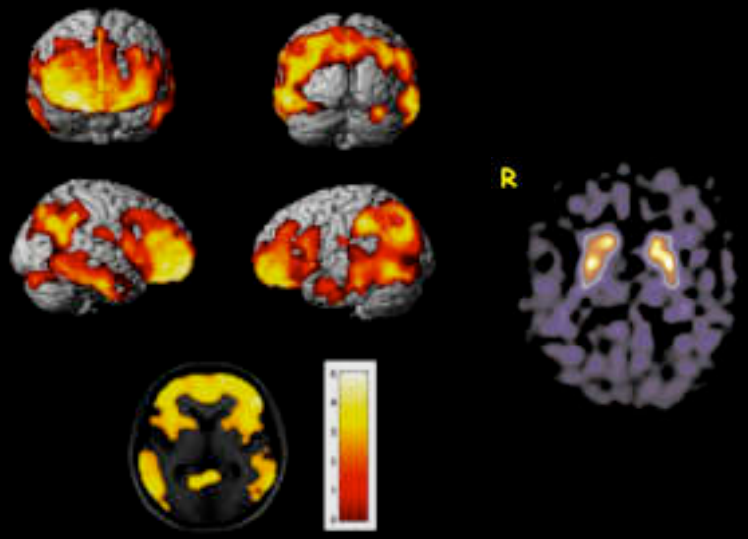
→ Avant une perte neuronale trop importante



- Imagerie métabolique +++

- Combinaison de marqueurs

→ Vérifications anatomiques ++



- Suivi thérapeutique