Neuropsychologie et neuroimagerie de la maladie d'Alzheimer

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Inserm

Cyceron
PLATEFORME D'IMAGERIE BIOMÉDICALE

CHUCaen

UNICAEN
université de Caen
Basse-Normandie

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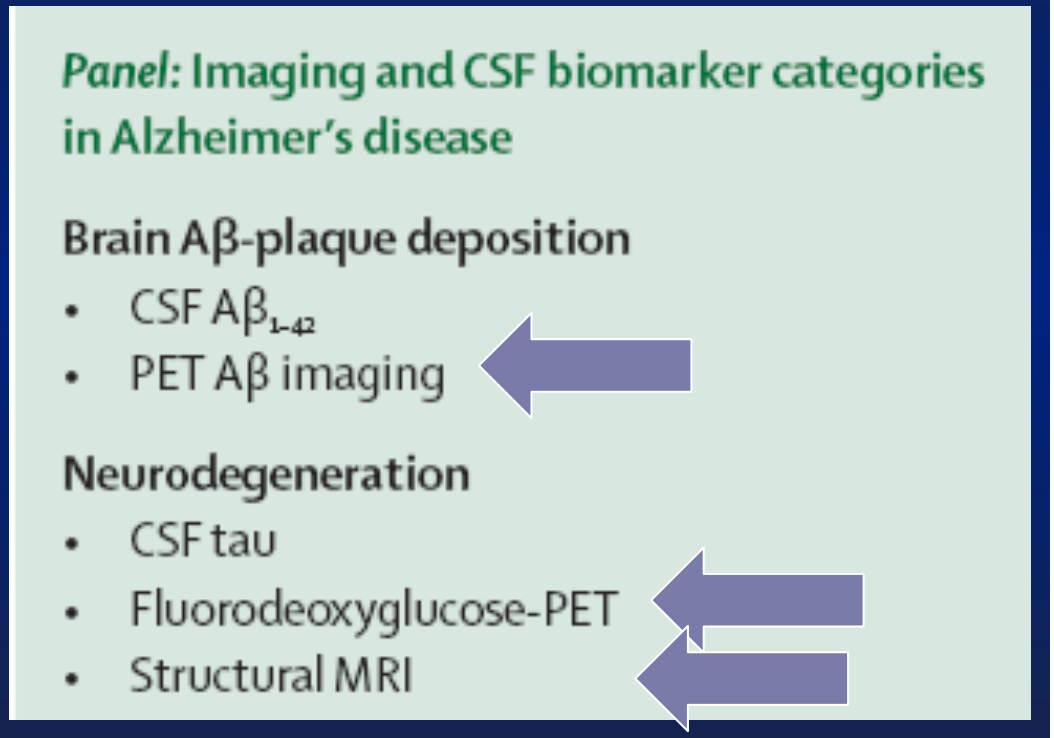
Biomarqueurs

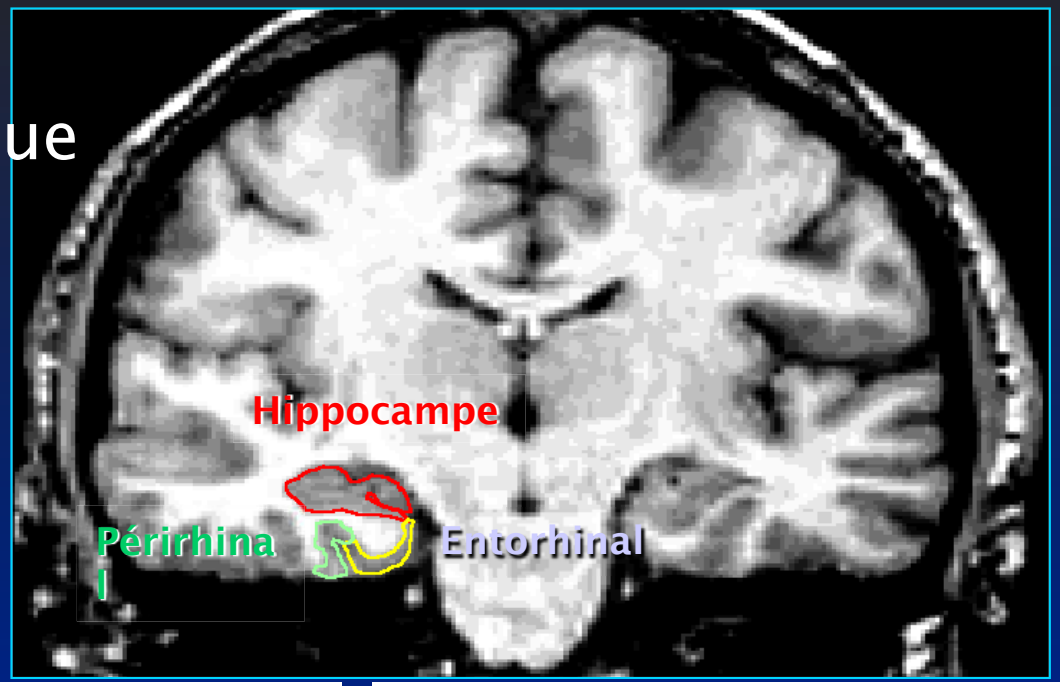
- Variables (physiologiques, biochimiques, anatomiques) qui peuvent être mesurées *in vivo* et peuvent renseigner sur les modifications liées à la maladie
- Imagerie et biomarqueurs LCR
- 5 plus courants : diminution de Aβ (LCR), augmentation de Tau (LCR), atrophie (IRM), hypométabolisme (TEP), augmentation de la fixation amyloïde (TEP)
- Autres : SPECT, IRMf repos…



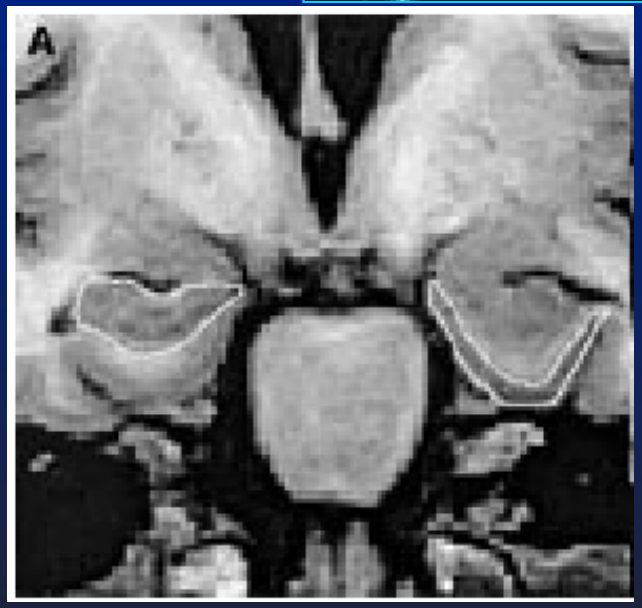
Jack et al. Lancet Neurol, 2010

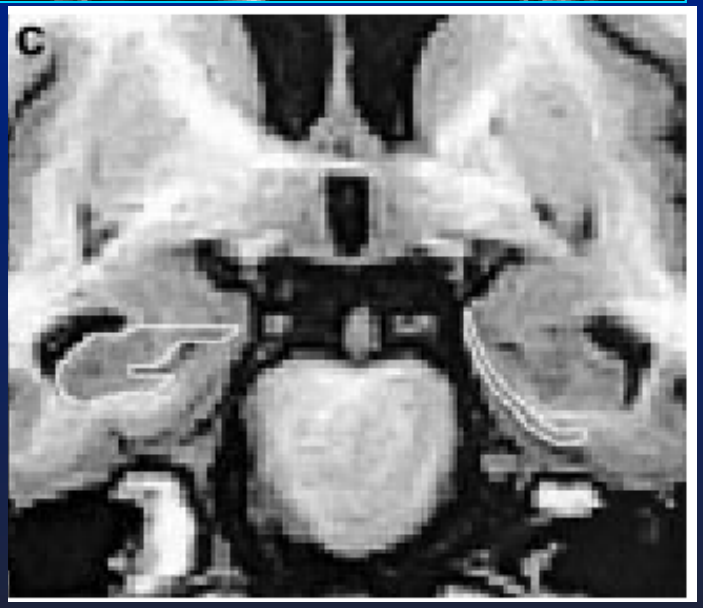
Atrophie hippocampique

Analyse par régions d'intérêt (ROI)



SS





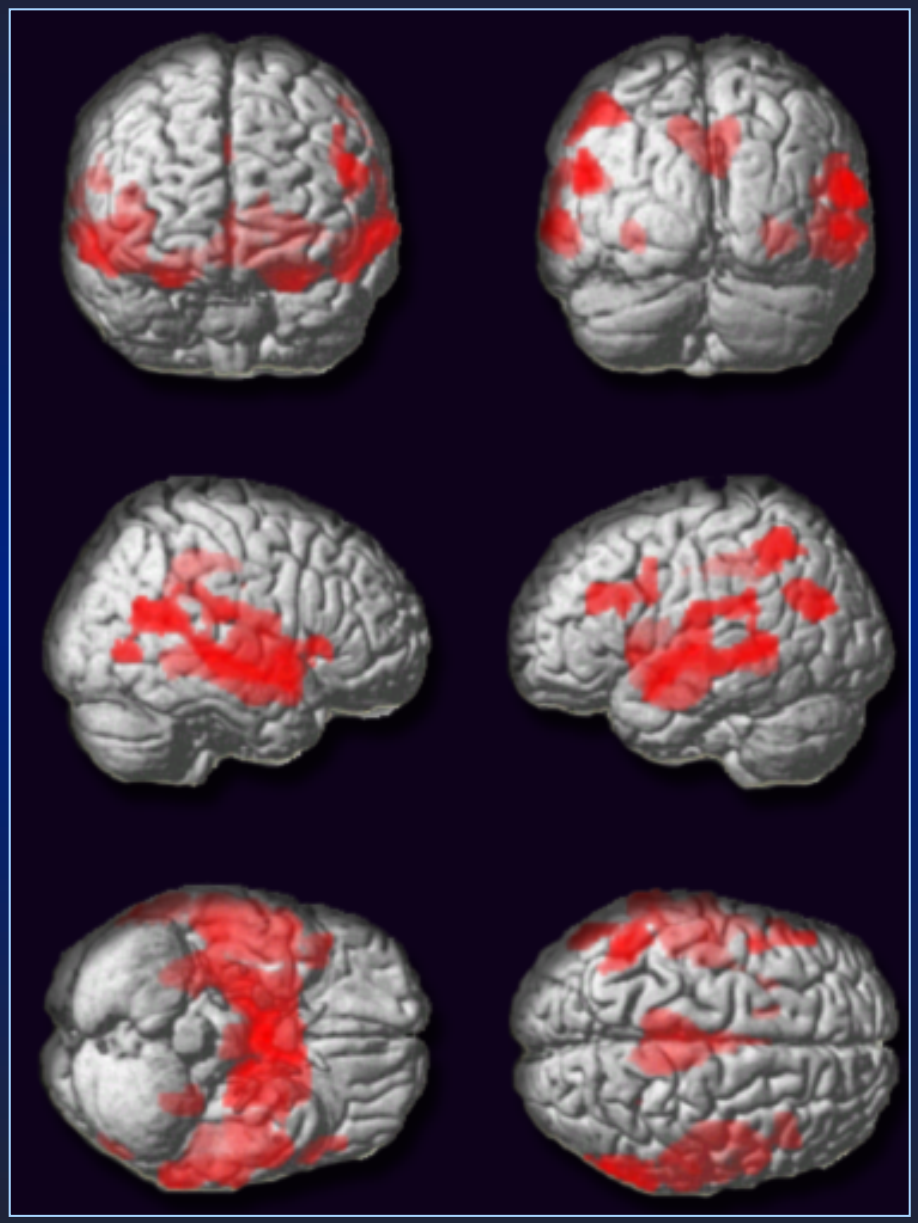
MA

Du et al., JNNP 2001

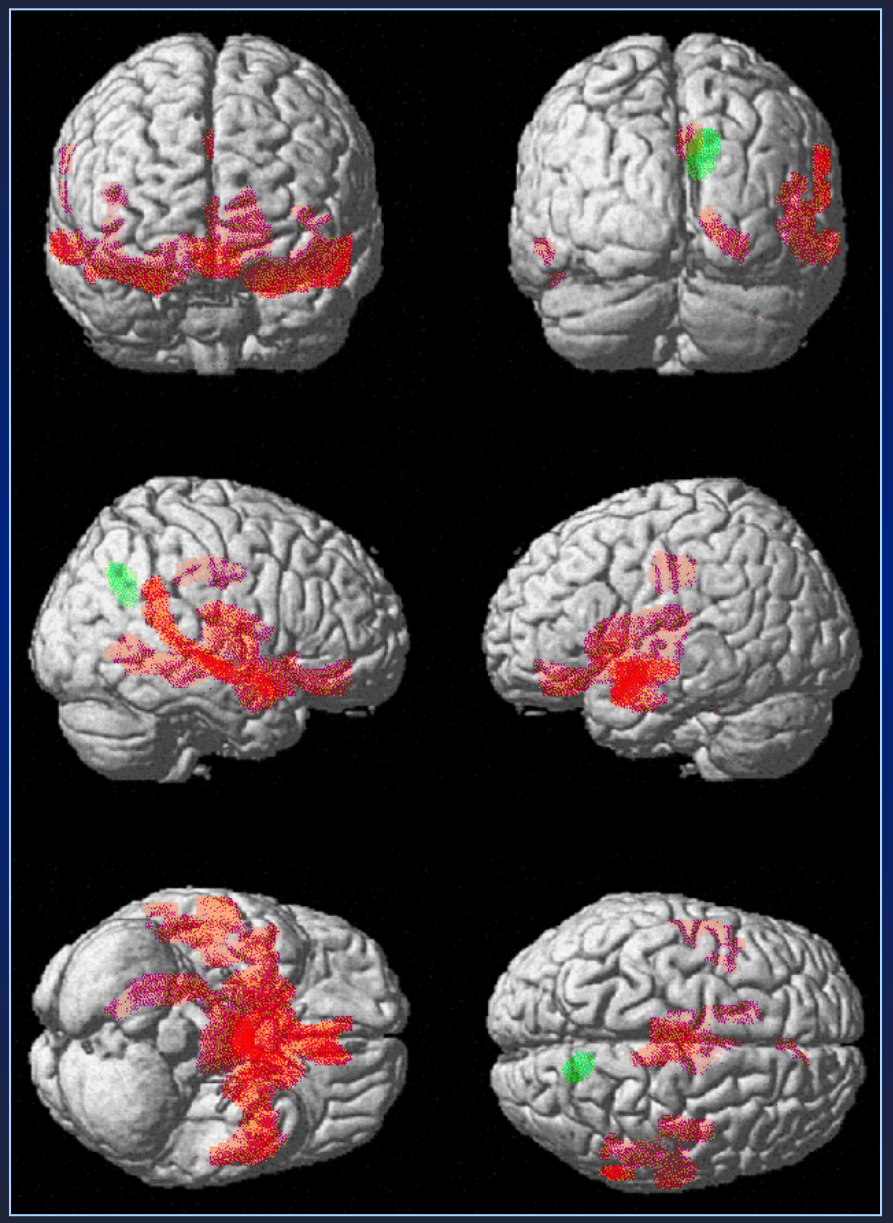
Hi et entorhinal entorhinal↘↘

Hi↘ et

ATROPHIE SUR L'ENSEMBLE DU CERVEAU (SPM)



MA : Baron et al., 2001



MCI : Chételat et al., 2002

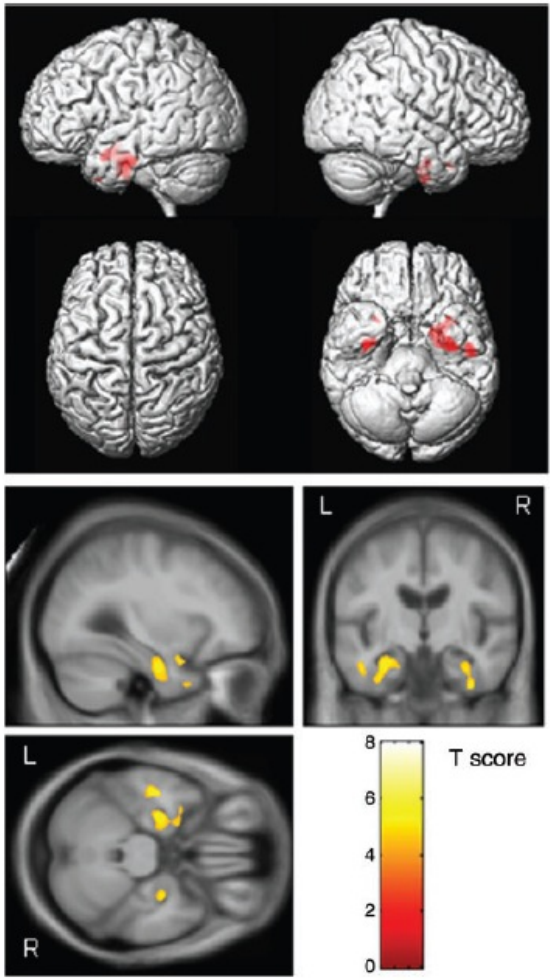


Fig. 2 Patterns of grey matter atrophy in the aMCI progressors ~3 years (18–54 months) before progression to AD. The results are shown on a 3D surface render (top) and overlaid on representative axial, coronal and sagittal slices (bottom). L = left; R = right.

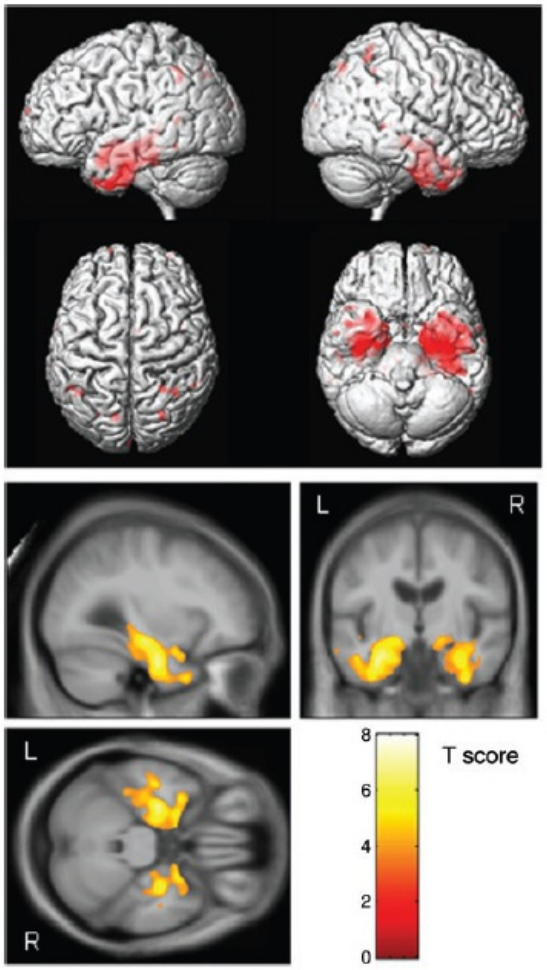


Fig. 3 Patterns of grey matter atrophy in the aMCI progressors ~1 year (9–18 months) before progression to AD. The results are shown on a 3D surface render (top) and overlaid on representative axial, coronal and sagittal slices (bottom). L = left; R = right.

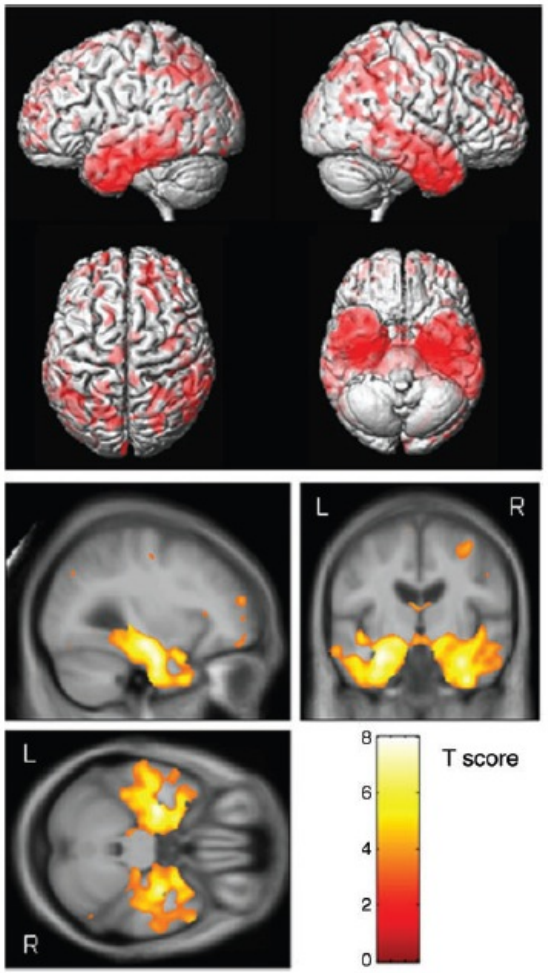


Fig. 4 Patterns of grey matter atrophy in the aMCI progressors at the time of a diagnosis of AD. The results are shown on a 3D surface render (top) and overlaid on representative axial, coronal and sagittal slices (bottom). L = left; R = right.

3 ans avant

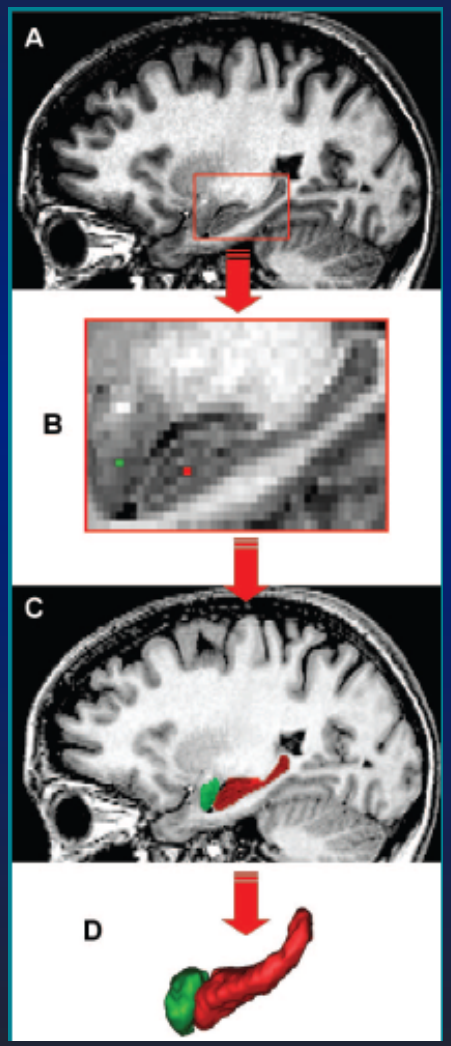
1 an avant

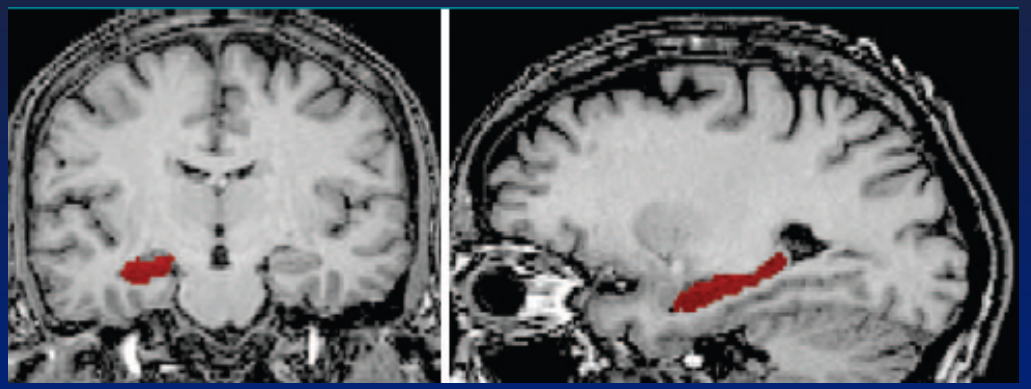
Au moment du diagnostic de M

Whitwell et al., Brain, 20

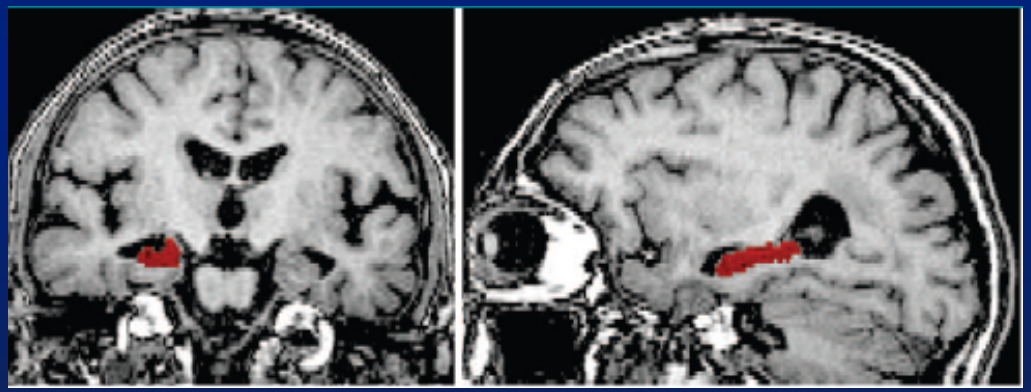
Segmentation automatique (Colliot et al., Radiology, 2008)

Logiciel M Chupin
(« graines »)



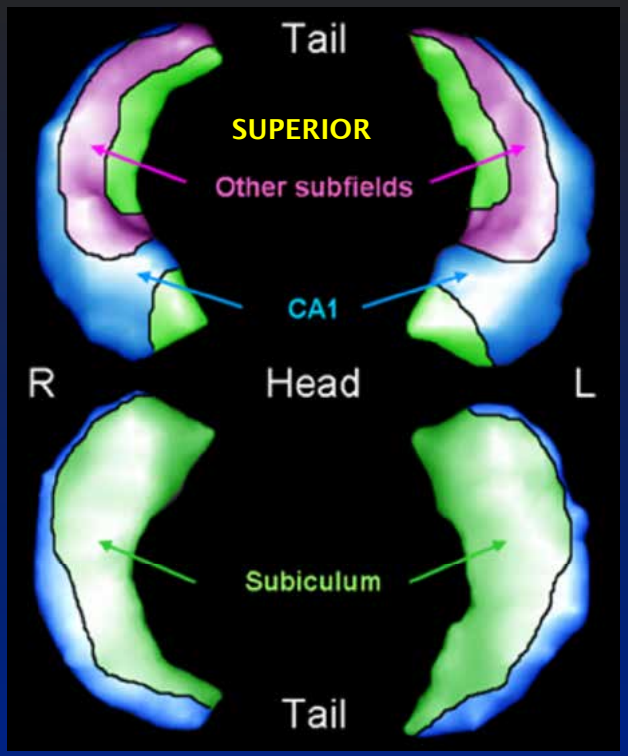


SAS



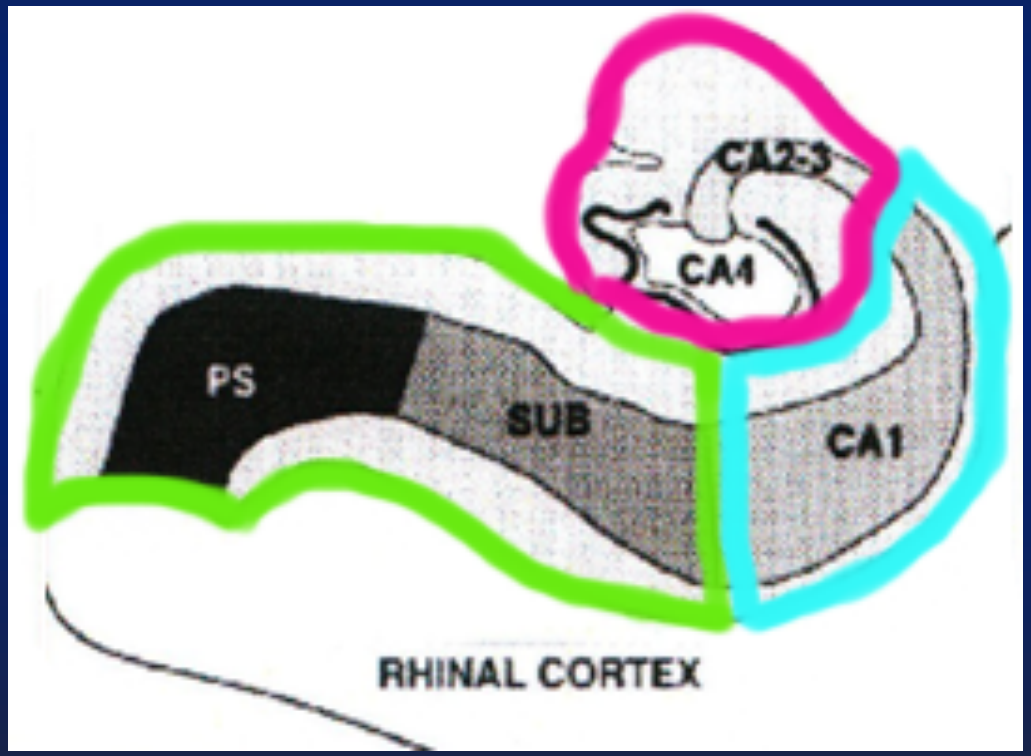
MA

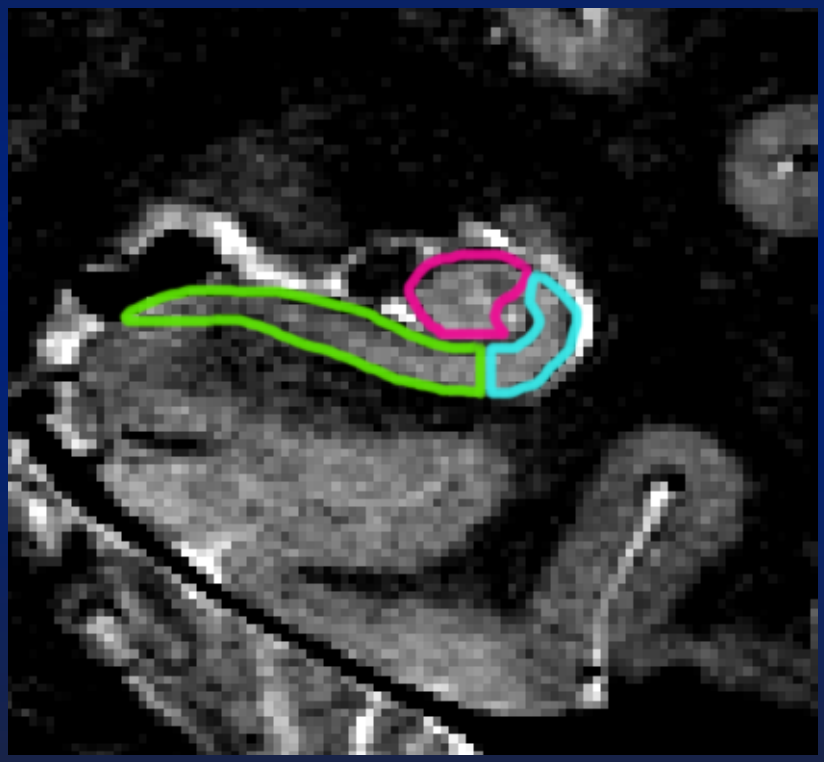
Group	Normalized Hippocampal Volume (cm^3)	Volume Reduction (%)	*P* Value
AD vs controls	1.95 vs 2.86	−32	<.001
MCI vs controls	2.30 vs 2.86	−19	<.001
AD vs MCI	1.95 vs 2.30	−15	<.01



Chételat et al., Neuropsychologia, 2008

Sous-régions hippocampiques

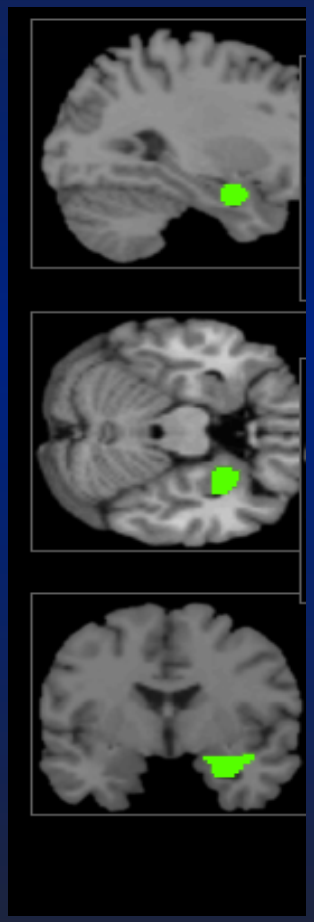




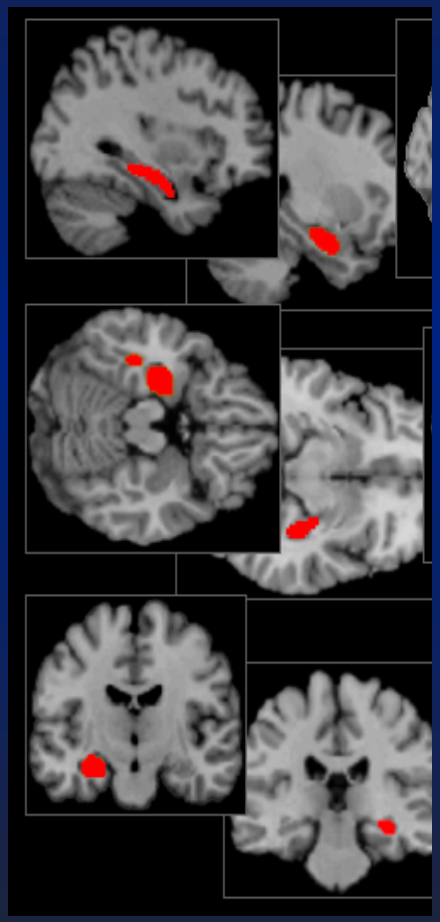
La Joie et al. NeuroImage, 2010

Corrélations entre les données morphologiques et la mémoire épisodique chez des MCI

Chételat et al.
Brain, 2003

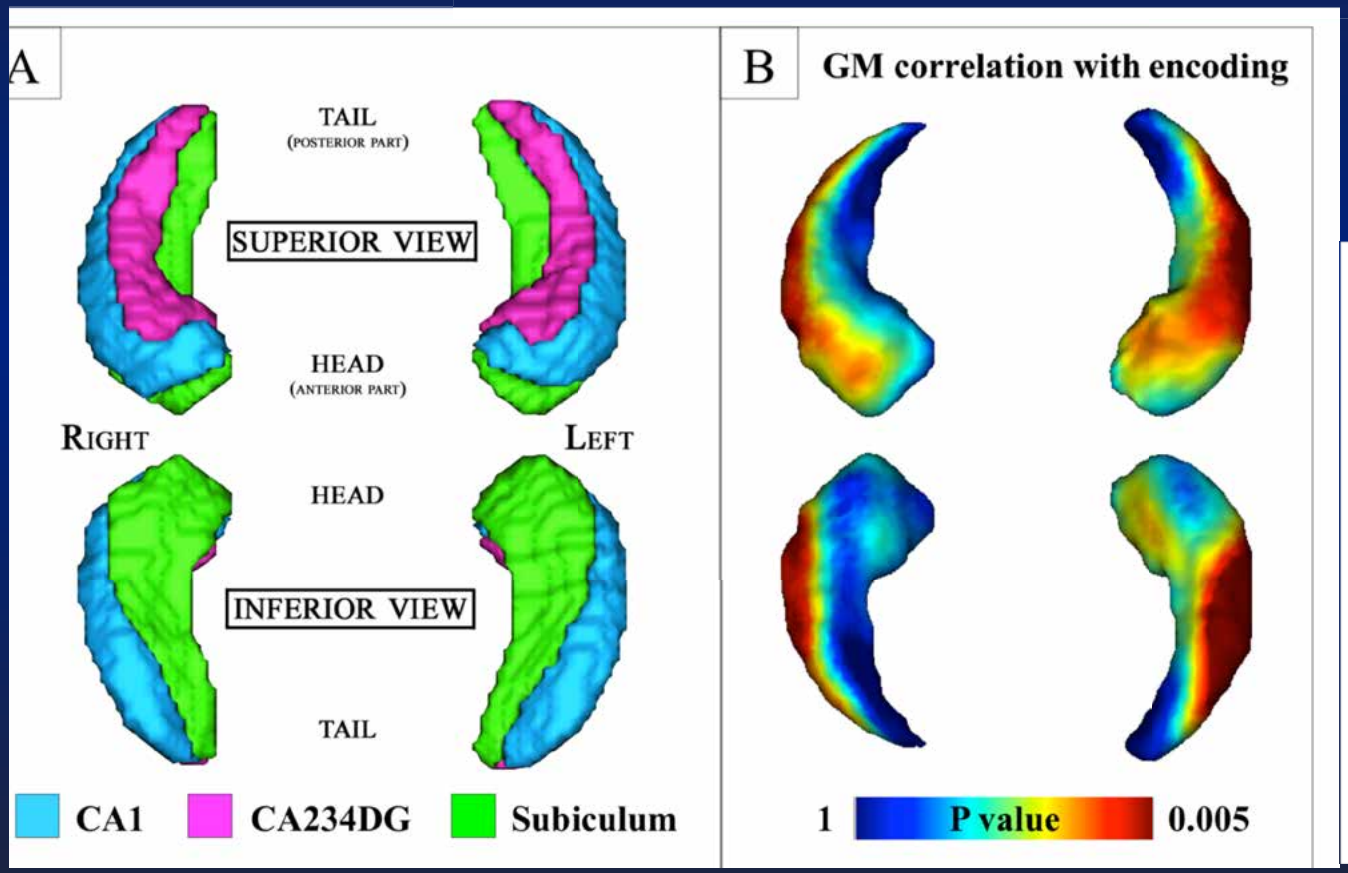


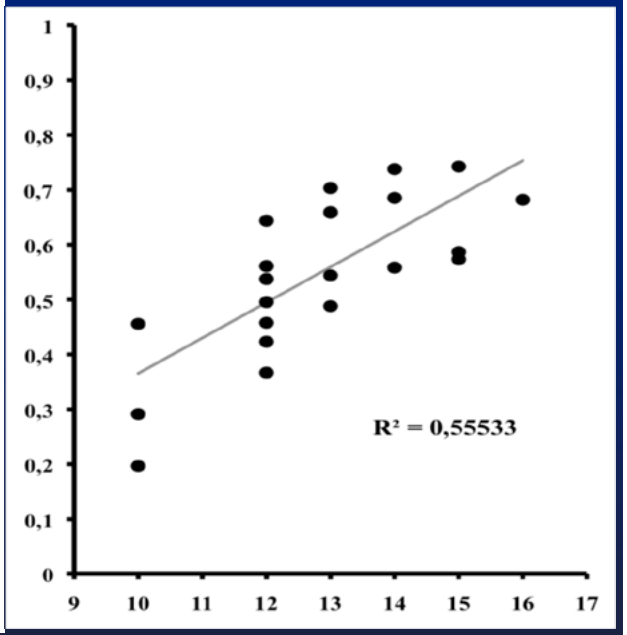
Encodage



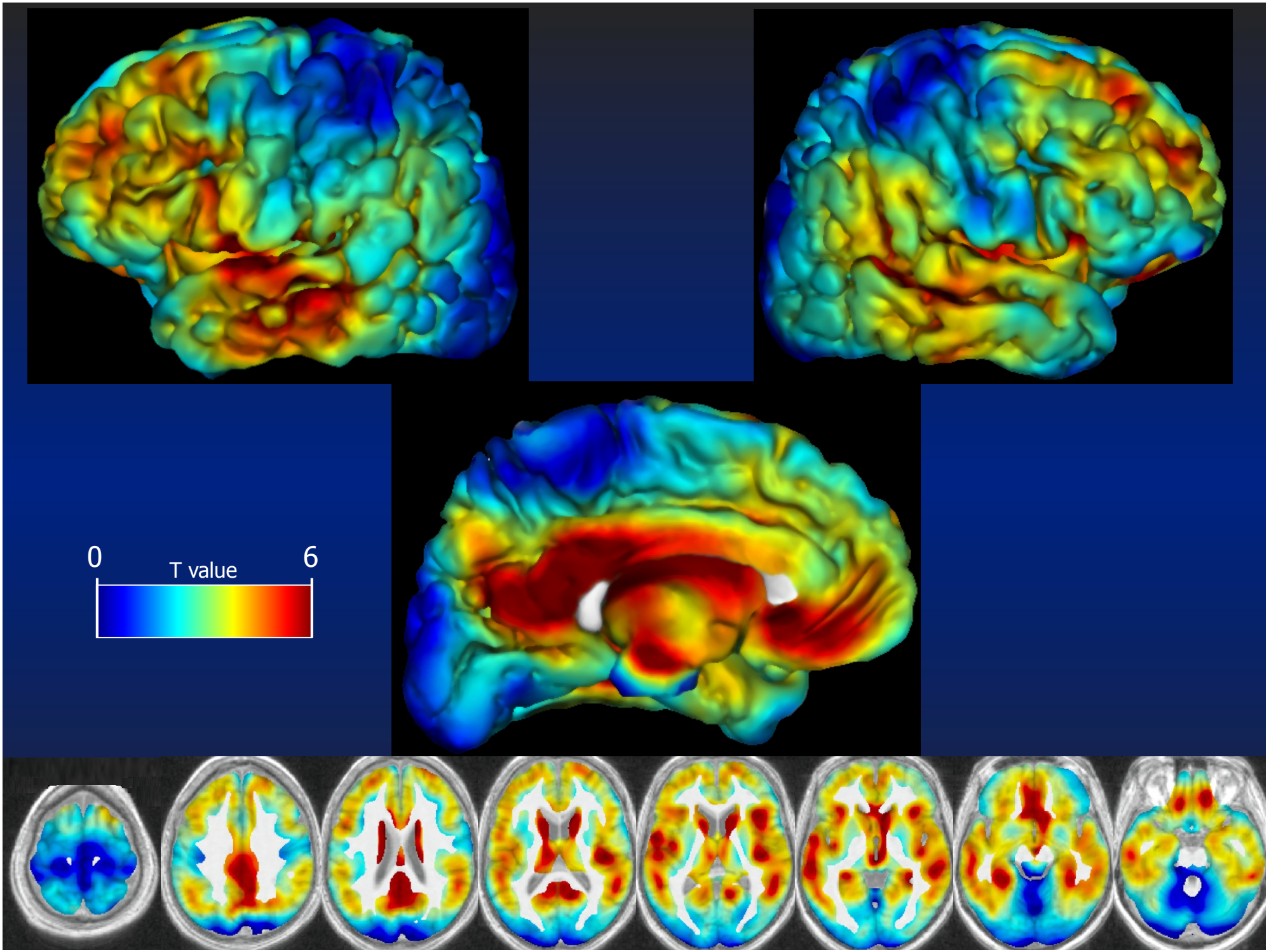
Récupération

MCI : Corrélations entre le score d'encodage et CA1



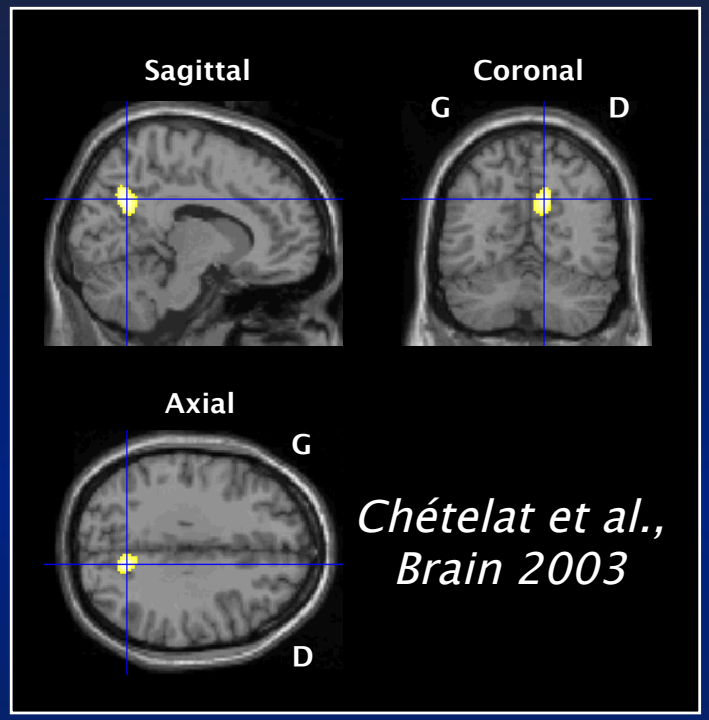


Fouquet et al., 2012

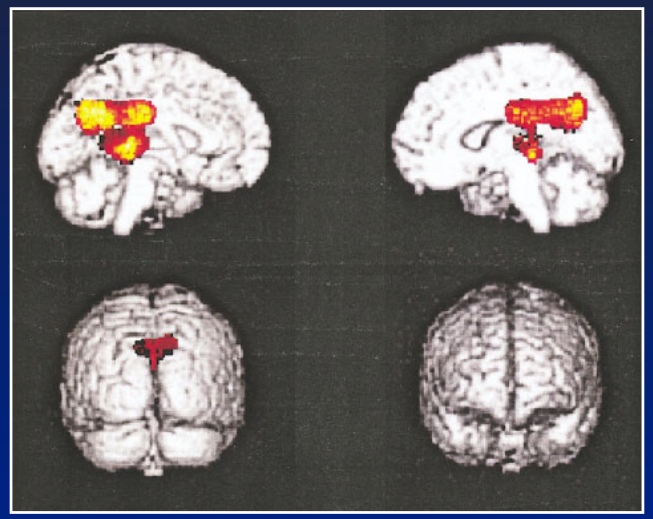

0
T value
6

MCI

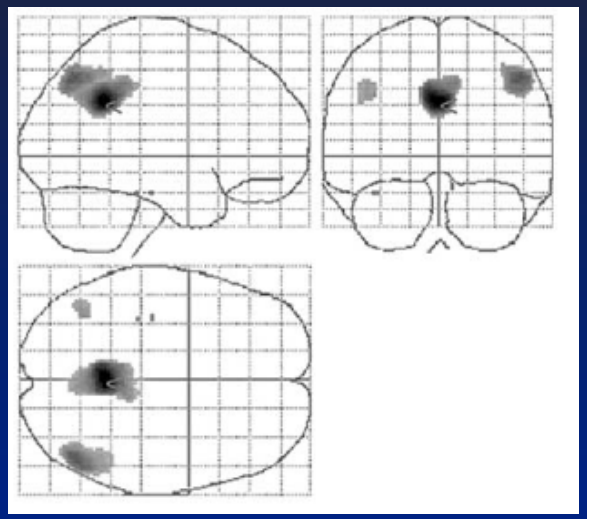
➡ CORTEX CINGULAIRE POSTERIEUR– PRECUNEUS



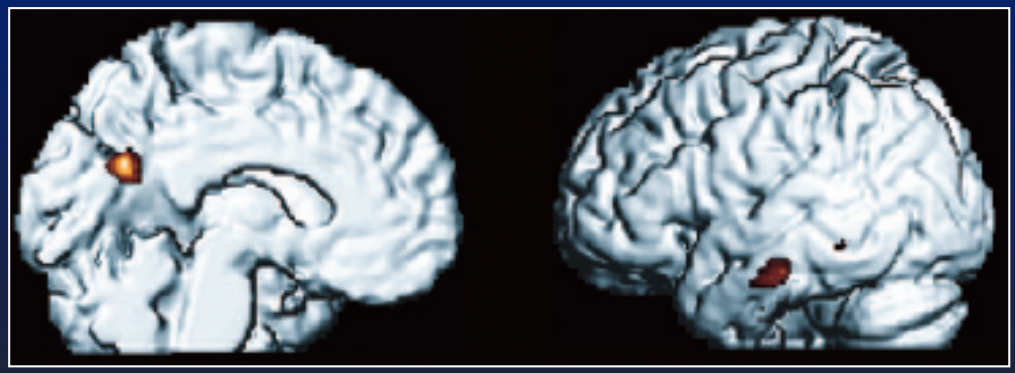
Chételat et al., Brain 2003



Nestor et al., Ann Neurol 2003



Hirao et al., NeuroImage 2005 (SPECT)

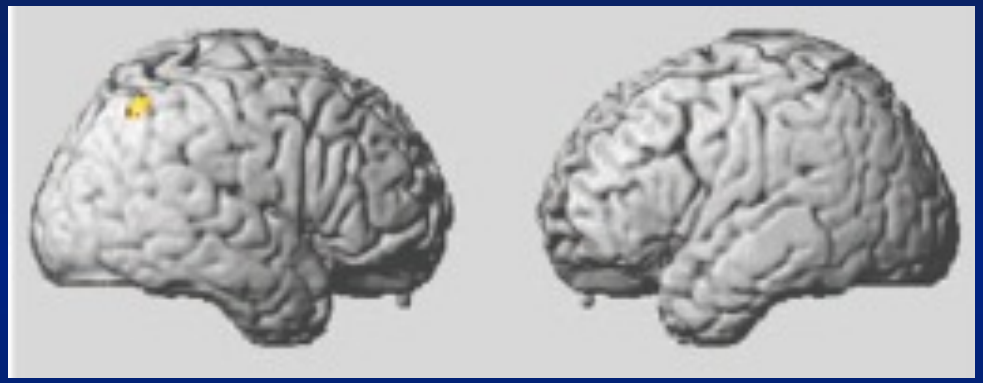


Mosconi et al., Neurology 2005 (SPECT)

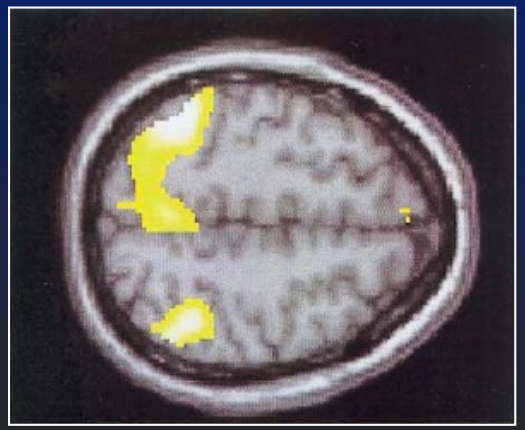
Converteurs/non converteurs (prédit la conversion vers la MA)

Chételat et al., Neurology 2003

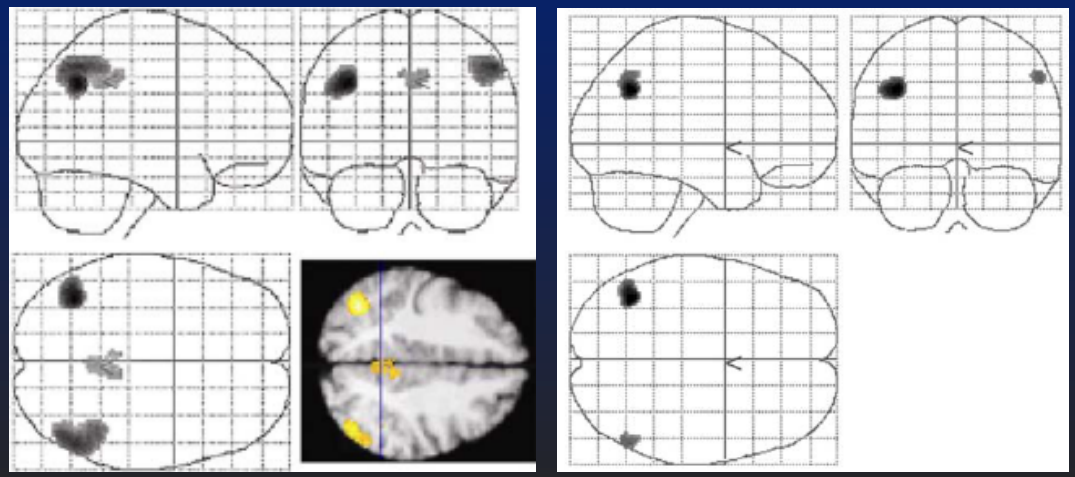
Mosconi et al., Neurology 2004



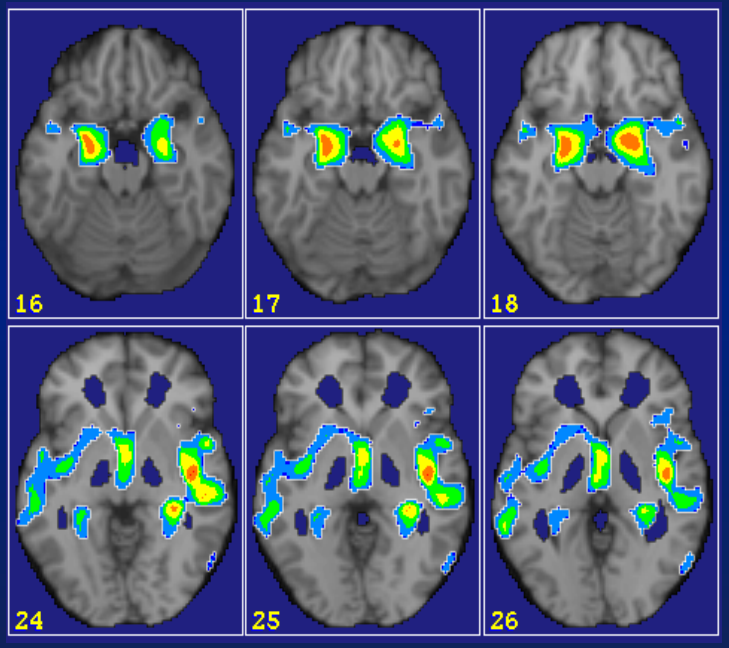
Huang et al., NeuroImage 2003 (SPECT)



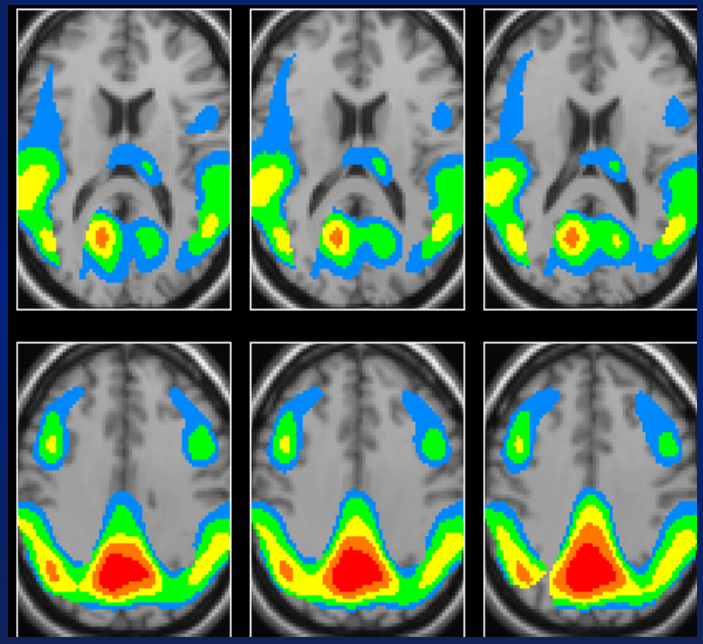
Hirao et al., NeuroImage 2005 (SPECT)



Discordance entre les profils

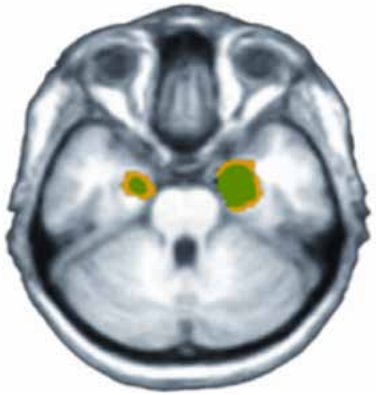
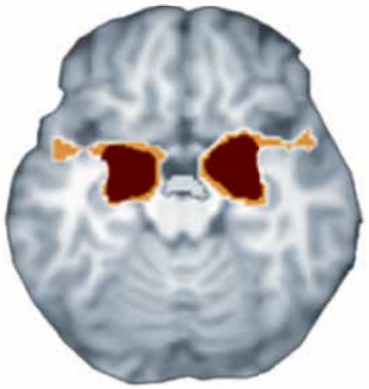
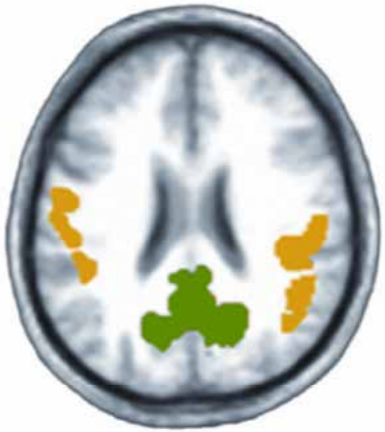
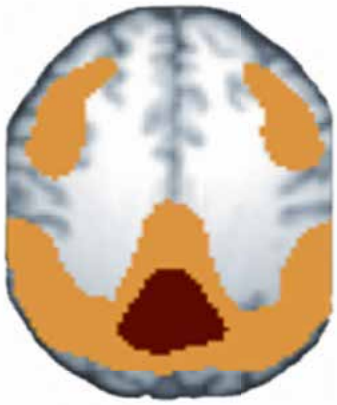


IRM : Atrophie
Hypométabolisme

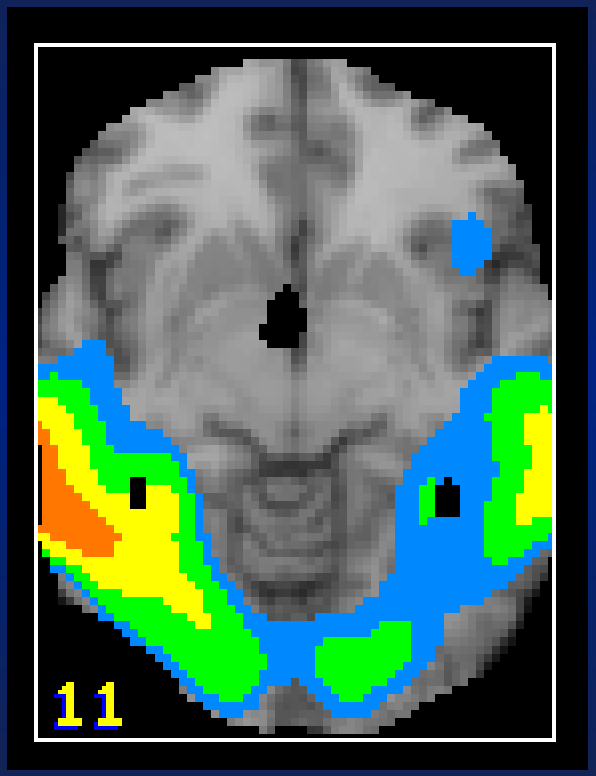


TEP :

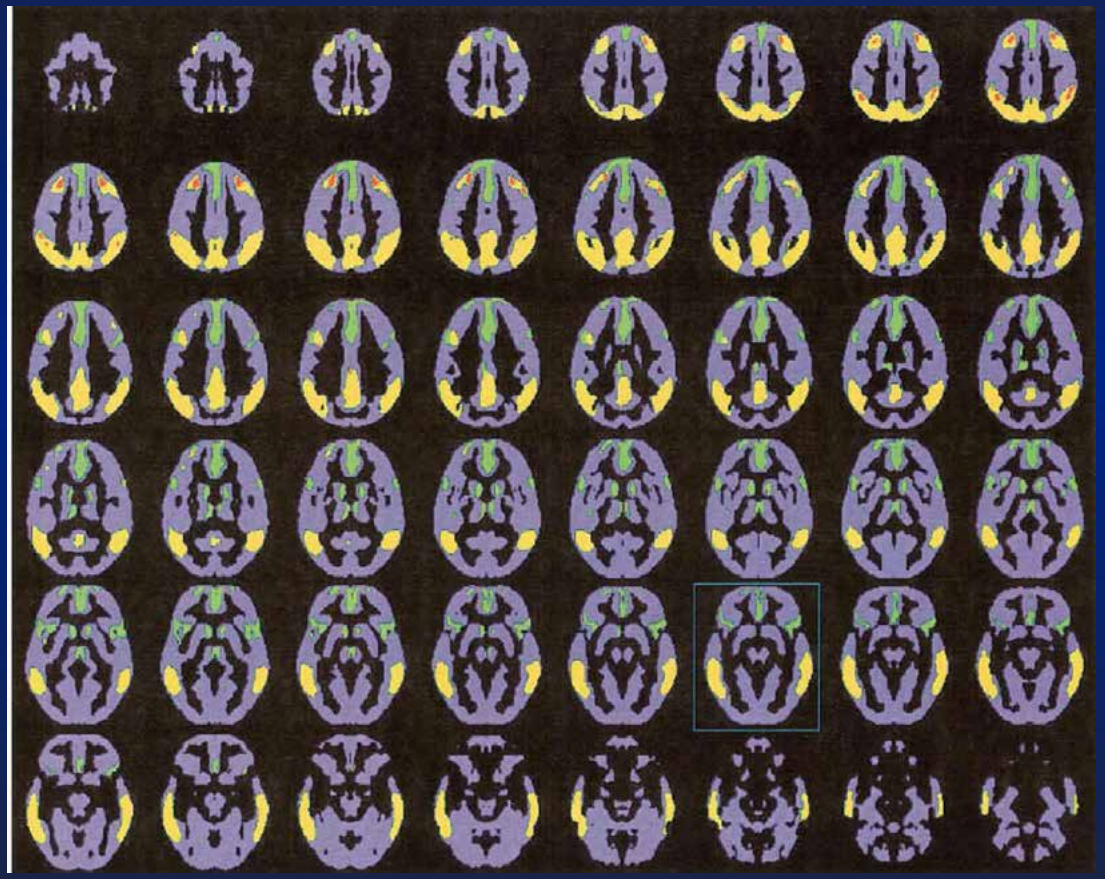
Contraste entre VN et MA

	Vieillissement normal	Maladie d'Alzheimer
IRM		
TEP-FDG		

1) Le paradoxe hippocampique

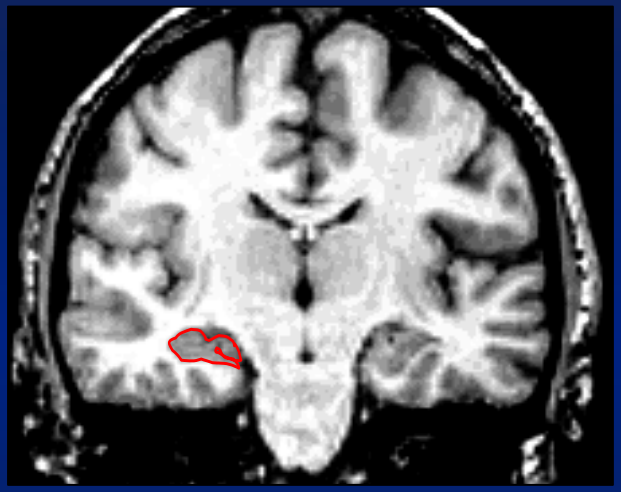


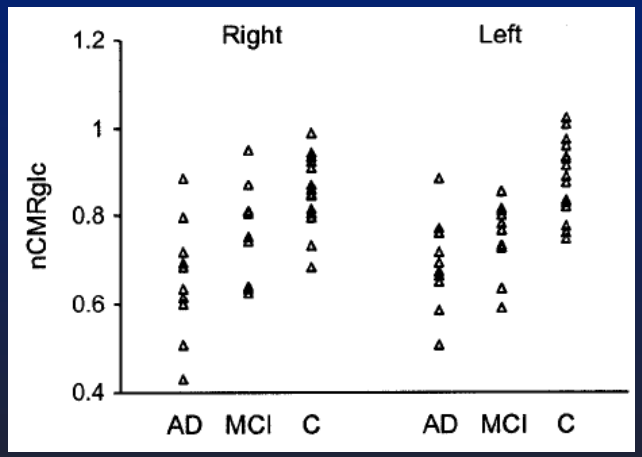
Résultat retrouvé dans la plupart des études TEP – MA ou MCI (Mosconi et al., 2005)



Herholz et al., NI, 2002 (N = 395)

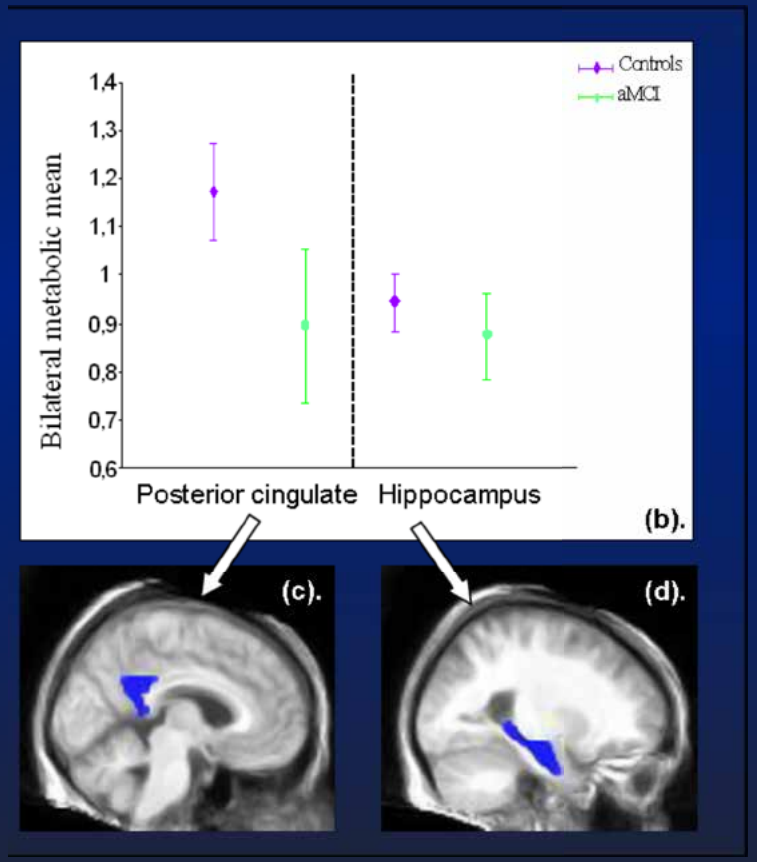
SPM vs ROI individuelles





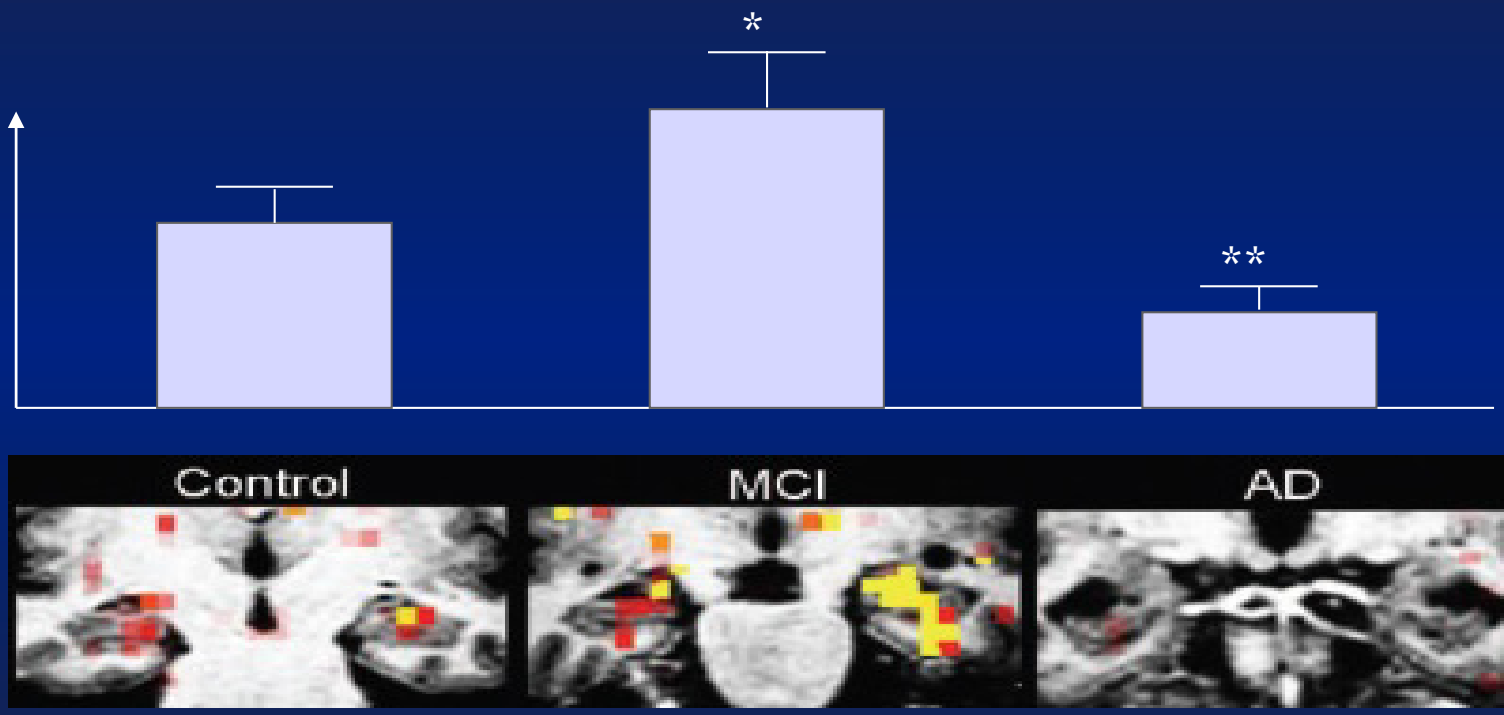
Nestor et al., 2003

EVP, vermis, ROI template commun SPM



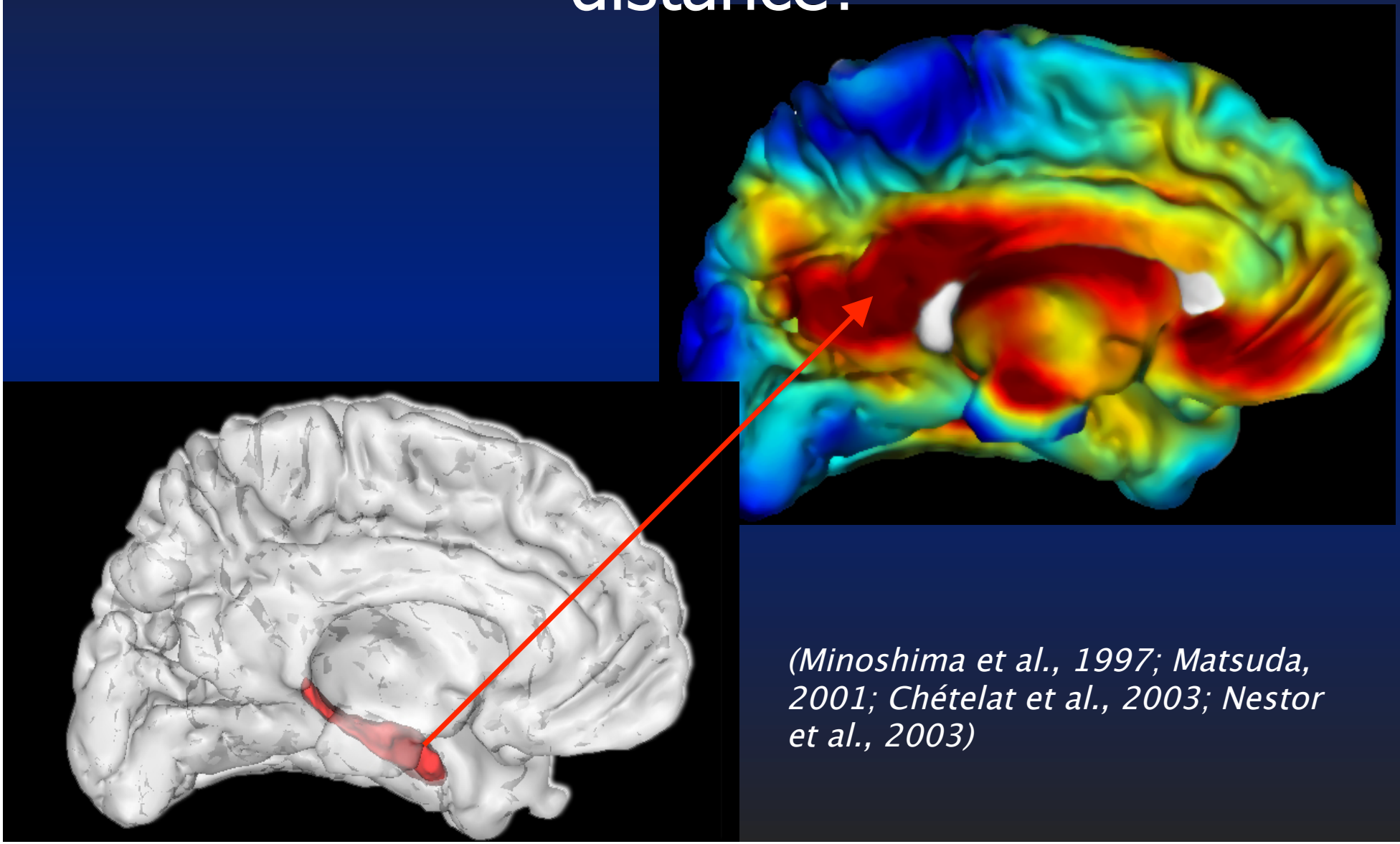
Mevel et al., NI, 2008 (N= 28 MCI)

Mécanismes compensatoires?



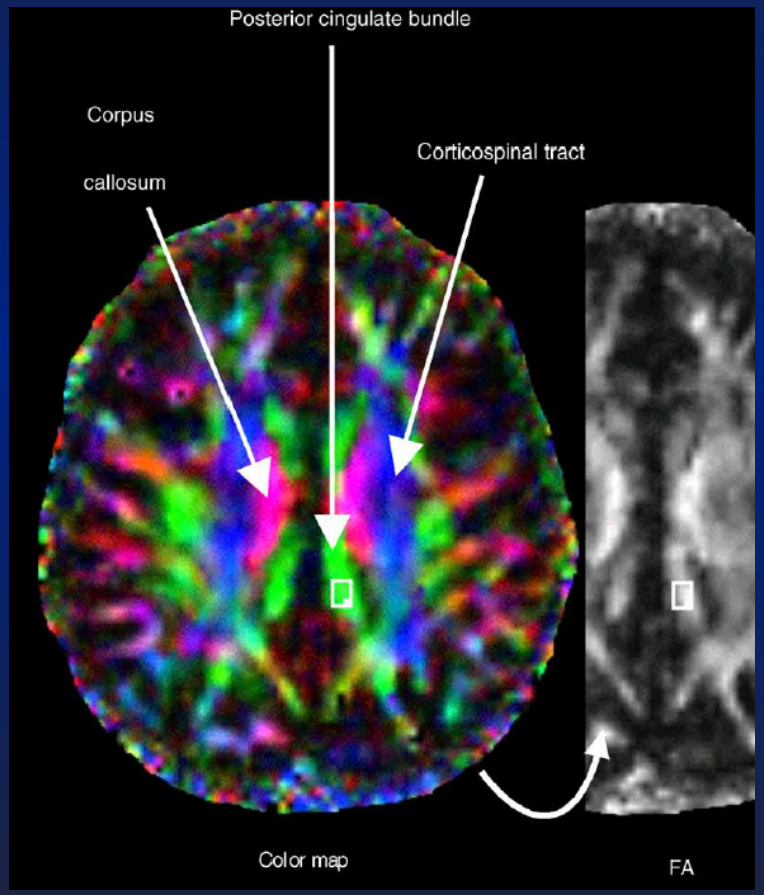
Dickerson et al., 2005

2) Atteinte cing post = Effet à distance?



(Minoshima et al., 1997; Matsuda, 2001; Chételat et al., 2003; Nestor et al., 2003)

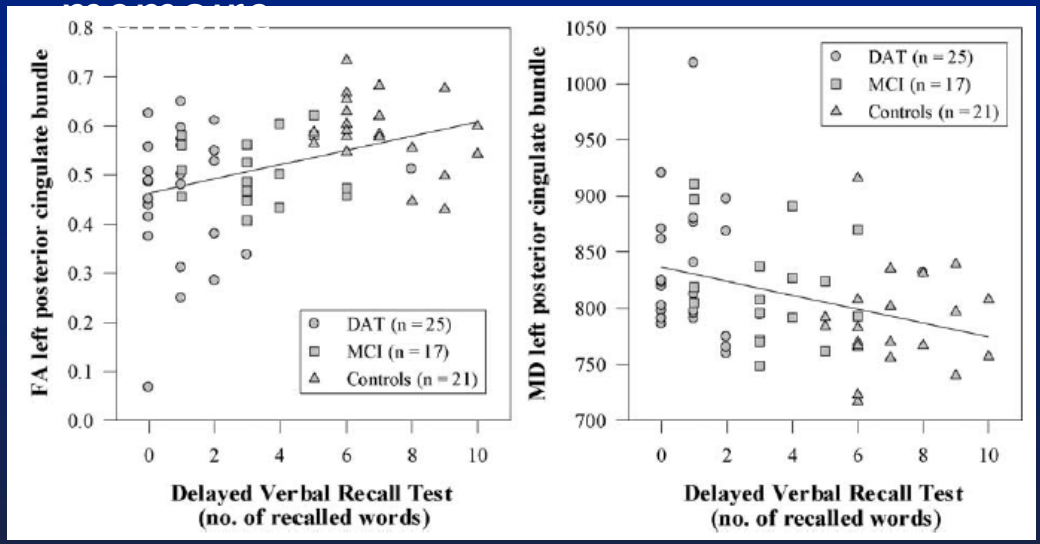
Cingulum (Hippocampe-cing post)



augmentation de la diffusivité (altération du tissu cérébral)

et diminution de l'anisotropie (intégrité de la SB)

corrélations avec les scores de mémoire

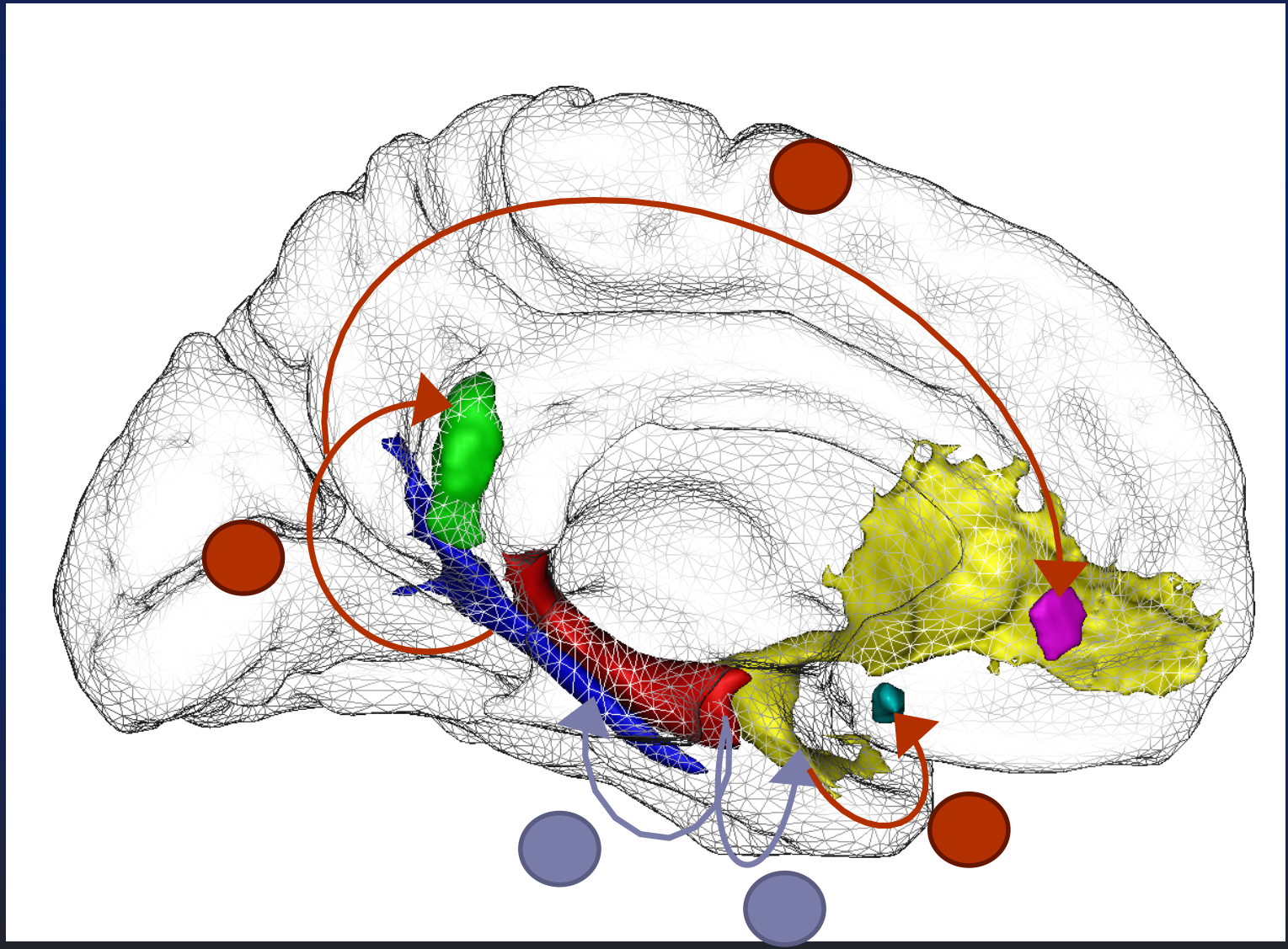


Supporte l'hypothèse de dysconnexion hypo cing post

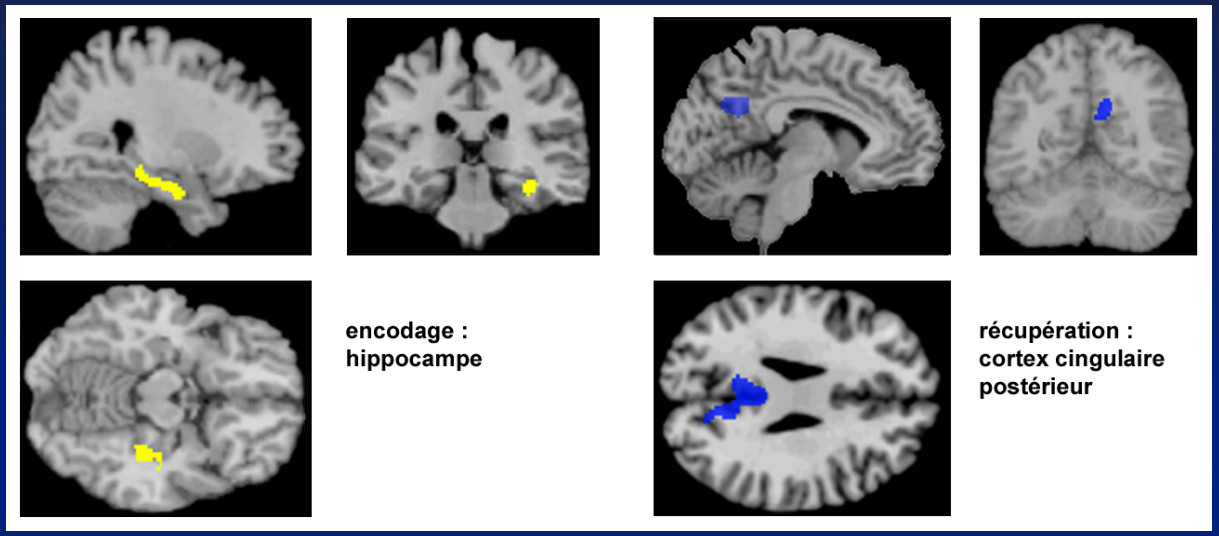
Fellgiebel et al., N of Aging, 2005

MA = syndrome de dysconnexion?

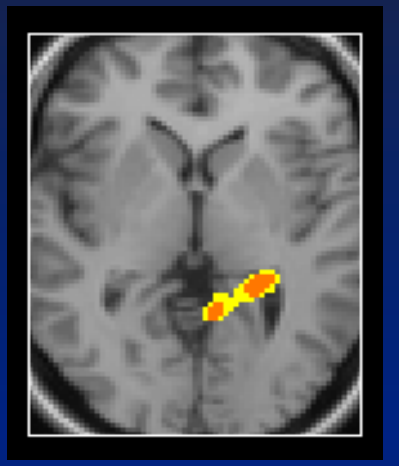
Villain et al., JN, 2008; Brain, 2010



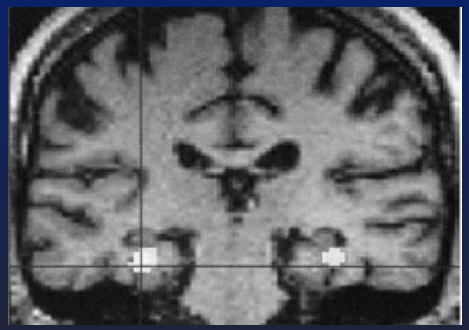
Corrélations cognitivo-métaboliques

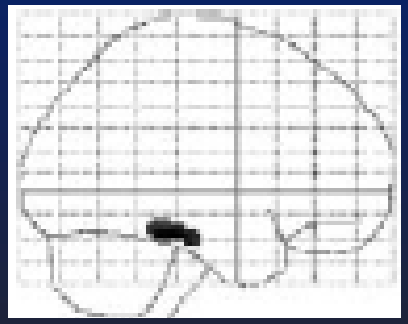


MCI (Chételat et al., 2003)

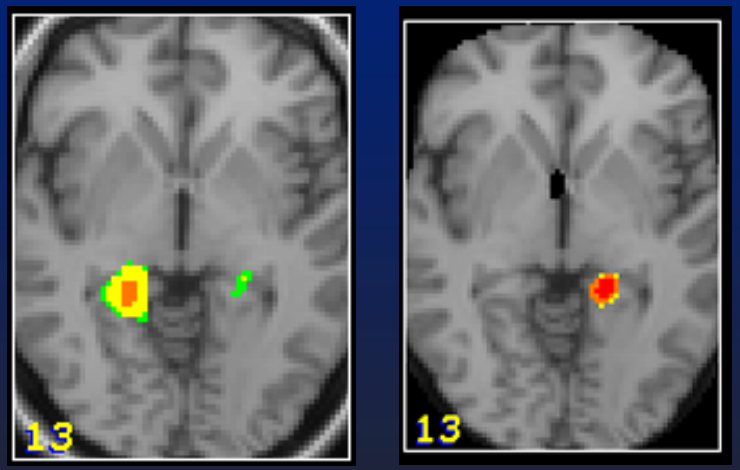


Eustache et al., 2004





Lekeu et al., 2003 ; Teipel et al., 2006



Desgranges et al., 1998 ; 2002

Réseau par défaut

- Emerge spontanément lorsque activité cognitive non contrainte (repos) => propriété intrinsèque du cerveau

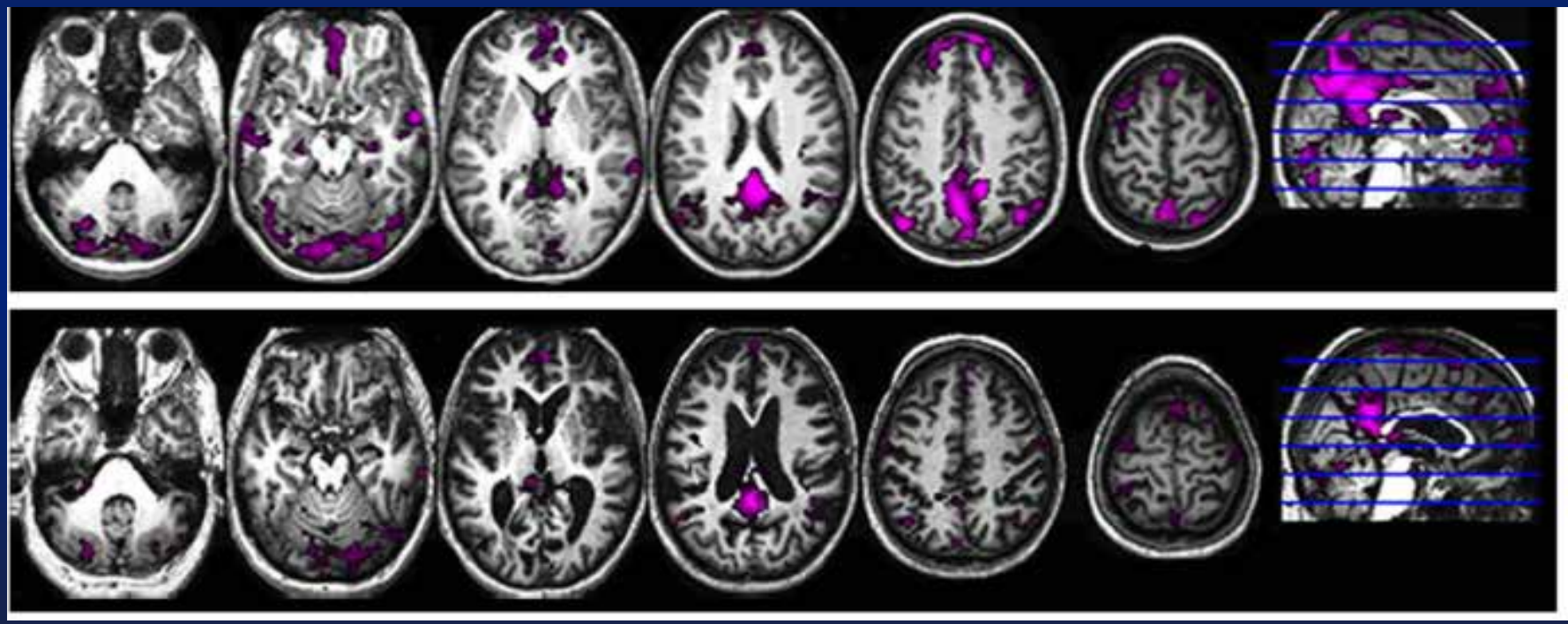
- **Synchronisation temporelle** de fluctuations basse fréquence (0.01-0.1 Hz ; Cordes *et al.*, 2001) = connectivité fonctionnelle

- ... Et **spatiale** = entre plusieurs régions cérébrales (nœuds ; 'hubs', Buckner *et al.*, 2009) anatomiquement reliées (SB; voir van den Heuvel *et al.*, 2010 pour revue):

Réseau par défaut

IRMf repos et connectivité fonctionnelle (synchronisation de l'activité cérébrale régionale)

Mevel et al., 2010



Altération des désactivations dans la MA (régions pariétales et frontales médian
Similitude avec les régions hypométaboliques

Rôle cognitif du DMN ?

Voir Mevel et al., 2010 pour revue

- Deux hypothèses :
  - **Activité introspective**
    - ***Voyage dans le temps :***
      - **Passé** : rappel d'évènements en mémoire autobiographique (Andreasen *et al.,* 1995; Buckner & Carroll, 2007; Buckner *et al.,* 2008) pour...
      - **Futur** : 'prospective brain' = projection de Soi dans le futur (Schacter *et al.,* 2005, 2007)
    - ***Rêveries diurnes et pensées intrusives*** ('Mind wandering', 'task unrelated thoughts'; Mason *et al.,* 2007)
  - **Fonction de Sentinelle:**
    - Fonction de surveillance diffuse de l'environnement (Ghatan *et al.,* 1995; Shulman *et al.,* 1997; Gusnard & Raichle 2001; Gilbert *et al.,* 2007; Buckner *et al.,* 2008)

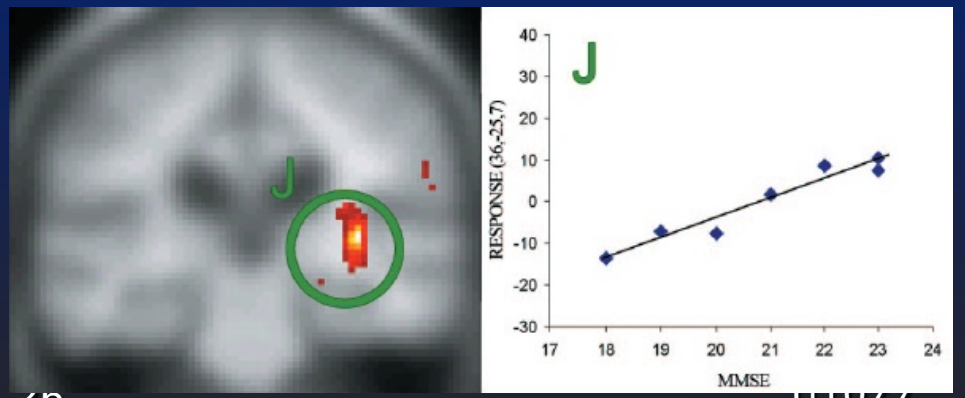
Imagerie fonctionnelle de la mémoire aux stades précoces de la maladie d'Alzheimer : dysfonctionnements et mécanismes compensatoires

Alexandre Bejanin, Nicolas Villain, Armelle Viard, Mickaël Laisney, Francis Eustache, Béatrice Desgranges

Rev Neuropsychol

2010 ; 2 (2) : 145-56

- Peu d'études MA ou MCI : 45 articles entre 1996 et 2010
- 50% pendant l'encodage; 25% pendant la récup; 25% les deux
- MA : résultats attendus : hypoactivation de l'hippocampe, corrélation avec l'atrophie hippocampique, les performances et le MMS



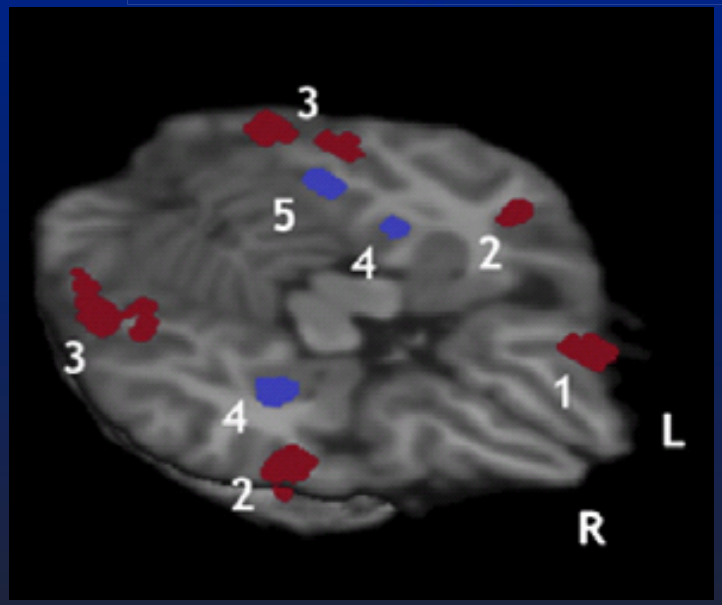
Activation hippocampique corrélée au MMS (Golby et al., Brain, 2005)

Méta-analyse 14 études Hypoactivations dans l'hippocampe

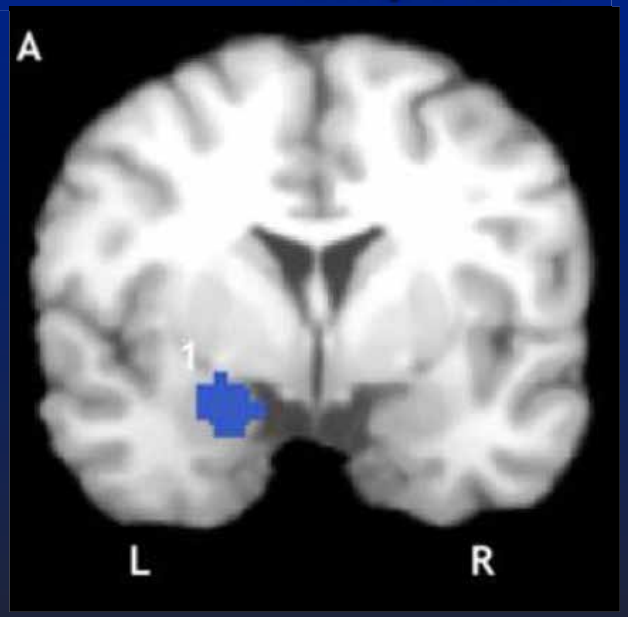
Schwindt et Black., NeuroImage, 2009

Backman et al., (1999)
Becker et al., (1996)
Celone et al., (2006)
Diamond et al., (2007)
Golby et al., (2005)
Gould et al., (2006)
Gron et al., (2002)
Hamalainen et al., (2007)
Pariente et al., (2005)
Petrella et al., (2007)
Rémy et al., (2005)
Rombouts et al., (2002)
Solé-Padullés et al., (in press)
Sperling et al., (2003)
Total foci

Encodage (4)



Récupération

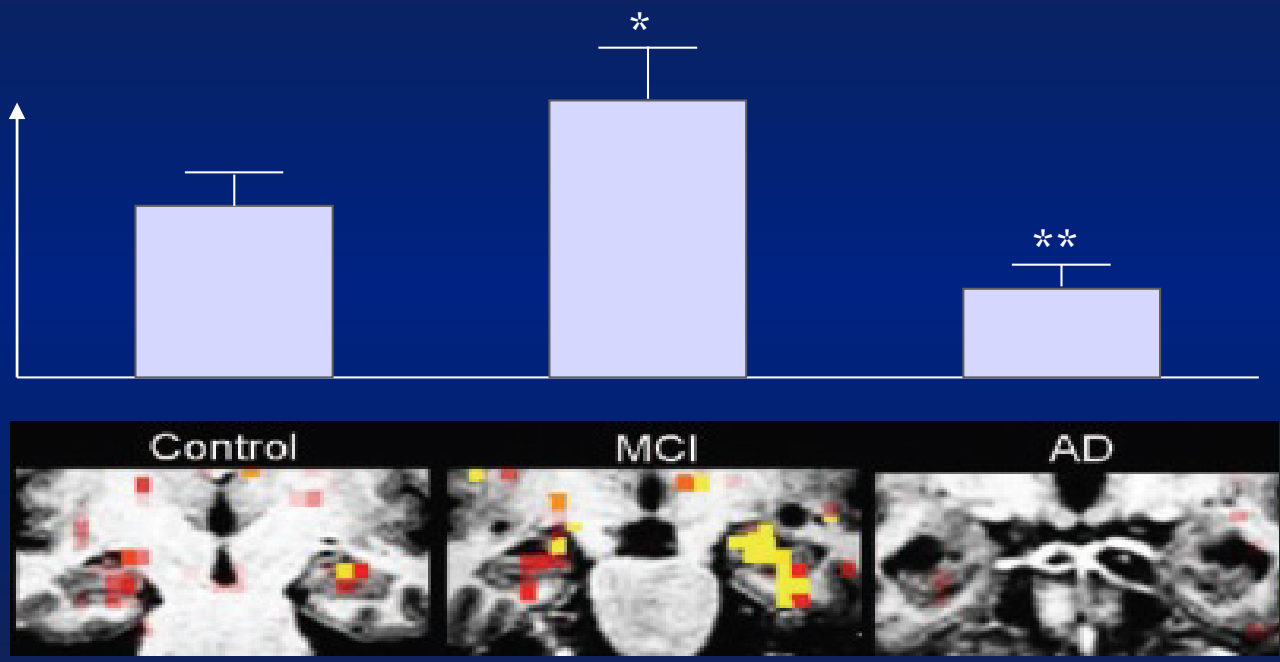


Et chez les patients MCI? Augmentation de l'activité hippocampique

IRMf : Encodage de paires visages-noms

Perf. en reconnaissance : SAS = MCI > MA

Dickerson et al.,2004; 2005

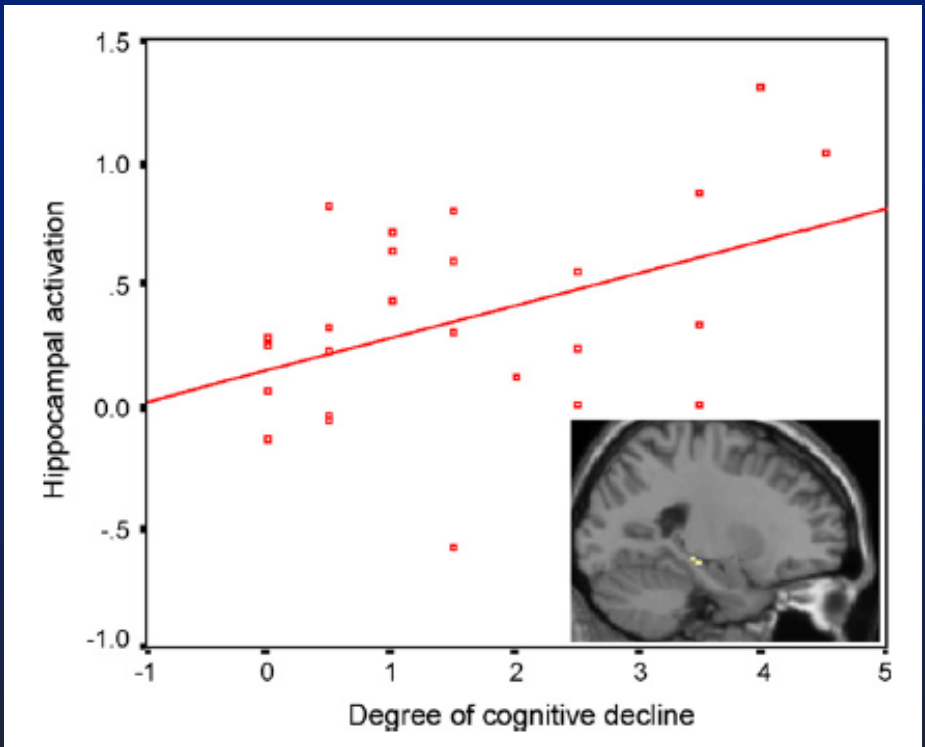


Répliqués : Celone *et al.*, 2006 ; Kircher *et al.*, 2007 ; Hamalainen *et al.*, 2007a ; Heun et al., 2007; Trivedi *et al.*, 2008 (E) ; Yassa et al., 2010; Putcha et al., 2011

Non répliqués : Machulda *et al.*, 2003 ; Petrella et al., 2006 ; Johnson *et al.*, 2006; Trivedi et al., 2008 (R); Mandzia et al., 2009 ; Hanseeuw et

Phénomène transitoire - Caractère prédictif

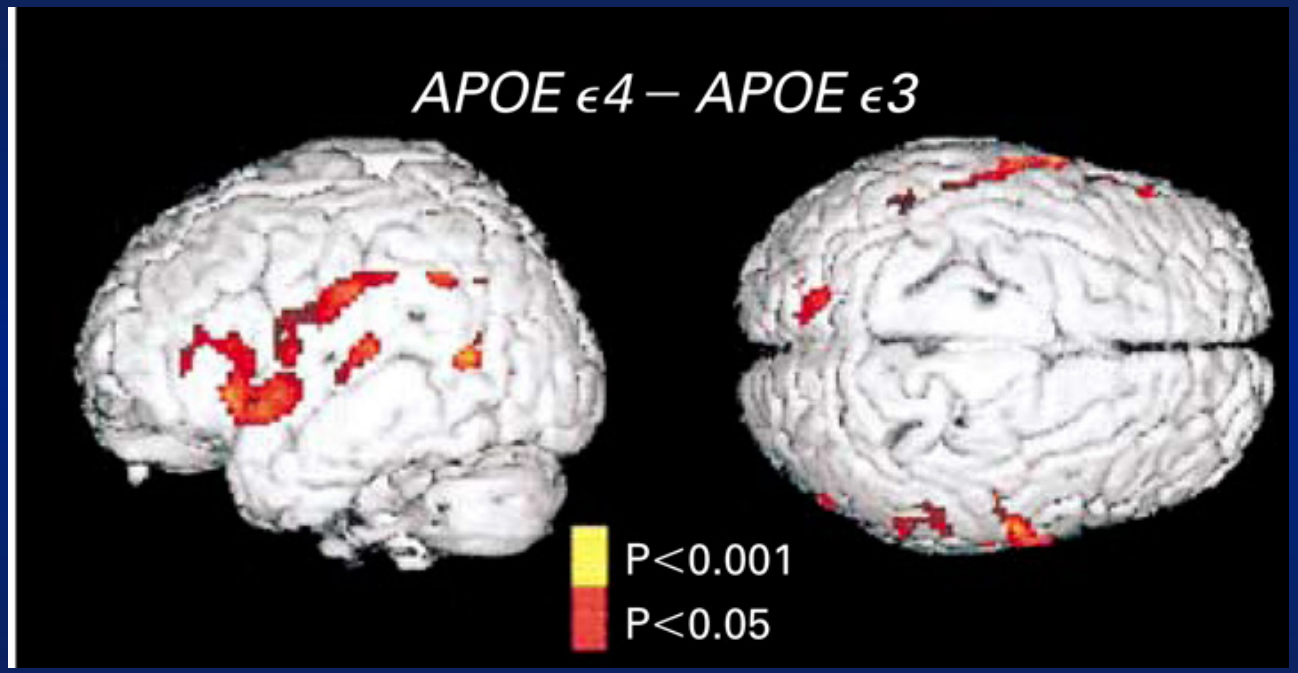
- Facteurs invoqués : processus (E) ; type d'encodage (intentionnel)
- Stade de la maladie : (Celone et al., 2006)
  - Hyperactivation chez les MCI les moins altérés
  - Hypoactivation chez les plus atteints



Le degré d'hyperactivation initiale prédit le déclin cognitif 4 ans plus tard (Miller et al., 2006)

Sujets sains APOE4

- Bookheimer et al., 2000, IRMf



Encodage de paires de mots

16 sujets $APOE_4$ (14 4-4 et 2 4-4)

14 sujets $APOE_3$

$APOE_4$= Activations plus importantes dans l'hippocampe

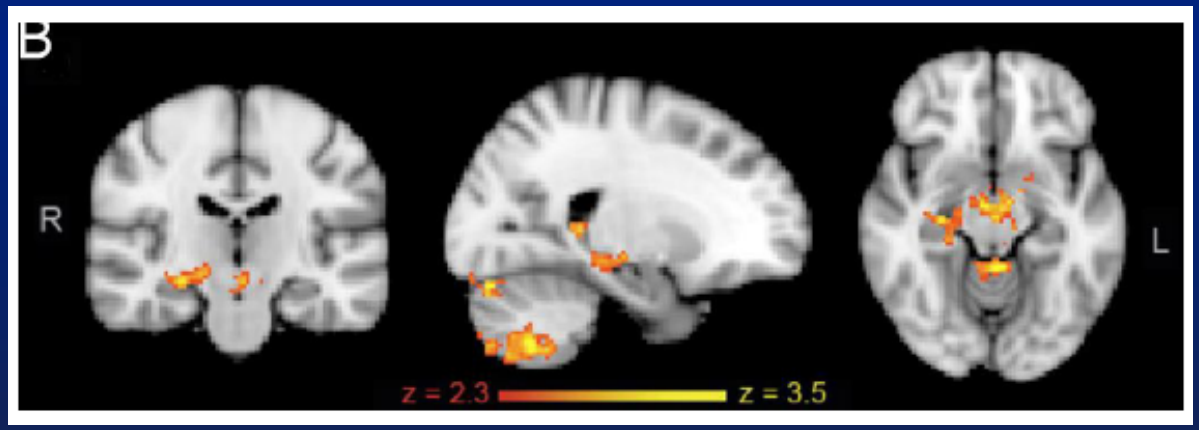
Caractère prédictif : corrélation entre ces activations et le déclin mnésique 2 ans après

Sujets sains APOE4

Puis autant d'études dans un sens que dans l'autre :

Hyperactivations : Bondi et al., 2005, Smith et al., 2002; Wishart et al., 2004; Fleisher et al., 2005; Han et al., 2007 ; Filippini et al. 2009

Filippini et al. 2009

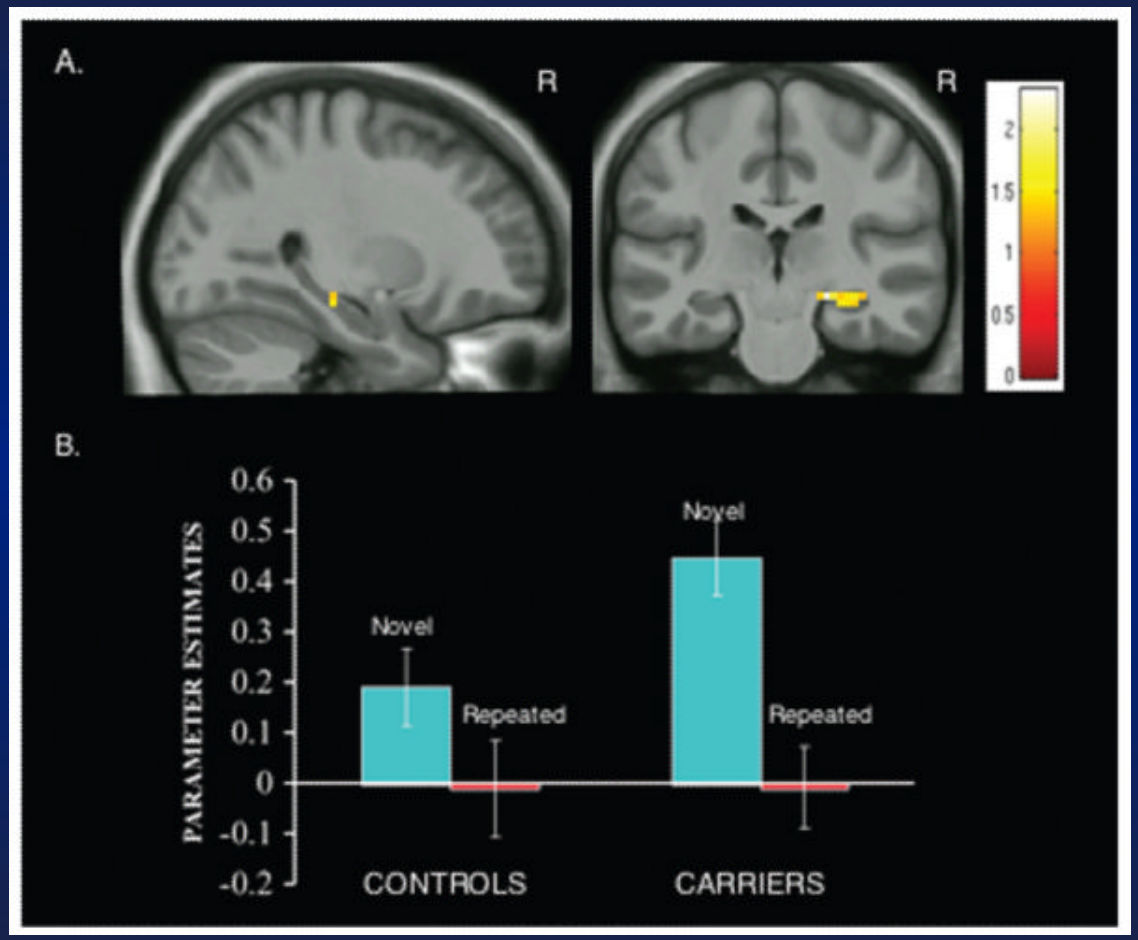


Hypoactivations : Smith et al., 1999; Lind et al., 2006; Trivedi et al., 2006; Mandadori et al., 2007; Borghesani et al., 2007)

Sujets porteurs de mutations PS1

20 sujets (m = 33 ans), vs 19 non porteurs, membres de la famille)

Quiroz et al., Ann Neurol, 2010

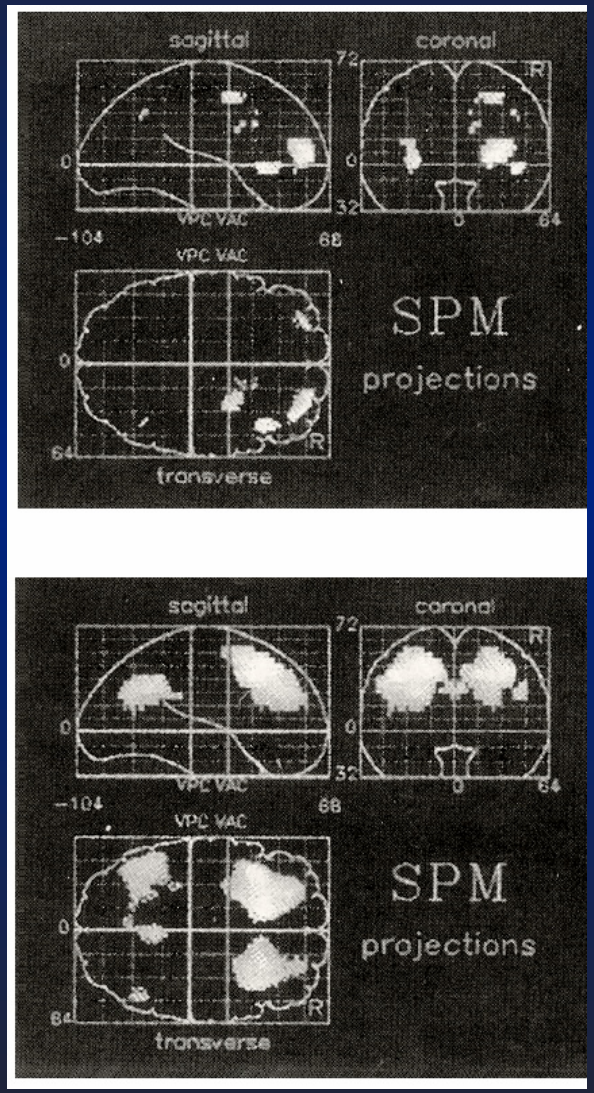


Encodage de paires visages-noms
Perf identiques

Pas d'atrophie hip

IRMf peut détecter des modif présymptomatiques et suggère que « cette approche pourrait être un biomarqueur utilisable dans la MA sporadique »

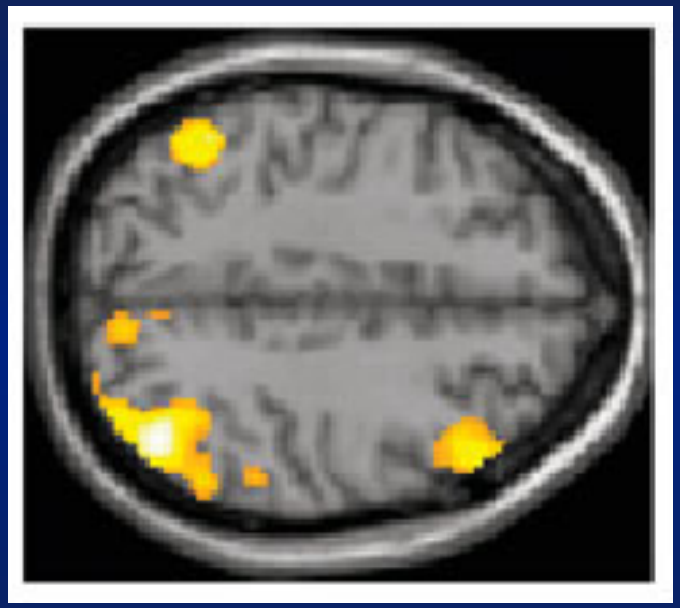
Hyperactivations dans la MA : Cortex frontal



Becker et al. 1996, TEP

Sujets contrôles

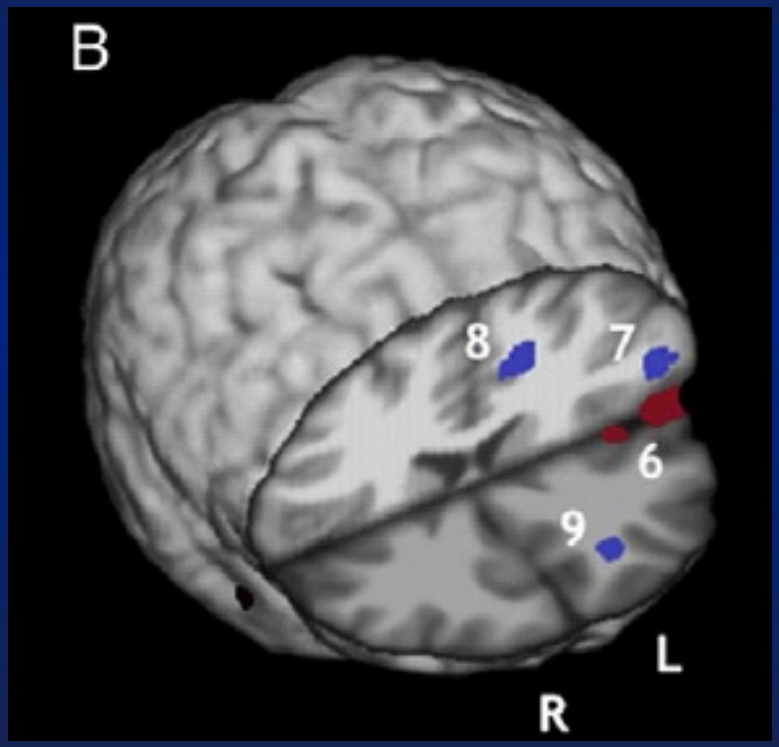
Patients MA



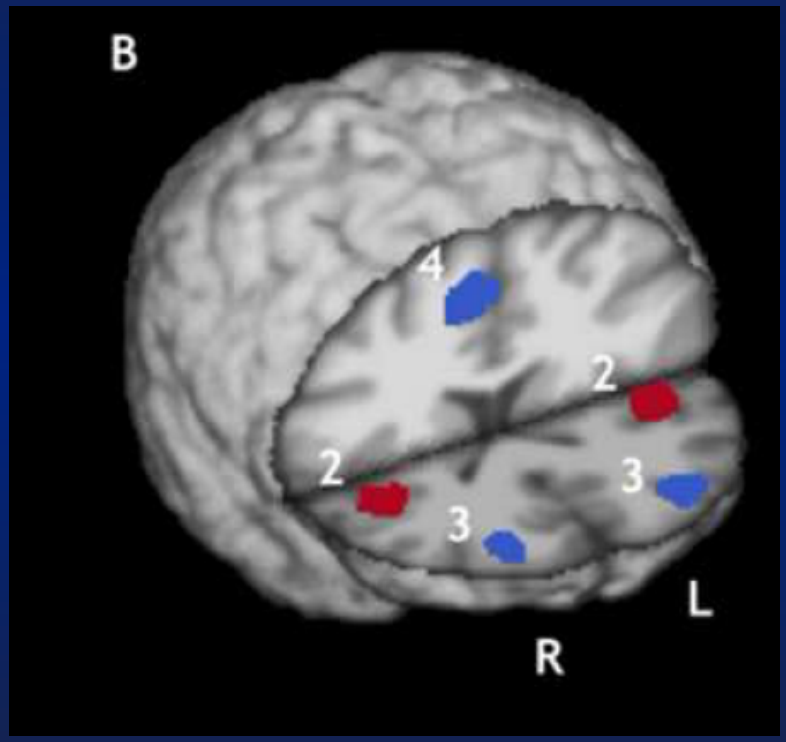
Pariente et al., 2005

Hyperactivations frontales

Encodage



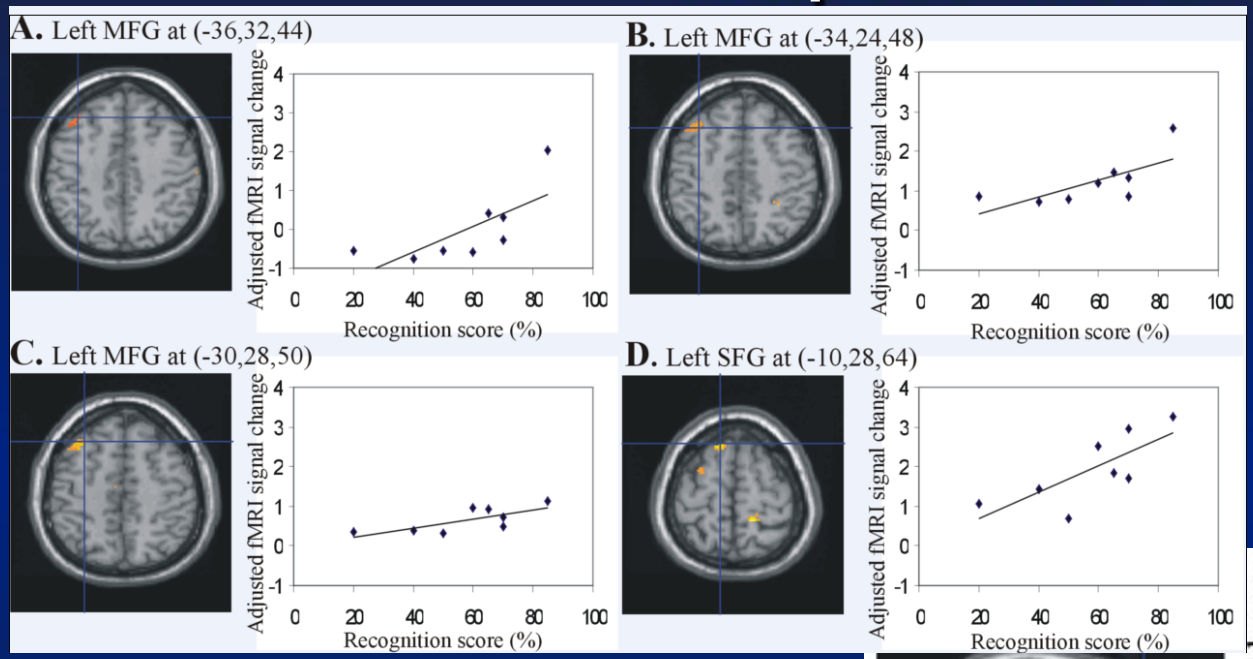
Récupération



Hyper-activation : Cortex frontal Ventro-latéral (en rouge)

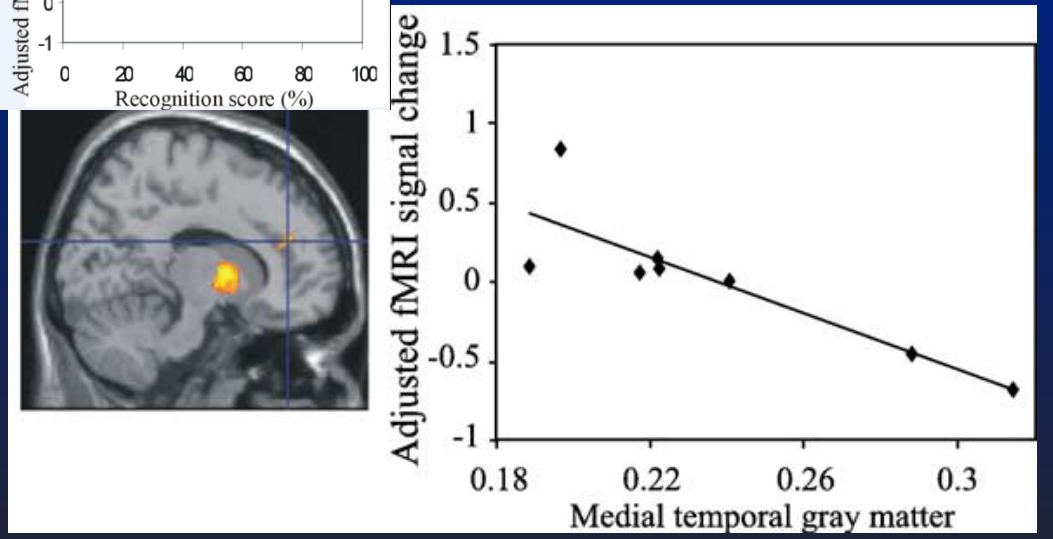
Schwindt et Black, 2009, NI

Reflet de l'effort ? Phénomène compensatoire?



Hyperactivations

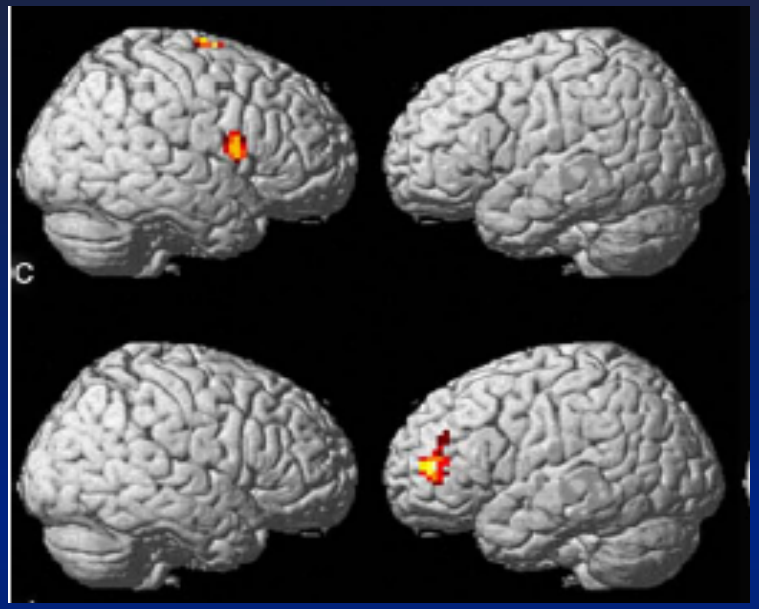
Corrélées positivement avec les performances



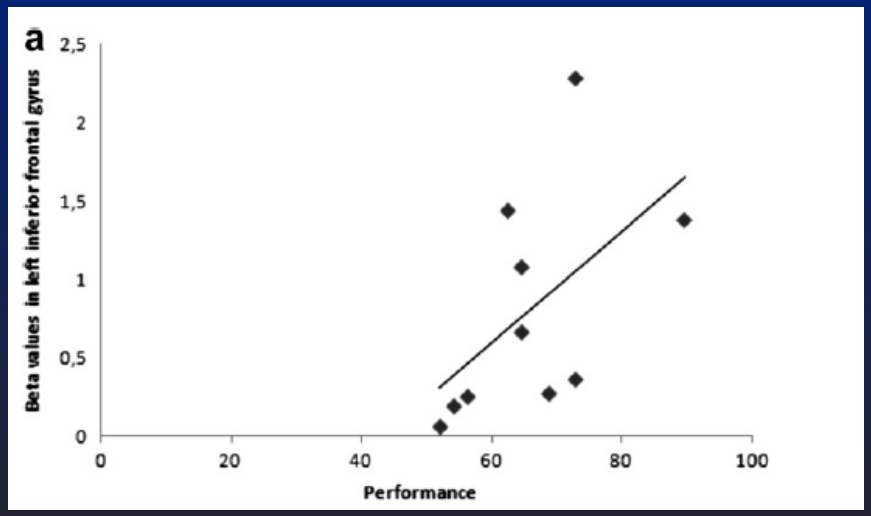
Corrélation négative avec le volume hippocampique

Rémy et al., NeuroImage, 2005, IRMf

Chez les patients MCI



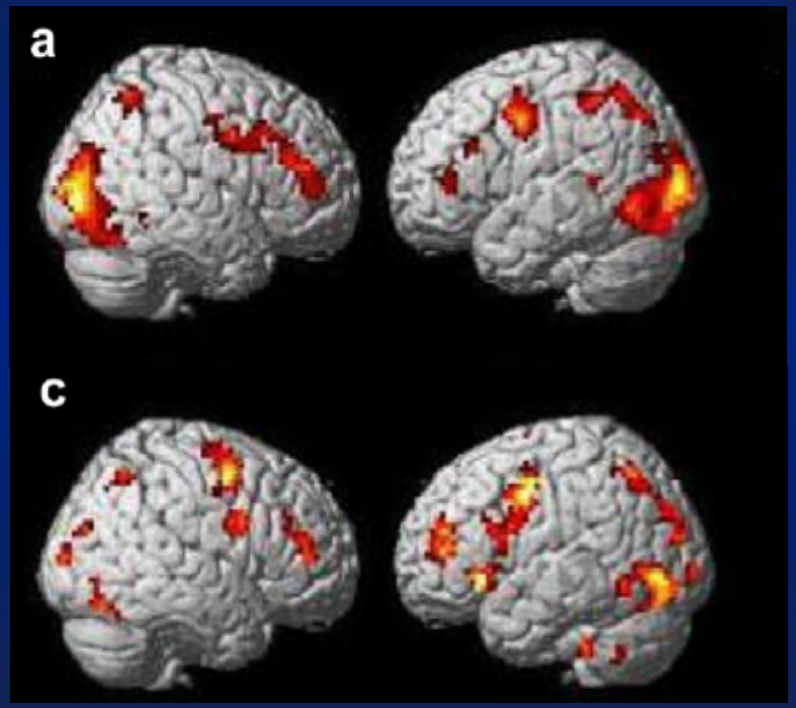
Heun et al.,2006



Clément et al., 2009

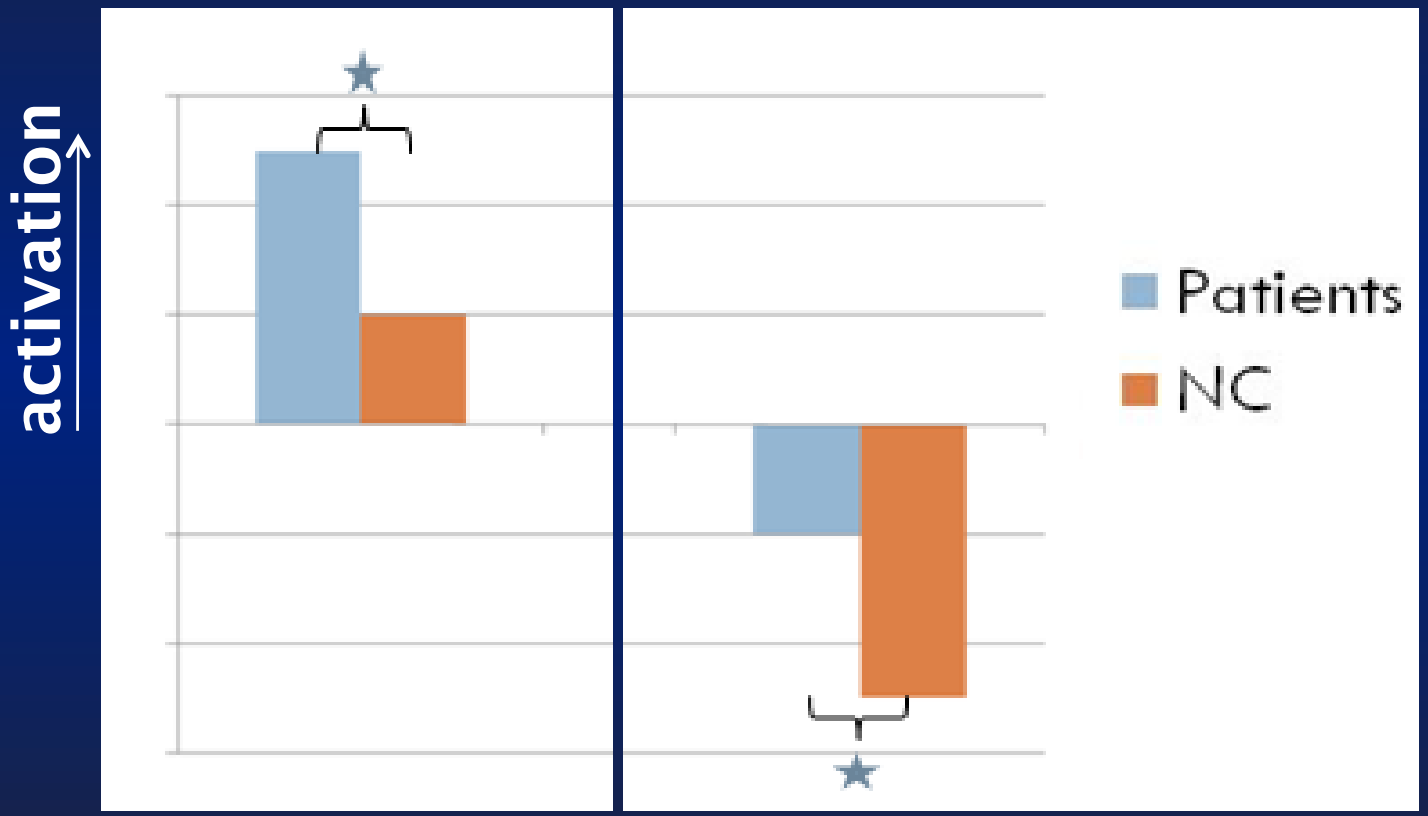
SS

MCI



Hyperactivation frontale pendant l'encodage, corrélée avec les performances

Hyperactivation ou défaut de déactivation?



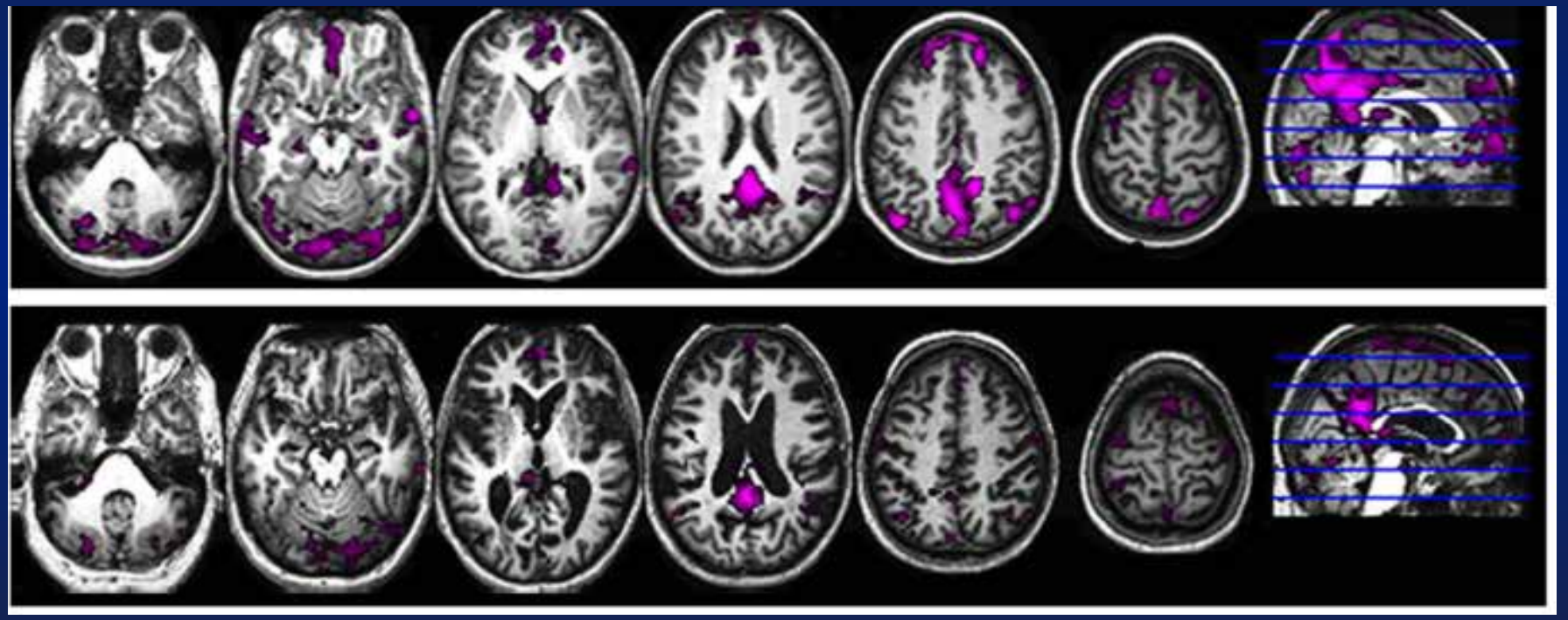
Réalisation d'une tâche cognitive : Activations mais aussi désactivations

Réseau par défaut (IRMf repos)

Mevel et al., 2010

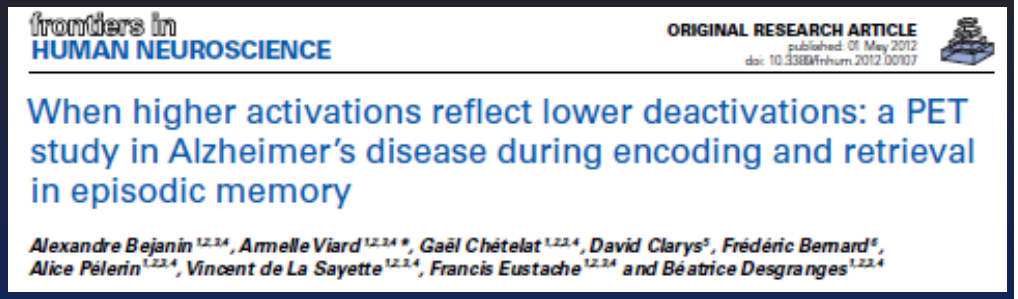
SAS

MA



Altération de ce réseau dans la MA (régions pariétales, cortex cingulaire postérieur et frontal médian) ; Similitude avec les régions hypométaboliques

Etude TEP-$H_2{}^{15}O$

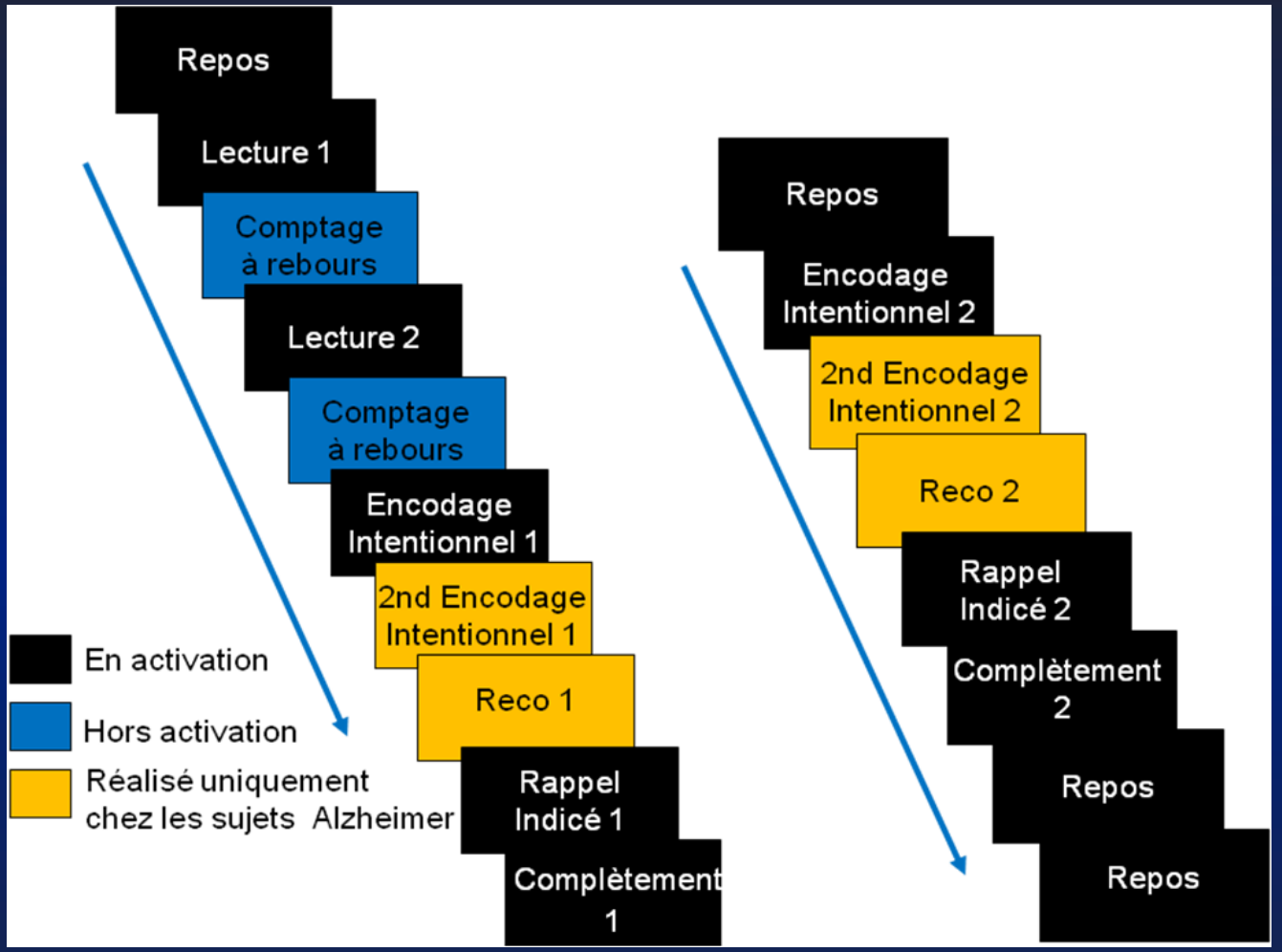


11 patients atteints de MA (MMS: 24,3 ± 3,3) vs 12 sujets sains

	Encodage	Récupération
Tâche cible	Encodage intentionnel (moto, baleine…)	Rappel indicé (Mo…, Ba…)
Tâche de référence	Lecture silencieuse (escabeau, tulipe…) + décision vivant/non vivant	Complétion de bigrammes (Bi…, Ep…)

Lecture de 24 mots

Rappel : 24 bigrammes

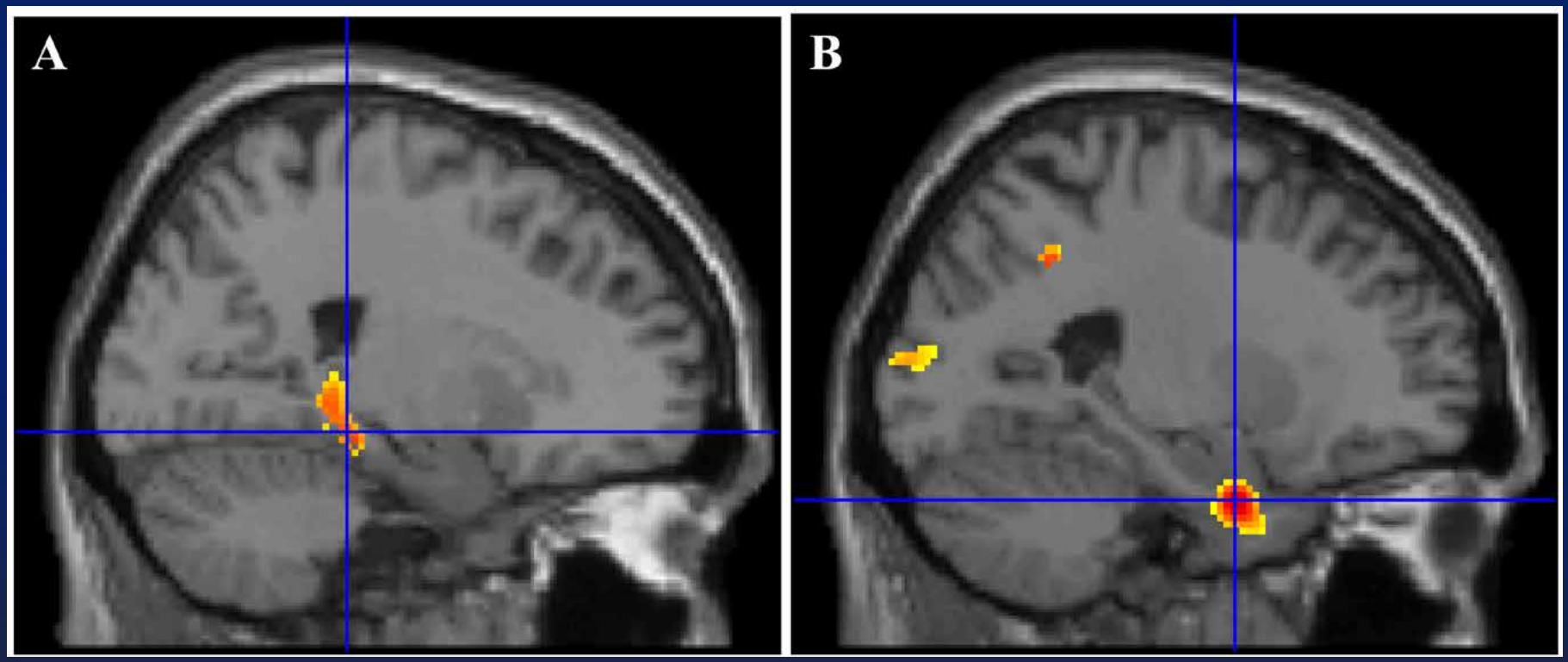


12 mesures, dont 4 conditions de repos
Performances déficitaires (11 vs 20 mots)

Hypoactivations de l'hippocampe

Encodage – lecture complétion

Rappel indicé –

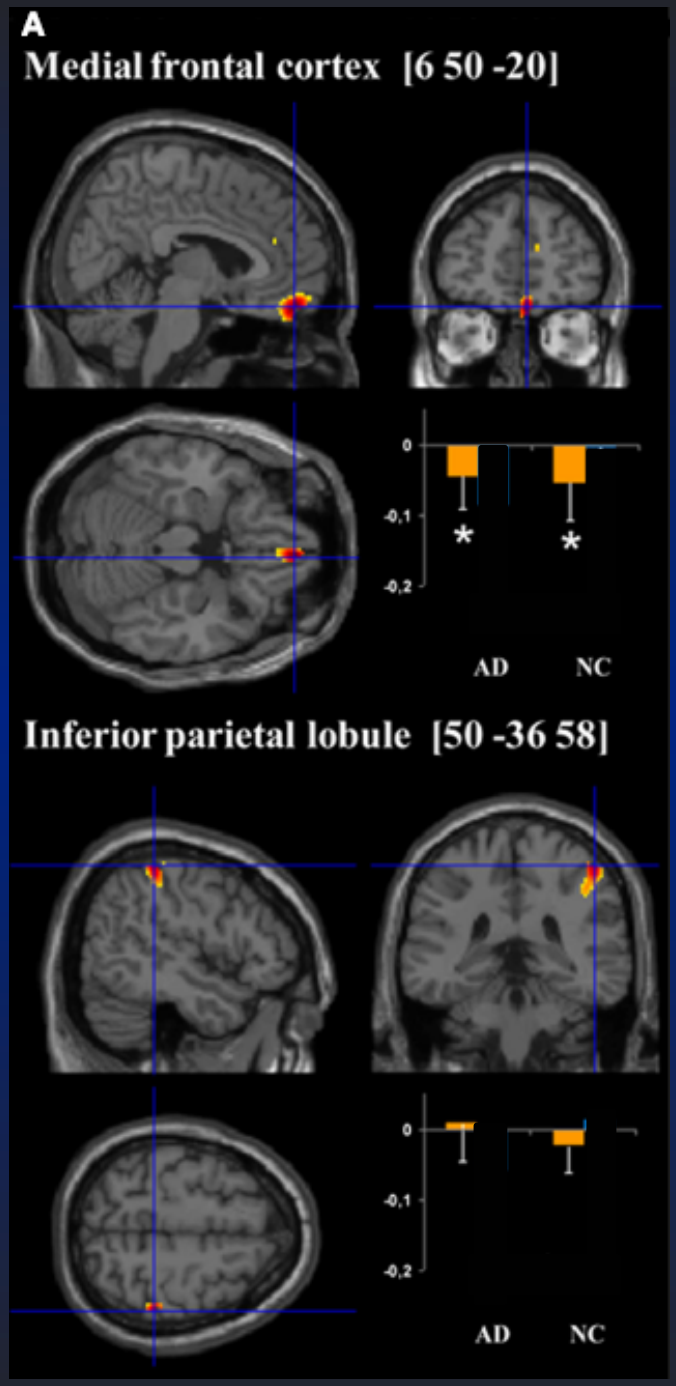


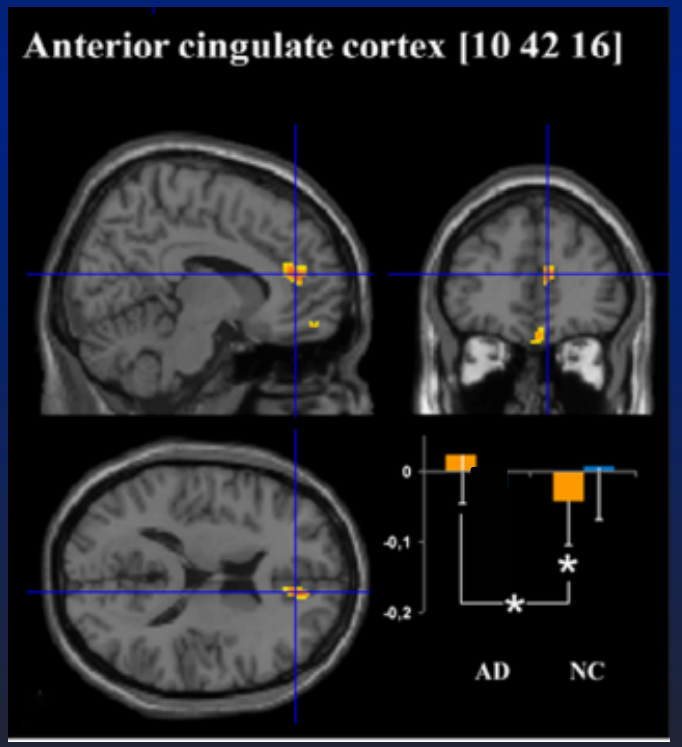
Cingulaire antérieur pariétal G

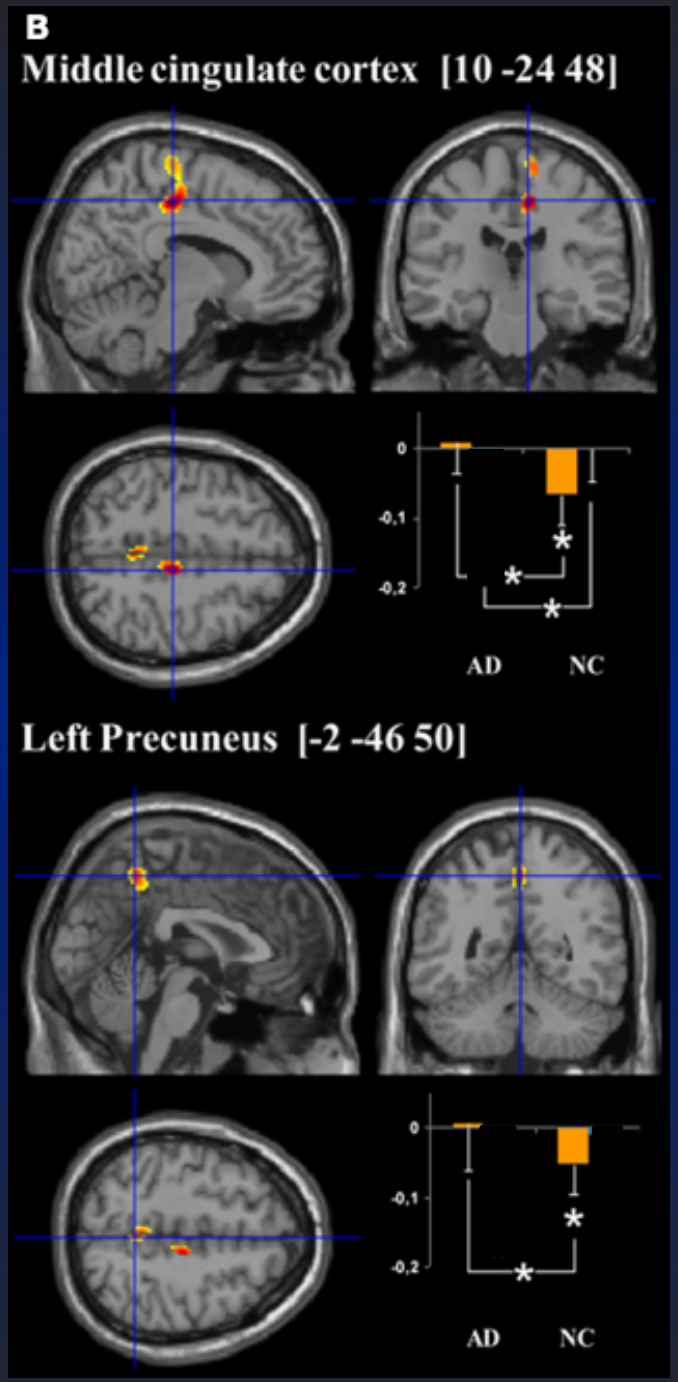
Cortex frontal D et temporo-

Hyperactivations

Encodage – Lecture

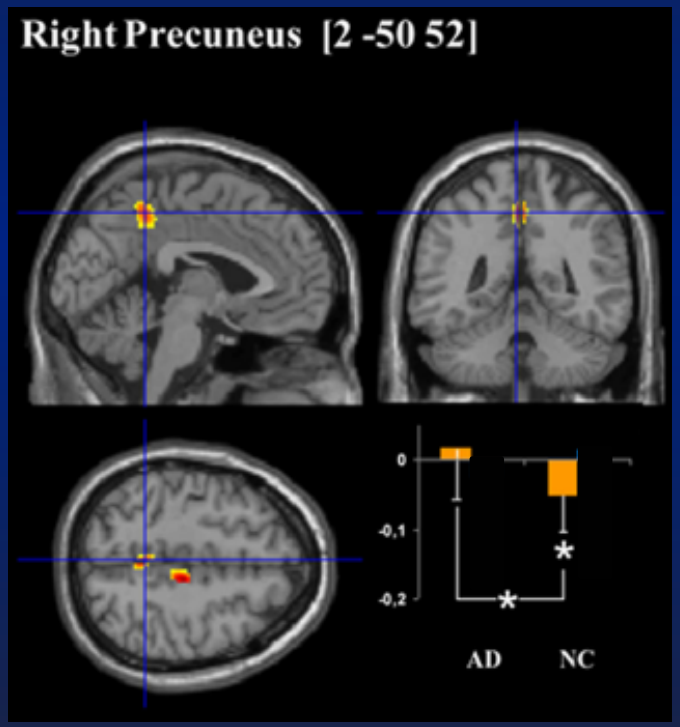






Hyperactivations

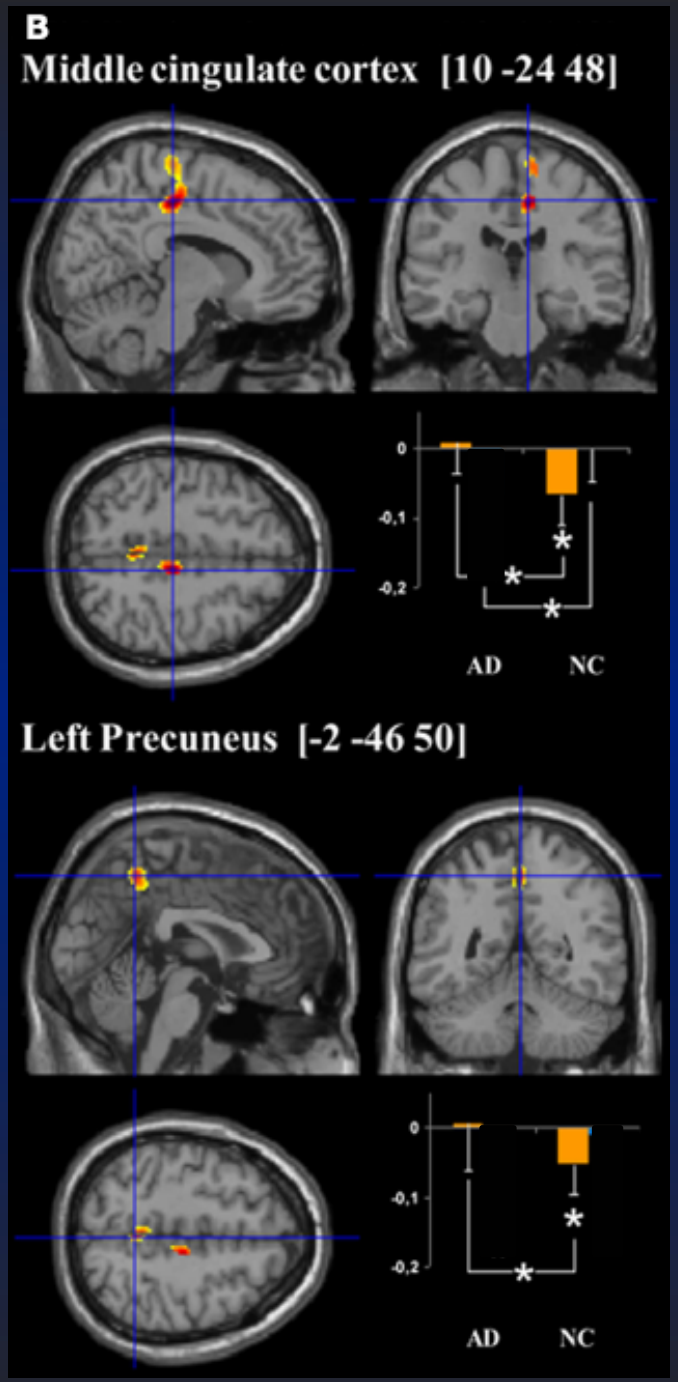
Rappel – complétion



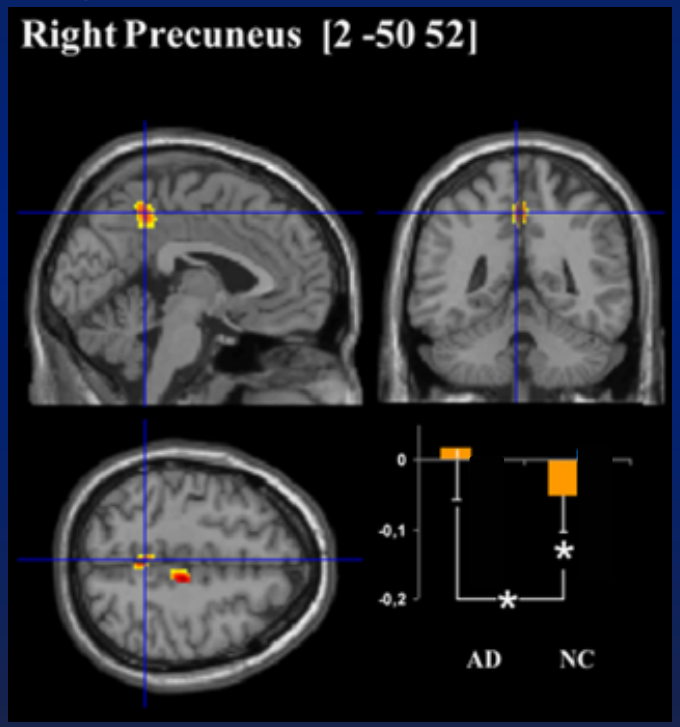
Hyperactivations

Rappel – repos

Analyse par ROI
(histogrammes)



S. sains : déactivent
MA non



Défaut de déactivation chez les patients, dans des régions qui se déactivent chez les sujets sains (Daselaar et al., 2004)

Conclusion

- Hypoactivations hippocampiques dans la MA (et autres régions, cingulaire postérieur)
- Hyperactivations concernent des régions différentes selon le stade de la maladie (hippocampe, puis cortex frontal)
- Preuve de plasticité cérébrale, y compris au stade démentiel
- Au moins parfois efficaces
- Mais prudence : elles ne sont pas toujours authentiques

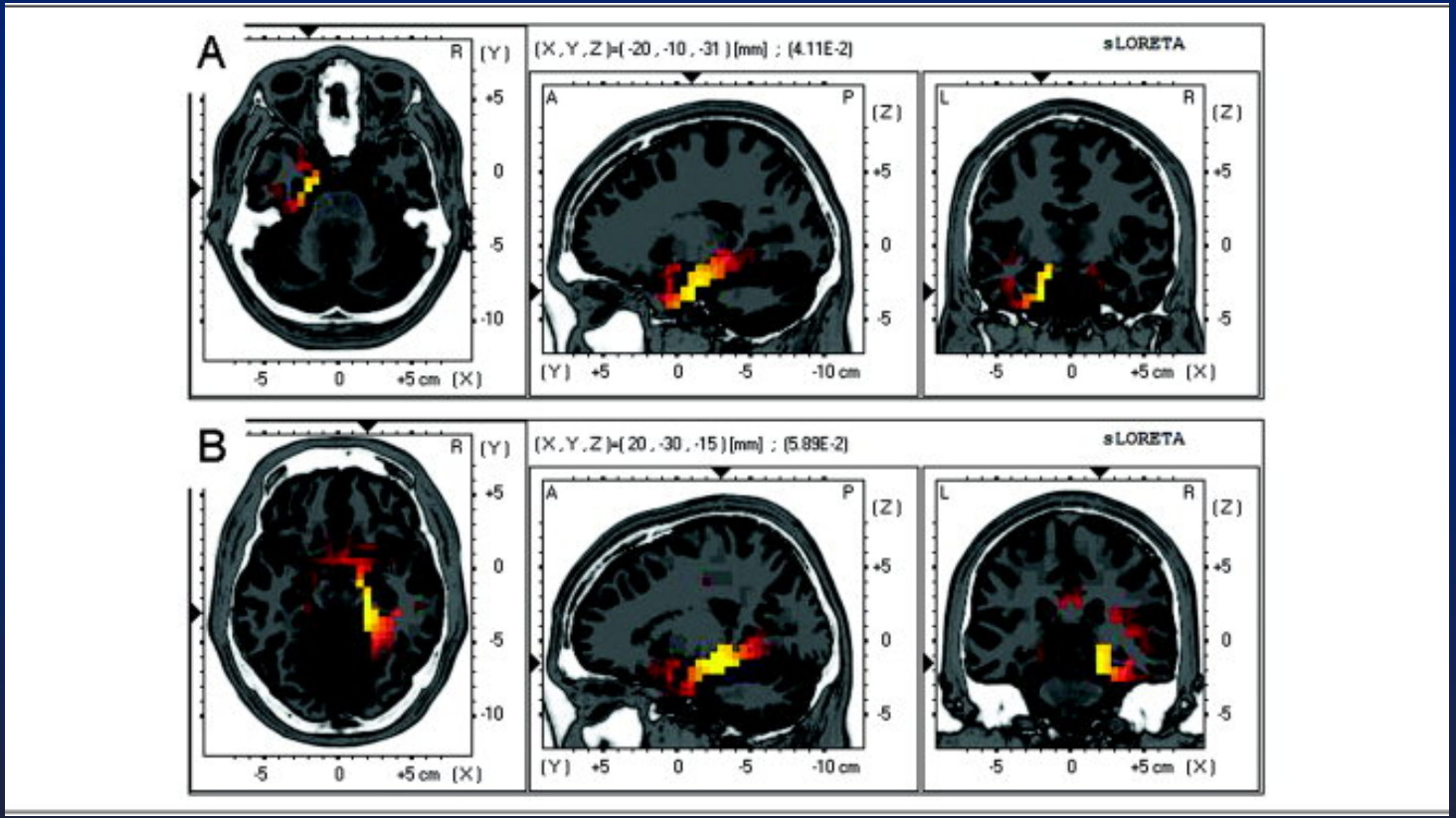
Stimulation corticale profonde

(hypothalamus/fornix bilatéral) chez un patient obèse:

-Souvenirs autobiographiques détaillés

- EEG (Loretta) : augmentation de l'activité dans le LTI

- Augmentation des performances mnésiques



Hamani et al., 2008

Test	Baseline	Postoperative
WAIS Full-Scale Intelligence Quotient[a]	125	134
WAIS Attention Index[a]	108	119[b]
Trail Making Test of processing speed (average Parts A and B)[c]	60	50
Verbal Fluency (average phonemic and semantic)[c]	43	50
California Verbal Learning Test (total learning)[c]	40	77[b]
California Verbal Learning Test (short-delay recall)[c]	40	70[b]
California Verbal Learning Test (long-delay recall)[c]	55	70[b]
Spatial Associative Learning (trials to criterion)[c]	39	54[d]
Wechsler Memory Scale-III Face Recognition (Immediate)[c]	62	58
Wechsler Memory Scale-III Face Recognition (Delay)[c]	68	63
Behavioral Evaluation of Memory Figural Learning[c]	77	81
Behavioral Evaluation of Memory Figural Recall[c]	79	79
Beck Depression Inventory (raw scores)	29	27
Spielberger State Anxiety[c]	76	79

Postoperative scores were obtained after 3 weeks of continuous stimulation (bilateral stimulation, 2.8 volts, 130Hz, 60-microsecond pulse width, contacts 0 and 4 as cathodes, case as anode). Stimulation was initiated at the first postoperative office visit. The settings chosen did not produce any acute overt memory, behavioral, sensory, or autonomic effects.

[a]Scaled scores: mean = 100; standard deviation (SD) = 15.

[c]T scores: mean = 50; SD = 10.

[b]Measures in which pre-post change exceeds the 95% confidence interval for reliable change.

[d]Measures showed performance increase of greater than 1.5 SD units; normative test-retest data for reliable change computation are not available. WAIS = Wechsler Adult Intelligence Scale.

Condition	Task 1		Task 2	
	Recollection Index[a,b]	Familiarity Index[c]	Recollection Index[b,d]	Familiarity Index[e]
Stimulation "off"	0.17	0.45	0.13	0.57
Stimulation "on"	0.38	0.28	0.38	0.47
95% CI[f]	0.11	0.25	0.18	0.37

Results of associative recognition tasks with the patient tested in a double-blinded manner with the stimulation randomly assigned to being "on" or "off."

[a]Proportion of correct *remember* responses in the *remember/know* task. Mean and standard deviation (SD) from 10 healthy control subjects tested in a concurrent study = 0.22 ± 0.10 (unpublished data).

[b]Measures in which the magnitude of test-retest change exceeded the 95% confidence interval (CI) for reliable change based on control data.

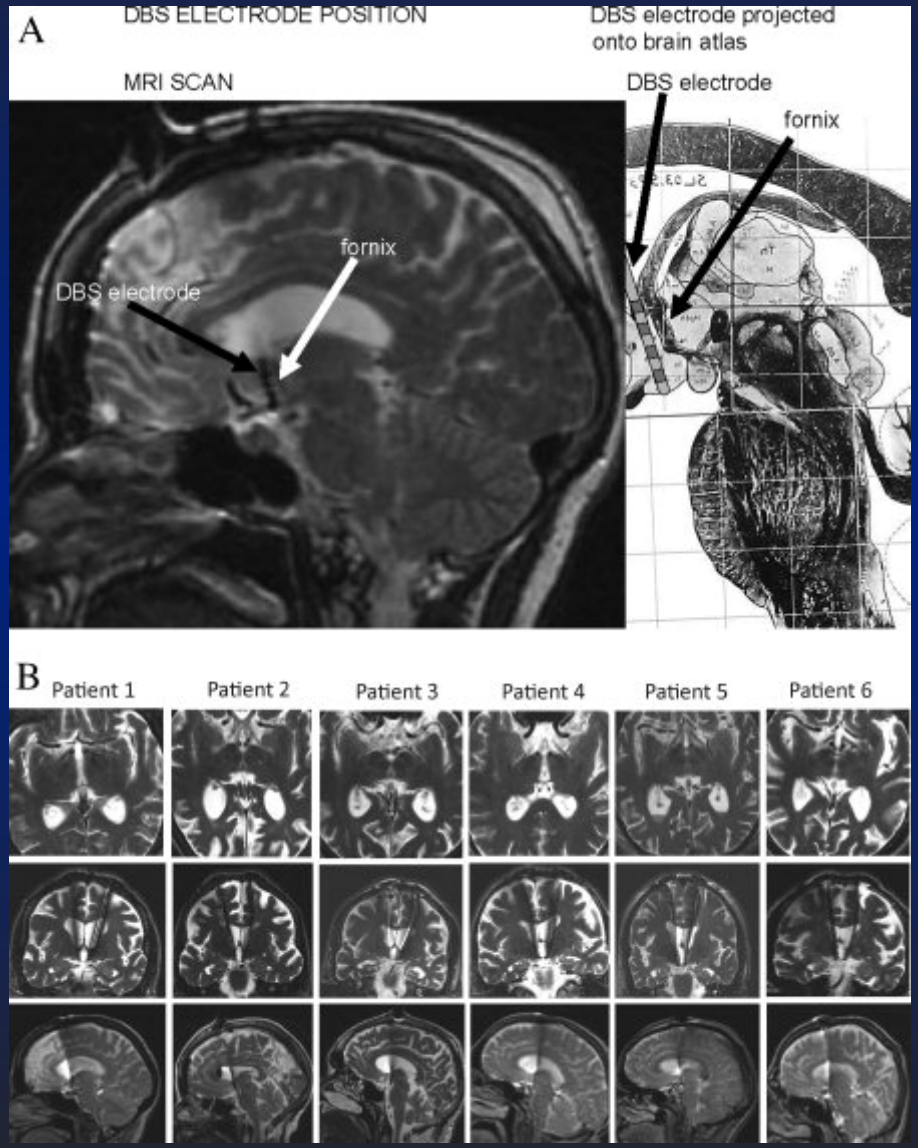
[c]Familiarity estimate for the remember/know task based on assumption of independent recollection and familiarity processes (ie, Yonelinas and Jacoby's[13] Independence Remember/Know procedure); Familiarity = [Know/(1 − Remember)]. Mean and SD from 10 healthy control subjects tested in a concurrent study = 0.24 ± 0.14 (unpublished data). Note that false-positive rates are similar for the patient on the two sessions ("off" = 0.11; "on" = 0.14) and control subjects (mean = 0.10 ± 0.05).

[d]Proportion of correctly recognized *recombined* word pairs when task required positive response to both intact and recombined pairs − falsely recognized *recombined* pairs when asked to identify only intact pairs. Mean and SD from 24 healthy control subjects tested in a concurrent study = 0.48 ± 0.17.[11]

[e]Proportion of falsely recognized *recombined* word pairs/[1 − Recollection Index]. Mean and SD from 24 healthy control subjects tested in a concurrent study = 0.31 ± 0.18.[11]

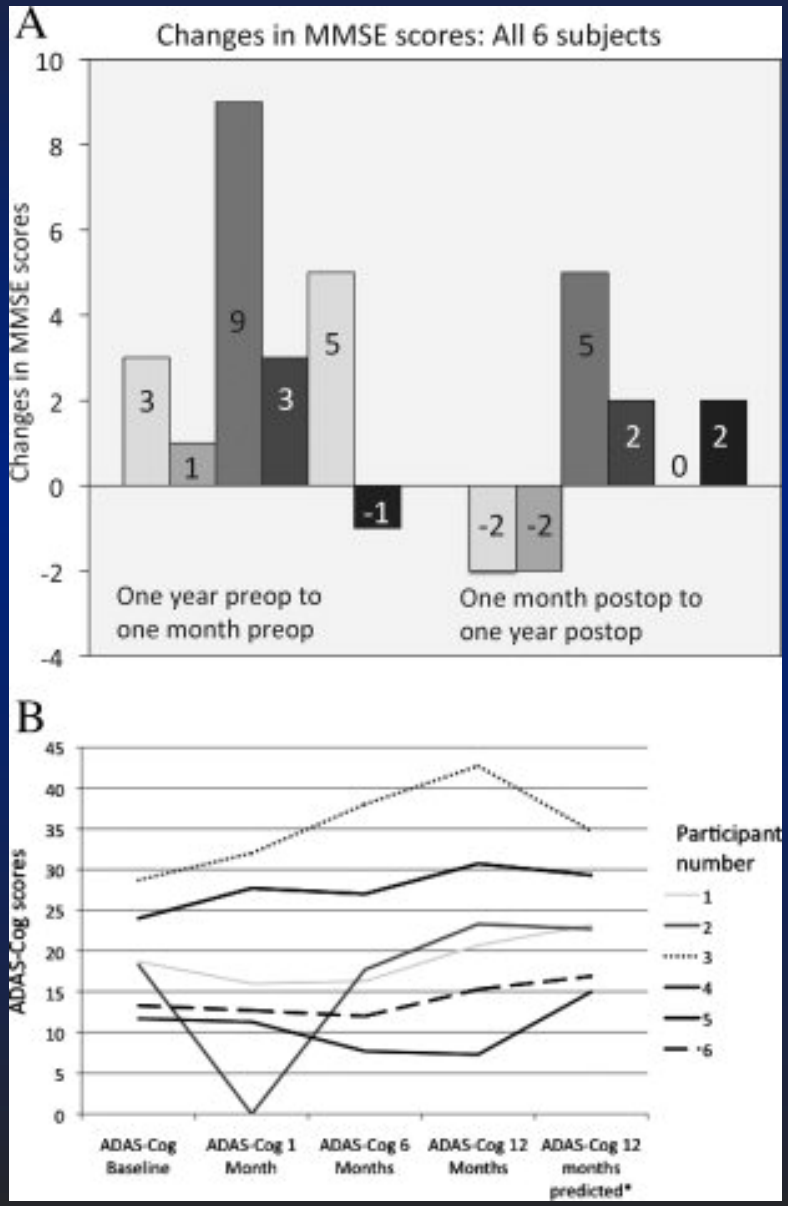
[f]Change required to exceed 95% CI on normative test-retest sample.

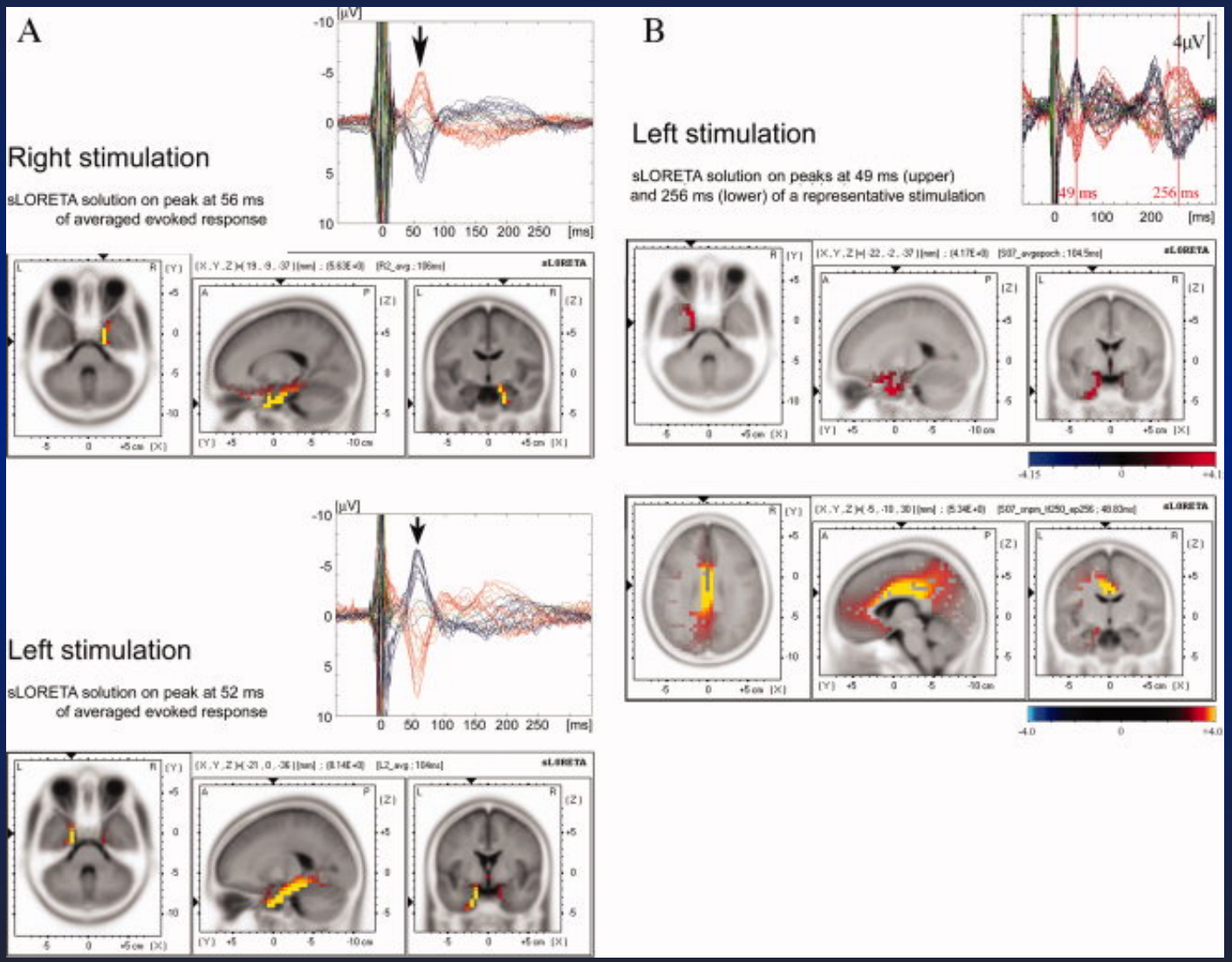
A phase I trial of deep brain stimulation of memory circuits in Alzheimer's disease

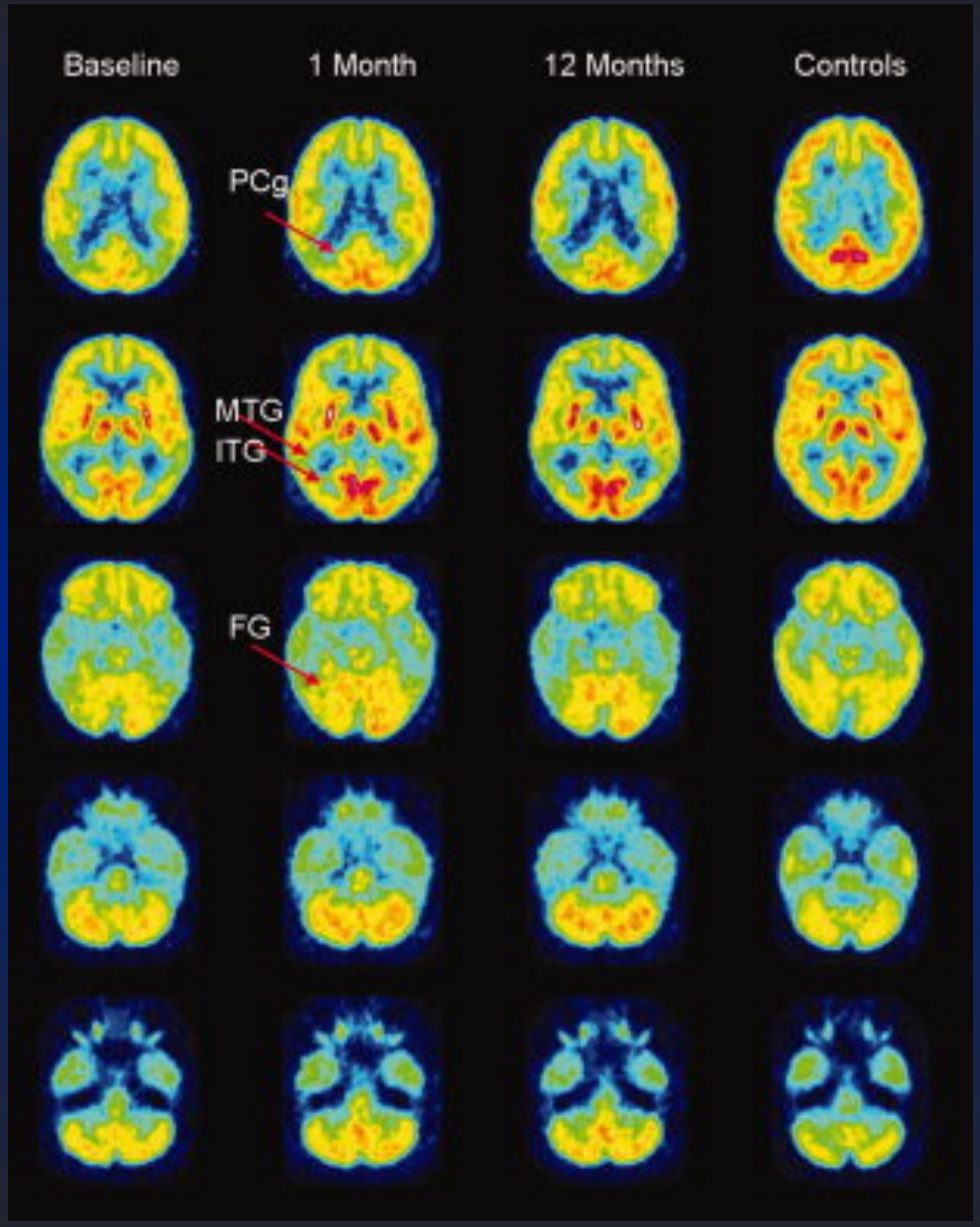


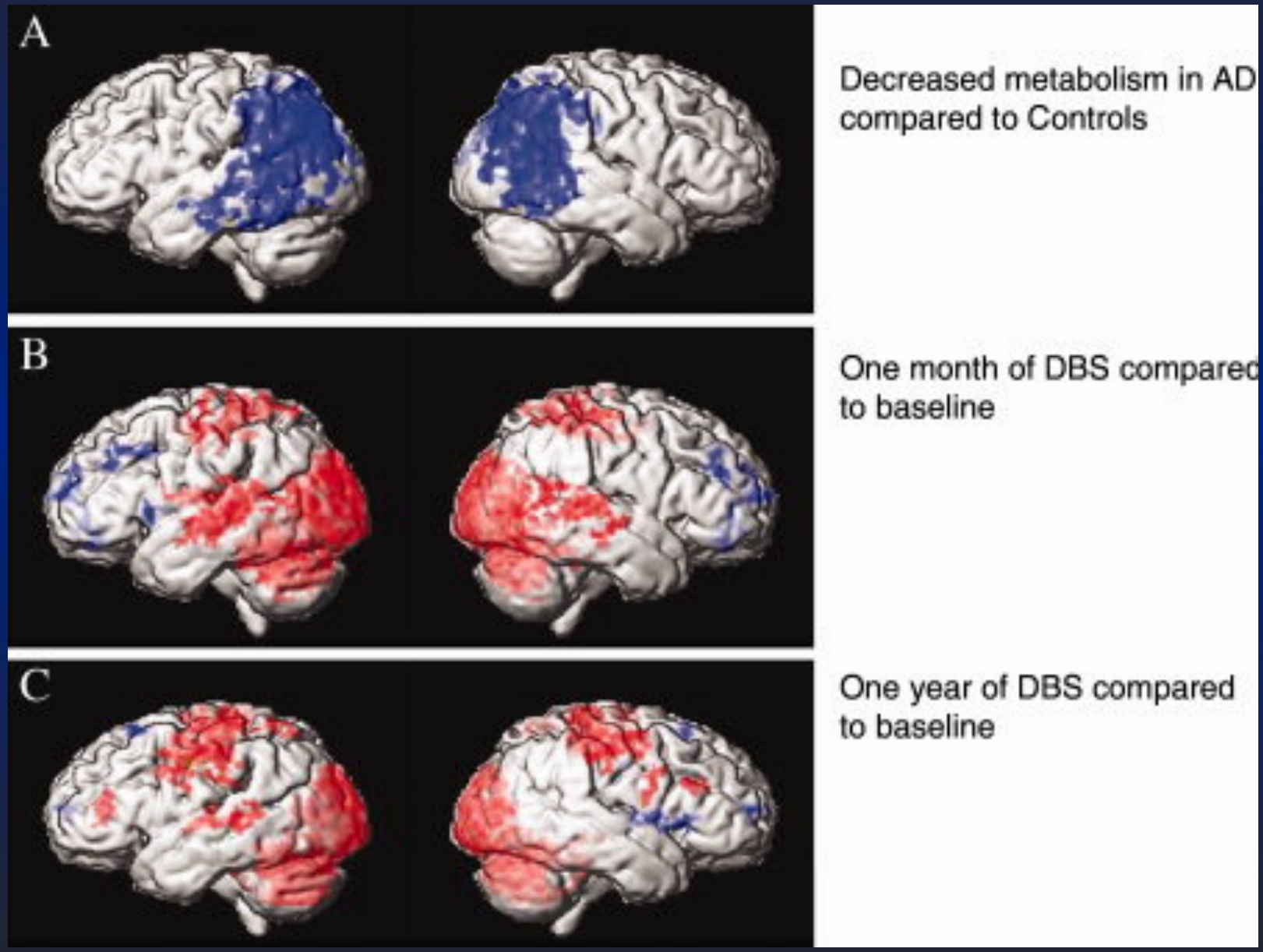
Laxton et al., 2010

A phase I trial of deep brain stimulation of memory circuits in Alzheimer's disease

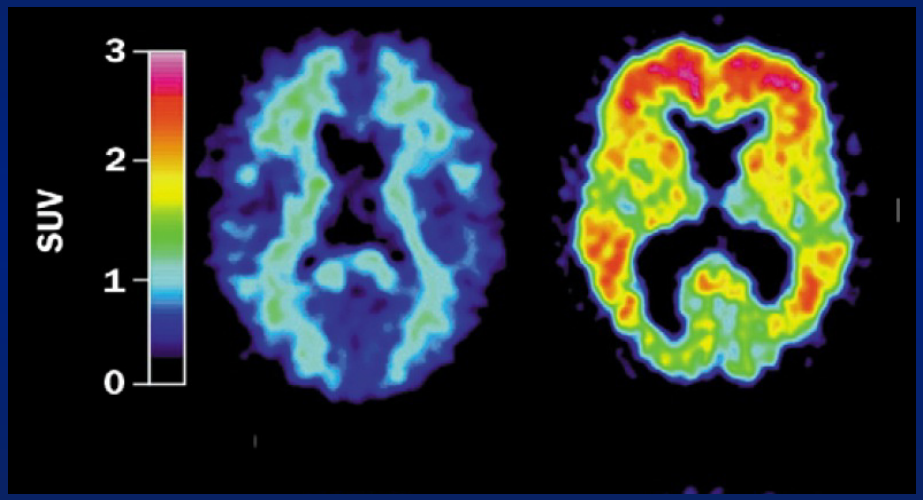



A
Right stimulation
sLORETA solution on peak at 56 ms
of averaged evoked response
Left stimulation
sLORETA solution on peak at 52 ms
of averaged evoked response
B
Left stimulation
sLORETA solution on peaks at 49 ms (upper)
and 256 ms (lower) of a representative stimulation
4μV
49 ms
256 ms
[μV]
[ms]
sLORETA

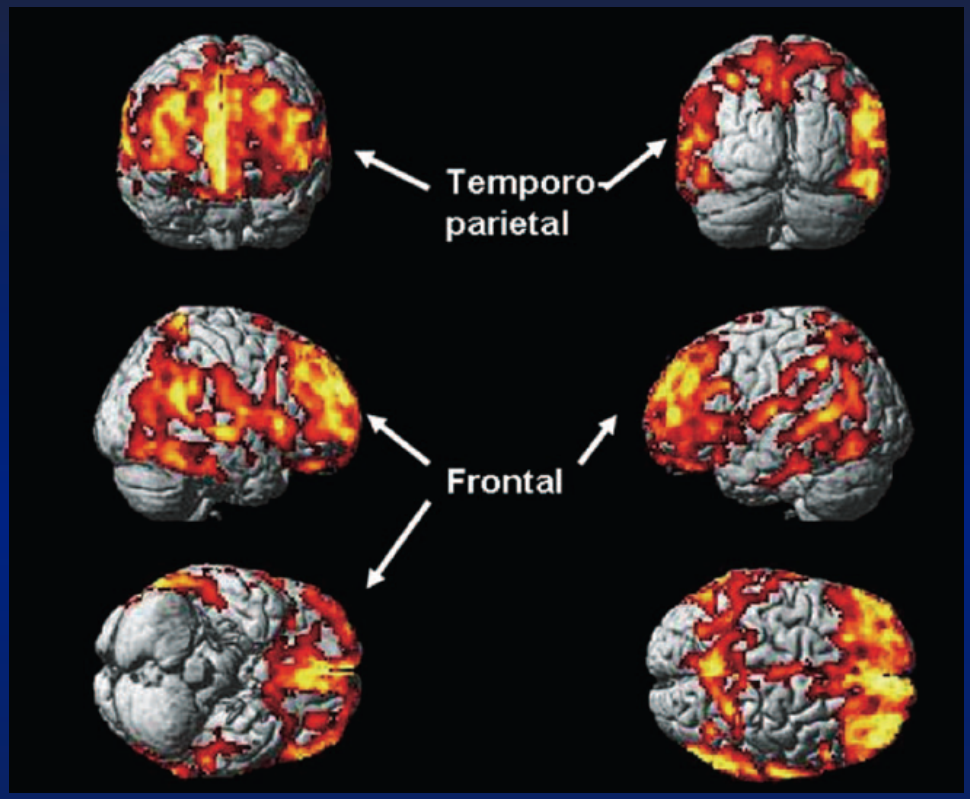

Baseline
1 Month
12 Months
Controls
PCg
MTG
ITG
FG


A
Decreased metabolism in AD compared to Controls
B
One month of DBS compared to baseline
C
One year of DBS compared to baseline

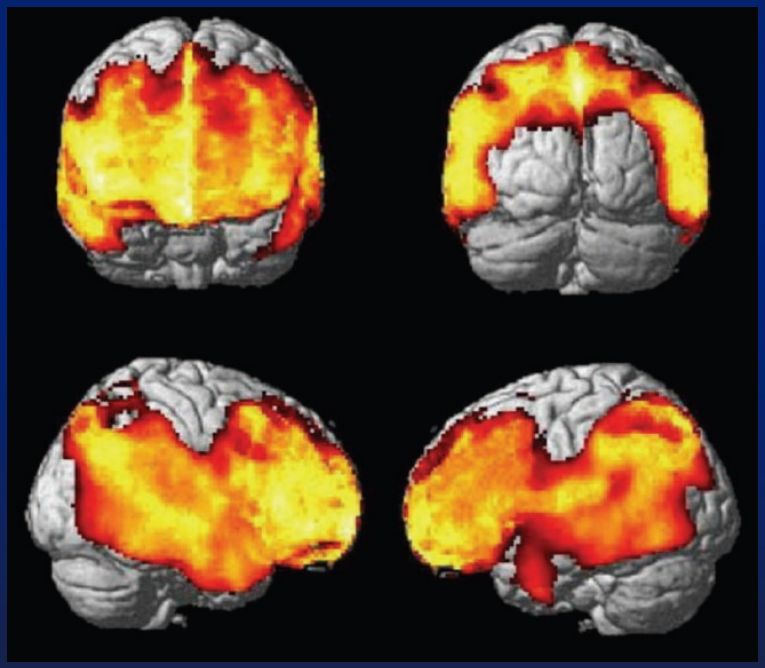
IMAGERIE MOLÉCULAIRE



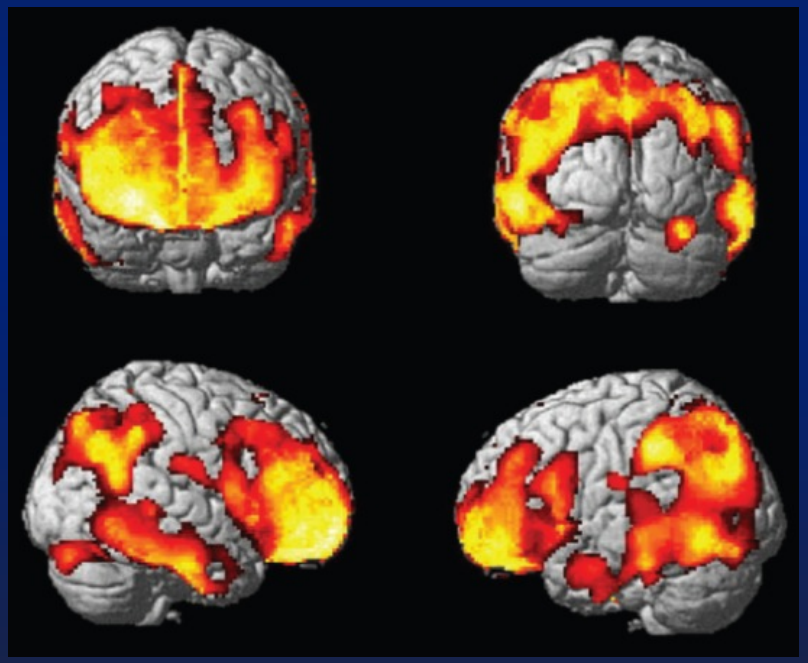
Klunk et al., Ann Neurol, 2004



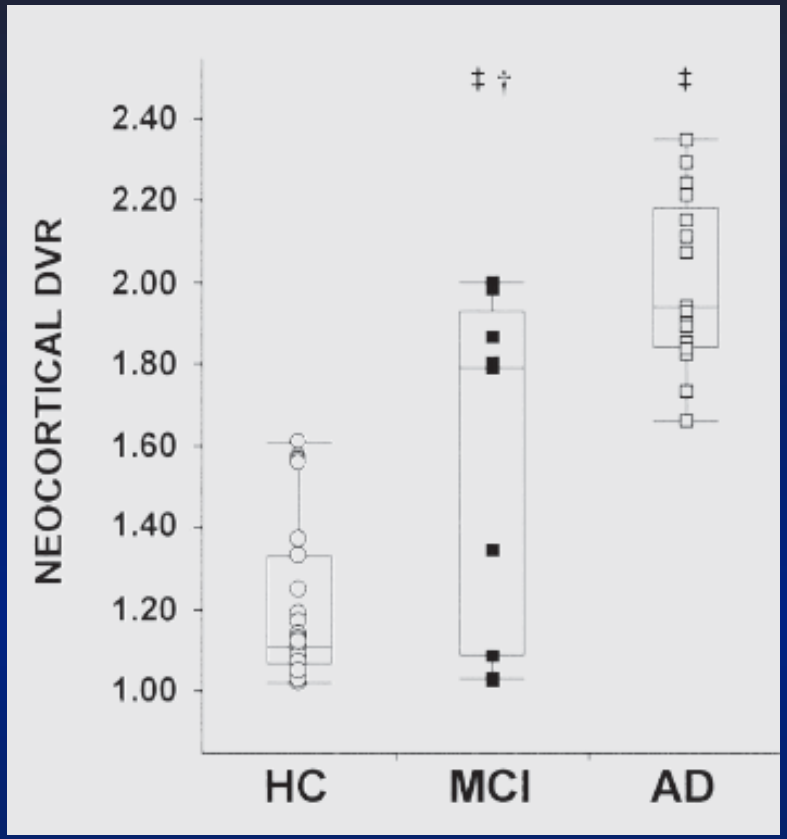
Edison et al., 2007



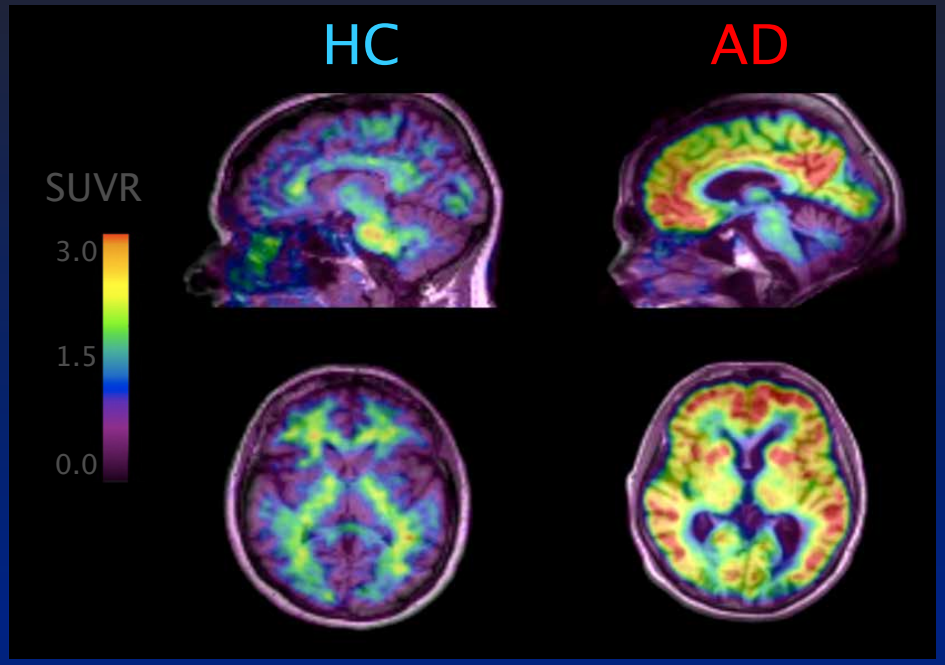
Kemppainen 2006

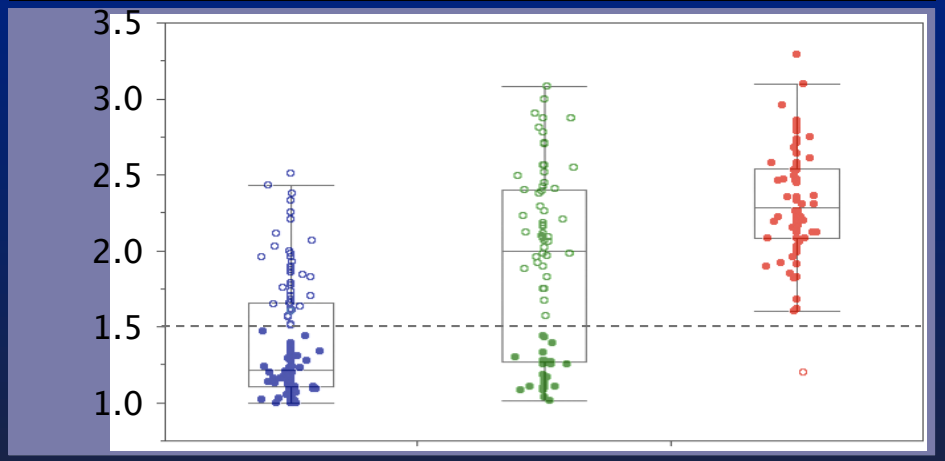


Kemppainen 2007



Rowe et al., Neurology, 2007





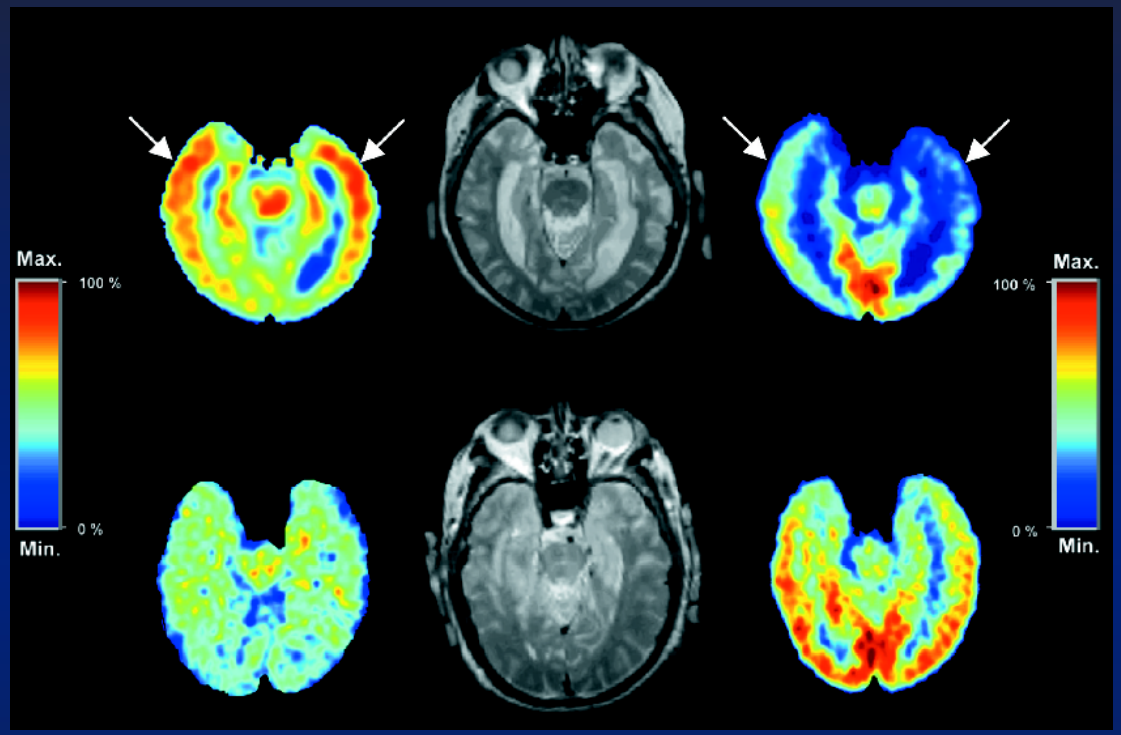
PIB global/PIB cervelet
Cut-off = 1,5

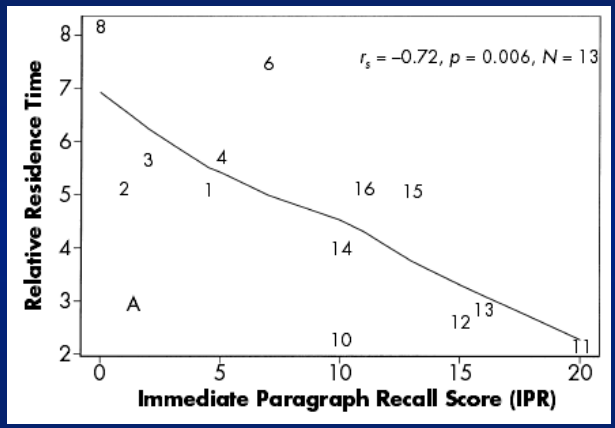
Chételat et al., ENJ, in press

FDDNP IRM TEP

MA

SS





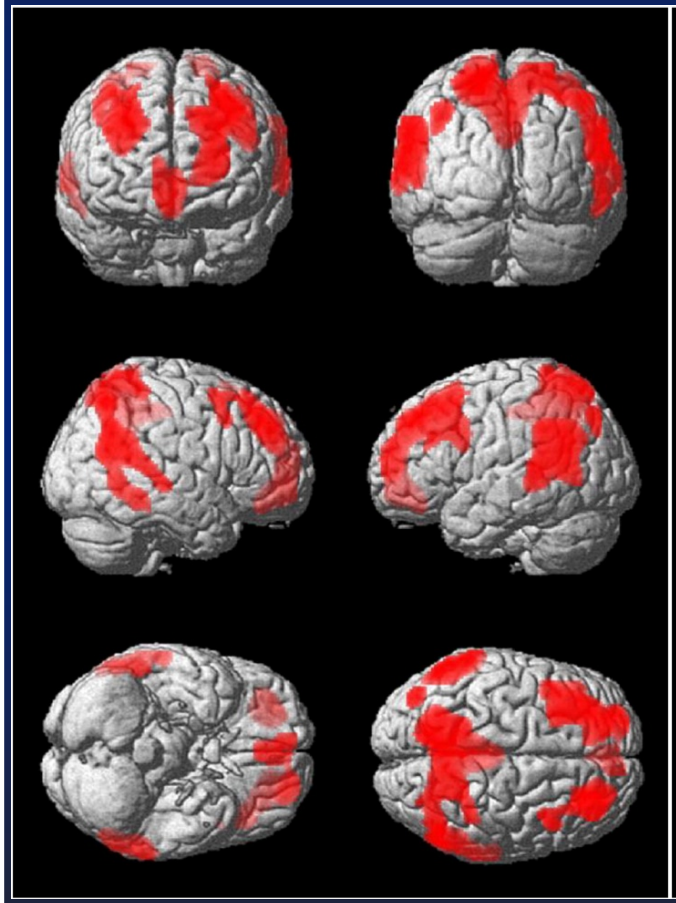
Shoghi-Jadid et al., 2002

Augmentation de la rétention FDDNP dans la MA
LTM -> temporal -> pariétal -> tout le néocortex

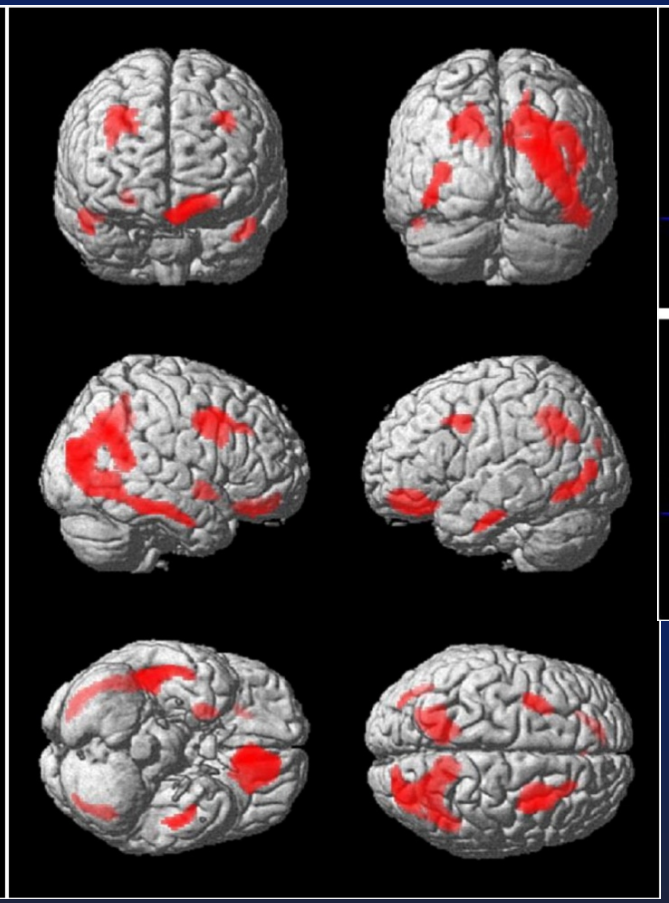
Bonne corrélation avec les déficits cognitifs

PIB et FDDNP

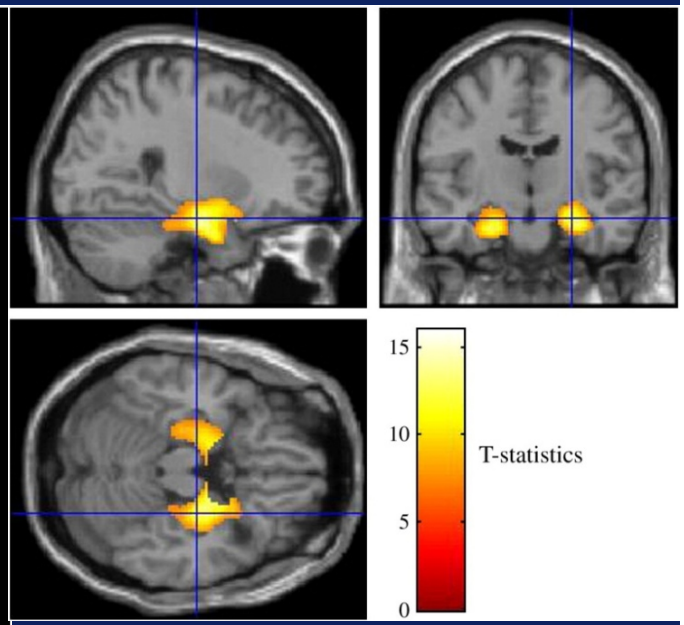
Shin et al., NeuroImage, 2010



PIB

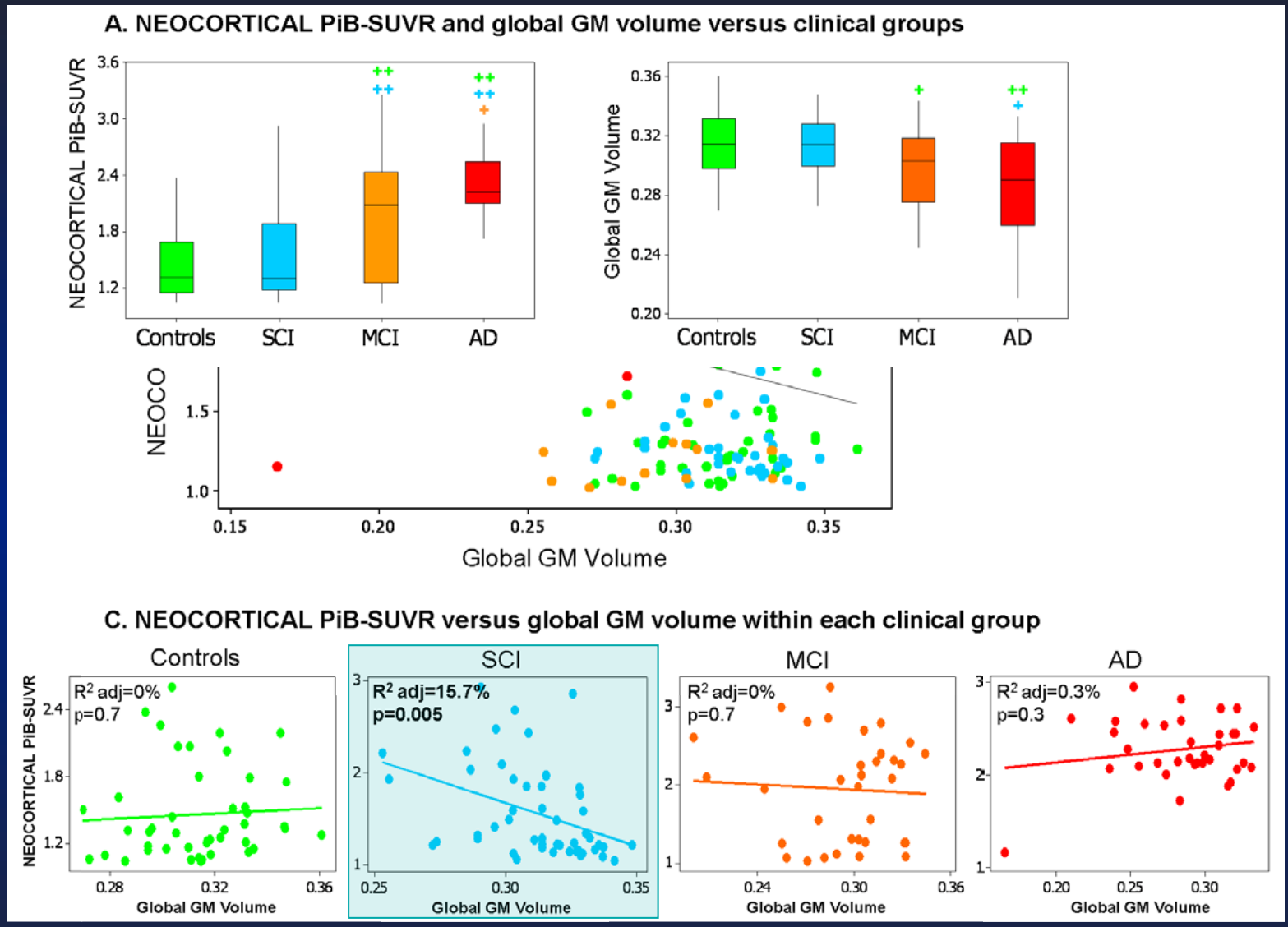


FDDNP



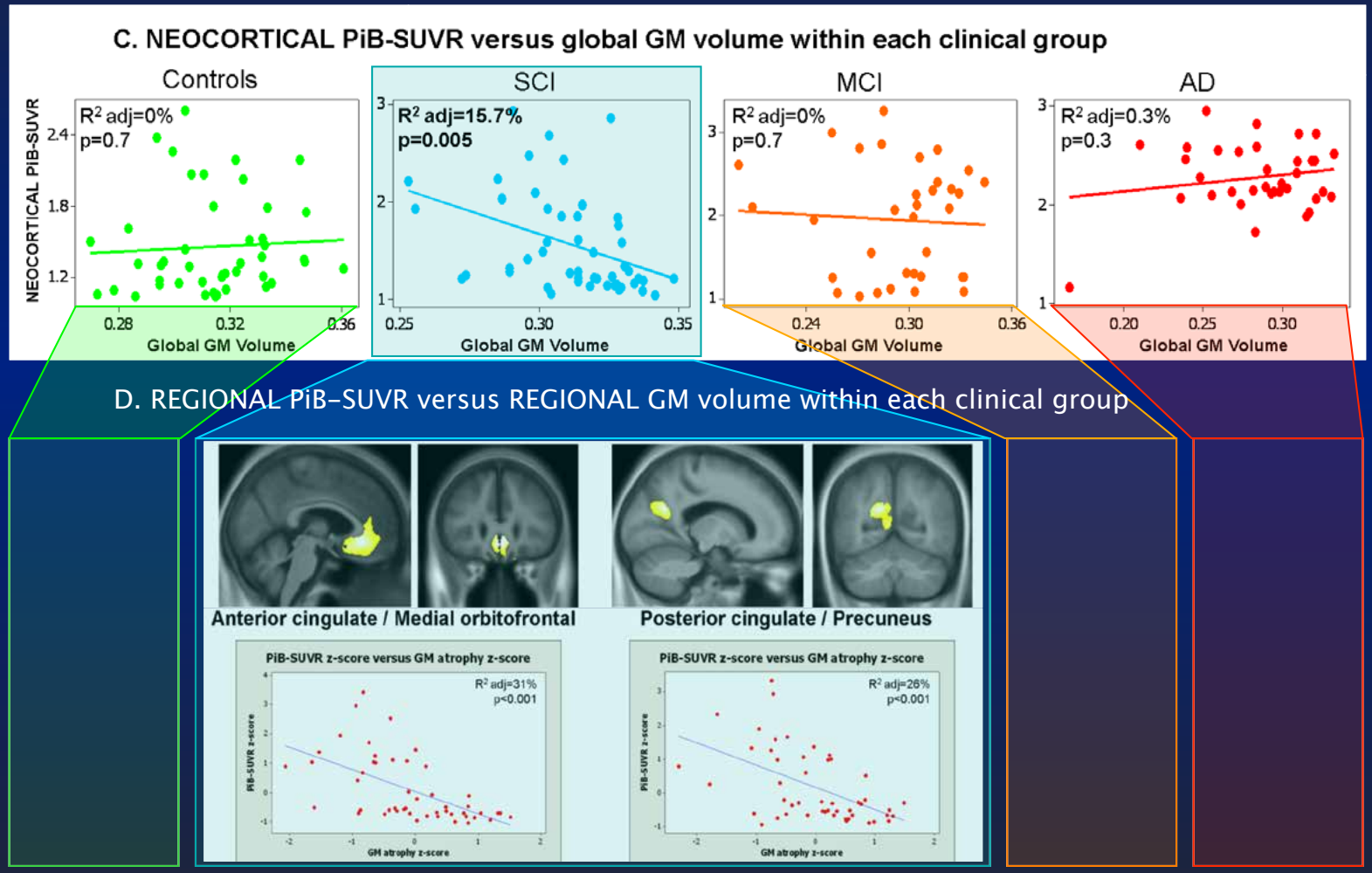
FDDNP–PIB :
Hippocampe

Relations PiB – atrophie



Chételat et al., Annals of Neurology, 2010

Relations PiB – atrophie (corrélations)



Chételat et al., Annals of Neurology, 2010

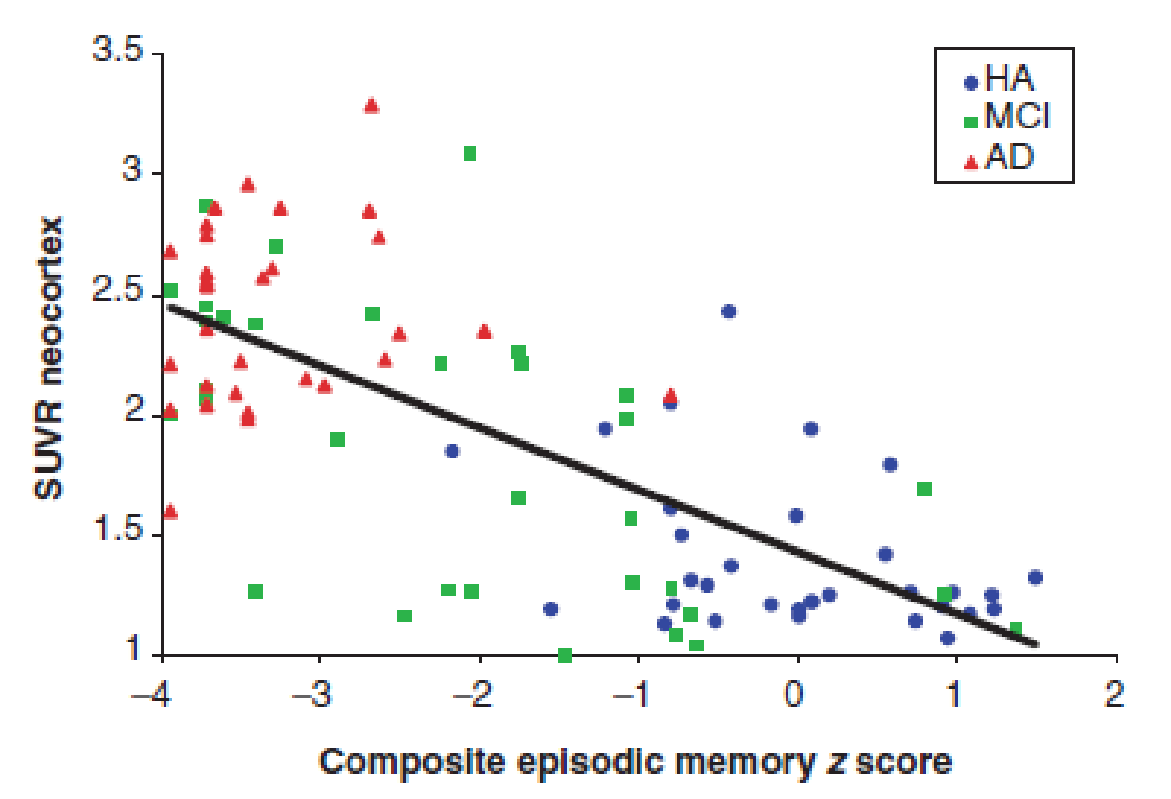
Liens avec l'hypométabolisme

- Peu de corrélations entre PIB global et FDG
- PIB régional : corrélations cx pariétal et temporal, pas cx frontal (Edison et al., 2007)

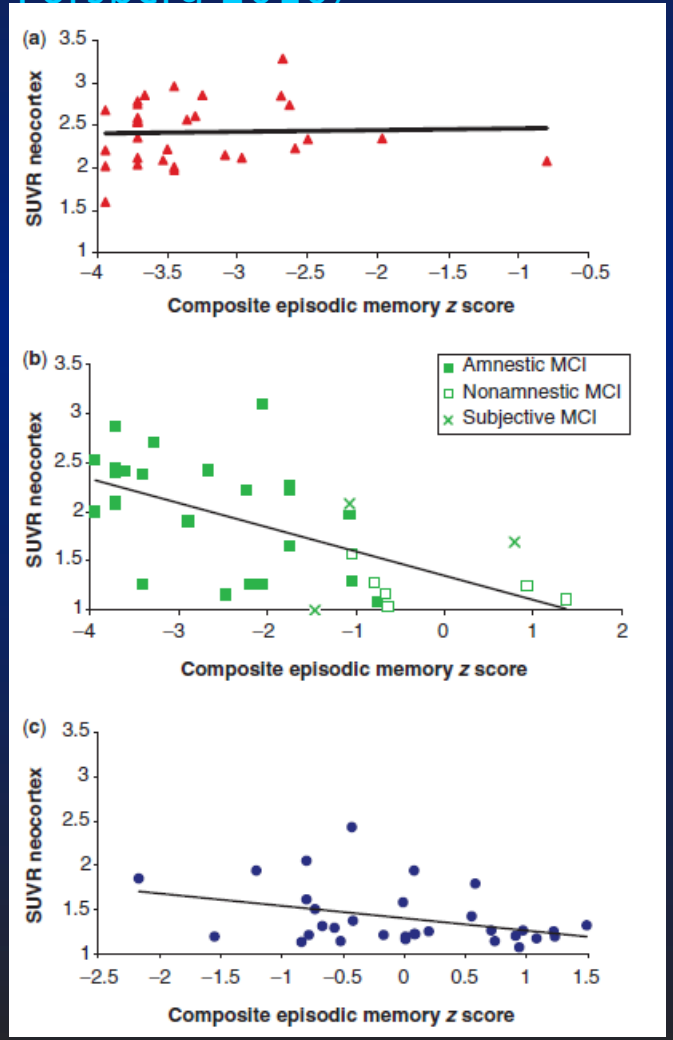
PIB et Mémoire épisodique

PIB Global : résultats contradictoires

- **OUI** (Forsberg et al., 2008, Pike et al., 2007; Rentz et al., 2010; Mormino et al., 2009)
- **NON** (Sperling et al., 2009; Storandt et al., 2009; Forsberg 2010)



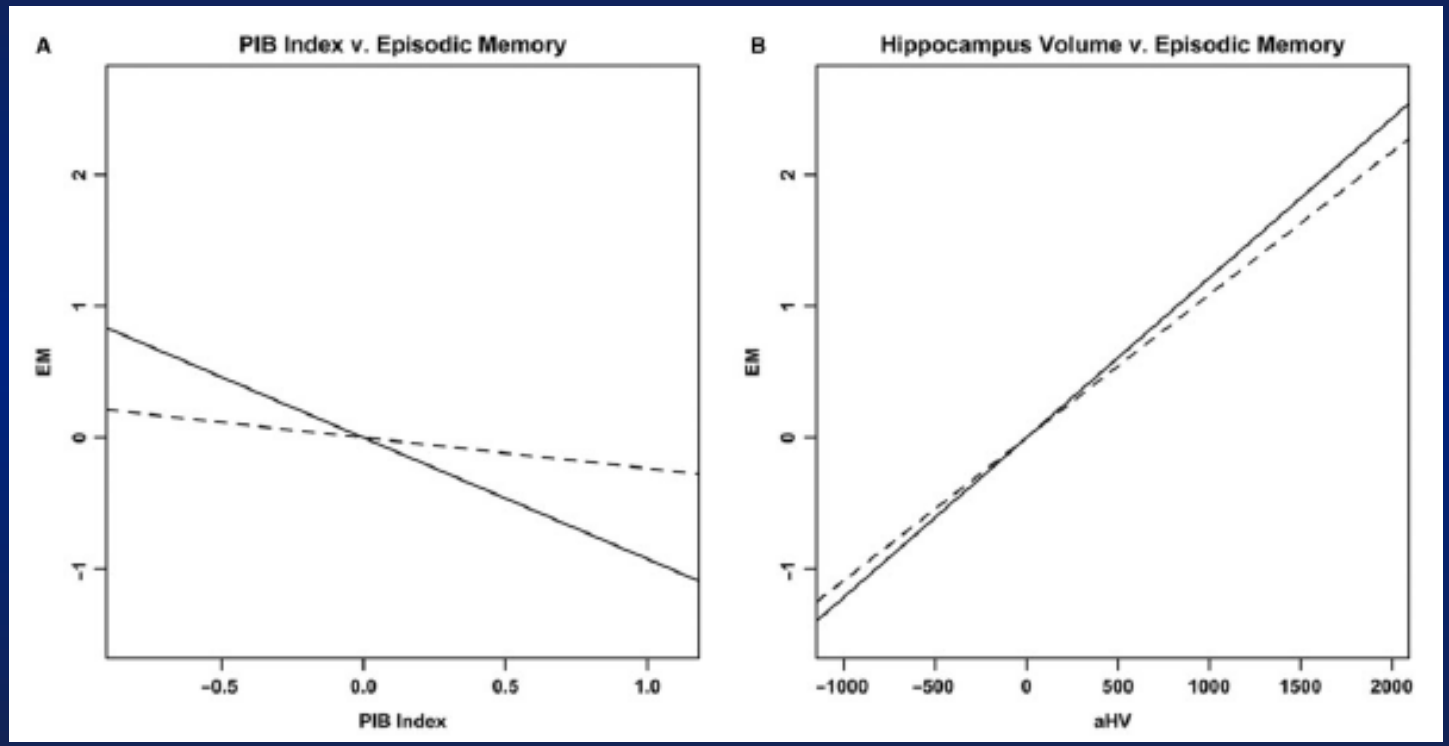
Pike et al., Brain, 2007



Tous groupes : oui; groupes isolés : MCI : oui

PIB et Mémoire épisodique

Tenir compte de l'effet d'autres facteurs connus pour avoir un impact sur la mémoire comme l'atrophie hippocampique



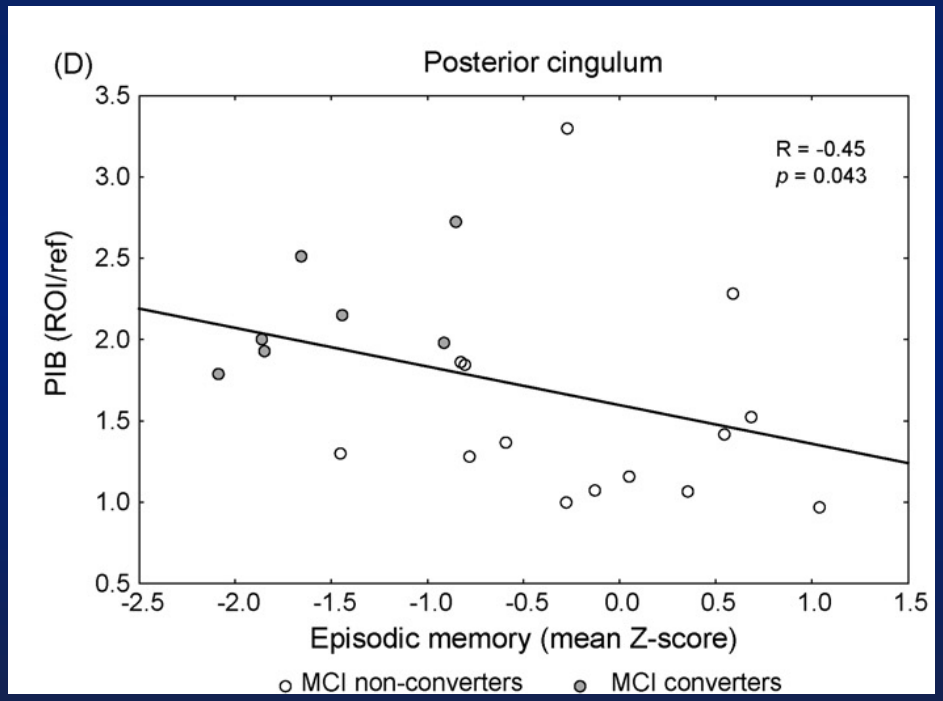
Corrélation entre PIB global et mémoire avant et après contrôle de volume hipp

Corrélation entre volume hipp et mémoire, avant et après contrôle de PIB

Mormino et al., 2009 (MCI + SAS)

PIB / FDDNP et Mémoire épisodique

PiB régional (Forsberg et al., 2008; Rentz et al., 2010; Tolboom et al., 2009)

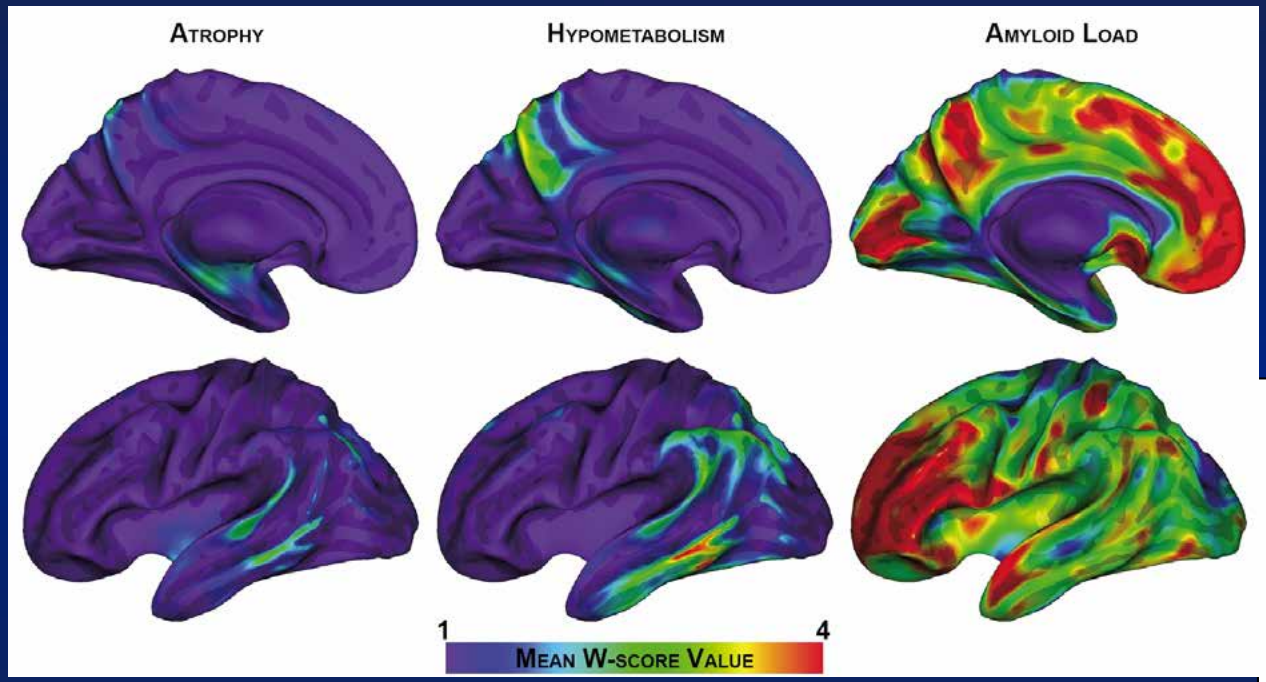


Forsberg et al., 2008

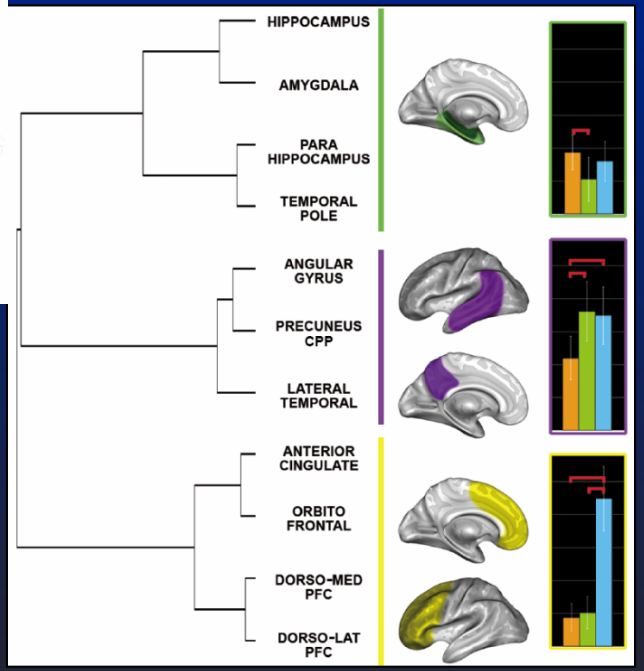
	PIB	FDDNP
MMS	**-0.67**	**-0.43**
Empan endroit	0.05	-0.07
Empan envers	-0.09	-0.09
Rappel imm. mots de Rey	**-0.56**	**-0.52**
Rappel différé mots de Rey	**-0.77**	**-0.50**
Tâche d'association visuelle	-0.50	-0.22
Dénomination d'images	-0.15	-0.11
TMT A	0.32	0.11
TMT B	**0.47**	0.22
Stroop lecture	0.27	0.14
Stroop déno	0.24	0.03

Tolboom et al., 2009

Comparaison des 3 types d'anomalies



15 patients MA



La Joie et al., soumis

Séquence temporelle des anomalies?

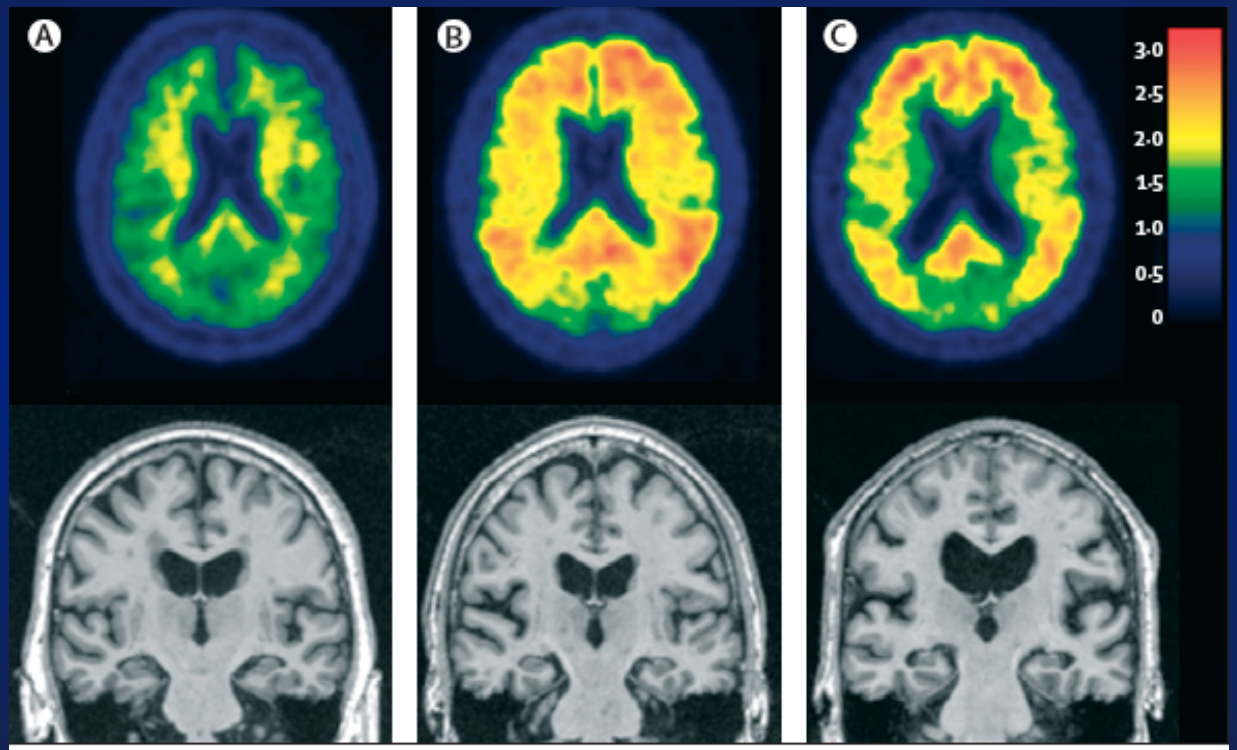


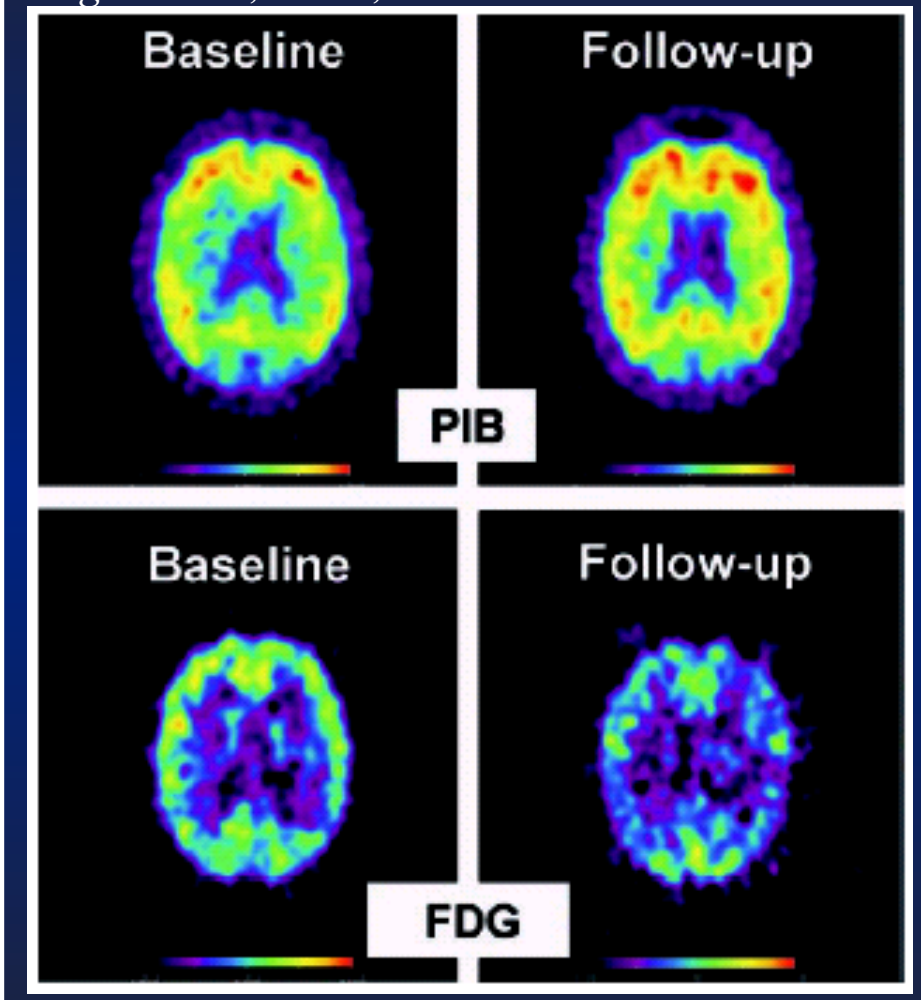
Figure 1: **Illustration of biomarker staging of Alzheimer's disease**
Three elderly individuals are placed in order from left to right by use of our proposed biomarker staging scheme. (A) A cognitively normal individual with no evidence of Aβ on PET amyloid imaging with PiB and no evidence of atrophy on MRI. (B) A cognitively normal individual who has no evidence of neurodegenerative atrophy on MRI, but has significant Aβ deposition on PET amyloid imaging. (B) An individual who has dementia and a clinical diagnosis of Alzheimer's disease, a positive PET amyloid imaging study, and neurodegenerative atrophy on MRI. Aβ=β-amyloid. PiB=Pittsburgh compound B.

B : sujet normal, sans atrophie mais PIB+

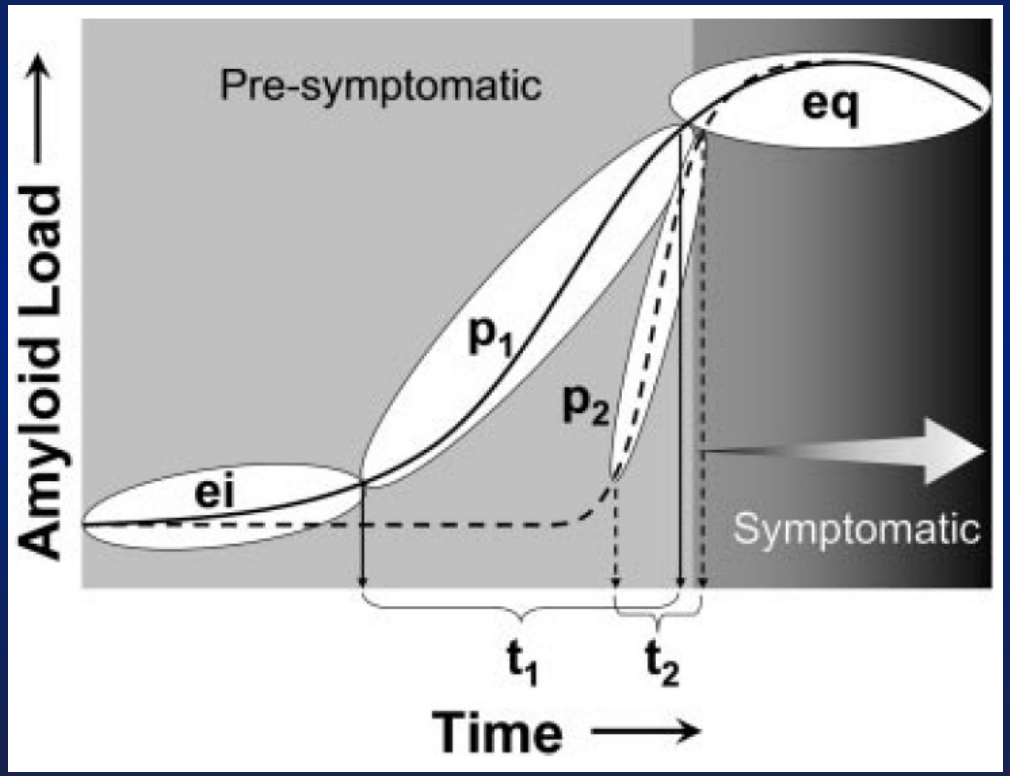
Jack et al., 2010

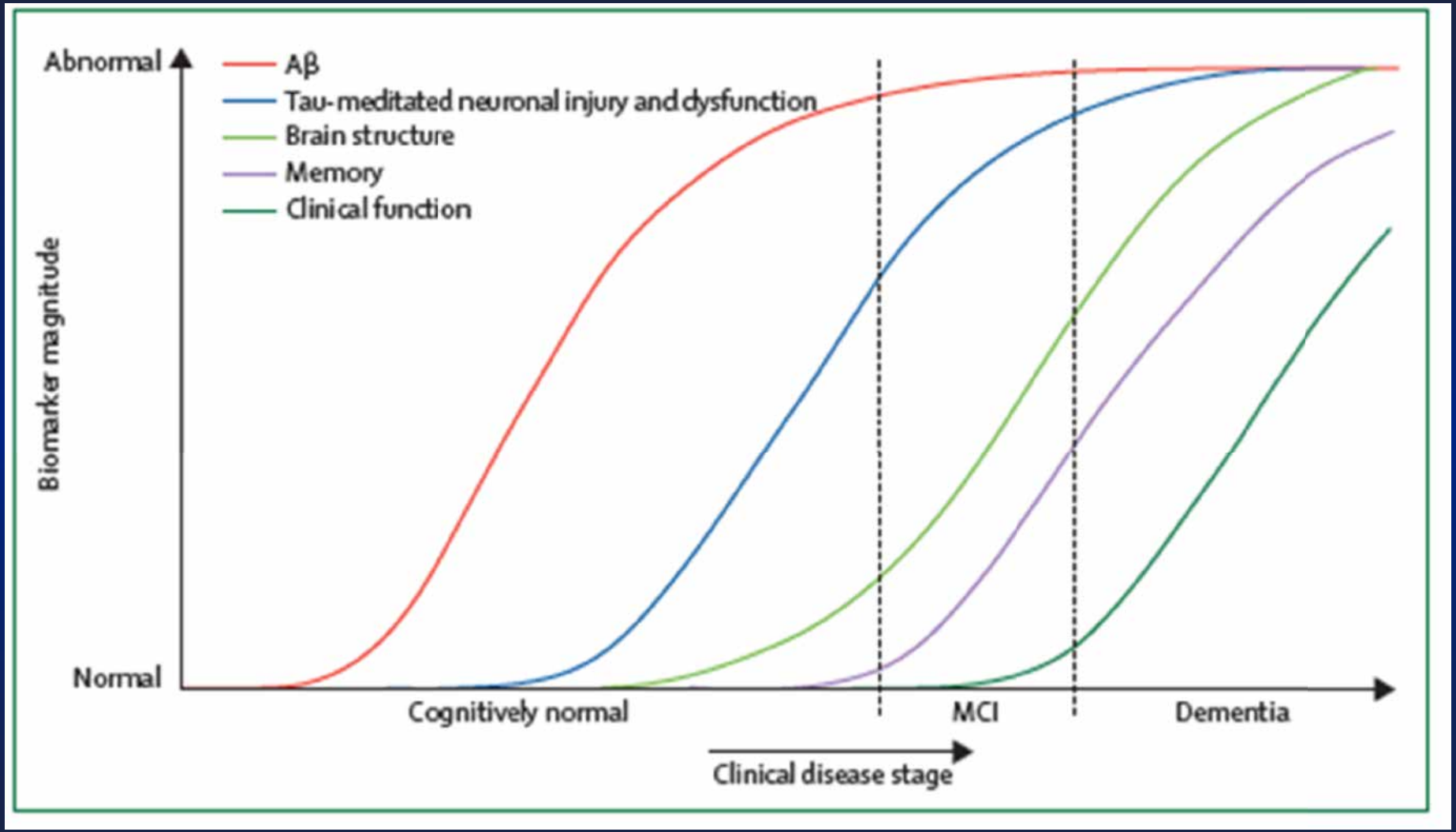
ETUDES LONGITUDINALES

Engler et al., Brain, 2006



Klunk et al., Brain, 2006



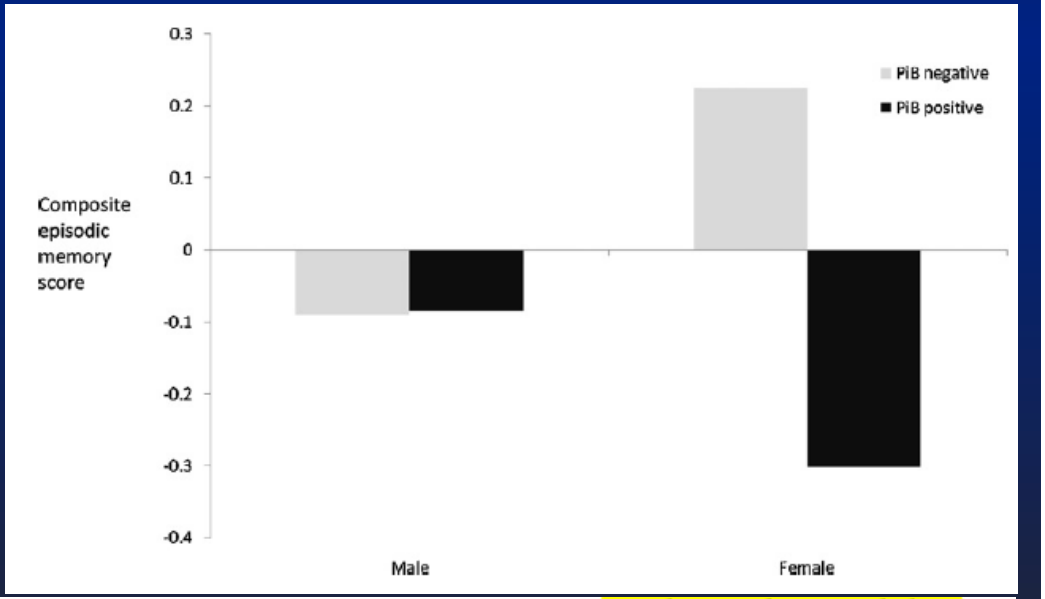


Jack et al., Lancet Neurol 2010

Facteurs à prendre en compte

- Statut génétique (APOE4…, Lambert et al.)
- Réserve cognitive (Rentz et al. 2010)
- Co-morbidités
- Age
- Sexe?

177 sujets âgés sains
33% PIB+
Pas de lien entre PIB et cognition dans tt le groupe, mais interaction avec le sexe
Pike et al., 2011



We have observed that males with AD have significantly higher PiB binding than females (Rowe et al., 2010), possibly indicating that a greater amyloid load is necessary before men manifest the disease.

CONCLUSION

Intérêt des biomarqueurs pour comprendre la physiopathologie de la MA et diagnostic précoce

Liens limités entre PIB et atrophie, hypométabolisme et troubles cognitifs ; Mesures complémentaires (combinaison)

Question des 30% de sujets sains PIB+ ?

Modèles postulent Aβ en premier, pas en accord avec Braak et Braak (DNF précèdent)

Limites : Pas de ligand spécifique de DNF

En clinique, place de la neuropsychologie

Autres marqueurs

Biomarkers under examination for AD
Biomarkers of Aβ deposition
CSF $A\beta_{42}$
PET amyloid imaging
Biomarkers of neuronal injury
CSF tau/phosphorylated-tau
Hippocampal volume or medial temporal atrophy by volumetric measures or visual rating
Rate of brain atrophy
FDG-PET imaging
SPECT perfusion imaging
Less well validated biomarkers: fMRI activation studies, resting BOLD functional connectivity, MRI perfusion, MR spectroscopy, diffusion tensor imaging, voxel-based and multivariate measures
Associated biochemical change
Inflammatory biomarkers (cytokines)
Oxidative stress (isoprostanes)
Other markers of synaptic damage and neurodegeneration such as cell death

Albert et al., 2011


les chemins
NOS CONNAISSANCES SUR LA STRUCTURE ET LE FONCTIONNEMENT DE LA
de la mémoire
MÉMOIRE HUMAINE ONT BEAUCOUP PROGRESSÉ. L'ÉTUDE DES MALADIES NOUS RENSEIGNE,
f. eustache et
MIEUX QUE TOUTE AUTRE DÉMONSTRATION, SUR CETTE FONCTION MENTALE QUI
b. desgranges
SE TROUVE AU CŒUR DE NOTRE SUB- JECTIVITÉ ET DE NOTRE IDENTITÉ.
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[LES ESSAIS DU POMMIER !]