Imaging biomarkers to predict AD

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Disclosures

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-Stichting Vumc fonds

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-Dr Scheltens and staff receive <u>no personal</u> compensation from any of the above.

-www.alzheimercentrum.nl/fondsenwerving

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Contents

- Overview imaging modalities
- Case vignette
- Clinical value amyloid PET
- Imaging biomarkers in MCI
- Imaging and CSF in MCI
- From simple to complex methodology
- Conclusions

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# Imaging modalities differ in many aspects (example)
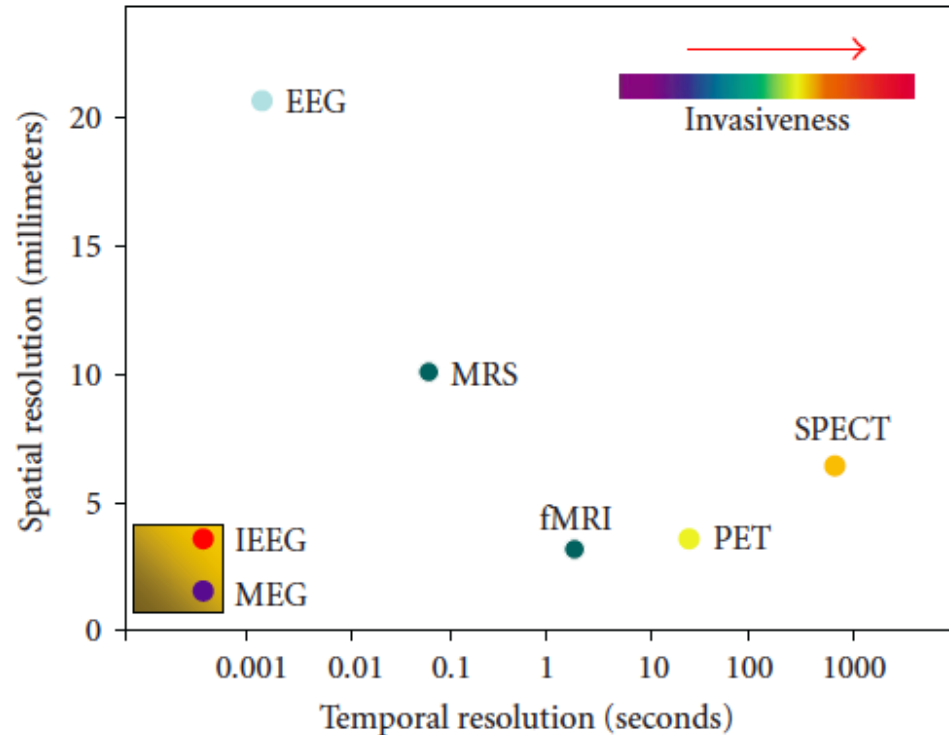
CASE

- 59 year old male for second opinion.

- memory problems and spatial disorientation. Behavioural problems: aggression and apathy.

- Neuropsych: visuo-spatial disturbances, memory deficits and low MMSE (22) and CAMCOG (80) scores.

- Fronto-temporo-parietal brain atrophy was observed on MRI, most pronounced in the right hemisphere.

- Differential diagnosis: 1) atypical Alzheimer's disease (AD), 2) corticobasal syndrome (CBS), or 3) behavioural variant frontotemporal dementia.

- For this study, the probability diagnosis was set to AD with a diagnostic certainty of 50%.
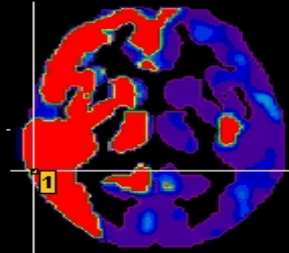
Case A

[^{11}C]PIB BP$_{ND}$
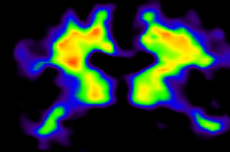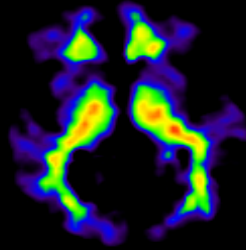
[^{18}F]FDG SUVr
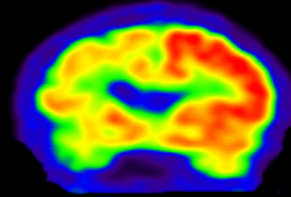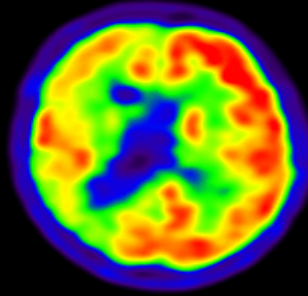
[^{18}F]FDG PALZ
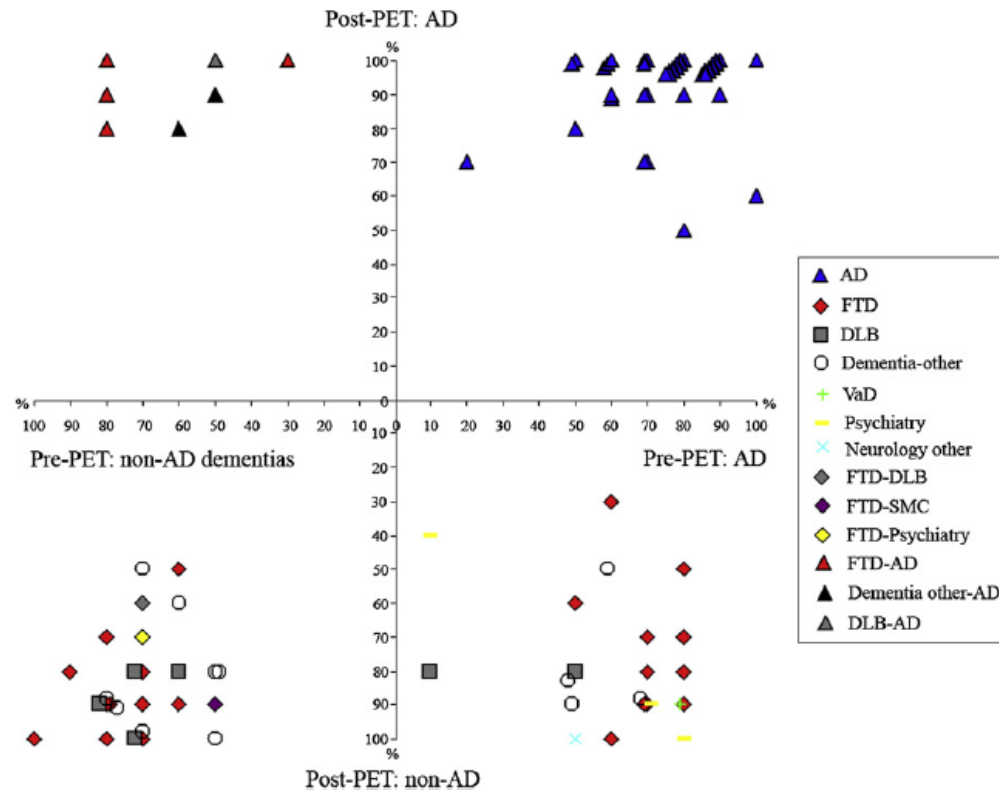
Clinical Value Molecular Imaging

- N= 154 (<70y) patients underwent [^{11}C]PIB and [^{18}F]FDG

- [^{11}C]PIB positive in:
    - 40/66 (61%) patients with a clinical diagnosis AD
    - 5/18 (28%) patients with clinical diagnosis FTD
    - 4/5 (80%) patients with clinical diagnosis DLB
    - 3/10 (30%) patients with other dementias

- [^{18}F]FDG positive in:
    - 38/66 (58%) of AD patients,
    - 6/18 (33%) of FTD patients.

Clinical Value Molecular Imaging

- PET results led to a change in diagnosis in 35 (23%) patients.
- This only occurred when prior diagnostic certainty < 90%.

- Diagnostic confidence increased from 71±17% before to 87±16% after PET (p<0·001)

Impact of molecular imaging on the diagnostic process in a memory clinic

Rik Ossenkoppele[a,b,*], Niels D. Prins[a], Yolande A. L. Pijnenburg[a], Afina W. Lemstra[a],
Wiesje M. van der Flier[a,c], Sofie F. Adriaanse[a,b], Albert D. Windhorst[b], Ron L. H. Handels[d],
Claire A. G. Wolfs[d], Pauline Aalten[d], Frans R. J. Verhey[d], Marcel M. Verbeek[e,f],
Mark A. van Buchem[f,g], Otto S. Hoekstra[b], Adriaan A. Lammertsma[b], Philip Scheltens[a],
Bart N. M. van Berckel[b]

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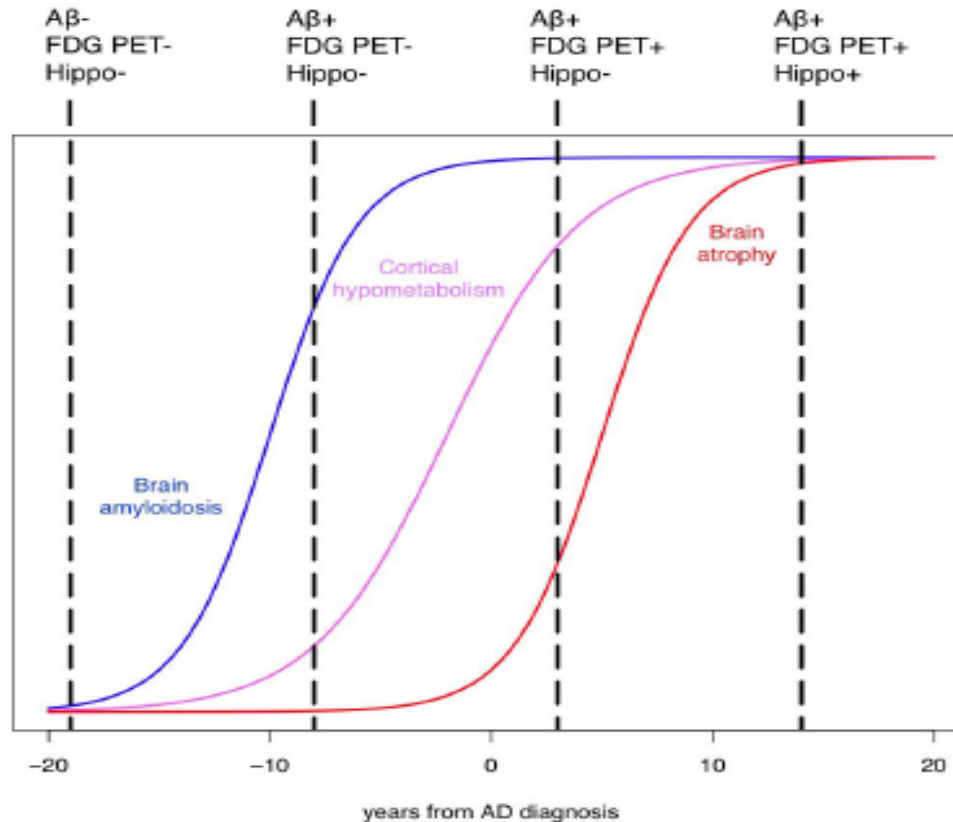Bart N. M. van Berckel[b]

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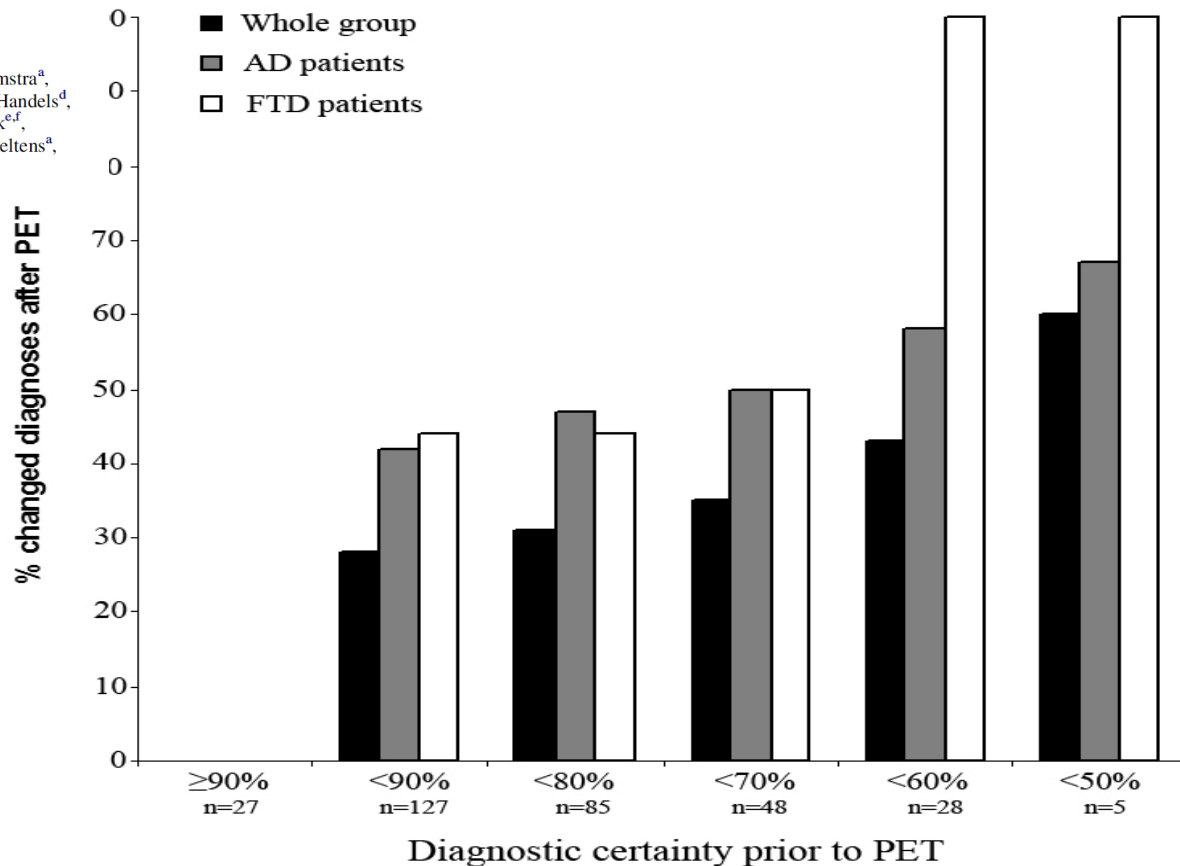
Prediction of dementia in MCI patients based on core diagnostic markers for Alzheimer's disease

[a] Prestia A, PsyD, [a, b] Caroli A, PhD, [c,d] van der Flier WM, PhD, [c,e] Ossenkoppele R, MSc, [e] Van Berckel B, MD, [f] Barkhof F, MD, PhD, [g] Teunissen CE, PhD, [h] Wall A, PhD [i] Carter SF, PhD [i] Schöll M, PhD [i,j] Choo IH, MD, PhD, [i,k] Nordberg A, MD, PhD, [c] Scheltens P, MD, PhD, [a] Frisoni GB, MD.

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Variation on a model.....
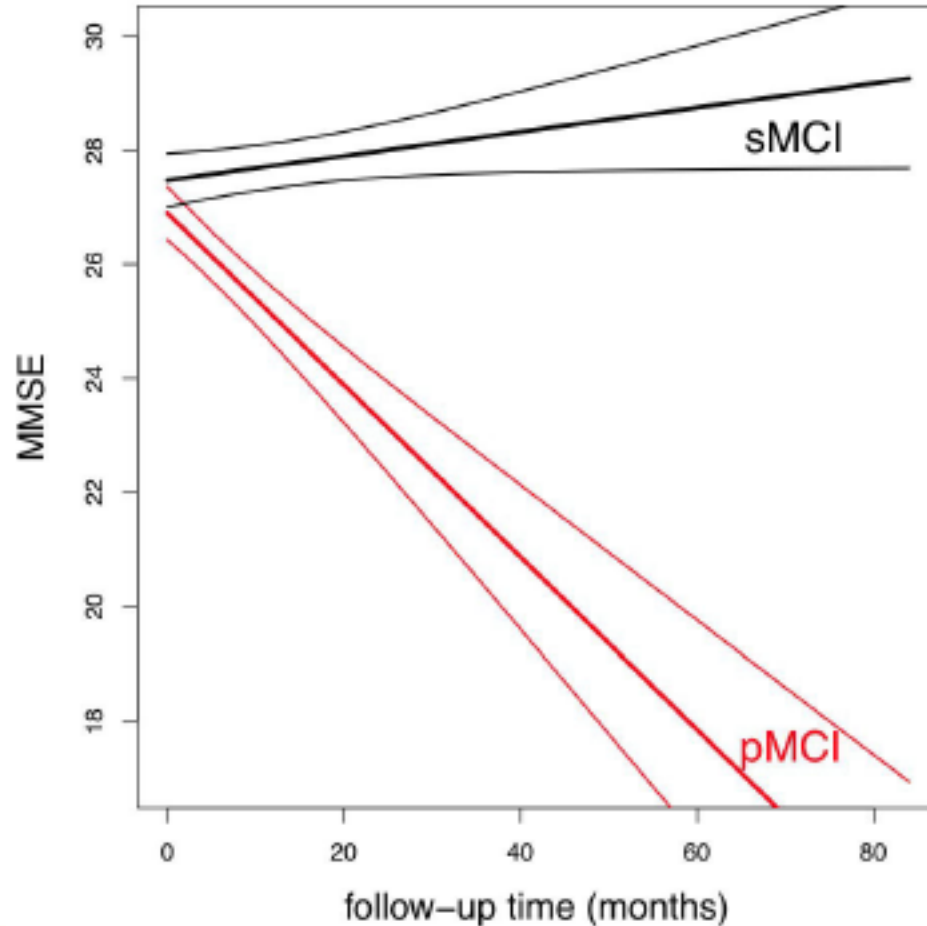
Two groups of MCI

B)

All MCI (N=73)

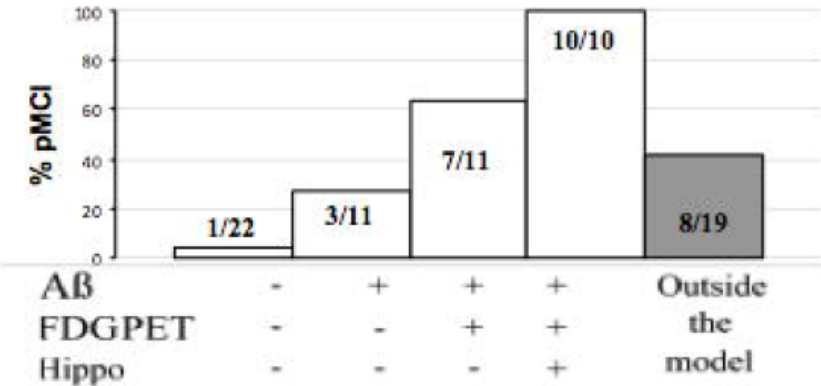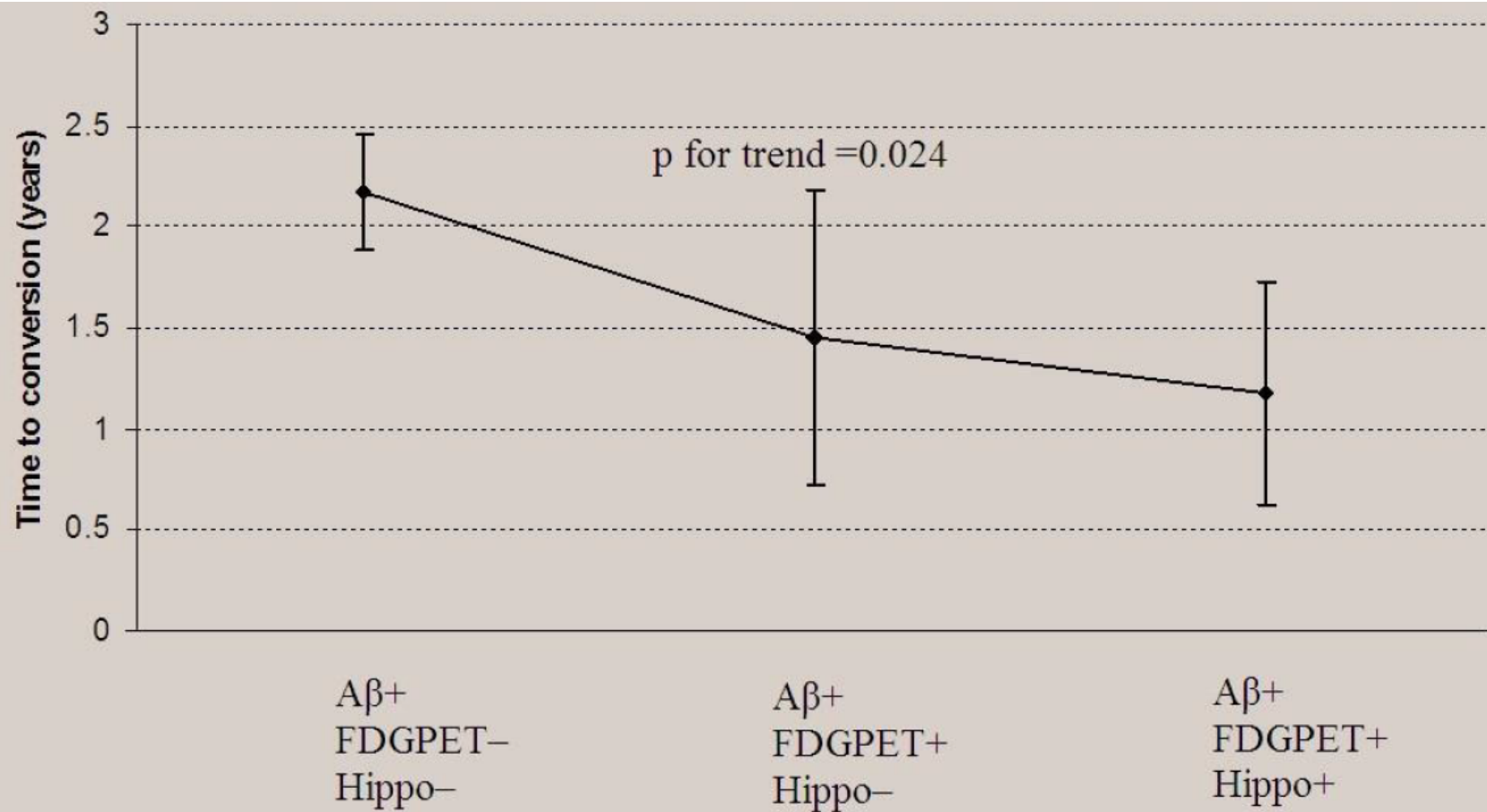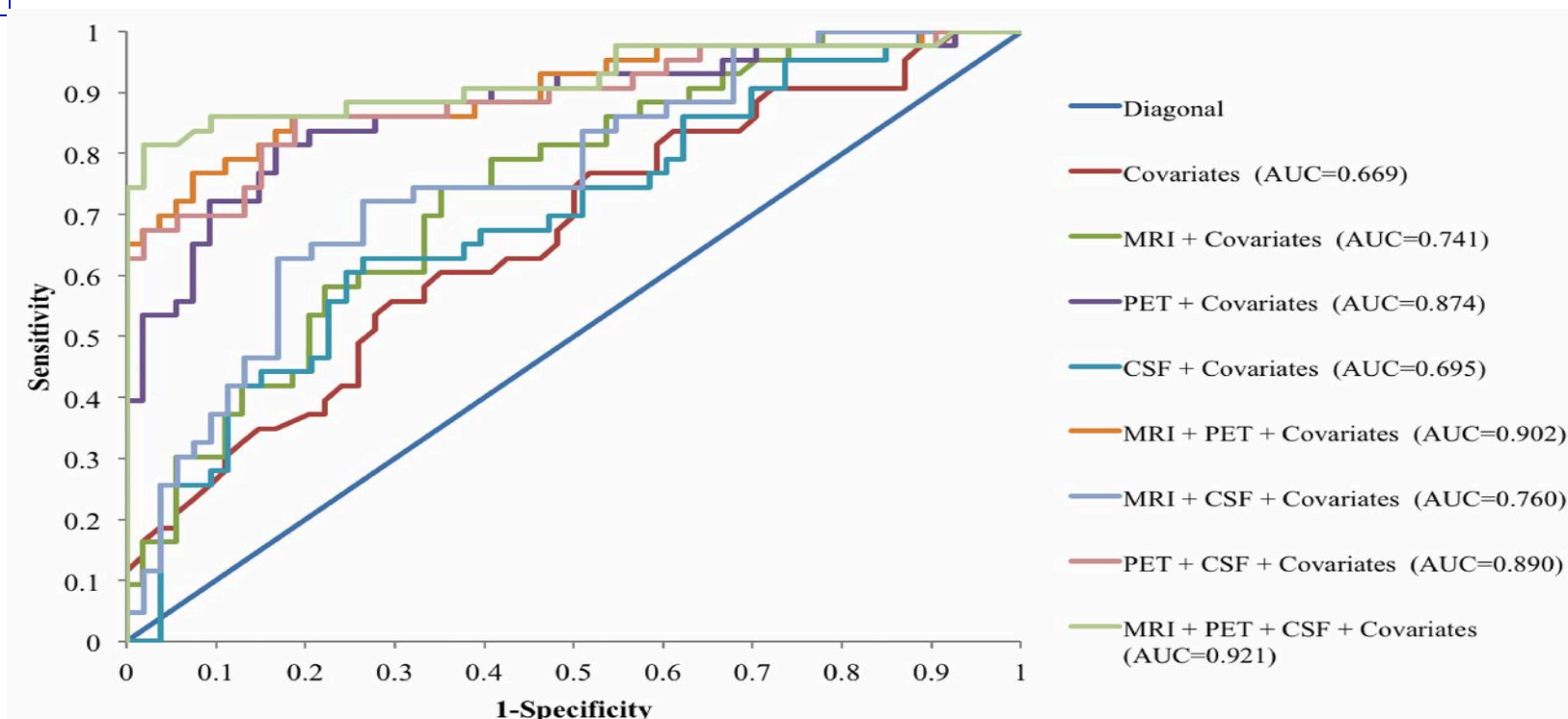| Aß | - | + | + | + | Outside |
| FDGPET | - | - | + | + | the |
| Hippo | - | - | - | + | model |

Predicting Cognitive Decline in Subjects at Risk for Alzheimer Disease by Using Combined Cerebrospinal Fluid, MR Imaging, and PET Biomarkers.
Shaffer JL, Petrella JR, Sheldon FC, Choudhury KR, Calhoun VD, Coleman RE, Doraiswamy PM; For the Alzheimer's Disease Neuroimaging Initiative.

Radiology 2012; dec 11

Receiver operating characteristic curves for all of the logistic regression models for predicting conversion from MCI to AD. Of the three biomarkers alone, FDG PET added the most prognostic information with an area under the curve (AUC) of 0.874, compared w...

Legend:
- Diagonal
- Covariates (AUC=0.669)
- MRI + Covariates (AUC=0.741)
- PET + Covariates (AUC=0.874)
- CSF + Covariates (AUC=0.695)
- MRI + PET + Covariates (AUC=0.902)
- MRI + CSF + Covariates (AUC=0.760)
- PET + CSF + Covariates (AUC=0.890)
- MRI + PET + CSF + Covariates (AUC=0.921)

Axes: Sensitivity (y-axis), 1-Specificity (x-axis)

Shaffer J L et al. Radiology doi:10.1148/radiol.12120010

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DIAGNOSTIC NEURORADIOLOGY

Is radiological evaluation as good as computer-based volumetry to assess hippocampal atrophy in Alzheimer's disease?

Claire Boutet · Marie Chupin · Olivier Colliot ·
Marie Sarazin · Gurkan Mutlu · Aurélie Drier ·
Audrey Pellot · Didier Dormont · Stéphane Lehéricy ·
And the Alzheimer's Disease Neuroimaging Initiative

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a Right hemisphere

b Left hemisphere

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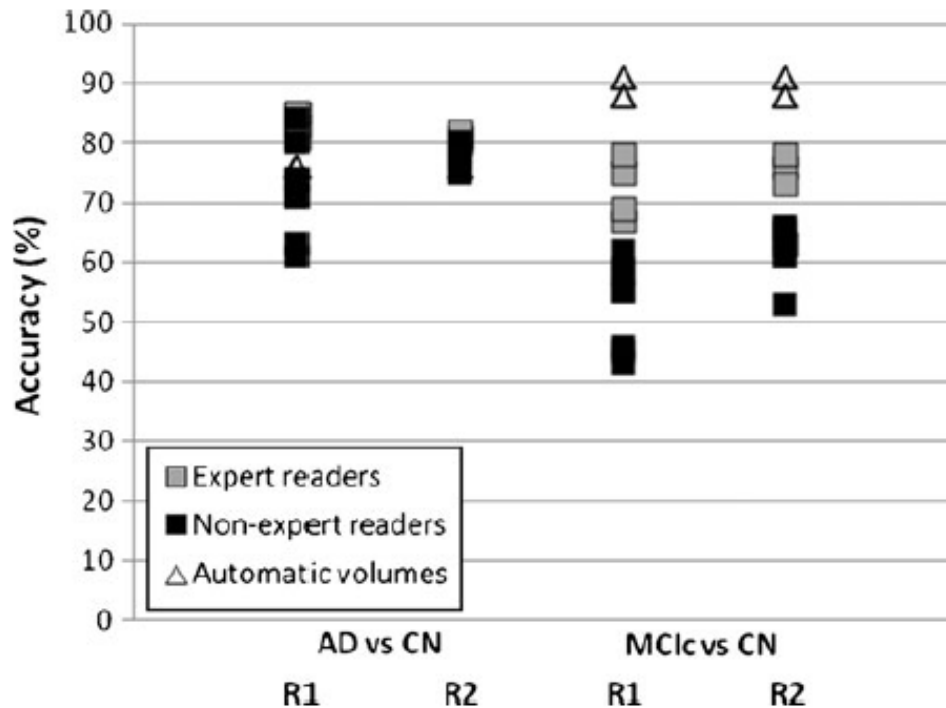
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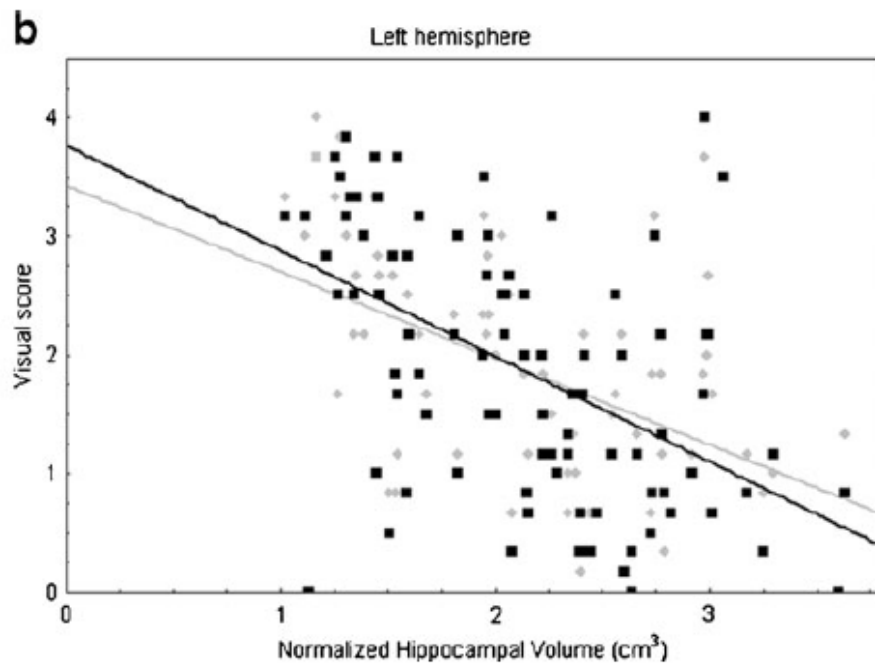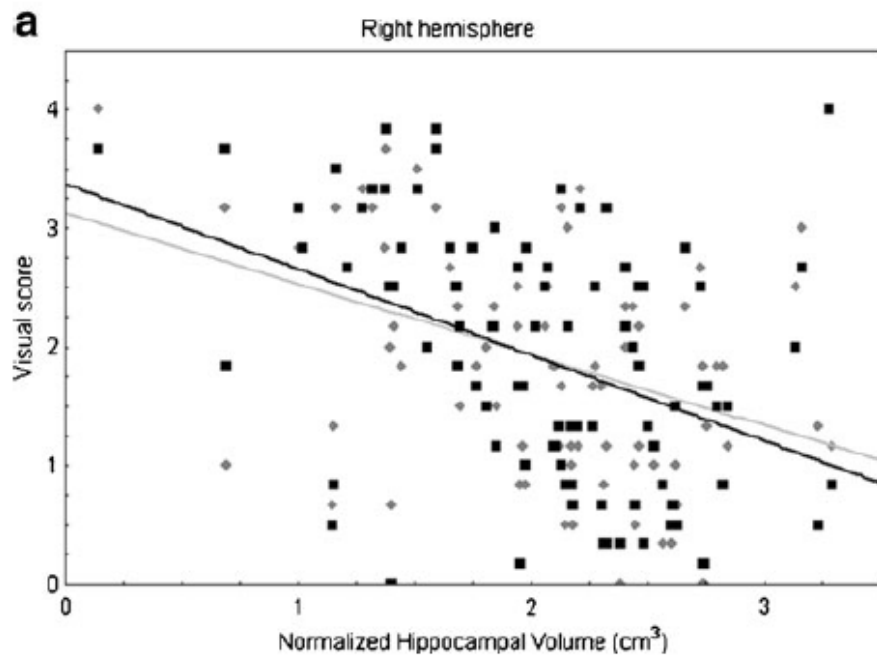
Fig. 3 Classification accuracy for AD, MCIc and CN for readings 1 (*R1*) and 2 (*R2*) compared with the results derived from the automatic volumes

Conclusions Visual assessment of medial temporal lobe atrophy by radiologists was well correlated with hippocampal volume. Radiological assessment is as good as computer-based volumetry for the classification of AD, MCI non-converter and CN and less good for the classification of MCI converter versus CN. Use of Scheltens scale for assessing hippocampal atrophy in AD seems thus justified in clinical routine.

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Dementia
and Geriatric
Cognitive Disorders

Associations between Patterns of EEG Abnormalities and Diagnosis in a Large Memory Clinic Cohort

M. Liedorp[a]   W.M. van der Flier[a]   E.L.J. Hoogervorst[c]   P. Scheltens[a]   C.J. Stam[b]

Table 2. Prevalences of the main diagnostic groups according to the EEG pattern and PR (prevalence of diagnosis with specific EEG pattern/prevalence of diagnosis in total population)

	Total population, %	Prevalence per EEG pattern, % (n = 1,313)				PR (prevalence per EEG pattern/total prevalence)			
		normal (n = 530)	only focal abnormalities (n = 372)	only diffuse abnormalities (n = 151)	focal and diffuse abnormalities (n = 260)	normal	only focal abnormalities	only diffuse abnormalities	focal and diffuse abnormalities
SC	21	33	19	8	6	1.6[1]	0.9	0.4[2]	0.3[2]
Psychiatry	9	13	9	5	4	1.4[1]	1.0	0.6	0.4[2]
FTLD	5	5	6	5	2	1.1	1.2	1.1	0.5
MCI	14	16	19	12	7	1.1	1.3[1]	0.8	0.5[2]
AD	29	19	26	45	45	0.7[2]	0.9	1.5[1]	1.5[1]
VaD	4	1	5	3	9	0.3[2]	1.2	0.8	2.3[1]
DLB	3	0.2	1	5	10	0.1[2]	0.3[2]	1.8	3.5[1]

[1] Lower-bound 95% CI >1. [2] Upper-bound 95% CI <1.
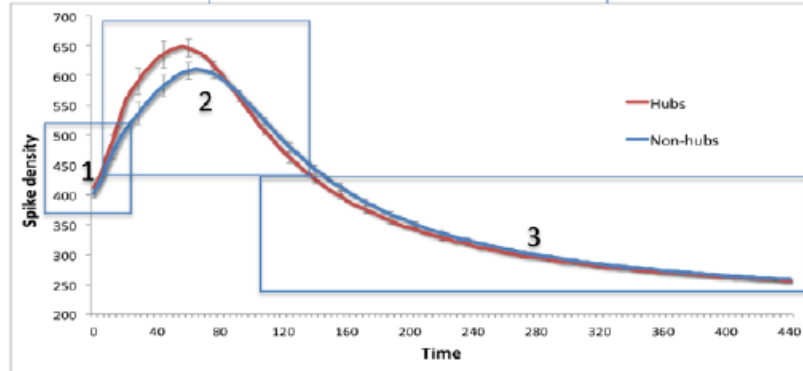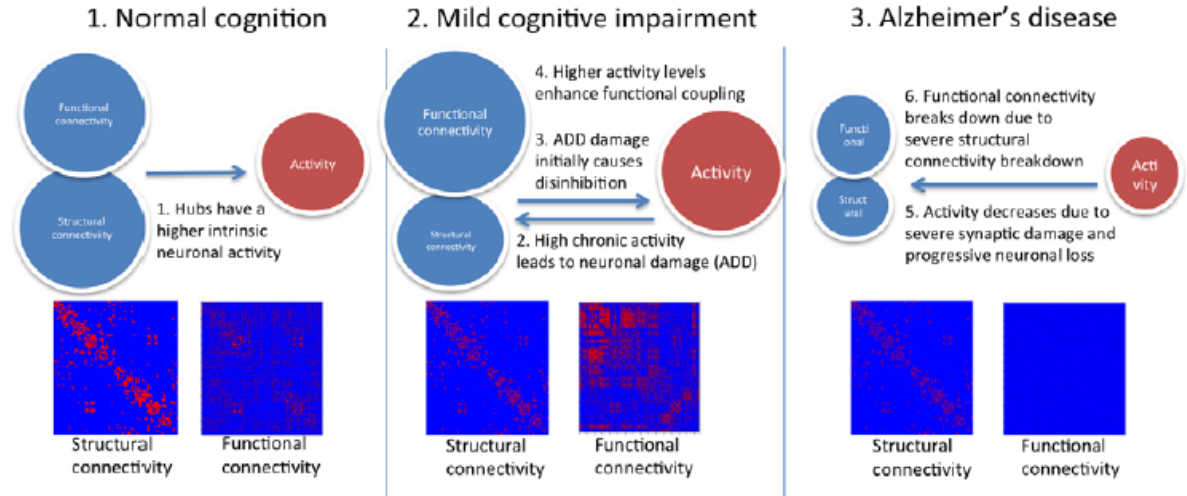
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Table 3. Clinical relevance of EEG patterns

EEG pattern	Argues for	Argues against
Normal	SC	DLB
	Psychiatric diagnosis	VaD
		AD
Only focal abnormalities	MCI	DLB
Only diffuse abnormalities	AD	SC
Focal and diffuse abnormalities	DLB	SC
	VaD	Psychiatric diagnosis
	AD	MCI

In a network state of mind…