

Biomarqueurs du LCR MA / DLFT

Réunion de référence des démences rares
Jeudi 17 juin 2010

Du syndrome topographique au dg biologique

Phénotype

Information sur la
localisation des lésions

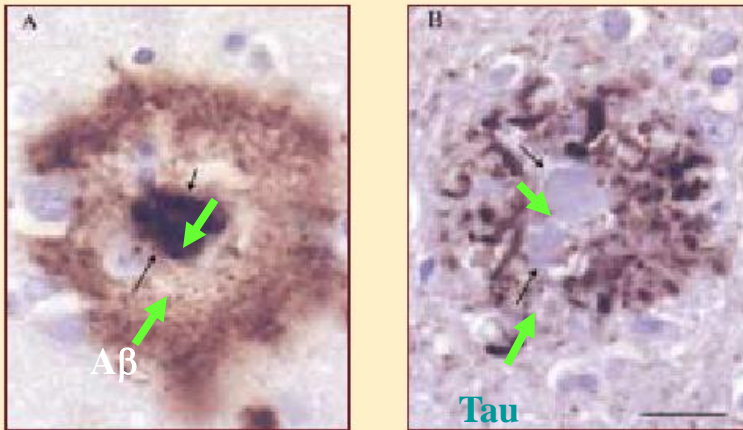
- Neuropsychologie
- IRM: Atrophie focale
- Imagerie fonctionnelle (SPECT / TEP FDG)

Processus biologique

Information sur le
mécanisme causal

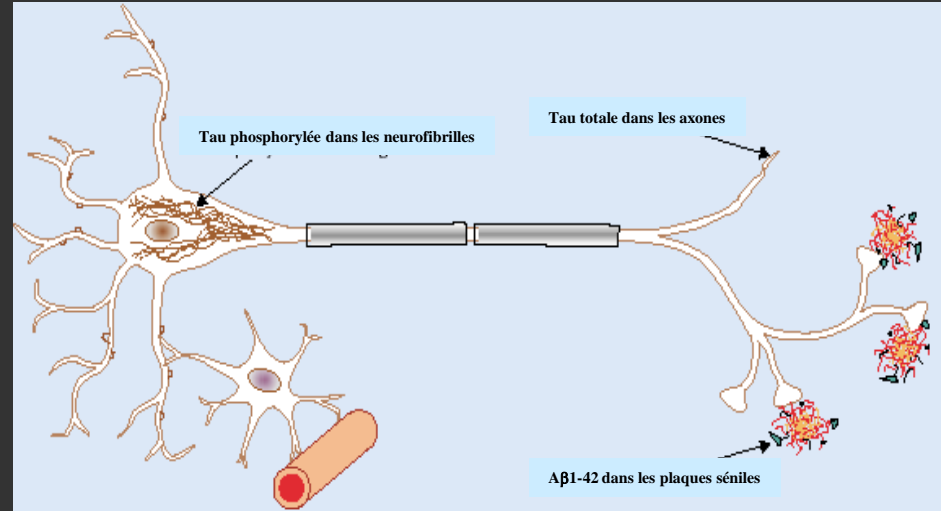
- **Biomarqueurs Tau et A β (LCR)**
- PET – PIB (Pittsburgh Binding Compound)

Marqueurs biologiques de MA



Plaque sénile avec ses 2 principaux composants

Charles Duyckaerts, Pitié-Salpêtrière



Bleenow and Hampel, 2003

Peptide A β

Protéine tau et P-tau

Diminué

LCR

Augmentées

Biomarqueurs du LCR et DLFT

- études neuropathologiques
- études cliniques

Validité du diagnostic biologique pour des dg confirmés

		sensibilité	spécificité
MA vs T (Tapiola 2009)	P-Tau/A β 42	91,6 %	85,7 %
MA vs DFT (Bian 2008)	Tau/A42	78.9%	96.6%,

Validité du diagnostic biologique par l'autopsie

P-Tau / A β 42 (dg MA) :

sensibilité = 91,6 %

spécificité = 85.7%

overall accuracy =

90.2%

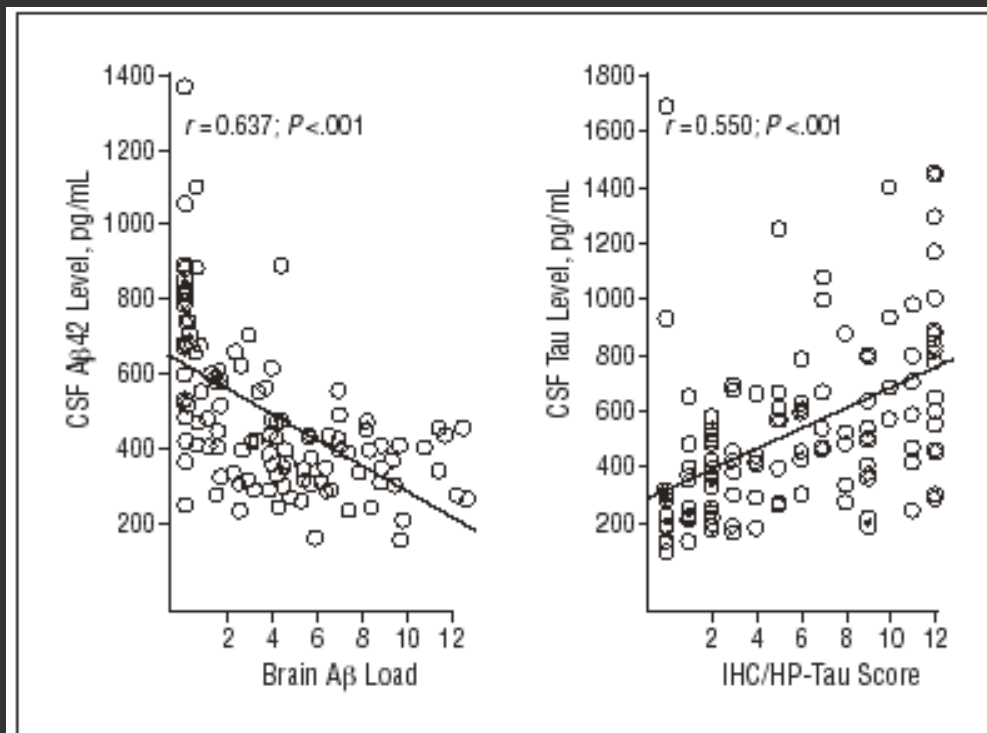


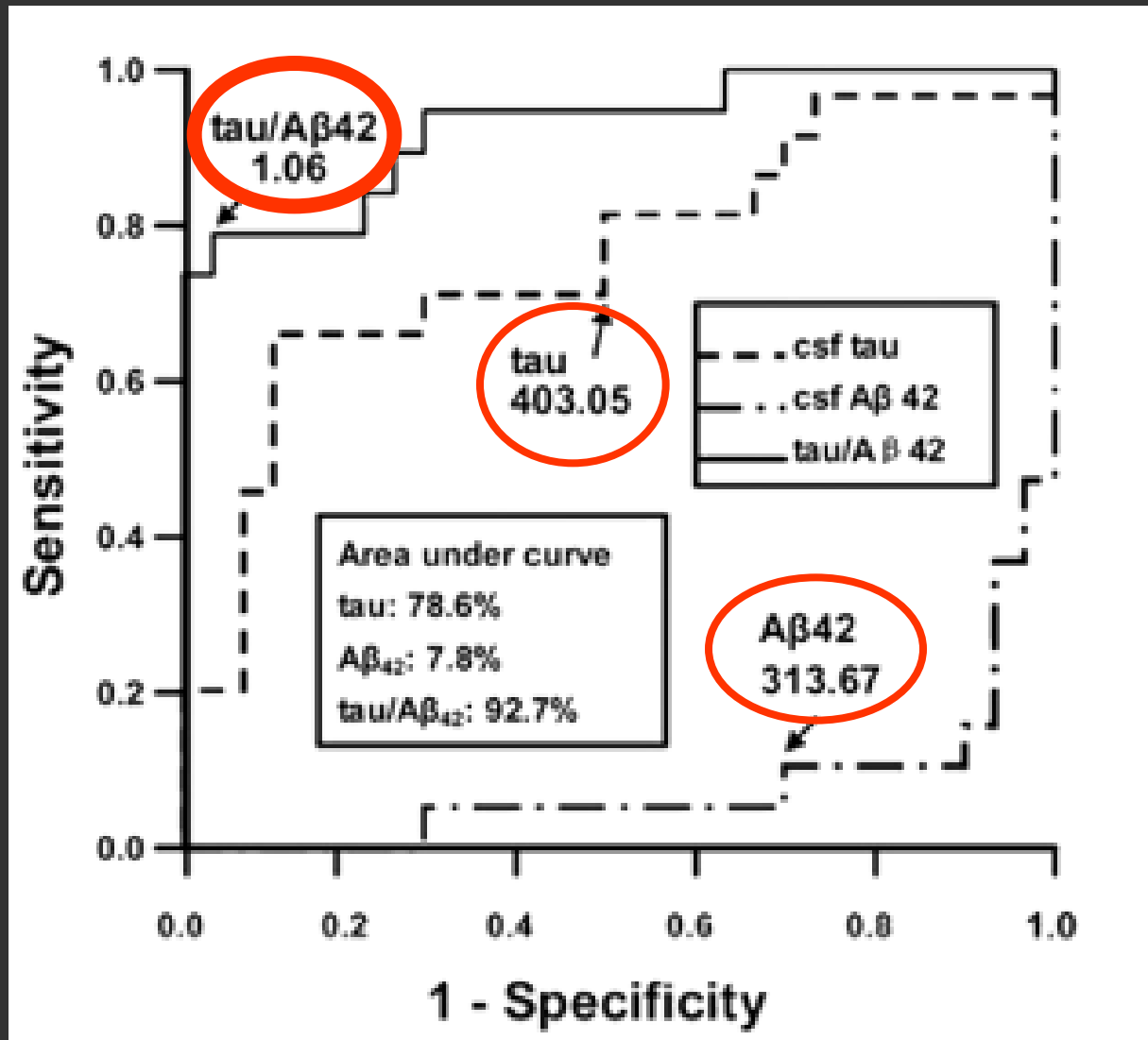
Figure 3. Correlation between cerebrospinal fluid (CSF) biomarkers and total β -amyloid (A β) load in the brain (stained area fraction) and hyperphosphorylated tau immunoreactivity on immunohistochemistry (IHC/HP-tau semiquantitative assessment scores).

N=123

Tapiola et al, 2009

CSF biomarkers in frontotemporal lobar degeneration with known pathology

Bian et al.
Neurology, 2008

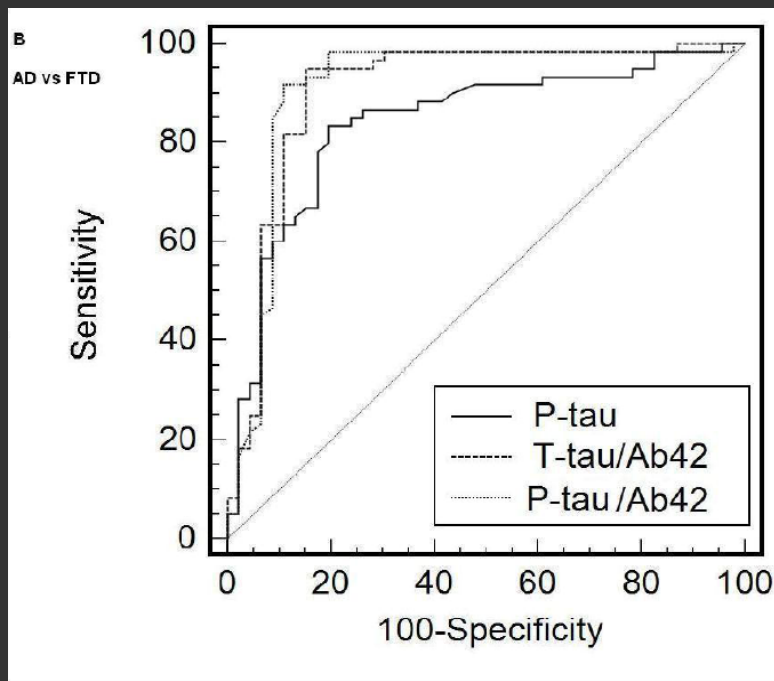


Cerebrospinal fluid biomarkers in the differential diagnosis of Alzheimer's disease from other cortical dementias

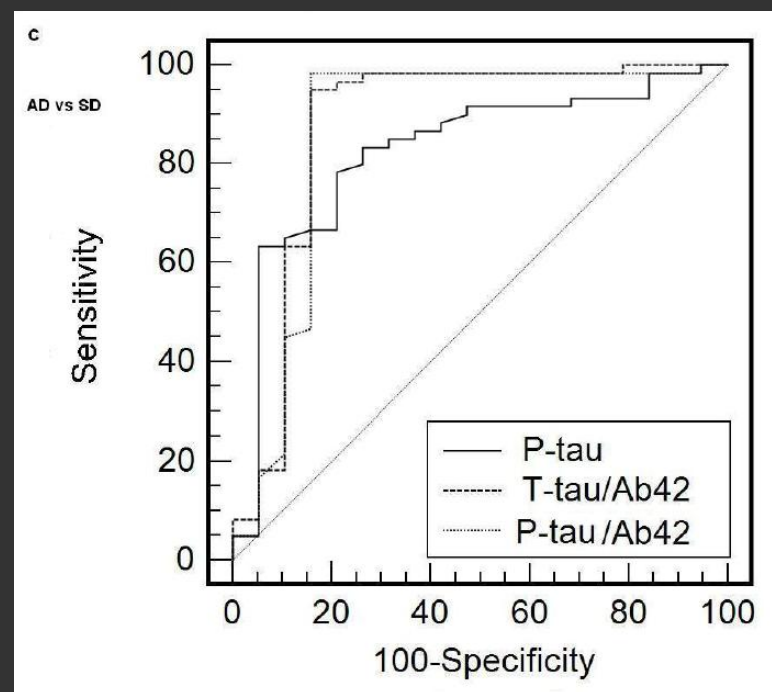
Leonardo Cruz de Souza (MD)^{a,b *}, Foudil Lamari (MD, PhD)^{c *}, Serge Belliard (MD, PhD)^d, Claude Jardel (MD, PhD)^c, Caroline Houillier (MD)^b, Raphael De Paz (MD)^b, Bruno Dubois (MD, PhD)^{a,b} and Marie Sarazin (MD, PhD)^{a,b}.

	AD	FTD	SD	FCD
N	60	27	19	17
Age	63.6 (57-72)	66 (59-73)	60 (57-68)	56 (52-58) ^b
Sex ratio (M/F)	30/30	15/12	9/10	12/9
Disease duration (years)	3 (2-4)	3 (2-5)	4 (2-7)	Not applicated
MMSE	20 (17-24)	21 (18-23)	22 (21-27) ^c	27 (26-28) ^{a,d}
FAB	13 (11-14)	13 (6-14)	15 (12-17)	15 (13-17) ^a
Aβ42 (ng/ml)	237.6 (155.5-315.5)	394 (306.2-473) ^a	532 (308.2-682.2) ^a	500 (417-614.5) ^{a,d}
T-tau (ng/ml)	571 (419-796.5)	239 (137-407.4) ^a	317 (209.5-433.7) ^a	185 (141.2-262.7) ^a
P-tau (ng/ml)	84.2 (69-107.5)	43.5 (32.5-57) ^a	46.2 (38.4-67.0) ^a	34 (30.2-56.9) ^a
T-tau/Aβ42	2.450 (1.688-3.433)	0.582 (0.396-1.055) ^a	0.492 (0.35-0.928) ^a	0.335 (0.31-0.51) ^{a,d}
P-tau/Aβ42	0.43 (0.26-0.48)	0.13 (0.08-0.15) ^a	0.18 (0.06-0.13) ^a	0.074(0.066-0.093) ^{a,d}

MA vs DFT-f (N = 60; n = 27)



AD vs demence sémantique (n = 60; n = 19)



	Se	Spe
MA vs DFT (0.211)	98.3%	84.2%
MA vs DS (0.143)	91.7%	92.6%
MA vs DLFT (0.211)	91.7%	89.1%

Dg différentiel MA vs DFT

	n	LCR ratios	sensibilité	spécificité
Kapaki 2008	76 MA 34 DLFT 93 T Dg clin x 2 ans	P-Tau / Aβ Tau / Aβ	77.2% 90.3%	80.7% 64.5%
Bian 2008	19 MA 30 DFT 13 T Dg confirmés	Tau/A42	78.9%	96.6%,
De sousa 2010	60 MA 27 DFT Dg clin x 2 ans	P-Tau/Abeta	98.3%	84.2%

Number of patients (%) with altered values of individual CSF biomarkers

	AD	FCD	FTD	SD
A β 42 < 379 pg/ml	55/60 (91.6)	3/17 (17.64)	12/27 (44)	6/19 (31.5)
T-tau > 465 pg/ml	41/60 (68.3)	2/17 (11.76)	3/27 (11.1)	4/19 (21.05)
P-Tau > 64.3 pg/ml	50/60 (83.3)	1/17 (5.88)	4/27 (14.81)	5/19 (26)
T-tau/A β 42 > 1.23	57/60 (95)	0/17	4/27 (14.81)	3/19 (15.8)
P-tau/A β 42 > 0.211	54/60 (90)	0/17	2/27 (7.4)	3/19 (15.8)
T-tau/A β 42 >1.23 and P-tau/A β 42 > 0.211	54/60 (90)	0/17	1/27 (3.7)	3/19 (15.8)

The employed cut-offs were those found from ROC curves for discriminating AD from FTD pooled with SD.

	PCA	PNFLA
Âge	N=15	N=26
MMSE	62 (57-67)	65.5 (62-71)
	19 (16-22)	21 (20-24)
Tau/Aβ42	1.33	1.678
Se / Spe	88.3 / 46.7	75 / 65.4
Analyse indiv.	N = 11/15 (73%)	N = 17/15 (65%)
P-Tau/Aβ42	0.311	0.296
Se / Spe	61.7 / 80	68.3 / 69.2
Analyse indiv.	N = 9/15 (60%)	N = 16/15 (61%)