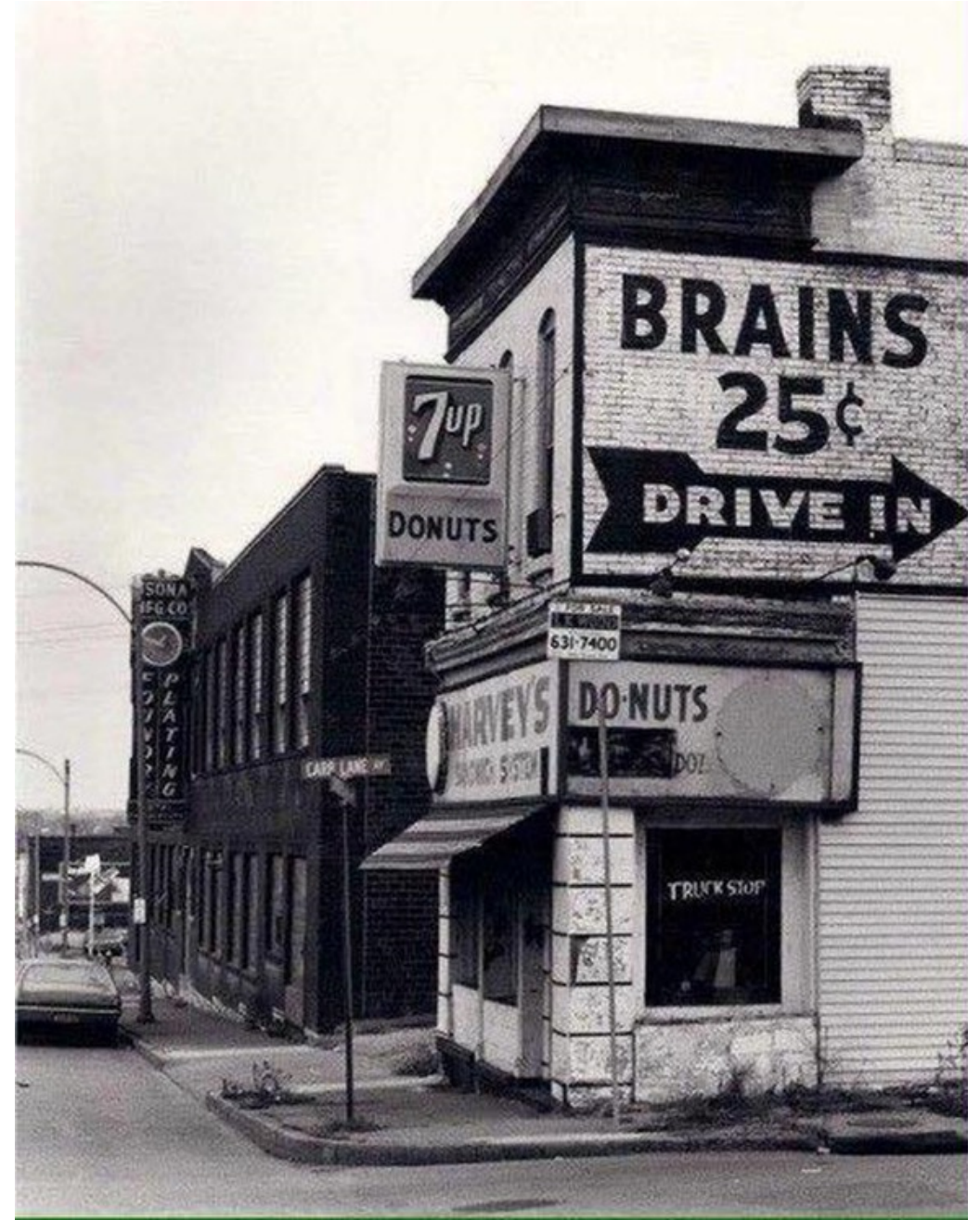


When to refer a patient to a memory clinic? Practical and ethical issues

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Neurology Dept
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Dementia is not a diagnosis

- Acquired
- Progressive
- Cognitive decline (not always memory)
- Loss of autonomy

Never explained by age

early on: difficulties with

administration

drug compliance

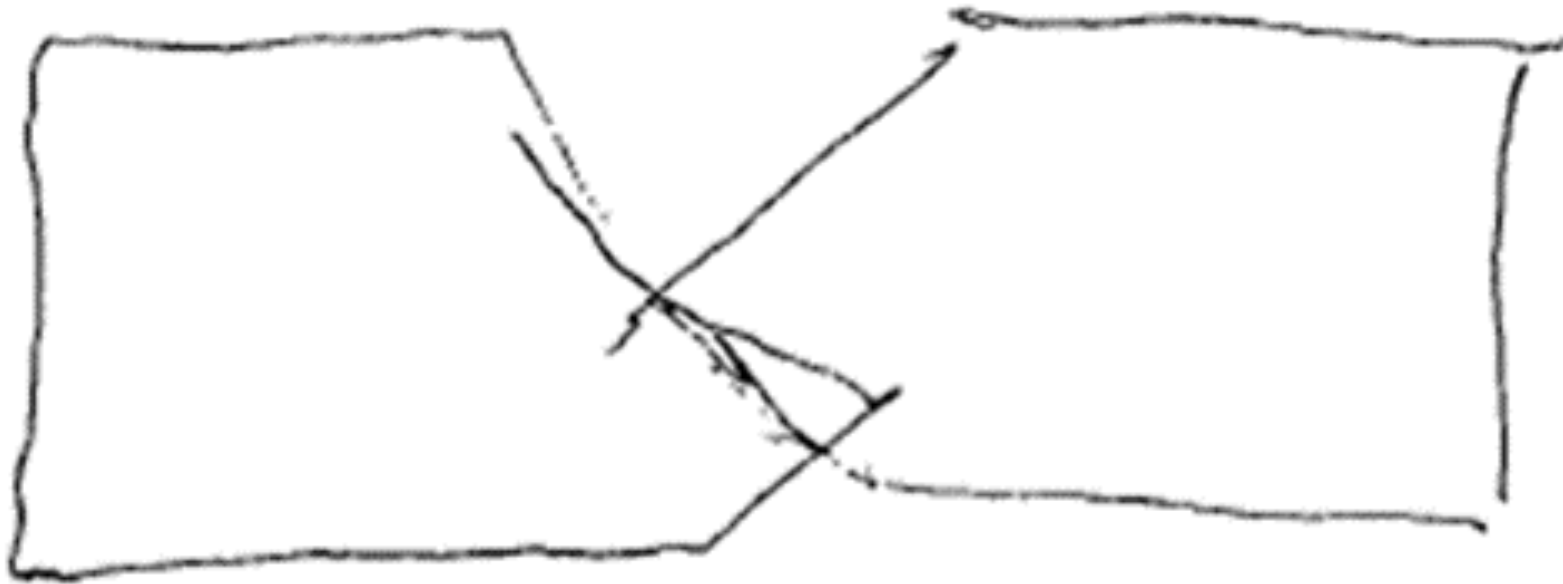
appointments

electronic devices

use of public transport



Loss of autonomy implies knowledge about
past autonomy



Most common causes of dementia

- Alzheimer's disease: accumulation of amyloid β 42 inside and p-tau
- Vascular dementia
- Dementia with Lewy bodies: accumulation of α -synuclein
- Frontotemporal dementias: many different rare diseases, language and behavioral difficulties

Many patients, even the young, have multiple pathologies (+ alcohol, drugs, SAS...)

Alzheimer's disease is not curable, but treatable

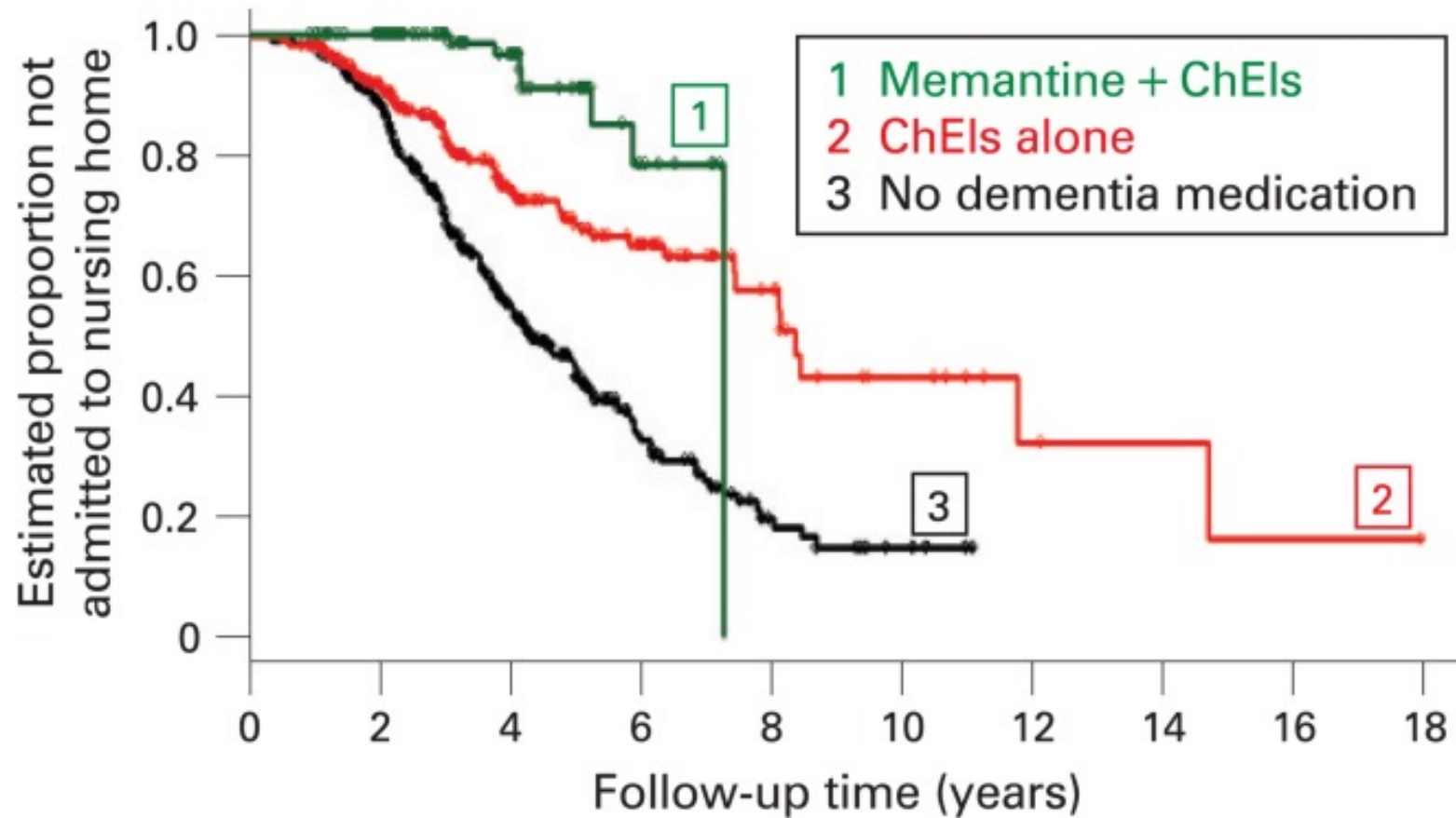


Figure 2.

Alzheimer is not a disease of short time memory but of encoding of new memories in the episodic long term memory

Banana
Taxi
Sheep

Short term memory



Banana
Taxi
...

Long term memory

No help of semantic cueing = hippocampus problem:

- AD
- Anticholinergics: not rare
- Stroke in hippocampus: rare

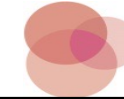
The third word was an animal

Cat?



Médicaments pouvant entraîner une confusion par leurs effets anticholinergiques

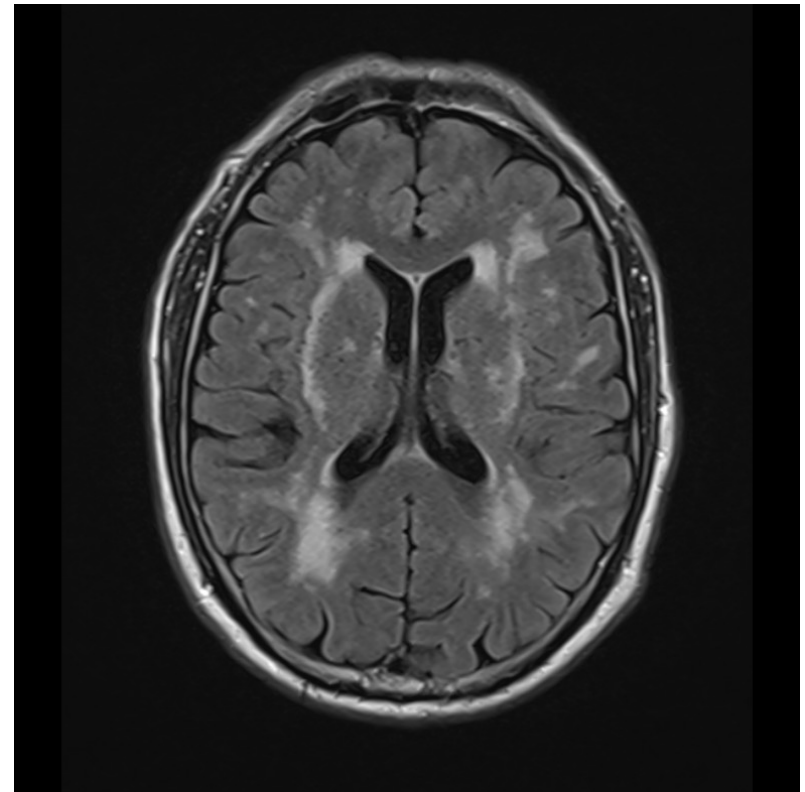
Neurologie	Antiparkinsoniens anticholinergiques	Trihexyphénidyle (Artane) Bipirédène (Akineton) Procyclidine (Kemadrin)
Psychiatrie	Antidépresseur 3C	Clomipramine (Anafranil) Amytryptiline (Redomex)
	Neuroleptique phénothiazinique/thioxanthène	Prothipendil (Dominal) Lévomépromazine (Nozinan) Flupenthixol (Deanxit)
	ISRS	Paroxetine (Seroxat)
	Neuroleptique atypique	Clozapine (Leponex) Olanzapine (Zyprexa)
	Myorelaxant	Tizanidine (Sirdalud)
Gastroentérologie	Antiémétiques (neuroleptiques)	Metoclopramide (Primperan)
Urologie	Antispasmodiques dans l'instabilité vésicale	Oxybutinine (Ditropan) Tolterodine (Detrusitol) Solifenacine (Vesicare) Darifénacine (Emselex) Fesoterodine (Toviaz) Flavoxat (Urispass) Tous : strong anticholinergic properties (BEERS)
Immuno-allergologie	Antihistaminiques phénothiaziniques	Prométhazine (Phenergan) Alimémazine (Theralène)
	Antihistaminiques H1	Cétirizine (Zyrtec) Desloratadine (Aerius) Dimetendène (Fenistil) Hydroxyzine (Atarax)
Pneumologie	Antitussifs antihistaminiques H1	Oxomémazine (Toplexil sirop)
	Bronchodilatateurs anticholinergiques	Ipratropium (Atrovent) Tiotropium (Spiriva)
Cardiologie	Troubles du rythme	Dysopiramide (Rythmodan)
Divers	Antispasmodiques anticholinergiques	Atropine Scopolamine

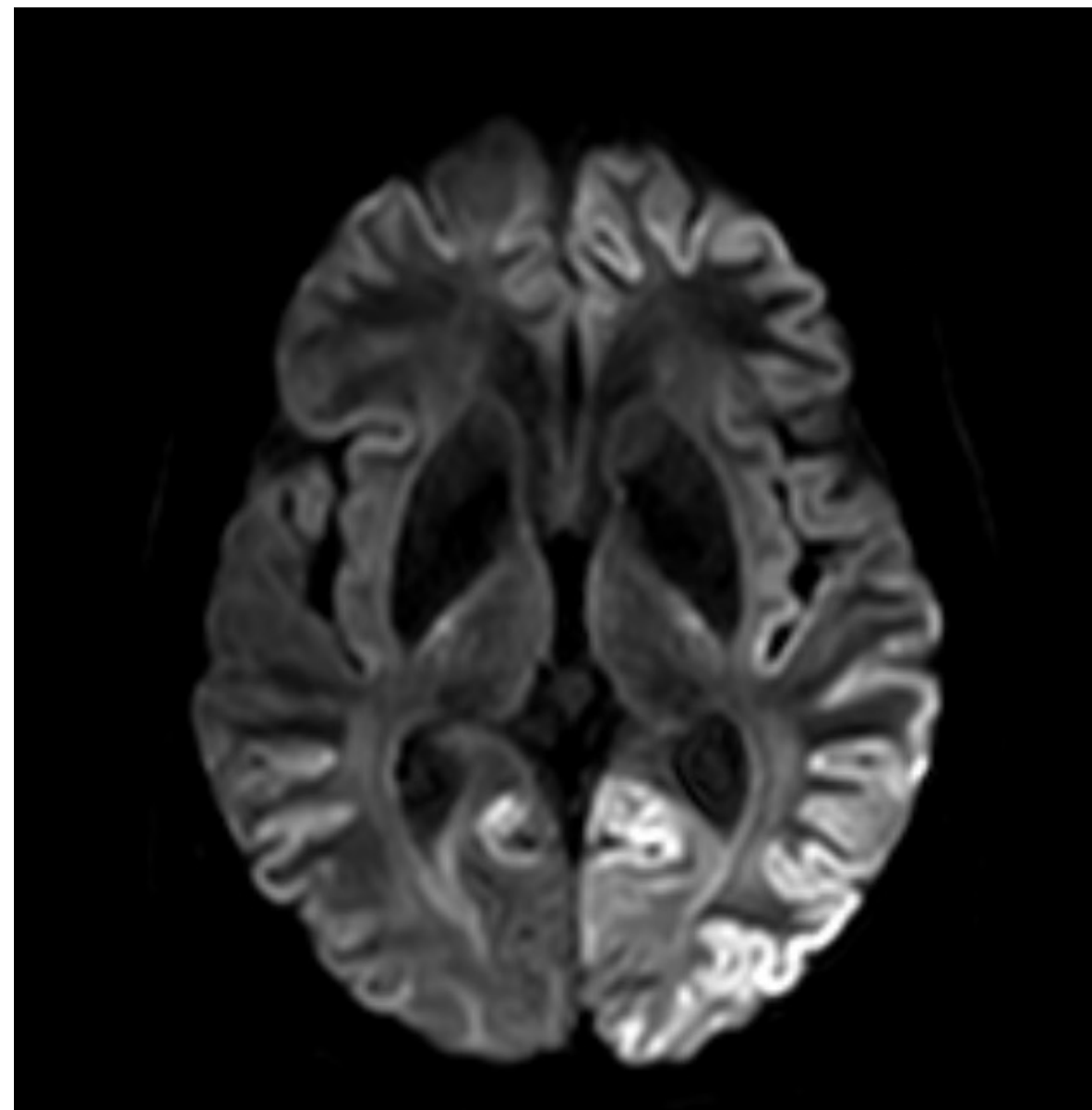


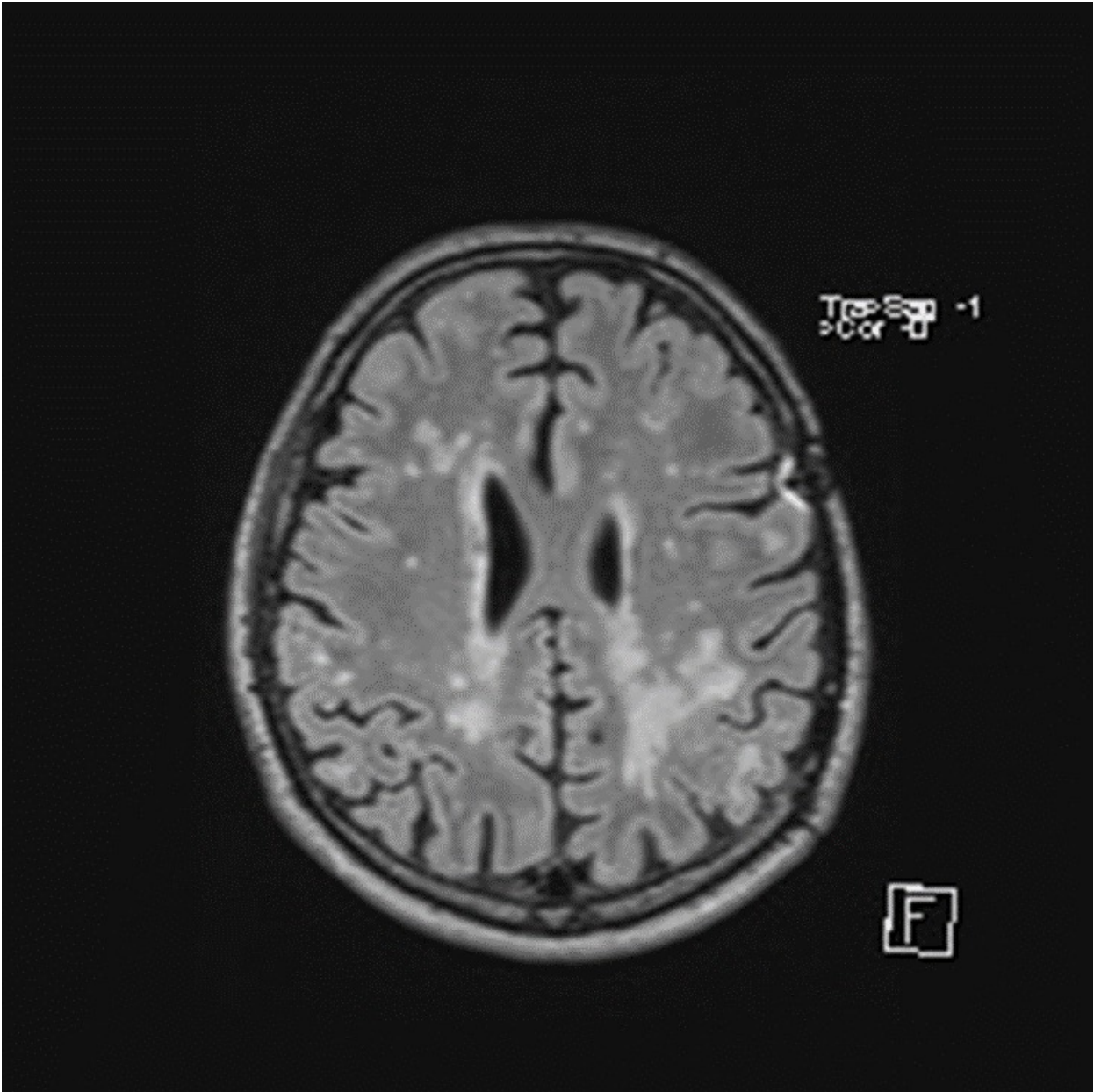
C H U I U V C
B R U G M A N N

Vascular dementia

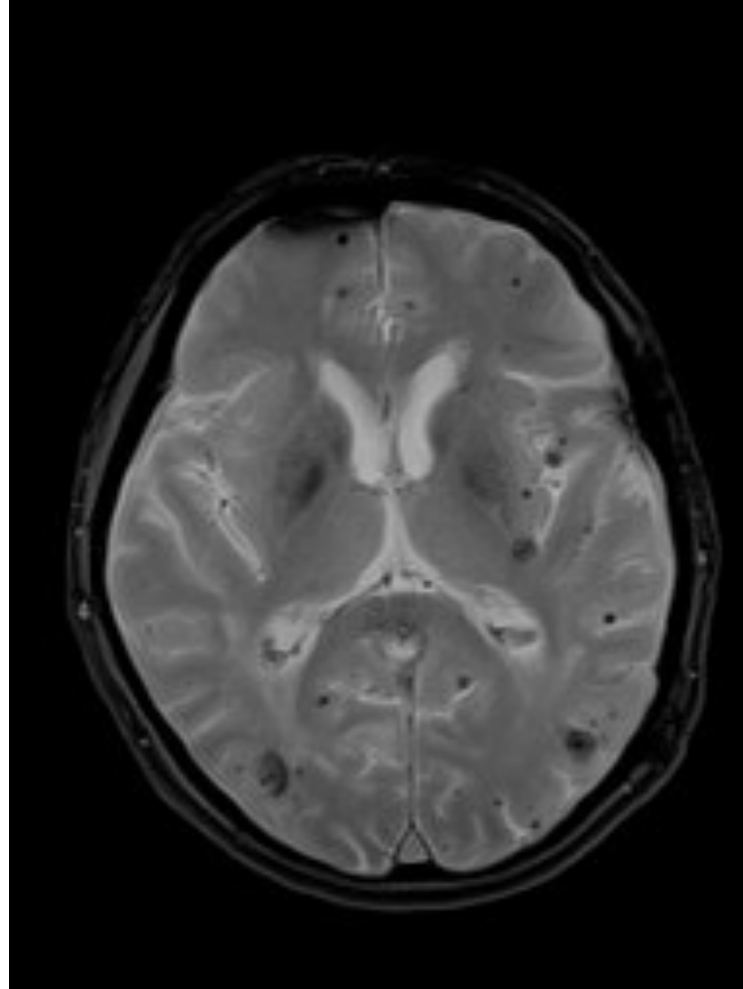
- Small subcortical infarcts
- Dysexecutive functioning, frontal behavior, early urinary incontinence and walking difficulties
- Memory is spared (MMSE often high)
- Choose MRI, not CT: you might miss things







Cerebral amyloid angiopathy: absolute contraindication for anticoagulation and even anti-
aggregation

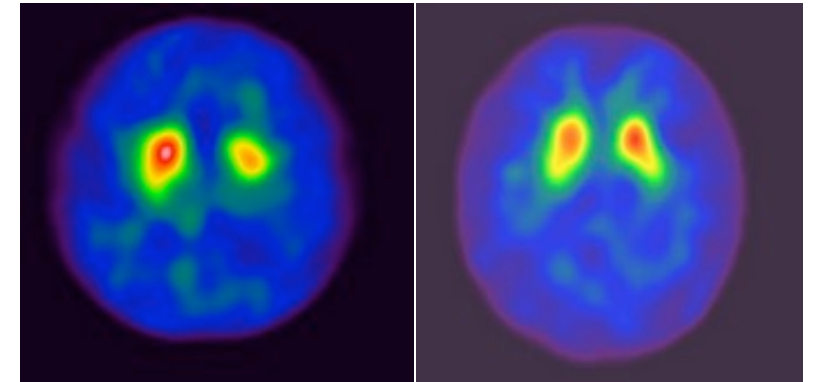


Dementia with Lewy bodies

- Inversed Parkinson disease: cognitive and behavioral changes before extrapyramidal signs
- Younger patients -> often mistaken for depression and other psychiatric disorders
- Think LBD when
 - (Visual) hallucinations
 - Cognitive fluctuation
 - Parkinsonism
 - Parasomnia
 - Hypophonia

Core criteria

 - Anxiety needing medical care
 - Intolerance to neuroleptics (if necessary: clozapine)
 - Orthostatic hypotension
 - Constipation
 - Delusions
 - Cognitive slowing
 - Early spatial disorientation



Problem: lone wolves

- Hallucinations: 20% will never have
- Extrapramidal signs: easy to recognize but late
- Parasomnia: difficult to establish without a bedpartner
 - Falls from bed?
 - Some patients awaken from hearing themselves
- Cognitive fluctuation: rarely noticed by patients themselves

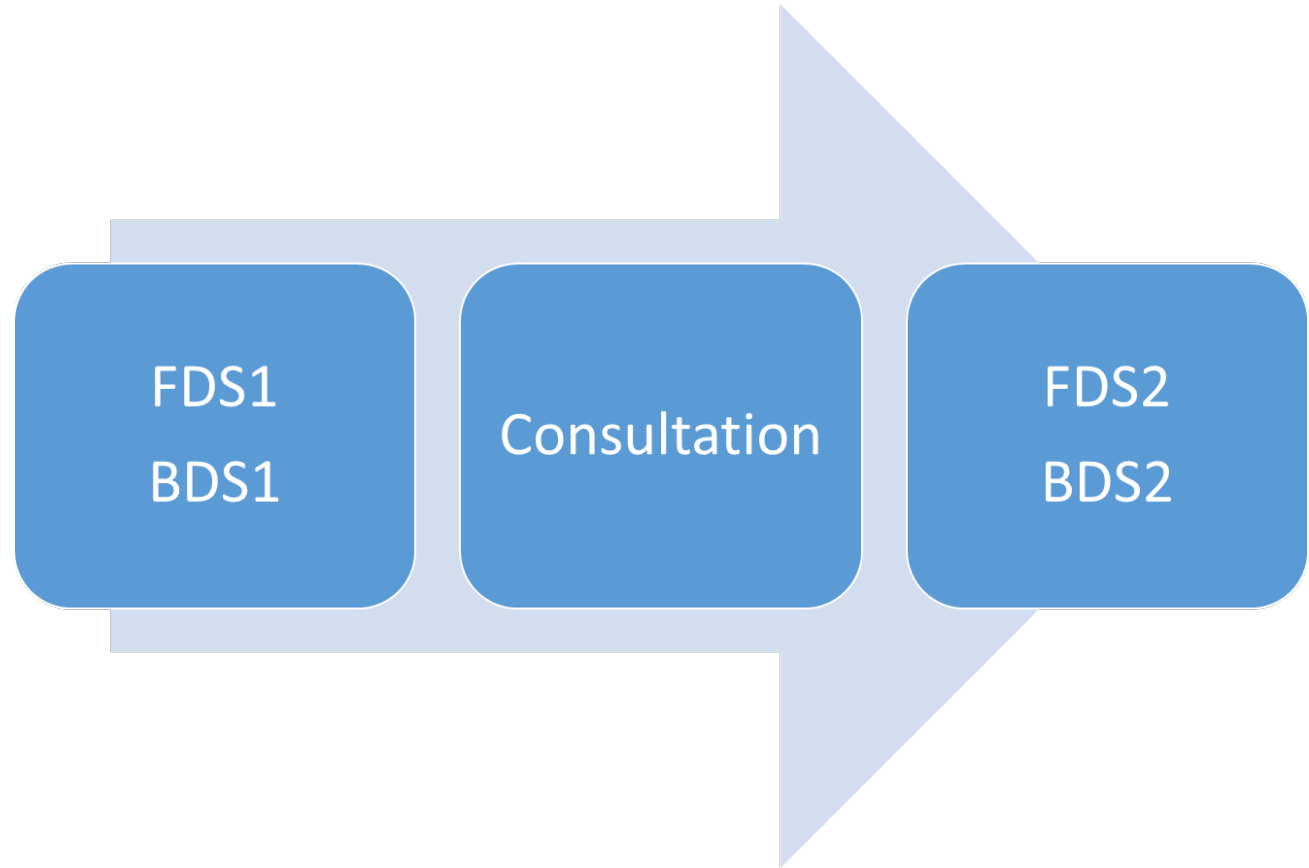


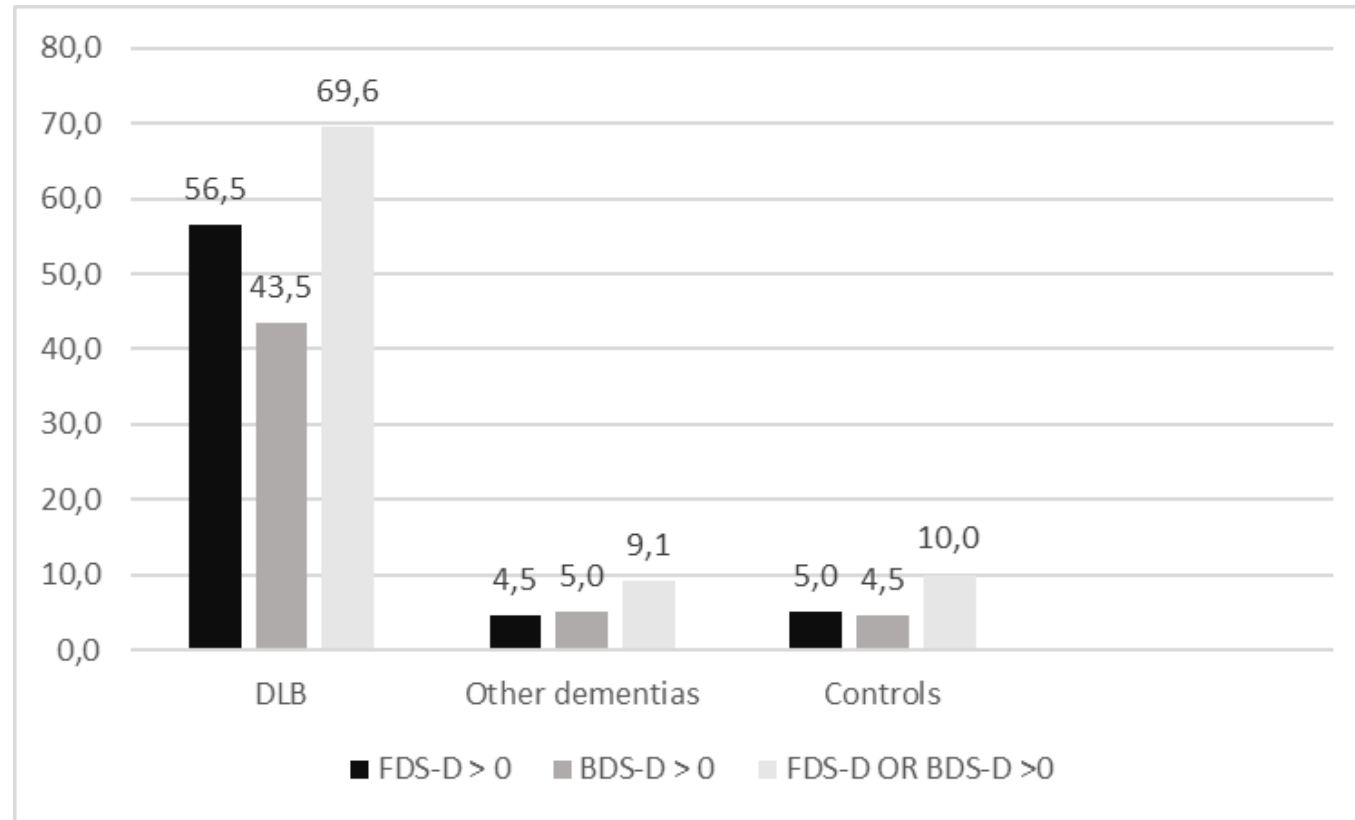
Cognitive fluctuation

- Variations of attention and vigilance:
 - From seconds to weeks
 - Somnolence or lethargy despite good night rest
 - « He slept for 48 hours »
 - Moments of perfect lucidity: « Sometimes she is completely normal again»
 - DD absences: can be interrupted
 - DD sundowning: no specific rhythm
 - DD « cognitive blocking » in Alzheimer: spontaneous

Forward et backward digit span

- 2 5 7
- 3 8 6
- 5 1 9 3
- 4 2 7 8
- 7 9 3 1 6
- 2 8 5 3 4
- 1 7 8 9 2 5



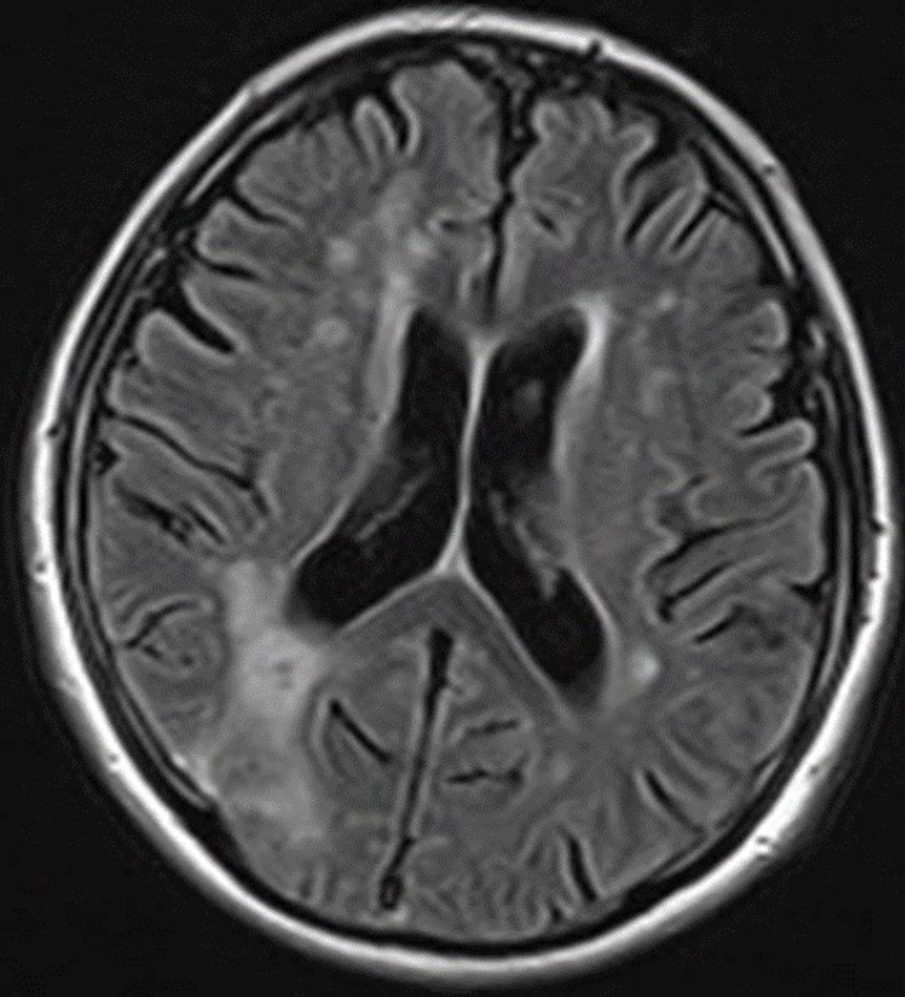


Frontal lobe behavior

- Not specific: AD, vasc, LBD, FTD, alcohol, trauma
- Inappropriate behavior during consultation: intolerance for waiting, misplaced familiarity, jocularity (Witzensucht), hypersexuality, need to touch objects on your desk (utilization behavior)
- Imitation (test visual fields!)
- Head turning sign: AD
- “Emotional incontinence”: responds often well to SSRI

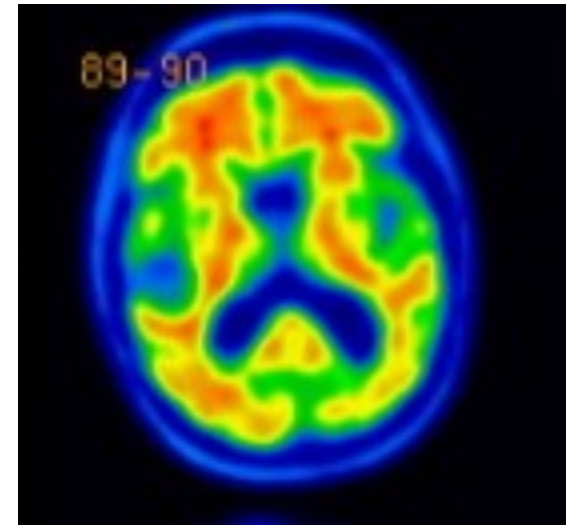
Albanian construction worker, 48 y, cries since recently when he sees a romantic film





Anosognosia

- Inability to perceive one's own cognitive dysfunction
- NOT a psychological defense mechanism
- It will not disappear with reasoning
- Always pathological (frontal lobe dysfunction)
- Even present in prodromal Alzheimer's disease (40%)
- Interferes with treatment compliance +++



Observe the patient in the waiting room

- Extrapiramidal walking difficulties are not exclusively a motor problem
 - Improves with attention
 - Might deteriorate when thinking about other things (risk falls)
 - Might deteriorate when passing a door (freezing)
- Sleep apnea syndrome?

Cognitive function and treatment compliance

- Call the pharmacist, not the GP.
- Temporal disorientation? A pillbox for the week won't help
- Avoid polypharmacy and multiple intakes a day
- Avoid cascades (amlodipine -> furosemide -> anticholinergics->donepezil)

Careful with screening tools (MMSE)

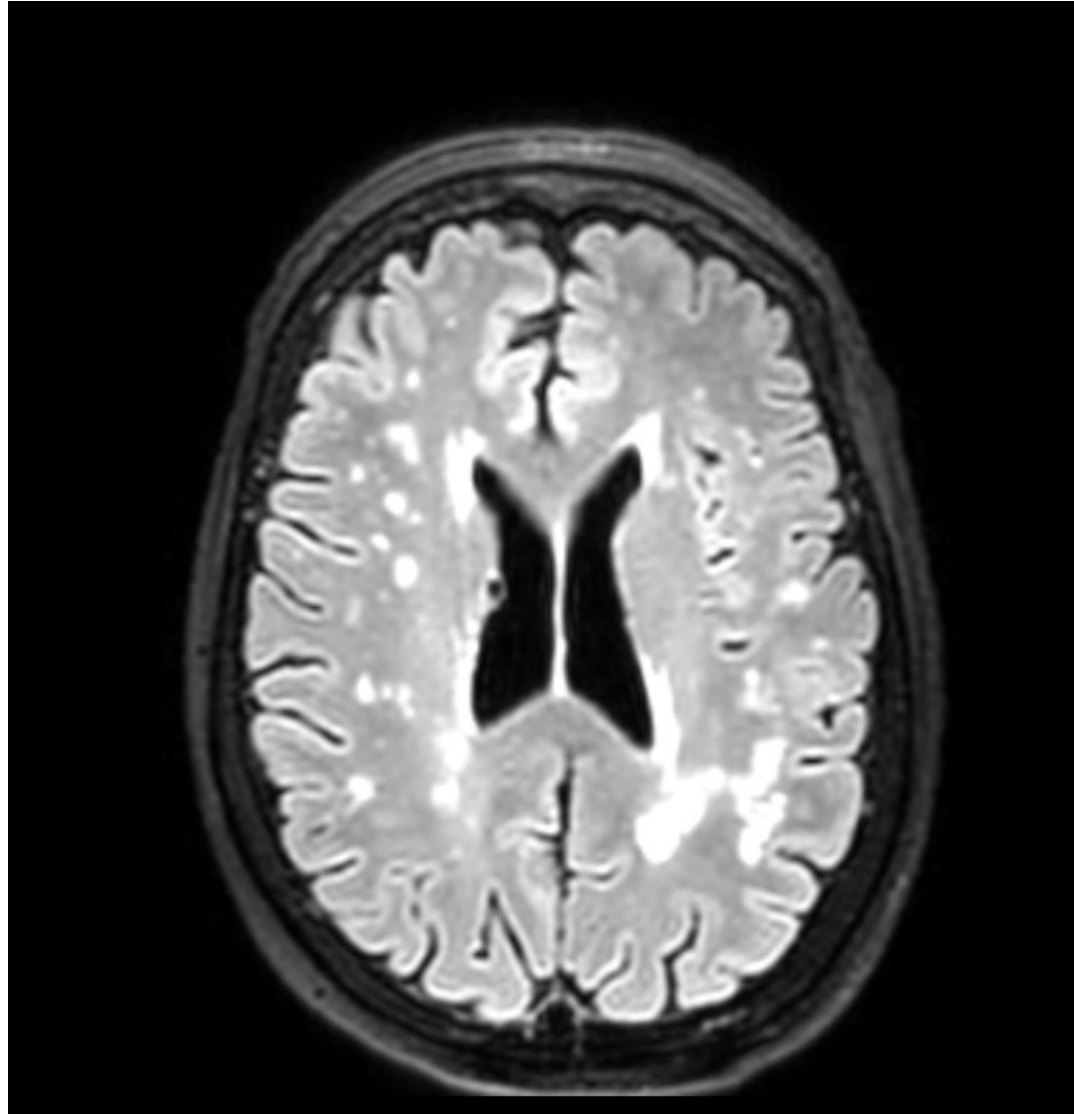
Underdiagnosis (high MMSE)

- highly educated patients
- vascular cognitive disorder: use MoCA

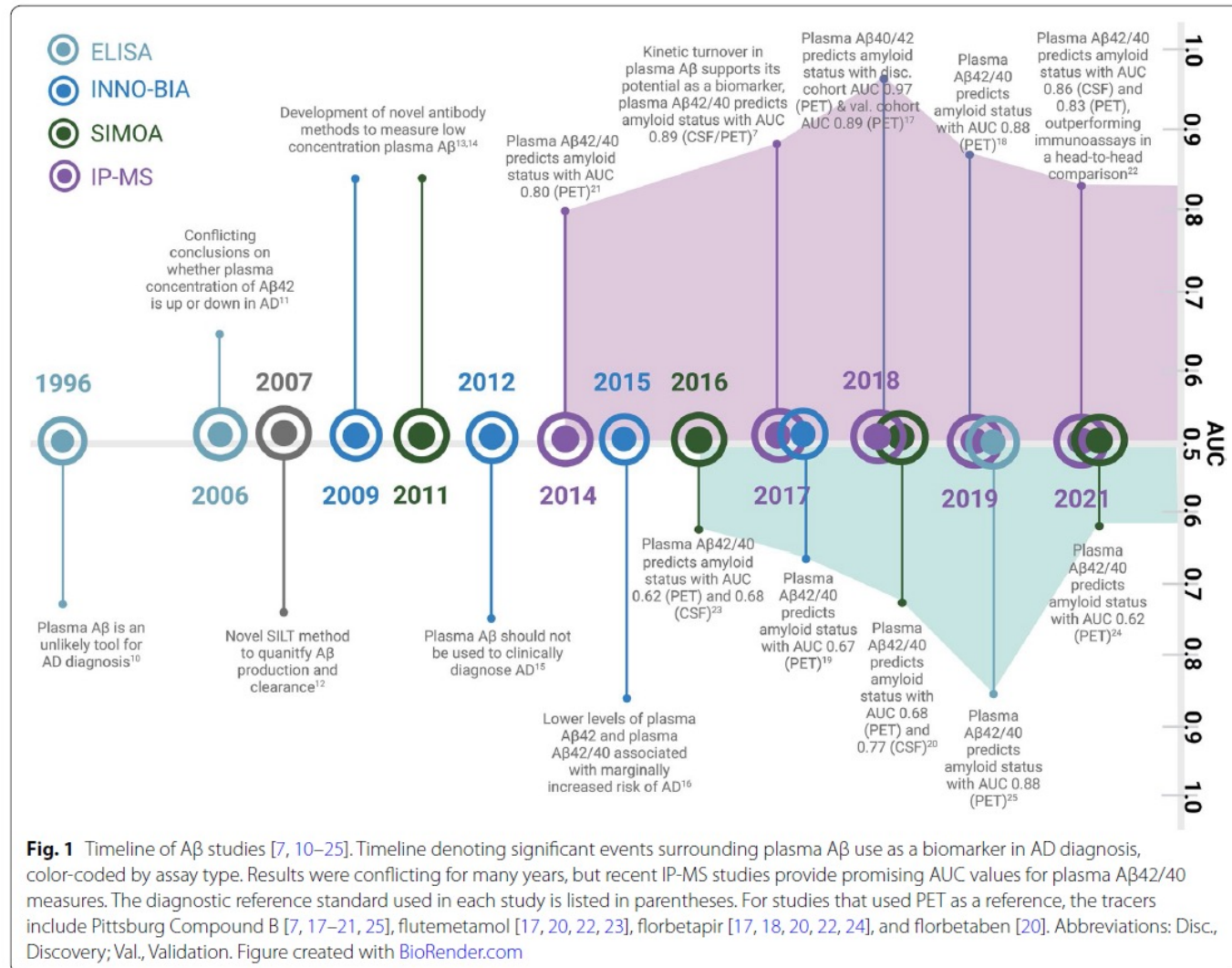
Overdiagnosis (low MMSE)

- unschooled patients (Ardilla effect)

Pharmacist, 75 y, MoCA 30/30



There will be blood



Blood based biomarkers: difficulties

- Quantity of proteins associated with neurodegeneration:
 - CSF: 1 in 1 million proteins
 - Blood: 1 in 10 billion proteins
 - Moreover:
 - amyloid β sticks to hydrophobe molecules
 - difference normal/abnormal values of index A β 42/40 in CSF is 50%, 20% in blood

Plasma amyloid

- Ovod et al, 2017: Lower index amyloid $\beta 42/\beta 40$ in AD patients
- Abnormal index in people with normal amyloid-PET: risk AD x 15
- SIMO index $A\beta 42/A\beta 40$ in controls and patients with subjective memory decline predicts CSF and PET amyloid status
- Sooner abnormal than CSF and PET
- USA: authorisation for clinical use since octobre 2020 for symptomatic patients

Paczynski MM & Day GS, J Primary Care & Comm Health 2022

Giampetri L et al, Diagnostics 2022

Brand AL et al, Alz Research & Ther 2022

Sérum tau

- ECLIA with p-tau-181: good discrimination AD-FTD
- SIMOA with p-tau-181: good discrimination with other dementias
- P-tau-217: better predictor than PET-tau, earlier than p-tau-181 (in genetic forms: 20 vs 16 years before clinical onset)
- Earlier changes than CSF
- Might be useful for AD in Down-syndrome

Giampetri L et al, Diagnostics 2022

Park SA et al, J Clin Neurolo 2022

Padala SP & Newhouse PA, Metabolic Brain Dis 2023

Gonzalez-Ortiz F et al, Mol Neurodeg 2023

When you refer a patient

- Exact treatment?
- Consider asking MRI to speed up workout
- No neuropsychological tests
 - During use of anticholinergics
 - For advanced dementia
 - In the acute phase of a disease
 - Untreated but treatable SAS
- Ask someone to come with them

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Stempel van de voorschrijver	Datum en handtekening van de voorschrijver
	 Uitvoerbaar vanaf voornoemde datum of vanaf: <i>6/10/15</i>

GENEESMIDDELENVOORSCHRIFT

New ethical considerations arise

- Isolated parasomnia: what should we tell?
- Blood based biomarkers:
 - Should not be used for screening asymptomatic people
 - Should be confirmed by LCR in young patients

Suggested reading:

- Johnson JCS, McWhirter L, Hardy CJD, et al. Suspecting dementia: canaries, chameleons and zebras. Practical Neurology 2021;21:300-312.