Recent updates in the field of Alzheimer's disease

LATE-NC and AD co-morbidity

LATE-NC, a comorbidity of AD (>50% of cases),[1] is characterized by the abnormal accumulation of TDP-43 and amnestic dementia syndrome[1,2]

Tomé et al, reported that P-tau seeding severity increased in mice treated with brain homogenates from patients with **AD+LATE-NC**, and that hippocampal tau pathology and neuronal loss were higher in patients with AD+LATE-NC than controls[3]

Retinal biomarkers and microglia

Sustained **microglial activation may exacerbate tau propagation** and promote AD progression[4]

Hart de Ruyter et al, reported **higher levels of P-Tau** in patients with AD and primary tauopathies versus controls **in the retina**, and these correlated with retina microglia counts[5,6]

Sleep disturbances

Disrupted sleep is a common feature of early AD[7]

Son et al, reported that the master regulator of sleep, the **suprachiasmatic nucleus is differentially affected by tau toxicity** in AD vs neighbouring nuclei, contributing to disrupted sleep[8]

Role of GnRH in AD

A mouse model of trisomy 21 has a **loss of GnRH neurons and pulsatile production**[9]

Prevot et al, reported that in mouse models of AD and trisomy 21, restoring normal GnRH levels **improves memory,** and in pilot study of humans with Down's syndrome **improves cognition and brain functional connectivity**[9]

AD, Alzheimer's disease; GnRH, gonadotropin-releasing hormone; LATE-NC, limbic-predominant age-related TDP-43 encephalopathy neuropathological changes; P, phosphorylated.

1. Meneses A, et al. *Molecular Neurodegeneration.* 2021;16(1):84; 2. Nelson PT, et al. *Brain.* 2019;142(6):1503-27; 3. Tome SO, et al. *Alzheimer's Dement.* 2023; 19(Suppl. 12): e073996; 4. Leng F, Edison P. *Nat Rev Neurol.* 2021; 17(3): 157-72; 5. Hart de Ruyter FJ, et al. *Alzheimer's Dement.* 2023; 19(Suppl. 12): e07666; 6. Hart de Ruyter FJ, et al. *Acta Neuropathol* 2023; 145(2):197-218; 7. Lew CH, et al. *Sleep Med Rev.* 2021; 60:101541; 8. Son G, et al. *Alzheimer's Dement.* 2023; 19(Suppl. 12): e074494; 9. Prevot V et al. *Alzheimer's Dement.* 2023; 19(Suppl. 12): e074955.

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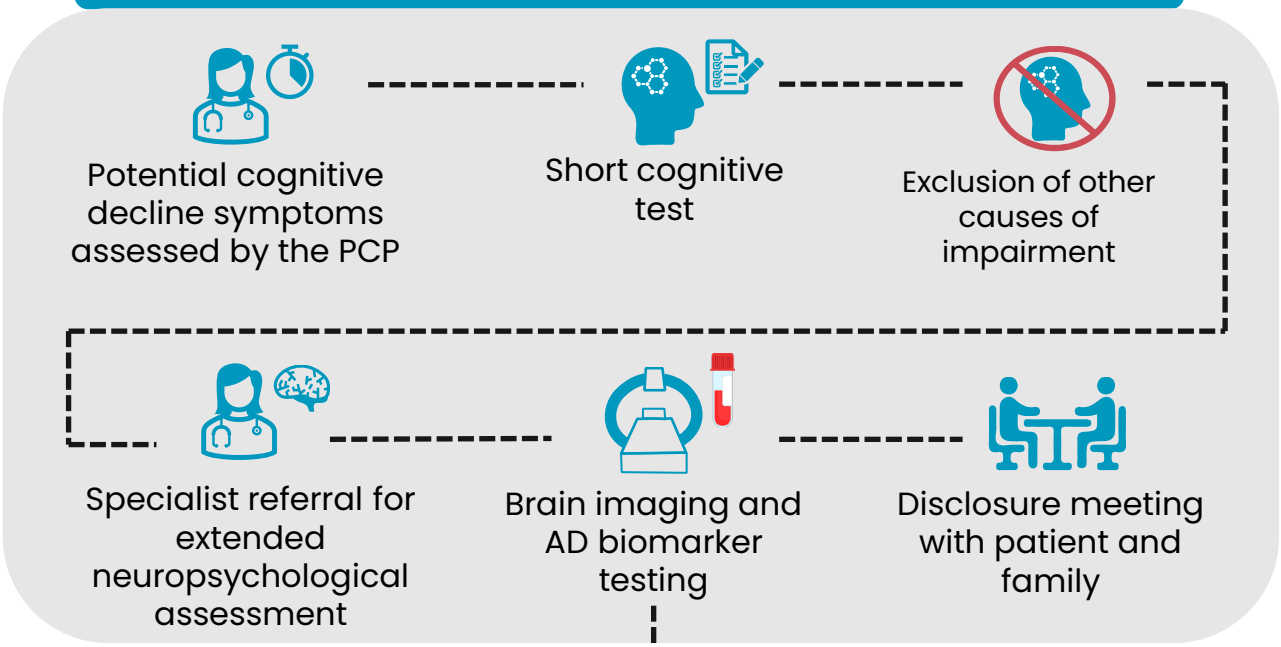
Optimal diagnostic pathway for suspected early AD[1,2]



Utility of biomarkers

- Early differential diagnosis[3]
- Diagnosis of atypical AD presentations[3,4]
- Estimate prognosis and guide treatment decisions[5]
- Patient and family involved in shared decision-making[6,7]

Biomarkers for diagnosis and staging[3,5,8]

- CSF Aβ42 and Aβ42/40 ratio
- Amyloid PET
- CSF P-tau 181 and 217
- Tau PET*

*requires further studies to define the role of tau PET in AD.

AD, Alzheimer's disease; CSF, cerebrospinal fluid; PCP, primary care physician; P, phosphorylated; PET, positron emission tomography
1. Porsteinsson A.P. et al. *J Prev Alz Dis.* 2021;3(8):371-386; 2. Iliffe S. et al. *Int J Geriatr Psychiatry.* 2009;24:895–901; 3. Luebke M. et al. *Biomark Neuropsychiatry.* 2023;8:100062; 4. Graff-Radford J, et al. *Lancet Neurol.* 2021;20(3):222-234; 5. Dubois B, et al. *Alzheimers Res Ther.* 2023;15(1):175; 6. Dubois, B, et al. *J Alzheimers Dis.* 2016;49(3):617-31; 7. Liss JL, et al. *J Intern Med.* 2021;290(2):310-334; 8. Andersen E. et al. *Biomark Neuropsychiatry.* 2021;5:100041.

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