Giornata dello Specializzando 2019

MALATTIA DI ALZHEIMER, **ENTITÀ BIOLOGICA** VS ENTITÀ CLINICA

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NIA-AA Research Framework

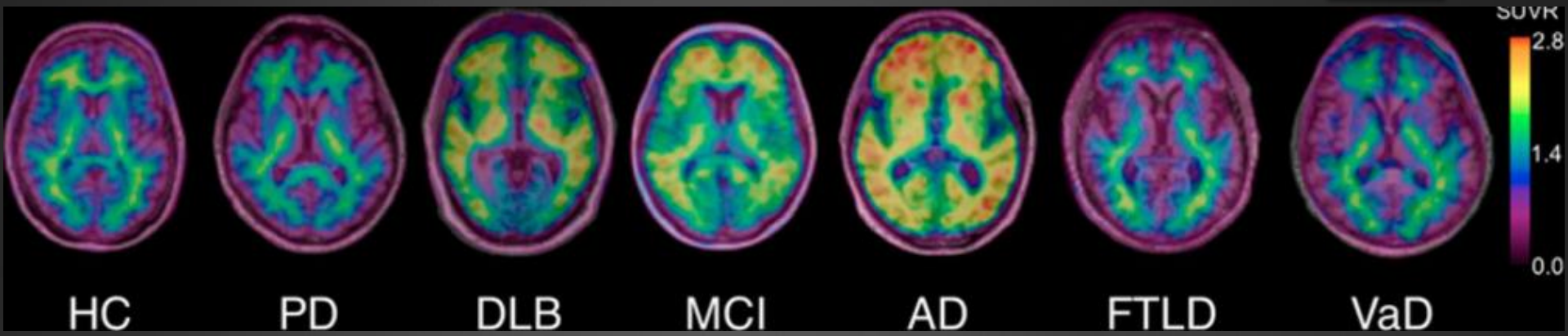
4. The term "Alzheimer's disease" refers to an aggregate of neuropathologic changes and thus is defined *in vivo* by biomarkers and by postmortem examination, not by clinical symptoms

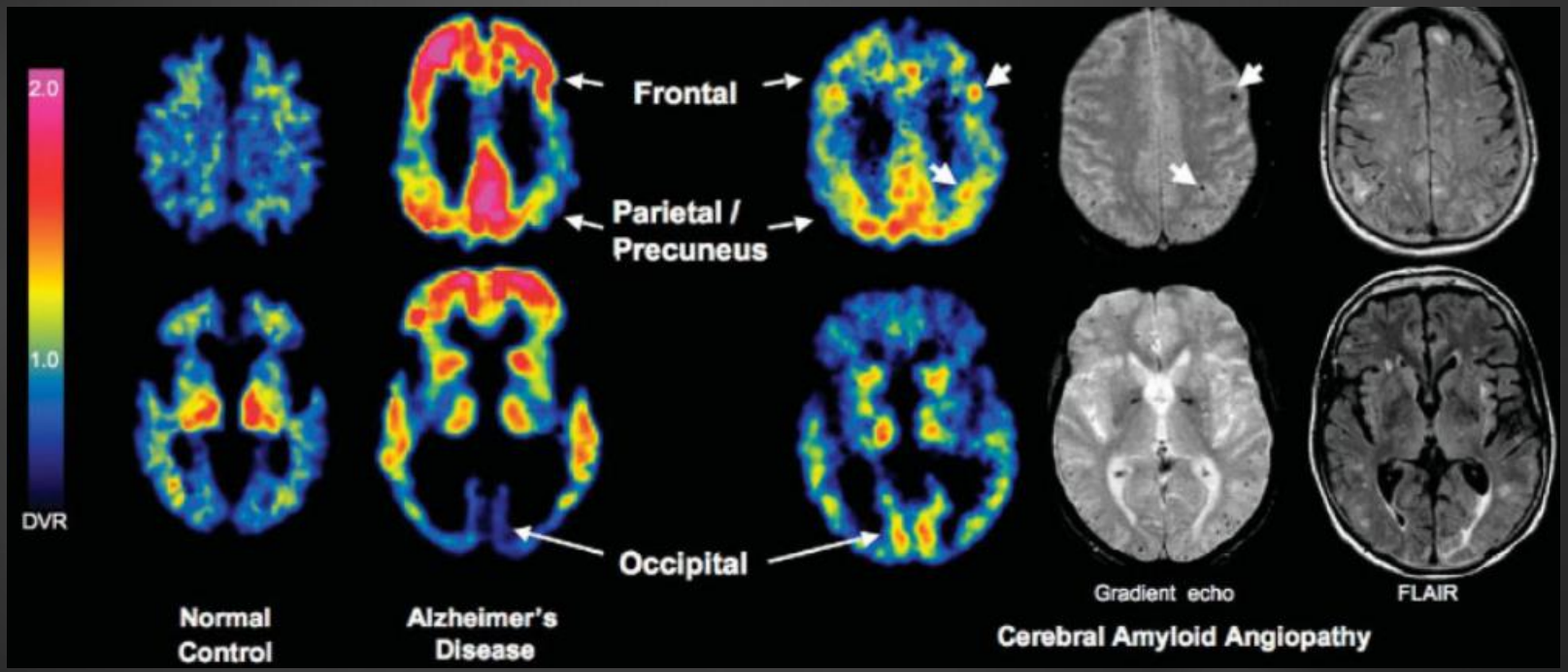
Jack, C. R., Bennett, D. A., Blennow, K., Carrillo, M. C., Dunn, B., Budd, S., … Silverberg, N. (2018). NIA-AA Research Framework : Toward a biological definition of Alzheimer ' s disease. *Alzheimer's & Dementia*, *14*(4), 535–562. https://doi.org/10.1016/j.jalz.2018.02.018

NIA-AA Research Framework

		Cognitive stage		
		Cognitively Unimpaired	**Mild Cognitive Impairment**	**Dementia**
Biomarker Profile	$A^- T^-(N)^-$	normal AD biomarkers, cognitively unimpaired	normal AD biomarkers with MCI	normal AD biomarkers with dementia
	$A^+ T^-(N)^-$	Preclinical Alzheimer's pathologic change	Alzheimer's pathologic change with MCI	Alzheimer's pathologic change with dementia
	$A^+ T^+ (N)^-$	Preclinical Alzheimer's disease	Alzheimer's disease with MCI(Prodromal AD)	Alzheimer's disease with dementia
	$A^+ T^+(N)^+$			
	$A^+ T^- (N)^+$	Alzheimer's and concomitant suspected non Alzheimer's pathologic change, cognitively unimpaired	Alzheimer's and concomitant suspected non Alzheimer's pathologic change with MCI	Alzheimer's and concomitant suspected non Alzheimer's pathologic change with dementia
	$A^- T^+(N)^-$	non-Alzheimer's pathologic change, cognitively unimpaired	non-Alzheimer's pathologic change with MCI	non-Alzheimer's pathologic change with dementia
	$A^- T^-(N)^+$			
	$A^-T^+(N)^+$			

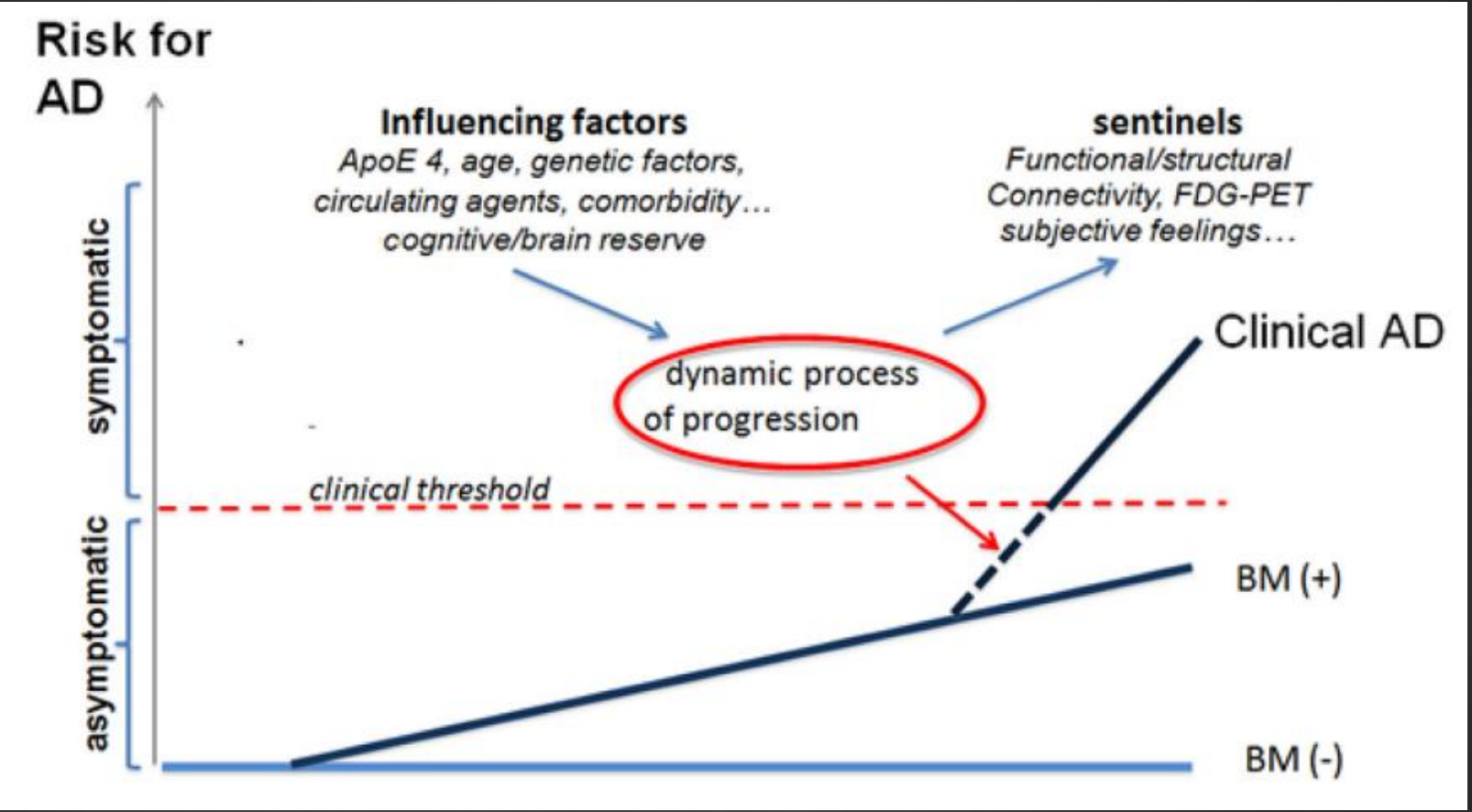
Jack, C. R., Bennett, D. A., Blennow, K., Carrillo, M. C., Dunn, B., Budd, S., … Silverberg, N. (2018). NIA-AA Research Framework : Toward a biological definition of Alzheimer ' s disease. *Alzheimer's & Dementia*, *14*(4), 535–562. https://doi.org/10.1016/j.jalz.2018.02.018





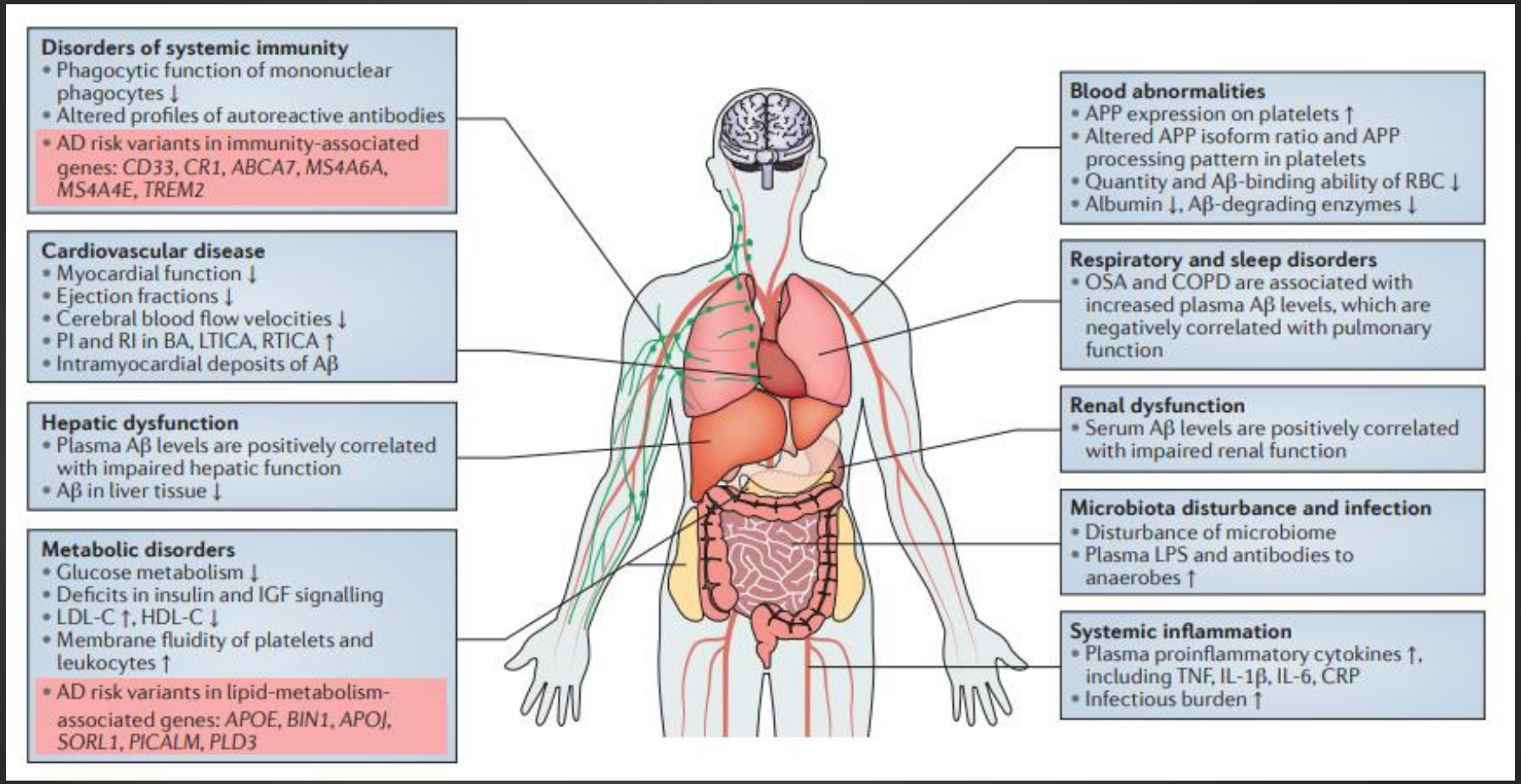
Catafau, A. M., & Bullich, S. (2015). Amyloid PET imaging : applications beyond Alzheimer ' s disease, 39–55. https://doi.org/10.1007/s40336-014-0098-3

La malattia di Alzheimer ha una fase preclinica



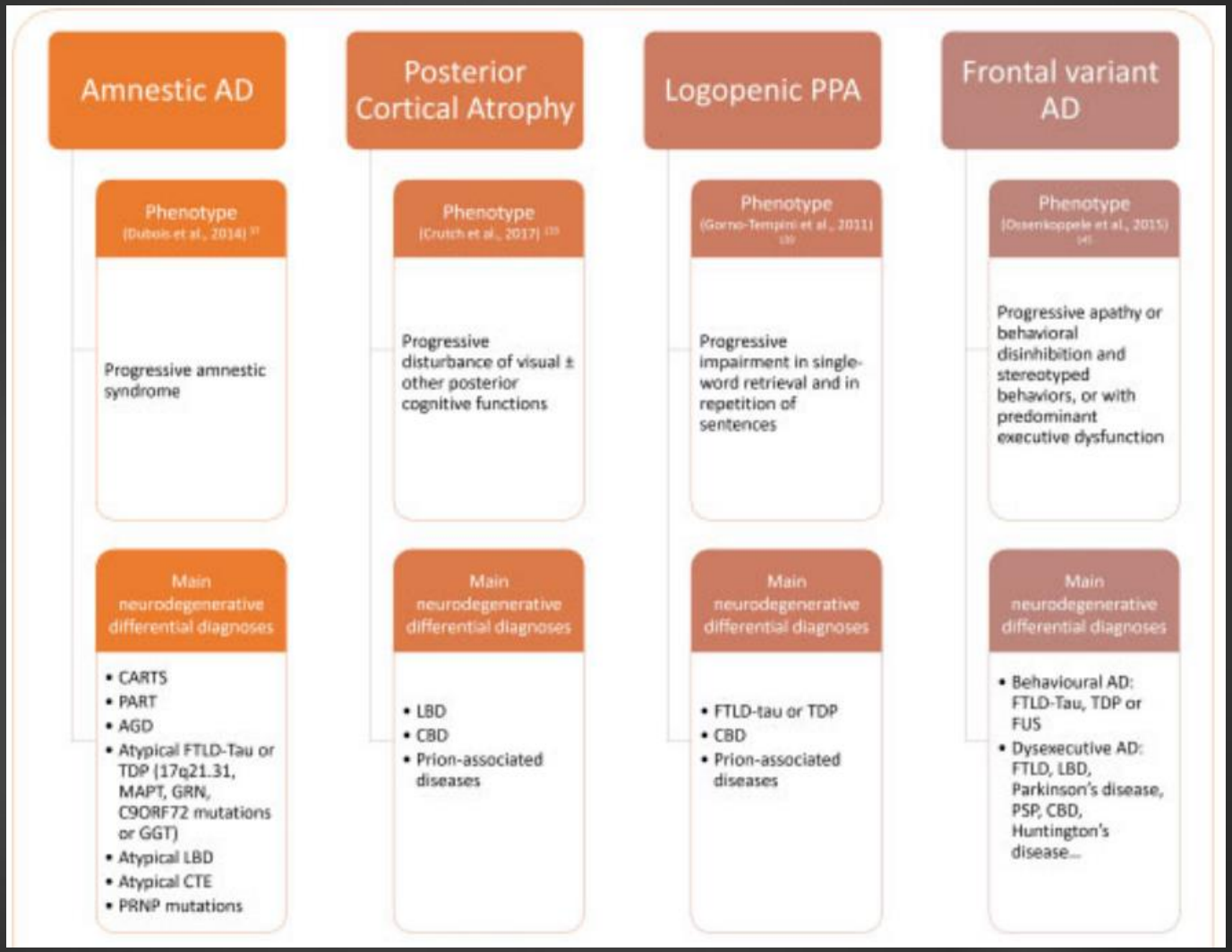
Dubois, B., Hampel, H., Feldman, H. H., Scheltens, P., Aisen, P., Andrieu, S., … Working, I. (2016). *Preclinical Alzheimer ' s disease : Definition , natural history , and diagnostic criteria* (Vol. 12). https://doi.org/10.1016/j.jalz.2016.02.002

La malattia di Alzheimer è un'entità biologica con aspetti sistemci



Wang, J., Gu, B. J., Masters, C. L., & Wang, Y. (2017). *REVIEWS A systemic view of Alzheimer disease — insights from amyloid - β metabolism beyond the brain*

La malattia di Alzheimer è clinicamente eterogenea, altre entità possono avere clinica simile



Villain, N., & Dubois, B. (2019). Alzheimer ' s Disease Including Focal Presentations.

SNAP

- Suspected non-Alzheimer disease pathophysiology (SNAP) is a biomarker-based concept that applies to individuals with normal levels of amyloid-β biomarkers in the brain, but in whom biomarkers of neurodegeneration are abnormal.

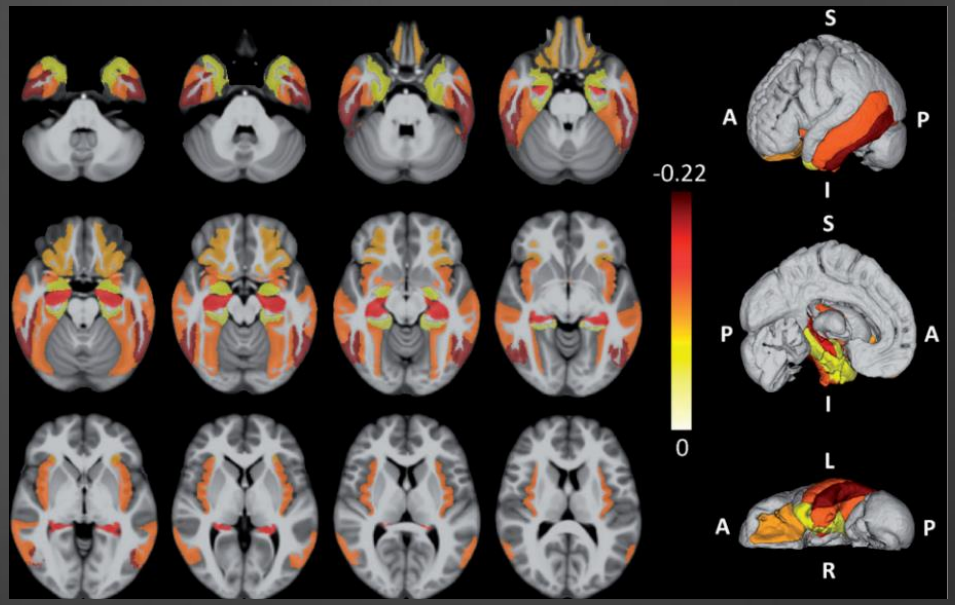
- In the Alzheimer disease Disease Neuroimaging Initiative, 7% of participants who were **clinically diagnosed** as having AD dementia met the criteria of SNAP.

Nat Rev Neurol. 2016 Feb;12(2):117-24. doi: 10.1038/nrneurol.2015.251. Epub 2016 Jan 18.
Suspected non-Alzheimer disease pathophysiology--concept and controversy.
Jack CR Jr[1], Knopman DS[2], Chételat G[3], Dickson D[4], Fagan AM[5], Frisoni GB[6], Jagust W[7], Mormino EC[8], Petersen RC[2], Sperling RA[8], van der Flier WM[9],Villemagne VL[10], Visser PJ[11], Vos SJ[11].

Limbic-predominant age-related TDP-43 encephalopathy (LATE)

- LATE neuropathological change (LATE-NC) is defined by a stereotypical TDP-43 proteinopathy in older adults, with or without coexisting hippocampal sclerosis pathology.

- LATE-NC is a common TDP-43 proteinopathy, **associated with an amnestic dementia syndrome that mimicked Alzheimer's-type dementia in retrospective autopsy studies.**



Nelson, P. T., Dickson, D. W., Trojanowski, J. Q., Jr, C. R. J., Boyle, P. A., Arfanakis, K., … Schneider, J. A. (2019). Limbic-predominant age-related TDP-43 encephalopathy (LATE): consensus working group report.

Conclusioni

- Nonostante il ruolo dell'amiloide nella malattia di Alzheimer non sia chiaro, questa è un elemento costante e (con alcuni caveat) specifico
- La malattia di Alzheimer ha aspetti biologici extranervosi
- La presentazione clinica della malattia di Alzheimer è eterogenea ed aspecifica. La clinica non è sufficiente ad individuarla
- Definire la malattia di Alzheimer come entità clinica porta ad ignorare i pazienti preclinici