A case of suspected non–Alzheimer disease pathology (SNAP) and mild cognitive impairment (MCI): clinical progression and 7 Tesla MRI and FDG PET characterization

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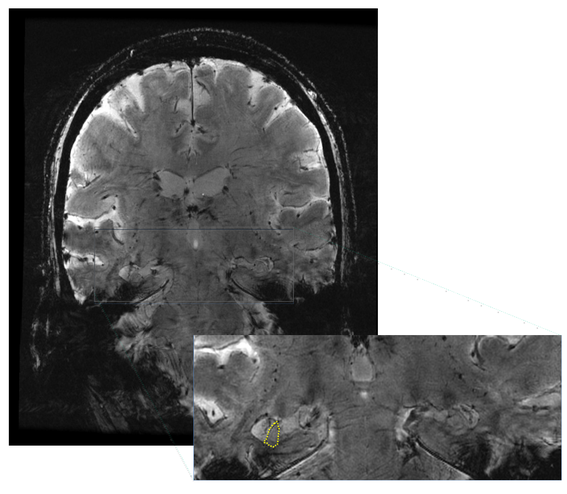
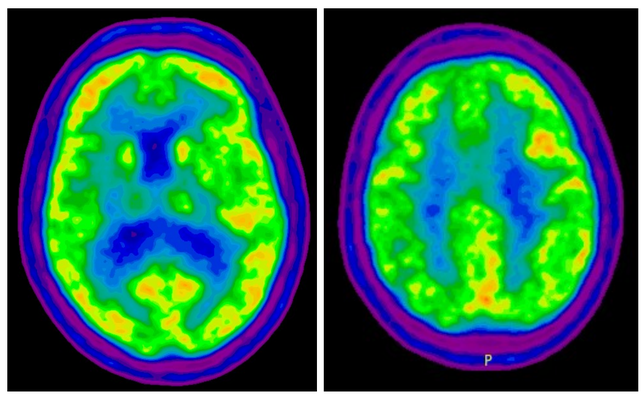
INTRODUCTION

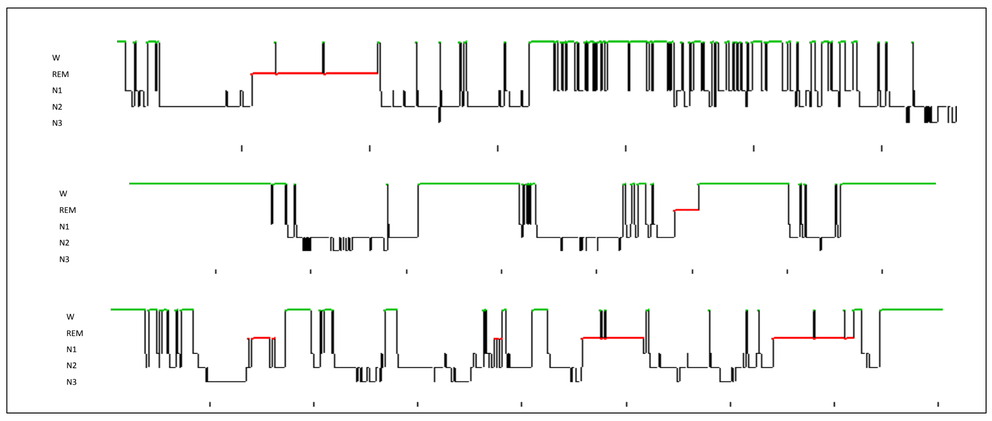
The NIA-AA criteria for preclinical AD propose ordered stages for cognitively normal individuals with abnormal β amyloid markers (stage 1), abnormal amyloid and neuronal injury markers (A+N+) (stage 2), and abnormal amyloid and neuronal injury markers and subtle cognitive changes (stage 3)[1]. Beside these stages, the nosological entity of suspected non-Alzheimer pathophysiology (SNAP) was described, charaterized by abnormal t-tau or p-tau in the presence of normal Aβ1–42 [2]. The clinical and pathological features of patients with SNAP and cognitive impairment have been described only in few reports. We here report the clinical and neuroimaging features of a patient with SNAP and mild cognitive impairment (MCI) with progression to dementia.





CASE REPORT

- A 66 years old female developed initial and progressive isolated memory deficits and mild irritability.
- After 6 months, neurologic examination was normal and in particular did not show extrapyramidal signs. The neuropsychological examination suggested a diagnosis of amnestic MCI (aMCI). Brain MRI showed moderate atrophy of the right head and body hippocampus.
- One year later, her neuropsychological tests confirmed the MCI profile with a worsening of learning, memory and executive functions. The Free and Cued Selective Reminding Test (FCSRT) free and total recall scores were below the normal range[3]. MMSE score was 27/30. The neuropsychiatric inventory (NPI) evidenced moderate irritability and mild disinhibition.
- CFS analysis showed normal values of CSF Aβ42 (1257 pg/ml), with mild higher levels of t-tau (578 pg/ml) and p-tau (91 pg/ml).
- A 7 Tesla MRI evidenced marked atrophy of right hippocampus and milder atrophy of contralateral one. The FDG PET showed a right parieto-temporal hypometabolism.
- After 6 months there was a rapid worsening of cognitive impairment, with difficulties in activities in everyday life (MMSE 19/30; ADL 6/6; IADL 4/6) with increase of irritability, disinhibition and mild insomia, so that she underwent a polysomnograpy. Olanzapine 2,5 mg was introduced to control irritability, with a good response. Treatment with Rivastigmine 9,5 mg was started with initial poor response.



a) Hypnogram of the patient; b) Hypnogram of AD (CDR 1) c) Hypnogram of healthy elderly

CONCLUSIONS

- Our MRI data confirm the severe hippocampal atrophy described in SNAP that is higher than than A+N+ patients [4], with the peculiarity of our patient of a predominantly right atrophy and FDG PET hypometabolism.
- Clinically the patient showed a rapid worsening of memory and executive functions with consequent dementia. During the disease irritability and disinhibition with excessive playfulness occurred, so that a treatment with neuroleptic was necessary to treat them.
- A clear reduction of NREM sleep and of slow activities was observed, more marked than typical MCI or mild AD subjects while REM sleep is preserved. Slow wave NREM sleep and activities have been related to hippocampus-dependent memory and reactivation of hippocampal-neocortex connectivity during sleep [5]. REM preservation suggests that basal forebrain structures (such as nucleus basalis of Meynert), and brainstem areas that are needed for REM generation are functionally intact in NSAID than in typical MCI.
- Further clinical studies are warranted in order to better describe these new clinical entities.

References:

1. Sperling RA, Aisen PS, Beckett LA et al. Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's & Dementia 7 (2011) 280–292.

2. Jack CR, Knopman DS, Weigand SD et al. An Operational Approach to National Institute on Aging–Alzheimer's Association Criteria for Preclinical Alzheimer Disease. Ann Neurol 2012;71:765–775

3. Sarazin M, Berr C, De Rotrou J et al. Amnestic syndrome of the medial temporal type identifies prodromal AD: a longitudinal study. Neurology 2007; 69; 1859-67.

4. Caroli A, Prestia A, Galluzzi S et al. Mild cognitive impairment with suspected nonamyloid pathology (SNAP) Prediction of progression. Neurology 2015; 84; 1-8.

5. Vorster AP, Born J. Sleep and memory in mammals, birds and invertebrates. Neurosci Biobehav Rev. 2015 Mar;50C:103-119.