PROJECT SUMMARY

Dr S. Epelbaum
Dpt. de Neurologie/Institut de la mémoire et de la maladie d'Alzheimer
Hôpital de la Salpêtrière

Scientific background and objectives:

In a recent article (Cacciamani et al., 2017, *JAD*), we derived an index of awareness of cognitive decline in cognitively healthy memory complainers (INSIGHT- PreAD cohort [Dubois et al., 2018, *Lancet Neurol*]), by resorting to the discrepancy between self- and informant-reports of decline. Participants with low versus high awareness were compared. Interestingly, subjects poorly aware showed greater amyloid burden and decreased glucose metabolism. The purpose of the present project is to better understand the potential role of low awareness as an early marker of AD, and to provide further insights into its neural correlates. Our specific aims are:

1. to extend the above-cited work, comparing the two groups on additional measures;
2. to replicate the study design with other large cohorts;
3. to explore awareness trajectories over 36 months;
4. to track how imaging and cognition change in the two groups after 36 months;
5. to develop a new measure of cognitive awareness.

Rationale & methods:

In INSIGHT-PreAD, further analysis will be performed to test differences between the two defined groups. Other large cohorts of elderly memory complainers either with or without cognitive impairment (ADNI [adni.loni.usc.edu], Memento [memento-cohort.org], Constances [constances.fr]) will be analyzed. Low and high awareness groups will be defined in these other cohorts, and compared in baseline genetic, imaging, cognitive and psycho-behavioural measures. In all cohorts, awareness trajectories will be longitudinally explored, and correlations will be performed between awareness level at baseline and neuroimaging/cognitive measures at follow-up. Furthermore, we will develop a new comprehensive test to assess self and informant's perception of decline, which allows deriving an index of cognitive awareness. Psychometric properties will be tested in INSIGHT-PreAD cohort, as well as the association with AD markers. In collaboration with Dr Durrleman at the ARAMIS Lab (Paris), we will include these awareness indices in algorithms aimed at improving preclinical AD diagnosis as already initiated in the ARAMIS lab (Shiratti et al., 2017, *J Mach Learn Res*).

Expected results:

Identifying the earliest symptoms of AD is crucial for preventing subsequent cognitive decline, and selecting appropriate populations for preclinical trials.

Phases of production:

1. Extension of our pilot study (Cacciamani et al., 2017, *JAD*);
2. Generalizability study within other cohorts of interest;
3. Development of a new test to measure awareness of cognitive decline;
4. Integration of the cognitive awareness index into diagnostic/prognostic algorithms.

Three publications on the subject:

Cacciamani F, Tandetnik C, Gagliardi G, Bertin H, Habert MO, Hampel H, Boukadida L, Révillon M, Epelbaum S, Dubois B. (2017) Low Cognitive Awareness, but Not Complaint, is a Good Marker of Preclinical Alzheimer's Disease. *J Alzheimers Dis*

Orfei MD, Varsi AE, Blundo C, Celia E, Casini AR, Caltagirone C, Spalletta G (2010) Anosognosia in mild cognitive impairment and mild Alzheimer's disease: frequency and neuropsychological correlates. *Am J Geriatr Psychiatry*

Michon A, Deweer B, Pillon B, Agid Y, Dubois B (1994) Relation of anosognosia to frontal lobe dysfunction in Alzheimer's disease. *J Neurol Neurosurg Psychiatry*