

PIA Day at AAIC 2016

Subjective Cognitive Decline

Scientific Session

Date: July 23rd, 2016
 Start: 04:45 PM
 End: 06:15 PM
 Location: Conference room Harbour A,
 Westin Harbour Castle Hotel,
 Toronto

Chair/Co-Chair	Site
Frank Jessen (Chair)	Cologne
Wiesje van der Flier (Co-Chair)	Amsterdam
Andrew Saykin (Co-Chair)	Indianapolis

Welcome remarks (Frank Jessen)
SCD-I Item Analysis Project: UPDATE (Laura Rabin, Sietske Sikkes, Rich Jones)
<p>Joint effort among 19 working groups representing 8 countries and 5 languages <u>Goal:</u> Item response theory (IRT) approach to data analysis <u>Projected Project Outcomes:</u> Relationship of SCD to clinical progression and AD biomarkers and identification of subset of items with strongest psychometric properties <u>Empirical harmonization:</u> Pre-statistical harmonization, testing algorithm (via simulation), Choice of reference sample (ADNI e.g.), Weighting reference sample, Running algorithm (while using IRT); Validation strategy</p>
Operationalization of SCD-Consensus Paper (José Luis Molinuevo)
<p>José Luis Molinuevo summarizes the work on a manuscript regarding the implementation of SCD criteria in research studies. <u>Methods:</u> writing group met to identify and agree upon topics relevant to the operationalization of SCD <u>Results:</u> see publication (to come out soon)</p>
SCD Non-Pharmacological Interventions Project: Systematic Review & Meta-Analysis (Colette Smart)
<p>SCD-I Special Interest Group on Non-Pharmacological Interventions (NPI)</p> <ul style="list-style-type: none"> • formed at AAIC SCD PIA in July 2015 (Goals: ascertain current state of science; work towards implementing multi-center trial with SCD-I workgroups) • in fall 2015: completion of an initial systematic review <p><u>Methods</u> (based on PRISMA guidelines):</p> <ul style="list-style-type: none"> • Eligibility: controlled trials of any NPI • Target participants: ages 55+; SCD broadly defined • Several authors devised a list of most important keywords • Rigorous search protocol designed and run by 3 independent raters in common databases • Search results screened for duplication and articles clearly not eligible • Each article adjudicated for appropriateness by 2 separate raters • Data extraction on each eligible article by 2 separate raters

Results:

- Overview of the preliminary and unpublished findings. The meta-analysis and the results will be forthcoming in the publication which is planned for submission in fall 2016.

Conclusions and Recommendations:

- Insufficient evidence to make definitive conclusions
- Large number of studies excluded because of very poor participant characterization and insufficient data reporting (use *Jessen et al. 2014* and *Molinuevo et al 2016* for guidance in future studies)
- Use existing theory to inform development and implementation of interventions, with sufficiently sensitive outcome measures to match

Next steps:

- Submit systematic review/meta-analysis for publication (early fall 2016)
- Potential grant application for multi-center clinical trial of NPI in SCD (Spring 2017) - harmonization of methods and measurements across sites

SCD and Conversion to Non-AD Dementias (Rosalinde Slot)

- Presented were the preliminary results of the collaborative project of SCD conversion to non-AD dementia lead by the Amsterdam group
- Key points: Data of 10 cohorts have been assembled. Differences amongst cohorts in SCD criteria, setting, demographics are large, and determine for a large part the outcomes. This is a methodological challenge, that the group is still addressing (work in progress).
- Interim conclusion: rate of progression to dementia may be somewhat higher than in normal population. Progression to non-AD dementia in about 1 out of 3 cases.

European Initiative on Harmonization of SCD in Preclinical AD and on a Life-style Based Prevention Strategy - Euro-SCD, JPND, Amsterdam, Barcelona, Cologne (Steffen Wolfsgruber)

Background and Aims:

- 1.) Create a transnational, harmonized protocol for case definition and assessment of SCD
- 2.) Develop an internet-based, lifestyle modification strategy for AD prevention in subjects fulfilling the Euro-SCD criteria

Method (Euro-SCD part 1):

- 1.) Collection of data from representative SCD cases from each site with available CSF
- 2.) centralized CSF analysis in VUmc Amsterdam to reduce (method) variability
- 3.) Comparison of each center's initial SCD recruitment criteria and rates of biomarker abnormalities in each sample
- 4.) Investigate predictors of biomarker abnormality across samples

Results (Euro-SCD part 1):

- Difference in SCD definition across sites
- Variation of AD biomarker positivity across sites
- Harmonized protocol will be defined by inclusion and exclusion criteria within ongoing recruitments at all sites
- Comparability of prevalence of AD pathology, if the same incl/excl. criteria across the sites are applied will be assessed - ongoing

Tau-PET in SCD: Findings from HABS and AIBL (Rebecca Amariglio presented Rachel Buckley data)

Aims and hypotheses: HABS

Elucidate the relationship between entorhinal cortical (EC) and inferior temporal (IT) tau, neocortical A β and SCD in clinically-normal (CN) older adults: it is predicted that EC tau and IT tau would exhibit differential patterns of relationships according to their temporal pattern of topographical distribution, particularly when A β burden is considered

- Cross-sectional study; 73 clinically-normal older adults
- SCD strongly associated with EC tau, but disappears when A β *EC tau considered
- SCD less strongly associated with IT tau, and appears with A β *IT tau

Summary:

- First study to demonstrate regionally-specific patterns of association between tau burden and SCD

- EC tau was associated with greater SCD, but the effect was independent of A β burden
- Increasing IT tau, on the other hand, was related to greater SCD only within the context of increasing A β burden
- IT tau-driven SCD reflects individuals likely on the AD trajectory, whereas EC-related SCD captures a range of phenomena including normal aging, in which higher levels of EC tau burden is very common

Aims and Hypotheses: AIBL

Does amount of medial (MTL) temporal tau burden reflect the presence of SMC?

Can SMCs provide additive information about an individual's cognitive performance beyond their biomarker status?

Methods:

106 clinically-normal older adults; dichotomized into high and low SMC: "Do you have difficulties with your memory, yes or no". (Ellis et al., 2009)

Greater SMC across preclinical AD stages: the clinically normal group was divided into their preclinical stages according to their status on amyloid and global tau burden.

Summary

Amplified SCD in high MTL tau mirroring of preclinical AD stages

Take home points:

- a relationship between SCD and tau exists
- Future directions:
 - o Look in other regions (i.e. temporoparietal/neocortical tau, etc.)
 - o Determine whether A β +/tau+/SCD+ will exhibit steepest cognitive decline trajectory
 - o Using more fine-grained measures, is there a pattern of "SCDness" that gives a clearer indication of your likely path on the AD trajectory?

Closing Remarks (Frank Jessen)

- Much new interesting data
- Next projects to be discussed at the business meeting
- Zahinoor Ismail reported on the Mild Behavioral Impairment (MBI) Change Checklist