

**Chairs: Holly Posner, MD (Pfizer\*) & Philip Harvey, PhD (University of Miami School of Medicine)**

***Speakers:***

**Michael Arrighi**, Senior Director, Epidemiology at Janssen Research & Development

A description of the Cognitive Health in Aging Register: Investigational, Observational, and Trial studies in dementia research (CHARIOT): Prospective Readiness cOhort study (PRO), an approach to improve the enrollment of clinical trials in early Alzheimer's disease, which identifies likely participants who will more closely match the trial requirement and to address a few critical questions.

**Jeffrey Kaye**, Layton Professor of Neurology and Biomedical Engineering, Director, NIA - Oregon Center for Aging & Technology & Layton Aging & Alzheimer's Disease Center, University of Oregon

Sensing Life Kinetics: Objective, continuous, unobtrusive and ecologically valid, clinical trial assessments. The presentation briefly reviewed key shortcomings of current dementia-focused clinical trial assessment methods followed by a summary of new methods using embedded sensing and pervasive computing technologies to assess clinical function in everyday life. Examples of the kind of data generated from these approaches was presented.

**Daniel Marson, Prof of Neurology, Director, Division of Neuropsychology, Univ of Alabama at Birmingham**

Detecting Functional Change in Preclinical AD: The Financial Capacity Instrument—Short Form

The presentation addressed the question of functional decline in preclinical AD and how it can be detected and measured using a brief performance measure of financial skills (FCI-SF), which was described. Recent, previously unreported empirical findings from the Mayo Clinic Study of Aging in Olmsted County, Minnesota were presented.

***Providing additional insight and commentary:***

Nick Kozauer, recent former FDA

Karl Broich, bfarm

Nina Silverberg, NIA

Jim Hendrix, Alzheimer's Association

- The Cognitive Health in Aging Register – Prospective Readiness Cohort Study (CHARIOT-PRO)
- Collaboration between Imperial College, London & Janssen – 4 year study
- GP practices in West London identified 6000 individuals for study registry to enter Prospective Readiness Cohort Study
- 4 clinical trial arms – cognition assessments & raters standardised
- RBANS delayed memory score used for enrolment – Low, Medium & High Risk groups
- Which cognitive measures are most sensitive in pre-dementia?
  - Largest comparative study ever run
  - Computerised & non-computerised tests
    - NAB, CDR, MMSE, DKEFS, CogState, CDR System
- Designed as interventional study – low cost high value
- Designed to measure change in cognition
- Other assessments mood, QoL, Sleep, Life Style, Work productivity
- APoE Genotyping & biobank blood, saliva & urine
- So far (5.5 months) 285 screened 242 enrolled
  - Low risk group – 87%
  - Mean age 70, M:F Ratio 40:60, 64% non E4, 34% hetero, 2% homozygotes
- Questions & Comments
  - RBANS – will also use other tests retrospectively to screen
  - Frailty & Apathy measures – will these be used?

## Detecting functional change in preclinical AD: The Financial Capacity Instrument– Short Form (FCI-SF)

- Problem – no functional impairment in preclinical AD
  - But IADL loss in MCI & functional differences in individuals destined to decline
- Possible that *demanding* ADL measures may prove sensitive
- Need to measure accuracy (termed performance) & speed
- Financial Capacity (FC) is cognitively complex
- Original FCI-9 takes 60 minutes, 18 tasks & 9 domains
- Short Form FCI-SF
  - Based on measures which detect declines from MCI to AD
  - 15 minutes, range 0 to 74 units, time range per test 0 to 720 minutes
- Validation Study
  - Done @ Mayo
  - Amyloid detected using PIB – n=186 all cognitively normal
    - A+ n=66 A- n=120 (no cognitive diffs between them)
  - How did FCI-SF predict amyloid classification?
- 3 FCI-SF items showed significant differences on performance (accuracy) (p value range 0.011 – 0.028)
  - Quarters Item, Deposit Slip, Bank Statement Checks Item
- 4 items showed sig diffs on speed
  - Overall Composite Time (p=0.002)
- Logistic Regression showed completion time, quarters item & Checks item all significant predictors
- Conclusion subtle financial skill declines occur in preclinical AD & may outperform the cognitive assessments used
- Next stage longitudinal testing
- Comments
  - **Nick Kozauer (ex FDA) data compelling – this might be a single endpoint in a preclinical AD study**
  - **Karl Broich (EMA) – results look exciting**
  - Gary Kay – can mathematical ability predict these failures?

- Embedded wireless sensors and pervasive computing in the home -
- Big Data
- Outcome measures could be a change in day to day variability
- Have 'mock apartment' @ ORCATECH & Life Lab - community wide
  - Passive infra red activity sensors - activity, mobility & sleep
  - Balance, HR, body comp, temp, CO2
  - Med Tracker
  - Time on telephone
  - Door sensors
  - Monitor PC use
- Home Kiosk – touch screen tests does cognitive assessments using speech recognition etc
- Life Space & Event Analysis – Use Spiral Plots
- Norovirus outbreak– could detect those affected using room enterings
- Assess in home walks from 2 to 7000 per year
- Variance in walking speed & total activity differentiates normal from MCI followed for 315 days
- MCI patients 9x more likely to be in slow walking group
- Medication adherence – ADAS cog hi & low group - latter less adherent to taking vitamins twice per day
- Computer use declines over 28 months in MCI
- Wake after sleep onset shorter in MCI
- Hi frequency measures provide more precise trajectory changes over time
- Such technology requires smaller sample sizes & time taken to detect effect
- Questions
  - Any plans to use AD biomarkers?
  - Future roll out by Apple, Google, Intel etc?
  - Technology advances is standardising required technical skills – making such tests more widely applicable
  - Being set up in Japan and China

## Question to Industry Members on relevance and practicality of techniques

- Financial Capacity will be attractive as well as sample size reduction
- Wearable technology options?
  - Kaye
    - Need to be sure about what trying to measure & battery power problems
    - Wearable with ease of use is attractive option
- Further, smart technology can provide cueing to subjects