The majority of the neuropsychological tests used in ADNI are not suitable instruments for research in Preclinical Alzheimer’s Disease

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BACKGROUND

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Trials in preclinical AD will involve repeated cognitive testing of middle aged and elderly individuals with generally normal cognitive function.2011 Diagnostic guidelines for preclinical Alzheimer’s disease.

Healy et al. (2012) have called for these guidelines to be updated for the preclinical AD cohort.

METHODS

Data from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) Database

- 226 Healthy Controls mean age 76 years (range 60-90), MMSE 24-30
- 234 amnestic MCI patients
- Administered a range of neuropsychological tests repeatedly over 5 years
  - Rey AALT
  - WMS Logical VI
  - Category Fluency
  - DSST
  - Digit Span
  - Boston Naming Test
  - Trail Making Tests
  - Clock Copying Task
  - Clock Drawing Task

Analysis

- Data analysed using mixed-effects model repeated measures approach (MMRM) with SAS PROC MIXED
- Data are plotted as least squares means changes from study entry, with 95% confidence intervals (CI)
- Improvements are plotted to ascend
- Where CIs do not cross zero line, improvement or impairment is significant

RESULTS

Healthy Controls vs. Amnestic MCI Patients

- Can impairment be detected by cognitive tests over 5 years in the healthy but elderly?
- In presentation (P3-247) at the present meeting, consistent declines over a 5 year period were detected in a population of 256 elderly volunteers directly comparable to the ADNI controls - mean age 76, range 70 to 90, MMSE 28.8.
- These deficits were detected using computerised tests of attention, information processing, working and episodic memory.
- Deficits started by year 1 for 2 measures, and for all 4 by 3 years onwards.
- The deficits were of medium effect sizes for 3 measures and a large effect for attention and information processing.

CONCLUSIONS

- Large long-term clinical trials in preclinical AD are underway and many are being planned.
- These will involve populations comparable, or in several cases considerably younger than the ADNI cohort.
- The analyses presented here indicate that traditional neuropsychological tests are unlikely to prove suitable outcome measures in such trials.
- Sperling et al (2011) have called for the development of sensitive tests for such trials, but the possibility exists that such procedures are currently available, and like the CDR System (P3-247) at the present meeting, have been used in clinical trials in normal and pathological ageing since the mid-1980s.