

The Deep and Frequent Phenotyping (DFP) CANTAB cognitive assessment from the feasibility study

Rosemary Abbott¹, Simon Lovestone², Jennifer Lawson², Jenny H. Barnett¹ and Barbara J. Sahakian³ on behalf of the DFP Study Team

¹ Cambridge Cognition, UK; ² University of Oxford, UK; ³ University of Cambridge, UK.

Background

- The Deep and Frequent Phenotyping Study (DFP) is a multi-centre, observational study of prodromal Alzheimer's disease (AD).
- The study includes a wide range of established and novel biomarkers and aims to identify a set of multi-modal markers for phenotyping prodromal AD.
- Prior to study initiation, a pilot study was conducted as a proof of concept to assess task suitability and participant acceptability of extensive and repeated phenotyping.
- Here, we report the results of the CANTAB cognitive testing (Barnett, 2016) completed during the pilot study.

Methods

- Pilot data were collected at six centres (Oxford, Cambridge, Newcastle, University College London, Imperial College, and Kings College London)
- Participants were classified as early AD (NIA-AA) with MMSE >20, with a Rosen Modified Hachinski Ischemic score of <4.
- Following screening and enrolment participants undertook four assessments over six months; Baseline, Day 29, Day 85 and Day 169.
- Measurements included clinical, cognitive, gait and ophthalmological assessment, molecular markers of AD and imaging technologies (e.g. PET, MEG, MRI, EEG). Feedback on the experience of completing the computerised CANTAB tasks was also collected at Day 169.
- Cognition, measured with the CANTAB battery covered the following cognitive domains:
 - Episodic Memory - Paired Associates Learning (PAL)
 - Working Memory - Spatial Working Memory (SWM)
 - Sustained Attention - Rapid Visual Processing (RVP)
 - Processing Speed - Reaction time task (RTI)
- Data were analysed using a repeated measure mixed model. Performance on CANTAB tasks were compared against normative data from a large epidemiological sample (Abbott, 2015).

Results

CANTAB Task Completion and Engagement

- Twenty-two participants (M=10, F=12) completed screening assessments and 19 were followed up to Day 169. Age ranged from 54-84 years (mean=72, SD=8.6).
- 97% of CANTAB tasks were completed, with only 3% aborted or not run.
- Participant feedback showed (Figure 1, A-C) showed the majority found the test instructions to be clear and would be happy to complete the tests again.

- At baseline 75% reached the 6 pattern stage of PAL and 25% progressed to the 8 pattern stage. This supports the suitability of the task in this cohort, with graded assessment and adaptation according to ability. This performance is as expected for early AD. Comparable figures for the general population are 85% and 40% respectively (Figure.2)

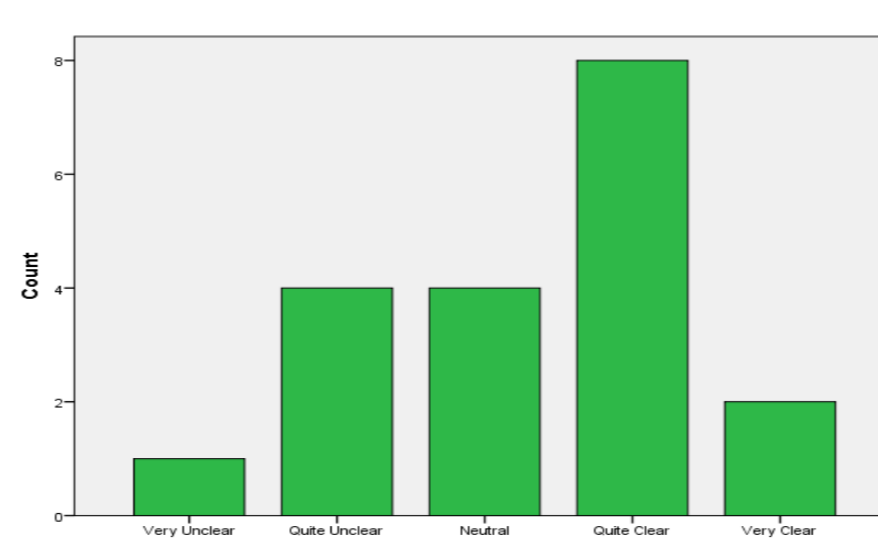
Performance on CANTAB Tasks - Sensitivity to Change

- There was notable decline in performance on PAL, (+ 5.5 errors over 6 months), spatial working memory (+3.1 errors) and processing speed (+12ms) (Figure. 3A-C).
- There was no significant change in attention (RVP A' prime) over 6 months. However, mean scores at baseline (0.83) showed a deficit compared to expected norms (0.87) (ES =0.5).
- Performance on all tasks showed a deficit compared to age adjusted norms. (Figure. 4)
- Deficits reflect those reported for an aMCI sample (Nathan, 2017)

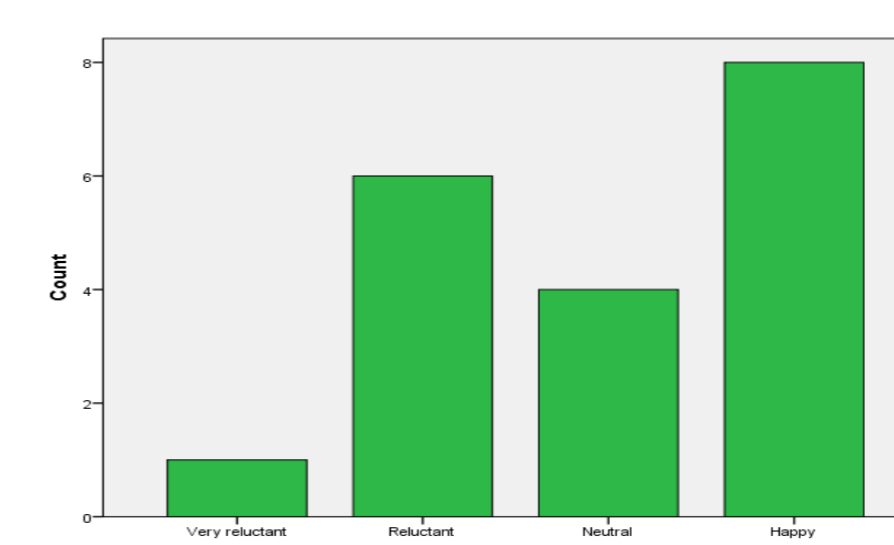
Task Acceptability and Engagement

Figure 1: Participant Feedback

A - How clear did you think the test instructions were?



B - How happy would you be to complete the iPad tests again?



C - How easy was it for you to use the iPad tablet computer?

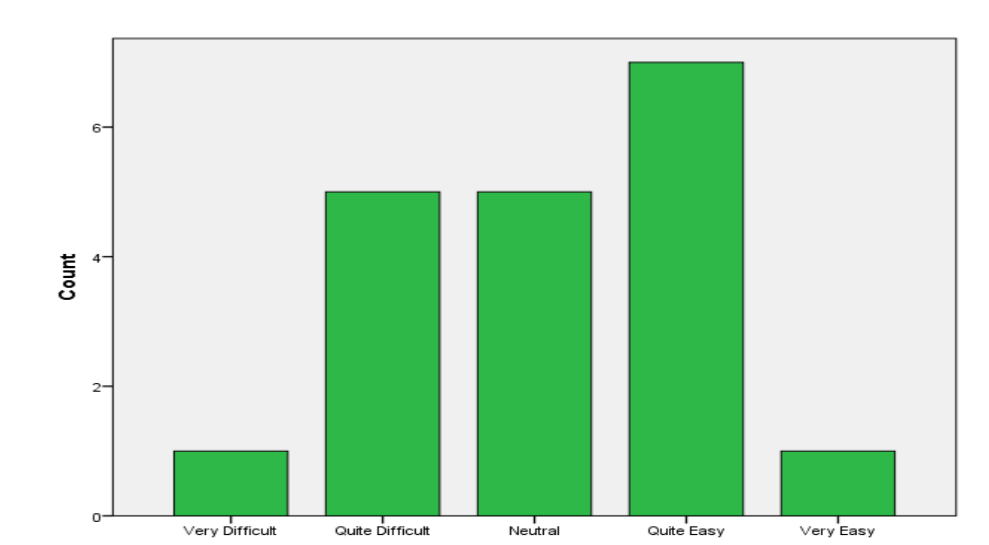
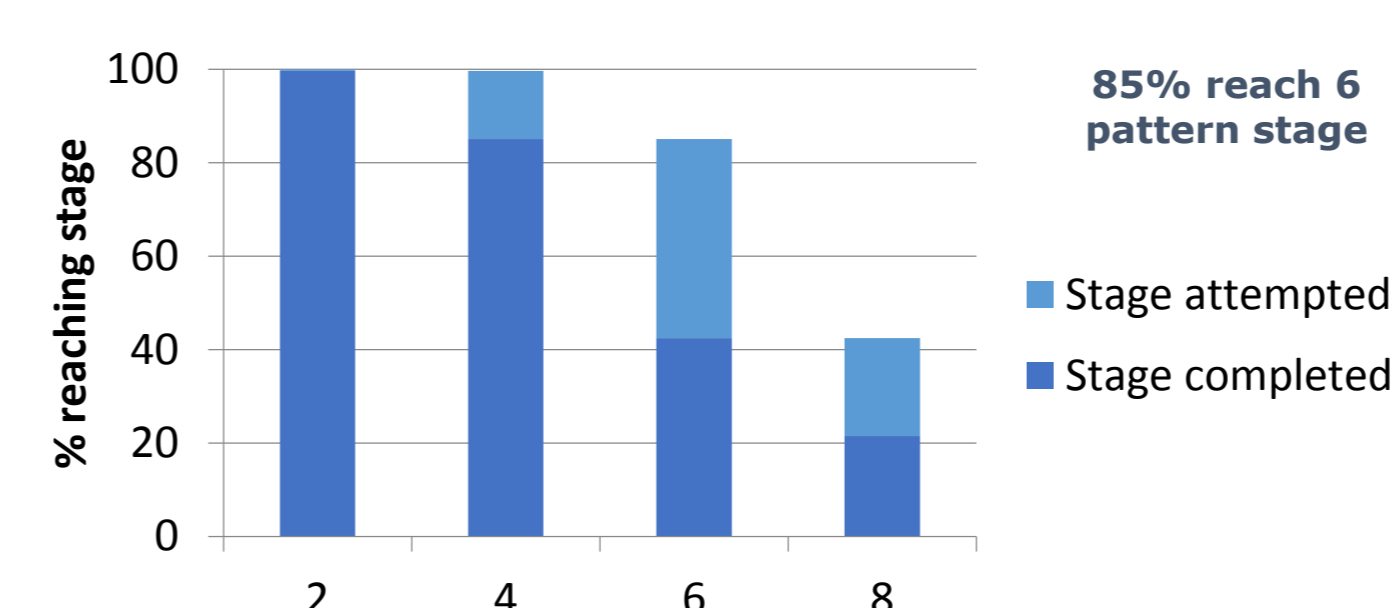


Figure 2: Performance on the PAL task.

General Population (Aged 60-80 years)



Feasibility Study (Baseline) 75% of participants reach the 6 pattern stage, 25% progress to 8 patterns.

Performance on CANTAB Tasks – Sensitivity to Change

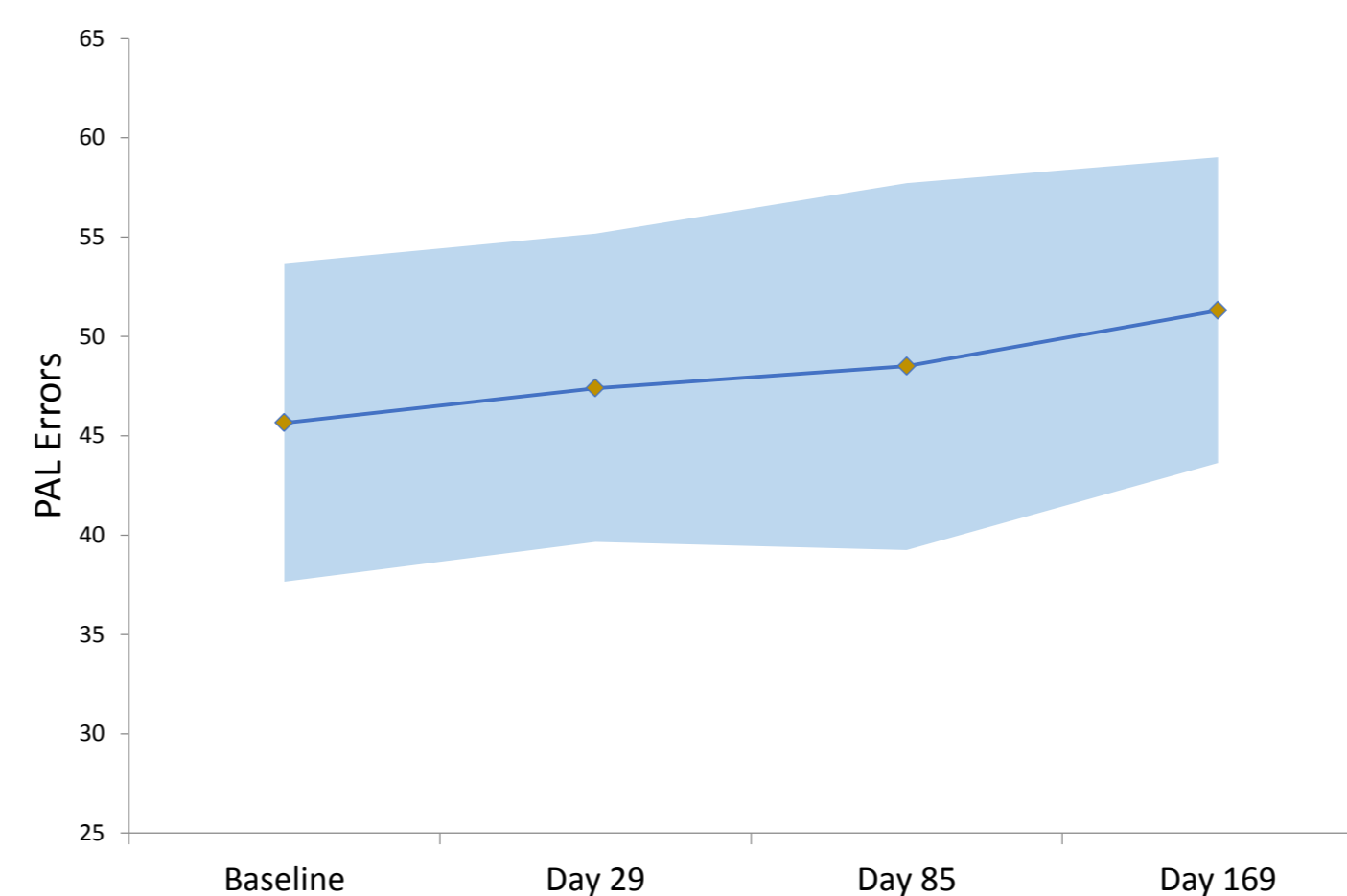


Figure 3A: PAL Errors – Increase 5.5 errors Baseline to Day 169. Expected age related change, 0.6 errors per year of age. LS means adjusted for age and education.

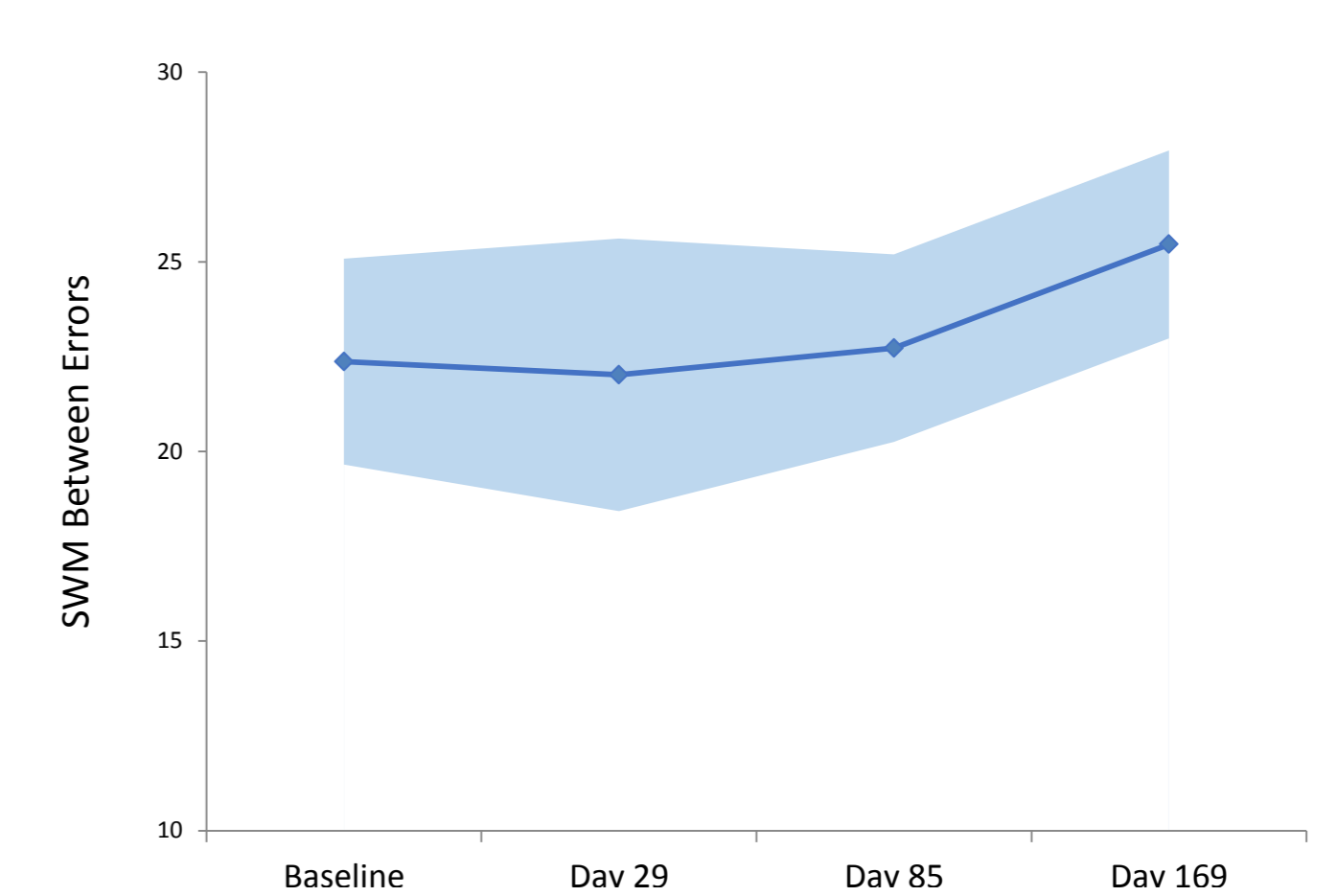


Figure 3B: SWM Errors – Increase 3.5 errors Baseline to Day 169. Expected age related change, 0.4 errors per year of age. LS means adjusted for age and education.

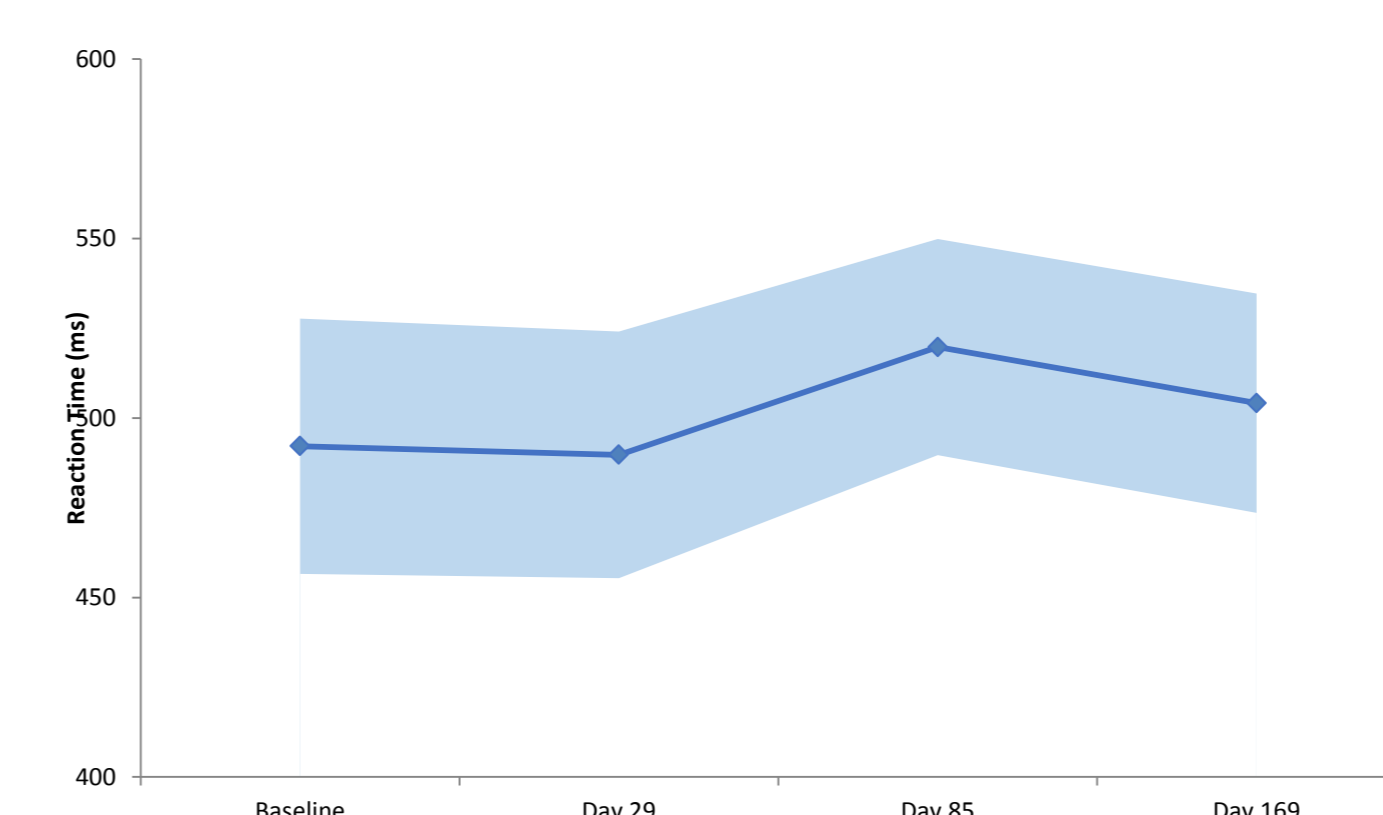


Figure 3C: Reaction Time - +12 ms Baseline to Day 169. Expected age related change, 1.1 ms per year of age. LS means adjusted for age and education.

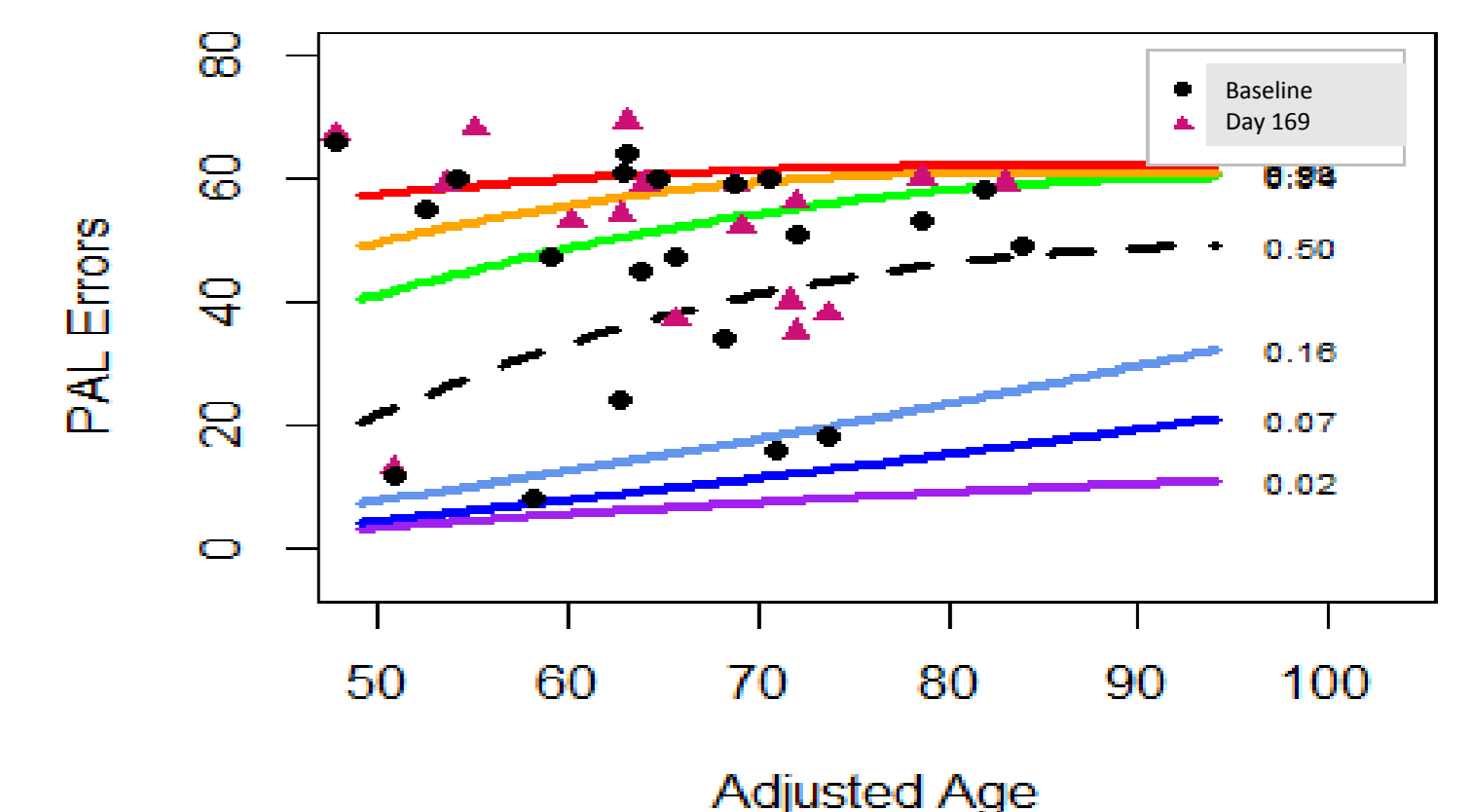


Figure 4. Graph shows performance on PAL from the feasibility study compared to normative data. Coloured lines indicate quantile boundaries. Black dots=baseline, Pink triangles Day 169.

Conclusions

- The CANTAB tasks were well tolerated by participants with a high completion rate
- Cognitive profiles reflected those expected for an early AD sample.
- The pilot results show sensitivity to decline in performance over six months
- The CANTAB results are similar to those reported for aMCI participants in the Pharmacog (EU_ADNI Study)
- The CANTAB computerised platform provides a validated sensitive cognitive assessment for assessment in prodromal AD (Barnett, 2016).

Illustration Right
CANTAB's cloud based software



References

- Abbott RA, Dlugaj M, Streffer J, et al (2015) Cross sectional normative CANTAB data in an epidemiological sample of elderly subjects: data from the Heinz Nixdorf Recall Study. *Alzheimers Dement* (2015);11(7 suppl): P564-P565.
- Barnett JH, Blackwell AD, Sahakian BJ & Robbins TW(2016) The paired associates learning (PAL) test: 30 years of CANTAB translational neuroscience from laboratory to bedside in dementia research. In: *Translational Neuroscience* (TW Robbins & BJ Sahakian eds) Current Topics in Behavioural Neurosciences, Volume 28, Springer.
- Nathan P, Lim YY, Abbott RA et al (2017) Association between CSF biomarkers, hippocampal volume, and cognitive function in patients with amnesic mild cognitive impairment (MCI). *Neurobiology of Aging*, 53