The transition of cognitive decline from normal aging to mild Cognitive Impairment and Alzheimer's disease

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BACKGROUND

- Following the recent development of research criteria for pre-clinical dementia (Sperling et al, 2011), trials are now being planned with compounds designed to prevent or reduce cognitive decline in healthy older individuals identified to be at risk of developing Alzheimer’s disease.

- The ADAS-cog will not be suitable for trials in preclinical AD, and thus cognitive tests need to be identified which can be used in healthy individuals as well as patients with dementia.

- Automated tests can assess aspects of cognitive function, such as the speed of retrieval of information held in memory, which cannot be assessed using traditional non-automated techniques.

- The present study assesses the transitions of cognitive functioning from normal aging to MCI cognitive impairment (MCI) and Alzheimer’s disease (AD) as identified using automated tests of cognitive function.

THE CDR SYSTEM

BACKGROUND TO DATE

- The CDR System is an integrated set of automated cognitive tests which has been widely used in healthy volunteers and all of the major dementias (see references).

- The tests assess core aspects of attention, vigilance, information processing, working and episodic memory.

- The three CDR System tests of attention were used which yield two validated composite scores:
  - Power of Attention – based on the speed scores from the tasks which assesses focused attention and information processing.
  - Continuity of Attention – based on the accuracy scores from the attention tests and reflects the ability to sustain attention.

- CDR System tests of working memory, delayed word recognition and delayed picture recognition were also used.

- Testing is brief, no last testing longer than 5 min, and has been shown to be acceptable to the elderly and patients with dementia (Simpson et al., 1991;Nicholl et al., 1996; Collerton et al., 2007).

POPOPULATIONS

- Amnestic MCI (aMCI) – 74 patients aged 55 to 92 years. Diagnosis utilised the current Petersen criteria for amnestic MCI: age 55 or over; memory complaints and memory difficulties verified by an informant; normal memory function documented by scoring below the education-adjusted cut-off on the Logical Memory II subtests from the Wechsler Memory Scale-Revised; Mini-Mental State Examination score between 24 and 30; Clinical Dementia Rating (CDR) of 0.5 with a memory box score of 0.5 or 1.0.

- Alzheimer’s disease (AD)
  - 715 patients aged 55 to 91 years, with Global Deterioration Score ratings of mild, moderate and mildly-severe AD, MMSE in range 12 to 24, objective evidence of cognitive decline and diagnosis supported by MRI scan.

- Healthy Controls
  - Males and females who had volunteered for Phase I clinical trials, free of cognitive decline from normal aging to Mild Cognitive Impairment and Alzheimer’s disease (AD) becomes more severe in AD. It is further compromised in MCI, but clearly declines in AD.

SPEED OF RETRIEVAL OF INFORMATION HELD IN WORKING AND EPISODIC MEMORY

The time taken to retrieve information held in working & episodic memory declines with normal aging, significant declines occurring between each age group (p<0.0001) with large effect sizes between the youngest and eldest cohorts (working memory > 3, episodic memory > 2). It is further compromised in MCI, to the level of Mild AD for working memory and very close for episodic memory, and in a function of disease severity fashion in modernd and severe AD.

DELADED PICTURE RECOGNITION

The ability to correctly identify previously presented pictures does not decline with normal aging, nor is it influenced by MCI, but it is compromised as disease becomes more severe in AD.

CONCLUSIONS

- Automated tests of cognitive function can provide a fuller evaluation of the deficits in aMCI & AD than traditional tests which do not assess speed, particularly for working and episodic memory.

- Tests which can be used throughout the normal age span as well as in pathological aging will be better suited as outcome measures in trials of Preclinical AD.

- Overall the accumulating evidence is that automated cognitive tests are appropriate for use in all areas of dementia research.