The Measurement of Normal and Abnormal Age-Related Declines in Human Cognitive Function

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INTRODUCTION

Interest is growing in identifying the onset and progression of abnormal age-related cognitive declines which reflect presymptomatic Alzheimer's disease (AD). At ICAD 2010, NIA-Alzheimer’s Association workgroup developed criteria both for preclinical AD and MCI due to AD (Sperling et al, 2011; Albert et al, 2011). The figure above from Sperling et al illustrates the concept that cognitive decline will begin many years before the onset of MCI, and that measured change over time will be more sensitive to identify such declines than one-time measures. Albert et al (2011) recognised that the declines would occur in other domains besides memory, including attention, executive function and visuospatial skills.

NORMAL AGE-RELATED COGNITIVE DECLINE

TIMOTHY SALTHOUSE, UNIVERSITY OF VIRGINIA

A research group led by Salthouse has conducted an extensive series of studies into the declines seen in cognitive function in normal aging (see example to the right from Salthouse & Ferrer-Caja, 2003). The major conclusions from this extensive programme are that a wide range of aspects of cognitive function declines in normal ageing, that these declines start in the 20s, that these declines are large in magnitude and the declines occur for the majority of individuals (Salthouse, 2010).

THE CDR SYSTEM DATABASE

The CDR System is an automated set of computerised tests of major aspects of cognitive function which has been used in more than 1100 clinical trials worldwide over the last 25 years. A database has been established of 5324 healthy volunteers:

- Age 18 to 87 (3800 males & 1424 females)
- Years of education mean 13.4 years, sd 5.7
- Nationalities: American, Belgian, Danish, Dutch, English, French, German, Swedish & Swiss
- All participated in Phase I trials and were free from major medical, neurological or psychiatric disease

The figures below illustrate the declines in performance from the early twenties onwards on a range of tests of attention (simple and choice reaction time, digit vigilance), working memory (numeric and spatial) and episodic memory for words and pictures. The data show a continuum of decline from MCI through the stages severity of AD. This posterior is financially supported by Bracket (formerly United BioSource Corporation). All authors are currently employed by Bracket.

DISCUSSION

Longitudinal studies have shown cognitive impairment to precede the onset of MCI by several years (eg Howesoon et al, 2008), and therefore to identify precocious dementia, repeated cognitive assessments over many years will be necessary. Knowing that function is declining in normal aging, an important approach to the treatment of the trajectories of decline which signal pathological ageing. For preclinical dementia, Sperling et al (2011) recommend studies to determine whether the presence of biomarkers such as Aβ is predictive of increased decline, and also trials of disease modifying agents. The ideal cognitive tools for such programmes will be those which capture a full range of relevant aspects of cognitive function, and which can be administered repeatedly without showing confounding training effects. Computerised test systems are available which fulfil these requirements (eg Wesnes and Pincock, 2002), and some can be administered via the internet which may be important in large scale studies. Similarly, in MCI programmes, an important outcome measure besides delaying conversion to AD would be to reduce the rate of cognitive decline during the treatment period.

REFERENCES