As human longevity steadily grows in more fortunate world regions, cognition enhancement has become a "hot topic" and is currently arousing intense public and scientific debate. While definitions vary, cognition enhancement can be defined as improved ability to perform tasks involving mental ability, either by counteracting impairment, or by producing improvement above existing levels. The principal, and arguably only direct, objective measure of cognitive ability involves the use of tasks that demand mental efficiency, ie cognitive tests. This paper concerns a computerised test system designed by the author which had to six in a PhD program which started at Reading University (UK) in 1972. The research used nicotine and scopolamine as tests to determine whether the brain’s cholinergic systems were involved in the control of human attention. It rapidly became evident that to detect subtle cognitive improvements in healthy young subjects with nicotine, automated procedures that captured speed of cognitive processes as well as the accuracy of performance were essential. Static laboratory based computers of the 1970s offered the first solutions, while the portable laboratory microcomputers of the early 1980s allowed cognitive testing to migrate from the laboratory to diverse clinical settings and even patients homes.

**THE CDR SYSTEM**

- 186 clinical trials conducted from 1975 to the present described in:
  - 146 peer-reviewed publications
  - 29 published conference abstracts
  - 3 unpublished conference abstracts
  - 7 peer-reviewed publications of studies with negative results

Data from:
- 5,765 Healthy volunteers
  - 1,467 - Aged 5 to 17 years
  - 2,696 - Aged 18 to 40 years
  - 968 - Aged 40 to 60 years
  - 436 - Aged 60 and above
- 8,165 patients from 33 different clinical conditions

**CLINICAL POPULATIONS**

- 18 Age-Associated Memory Impairment (AAMI)
- Alzheimer’s disease (AD)
- ACHD both Childhood & Adult
- Coronary artery bypass patients (CABG)
- Carotid Endarterectomy Patients
- Chronic Fatigue Syndrome (CFS)
- Cocaine Dependents
- Dental Anaesthes Patient
- Dementia with Lewy bodies (DLB)
- Epilepsy
- Fibromyalgia
- Hepatic Encephalopathy
- Hypertension
- Kidney dialysis Patients
- Mild Cognitive Impairment (MCI)
- Major Depressive Disorder (MDD)
- Narcolepsy
- Neuropsychiatric Oncology
  - Breast cancer
  - Haematological disorders
  - Tumours
- Parkinson’s disease
- Parkinson’s disease dementia (PDD)
- Post-Operative Cognitive Decline (POCD)
- Post-Menopausal females
- Recreational Drug Users
- Reduced Cardiac Vascular Reserve
- Shift Work, Sleep Disorder
- Sleep Apnoea
- Stimulant Abusers
- Stroke
- URTI

**QUESTIONS TO BE ADDRESSED**

- Can a single system detect improvement to cognitive function in a wide range of studies?
- Can patients involving the patients with dementia perform the same tests as those used in volunteers?
- Do separate cognitive test systems need to be developed for each individual clinical condition to detect enhancements, or can one system work for all?

**CONCLUSIONS**

- To our knowledge, this is the largest database ever assembled of cognitive enhancements in recent years
- Most tests commonly used in drug development have no or only limited alternate forms, ie most neuropsychological tests as well as the ADAS-cog, NTB & MATRICS battery, this absence being the cause of numerous failures by such tests to detect improvements in recent years
- This major problem was recognised early in the development of the CDR System & every test has numerous validated and alternate forms, such that no set of test stimuli is ever repeatedly presented to a study participant in any clinical trials

**DISCUSSION**

- Why has the CDR System been developed to detect enhancements in cognitive function?
- The CDR System was developed to detect enhancements in cognitive function
- Each task was introduced only once its ability to detect enhancement had been confirmed
- Important, to detect enhancement, cognitive testing needs to be repeated over hours, days, weeks or even years in clinical trials
- An early feature in the development of the System was the recognition that training or practice effects could obscure therapeutic improvements to cognition
- Repeated pre-study training of volunteers and all patients populations on all CDR System tests has always been an essential requirement for the CDR System
- Training effects also regularly occur in clinical trials due to the absence or insufficient number of validated and equivalent alternate forms of the tests employed
- Volunteers and even patients with dementia show gains with repeated testing due to familiarity with the task materials
- Most tests commonly used in drug development have no or only limited alternate forms, ie most neuropsychological tests as well as the ADAS-cog, NTB & MATRICS battery, this absence being the cause of numerous failures by such tests to detect improvements in recent years

Keith Wesnes is a Co-Founder of the CDR Systems. Wesnes K
Bracket, Goring-on-Thames, United Kingdom and Centre for Human Psychopharmacology, Swinburne University, Melbourne, Australia

Keith.Wesnes@BracketGlobal.com

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