The Application of Cognitive Neuroscience to Clinical Research I: Detecting Cognition Enhancement in Man

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BACKGROUND

As human longevity steadily grows in more fortunate world regions, cognition enhancement has become a ‘hot topic’ and is currently ensuring intense public and scientific debate.

While definitions vary, cognition enhancement can be defined as improved ability to perform tasks involving mental activity, 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 tests that demand mental efficiency, i.e., cognitive tests.

This paper concerns a computerized test system designed by the author which had its roots in a PhD program which started at Reading University (UK) in 1972.

The research used nicotine and scopolamine as tools to determine whether the brain norepinephrine 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 emerged from this early research and has been used in approaching 1400 clinical trials worldwide.

The core tests have remained constant over the last 3 decades while being steadily supplemented with others as required.

Three major domains are evaluated:

- Sustained as well as focussed attention & the quality of information processing
- Working memory & executive control/function
- Long-term episodic memory, both verbal & non-verbal

The public domain studies in which the System has been used to identify potential cognition enhancement are reviewed in this paper.

For each study the Tables indicate whether or not the domain was assessed, and if so whether significant improvement was identified, or significant impairment, or no change.

Questions To Be Addressed

- Can a single system detect improvement to cognitive function in a wide range of studies?
- Can patients including those 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?

DISCUSSION

Why has the CDR System Proven to be so Sensitive to Detecting Cognition Enhancements?

- 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
- Importantly, 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 patient 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 of sufficient validated and equivalent alternate forms of the tasks 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, i.e., 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 equivalent forms of the tests employed
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CONCLUSIONS

- To our knowledge, this is the largest database ever assembled of cognitive enhancement identified with a single test or test system
- The answer to the question of whether a single system can be used in a diverse range of conditions to detect cognition enhancement appears to be a positive one
- Further versions of these Tables will include the identification of the relative effect sizes of the various improvements detected