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ALZHEIMER'S DISEASE
CDR SYSTEM SUMMARY
JULY 26, 2024

The CDR System is a widely used, extensively validated and a highly sensitive computerized cognitive assessment battery. The CDR System comprises of a range of tasks assessing essential cognitive domains (including attention, information processing, decision-making, episodic and working memory) relevant to everyday life activities and, for over 35 years, has been used in international clinical trials of a wide variety of diseases and clinical conditions, including non-CNS disorders. The System was designed for repeated use in clinical trials to provide a non-invasive, brief but comprehensive, set of cognitive tasks (30 minutes) in order to maximize both patient acceptability and compliance. It is virtually devoid of floor or ceiling effects, thus having bi-directional sensitivity, which together with pre-study training ensures definitive and highly sensitive longitudinal assessment of core domains of cognitive function in any clinical trial situation.

The CDR System has identified drug-induced enhancements to cognitive function in over 200 clinical trials in a range of populations ranging from healthy volunteers to Alzheimer's disease (AD). Deficits to attention have been established to be central to normal ageing, Mild Cognitive Impairment (MCI) and Alzheimer's disease. The CDR System attention tests have been shown to identify progressive impairment in normal ageing, MCI and AD (Nicholl et al. 1995; Wesnes KA 2000; McGuiness et al. 2010; Walker et al. 2000). Test-retest reliability of the individual and composite scores from the CDR System in AD has been established over periods as long as 6 months (Wesnes et al. 2005; Wesnes et al. 2010).

The CDR System has been used extensively in MCI patients (Dunbar et al. 2003; Ellis et al. 2008; Newhouse et al. 2012) and mild to moderate AD patients (Galvin et al. 2008; O'Brien et al. 2002; Rinne et al. 2016; Allain et al 1997; Ballard et al. 2001; Frolich et al. 2011;Sigfried et al. 1991; Vellas et al. 2005; Templeton et al. 1999), including a Phase III AD program in which it was approved by the FDA as a primary outcome (Fakouhi et al. 1995; Mohr et al. 1995). Further the CDR System has been used in a Phase I study assessing the effects of a novel M1-receptor partial agonist for the treatment of dementias (Bakker et al 2021) and has been used with patients scoring as low as 6 on MMSE (Simpson et al 1991).

Additionally, the CDR System picture recognition task can also provide a measure of pattern separation, a surrogate marker of hippocampal neurogenesis. Data from the CDR System database, has provided evidence of impaired pattern separation, but preserved pattern completion in both MCI (Wesnes KA 2010) and AD patients (Wesnes et al. 2014). Moreover, positive drug effects upon pattern separation have been detected in AD clinical trials (Goetghebeur et al. 2019).

The utility of the CDR System database will be discussed on a study-by-study basis, where the details of the population will be considered and appropriate cognitive test battery proposed. The CDR System offers both a standard and impaired cognitive test battery.

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