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OBJECTIVE METAMEMORY TESTING CAPTURES AWARENESS OF DEFICIT IN ALZHEIMER'S DISEASE

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ABSTRACT

For reasons that remain unknown, there is marked inter-person variability in awareness of episodic memory loss in patients with Alzheimer's disease (AD). Existing research designs, primarily subjective in nature, have been at a relative disadvantage for evaluating disordered metamemory and its relation to the clinical and neuropathological heterogeneity of AD, as well as its prognosis for various disease outcomes. The current study sought to establish an objective means of evaluating metamemory in AD by modifying traditional metacognitive paradigms in which participants are asked to make predictions regarding their own memory performance. Variables derived from this measure were analyzed in relation to clinically rated awareness for memory loss. As predicted, a range of awareness levels existed across patients with mild to moderate AD (n = 24) and clinical ratings of awareness (CRA) were significantly associated with verbal episodic memory monitoring (r = .46, p = .03). Further, patients who were rated as aware of their memory loss remained well calibrated over the course of the task whereas those rated as relatively unaware grew over-confident in their predictions [F (1, 33) = 4.19, p = .02]. Findings suggest that over-confidence may be related to impaired online error recognition and compromised use of metamemory strategies such as the Memory for Past Test (MPT) heuristic. Importantly, clinically rated awareness did not vary as a function of demographic variables, global cognition, or verbal memory. However, participants characterized as relatively unaware were impaired on a nonverbal memory task as compared to aware participants [F (1, 20) = 6.98, p = .02]. The current study provides preliminary support for the use of a recognition-based verbal episodic memory monitoring task as a quantitative measure of awareness for memory loss in AD, and offers insight into the manner in which metamemory breaks down. Discrepancies in nonverbal memory across the two awareness groups provide preliminary support for the idea that metamemory variability in AD may be related to the neuroanatomic presentation of the disease, with disordered awareness potentially reflective of a critical level of right hemisphere involvement.

Key words: metamemory, AD, awareness, anosognosia, insight

Episodic memory loss, the earliest and most striking signature of Alzheimer's disease (AD), is directly attributable to neuropathological changes in the hippocampus (Hyman et al., 1984; Braak et al., 1991; Squire, 1992; Storandt et al., 1984). Prerequisite for the diagnosis of AD, episodic memory loss is common to all patients. In contrast, for reasons that remain unknown, there is marked inter-person variability in awareness of this episodic deficit (metamemory) (Neary et al., 1986; Reed et al., 1993; Smith et al., 2000). Disordered awareness of memory loss in dementia challenges patient safety (Hunt et al., 1993; Cotrell et al., 1999), the efficacy of behavioral interventions (Koltai et al., 2001), and caregiver quality of life (Clare et al., 2004; Seltzer et al., 1997; Spitznagel et al., 2006). Despite its frequency and clinical relevance, the etiology, nature, clinical correlates, and prognostic value of impaired awareness for memory loss remain poorly understood (Agnew et al., 1998; Morris et al., 2004; Cosentino et al., 2005). Although numerous studies have examined these issues, discrepant results across investigations highlight the complexity of the construct of awareness, and the limitations of using subjective methodological approaches to clarify the phenomenon of disordered awareness (Clare, 2004a).

Historically, disordered awareness in dementia (also referred to as anosognosia) has been characterized using clinician ratings (Zanetti, 1999; Reed et al., 1993; McDaniel, 1995; Derouesne, 1999), or discrepancy scores that reflect differences between patients' report of their own functioning and caregivers' reports (Smith et al., 2000; Mangone et al., 1991; Michon et al., 1994; DeBettignies et al., 1990; Kotler-Cope et al., 1995). While these measures are informative, their subjectivity limits their ability to probe the nature and extent of disordered awareness, and to reliably assess this clinical phenomenon over time and across studies. Further, in the case of discrepancy scores, patients who endorse memory problems may still be characterized as having some degree of reduced awareness if their caregiver reports more severe problems. While caregiver impression is important, it cannot be considered an unbiased standard of accuracy, particularly given the psychological, economic, functional, and social adjustments involved with caring for a family member with dementia (Clare, 2004a). In the absence of objective methodology, we are impeded

in our investigation of the etiology, components, clinical correlates, neurocognitive substrates, and prognostic value of disordered awareness in AD.

In all likelihood, disordered awareness for memory loss or other disease symptoms is influenced by a combination of neurocognitive, psychological, social, and cultural variables. (Saravanan et al., 2004; White et al., 2000; Sussman, 2004; Prigatano et al., 1996; Ownsworth et al., 2006; Clare, 2004b; Markova et al., 2005). According to Clare's biopsychosocial model, neurocognitive features likely determine the domains of unawareness (e.g., memory, executive abilities), whereas psychological variables (e.g., coping style and premorbid personality traits), and social factors (e.g., interaction with friends, family, and healthcare professionals) contribute to the overall extent and presentation of unawareness in each individual. The complex manner in which these factors interact likely contributes to the variability in the degree and type of awareness for disease related deficits seen across individuals with AD (Ownsworth et al., 2006). Clarification of the components of awareness, such as memory monitoring abilities, may advance understanding of the construct as a whole and shed light on important aspects of disease heterogeneity.

Objective test frameworks such as Judgment of Learning (JOL) and Feeling of Knowing (FOK) are commonly used tasks to evaluate memory monitoring in healthy adults (Metcalfe, 1994) and have the potential to inform metamemory changes in the context of AD. Both types of judgments involve making predictions regarding future performance on specific test items related to general knowledge (semantic memory; Hart, 1965; Nelson, 1980) and newly learned (episodic) information (Leonesio et al., 1990; Schacter, 1983). Traditionally, JOLs are acquired for all items in a memory test, and evaluated in a cued recall format whereas FOKs are acquired for non-recallable items and tested in recognition format (or another context that does not rely on recall) (Nelson et al., 1994). Both types of judgments offer the opportunity to evaluate several aspects of memory monitoring including: 1) resolution (relative accuracy), or the extent to which accuracy is high when predictions are high, and accuracy is low when predictions are low; and 2) calibration (absolute accuracy), the degree to which individuals are over or under-confident on average. Calibration can also be measured on a global level by having the participant make a judgment regarding the total number of items that he or she expects to achieve and comparing this global estimation to the total memory score. There is some evidence to suggest that on multi-trial learning tasks, healthy adults are overconfident on the first trial, and subsequently become underconfident, an effect that has been described as the underconfidence with practice (UWP) effect (Koriat et al., 2002). Recent work has suggested that this may be due to the use of the Memory for Past Test (MPT) heuristic to construct predictions after the first trial (Finn et al., 2007). That is, predictions are based in part on performance at the previous trial rather than exclusively on current memory for items, a strategy that seems to result in predictions that underestimate accuracy.

Studies of older adults generally suggest that both semantic (Butterfield et al., 1988; Connor et al., 1997; Pappas et al., 1992) and episodic memory monitoring (Hertzog et al., 2002; Dunlosky et al., 2000; Lovelace et al., 1985; Shaw et al., 1989; Rabinowitz et al., 1982; Pappas et al., 1992) are intact. An exception is Souchay et al.'s (2000, 2004) finding that episodic FOK, but not JOL, is impaired in older adults secondary to executive dysfunction. The link between FOK and executive function has previously been demonstrated in individuals with frontal lobe lesions (Vilkki et al., 1998; Janowsky, 1989) and Korsakoff's syndrome (Shimamura and Squire, 1986), and may reflect the fact that individuals construct FOKs with regard to non-recallable items, a process that may place greater demands on executive abilities than JOLs (which are constructed for all items). The extent to which participants included in Souchay's study were differentially impaired with regard to executive abilities, or whether executive changes that occur even in the course of "healthy aging" are sufficient to reduce the accuracy of FOK judgments, is unclear.

Similar to healthy elders, patients with AD generally demonstrate intact memory monitoring for general knowledge (semantic memory; Backman et al., 1993; Lipinska et al., 1996) although this is not fully supported (Pappas et al., 1992). A more consistent finding seems to be that episodic memory monitoring is impaired in participants with AD using both JOL (Moulin et al., 2000b; McGlynn, 1991; Moulin et al., 2000a; Ansell et al., 2006; Lopez et al., 1994) and FOK (Souchay et al., 2002). Most studies have used global level judgments which require participants to predict the total number of list items that they will recall, and have found that AD groups overestimate performance as compared to healthy controls. Moulin and colleagues have raised the concern that severely impaired recall in AD may hamper the interpretation of recall-based metacognitive assessment, focusing instead on evaluating metamemory processes that operate during encoding (Moulin et al., 2000b; Moulin, 2002). For instance, this group has demonstrated that despite being over-confident in global pre-study predictions, participants with AD generally revise post-study predictions downward (Moulin et al., 2000b). Additionally, participants are sensitive to objective differences in item difficulty, predicting that they are less likely to recall the