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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 more difficult words. However, Moulin (2002) acknowledges that the sensitivity approach does not necessarily reflect participants' awareness of their *own* memory processes.

Existing work has thus provided evidence that aspects of episodic memory monitoring are impaired in participants with AD in comparison to healthy elders. However, an important issue is that nearly all studies have examined AD as a homogenous group without taking into account the marked variations in clinically observed awareness of memory loss across individuals. This approach has limited investigation of the nature and extent of metamemory deficits in AD. For example, Ansell and Bucks (2006) used a JOL format to evaluate the applicability of the Cognitive Awareness Model (CAM; Agnew et al., 1998; Morris et al., 2004), a neurocognitive model outlining three forms of anosognosia potentially applicable to AD (Ansell et al., 2006). Briefly, according to the CAM, information regarding a memory failure is filtered through a comparator mechanism where the failure is compared with the personal database and recognized as an aberrant occurrence; this discrepancy is then processed in explicit awareness via the Metacognitive Awareness System. Disturbances in this multi-step process may result in one of three forms of anosognosia: *executive anosognosia* in which there is a failure at the comparator level such that memory errors are never recognized as aberrant occurrences; *mnemonic anosognosia* in which memory errors are recognized as aberrant but are never incorporated into the personal knowledge base; and *primary anosognosia* in which the final Metacognitive Awareness System is disrupted resulting in complete absence of explicit awareness of memory or other cognitive errors.

Ansell and Bucks (2006) tested the applicability of mnemonic anosognosia in participants with AD expecting that memory errors may be recognized as failures, but are not integrated into the personal database and therefore do not influence participants' judgments of their memory despite repeated testing. Indeed, the authors found that in comparison to healthy adults, the AD group overestimated their recall abilities across all three trials of a list-learning test. However, predictions in the AD group decreased over each trial, moving closer toward their accuracy scores, and explicit post-test ratings revealed that the AD group was aware that they had performed below predicted levels. After a delay, this awareness diminished to some extent but did not return to pre-test levels, offering only partial support for the model of mnemonic anosognosia.

A critical issue is the extent to which patient metamemory patterns differed as a function of the individual's overall awareness of memory loss. Given the heterogeneity of awareness in AD, it is possible that relatively aware participants may have achieved metamemory scores in line with healthy elders whereas relatively unaware participants may have been less able to update their personal knowledge base over the course of the study, particularly after a delay. In fact, a study by Reed et al. (1992) suggested that clinical ratings of awareness (CRA) based on a structured interview were moderately correlated with discrepancies between participants' predictions and performance on a memory test.

The aim of the current study was to examine metamemory heterogeneity within AD in relation to clinically rated awareness of memory loss. Comprehensive examination of memory monitoring in early AD might generate an objective assessment of awareness for memory loss that has the potential to advance our conceptualization and study of disordered awareness. Metacognitive studies in patients with AD have established the feasibility of such techniques in this population while raising important methodological issues to be considered in future studies. We evaluated memory monitoring in the context of an objective battery designed specifically for individuals with mild to moderate dementia to determine whether or not test scores would capture variations in clinically rated awareness for memory loss. We hypothesized that a range of clinically rated levels of awareness would exist across participants, and we expected CRA for memory loss to be selectively associated with memory monitoring deficits related to new learning (episodic memory) rather than general knowledge. Furthermore, CRA was not expected to vary as a function of global cognition, verbal memory, or demographic variables such as age, education, ethnicity, or sex. Our overall goal was to establish an objective task that captured variability in awareness for episodic memory loss that might be used in future investigation of the etiology, clinical correlates and prognostic value of disordered awareness in AD.

METHODS

Participants

24 participants with AD were recruited through the Columbia University Medical Center Alzheimer's Disease Research Center and received comprehensive neurologic and neuropsychological evaluations that were reviewed in a diagnostic consensus conference attended by neurologists and neuropsychologists. Diagnoses of AD were made according to the National Institute of Neurologic Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINDS-ADRDA) criteria. Given the cognitive demands of the experimental tasks and our interest in studying awareness in early AD, only patients with mild to moderate AD, defined as a score of 20 or greater

on the Mini-Mental State Examination (Folstein et al., 1975) were selected for participation. Individuals with ongoing moderate to severe psychiatric conditions were excluded from the study, as were individuals with history of head injury, stroke, and other neurologic illnesses that might impact cognition and/or the presentation of AD. All participants provided informed consent and were reimbursed $30.00 for participation.

20 healthy elderly volunteers were recruited from senior centers in the New York City area. Participants underwent medical and neuropsychological evaluations to ensure the absence of dementia, mild cognitive impairment (MCI), psychiatric illness, neurologic illness, or other conditions with cognitive sequelae.

Procedures

The study visit included examiner ratings of awareness using a modified version of the Anosognosia Rating Scale (Reed et al., 1993), participants' self-ratings, the MMSE, and our experimental metamemory battery.

Measures

Clinical Ratings of Awareness

Testing sessions began with a brief interview to allow the examiner to make a clinical judgment regarding participant awareness of memory loss. This was done only with participants in the AD group for the purposes of establishing a clinical rating of awareness. Scores could not be assigned in healthy elders as clinical diagnosis of AD was the criteria against which self- report was measured. Examiners asked participants to discuss their opinions of their memory abilities at the current time, and assigned a score ranging from 1 to 5 on a modified version of the Anosognosia Rating Scale (Reed et al., 1993). Participants were scored according to the following five point ordinal rating system: 5 = *Full Awareness* (Spontaneous complaint or ready admission of memory loss along with the recognition that the loss is consequential. Loss related to dementia or an abnormal process); 4 = *Moderate Awareness* (Spontaneous admission of memory loss; however, loss is discussed in the context of "normal" age related changes. No discussion of diagnosis); 3 = *Shallow Awareness* (Inconsistent or transient recognition of memory loss, or uncertainty regarding memory loss. Patients may acknowledge inconsequential memory loss); 2 = *No Awareness* (Matter-of-fact denial of impairment in response to direct questions regarding memory loss); 1 = *Explicit Denial* (Questions regarding memory elicit vigorous denial of impairment or angry assertions of normal function). If spontaneous responses did not clearly fit into a specific rating category (e.g., 'My memory is bad'), the examiner queried as appropriate (e.g., 'Do you have a sense of why your memory is bad?') to extract sufficient information for assigning a score of 1-5. Responses were recorded verbatim and scored independently by two neuropsychologists (the examiner and a second rater uninvolved in the current study) to determine an inter-rater reliability coefficient. The final assigned awareness score was the mean rating from the two raters.

Self-Ratings

Following examiner ratings, participant self-ratings were obtained using a brief anosognosia scale (Deckel and Morrison, 1996) that prompts participants to judge themselves in comparison to others their age on eight abilities (walking; accurately and quickly using hands and fingers; speaking clearly; remembering; concentrating and attending; sitting still and quietly; saying the word you are thinking of; and controlling your emotions). Participants selected one of five ratings from a visual chart with the ratings arranged vertically (excellent; above average; average; below average; very impaired).

Mini Mental State Examination (Folstein et al., 1975)

This commonly used 30-item test assessing orientation, attention, language, visuospatial functioning and memory was included in the current study as a measure of global cognition.

Metamemory Battery

Training Procedure. Throughout the metamemory tasks, participants were required to predict whether or not they would achieve the correct answer using a three-point scale (Yes, Maybe, or No). In order to establish that participants could use this scale appropriately, and appreciate the difference between these judgments, we implemented a basic training procedure for this rating scale. We gave particular attention to whether or not participants appreciated the concept that "Maybe" is the best response when they are uncertain ('Will it rain three weeks from today?'). The first six participants completed a brief training procedure including 6 questions about themselves ('Are you seated?'), the examiner ('Am I eating?'), and general information ('Is this table red?') that required specific responses of Yes, No, or Maybe. Beginning with the seventh participant, a more comprehensive training procedure with 26 questions was implemented after a relatively impaired participant (not included in the current data set) demonstrated significant difficulty using "Maybe" appropriately. Following this training, all participants completed the three tasks described below.

1) General Knowledge (GK). Inclusion of the GK paradigm served two purposes. First, it acquainted participants with the test format and established that participants understood the testing framework. Second, establishing comparable performance on this measure across awareness ratings would strengthen the predicted dissociation on the Episodic JOL tasks below. The GK task consisted of thirteen general knowledge questions with a broad range of difficulty (1 to 100) defined as the percentage of healthy controls able to provide the correct answer to the specific question as reported in the Nelson and Narens trivia set (Nelson, 1980). The rating scale was printed on 8.5” × 11” paper, with the rating items (Yes – Maybe – No) written vertically in the center of the page, and was placed directly in front of the participant for the duration of the metamemory battery. Participants were provided with two practice items intended to acquaint them with the task, and to provide the examiner with the opportunity to correct misunderstanding of the directions. Questions were printed on 8.5” × 11” paper with a reminder not to answer aloud at the top of each page. For example, the first practice item read, “What instrument did Miles Davis play?”. After participants read the question aloud, the examiner provided the following prompt: “There are eight possible answers on the next page. Will you know which one is right – Yes, Maybe, or No?”. The examiner then directed the participant to make a prediction using the rating scale. Once ratings were recorded, participants were provided with eight answer choices and asked to select the correct answer. The examiner repeated the question as necessary. Distractors were semantically related to the correct answer (e.g., trumpet, clarinet, oboe, piano, etc.). While participants were encouraged to make their best guess, “I don’t know” was also accepted and scored 0 for accuracy. Once participants selected an answer choice, the examiner provided feedback regarding accuracy.

2) Verbal Episodic Judgment of Learning (VJOL). In contrast to the GK metamemory test, this episodic task required participants to retain newly learned information, and to make ratings about the likelihood of recognizing each newly learned item. A recognition-based format was adopted to minimize the number of participants who performed at floor level as might occur on a recall measure. Stimuli for this task were selected to parallel stimuli in the GK task as closely as possible. Participants were asked to remember 5 pieces of factual information drawn from a subset of the Nelson and Narens (Nelson, 1980) items that less than 1% of healthy adults answered correctly (e.g., ‘Charles Ford supposedly killed Jesse James’). The examiner read the following instructions, “In the next part of the task, I will teach you five facts. Your task is to remember this information as best you can. Then I will test your memory, giving you answer choices like before. Here are the facts”. Immediately after stimuli were presented, participants were asked to predict how many of the five facts they would get right when tested in recognition format. (i.e., ‘Now I am going to test your memory for those facts. How many of the five do you think you will get right if I give you answer choices like before?’). These trial-based judgments enabled examination of global metamemory judgments and were used as a measurement of global calibration (over/under confidence). Following the global judgments, participants were provided with the rating scale (Yes – Maybe – No) and the first test question. Questions were presented in the same format as in the GK task such that a reminder not to answer aloud was written at the top of the page, with the test question printed in the center of the page. The examiner stated: “Here is the question. There are eight answer choices on the next page. Will you know which one is right?”. Participants used the rating scale to make their prediction, and then chose an answer on the following page. In contrast to the GK task, feedback regarding accuracy was *not* provided throughout the VJOL task so as to enable evaluation of participants’ spontaneous adjustments to metamemory judgments over the course of the list-learning task. To control for basic familiarity effects and to ensure that participants encoded the information in a paired-associates format, the 8 answer choices included the correct response to the item, as well as 4 distractor items that are the correct answers for the remaining 4 stimuli, and 3 new distractors. The procedure was repeated three times using the same memory items. Stimuli were presented in the same order during the study phase in each trial; however, the questions and answer choices were presented in a pseudorandom order for each test trial. A delayed trial was administered after approximately 15-20 minutes.

3) Nonverbal Episodic Judgment of Learning (NJOL). This task was designed to resemble the format of the VJOL task such that participants studied five new pieces of information over the course of four learning trials. The stimuli for this task were taken from a children’s visual memory test (Adams et al., 1990) and consisted of geometric designs located on a 4 × 2 grid of squares (5 stimuli and 3 distractors), each of which was concealed by a lid at the start of the test. The five stimuli were exposed one at a time, for five seconds each. Participants were instructed to study the design for the entire time so that they would remember the location of the design in the grid. Following study, participants were asked to estimate the number of designs out of five that they would get right (‘Now I am going to test your memory for the location of the five designs. How many do you think you will get right?’). The examiner then showed the participant the first

TABLE I
Demographic and cognitive scores in Healthy Elders compared to entire AD Group
Mean (SD)

	HE	AD	F	df	p
Age	73.70 (6.85)	76.96 (7.12)	2.35	1, 42	.13
Education	15.70 (2.47)	15.50 (3.51)	.05	1, 42	.83
% Female	50	50	–	1	1.00
% Caucasian	95	71	–	1	.05
MMSE (0-30)	28.75 (.85)	25.13 (2.38)	41.70	1, 42	.00
General Knowledge Total (0-13)	9.20 (2.04)	7.21 (2.52)	8.07	1, 42	.01
Verbal Episodic Total (0-20)	18.00 (4.17)	10.39 (5.44)	25.87	1, 37	.00
Verbal Episodic Delay (0-5)	4.60 (1.09)	2.48 (1.40)	29.05	1, 39	.00
Nonverbal Episodic Total (0-20)	18.90 (2.29)	9.64 (5.98)	42.26	1, 40	.00

Note. HE = Healthy Elders; AD = Alzheimer's disease (combining awareness groups); MMSE = Mini-Mental State Examination (Folstein, et al., 1975).

design from the stimuli book in conjunction with the rating scale, stating, "Do you think you know where this design is – Yes, Maybe, or No?". After assessing JOL and accuracy for each of the five designs, the examiner repeated this entire procedure using the same designs for trials two, three, and four. Similar to the VJOL procedure, stimuli were presented in the same order during the study phase in each trial while the prompts were presented in a pseudorandom order for each test trial. Although a delayed trial was administered after approximately 15-20 minutes, data are not presented in the current study since this was introduced after the beginning of the study and is available for only a subset of the participants.

Metamemory Scoring

Resolution. Resolution was calculated using the gamma statistic, a rank-order correlation representing the degree to which higher ratings were paired with higher accuracy scores (scored as 0 or 1) and lower ratings were paired with lower accuracy scores. In this calculation, each rating – accuracy pair is compared with the others to determine the number of concordant pairs (instances in which both the rating and accuracy are higher in one pair than another) and discordant pairs (instances in which the rating in one pair is higher than that in the second pair, but accuracy is lower). Gamma represents the number of concordant minus discordant pairs divided by the total number of discordances and concordances (C – D)/(C + D). Gamma scores were calculated for each of the three metamemory tasks using all items in each task.

As the purpose of gamma is to describe the manner in which accuracy rises and falls as a function of the participant's prediction, calculation of gamma discards ties, or instances in which either rating or accuracy in one pair is equal to that in another pair. For example, all instances in which "Yes" is selected as the rating are not compared to one another in the calculation of gamma, regardless of the accuracy of the items. While this characteristic of the gamma calculation results in a "noisy" estimation of resolution, it is important for data in which many "ties" arise due to restricted range in either rating or accuracy (Nelson, 1984). Although implementation of a scale with broader range would have offered a more precise measure of resolution, we prioritized a restricted range to ensure valid use in patients with dementia.

Item by Item Calibration. In order to calculate item-by-item calibration scores, ordinal ratings (Yes – Maybe – No) were translated into interval data (1, 0.5, and 0). Average accuracy was then subtracted from the average rating to determine the extent to which individuals were over or under confident on an item-by-item basis. A score of zero indicates perfect calibration, positive scores indicate overconfidence, and negative scores indicate underconfidence.

Global Calibration. We also calculated global calibration at each learning trial and the delay trial to evaluate individuals' ability to make pre-test predictions regarding the overall number of items that they would correctly remember out of the five studied. Global calibration scores were determined by subtracting the actual accuracy at each trial from the predicted global accuracy, and dividing by the total number of items.

RESULTS

Demographic and cognitive variables are presented for the healthy elders and the entire AD group in *Table I*, and for the two AD awareness groups in *Table II*. Bivariate correlations were used within the AD group to evaluate the relationship between CRA and metacognitive variables. One-way analyses of variance (ANOVAs) were used to evaluate between group differences on continuous variables. Chi-square tests were conducted to analyze the distribution of sex and ethnicity by awareness group.

Awareness Ratings

An intraclass coefficient of .90 ($p < .001$) demonstrated a high degree of inter-rater reliability between the two raters applying the modified Anosognosia Rating Scale. Using the average rater

TABLE II
Demographic and cognitive scores in Aware versus Unaware AD Groups
Mean (SD)

	AAD	UAD	F	df	p
Age	76.87 (6.41)	77.11 (8.58)	.01	1, 22	.94
Education	14.67 (3.56)	16.89 (3.14)	2.39	1, 22	.14
% Female	60	33	–	1	.40
% Caucasian	67	78	–	1	.67
MMSE (0-30)	25.73 (2.09)	24.11 (2.62)	2.81	1, 22	.11
General Knowledge Total (0-13)	7.27 (2.46)	7.11 (2.76)	.02	1, 22	.89
Verbal Episodic Total (0-20)	11.27 (5.50)	8.75 (5.28)	1.12	1, 21	.30
Verbal Episodic Delay (0-5)	2.50 (1.45)	2.43 (1.40)	.01	1, 19	.92
Nonverbal Episodic Total (0-20)	11.67 (5.85)	5.29 (3.59)	6.98	1, 20	.02

Note. AAD = Aware AD group; UAD = Unaware AD group; MMSE = Mini-Mental State Examination (Folstein et al., 1975).

score, there was a range of clinically rated awareness levels such that 8 participants were classified as Fully Aware, 7 as Moderately Aware, 6 with Shallow Awareness, 2 with No Awareness, and 1 participant who vigorously denied memory loss. Due to the relatively small sample, we created two awareness groups for certain analyses by combining the full and moderate groups into an Aware AD (AAD) group (n = 15), and the remaining three awareness categories into an Unaware AD (UAD) group (n = 9).

On a self-report inventory that queried participants about specific cognitive and functional abilities in comparison to others their age (1 = Very Impaired; 2 = Below Average; 3 = Average; 4 = Above Average; 5 = Excellent), ANOVA revealed that both AD groups and healthy elders rated themselves similarly for *walking, accurately and quickly using their hands and fingers, sitting still, saying the word you are thinking of,* and *controlling emotions.* In contrast, there were significant overall group differences for ratings regarding *remembering* [F (2, 41) = 8.54, p < .01], *speaking clearly* [F (2, 41) = 3.66, p = .04], and *concentrating* [F (2, 41) = 4.81, p = .01]. Planned comparisons demonstrated that the UAD group generally rated *remembering* as average (mean = 3.22; SD = .83), comparable to ratings by healthy elders (mean = 3.60; SD = .88); in contrast, the AAD group assigned themselves ratings for *remembering* in the below average range (mean = 2.40; SD = .83), significantly lower than both the healthy elders (p < .01) and UAD group (p = .03). Self-Ratings for *speaking clearly* paralleled the ratings of *remembering*, with the AAD group assigning ratings that were significantly lower than the HE (p = .02) and UAD (p = .05) ratings. The AAD group's ratings of *concentrating* were in the below average range, significantly lower than the HE ratings in the average range (p < .01); UAD group ratings did not differ significantly from the other groups.

Rating Scale Training Procedure

The first six participants in the study completed a six-item training procedure; all but one participant achieved perfect scores with the final participant answering one item incorrectly. The comprehensive training for the rating scale was implemented for the remaining 18 participants (UAD = 7; AAD = 11). There was no significant difference in each group's ability to answer No, Yes, or Maybe when appropriate [F (1, 16) = 1.88, p = .19]. Of note, both groups used the Maybe response correctly during training [F (1, 16) = 1.42, p = .25]. Out of 13 items that required Maybe as a response, the means and standard deviations for the AAD group were 11.82 (1.60) and 12.57 (.53) for the UAD group. These results provide evidence that participants understood the rating choices and used the scale correctly in a context that was independent of the metamemory tasks.

Experimental Task Accuracy: General Knowledge and Episodic Memory

Prior to examining metacognitive scores, ANOVAs were used to evaluate between-group difference in accuracy on four dependent variables (general knowledge, verbal episodic memory – immediate and delayed, and nonverbal episodic memory – immediate). As expected, there were significant differences on all accuracy indices between healthy elders and the AD group (Table I). Evaluation of within-AD group differences revealed similar accuracy scores for general knowledge and verbal episodic memory; however, the UAD group scored significantly lower than the AAD group on the nonverbal episodic memory task (Table II).

Metacognitive Scores

We conducted bivariate correlations to examine the relationship between CRA and metacognitive scores (resolution and calibration) on the general knowledge, verbal episodic, and nonverbal episodic metamemory measures. In a subsequent step to establish divergent validity, metacognitive variables that correlated significantly with CRA were then examined in relation to cognitive and demographic variables.

TABLE III

Correlational analyses relating clinical ratings of awareness to metacognitive, cognitive, and demographic variables in Alzheimer's disease

	CRA		Verbal Episodic Gamma		NV Global Calibration	
	r	p	r	p	r	p
Metacognitive						
Verbal Episodic Gamma	**.46**	**.03**	NA	NA	.00	.99
Verbal Episodic Global Calibration	.30	.19	.11	.63	.73	.00
Verbal Episodic Item Calibration	.18	.44	.00	.99	.00	.99
Verbal Episodic Delayed Calibration	– .16	.49	– .14	.56	.53	.02
NV Episodic Gamma	– .03	.90	– .22	.38	.22	.40
NV Episodic Global Calibration	**– .50**	**.03**	.00	.99	NA	NA
NV Episodic Item Calibration	– .41	.08	– .13	.60	.63	.01
General Knowledge Gamma	.30	.15	.36	.09	– .28	.23
General Knowledge Calibration	– .12	.59	– .27	.23	.25	.30
Cognitive						
MMSE	.29	.18	– .02	.94	– .30	.21
Verbal Episodic Total	.06	.79	– .05	.83	– .24	.32
Verbal Episodic Delay	– .04	.85	– .04	.86	– .24	.30
Nonverbal Episodic Total	.31	.16	.08	.72	– .78	.00
General Knowledge Total	.04	.86	.13	.55	.25	.29
Demographic						
Age	– .01	.96	– .13	.55	– .16	.49
Education	– .19	.37	– .21	.34	.40	.08
Correlations controlling for MMSE						
Verbal Episodic Gamma	**.48**	**.02**				
NV Episodic Global Calibration	**– .53**	**.02**				

Note. NV = Nonverbal.

Resolution Scores

As predicted, gamma scores on the general knowledge task were not related to CRA, however, verbal episodic gamma scores were significantly and selectively correlated with CRA (r = .46, p = .03) such that participants who achieved higher gamma scores had higher awareness ratings (Table III). To evaluate the extent to which disease severity might impact this association, we used a partial correlation procedure to control for Mini-Mental State Examination (MMSE). The correlation between verbal episodic gamma and CRA was increased (r = .48, p = .02). Contrary to expectations, awareness ratings were not associated with the nonverbal episodic gamma score (r = – .03, p = .90). Mean gamma scores for each group were also calculated and ANOVAs with planned comparisons were used to evaluate between group differences for all metacognitive scores across the healthy elders, AAD, and UAD groups (see *Table IV*). In support of the above correlational results, the UAD group achieved significantly lower verbal episodic gamma scores than the AAD group.

Calibration

As predicted, calibration scores for the test of general knowledge were unrelated to CRA. Contrary to predictions, neither item-level (r = – .18, p = .44) nor global level calibration scores (r = – .30, p = .19) on the verbal episodic test were

TABLE IV

Mean metacognitive scores by group Mean (SD)

	HE	AAD	UAD
Verbal Episodic Gamma	.69 (.66)	.76 (.36)	.28 (.83)^
Verbal Episodic Global Calibration	– .03 (.07)	– .06 (.28)	.15 (.23)*^
Verbal Episodic Item Calibration	.00 (.07)	.06 (.16)	.12 (.14)*
Verbal Episodic Delayed Calibration	– .11 (.18)	– .10 (.28)	.04 (.27)
NV Episodic Gamma	.55 (.78)	.39 (.73)	.63 (.47)
NV Episodic Global Calibration	– .23 (.36)	– .07 (.33)	.37 (.16)*^
NV Episodic Item Calibration	.03 (.12)	.10 (.14)	.30 (.30)*^
General Knowledge Gamma	.57 (.48)	.62 (.27)	.43 (.40)
General Knowledge Calibration	– .02 (.13)	– .05 (.15)	.05 (.11)

Note. *Indicates performance is significantly different from healthy elders (p < .05). ^Indicates performance is significantly different within AD groups. NV = Nonverbal.

TABLE V
Use of Memory for Past Test Heuristic

	Verbal Episodic			Nonverbal Episodic		
	Mean (SD)	*t*	*p*	*Mean (SD)*	*t*	*p*
Healthy Elders						
Trial 2	.40 (.68)	2.63	.02	.00 (1.21)	.00	1.0
Trial 3	.33 (.78)	1.48	.17	.00 (1.63)	.00	1.0
Trial 4	.00 (.00)	NA	NA	.33 (.82)	1.00	.36
Aware AD						
Trial 2	.43 (1.27)	1.32	.21	– .46 (1.14)	– 1.45	.17
Trial 3	– .40 (1.76)	– .88	.40	.00 (1.49)	.00	1.00
Trial 4	– .21 (1.29)	– .56	.59	– .08 (1.72)	– .17	.87
Unaware AD						
Trial 2	.83 (1.27)	1.96	.09	1.25 (1.28)	2.76	.03
Trial 3	.81 (1.25)	1.83	.11	1.86 (1.07)	4.60	.00
Trial 4	1.00 (.75)	2.37	.05	2.17 (.75)	7.05	.00

Note. Results are from one-sample t-tests conducted in each group to determine if MPT values were significantly different from zero. Positive mean values represent predictions that were higher than the accuracy achieved on the former trial and negative values represent predictions that were lower than the accuracy achieved on the former trial.

related to CRA. However, follow-up analyses of between group differences revealed that, as a whole, the UAD group demonstrated overconfidence on measures of global and item-level calibration for the verbal episodic test (see Table IV). With regard to the nonverbal episodic task, awareness ratings were significantly correlated with global calibration (r = – .50, p = .03) and this association persisted when the effects of disease severity (MMSE) were removed (r = – .53, p = .02).

Trial-Based Analyses. We conducted further analyses to examine potential changes in calibration over the course of the episodic tests. Unlike the calculation of gamma scores (which required combination of all 20 items for each episodic task), item level and global calibration scores were generated for each of the four trials in the verbal and nonverbal episodic JOL tasks. To get a general sense of calibration at the beginning and end of the episodic tests, we averaged calibration scores for the first two trials and the second two trials to represent calibration scores over the course of the test.

Repeated measures ANOVAs with a 3 (healthy elder, aware, unaware) × 2 (Trials 1/2, Trials 3/4) design were used to evaluate the presence of interaction effects between group and trial. A significant interaction was found for item-level calibration on the verbal episodic test such that the AAD group remained evenly calibrated over time whereas the UAD group moved toward overconfidence and the healthy elders moved toward under-confidence [F (1, 33) = 4.19, p = .02]. Planned comparisons revealed that average item-level calibration for Trials 3/4 was significantly higher in the UAD group than in the healthy elder (p < .01) and AAD groups (p = .04). There was no significant difference between scores in the latter two groups (Figure 1). Interactions were not detected for global level calibration on the verbal test [F (1, 26) = 1.91, p = .17], nonverbal global calibration [F (1, 29) = .13, p = .88], or nonverbal item level calibration [F (1, 30) = .28, p = .76].

Factors Underlying Metacognitive Deficits

We ran preliminary analyses to examine potential factors that may underlie deficits in resolution and calibration. One possibility is that failures in the online recognition of errors may contribute to both impaired resolution and calibration in the UAD group. We examined this by comparing the nature of errors during the verbal episodic task (this data was unavailable for the Nonverbal Episodic task). Specifically, we

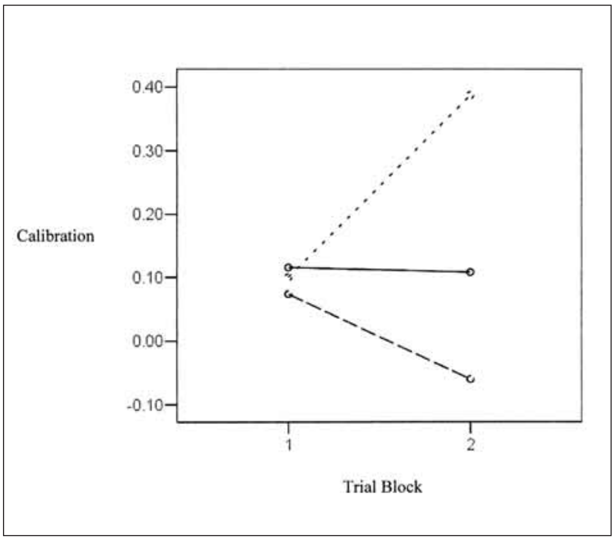

Fig. 1 – *Item-level calibration scores for trials blocks on the Verbal Episodic Task.*
Solid Line = Aware AD; Small Dotted Line = Unaware AD; Large Dotted Line = Healthy Elders.

compared the frequency with which participants in the two awareness groups responded "Don't Know" for incorrect items (*vs.* selecting a distractor item). When controlling for total number of errors, the UAD group answered "Don't Know" less frequently (mean = 2.33, SD = 3.01) than the AAD group (mean = 5.33; SD = 5.61): F (1, 11) = 7.20, p = .01.

Another possible factor contributing to discrepant metamemory scores across the UAD and AAD groups may have been the degree to which each implemented a metacognitive heuristic known as the MPT heuristic (Finn et al., 2007). The MPT score that we used reflects the extent to which global predictions for a given trial are related to overall accuracy on the former trial. An MPT score of zero indicates that global predictions match overall accuracy on the former trial. We used one-sample t-tests to evaluate whether or not each group's MPT scores ($\text{Prediction}^{\text{Trial N}}$ – $\text{Accuracy}^{\text{Trial N-1}}$) differed significantly from zero at trials two, three, and four (see Table V). Scores in the healthy elders and AAD group were not significantly different from zero at any time, suggesting that accuracy on the former trial may have guided predictions on the subsequent trial in these groups. In contrast, MPT scores in the UAD group rose significantly above zero in the final trial of the verbal episodic test and were consistently above zero throughout all trials of the nonverbal episodic test.

Although the global MPT score provides an indication of the importance of MPT at a cumulative level, use of the MPT heuristic is also believed to reflect the extent to which individuals make predictions for specific items on upcoming trials based on accuracy for those individual items at the previous trials. To determine whether or not the awareness groups differed in the use of this item-level approach, we calculated a backward gamma score relating item based predictions at trial N to accuracy for those specific items at trial (N-1). In fact, bivariate correlations revealed a highly significant relationship to CRA (r = .71, p < .01) and verbal episodic gamma (r = .74, p < .01). Further examination of mean backward gamma scores revealed a significant difference between the aware (mean gamma = .73, SD = .34) and unaware groups (mean gamma = .03, SD = .85): F (1, 17), = 6.89, p = .02. This data was not available for the nonverbal episodic task.

Discussion

Countless works have been dedicated to establishing a coherent understanding of syndromes of anosognosia, their etiology, and neurologic and cognitive correlates (Bisiach et al., 1986; Cutting, 1978; Feinberg, 2001; Geschwind, 1965; Heilman, 1993b; Marcel et al., 2004; Prigatano et al., 1991; Ramachandran, 1995; Schacter, 1990; Shimamura, 2000; Vuilleumier, 2004; Weinstein et al., 1955; Kaszniak et al., 1996). Impaired awareness for memory loss in AD represents a form of anosognosia, and may very well reflect the regional distribution of neuropathology. Disordered awareness for memory loss in AD is a clinical phenomenon that has yet to be measured in an objective framework. Historically, measurement of awareness in clinical populations has been largely subjective, and very frequently restricted to qualitative comments regarding a patient's degree of insight into the cognitive or physical sequelae related to injury or illness. The main aim of this study was to modify an objective metacognitive methodology to capture variability in clinically rated awareness of episodic memory loss in patients with AD.

Awareness Ratings

In the current study, the CRA was made on the basis of a brief interview that preceded all formal testing. These ratings were compared against participants' self-ratings on a separate measure that queried regarding memory and other abilities in comparison to others in their age group. Interestingly, the UAD group rated themselves as average, and comparable to healthy elders for abilities including remembering and speaking clearly, for which the AAD group provided ratings that were significantly lower than both groups. In contrast, all three groups rated themselves as average for walking, accurately and quickly using hands and fingers, saying the word that you are thinking of, sitting still, and controlling emotions, offering some degree of specificity for the difference in memory ratings across the groups.

Metacognitive Training Procedure

We implemented a three-point rating scale for predicting memory performance. While past studies have implemented more finely graded rating scales that offer the opportunity to assess a wider range of confidence judgments (Moulin et al., 2000a, 2000b; Pappas et al., 1992), we felt that a three-point scale would introduce fewer demands on cognitive estimation skills thus minimizing the likelihood that metacognitive ratings are confounded by poor conceptualization and improper use of the rating scale. An important component of this study was to demonstrate that participants with AD are able to use the metacognitive rating scale in a valid manner, and that this ability did not vary as a function of awareness level. As such, we implemented a training procedure that required participants to demonstrate appropriate use of the answers Yes, No, and Maybe in response to basic questions about themselves, the examiner, and the world. In fact, all participants used these answer choices accurately in a context independent of the metacognitive testing. This enhances our ability to interpret differential performance as a function of memory monitoring rather than non-specific cognitive factors.

Awareness Ratings and Metacognitive Scores

We evaluated clinically rated awareness in relation to two types of memory monitoring abilities, resolution and calibration. Resolution was measured with the gamma statistic, and represents the relative frequency with which higher predictions were paired with higher accuracy and lower predictions were paired with lower accuracy throughout the test. We also assessed calibration scores to evaluate over or under confidence for particular memory items as well as in the context of a global self-evaluation at each study trial.

Resolution

A main aim of this study was to demonstrate a relationship between clinically rated awareness and objective measures of episodic memory monitoring in contrast to general knowledge monitoring, global cognition, demographics, and severity of episodic memory loss. As predicted, participants with mild to moderate AD demonstrated a range of clinically rated awareness for memory loss, and these ratings correlated significantly with gamma scores on the verbal episodic task. That is, the higher a patient's level of awareness, the more likely he or she was to adjust predictions in accord with accuracy scores. There was no relationship between general knowledge gamma scores and awareness ratings. This provides an important aspect of divergent validity, demonstrating that the association was not driven by the format of metamemory testing, but was related specifically to judgments of new learning. Further divergent validity derives from the fact that neither CRA nor verbal episodic gamma scores were correlated with demographic variables, global cognition, general knowledge, or verbal memory.

To our knowledge, this is the first study to document selective differences in episodic memory monitoring as a function of clinically rated awareness for memory loss. Although Reed et al. (1992) demonstrated this relationship over a decade ago, awareness ratings in that study were also correlated with global cognition and memory deficit. Such a pattern is not entirely surprising particularly if participants were further into the disease course than participants in the current study. As awareness for memory may worsen within individuals over time, low memory scores would likely be associated with lower awareness when studying individuals in a more advanced disease stage.

Contrary to our predictions, awareness ratings were not correlated with gamma scores for the nonverbal episodic memory task. This may be related to the fact that accuracy on the nonverbal task was significantly different across the awareness groups (a finding that is discussed below), and that gamma scores were incalculable for six participants due to a lack of variability in predictions, accuracy, or both across the 20 items. Gamma is calculated by comparing the rating and accuracy for one item with the rating and accuracy for another item. If either the rating or accuracy is "tied" with that in the second pair, the comparison does not enter into the calculation. For example, if an individual chose "Yes" as the rating for every item, gamma would be incalculable because it would be impossible to determine whether accuracy scores varied as a function of ratings. This is a limitation to the use of the gamma statistic, but can be reconciled by adding more items to the test to increase the likelihood that either ratings or accuracy will vary. We are currently revising our tasks to improve the calculability of gamma.

Calibration

Of the four calibration measures, only the global score on the nonverbal episodic task was significantly correlated with CRA. However, follow up analyses revealed that this calibration score was associated with accuracy on the nonverbal memory task as well as several other measures, obscuring the extent to which this score reflects specific metamemory processes, and rendering it less compelling than the verbal episodic gamma score discussed above. In contrast to correlational analyses, between-group analyses revealed a significant difference in verbal calibration in the aware *versus* unaware groups with the latter group being over-confident in their predictions. Further, different patterns emerged in each group over the course of the verbal test such that the unaware group increasingly overestimated their performance whereas the aware group remained evenly calibrated and not significantly different from the healthy elders who demonstrated reduced confidence over time. This UWP effect has been demonstrated in several previous studies and suggests that the healthy elders, and potentially the UAD group, based current predictions on accuracy from the former trial (Koriat et al., 2002; Finn et al., 2007). We discuss this possibility below.

Factors Underlying Metacognitive Deficits

Miscalibration is not necessarily related to resolution deficits. The fact that the UAD group demonstrates impairment in both aspects of episodic memory monitoring may implicate primary impairments in each, or a single impairment that affects both. The most parsimonious interpretation of the data is that both resolution and calibration scores are impaired secondary to a common deficit. One possibility is that the UAD group has deficient online error recognition, comparable to the executive anosognosia subtype described by the CAM. At the beginning of the verbal episodic test, the aware and unaware groups were equally calibrated, suggesting that both groups start with a relatively accurate sense of how they will perform with only one presentation of the stimuli. However, the groups diverged in their self-assessments with repeated exposure to the stimuli. Similar to patterns seen in healthy adults (Finn et al., 2007), the aware group appeared to implement the MPT heuristic (predicting that they would achieve the same amount correct as the last trial). Backward gamma scores on the verbal task suggested that they did this by assessing the accuracy of specific items from the previous trial and using this assessment to make predictions for upcoming accuracy at both the item and global level. In contrast, the unaware group did not implement these strategies, and became over-confident over the course of the episodic test. Taken together, these results suggest that the unaware group may not recognize memory failure as it occurs and thus cannot accurately predict future performance; perhaps this group relies on a current but inaccurate assessment of performance, or reverts to pre-existing ideas of their memory abilities. Interestingly, after a delay, both the aware and unaware groups are equally and accurately calibrated (similar to the first trial of the learning test). That is, when there is no trial immediately preceding the prediction (such as at trial one and at delay), the groups are indistinguishable with regard to calibration. It thus appears that calibration discrepancies in the current study occurred in direct relation to the repeated presentation of stimuli, and the extent to which each group based upcoming performance on past performance. Either failure to use the MPT strategy altogether, or use of MPT with impaired recognition of errors in the preceding trial, had a direct impact on calibration scores.

Further evidence for poor online error recognition derives from examination of errors across the verbal episodic task. Specifically, when controlling for total accuracy, the UAD group made fewer "don't know" responses than the AAD group. That is, when the UAD group made errors, they were more likely to endorse distractor items than to say "I don't know", a pattern of performance that may indicate that the UAD group did not recognize when they were wrong. This would lead to overconfidence in general (calibration), as well as difficulty adjusting item-by-item ratings in accord with accuracy (resolution). Although results offer some support for deficits in online error recognition, data from the current study do not clearly evaluate the degree to which participants explicitly recognize each memory error. Another possibility is that the UAD group recognized errors but were unable to incorporate these errors over time, a pattern that would be consistent with the mnemonic model of anosognosia outlined by the CAM. We are exploring these two possibilities in a follow up study in which participants are asked directly to comment on their accuracy after they provide their response. It is important to note that even within the unaware participants, there may be heterogeneity in the etiology and profile of metamemory deficits (Agnew et al., 1998). Overall, however, the pattern of metamemory errors seen on objective testing in the current study offers a plausible perspective regarding the syndrome of disordered awareness for memory loss seen in the daily lives of these patients.

The Neuroanatomy of Metacognitive Deficits

A broader question underlying the current line of research is the nature of the neuropathologic substrate of self-awareness (in this case metamemory) in AD. Early AD is marked by a core amnestic syndrome and heterogeneous deficits in visuospatial functioning, language abilities, and executive skills. Certainly, this disease is a progressively global illness; however, studies of the varied neuropsychological and clinical presentations of this illness have demonstrated that, within the general profile of AD, the illness is heterogeneous in its manner of presentation (Caine et al., 2001; Haxby et al., 1988; Cummings, 2000; Mann et al., 1992; Strite et al., 1997). The various cognitive profiles seen in AD are thought to reflect the relative distribution of neuropathology, and have been associated with distinct functional neuroimaging patterns (Aharon-Peretz et al., 1999; Binetti et al., 1996; Galton et al., 2000; Johnson et al., 1999; Kanne et al., 1998; Lambon Ralph et al., 2003).

Wide metacognitive variability across individuals in the mildest stages of AD may signal dissociations in the underlying distribution of disease, although the relevant neural networks are not yet known. Most neuropsychological studies in AD have suggested a relationship between frontal lobe functioning and awareness (Mangone et al., 1991; Michon et al., 1994), and this relationship has been supported by several functional neuroimaging studies pointing to decreased activation in areas of the right frontal lobe (Vogel et al., 2005; Reed et al., 1993; Starkstein et al., 1995). This is largely consistent with research in stroke (Bisiach et al., 1986; Critchley, 1953; Heilman, 1993a, 1993b; Prigatano et al., 1991; Schnyer et al., 2004; Rainville et al., 2003), dementia (Reed et al., 1993; Miller et al., 1993; Edwards-Lee et al., 1997; Rankin et al., 2006; Marshall et al., 2004), and MCI (Adair et al., 2006) that has implicated the importance of right rather than left hemisphere areas in supporting self-awareness related to a wide range of cognitive and behavioral changes. For example, unawareness of hemiplegia is a form of anosognosia reported largely in the context of right rather than left parietal lesions (Young, 1983; Critchley, 1953; Heilman, 1993b). Conversely, altered awareness of one's behavior and social appropriateness is a key feature of the behavioral disorder subtype of frontotemporal dementia (FTD) that may reflect a critical involvement of the right prefrontal cortex in contrast to the primary aphasia syndrome associated with predominantly left hemisphere pathology (Grossman, 2000). Other syndromes of disordered self-awareness such as reduplication and misidentification have been tied to right-sided frontal and parietal injuries (Feinberg, 2001; Feinberg et al., 1994, 1999, 2000), and a recent case study of a commissurotimized patient found a critical role for the right hemisphere in self-voice recognition (Rosa et al., 2006). Interestingly, the right hemisphere's role in evaluating aspects of the self has been echoed in studies of healthy adults as well (e.g., face recognition) (Fink et al., 1996; Keenan et al., 1999, 2000; Platek et al., 2004).

Prigatano and colleagues have insightfully suggested that awareness for specific abilities may be supported by the cortical areas implicated in production of the relevant skill such that the parietal lobes play a primary role in mediating self-awareness for spatial abilities while the prefrontal cortex may be critical to aspects of social self-awareness (Prigatano, 1991; Prigatano et al., 1991). This notion of domain relevant anosognosia might predict a role for the medial temporal cortex, right greater than left, in supporting awareness for memory deficits. Interestingly, results from the only neuropathological study evaluating anosognosia in AD are fairly consistent with this idea, pointing to decreased cell count in the prosubiculum region of the right hippocampus in unaware patients (Marshall et al., 2004). Current results also lend preliminary support to the idea that decreased awareness may be related to right rather than left medial temporal integrity. Specifically, while the UAD and AAD groups achieved comparable scores on several measures of cognition and memory, the UAD group scored well below the AAD group on a measure of nonverbal memory. The nonverbal episodic memory task required participants to pair five designs with specific locations in a 4×2 grid, exerting demands on the formation of new associations, a function believed to be specifically dependent on hippocampal functioning. Unfortunately, the current study did not include a comprehensive neuropsychological battery; however, ongoing data collection is dedicated to evaluating a broad range of neuropsychological abilities related to both right and left hemisphere functioning. Future neuroimaging studies are needed to more fully investigate the neuroanatomic profile associated with impaired awareness for memory loss, and objective evaluation of memory monitoring may facilitate such investigations.

This study has several limitations. Notably, gamma cannot be calculated when there is no variability in ratings or accuracy, and increasing the number of items on the test will likely introduce the needed variability. This was particularly an issue for the nonverbal episodic task. Further, gamma is sensitive to individual items, and increasing the number of test items may stabilize this variable; this modification has been introduced into a follow up study. Nonetheless, verbal episodic gamma scores correlated significantly with CRA made prior to all cognitive and metacognitive testing, but with no other clinical or demographic variables. Further, calibration scores and implementation of the MPT heuristic differed as a function of awareness.

The current study indicates that with further refinement, the verbal episodic memory monitoring task has the potential to serve as a quantitative measure of metamemory in AD, and may offer important insight into the manner in which metamemory breaks down. Additional work is being conducted to determine the stability of performance on these measures over time, as well as to refine the metacognitive tasks. The utility of a metamemory task as a research instrument is specifically driven by objective administration and scoring. Such psychometric qualities increase the likelihood of reliable measurement across time in longitudinal analyses as well as across studies. The current study suggests that the verbal episodic JOL task is a promising approach to assessing metamemory in AD and relating such abilities to disease variables. Further, for practical purposes, our results support the use of ordinal clinical ratings as efficient and qualitative means of characterizing patients' level of awareness of memory loss in the clinic. Finally, metacognitive tasks such as the one included in this paper may have important implications for the diagnosis of MCI and we are currently collecting data to examine this issue. Individuals with MCI are considered to be more aware of memory difficulties than individuals with AD; however, this is directly related to the diagnostic criteria for this condition which require subjective memory complaint by either the individual or an informant (Petersen, 2004). Studies have begun to document that the heterogeneity in awareness in early AD is mirrored in individuals who meet the memory criteria for MCI (Vogel et al., 2004; Adair et al., 2006). Longitudinal studies are required to fully appreciate the spectrum of awareness for memory loss that exists at the transition from healthy aging to MCI and to AD.

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