Neuropsychology Review, Vol. 15, No. 3, September 2005 (© 2005)
DOI: 10.1007/s11065-005-9026-7

Unawareness of Deficits in Alzheimer's Disease and Other Dementias: Operational Definitions and Empirical Findings

Eric Ecklund-Johnson[1,5] **and Ivan Torres**[2,3,4]

Individuals with dementia frequently demonstrate decreased awareness of their cognitive difficulties. Empirical research examining this phenomenon has addressed a number of aspects of unawareness in Alzheimer's disease and other dementias, including occurrence in various disorders; possible neuroanatomical substrates; relationship to general cognitive functioning, executive functioning, and psychiatric symptomatology; and progression over time and across cognitive domains. Limitations of the current research literature are discussed, particularly issues surrounding operational definitions of unawareness and the current limited understanding of the role of the frontal lobes. A number of conclusions regarding unawareness that appear to be supported by the current body of empirical research and possible future directions are discussed.

KEY WORDS: unawareness; dementia; anosognosia; denial of deficits.

INTRODUCTION

Over the past century, observations have been made of unawareness of various deficits in cognitive functions such as memory, visual perception, etc. in dementing disorders. However, it is only within the past 10–15 years that most of the existing empirical studies of these unawareness phenomena have been conducted (Kaszniak and Christenson, 1996). Much of the work that has been done to date on unawareness phenomena in dementia has focused on Alzheimer's disease (AD), which is the most frequently occurring dementing illness in older adults, affecting an estimated 7–10% of the population over the age of 65 and up to 40% of individuals over the age of 80 (Sisodia, 1999). Increasingly, however, studies of unawareness have also been conducted in patients suffering from other dementia etiologies (e.g., McGlynn and Kaszniak, 1991a; Seltzer et al., 2001; Starkstein et al., 1996a, 1996b; Tabert et al., 2002; Vanderploeg et al., 2001).

In this review, we will attempt to summarize the research literature pertaining to unawareness of cognitive deficits in Alzheimer's disease and other forms of dementia. First, we will briefly review three broad explanations that have been proposed to explain unawareness. Next, we will discuss the important issue of operationalization of unawareness and the major approaches that various investigators have taken to defining unawareness. The remainder of the review will focus on relevant empirical studies addressing issues related to unawareness in dementia, including brain systems/regions involved, neuroimaging studies, relationship to functioning in various cognitive domains, relationship to psychiatric symptomatology, longitudinal progression, unawareness of functional abilities, and comparisons of unawareness across diagnostic groups. We performed searches of Medline and Psychinfo databases for studies including relevant keywords ("awareness," "unawareness," "anosognosia," "denial of deficit") and refined these searches by using conjunctions such as "dementia" or "Alzheimer's disease." Additional studies were identified from references of articles obtained, resulting in an exhaustive search of published studies addressing unawareness in dementia.

[1]Allied Services Psychology Service, Scranton, Pennsylvania.
[2]Department of Psychology, Simon Fraser University, Burnaby, British Columbia, Canada.
[3]Department of Medicine and Research, Riverview Hospital, Coquitlam, British Columbia, Canada.
[4]Centre for Complex Disorders, Vancouver Coastal Health Research Institute, Vancouver, British Columbia, Canada.
[5]To whom correspondence should be addressed at Allied Services Psychology Service, P.O. Box 1103, 475 Morgan Highway, Scranton, Pennsylvania 18501-1103; e-mail: eecklu@allied-services.org.

GENERAL MODELS OF UNAWARENESS

Explanations of unawareness of cognitive deficits in dementia have fallen into three broad categories. The first explanation contends that unawareness of cognitive deficits is simply the result of severe impairment in learning new information (Sunderland et al., 1983). Little empirical evidence is available to support this explanation, however. Individuals with severe impairment of new learning resulting from various amnesic disorders that are not accompanied by dementia, such as transient global amnesia, are typically well aware that their memory is not functioning normally (Schacter, 1990). However, memory deficits may help to perpetuate a lack of awareness by preventing an individual from recalling moments of realization about his or her memory difficulties.

The second broad category of explanation is that unawareness of deficits (usually termed "denial" by authors who favor this hypothesis) primarily reflects a psychological defense against the terrible realization that one is suffering irreversible cognitive decline (Reisberg et al., 1985; Sevush and Leve, 1993; Weinstein and Kahn, 1955). According to Weinstein (1991), this defensive denial, while it can occur even in individuals without any structural brain damage, happens frequently in the context of extensive, acute brain damage, usually involving limbic structures. In such cases, the denial is an exacerbation of a normal human tendency to deny threats to the self. The type of brain insult described by Weinstein is believed to impair one's ability to make sense of various internal, as well as external, stimuli, allowing the normal tendency toward denial to become more pronounced. As evidence for this more "functional" explanation of unawareness of deficits, Reisberg and colleagues (1985) pointed to their finding that while their participants with Alzheimer's disease appeared to underestimate their own deficits, they were generally accurate in their assessments of their spouses' functioning. They contended that this pattern is indicative of defensive denial.

The third explanation is that unawareness of deficits primarily reflects damage to specific brain systems that are crucial for self-awareness. Authors who support this explanation have put forth several arguments for a primarily "organic" explanation of unawareness (which they often label anosognosia). Baars and Banks (1992) argued that unawareness frequently occurs without a general loss of cognitive functioning in other areas, and that damage to brain regions outside those hypothesized to be involved in unawareness phenomena do not usually result in unawareness of deficits. Furthermore, Baars and Banks cited cases of people who are completely unaware of a deficit in a particular cognitive function, but are well aware of others. This observation was also made many years ago by Anton (as cited in Prigatano, 1999) in his description of unawareness of cortical blindness. Prigatano (1999) reviewed case studies that indicate that even very knowledgeable individuals (e.g., neurologists, neuroscientists) can be subject to unawareness of deficits following brain insult, which would appear to argue for an "organic" explanation. McGlynn and Schacter (1989) pointed out that, in dementing illnesses, the loss of insight into one's condition tends to increase gradually over the course of the disease process, sometimes resulting in unawareness of certain deficits while awareness of others is preserved until later in the disease course. Kaszniak et al. (1993) argued that an inverse relationship between unawareness and depressive symptomatology (which might be expected if in fact unawareness is a defense against a catastrophic realization) had been found inconsistently in the literature, and when present, was usually weak. Other authors (Gibson, 1992; Kaszniak and Christenson, 1996) have argued that findings that distinct types of unawareness syndromes consistently accompany damage to particular neuroanatomical sites suggest that there are specific brain systems underlying awareness of functioning. These systems are thought to involve multiple brain regions, and damage to different portions of these systems might result in different types of unawareness phenomena.

Most of the recent empirical work addressing unawareness of deficits in dementia has been conducted within the theoretical framework that unawareness of deficits is primarily the result of damage to specific awareness systems. Within this broad explanation, there are several major theoretical approaches that attempt to explain the underlying systems necessary for normal self-awareness and how damage to them might result in unawareness of deficits.

Models of Brain Systems in Self-Awareness

Schacter (1990) noted the work of Bisiach et al. (1986) demonstrating dissociability of unawareness syndromes and applied what he termed the Dissociable Interactions and Conscious Experience (DICE) model to explain various types of unawareness. Interested readers are encouraged to consult Schacter's (1990) paper for a more complete description of the model. Briefly, the DICE model proposes that there are specific modules that contain knowledge related to a particular domain (e.g., language, memory), each of which is capable of causing a change in an individual's behavior without conscious awareness. It is only when a Central Awareness System (CAS) is activated that conscious awareness of the

knowledge within a specific module will occur. If the CAS is disconnected from a particular module, the knowledge from that module will no longer be consciously monitored, although the module itself remains capable of influencing behavior. Thus, knowledge about the functioning of a particular system would cease to be updated, and the CAS would behave as if the module were functioning as it had before the disconnection. According to McGlynn and Schacter (1989), the CAS is thought to have both parietal lobe components (for awareness of individual modules), and frontal lobe components (for more global planning and execution of behavior in response to awareness of the functioning of the modules), which are connected to each other and to limbic structures. With this model, it is possible to understand how different types of unawareness could occur. For example, unawareness of a deficit in motor functioning (as in anosognosia for hemiplegia) might occur with a disconnection of the posterior (parietal) component of the CAS from the module devoted to motor functions, while a higher level impairment (i.e., unawareness of higher cognitive functions) might occur with damage to the anterior (frontal) component of the CAS or disconnection of the anterior from the posterior component. This model is capable of explaining how unawareness for different functions might occur; however, it has difficulty explaining certain aspects of unawareness phenomena. For example, McGlynn and Schacter acknowledged that this model, in its current state, cannot explain why anosognosia appears to occur more frequently with right hemisphere damage. Further, as Scheibel (1992) pointed out, there is, as yet, little anatomical evidence for the existence of the CAS.

Stuss (1991) emphasized the role of the frontal lobes in awareness of complex functions. He cited previous theoretical and empirical work on the functions of the frontal lobes (Stuss and Benson, 1986) in outlining his "Hierarchy of Brain Function" model. Within this approach, various processes such as language, attention, memory, etc. are thought of as individual functional systems capable of working at an automatic level. Each of these systems involves various cortical and subcortical areas from both hemispheres that normally work together relatively seamlessly. These specific domains of function are handled by the "posterior/basal" systems, located in portions of cortex and subcortical areas outside of the frontal lobes. The function of the frontal lobes within the hierarchy is to interact with these various systems to provide drive, sequencing, and executive functions (i.e., the impetus, planning, and actual commands necessary to carry out behaviors based on input from the posterior/basal systems). The posterior/basal systems are generally capable of handling routine, well-learned tasks without assistance from the frontal lobes. However, when novel and/or complex situations are encountered, the conscious direction of the frontal executive system is required. Within this model, self-awareness is hypothesized to be the "highest" cognitive function. Thus, damage to the frontal lobes, in addition to potentially causing deficits in drive, sequencing, and execution, may result in impaired self-awareness, as opposed to more focal disturbances of awareness that might occur with damage to the posterior/basal systems. This impaired self-awareness may show different patterns with lesions to different locations within the system. Thus, while damage to the various posterior/basal systems can cause deficits in knowledge of the outside world, only damage to the frontal system would cause deficits in awareness of the internal world of the individual. The same criticisms that apply to Schacter's model can also be leveled against Stuss' model: it fails to explain why right hemisphere dysfunction might more often lead to unawareness (although Prigatano's model, described below, would suggest that bilateral involvement is likely present when there is more complete and lasting unawareness), and it is a step removed from a detailed understanding of the various anatomical structures that might underlie the function of self-awareness.

Prigatano (1999) put forward a model of unawareness following brain injury that likely has relevance to other disorders, including dementia. He noted that unawareness can be very specific and related only to particular deficits (e.g., aphasia, hemiplegia). It can also occur in the absence of more general cognitive impairment. As Bisiach and colleagues (1986) have demonstrated, unawareness for different types of deficits (hemianopiaversus hemiplegia) can be dissociated and does not simply reflect inattention. Prigatano proposed that the specificity of unawareness phenomena suggests that it results from damage to various areas of heteromodal association cortex. For example, unawareness of aphasia (e.g., in jargon aphasia) would be expected to occur with damage to or disconnection of the angular gyrus. Further, Prigatano contended that, in order for complete and lasting unawareness to occur, damage would need to be present in homologous regions bilaterally. Unilateral damage to a particular area of heteromodal association cortex would generally result only in partial and perhaps transient unawareness. This model does not propose a specialized role of the right hemisphere in awareness as some others have and, in fact, emphasizes that both left and right hemisphere must be involved for complete unawareness to occur. Presumably, this model could be applied to progressive dementing disorders in which progressive degeneration of cortex results in a similar but more slowly advancing (and probably eventually more global) unawareness

syndrome similar to those seen in stroke and traumatic brain injury. While raising an intriguing explanation as to why unawareness can be very specific in certain disease processes, Prigatano's model does not provide a great deal of detail regarding the proposed working of whatever system(s) involving heteromodal association cortex are responsible for awareness.

Operationalization of Unawareness

Although theoretical explanations of the construct of unawareness remain tentative and somewhat vague, empirical studies have begun to elucidate aspects of unawareness in dementia. Several different methods have been used to operationalize the construct of unawareness in dementia. The approaches generally fit within one of three categories: (1) derivation of a discrepancy score based on the difference in impairments reported by the individual with dementia and those reported by an informant (often a spouse), who is familiar with his/her current cognitive functioning (see, e.g., numerous studies of Starkstein and colleagues below); (2) examination of group differences between quasi-experimental groups (aware vs. unaware) created based on clinical observation (see, e.g., Reed et al., 1993); or (3) comparison of patients' reports or predictions of their functioning with objective measures of cognitive functioning (see, e.g., Anderson and Tranel, 1989). All of these methods have inherent strengths and weaknesses.

The patient-informant discrepancy score method appears to be the most commonly used approach, likely because it is relatively easy to obtain by using a self (and informant) report questionnaire measure, which can be designed to meet the investigator's specific purpose. However, as Trosset and Kaszniak (1996) pointed out, the discrepancy score method has the inherent weakness that it cannot distinguish underestimation of deficits on the part of the patient from overestimation on the part of the informant. Indeed, evidence has been found of a significant relationship between the level of burden reported by caregivers and the degree of impairment they report on such measures (DeBettignies et al., 1990; Zanetti et al., 1999a). Nevertheless, informant ratings of cognitive problems in patients with possible prodromal symptoms of dementia have been shown to be a strong predictor of a subsequent dementia diagnosis, whereas patient ratings have not (Carr et al., 2000; Tabert et al., 2002), suggesting that informants at least come closer to an accurate reporting of symptoms. Adding to the difficulty in reaching firm conclusions based on discrepancy scores, many different measures have been developed and used, and rarely has more than one group of investigators used the same measure. Compounding this issue, there are few data addressing the reliability or validity of any of the measures for their intended purpose.

Another commonly used operational definition of unawareness of deficits is based on the judgment of a clinician (who is usually blind to the other variables in the study) as to each patient's insight into his/her cognitive impairment. In some cases, archival data is used both in arriving at the determination of unawareness and investigating the relationship between unawareness and demographic, neuropsychological, and psychiatric variables. This method is attractive in that ratings of awareness are relatively easily obtained, and some researchers have even developed structured interview questions to increase standardization. However, the difficulty with this method is its dependency on clinical ratings usually based on just a few interview questions or post hoc determinations of awareness from records, with no established validity in predicting whether patients actually demonstrate unawareness of deficits in their daily life.

The other method of operationalizing unawareness of deficits that has appeared with some frequency in the literature relates patients' reports or specific a priori predictions regarding their performance in various cognitive domains or tasks to objective measures of their performance (either formal neuropsychological tests or other similar measures developed for the specific study). Some investigators have used techniques similar to those used in the clinical judgment method to elicit self-ratings from study participants, and related these to performance on a number of neuropsychological instruments. The major flaw with this method, as pointed out by Trosset and Kaszniak (1996), is that it often compares patient responses to very general questions about cognitive functioning with very specific, focused, and usually unfamiliar tasks. These authors concluded that the best method of measuring unawareness is elicitation of very specific predictions of both the patient's and the informant's performance on a particular task from both the patient and the informant. From this approach, Trosset and Kaszniak derived a ratio score that allowed them to rule out alternative explanations (e.g., lack of understanding of how memory processes function, generally impaired judgment) when discrepancies in predictive accuracy were found. This approach would appear to allow for greater confidence than the other methods that what one is observing is actually impaired awareness of deficits, but it too has several drawbacks. One is that the method only allows the researcher to determine unawareness of deficits in very specific (and typically novel) tasks, without necessarily gaining any information about how this relates to what the patient believes about his/her daily functioning. In addition, this approach

is difficult to implement in clinical settings because describing the tasks beforehand and eliciting patient and caregiver predictions may invalidate many standardized neuropsychological measures. Clearly, there is no ideal or consensual approach to the operationalization of unawareness of deficits, and there is no existing "gold standard" to which each individual approach can be validated. Given this lack of consensus, work is perhaps needed in developing standardized measures of unawareness. It is probable that the data one collects as well as the conclusions one reaches about those data are colored to some extent by the operational definitions one uses. However, it should also be recognized that unawareness phenomena are quite complex and varied and that the study of various types of unawareness syndromes in different neuropsychological disorders might require the use of multiple methods of assessing unawareness. In light of this, it is perhaps most important that investigators and theoreticians keep in mind the potential influence of operational definitions in comparing findings of various studies of unawareness.

The remainder of this review will focus on core issues in the literature investigating unawareness in dementia, and the relationship between unawareness and a number of other variables of interest. Given the lack of agreement regarding operational definitions of unawareness, this will be followed by analysis of emerging trends or contradictions based on the various operationalizations of the construct. To this end, a table of empirical studies reviewed in this article is included that groups studies according to operational definitions and includes summary data about study findings (see Table 1).

Brain Dysfunction Underlying Unawareness

Several investigators have attempted to address the question of whether unawareness in dementia is related primarily to a psychological defense of denial or a disruption of specific brain systems that normally allow individuals to maintain awareness of their functioning. In an early study using the patient-informant discrepancy score method to operationalize unawareness of deficits, Reisberg and co-workers (Reisberg et al., 1985) found that, while patients with AD appeared to underestimate their own deficits when compared to their relatives' ratings of them, they were generally accurate in their assessment of their relatives' memory abilities. The authors interpreted this finding as evidence for defensive denial, since patients with AD appeared to maintain the ability to report accurately on the memory functioning of someone else, even as they overestimated their own functioning.

In contrast, McGlynn and Kaszniak (1991a), operating under the hypothesis that impaired awareness of deficits results from dysfunction of brain systems necessary for self-monitoring rather than defensive denial, attempted to rule out alternative explanations of unawareness of deficits by developing a method which required both patients and their caregivers to predict their own performance on various cognitive tasks and required patients to predict their caregivers' performance, thus controlling for the novelty of the tasks and the ability to predict performance on them in general (however, see Trosset and Kaszniak, 1996, for a discussion of problems of interpretation in this and other methods and a proposed method to remedy these shortcomings). In addition to making performance predictions, each patient and each informant was asked to rate both him- or herself and each other on an instrument called the Daily Difficulties Questionnaire, developed by the authors to assess difficulties in everyday memory functioning. On this questionnaire, patients rated their own problems in everyday memory functioning as less severe than their caregivers rated them. There was also a significant interaction between degree of cognitive impairment and rater, indicating that more impaired cognitive functioning was associated with a larger discrepancy score (i.e., patients rated their problems as less severe, caregivers rated them as more severe). In contrast to the discrepancy between patients' and caregivers' ratings of patient functioning, patients' ratings of their caregivers on the Daily Difficulties Questionnaire were consistent with the caregivers' own ratings. Turning to the performance predictions, McGlynn and Kaszniak found significant differences between the patient predicted/actual performance ratio and the caregiver predicted/actual performance ratio for several cognitive tasks. While the comparison of the accuracy ratios suggests that patients were generally less accurate than caregivers in predicting their own performance, patients were largely accurate in their prediction of caregiver performance. In contrast to the argument of Reisberg and colleagues, McGlynn and Kaszniak suggested that this pattern indicates that patients maintained an accurate understanding of how memory works in general, but were largely unaware of the extent of their own impairment.

Feher and colleagues (1991), also taking issue with the denial explanation of unawareness of deficits in AD, administered a memory questionnaire and several memory measures to patients with probable AD. They found significant positive correlations between the memory measures and informants' ratings of patient memory functioning, but nonsignificant negative correlations between the patients' own ratings and their scores on the memory measures. Interestingly, the authors reported that, based on

Table 1. Summary of Studies of Unawareness in Dementia

Study	Method	*N*	Findings	F/E	Dep	Cog
DeBettignies et al. (1990)	Patient-informant discrepancy	36 (12 AD; 12 VaD; 12 Control)	Unawareness: AD > VaD = Controls; no significant relationship between unawareness & general cognitive functioning or unawareness and depression	NA	None	None
Feher et al. (1991)	Patient-informant discrepancy	38 AD	Informant ratings correlated with patient memory performance, patient ratings were not; significant but weak relationship between unawareness & general cognitive functioning & between unawareness & depression	NA	None	None
Kaszniak et al. (1993)	Patient-informant discrepancy	19 AD	Patients & caregivers differed significantly in ratings of cognitive functioning, but not in ratings of emotional functioning; relationship between MMSE & unawareness approaching $p < .05$	NA	None	+
Kotler-Cope and Camp (1995)	Patient-informant discrepancy	13 AD	Patients & caregivers differed significantly in ratings across domains of cognitive functioning, but not emotional/behavioral domain, although differences in these ratings might have reached significance in larger sample	NA	None	NA
Mangone et al. (1991)	Patient-informant discrepancy	41 AD	Best predictors of unawareness included global deterioration ratings & neuropsychological measures assessing attention & visual memory	+	NA	+
Michon et al. (1994)	Patient-informant discrepancy	24 AD	Unawareness significantly correlated with frontal/executive functioning score & modified WCST; not significantly correlated with MMSE	+	NA	None
Migliorelli et al. (1995a)	Patient-informant discrepancy	103 AD	Participants who experienced delusions scored higher in unawareness than those who did not experience delusions; no significant relationship between unawareness and neuropsychological measures of frontal/executive functioning	None	NA	None
Migliorelli et al. (1995b)	Patient-informant discrepancy	103 AD	No differences between aware & unaware groups on frontal/executive functioning measures; only significant correlation was with performance on a verbal memory measure	None	NA	None
Reisberg et al. (1985)	Patient-informant discrepancy	35 (25 AD; 5 "senescent forgetfulness"; 10 Control)	Patients & caregivers differed significantly in ratings of impairment; increasing impairment (based on objective measures) was associated with lower patient ratings of severity of impairment	NA	NA	NA
Seltzer et al. (2001)	Patient-informant discrepancy	63 (31 AD; 31 Parkinson's [PD])	Discrepancy scores: AD > PD; no significant relationship between measure of executive functioning and unawareness	None	NA	NA
Sevush (1999)	Patient-informant discrepancy	203 AD	Caregiver ratings showed a much higher correlation with MMSE score than patient ratings; little progression in discrepancy scores at follow up (possible ceiling effect?)	NA	NA	+
Smith et al. (2000)	Patient-informant discrepancy	23 AD	When depression controlled for statistically, unawareness significantly correlated with several neuropsychological measures	+	−	+
Starkstein et al. (1995)	Patient-informant discrepancy	24 AD	Patients in unaware group showed reduced regional cerebral blood flow in right frontal region on SPECT imaging	+	NA	NA

Table 1. Continued

Study	Method	*N*	Findings	F/E	Dep	Cog
Starkstein et al. (1996a)	Patient-informant discrepancy	170 AD	Two factor solution for unawareness measure (factor 1 = cognitive, factor 2 = emotional); cognitive factor related to neuropsychological performance, emotional factor unrelated	NA	NA	+
Starkstein et al. (1996b)	Patient-informant discrepancy	66 (33 AD; 31 PD)	Discrepancy scores: AD > PD; Depression: PD > AD	NA	−	NA
Starkstein et al. (1997a)	Patient-informant discrepancy	92 AD	Patients in unaware group did worse on test of procedural learning & on WCST	+	NA	NA
Starkstein et al. (1997a)	Patient-informant discrepancy	62 AD	Progression in discrepancy scores at follow up for aware and mildly unaware groups; significant relationship between unawareness & depression scores in dysthymic, but not major depression, group	NA	−	NA
Starkstein et al. (2001)	Patient-informant discrepancy	319 AD	Unawareness higher in group with apathy but not depression than in group with depression but not apathy	NA	None	NA
Tabert et al. (2002)	Patient-informant discrepancy	92 MCI	Informant ratings were a significant predictor of conversion to dementia at follow up, while patient ratings were not	NA	NA	NA
Vasterling et al. (1995)	Patient-informant discrepancy	43 AD	Discrepancies were domain specific, with significant discrepancies for cognitive, but not emotional/health functioning ratings	NA	NA	+
Vasterling et al. (1997)	Patient-informant discrepancy	28 AD	Informant ratings of functioning decreased over time while patient ratings remained relatively constant	NA	NA	NA
Anderson and Tranel (1989)	Test based discrepancy	49 dementia (29 AD, 5 VaD, 15 mixed), 32 CVA, 19 TBI	When severity of deficits on testing was controlled for, no differences in unawarenesss were found across groups	NA	NA	+
Dalla Barba et al. (1995)	Test based discrepancy	12 AD, 12 Depressed, 12 elderly NC, 12 young NC	Unawareness related to verbal fluency, but not to other frontal lobe measures administered	+	NA	NA
McGlynn and Kaszniak (1991a, 1991b)	Test based discrepancy	8 AD	Patients inaccurate in predicting their own performance, but more accurate in predicting their caregivers' performance	NA	NA	+
Wagner et al. (1997)	Test based discrepancy	73 AD, 23 VaD, 17 geropsych, 19 NC	Patients with AD showed greatest unawareness, with VaD falling between AD and both control groups; within AD group, greater disease severity associated with greater unawareness	NA	NA	NA
Auchus et al. (1994)	Clinical judgment	28 AD	Patients classified as unaware did more poorly only on executive/visuoconstructive tasks, which authors suggested relates to greater right hemisphere involvement	+	NA	None
Gil et al. (2001)	Clinical judgment	45 AD	Unawareness associated with impairment on frontal tasks, overall cognitive impairment	+	NA	+
Harwood et al. (2000)	Clinical judgment	91 AD	When general cognitive functioning and agitation were controlled for, there was an inverse relationship between unawareness and depressed mood	NA	−	+
Loebel et al. (1990)	Clinical judgment	32 AD	Unawareness more common in patients with better language fluency, suggesting possibly greater right than left hemisphere involvement	NA	NA	None
Lopez et al. (1994)	Clinical judgment	181 AD	Age and executive functioning were the best predictors of unawareness	+	NA	+

Table 1. Continued

Study	Method	*N*	Findings	F/E	Dep	Cog
Reed et al. (1993)	Clinical judgment	57 probable/possible AD	Unawareness related to decreased right dorsolateral frontal hypoperfusion on functional imaging (SPECT)	+	NA	None
Sevush and Leve (1993)	Clinical judgment	128 AD	Unawareness associated with cognitive impairment and depressed mood	None	−	+
Zanetti et al. (1999a, 1999b)	Clinical judgment	37 AD, 32 VaD	Unawareness significantly related to cognitive impairment only in the middle range of impairment (not significantly correlated in high & low impairment groups); no difference between AD & VaD groups in unawareness	NA	None	+

Note: F/E = performance on measures of frontal/executive functioning (e.g., WCST; positive relationship indicates association between greater impairment on tests & general cognitive impairment frontal/executive dysfunction greater unawareness); Dep: measures of depression (e.g., geriatric depression unawareness scale; negative relationship indicates association between higher depression scores and less unawareness); Cog: performance on measures of general cognitive functioning (e.g., MMSE; positive relationship indicates association between greater impairment on tests & greater unawareness); NA: not addressed in study; None: no relationship found in study; +: positive association; −: negative association.

previously obtained normative information from a neurologically normal population for the memory questionnaire used, 45% of their sample of patients with probable AD believed that their memory functioning was *above average*. In addition, they found a weak relationship between global dementia severity and unawareness of deficits, as well as a weak inverse relationship between unawareness and depressive symptoms. They cited McGlynn and Schacter's (1989) model in concluding that lack of awareness of deficits appears to reflect primarily dysfunction of systems dependent on the frontal lobes.

Neuroimaging of Unawareness

No structural imaging studies examining neuroanatomical correlates of unawareness in dementia were found in the existing literature. However, Starkstein et al. (1992) studied unawareness in a stroke population using CT scans. They found unawareness to be associated with more frequent right hemisphere lesions, particularly when the unawareness was severe They also found unawareness to be associated with greater subcortical frontal atrophy.

Evidence favoring the hypothesis that unawareness is related to dysfunction in specific, localizable brain systems comes from two functional neuroimaging studies that have examined unawareness. Reed et al. (1993) used clinical judgment to create "aware" and "unaware" groups from a larger group of patients with possible or probable AD. These patients underwent functional neuroimaging using single photon emission computed tomography (SPECT). The only significant difference in regional cerebral blood flow (rCBF) among the groups was a finding of decreased perfusion in the right dorsolateral frontal lobe of the patients rated as having shallow or no awareness compared to the patients rated as having full awareness. The authors interpreted their results as consistent with an explanation of impaired awareness related to frontal lobe dysfunction. They speculated that unawareness of deficits might occur with damage to a parietofrontal pathway involving inferior parietal cortex, limbic structures, dorsolateral frontal cortex, and the connections among them, particularly within the right hemisphere.

Starkstein and colleagues (1995) used the patient-informant discrepancy method to select a group of 12 patients with probable AD who were rated as severely anosognosic according to criteria derived from an earlier validation study of their instrument (Migliorelli et al., 1995b) and 12 patients with probable AD who were rated as not anosognosic. The two groups were matched on the variables of age, duration of illness, and general cognitive functioning. Both groups underwent SPECT to assess differences in rCBF. The only significant difference was a relative deficit in blood flow in the right frontal lobes in the group classified as anosognosic. The authors concluded that unawareness of deficits in AD may reflect a deficit in self-monitoring related to frontal lobe pathology or broader cognitive dysfunction affecting processes dependent on the frontal lobe (i.e., disruption of "metacognitive" processes that allow one to update knowledge of one's current performance).

In general, there appears to be some convergence of findings suggesting involvement of frontal, particularly right hemisphere frontal, systems in unawareness in individuals with dementia.

Relationship of Unawareness to Domains of Cognitive Functioning

A number of investigators have examined relationships among measures of unawareness and functioning within various cognitive domains, including general cognitive/intellectual functioning, memory, and executive functioning. Several theories of awareness, including those of Stuss (1991) and Schacter (1990) described previously, posit a major role of the frontal lobes in maintaining awareness. Speculation about frontal lobe involvement in unawareness has led to a large number of studies of the relationship between unawareness and measures of executive functions, also thought to be highly dependent on the frontal lobes.

Starkstein and collaborators examined the relationship between measures of executive function and a patient-informant discrepancy measure they developed to study unawareness in several investigations. They named this instrument the Anosognosia Questionnaire-Dementia (AQ-D; Migliorelli et al., 1995b). Briefly, the AQ-D is a 30-item questionnaire that asks respondents to rate aspects of the patient's cognitive and emotional/behavioral functioning with separate forms for the patient and an informant (usually a spouse). A discrepancy score is then derived from comparison of the patient and informant ratings. Migliorelli and coworkers gave the AQ-D to patients with probable AD and their caregivers. In addition, each patient was administered a number of neuropsychological measures. Not surprisingly, patients generally rated themselves as less impaired than their caregivers did on questions about their cognitive functioning. Cutoff scores for the classification of awareness/unawareness were determined using scores from the patient sample by considering all those scoring below the mean to be aware, all those scoring more than one standard deviation above the mean to be anosognosic, and all those scoring between the mean and the cutoff to be mildly anosognosic. Multivariate analysis did not reveal a significant group difference in neuropsychological performance. The only measure found to correlate significantly with anosognosia group was the delayed recall portion of the Buschke Selective Reminding Test. However, although the Wisconsin Card Sorting Test (WCST) was administered to all patients and can provide a number of scores that are often useful in understanding various aspects of executive functioning, the only score derived from it that was used in the analysis was the total categories completed, raising the possibility that some potentially interesting data were lost.

Migliorelli et al. (1995a) examined the relationship between psychiatric symptomatology (including unawareness of deficits) and measures of cognitive functioning in a sample of individuals with AD. They examined a number of psychiatric and neuropsychological instruments in the same sample described in Migliorelli et al., 1995b. They found that patients with AD who experienced delusions scored significantly higher on the AQ-D and mania than those who did not experience delusions, even after controlling for length of illness. The authors speculated that self-monitoring deficits (possibly secondary to frontal lobe dysfunction) that are thought to underlie anosognosia may also contribute to delusions. However, they were unable to find any significant differences between those who experienced delusions and those who did not in the various executive tasks from their neuropsychological battery.

Starkstein et al. (1997b) used the AQ-D in a study examining unawareness of deficits and procedural learning in AD. They hypothesized that a deficit in procedural learning, as opposed to declarative learning might occur in patients with AD who are unaware of deficits, thus making it difficult for them to gain knowledge of their limitations from failed attempts to perform tasks. If this were true, it might explain why some patients with AD continue to demonstrate awareness of their deficits well into the disease course despite a severe deficit in declarative memory. The investigators found that the group classified as severely anosognosic showed significantly decreased learning across Maze test trials compared to the non-anosognosic and mildly anosognosic groups. In addition, the authors found that the patients from the severe anosognosia group did more poorly on the WCST than patients from the no anosognosia group. They suggested that set-shifting and procedural learning deficits may contribute to unawareness of deficits, or at least share similar neuropathology and that patients with anosognosia might represent a distinct subgroup with more pronounced frontal lobe dysfunction than is typical in the classic AD pattern of deficits.

In a study investigating the relationship between unawareness of deficits and frontal lobe dysfunction, Michon and colleagues (1994) administered a rating scale of memory functioning to 24 patients with probable AD and their caregivers. The authors found no significant correlation between unawareness of deficits and general intellectual functioning (as assessed by the MMSE) or memory impairment (although this relationship might have reached significance in a larger sample, as the reported p-value was .11 in their relatively small sample). Impaired awareness did, however, show a highly significant correlation with a "frontal" functioning clinician rating ($r = .70$) and with a modified WCST ($r = .72$). The authors concluded that the data supported a role for frontal lobe dysfunction in impaired deficit awareness in Alzheimer's disease.

In a study using clinician ratings of unawareness, Gil and co-investigators (Gil et al., 2001) developed a questionnaire (the Self-Consciousness questionnaire) and administered it to a group of 45 individuals with AD. Patient responses were scored by three expert raters (there was no indication as to whether ratings were blinded), who achieved high interrater reliability. There was a significant correlation between an anosognosia score based on their questionnaire and impaired functioning on a brief battery of tests designed to assess frontal lobe functions. They also found a significant association between the anosognosia score and overall dementia severity.

Auchus and coworkers (1994) performed a retrospective study of awareness of deficits using archival data. A dichotomous rating of awareness/unawareness was made based on patients' reported complaints and responses to questions regarding memory difficulty during a clinical interview. The unaware group performed more poorly on two neuropsychological measures: a clock drawing to command, and the Block Design subtest from theWAIS-R. The two groups did not differ in dementia severity, as determined by WAIS-R Full Scale IQ scores and scores on the Mattis Dementia Rating Scale (DRS) or on any of the other neuropsychological variables, including a verbal fluency task, a finding that the authors argued indicated that the groups did not differ in terms of left frontal lobe dysfunction. Based on these findings, the authors concluded that patients with impaired awareness of deficits have greater visuoconstructive dysfunction, suggesting greater involvement of the right frontal and parietal lobes. Using this explanation of unawareness, they explained the inconsistency between studies that have found a relationship between dementia severity and unawareness and those that have failed to find this relationship by arguing that people with AD who have prominent right hemisphere involvement early in the disease course (and therefore, presumably, decreased awareness of deficits) may avoid medical attention because of their lack of awareness until later in the disease process when there is greater cognitive impairment, while those with more prominent left hemisphere involvement may be more likely to seek out medical attention earlier in the disease course. However, the authors' interpretations of test performances is open to question, since it is generally acknowledged that performance on tests of visuoconstructive functioning can be impaired for a number of reasons, and does not necessarily localize pathology to the right hemisphere (Kaplan, 1990). Indeed, clock drawing tasks are often used as indices of impairment in executive functioning as well as visual-perceptual impairment.

Another group of investigators (Smith et al., 2000) hypothesized that failure to find a relationship between unawareness and severity or stage of dementia in some studies may have been due to confounding effects of depression. They developed a patient-informant discrepancy measure addressing several domains of cognitive functioning as well as performance of daily activities and emotional functioning. Based on a significant correlation between this measure and scores on the geriatric depression scale (GDS), the authors controlled for GDS score in their hierarchical multiple regression analysis. Whereas they found no significant relationships between their measure of unawareness and any measures of dementia severity or cognitive functioning prior to controlling for GDS scores, they found significant relationships between unawareness and scores on the MMSE, judgment of line orientation (JLO), serial seven subtraction, and an immediate recall task when depressive symptoms were controlled for. The authors interpreted these findings as indicating that greater temporal and particularly frontal lobe pathology is likely related to impaired awareness in AD.

In a study focusing on unawareness of memory functioning, Dalla Barba et al. (1995) constructed the self-rating scale of memory function (SRSMF) in order to obtain self-ratings of memory from patients with AD, depressed patients, elderly normal controls, and middle aged normal controls. Self-ratings for each participant were then compared with a combined score on the Logical Memory and Paired Associates subtests of the Wechsler Memory Scale. The authors found that, although patients were more likely than controls to demonstrate impairment both on tests of "frontal" functions and in awareness of deficits, the only test used to measure frontal lobe functioning that was significantly correlated with awareness of memory deficits in their study was a verbal fluency task (several other executive measures were uncorrelated). Thus, Dalla Barba and associates concluded that, contrary to the suppositions of several theoretical models of deficit unawareness, frontal dysfunction, while frequently present in patients who are unaware of their deficits, should not be considered necessary for unawareness to occur.

Loebel et al. (1990) were interested in the relationship between awareness of memory deficits and fluency of speech production, hypothesizing based on clinical observation that there may be an inverse relationship between the two. Their participants were classified into three categories of speech fluency (normal, mild-to-moderate impairment, severe impairment) based on clinical evaluation of their conversational speech, and two categories of awareness of memory deficits (aware, unaware) based on clinical judgment of their responses to structured interview questions. There were no differences in MMSE score between the aware and unaware groups. Caregivers

accompanying the patients were also asked to rate patients' awareness, and simple agreement between informant and clinician judgments of awareness were correlated at .88. For the fluency ratings, simple agreement was .78 among three clinician raters (no kappa statistic was reported and the authors did not specify whether raters for one dimension were blind to ratings on the other). Chi-square analysis of cross-tabulated awareness and fluency ratings yielded a significant result, with unawareness associated with higher ratings of fluency. The authors argued that these findings suggest that patients who demonstrated unawareness of deficits likely had more right hemisphere pathology, while those who demonstrated impaired fluency likely had more left hemisphere pathology.

In a large study using archival data, Lopez et al. (1994) studied the records of 181 patients with probable AD. Their assessment of patient awareness was based on standard questioning from the clinical interview. When asked whether they had any memory problems that affected their everyday functioning, 80 of the patients denied problems, while 101 agreed with an accompanying caregiver that they experienced problems. Also, following a mental status exam given as part of a neurological evaluation, each patient was asked about his/her performance during the evaluation, and 119 of the patients admitted to abnormal performance, while 62 of the patients insisted that their performance was perfectly normal. For the purposes of the study, only the 42 patients who did not report everyday problems with their memory and also denied difficulty on the mental status exam were considered unaware of their deficits, while the other 139 (including those who denied either everyday problems or difficulty with the exam, but not both) were considered aware. Unaware patients were found to have significantly lower scores on the MMSE, but there was no difference between the two groups on the demographic variables of age, gender, and education. Multivariate comparisons with age and education as covariates (the authors did not use MMSE scores as a covariate, despite the finding that they differed between the two groups) approached significance ($p = .065$). Although the multivariate test narrowly missed reaching conventional levels of significance, the authors proceeded to examine univariate comparisons of the various neuropsychological variables, and found significant differences between the two groups on tests of language, executive functioning, attention, and perception. Finally, a logistic regression procedure was performed, and age and executive functioning were found to be the best predictors of awareness. The authors concluded that their finding of a relationship between executive functioning and awareness might reflect greater frontal lobe dysfunction, or possibly more widespread generalized pathology, in the unaware group.

Across studies, there was considerable variability in relationships identified between unawareness and various measures of cognitive functioning. Evidence of executive dysfunction in unawareness was indicated in some, but not all studies. The relationship of unawareness to general cognitive functioning and other domains were inconsistent and may reflect the influence different methods and samples characteristics to some degree.

Relationship of Unawareness to Depression and Other Psychiatric Symptomatology

Sevush and Leve (1993) gave a structured interview focusing on "denial" of deficits to patients with probable AD. Depressed mood was also assessed using a scale that combined the patient's self-report, a clinician assessment, and a caregiver assessment. Analysis of correlations among denial, depression, and various demographic variables revealed significant correlations between cognitive impairment and denial, greater denial among female than male participants, and a significant inverse relationship between denial and depressed mood. A stepwise regression identified a confrontation naming test as the only neuropsychological measure that was a significant predictor of the denial score. The authors concluded that unawareness might be primarily "functional" in nature because it was found to be inversely related to depressed mood, suggesting that denial may protect against depression in patients with Alzheimer's disease.

Starkstein et al. (1996b) used the AQ-D in a study comparing unawareness of deficits, depression, and other psychiatric symptoms in patients with probable AD and patients with Parkinson's disease (PD) with dementia. They found significantly higher discrepancy scores (decreased awareness of deficit) in the group of patients with probable AD, and significantly higher scores on a measure of depressive symptomatology in the group with PD. In addition, they found that the patients in the AD group were rated significantly higher on behavioral disinhibition based on data obtained from psychiatric interviews. The authors speculated that greater disinhibition and decreased awareness of deficits may be related to greater cortical dysfunction involving the frontal and anterior temporal lobes in the patients with AD, compared to the primarily subcortical dysfunction in the patients with PD.

In another study of psychiatric symptomatology and unawareness in AD, Starkstein et al. (2001) administered the AQ-D, neurological and psychiatric examinations, and measures of depression and apathy to a group of patients

with probable AD. The investigators found significantly greater anosognosia in a subgroup of patients rated as having apathy but not depression than in a subgroup with depression but not apathy. Apathy was significantly associated with cognitive impairment (MMSE scores) in this study, raising the possibility that both apathy and unawareness were related to underlying brain dysfunction, while depression was more "functional" in nature.

Harwood and colleagues (2000) used clinician ratings of unawareness based on an item from a structured interview to examine the relationship between unawareness and both cognitive and emotional/behavioral symptoms in a group of patients with AD. In a stepwise regression analysis, MMSE score, ratings of anxiety/depression, and ratings of agitation/disinhibition all emerged as significant predictors of unawareness. The authors further examined the relationship between depressed mood and unawareness while controlling for cognitive impairment and agitation/disinhibition, and found an inverse relationship (i.e., greater unawareness associated with decreased depressive symptomatology). In comparing their findings to those of other studies examining the relationship between unawareness and depressive symptomatology, Harwood et al., noted that studies focusing specifically on depressed mood have tended to find a significant relationship, while those including somatic symptoms of depression in addition to depressed mood often have not found such a relationship.

Overall, depression was inconsistently related to unawareness across studies. It may be that certain symptoms often associated with depression (e.g., apathy/lack of initiation) but that could also reflect dysfunction of certain brain systems, have influenced these results.

Domain Specificity of Unawareness

Kaszniak et al. (1993) examined unawareness of deficits in various domains of cognitive functioning in patients with probable AD. They found that patients underestimated their memory problems relative to caregivers' reports. The authors also found a trend approaching conventional levels of significance for larger discrepancy scores in patients with lower scores on the MMSE, possibly indicating a relationship between level of impairment in global intellectual functioning and unawareness of deficits. In addition, they found significant discrepancies between patient and informant ratings in the other cognitive domains, but no significant discrepancy between patients and caregivers on emotional variables. They also found that patients and caregivers showed better agreement in their assessments of patient memory for more remote than for more recent information. They interpreted this finding as suggesting that caregivers are likely more accurate in reporting on both the more intact remote memory and the more impaired recent memory abilities of the patients, while patients may tend to underreport impairment in memory for more recently learned information, while retaining a more accurate awareness of their relatively preserved memory for information learned much earlier.

Kotler-Cope and Camp (1995) administered the memory tests and behavior rating scales to patients with probable AD and their caregivers. From these measures, Kotler-Cope and Camp were able to obtain patient-informant discrepancy scores for nine areas of functioning (language, agitation, need for routine, depression, higher cognition, memory, dementia, apraxia, and disorientation). They found significant differences between patient and informant ratings in the areas of language, higher cognition, memory, dementia, and apraxia. They found no significant differences in agitation, need for routine, depression, or disorientation. However, p values for these comparisons ranged from .07 to .12 in their small sample, raising the possibility that the nonsignificant results were due to a lack of statistical power. Nevertheless, the differences in the relative size of p values for significant and nonsignificant findings, may suggest larger effect sizes for the cognitive domains and lend evidence for some domain-specificity in awareness of cognitive versus emotional/behavioral problems.

In another study examining domain-specific differences in awareness in AD, Starkstein et al. (1996a) performed an exploratory factor analysis on the AQ-D (with orthogonal rotation). The analysis yielded two factors for the AQ-D. The first factor loaded most heavily on items reflecting awareness of cognitive deficits, while the second factor loaded most heavily on items reflecting awareness of behavioral problems. The authors found that awareness of cognitive deficits (factor one) correlated significantly with duration of illness and several neuropsychological variables (the Token Test from the Multilingual Aphasia Exam and Buschke Selective Reminding Test delayed recall), but neither duration of illness nor any of the neuropsychological variables correlated significantly with awareness of behavioral problems (factor two).

Vasterling and colleagues (1995) also examined the question of whether different levels of awareness can be seen in different cognitive domains in AD. These investigators administered a questionnaire to patients with probable AD and their caregivers that asked respondents to rate on a five-point scale the patients' memory, general health, and self-care at the present time in comparison to their functioning in the same areas five years before. In addition, patients and informants were asked to rate how

anxious, depressed, and irritable the patient had been in recent weeks. The authors also administered a questionnaire designed to assess everyday memory functioning, one designed to assess patients' ability to perform various activities of daily living, and a measure of depression. They found a significant main effect for rater (patient, informant) and domain (e.g., memory, depression), and a significant rater by domain interaction. Planned comparisons revealed significant differences between raters on ratings of memory, self-care, anxiety, and irritability, but not on ratings of depression or general health status. Further analysis of the discrepancies between patients and informants demonstrated that the largest difference appeared on ratings of memory functioning. Examination of the correlations between discrepancy in memory ratings and other study variables established a significant relationship between lack of awareness in this domain and greater cognitive impairment as measured by the MMSE. The authors concluded that their study provides evidence for domain specificity in unawareness of deficits in AD, at least with regard to differences between certain cognitive versus emotional variables.

There appears to be fairly clear evidence of domain specificity, at least for cognitive versus emotional symptoms, across studies examining this. There is also some evidence for domain specificity within the broader domain of cognition, although findings are less consistent in this regard.

Longitudinal Studies of Unawareness

In a longitudinal study of deficit unawareness in AD, Vasterling and colleagues (1997) examined scores on the questionnaires assessing general functioning and everyday memory functioning (mentioned previously) in patients with probable AD and their caregivers at two time points (12–20 months apart). Global cognitive functioning, as assessed by the MMSE, showed a nearly significant trend toward decline from time one to time two ($p = .078$). The authors found a main effect of time for memory impairment, memory decline, health decline, self-care decline, anxiety, and irritability. There was also a significant main effect of rater, with informants rating patients more impaired overall, and a significant interaction for memory impairment, health decline, self-care decline, anxiety, and irritability, and a trend toward a significant interaction for depression ($p = .055$), but no significant interaction for memory decline. Interestingly, the patients' ratings were generally stable from time one to time two, whereas informants rated the patients as having greater memory impairment, health decline, self-care decline, anxiety, and depression at time two. None of the demographic variables that were examined (age, duration of illness, age at onset, education) were significant predictors of longitudinal progression in unawareness.

In another longitudinal study of unawareness of deficits in Alzheimer's disease, Starkstein et al. (1997a) initially recruited 116 patients with probable AD and their caregivers to complete the AQ-D, and were able to collect follow-up data for 61 of the initial participants 12–28 months later. On the basis of AQ-D cutoff scores determined from previous research (Migliorelli et al., 1995b), patients in the follow-up sample were classified into three categories: no anosognosia ($n = 37$), mild anosognosia ($n = 12$), and severe anosognosia ($n = 12$). Patients who scored within the depressed range on a depression measure at time one scored significantly lower (i.e., they reported less depression) at time two (the authors did not address the issue of possible regression toward the mean, although they did control for use of antidepressant medication). With regard to patient-informant discrepancies on the AQ-D, they found a significant increase over time (i.e., reduced awareness). Furthermore, the authors found a group by time interaction, with discrepancy scores for the no anosognosia and mild anosognosia groups higher at time two, and no difference in the severe anosognosia group (they did not address whether this finding could reflect a ceiling effect on their measure). In examining the relationship between unawareness of deficits and depression, the authors found a significant inverse relationship between scores on the AQ-D and depression in the group that was classified as dysthymic at time one, while there was a non-significant positive relationship between the two variables over time in the group initially classified as having major depression. They concluded that there is progression in impairment of awareness over time and that more moderate depressive symptoms at the initial evaluation may have reflected an early emotional reaction to the disease that tends to decrease over time and with decreased awareness of deficits. In contrast, more severe depressive symptoms at the initial evaluation may reflect an "organic" mood disturbance that is not correlated with awareness of disease/cognitive dysfunction.

Sevush (1999) performed another longitudinal study of unawareness in AD, with a specific focus on unawareness of memory deficits. He developed patient and informant versions of a memory questionnaire with six dichotomous (yes/no) items. In the sample of 203 patients completing the initial assessment, there was a small but statistically significant correlation between patient-reported deficits and MMSE performance, and a much stronger correlation between patient-informant

discrepancy scores and MMSE performance, with larger discrepancies being associated with worse performance on the MMSE. A clinician rating of awareness was also strongly correlated with MMSE scores. Of the original 203 patients, 106 completed a follow-up assessment (interval between assessments $M = 1.28$ years, $SD = .69$). Despite a significant decline in MMSE scores at follow-up, no differences were found in patient ratings, patient-informant discrepancy, or clinician ratings over time. However, a possible ceiling effect (mean caregiver rating at initial assessment was 5.08 out of 6) may have contributed to the failure to find any progression in unawareness. Alternatively, it is possible that the intervening time period was insufficient to demonstrate a noticeable difference, particularly on a scale focusing on problems with memory, which are likely to be evident even early in the course of the disease.

Tabert and co-workers (2002) used the patient-informant discrepancy method to examine awareness of deficits in instrumental activities of daily living in a sample of individuals with mild cognitive impairment (MCI). They examined a group of 92 patients initially meeting their criteria for MCI at two time points and compared those who met criteria for dementia at the follow-up ($n = 23$) to those who still did not meet criteria ($n = 69$). They controlled for age, education, and cognitive impairment and found that baseline patient-informant discrepancy scores were significantly higher in the group of patients who converted to dementia status than in the group of patients who did not meet criteria for dementia at follow-up. Additional analyses revealed that informant-reported deficits were a significant predictor of conversion to dementia, while patient-reported deficits did not predict subsequent dementia status.

In general, there appears to be a progression of unawareness over time, particularly when a sufficient range of awareness and cognitive functioning are present at the initial assessment and participants are followed for an adequate period of time.

Awareness of Functional Capacity

In addition to Tabert et al. (2002), several other investigators have examined awareness of functional abilities in dementia. DeBettignies and colleagues (1990) compared patients with probable AD, patients with a diagnosis of multi-infarct dementia, and a group of elderly controls on awareness of their functioning in activities of daily living. All three groups of patients and their informants completed several measures assessing the patients' ability to perform various basic (e.g., feeding, grooming) and instrumental (e.g., food preparation, handling of finances) activities of daily living. Informants were also asked to complete a measure designed to assess the magnitude of caregiver burden. The authors found significant group differences in patient-informant discrepancy scores, and pairwise comparisons indicated that the group of patients with AD differed significantly from both of the other groups, which did not differ significantly from each other. The investigators also found a relatively large and statistically significant correlation between the degree of reported caregiver burden and the magnitude of the discrepancy scores ($r = .52$). Following this finding, they repeated the analysis of the discrepancy scores while controlling for caregiver burden, and still found significant group differences between the patients with AD and the other two groups. Discrepancy scores were not found to be significantly related to age, education, general intellectual functioning, or depression. The authors also reported that all of the patients from the AD group showed some discrepancy from their caregivers in reporting deficits, while there appeared to be a good deal of variability in insight in the multi-infarct dementia group, with half of the patients showing no discrepancy and the rest showing discrepancies that ranged from very small to quite large. The authors concluded that the discrepancy found between patients' and informants' reports of patient functioning is the result of both overestimation of functioning by patients and underestimation by caregivers, likely related to the burden placed upon them in caring for their spouse/family member.

Mangone et al. (1991) also examined awareness of daily living skills in patients with probable AD. The authors made a distinction between the terms "anosognosia," which they used specifically to refer to impaired insight presumably related to right hemisphere (often parietal lobe) dysfunction, and "confabulation," which they used to refer to impaired insight presumably related to frontal lobe dysfunction. An "impaired insight score" was derived from patient-informant discrepancy scores on measures of activities of daily living. This impaired insight score was found to be significantly higher for patients who experienced paranoid delusions and was significantly positively correlated with a measure of psychiatric symptomatology. The discrepancy scores also showed significant negative correlations with scores on all of the measures of global deterioration (although they were not significantly correlated with duration of memory impairment) and with most neuropsychological tests administered. Regression analysis revealed that two measures of global deterioration were the only significant predictors of the impaired insight score among the demographic and global functioning variables, and that a continuous performance test assessing

attention and concentration, and the Visual Reproduction subtest from the Wechsler Memory Scale were the best predictors among the neuropsychological variables.

These studies indicate that impaired awareness of functional abilities tends to parallel unawareness of tested cognitive abilities. The work of DeBettignies and colleagues highlights a potential confound in using patient-informant scores (i.e., overestimation of deficits by caregivers).

Comparison of Awareness Across Diagnostic Groups

A number of studies have indicated that unawareness of deficits tends to occur more frequently in predominantly cortical dementias, such as AD, than in primarily subcortical dementias, such as Parkinson's disease (Danielczyk, 1983; Starkstein et al., 1996b). However, there is evidence from both clinical observation (Weinstein, 1991) and empirical studies (McGlynn and Kaszniak, 1991b) that unawareness of both motor and cognitive impairment can occur in Huntington's disease, which affects primarily subcortical structures.

Anderson and Tranel (1989) compared awareness of deficits in several neuropsychological disorders. Their sample included patients with dementia (including AD, multi-infarct dementia, and "mixed" dementia), patients with stroke, and patients with traumatic brain injury. The assessed various domains of awareness of functioning, including awareness of the reason for the patient's visit/testing; awareness of motor impairments; awareness of impairment in general intellectual functioning, awareness of impairment in orientation; awareness of impairment in memory; awareness of impairment in language; awareness of impairment in visual perception; and (after the completion of all testing) judgment of overall performance and rating of ability to return to normal daily activities. Awareness scores for each patient were then compared to his or her performances on neuropsychological tests in the relevant domain of cognitive functioning. For the domains for which neuropsychological tests were not relevant, each patient's functioning was rated according to clinical judgment. By comparing awareness scores neuropsychological testing, deviation scores were obtained. These scores were then summed across all of the domains to give an "Awareness Index." Because the degree of actual impairment shown in various domains could presumably affect the opportunity for unawareness to be detected, an overall "Impairment Rating" was computed and used in the analysis of the deviation scores to control for the severity of actual deficits. In comparing the three patient groups (while controlling for impairment rating, age, education, and gender), the authors found no significant differences in awareness among them. The Awareness Index was significantly correlated with WAIS-R VIQ and PIQ and with temporal disorientation, but not with memory or visual perception. Within the dementia group, the Awareness Index correlated significantly with VIQ and temporal disorientation. Anderson and Tranel concluded that unawareness of intellectual impairment results from diffuse neuropathology that impairs metacognitive functions necessary to update and maintain awareness of cognitive functioning.

Using a similar method, Wagner and colleagues (Wagner et al., 1997) studied awareness of deficits in patients with either probable or definite AD, patients with vascular dementia (VaD), geropsychiatric controls, and geriatric controls. Wagner et al. developed an instrument called the Unawareness Interview, containing seven domains of cognitive functioning: awareness of the reason for the patient's visit, everyday memory functioning, remote memory functioning, orientation, change in intellectual functioning, language, and perceptual functioning. As in the Anderson and Tranel (1989) study, the Unawareness Interview was compared to objective/clinical data to derive deviation scores. Using overall cognitive impairment (as defined by MMSE score, as this was found to differ significantly across diagnostic groups) as a covariate, the investigators found that the group of patients with AD were significantly less aware of impairment than all other groups (with awareness of memory functioning most prominently affected). Patients with VaD, while more aware than patients with AD, showed less awareness than the two control groups, which did not differ from one another. When the group of patients with AD was broken into mild, moderate, and severe subgroups, a pattern of progressively greater unawareness was found, reflected in unawareness in an increasing number of the domains of functioning with disease progression. The authors speculated that, when viewed in terms of McGlynn and Schacter's (1989) model, their findings might reflect an early disconnection of the CAS from temporal lobe structures, with progressive disconnection from other areas of cortex with disease progression. Alternatively, the pattern observed might simply reflect an initially selective impairment in awareness becoming increasingly more global over time.

In a study using patient-informant discrepancies to compare individuals with AD and individuals with PD, Seltzer and colleagues (2001) hypothesized that impaired awareness would be present in both groups and would be related to impairment in frontal functions across groups. Both patients and caregivers were asked to rate

patients in the areas of cognitive functioning, self-care, social/emotional functioning, and motor functioning. Results indicated that patients rated themselves as less impaired than caregivers across all domains. Multivariate comparisons of discrepancy scores between the two patient groups with MMSE score as a covariate showed that the AD group had larger discrepancies, with follow-up analyses revealing a difference in discrepancy scores for cognitive functioning, but not in any of the other domains. The authors also found a significant group by rater interaction in ratings of cognitive functioning, with significant patient-caregiver discrepancies in the AD group, but not in the PD group. Thus, while both groups appeared to show some reduced awareness of motor, self-care, and social/emotional functioning, individuals with AD demonstrated reduced awareness of cognitive functioning while individuals with PD did not. The authors were unable to find a relationship between unawareness and frontal lobe functioning, although measures of frontal lobe functioning used (Mattis DRS subscales) may have been relatively insensitive for this purpose.

Zanetti and colleagues (1999b) used a measure of unawareness based on clinical judgment. They administered this measure to patients with possible or probable AD and patients with possible or probable VaD. In contrast to some other studies, Zanetti et al. did not find significant differences between the two groups on their measure of unawareness. However, it is possible that their VaD group was fairly heterogeneous with regard to primary location (e.g., cortical vs. subcortical) of the vascular pathology, which might lead to large within group variability in awareness (Erkinjuntti et al., 2000). In the total sample (i.e., combining patients with VaD and AD), the authors found an interesting pattern of relationship between MMSE scores and unawareness. There was a significant positive linear relationship between the unawareness score and MMSE performance in the middle range (from 12/30 to 24/30 on the MMSE) and no significant relationship between them at the low ($<$12/30) and high ($>$24/30) ends of the distribution. Zanetti et al. suggested that this pattern reflects initial full awareness during early stages of the disease, followed by decreasing awareness in the middle stages, and, finally, complete unawareness in the later stages. The authors found no significant relationship between depression and unawareness.

Overall, unawareness was found more commonly in cortical dementias, although it can certainly occur with other types of brain dysfunction. The underlying pathological process may be less important than the brain systems affected and different patterns of unawareness in different patient groups may simply reflect anatomical predilections of different disease processes.

Limitations of the Research Literature

One potential barrier to drawing clear conclusions from this body of research is the diversity of methods of operationalizing the construct of interest. This is potentially problematic because particular findings could in some instances be confounded or driven by the use of a specific operationalization of unawareness. Examination of the summary presented in Table 1, for example, suggests that the association between unawareness and depression may depend at least partly on the type of unawareness measurement that was used. Specifically, whereas only a minority (38%) of the studies evaluating the depression/unawareness relationship using the patient-information discrepancy approach found a positive relationship between these variables, the majority of studies using the clinical judgment approach (67%) reported such an association. In other cases, there is a less clear pattern of findings with respect to the type of operational definition used. For example, studies using both the patient-informant and the clinical judgment methods yielded positive and negative results with respect to the relationship between unawareness and executive and general cognitive functioning. To the extent that the operationalization of unawareness remains varied and essentially unresolved, there is the potential for findings to be obscured. However, it could also be argued that unawareness is a multifaceted phenomenon that manifests differently in different neuropsychological disorders, which may necessitate the use of multiple strategies for assessing it. Furthermore, our understanding of unawareness is perhaps at an early stage of evolution and there is no clear empirically based reason for favoring one method over another. Studies that compare operational definitions within samples in order to examine the convergent validity of the various approaches to defining unawareness could be helpful in clarifying some of these issues.

Another limitation inherent in the study of unawareness of deficits in dementias such as AD is that the onset and course are often quite variable. Thus, large within-group variability may serve to obscure some potential findings. This is compounded by the problem of differential sensitivity across studies of the measures used to assess global cognitive functioning in patients with dementia (e.g., MMSE vs. IQ tests). The fact that there is a good deal of disagreement between studies that found a significant relationship between unawareness of deficits and global intellectual decline (e.g., Lopez et al., 1994; Mangone et al., 1991; Vasterling et al., 1995) and those that did not (e.g., Auchus et al., 1994; Michon et al., 1994; Reed et al., 1993) could be due in part to the variable range in dementia severity that was present in the samples and/or

the sensitivity of the measures used to characterize their cognitive functioning. It is generally acknowledged that, as a dementia such as AD progresses and the intellectual decline becomes more severe, all patients eventually begin to demonstrate decreased awareness of deficits, regardless of the level of awareness they had earlier in the disease course (Reisberg et al., 1985). Thus, studies with samples that included a large number of participants whose dementia had already progressed beyond early stages might be more likely to be influenced by this eventually widespread decline in awareness. Further complicating the picture is the fact that some investigators covaried for global cognitive impairment in their analyses, while others did not.

The use of informants to rate patient functioning also raises its own set of problems. While there is evidence that informants tend to be more accurate than patients (Carr et al., 2000; Tabert et al., 2002), there is also evidence that issues such as caregiver burden can contribute to their ratings of patient impairment (DeBettignies et al., 1990). In addition to caregiver burden, other aspects of the patient-informant relationship, including level of familiarity with the day-to-day functioning of the patient, could logically be expected to influence ratings. Therefore, it may be important to understand the relationship of the informant to the patient and studies that lump different types of informants together face a potential confound.

Still another challenge to interpreting the findings of studies of unawareness within a theoretical approach that emphasizes the role of a self-monitoring system is a lack of formal neuropsychological measures specifically designed to assess self-monitoring functions. Another related issue is that the construct of awareness/unawareness is likely theoretically complex and distinctions such as level, depth, or type of awareness have typically not been studied. For example, it is unclear whether frank unawareness and minimization of deficits represent points on a continuum or qualitatively different types of unawareness. In addition, tests used to explore the relationship between unawareness of deficits and "frontal" functions in general may not always differentiate patients with frontal lobe dysfunction from those with pathology elsewhere in the brain. For example, Anderson et al. (1991) have shown that impairment on the WCST, which was found to be related to unawareness of deficits in several studies, but not in others, is not necessarily a very specific index of frontal lobe dysfunction (i.e., many patients with lesions outside of the frontal lobes may perform poorly on this test as well). Efforts to establish a relationship between executive dysfunction and unawareness may also have been clouded by the use of a wide range of executive measures employed. This is particularly problematic given the possibility that unawareness may relate to some, but not all aspects of executive dysfunction. To complicate matters further, efforts to assess a relationship between executive deficits and unawareness may be obscured by the variable use of experimental or statistical control for general cognitive functioning, which has been employed variably in the literature. These difficulties in the operationalization of variables reflect the complexity of the constructs that are of interest within this body of research and our incomplete understanding of them.

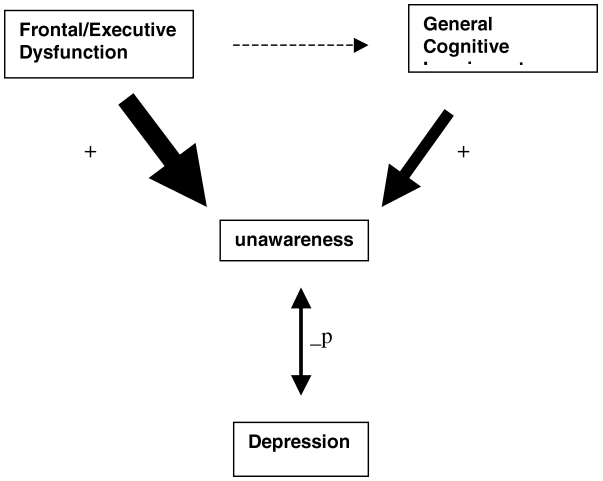

Fig. 1. Major variables associated with unawareness in dementia. The thickness of the arrow depicts the strength of the association, and the sign (+ or −) reflects the direction of the association. The dotted line indicates that influence of general cognitive impairment on unawareness may arise from executive/frontal dysfunction. Double arrow indicates possible biderectional relationship between depression and unawareness.

SUMMARY OF THE LITERATURE

Despite challenges to interpretation cited above, the existing body of literature appears to support a number of tentative conclusions (summarized in Fig. 1). The first conclusion is that memory deficits alone do not appear to be capable of explaining unawareness of deficits in Alzheimer's disease. Memory performance was rarely exclusively predictive of unawareness in studies in which this relationship was examined, and there is evidence from the study of people with circumscribed medial temporal lobe dysfunction that it is possible to have a severe amnesic deficit and yet be fully aware of memory impairment (Schacter, 1990).

Another conclusion that appears to be supported is that brain dysfunction, whether global or within a specific self-monitoring system, is involved in unawareness of

deficits. Evidence of "organic" dysfunction involving specific brain regions comes from the two studies (Reed et al., 1993; Starkstein et al., 1995) that employed functional imaging and converged in their findings of right frontal lobe hypoperfusion in patients with decreased awareness. The finding in the majority of studies addressing the relationship with general cognitive functioning that unawareness was related to measures of both general cognitive functioning (62%) and at least some aspect of executive functioning in studies addressing this relationship (71%) provides additional evidence for this explanation. Additionally, the finding that unawareness tended to be greater in individuals with AD than in individuals with other disease processes such as vascular dementia (DeBettignies et al., 1990; Wagner et al., 1997) and Parkinson's disease (Seltzer et al., 2001; Starkstein et al., 1996a, 1996b) also points to a specific neural basis of unawareness that can be differentially affected by different disease processes.

Longitudinal studies generally indicate that unawareness of deficits is progressive over time, involving increasingly more functional domains (Vasterling et al., 1997). Progression is also reflected in increasingly larger discrepancies between patients and their presumably more objective caregivers (Starkstein et al., 1997a). Initially, unawareness may be most pronounced in the domain of memory functioning (e.g., Tabert et al., 2002); however, this is likely due, at least in part, to the fact that memory function is most affected early in AD, allowing more opportunity for unawareness (at least when defined in terms of discrepancy scores) to be observed. It appears that there is not a uniform progression through stages of unawareness, as many patients with AD demonstrate impaired awareness relatively early, while others maintain awareness of at least some of their deficits well into the disease course, and a relationship between duration of illness and decreased awareness of deficits has been inconsistently found in the literature. Likewise, a relationship between depressive symptoms and unawareness, which some authors suggest is a key point in the debate over whether unawareness of deficits is primarily a defense against psychological distress, has not been consistently found in the literature (i.e., in 45% of studies in this review that addressed this question), and it was generally fairly weak in the studies in which it was found. However, as Harwood et al. (2000) point out, these discrepant findings may have been the result of some studies focusing specifically on depressed mood while others included somatic symptoms of depression. The use of different methods to assess depression could also contribute to this variability, as self-report measures and clinician rating scales might be expected to differ somewhat in populations with cognitive impairment and reduced insight. Notwithstanding these issues, in studies finding a significant relationship between depression and unawareness, the relationship was in the predicted direction. Clearly, the question of the nature of a possible association between unawareness and depression remains unresolved and awaits further prospective study. In addition to depression, several studies have investigated the relationship between other psychiatric symptoms and unawareness, and there is some suggestion that apathy (Starkstein et al., 2001) and delusions (Migliorelli et al., 1995a) may be positively associated with unawareness.

Finally, adding to the complexity of the unawareness construct, there is evidence that there may be some specificity to the unawareness of particular domains. For example, awareness of cognitive vs. emotional difficulties appear to be separate issues (Starkstein et al., 1996a). In this study, awareness of emotional difficulties appeared to be well preserved, even though awareness of cognitive deficits was decreased.

FUTURE DIRECTIONS

Further theoretical elaboration of the construct of unawareness in dementia and further validation of instruments to assess unawareness will be important in allowing investigators to begin to move toward increased understanding of the construct. In addition, increased understanding of executive or frontal lobe functioning from continued empirical research will be useful to help elucidate the possible system(s) that might underlie awareness and related "higher" brain functions. Functional or structural neuroimaging may offer a particularly promising avenue for further explanation of the systems underlying awareness/unawareness phenomena. Within the patient groups studied, some of the most suggestive evidence for regional brain specialization for awareness comes from existing functional neuroimaging studies. However, imaging studies utilizing theoretically driven tasks designed to elicit awareness and its complex constituents would add to our understanding of neural mechanisms underlying normal and impaired awareness. For example, Johnson et al. (2002) used functional MRI to study activation during a self-reflection task in normal adults and found anterior medial prefrontal and posterior cingulate activation. Additional studies such as this one in normal and patient groups will no doubt increase our understanding of awareness/unawareness and related phenomena. Although our understanding of functions such as awareness is still in an embryonic stage, impressive and accelerating strides have been made in the understanding of higher brain functioning within the past 50 years (Miller and Cummings, 1999) and there is reason for optimism that new theoretical and

empirical advances eventually will lead to a better understanding of these most elusive of neuropsychological phenomena.

REFERENCES

Anderson, S. W., Damasio, H., Jones, R. D., and Tranel, D. (1991). Wisconsin Card Sorting Test performance as a measure of frontal lobe damage. *Journal of Clinical and Experimental Neuropsychology* **13**: 909–922.

Anderson, S. W., and Tranel, D. (1989). Awareness of disease states following cerebral infarction, dementia, and head trauma: Standardized assessment. *The Clinical Neuropsychologist* **3**: 327–339.

Auchus, A. P., Goldstein, F. C., Green, J., and Green, R. C. (1994). Unawareness of cognitive impairments in Alzheimer's Disease. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology* **7**(1): 25–29.

Baars, B. J., and Banks, W. P. (1992). Introduction: The evidence for anosognosia. *Consciousness and Cognition* **1**: 148–151.

Bisiach, E., Vallar, G., Perani, D., Papagno, C., and Berti, A. (1986). Unawareness of disease following lesions of the right hemisphere: Anosognosia for hemiplegia and anosognosia for hemianopia. *Neuropsychologia* **24**(4): 471–482.

Carr, D. B., Gray, S. G., Baty, J., and Morris, J. C. (2000). The value of informant versus individual's complaints of memory impairment in early dementia. *Neurology* **55**: 1724–1727.

Dalla Barba, G., Parlato, V., Iavarone, A., and Boller, F. (1995). Anosognosia, intrusions, and 'frontal' functions in Alzheimer's disease and depression. *Neuropsychologia* **33**(2): 247–259.

Danielczyk, W. (1983). Various mental behavioral disorders in Parkinson's disease, primary degenerative senile dementia, and multiple infarction dementia. *Journal of Neural Transmission* **56**: 161–176.

DeBettignies, B. H., Mahurin, R. K., and Pirozzolo, F. J. (1990). Insight for impairment in independent living skills in Alzheimer's Disease and multi-infarct dementia. *Journal of Clinical and Experimental Neuropsychology* **12**(2): 355–363.

Erkinjuntti, T., Inzitari, D., Pantoni, L., Wallin, A., Scheltens, P., Rockwood, K., et al. (2000). Research criteria for subcortical vascular dementia in clinical trials. *Journal of Neural Transmission* **59**(Suppl.): 23–30.

Feher, E. P., Mahurin, R. K., Inbody, S. B., Crook, T. H., and Pirozzolo, F. J. (1991). Anosognosia in Alzheimer's disease. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology* **4**(2): 136–146.

Gibson, K. R. (1992). Toward an empirical basis for understanding consciousness and self-awareness. *Consciousness and Cognition* **1**: 163–168.

Gil, R., Arroyo-Anllo, E. M., Ingrand, P., Gil, M., Neau, J. P., Ornon, C., et al. (2001). Self-consciousness and Alzheimer's disease. *Acta Neurologica Scandinavica* **104**: 296–300.

Harwood, D. G., Sultzer, D. L., and Wheatley, M. V. (2000). Impaired insight in Alzheimer Disease: Association with cognitive deficits, psychiatric symptoms, and behavioral disturbances. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology* **13**(2): 83–88.

Johnson, S. C., Baxter, L. C., Wilder, L. S., Pipe, J. G., Heiserman, J. E., and Prigatano, G. P. (2002). Neural correlates of self-reflection. *Brain* **125**: 1808–1814.

Kaplan, E. (1990). The process approach to neuropsychological assessment of psychiatric patients. *Journal of Neuropsychiatry* **2**(1): 72–87.

Kaszniak, A. W., DiTraglia, G., and Trosset, M. W. (1993, February). *Self-Awareness of Cognitive Deficit in Patients with Probable Alzheimer's Disease*. Poster session presented at the annual meeting of the International Neuropsychological Society, Galveston, TX.

Kaszniak, A. W., and Christenson, G. D. (1996). Self-awareness of deficit in patients with Alzheimer's disease. In: Hameroff, S. R., Kaszniak, A. W., and Scott, A. C. (eds.), *Toward a Science of Consciousness: The First Tucson Discussions and Debates*. Cambridge, MIT Press, MA, pp. 227–242.

Kotler-Cope, S., and Camp, C. J. (1995). Anosognosia in Alzheimer disease. *Alzheimer Disease and Associated Disorders* **9**(1): 52–56.

Loebel, J. P., Dager, S. R., Berg, G., and Hyde, T. (1990). Fluency of speech and self-awareness of memory deficit in Alzheimer's disease. *International Journal of Geriatric Psychiatry* **5**: 41–45.

Lopez, E. L., Becker, J. T., Somsak, D., Dew, M. A., and DeKosky, S. T. (1994). Awareness of cognitive deficits and anosognosia in probable Alzheimer's disease. *European Neurology* **34**: 277–282.

Mangone, C. A., Hier, D. B., Gorelick, P. B., Ganellen, R. J., Langenberg, P., Boarman, R., et al. (1991). Impaired Insight in Alzheimer's disease. *Journal of Geriatric Psychiatry and Neurology* **4**: 189–193.

McGlynn, S. M., and Kaszniak, A. W. (1991a). Unawareness of deficits in dementia and schizophrenia. In Prigatano, G. P., and Schacter, D. L. (eds.), *Awareness of Deficit After Brain Injury: Clinical and Theoretical Issues*, Oxford University Press, New York, pp. 84–110.

McGlynn, S. M., and Kaszniak, A. W. (1991b). When metacognition fails: Impaired awareness of deficit in Alzheimer's disease. *Journal of Cognitive Neuroscience* **3**(2): 183–189.

McGlynn, S. M., and Schacter, D. L. (1989). Unawareness of deficits in neuropsychological syndromes. *Journal of Clinical and Experimental Neuropsychology* **11**(2): 143–205.

Michon, A., Deweer, B., Pillon, B., Agid, Y., and Dubois, B. (1994). Relation of anosognosia to frontal lobe dysfunction in Alzheimer's disease. *Journal of Neurology, Neurosurgery, and Psychiatry* **57**: 805–809.

Migliorelli, R., Petracca, G., Teson, A., Sabe, L., Leiguarda, R., and Starkstein, S. E. (1995a). Neuropsychiatric and neuropsychological correlates of delusions in Alzheimer's disease. *Psychological Medicine* **25**: 505–513.

Migliorelli, R., Teson, A., Sabe, L., Petracca, G., Petracchi, M., Leiguarda, R., et al. (1995b). Anosognosia in Alzheimer's disease: A study of associated factors. *Journal of Neuropsychiatry and Clinical Neurosciences* **7**: 338–344.

Miller, B. L., and Cummings, J. L. (1999). Preface. *The Human Frontal Lobes: Functions and Disorders*, Guilford Press, New York.

Prigatano, G. P. (1999). *Principles of Neuropsychological Rehabilitation*, Oxford University Press, New York.

Reed, B. R., Jagust, W. J., and Coulter, L. (1993). Anosognosia in Alzheimer's disease: Relationships to depression, cognitive function, and cerebral perfusion. *Journal of Clinical and Experimental Neuropsychology* **15**(2): 231–244.

Reisberg, B., Gordon, B., McCarthy, M., and Ferris, S. (1985). Clinical symptoms accompanying progressive cognitive decline and Alzheimer's disease: Relationship to "denial" and ability to give informed consent. In: Melnick, V. L., and Dubler, N. N. (eds.), *Alzheimer's Dementia*, Humana Press, Clifton, NJ, pp. 19–39.

Schacter, D. L. (1990). Toward a cognitive neuropsychology of awareness: Implicit knowledge and anosognosia. *Journal of Clinical and Experimental Neuropsychology* **12**(1): 155–178.

Scheibel, A. (1992). A cautionary note. *Consciousness and Cognition* **1**: 169–171.

Seltzer, B., Vasterling, J. J., Mathias, C. W., and Brennan, A. (2001). Clinical and neuropsychological correlates of impaired awareness of deficits in Alzheimer disease and Parkinson disease: A comparative study. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology* **14**(2): 122–129.

Sevush, S. (1999). Relationship between denial of memory deficit and dementia severity in Alzheimer disease. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology* **12**(2): 88–94.

Sevush, S., and Leve, N. (1993). Denial of memory deficit in Alzheimer's disease. *American Journal of Psychiatry* **150**(5): 748–751.

Sisodia, S. S. (1999). Alzheimer's disease: Perspectives for the new millennium. *Journal of Clinical Investigation* **104**(9): 1169–1170.

Smith, C. A., Henderson, V. W., McCleary, C. A., Murdock, G. A., and Buckwalter, J. G. (2000). Anosognosia and Alzheimer's disease:

The role of depressive symptoms in mediating impaired insight. *Journal of Clinical and Experimental Neuropsychology* **22**(4): 437–444.

Squire, L. R., and Zouzounis, J. A. (1988). Self-ratings of memory dysfunction: Different findings in depression and amnesia. *Journal of Clinical and Experimental Neuropsychology* **10**(6): 727–738.

Starkstein, S. E., Chemerinski, E., Sabe, L., Kuzis, G., Petracca, G., Teson, A., et al. (1997a). Prospective longitudinal study of depression and anosognosia in Alzheimer's disease. *British Journal of Psychiatry* **171**: 47–52.

Starkstein, S. E., Fedoroff, J. P., Price, T. R., Leiguarda, R., and Robinson, R. G. (1992). Anosognosia in patients with cerebrovascular lesions: A study of causative factors. *Stroke*, **23**(10): 1446–1453.

Starkstein, S. E., Petracca, G., Chemerinski, E., and Kremer, J. (2001). Syndromic validity of apathy in Alzheimer's disease. *American Journal of Psychiatry* **158**(6): 872–877.

Starkstein, S. E., Sabe, L., Chemerinski, E., Jason, L., and Leiguarda, R. (1996a). Two domains of anosognosia in Alzheimer's disease. *Journal of Neurology, Neurosurgery, and Psychiatry* **61**: 485–490.

Starkstein, S. E., Sabe, L., Garcia Cuerva, A., Kuzis, G., and Leiguarda, R. (1997b). Anosognosia and procedural learning in Alzheimer's disease. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology* **10**(2): 96–101.

Starkstein, S. E., Sabe, L., Petracca, G., Chemerinski, E., Kuzis, G., Merello, M., et al. (1996b). Neuropsychological and psychiatric differences between Alzheimer's disease and Parkinson's disease with dementia. *Journal of Neurology, Neurosurgery, and Psychiatry* **61**: 381–387.

Starkstein, S. E., Vazquez, S., Migliorelli, R., Teson, A., Sabe, L., and Leiguarda, R. (1995). A single-Photon Emission Computed Tomographic study of anosognosia in Alzheimer's disease. *Archives of Neurology* **52**: 415–420.

Stuss, D. T. (1991). Disturbance of self-awareness after frontal system damage. In: Prigatano, G. P., and Schachter, D. L. (eds.), *Awareness of Deficit After Brain Injury: Clinical and Theoretical Issues*, Oxford University Press, New York, pp. 63–83.

Stuss, D. T., and Benson, D. F. (1986). *The Frontal Lobes*, Raven Press, New York.

Sunderland, A., Harris, J. E., and Baddeley, A. D. (1983). Do laboratory tests predicteveryday memory? A neuropsychological study. *Journal of Verbal Learning and Verbal Behavior* **22**: 341–357.

Tabert, M. H., Albert, S. M., Boukhova-Milov, L., Camacho, M. S., Pelton, G., Liu, X., et al. (2002). Functional deficits in patients with mild cognitive impairment. *Neurology* **58**: 758–764.

Trosset, M. W., and Kaszniak, A. W. (1996). Measures of deficit unawareness for predicted performance experiments. *Journal of the International Neuropsychological Society* **2**: 315–322.

Vanderploeg, R. D., Yuspeh, R. L., and Schinka, J. A. (2001). Differential episodic and semantic memory performance in Alzheimer's disease and vascular dementias. *Journal of the International Neuropsychological Society* **7**: 563–573.

Vasterling, J. J., Seltzer, B., Foss, J. W., and Vanderbrook, V. (1995). Unawareness of deficits in Alzheimer's disease: Domain-specific differences and disease correlates. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology* **8**(1): 26–32.

Vasterling, J. J., Seltzer, B., and Watrous, W. E. (1997). Longitudinal assessment of deficit unawareness in Alzheimer's disease. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology* **10**(3): 197–202.

Wagner, M. T., Spangenberg, K. B., Bachman, D. L., and O'Connell, P. (1997). Unawareness of cognitive deficit in Alzheimer disease and related dementias. *Alzheimer Disease and Associated Disorders* **11**(3): 125–131.

Weinstein, E. A. (1991). Anosognosia and denial of illness. In: Prigatano, G. P., and Schacter, D. L. (eds.), *Awareness of Deficit After Brain Injury: Clinical and Theoretical Issues*, Oxford University Press, New York, pp. 240–257.

Weinstein, E. A., and Kahn, R. L. (1955). Denial of illness. Springfield, IL: Charles C. Thomas.

Zanetti, O., Geroldi, C., Frisoni, G. B., Bianchetti, A., and Trabucchi, M. (1999a). Contrasting results between caregiver's report and direct assessment of activities of daily living in patients affected by mild and very mild dementia: The contribution of the caregiver's personal characteristics. *Journal of the American Geriatrics Society* **47**(2): 196–202.

Zanetti, O., Vallotti, B., Frisoni, G. B., Geroldi, C., Bianchetti, A., Pasqualetti, P., et al. (1999b). Insight in dementia: When does it occur? Evidence for a nonlinear relationship between insight and cognitive status. *Journal of Gerontology: Psychological Sciences* **54B**(2): 100–106.