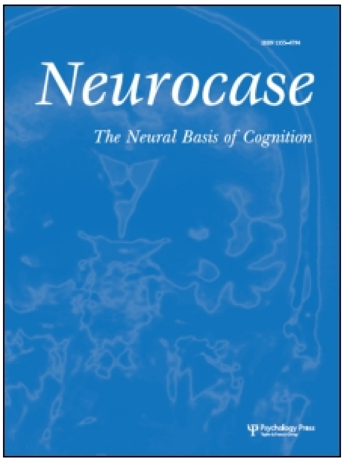

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The Cambridge Semantic Memory Test Battery: Detection of semantic deficits in semantic dementia and Alzheimer's disease

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The aims of this study were (a) to explore the utility of, and make more widely available, an updated and extended version of the Cambridge Semantic Memory test battery, and (b) to use this battery in conjunction with other tests to characterise the profile of several different forms of progressive cognitive impairment: semantic dementia (SD, $n = 15$), mild cognitive impairment (MCI, $n = 7$), established Alzheimer's disease (AD) ($n = 8$), all in comparison to normal controls ($n = 45$). The semantic battery is useful in a variety of ways for exploring the nature of semantic deficits; on its own, however, it does not provide sensitive differentiation between patients with AD and SD. An assessment including measures of episodic memory and visuospatial abilities as well as the semantic battery is recommended for good characterisation of the cognitive profiles associated with SD and AD.

Keywords: Memory; Neuropsychology; Memory disorders; Dementia; Semantic Dementia; Alzheimer's disease.

INTRODUCTION

Previously we have reported a battery of neuropsychological tests used within our clinic (e.g., Hodges, Salmon, & Butters, 1990; Hodges, Patterson, Oxbury, & Funnell, 1992a; Hodges & Patterson, 1995; Hodges et al., 1999) to assess semantic memory, episodic memory and other aspects of cognitive processing. Here, we describe the full battery of tests, including a newly devised measure of associative semantic memory (the Camel and Cactus Test), and compare the performance across different patient groups (Semantic Dementia, Mild Cognitive Impairment, and Alzheimer's disease).

The Cambridge Semantic Memory (CSM) test battery is a collection of tests that use the same set of stimulus items to assess semantic knowledge systematically across different input and output modalities. The original version consisted of 48 items, half living and half manmade, which were not well matched for familiarity or age of acquisition, factors known to have a significant influence on performance (Barry & Ellis, 1997; Funnell, 1992; Stewart, Parkin, & Hunkin, 1992). The updated battery contains 64 items representing three sub-categories of living things (*animals, birds* and *fruit*) and three sub-categories of artefacts (*household items, tools* and *vehicles*). It was not possible to create a single set of items matched across living and manmade categories for both concept familiarity and age of acquisition, so two stimulus subsets were assembled, each consisting of 16 living and 16

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non-living concepts (see Appendix A). One of these subsets was matched across the two domains for concept familiarity and the other for age of acquisition (see Garrard et al., 2001; Morrison, Chappell, & Ellis, 1997; Snodgrass & Vanderwart, 1980). The semantic memory tests on these 64 items and their sub-categories include: category fluency; picture naming (to the line drawings); word comprehension (word–picture matching); sorting by category at three levels (superordinate, basic and subordinate) for both pictures and words; and a more recently devised measure of semantic association, the Camel and Cactus Test (CCT, Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000). The CCT was designed along the principles of the Pyramids and Palm Trees test (PPT, Howard & Patterson 1992), and the PPT – despite not being based on the same items/sub-categories that are stimuli for all of the other semantic tests – was also included for comparison.

Our earlier studies (Hodges & Patterson, 1995; Hodges et al., 1999), using the original semantic memory test battery, reliably identified patients with advanced stage semantic dementia (SD). We have since been able to identify patients earlier in the course of the disease who show subtle, but definite, semantic deficits on our experimental measures. These patients have bilateral anterior temporal lobe atrophy, usually more notable on the left, and eventually progress to the typical profile as described in our earlier work (e.g., Bozeat et al., 2000; Bozeat, Lambon Ralph, Patterson, & Hodges, 2002; Hodges, Bozeat, Lambon Ralph, Patterson, & Spatt, 2000b; Lambon Ralph, McClelland, Patterson, Galton, & Hodges, 2001a; Rogers, Lambon Ralph, Hodges, & Patterson, 2003). These milder patients, however, do not always show deficits on the Pyramids and Palm Trees test or the word–picture matching task (e.g., Nestor, Fryer, & Hodges, 2006). It is in light of these findings that we devised a more difficult measure of semantic associative knowledge, the Camel and Cactus Test, which comprises the same 64 items as presented for naming and word–picture matching (see Bozeat et al., 2000) and hence 'inherits' the advantages of the basis for selection of those items (e.g., half living and half manmade, with familiarity and age-of-acquisition matching as described above). The test has two forms: in one, all items (targets and response choices) are presented as pictures; in the other form, all stimuli are words. Using a procedure similar to, but more taxing than, that in the PPT, here participants are required to choose the correct response from four same-category items (e.g., for the target camel, the four response choices are tree, sunflower, cactus (the correct response), and rose). The fact that chance level is therefore .25 (rather than .5 as in the PPT) should make this test more sensitive than its predecessor.

An important feature of the CSM battery is that knowledge of all items is assessed in both verbal and non-verbal modalities of stimulus and/or response, enabling the clinician or researcher to detect differential impairments across these domains of input/output. It is, however, important to emphasise that a non-verbal > verbal pattern of performance does not necessarily equate to a modality-specific deficit. This pattern of performance is also to be expected from an amodal, central semantic deficit on the basis of differences in the way in which objects vs. words relate to meaning (see Benedet, Patterson, Gomez-Pastor, & Luisa Garcia de la Rocha, 2006; Bozeat et al., 2000; Lambon Ralph & Howard, 2000; Patterson & Hodges, 2000). The mapping between the visual appearance of an object (either the whole form or parts of it) and its meaning is always more coherent than is the case for words, whose surface forms have an arbitrary relationship to their meanings.

We have previously published the performance of patients with Alzheimer's disease (AD) on the original semantic memory battery (Hodges & Patterson, 1995; Hodges, Salmon, & Butters, 1991; Hodges, Salmon, & Butters, 1992b; Hodges, Patterson, Graham, & Dawson, 1996; Lambon Ralph, Patterson, & Hodges, 1997) and some components of the new battery (Garrard, Lambon Ralph, Patterson, Pratt, & Hodges, 2005; Lambon Ralph et al., 2001b). Although the semantic memory impairment in AD is well documented (see for example Chertkow & Bub, 1990; as well as publications from our group), much of this research has tended to focus on the underlying cause of the deficit (e.g., 'access' vs. 'storage') rather than the stage of the disease process at which the impairment becomes detectable. Mild Cognitive Impairment (MCI) may represent the preclinical stage of early AD (Grundman et al., 2004; Petersen et al., 2001). Recent studies, however, highlight the heterogeneity in this patient population (e.g., Albert, Moss, Tanzi, & Jones, 2001; Blackwell et al., 2004; Chen et al., 2000; Chetelat et al., 2003; De Jager, Hogervorst, Combrinck, & Budge, 2003; Jack et al., 1999; Petersen et al., 1999), indicating that not all cases with MCI will go on to develop full-blown AD. It is of interest, therefore, to investigate whether patients with so-called MCI also have semantic memory deficits (e.g., Bennett et al., 2002; Bozoki, Giordani, Heidebrink, Berent, & Foster, 2001; De Jager et al., 2003; De Jager & Budge, 2005; Dudas, Clague, Thompson, Graham, & Hodges, 2005; Estévez-González et al., 2004; Lambon Ralph et al., 2003; Thompson, Graham, Patterson, Sahakian, & Hodges, 2002), when assessed on the updated CSM test battery.

It is, therefore, timely to determine whether the updated CSM test battery is sensitive to semantic deficits in MCI and AD, and to compare directly the performance of patients with MCI, AD and SD. This is a valuable goal for a variety of reasons, including the differentiation of MCI and AD from other forms of dementia early in the course of the disease. Such differential diagnoses determine appropriate information to be given to patients and their families regarding the nature and likely time-course of progression, possible genetic implications, etc; and as effective disease modifying interventions gradually become available, such early diagnosis will of course be of even greater significance.

In addition to the semantic memory measures, a general neuropsychological battery of tests was included. These measures include: short-term memory (digit span), episodic memory (story and design recall), executive function (letter fluency), and visuospatial perception. Compatible with a diagnosis of MCI or AD, previous studies have revealed episodic memory impairments in patients with MCI and AD (e.g., Dudas et al., 2005; Hodges et al., 1990, 1999; Perri, Carlesimo, Serra, & Caltagirone, 2005; Perry, Watson, & Hodges, 2000; Welsh, Butters, Hughes, Mohs, & Heyman, 1991, 1992), while patients with SD perform well on at least some measures of non-verbal episodic recall (e.g., Scahill, Hodges, & Graham, 2005). Furthermore, patients with AD, but not SD, have been shown to have deficits on measures of attention (e.g., Amieva, Phillips, Della Sala, & Henry, 2004; Perry & Hodges, 1999; Pignatti et al., 2005), visuospatial perception (e.g., Caine & Hodges, 2001; Perry et al., 2000; Ringman, 2005), and executive function (e.g., Perry & Hodges, 1999), early in the course of the disease. Therefore, in addition to exploring the nature of semantic memory in these patient groups, this study also aimed to characterise performance on more general neuropsychological measures.

In summary, the two main aims of this study were: (i), to make more fully available the updated Cambridge Semantic Memory (CSM) test battery, including a recently devised test intended to be sensitive to mild semantic impairment (the CCT); and (ii), to characterise and compare the neuropsychological profiles of different patient groups (i.e., MCI, AD, and SD).

METHODS

Participants

A total of 75 subjects took part in this study: 7 patients with a clinical diagnosis of amnestic MCI, 8 patients who had a fairly typical AD profile, 15 patients who fitted the criteria for SD, and 45 control subjects.

Controls were selected from the Medical Research Council Cognition and Brain Sciences Unit's participant panel. Twenty controls were administered the full semantic battery except for the Camel and Cactus Test (CCT) which was not yet developed at the time of this original data collection. An additional 25 controls were subsequently tested on the CCT.

The mean age range and years of education of the patient groups and the controls are shown in Table 1. Analysis revealed that the SD group was significantly younger than the AD group ($t(21) = 3.33$,

TABLE 1
The mean age at test and years of education

	MCI (range)	*AD (range)*	*SD (range)*	*Control (range)*	*Control CCTpic (range)*	*Control CCTword (range)*
Sex (F/M)	2/5	4/4	5/10	10/10	8/8	10/4
Years of education	10.7 (9–13)	10.1 (9–12)	11.07 (8–13)	11.0 (9–13)	12.7 (10–15)	12.0 (10–14)
Age at test (years)	65.4 (51–78)	72.4 (68–82)	61.4 (42–78)	68.1 (54–78)	63.6 (55–79)	61.0 (55–68)

The range is shown for each score. MCI represents mild cognitive impairment; AD represents Alzheimer's disease; SD represents semantic dementia; CCT represents Camel and Cactus Test.

p = .003). In addition, the control group who completed the picture version of the CCT had significantly more years of education relative to each of the patient groups (p < .0005–.007) and were significantly younger than the AD group ($t(22)$ = 2.82, p = .01). The control group who completed the word version of this test had significantly more years of education than the MCI ($t(19)$ = 2.16, p = .04) and AD ($t(20)$ = 3.79, p = .001) groups, and were significantly younger than the AD group ($t(20)$ = 5.77, p < .0005). In order to account for the potential impact of these differences in age at test and years of education, these variables were entered into analyses of covariance (see details in the Results section).

The patients presented to the Memory Clinic at Addenbrooke's Hospital, Cambridge where they were seen by a senior neurologist (JRH), a psychiatrist and a clinical neuropsychologist. In addition to a clinical assessment, all patients were given a number of standard psychiatric rating scales to exclude major psychiatric disorders such as depression or schizophrenia.

Patients with amnestic MCI (Grundman et al., 2004; Petersen et al., 2001) presented with complaints of poor memory with preservation of activities of daily life, both substantiated by a spouse/family member. Neuropsychological assessment (see Background Neuropsychology, Table 2) revealed impairment (≥2 *SD*s below normal) on at least one test of episodic memory but normal performance on a range of other routine tests administered in the memory clinic (Hodges et al., 2000a) and a score on the Mini-Mental State Examination (MMSE) of >24.

Patients with AD fulfilled NINCDS-ADRDA criteria (McKhann et al., 1984) and had evidence of impaired memory (see Table 2) plus deficits in at least one other cognitive domain, MMSE scores <24 (range: 19–23), and impairments in activities of daily living (based on reports from a family member).

The SD patients presented with a progressive loss of vocabulary affecting expressive and receptive language in the context of relatively fluent and phonologically correct speech production. They all fulfilled the cognitive criteria for SD previously reported (Hodges et al., 1992a; Neary et al., 1998), including marked anomia (e.g., on the Graded Naming Test, McKenna & Warrington, 1983), impairment in word comprehension (e.g., on the synonym judgement test of Warrington, McKenna & Orpwood, 1998) and impoverished semantic knowledge (e.g., on person knowledge tests, Thompson et al., 2004), with diagnosis arrived at by the consensus of a group of clinicians. Structural imaging by MRI in all cases revealed focal atrophy in one or both anterior temporal lobes.

TABLE 2

Summary of the means and standard error of the means (SEM) for the general neuropsychology assessments for each group

	MCI	*AD*	*SD*	*Control*
	Mean (SEM)	*Mean (SEM)*	*Mean (SEM)*	*Mean (SEM)*
MMSE (30)	25.6 (0.7)^{a,b}	20.9 (0.6) ^{a,d}	22.8 (1.6)^{a}	28.8 (0.2)^{b,c,d}
Digit span				
Forward	7.1 (0.3)	6.9 (0.4)	6.5 (0.3)	7.2 (0.2)
Backward	5.4 (0.4)	4.1 (0.2)	4.4 (0.4)	5.3 (0.3)
Letter fluency	34.9 (4.3)^{c}	34.3 (4.7)	19.5 (2.9)^{a,d}	41.7 (2.8)^{c}
Logical memory				
Immediate recall (24)	3.9 (0.9)^{a}	3.1 (0.7)^{a}	3.4 (0.8)^{a}	10.3 (1.0)^{b,c,d}
Delayed recall (24)	1.2 (0.4)^{a}	0.5 (0.4)^{a}	2.4 (0.8)^{a}	8.3 (0.9)^{b,c,d}
Rey Figure				
Copy (36)	32.7 (1.7)	30.2 (2.0)	32.2 (1.1)	34.0 (0.4)
Delayed recall (36)	4.6 (2.1)^{a}	1.1 (0.6)^{a,c}	14.5 (2.3)^{b}	18.4 (1.3)^{b,d}
VOSP				
Incomplete letters (20)	18.3 (0.5)	16.4 (1.5)^{a}	19.5 (0.2)	19.3 (0.2)^{b}
Object decision (20)	17.9 (0.9)	16.6 (1.1)	17.0 (0.7)	17.0 (0.5)
Dot counting (10)	9.1 (0.6)	9.8 (0.3)	10.0 (0.0)	10.0 (0.1)
Cube analysis (10)	8.6 (0.8)	7.8 (1.1)	9.2 (0.5)	9.7 (0.2)

MCI n = 7; AD n = 8, SD n = 15; Control n = 20. MCI represents mild cognitive impairment; AD represents Alzheimer's disease; SD represents semantic dementia; VOSP represents Visual Object and Space Perception battery. ^{a}, represents significant difference (with Bonferroni correction, $p \leq .008$) relative to controls; ^{b}, represents significant difference relative to AD; ^{c}, represents significant difference relative to SD; and ^{d}, represents significant difference relative to MCI.

All subjects gave informed consent to participate in the study, according to the Declaration of Helskini (BMJ 1991; 302: 1194), which was approved by the Ethical Committee of Addenbrooke's Hospital, Cambridge.

Background neuropsychology

The following battery of neuropsychological tests was administered: the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975); the digit span subtests (both forwards and backwards) of the Wechsler Memory Scale-Revised (WMS-R, Wechsler, 1987); verbal fluency for the letters F, A, S; copy and delayed recall of the Rey Complex Figure (Rey, 1941); various subtests from the Visual Object and Space Perception battery (Warrington & James, 1991); and the logical memory subtest of the Wechsler Memory Scale Revised (WMS-R, Wechsler, 1987).

Cambridge Semantic Memory Test Battery (CSM)

The following battery of tests was administered to investigate semantic memory performance. Each test (except for the Pyramids and Palm Trees test) used the same 64 items from the same six categories (animals, birds, fruits; household items, tools, and vehicles).

Category fluency

In this test, the subject is asked to produce as many exemplars as possible in one minute, for each of the six categories.

Naming

The subject is shown a line drawing of each of the 64 items and asked to produce its name.

Word-to-Picture matching

Subjects are presented with 64 picture arrays, one for each item, with each array consisting of 10 items from the same category (e.g., birds); the task is to point to the item named by the examiner. Across the arrays within one category, the target and foil items move around to different positions; furthermore, two of the 10 items in each category are never targets. These design factors prevent participants who remember their own previous choices within a category from working out subsequent correct responses by a simple process of elimination. The test sequence is consistent across subjects and is arranged so that each item is followed by an item from a different category.

Picture sorting

In this test, the subject is asked to sort pictures of the 64 items at a superordinate level, or Level 1 (*living* vs. *manmade*, maximum score 64), then into basic categories, or Level 2 (for living things: *animals* vs. *birds* vs. *fruit*; for artefacts: *household objects* vs. *tools* vs. *vehicles*, maximum score 64) and finally at subordinate level or Level 3 (for living things: *native* vs. *foreign, larger than a man* vs. *smaller than a man, meat-eating* vs. *non-meat eating*; for artefacts: *made mainly of metal* vs. *not made mainly of metal, wooden parts* vs. *no wooden parts, will fit in your pocket* vs. *will not fit in your pocket*, Level 3, maximum score 144).

Word sorting

The procedure is exactly same as above except that the participants sort cards with the written names of the items rather than pictures of them.

The Pyramids and Palm Trees Test (Howard & Patterson, 1992)

Subjects are asked to choose one of two items that is most closely associated with the target (e.g., for the target *pyramid*, the choice is between *palm tree* (the correct response choice) and *pine tree*). The stimuli are presented as either pictures or written words.

The Camel and Cactus Test (Bozeat et al., 2000)

This is a test of semantic association based on the principle of the Pyramids and Palm Trees test (Howard & Patterson, 1992). Subjects are asked to choose the correct one of four response-choice pictures or words that has an associative relationship with the target (n = 64). For example, in one of the trials the subject was asked to match the target *camel* to one of four types of vegetation: *tree*, *sunflower*, *cactus* (the correct response), or *rose*.

Statistical analysis

The data were analysed using separate analyses of variance. Age at test and amount of education were included as covariates in the analysis comparing the performance of the patients and controls on the Camel and Cactus Test. Significant main effects and simple main effects, following significant interactions, were analysed using one-way ANOVAs with corrections for multiple comparisons (Bonferroni correction). Details of the analysis are reported in Table 3.

RESULTS

Cambridge Semantic Memory Battery

Category Fluency Test

Separate one-way ANOVAs (see Table 3 and Figure 1) revealed that the control group generated significantly more items than the patient groups on both the living and manmade categories. The MCI patient group performed better than the SD group on the living and manmade categories, but only better than the AD group on the manmade category (however, these group differences did not survive Bonferroni correction, $p < .008$). The AD patient group's performance did not significantly differ from that of the SD group on either category.

Naming and word-to-picture matching

Separate one-way ANOVAs (see Table 3 and Figure 2) revealed that the SD group was significantly impaired relative to both controls and the MCI patient group on the naming task (no other group differences survived Bonferroni correction, $p < .008$). In contrast, both the SD and MCI patient groups were significantly impaired relative to controls on the word–picture matching task, with the MCI and AD patient groups performing marginally better than the SD group.

Sorting words and pictures

A previous study of semantic memory in SD from our research group reported better performance on tasks involving pictures compared to those using words (Bozeat et al., 2000), and attributed these differences to the nature of mapping between input modality and semantic memory. As noted in the Introduction, word forms have a completely arbitrary relationship with meaning, whereas object structure as revealed in pictures has a degree of systematicity with conceptual knowledge about the object, and therefore a more coherent mapping between appearance and meaning (e.g., Benedet et al., 2006; Lambon Ralph & Howard, 2000; Patterson & Hodges, 2000).

In order to investigate this issue in the current study, we analysed the category sorting data with a mixed-model ANOVA including a between-subjects factor of Group (MCI, AD, SD, control), a within-subjects factor of Modality (words, pictures) and a within-subjects factor of Level (level 1, level 2, level 3). Table 3 displays the results of this

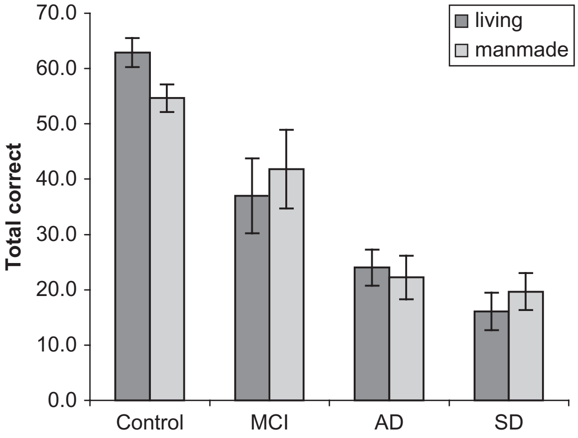

Figure 1. The mean number of correct items generated on the category fluency test for living and nonliving categories for each group. Standard errors are shown for each group. MCI represents mild cognitive impairment; AD represents Alzheimer's disease; SD represents semantic dementia.

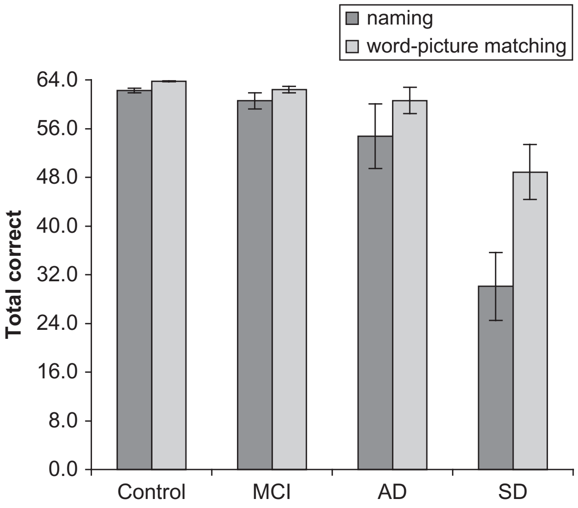

Figure 2. The mean number of correct items on the naming test and word picture matching tests (maximum = 64) for each group. Standard errors are shown for each group. MCI represents mild cognitive impairment; AD represents Alzheimer's disease; SD represents semantic dementia.

TABLE 3

Summary of the group statistical analyses for the Cambridge Semantic Memory Test Battery: Category fluency (living and manmade), and the 64-item task (naming and word–picture matching); Sorting task; Camel and Cactus Test (pictures and words), and Pyramids and Palm Trees test (pictures and words)

	F	*df*	*p-value*
Category fluency			
Living	43.18	3, 46	<.005
MCI vs. AD	3.25	1, 13	.10
MCI vs. SD	9.61	1, 20	.01
MCI vs. Control	19.31	1, 25	<.005
SD vs. AD	2.30	1, 21	.15
SD vs. Control	124.46	1, 33	<.005
AD vs. Control	71.29	1, 26	<.005
Manmade	26.82	3, 45	<.005
MCI vs. AD	6.61	1, 12	.02
MCI vs. SD	10.35	1, 19	.01
MCI vs. Control	4.73	1, 24	.04
SD vs. AD	0.23	1, 21	.64
SD vs. Control	74.13	1, 33	<.005
AD vs. Control	48.89	1, 26	<.005
64-item task			
Naming	18.48	3, 46	<.005
MCI vs. AD	1.01	1, 13	.33
MCI vs. SD	13.54	1, 20	.001
MCI vs. Control	2.66	1, 25	.12
SD vs. AD	8.3	1, 21	.01
SD vs. Control	44.75	1, 33	<.005
AD vs. Control	5.16	1, 26	.03
Word–picture matching	6.86	3, 45	.001
MCI vs. AD	0.57	1, 13	.47
MCI vs. SD	4.13	1, 20	.06
MCI vs. Control	15.29	1, 24	.001
SD vs. AD	3.36	1, 21	.08
SD vs. Control	14.07	1, 32	.001
AD vs. Control	5.2	1, 25	.03
Sorting task			
Group	5.07	3, 42	.004
MCI vs. AD	1.56	1, 12	.24
MCI vs. SD	3.39	1, 17	.08
MCI vs. Control	0.002	1, 25	.97
SD vs. AD	2.03	1, 17	.17
SD vs. Control	10.45	1, 30	.003
AD vs. Control	7.34	1, 25	.01
Level	64.98	1.83, 76.89	<.005
Modality	6.14	1, 42	.02
Group × Modality	4.45	3, 42	.008
Control pictures vs. words	5.16	1, 19	.04
MCI pictures vs. words	0.59	1, 6	.47
AD pictures vs. words	1.43	1, 6	.28
SD pictures vs. words	6	1, 11	.03
Group × Level	2.28	5.49, 76.89	.05
Level 1			
MCI vs. AD	0.96	1, 12	.35
MCI vs. SD	1.54	1, 17	.23
MCI vs. Control	2.23	1, 25	.15
SD vs. AD	0.71	1, 17	.41

(*Continued*)

TABLE 3
(*Continued*)

	F	*df*	*p-value*
SD vs. Control	6.29	1, 30	.018
AD vs. Control	9.41	1, 25	.005
Level 2			
MCI vs. AD	0.006	1, 12	.94
MCI vs. SD	3.16	1, 17	.09
MCI vs. Control	0.001	1, 25	.98
SD vs. AD	3.35	1, 17	.09
SD vs. Control	9.37	1, 30	.005
AD vs. Control	0.007	1, 25	.93
Level 3			
MCI vs. AD	2.68	1, 12	.13
MCI vs. SD	4.99	1, 17	.04
MCI vs. Control	0.27	1, 25	.61
SD vs. AD	1.70	1, 17	.21
SD vs. Control	12.96	1, 30	.001
AD vs. Control	5.99	1, 25	.02
Modality × Level	0.92	1.76, 73.84	.39
Group × Modality × Level	0.97	5.27, 73.84	.44
Pyramids and Palm Trees			
Pictures	3.15	2, 27	.06
MCI vs. AD	0.83	1, 13	.38
MCI vs. SD	5.35	1, 20	.03
SD vs. AD	2.15	1, 21	.16
Words	12.73	3, 46	<.005
MCI vs. AD	1.56	1, 13	.23
MCI vs. SD	7.17	1, 20	.01
MCI vs. Control	5.02	1, 25	.03
SD vs. AD	5.67	1, 21	.03
SD vs. Control	26.82	1, 33	<.005
AD vs. Control	14.4	1, 26	.001
Camel and Cactus Test			
Pictures			
MCI vs. AD	0.67	1, 9	.44
MCI vs. SD	6.90	1, 17	.02
MCI vs. Control	7.05	1, 19	.02
SD vs. AD	6.41	1, 16	.02
SD vs. Control	24.69	1, 26	<.005
AD vs. Control	3.93	1, 18	.06
Words			
MCI vs. AD	0.81	1, 7	.40
MCI vs. SD	7.94	1, 15	.01
MCI vs. Control	0.08	1, 16	.79
SD vs. AD	3.71	1, 14	.08
SD vs. Control	18.76	1, 23	<.005
AD vs. Control	0.012	1, 15	.92

MCI $n = 7$; AD $n = 8$, SD $n = 15$; Control $n = 20$; Camel and Cactus Control: picture $n = 16$, word $n = 14$. MCI represents mild cognitive impairment; AD represents Alzheimer's disease; SD represents semantic dementia.

analysis, and Figure 3a–c present the results (% correct between 100% and chance) for each participant group, comparing pictures and words, at each of the three levels.

Analysis revealed main effects of all three principal factors: Group, Modality (Pictures > Words) and Level (1 > 2 > 3). There was a significant Group × Level interaction, with the following results from follow-up analyses: At Level 1, two significant group differences were found, control > SD and control > AD, with the latter surviving Bonferroni correction ($p < .008$). At Level 2, the

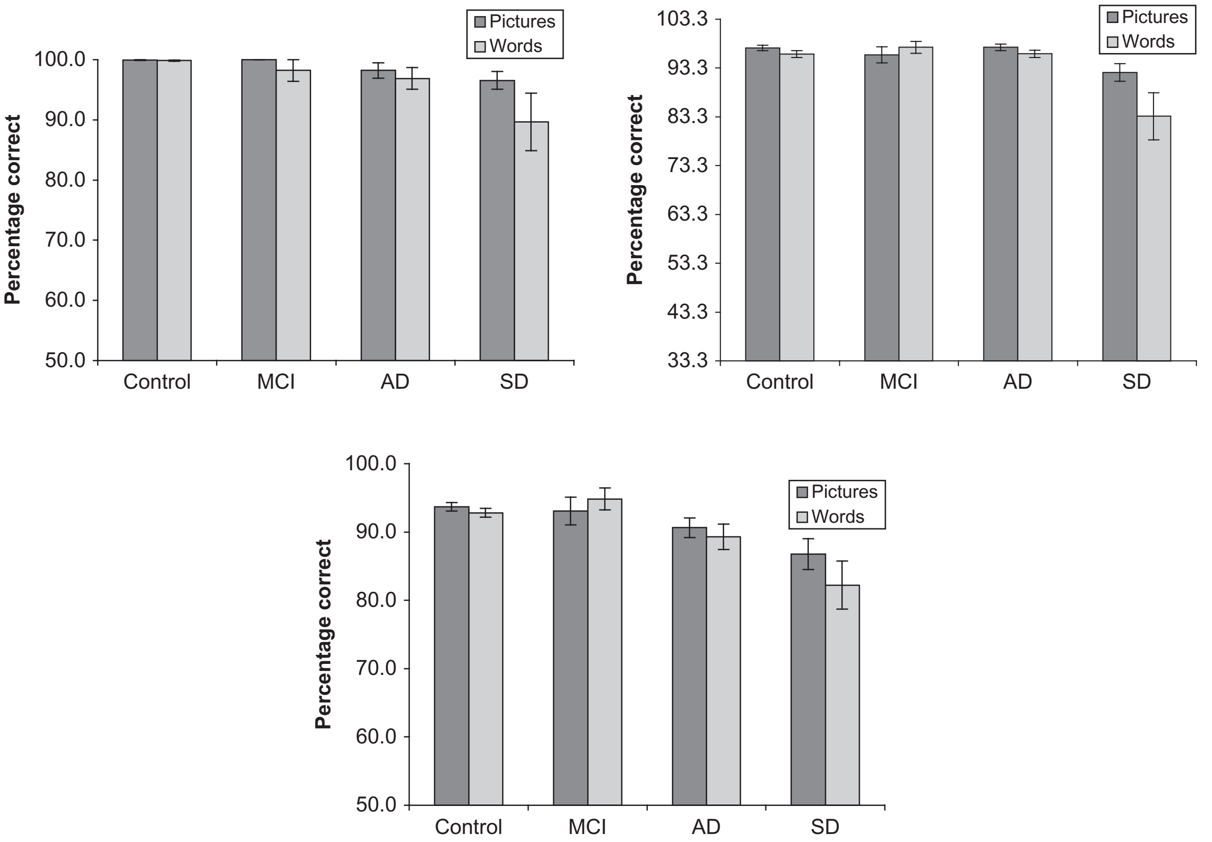

Figure 3. (a–c) The mean percentage of correct responses (between 100% and chance level) on the picture and word sorting tests for each category level: superordinate (level 1), basic (level 2) and subordinate (level 3), for each group. Standard errors are shown for each group. MCI represents mild cognitive impairment; AD represents Alzheimer's disease; SD represents semantic dementia.

only reliable significant group difference was control > SD. Level 3 engendered three group differences, control > SD, control > AD, and MCI > SD, with only the differences relative to the control group surviving Bonferonni correction. As for Modality effects, both the controls and SD patients performed better on the picture relative to the word version of the test (although neither of these survived Bonferonni correction, $p < .0125$).

The Pyramids and Palm Trees Test

As not all subjects received both versions of the task, separate one-way ANOVAs were carried out (Table 3 and Figure 4). The control group outperformed the patient groups on the word version of the task (although the control > MCI group comparison did not survive Bonferroni correction, $p < .008$). In addition, the MCI and AD patient groups performed better than the SD group (but not Bonferroni-corrected) and did not significantly differ from each other. As no age-matched control data were available for the picture version of this task, only patient group data were included in the analysis. A one-way ANOVA revealed a marginally significant Group effect, where only the MCI group performed significantly better than the SD group, although this did not survive Bonferroni correction ($p < .017$).

The Camel and Cactus Test

As with PPT data, not all subjects had been administered both versions of the task, so separate one-way ANCOVAs were conducted with the covariates of age at test and/or amount of education included (see Table 3 and Figure 5). On the word version of the task, the SD patient group were significantly impaired relative to controls, and showed a marginally significant (i.e., not Bonferroni-corrected) impairment relative to the MCI and AD patient groups.

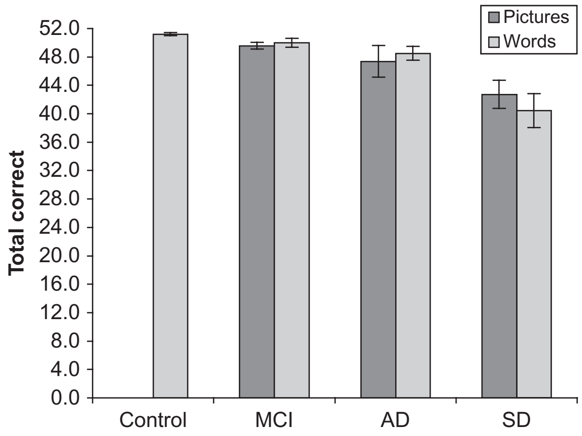

Figure 4. The mean number of correct responses on the Pyramids and Palm Trees Test for both pictures and words (maximum = 52) for each group. Standard errors are shown for each group. MCI represents mild cognitive impairment; AD represents Alzheimer's disease; SD represents semantic dementia.

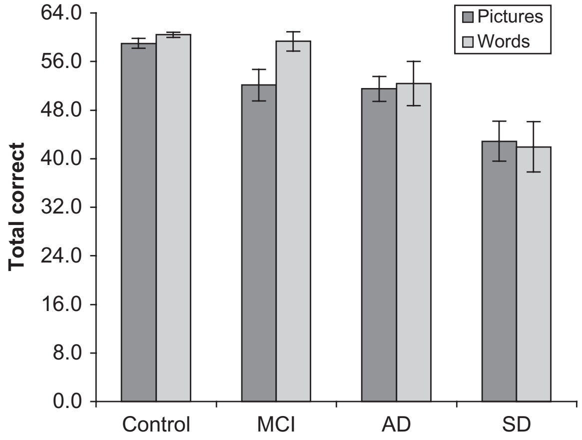

Figure 5. The mean number of correct responses on the Camel and Cactus Test for both pictures and words (maximum = 64) for each group. Standard errors are shown for each group. MCI represents mild cognitive impairment; AD represents Alzheimer's disease; SD represents semantic dementia.

For pictures, the SD patients were impaired relative to controls, while the MCI and AD patient groups showed a marginally significant impairment.

DISCUSSION

Although deficits of semantic memory as revealed by the revised CSM battery were most consistent and most prominent in the SD group, they were also measurable on a number of components of the battery in either or both of the AD and MCI groups. We would therefore not argue for sole reliance on the CSM battery if one's primary goal were to differentiate between these groups. When the semantic memory measures are considered together with episodic memory and visuo-spatial tests from the background neuropsychology assessment, however, a clearer picture emerges.

Consistent with previous studies of mild AD (Hodges et al., 1990, 1999; Perri et al., 2005; Welsh et al., 1991, 1992), the predominant deficits in both MCI and AD patients was in the domain of episodic memory, as reflected by their extremely impaired performance on delayed tests of both story recall and recall of a complex figure. Despite the differences in the severity of their disease (as measured by MMSE) the two patient groups did not significantly differ from each other on these episodic memory measures, owing to a floor effect in both groups.

The patients with SD were virtually as impaired as those with MCI or AD on tests of story recall, which is to be expected given that the ability to encode, store and retrieve a story relies on semantic as well as episodic memory. Patients with MCI and AD may have little difficulty comprehending the story content as they hear it, but show dramatic deficits in encoding and recalling any new material, a deficit associated with limbic system pathology/hypometabolism (Greene, Miles, & Hodges, 1996; Nestor, Fryer, Smielewski, & Hodges, 2003). By contrast, the SD impairment in story recall probably reflects deterioration of the semantic representations underlying language comprehension and production. In support of this proposal, the SD patients' recall of the Rey Complex Figure was better than that of the MCI and AD patients and, although numerically somewhat lower, not significantly different from that of the control group.

As demonstrated in many previous studies (e.g., Cerhan et al., 2002; Diaz, Sailor, Cheung, & Kuslansky, 2004; Hodges & Patterson, 1995; Hodges et al., 1999; Lambon Ralph et al., 2001b; Sailor, Antoine, Diaz, Kuslansky, & Kluger, 2004; Vogel, Gade, Stokholm, & Waldemar, 2005), category fluency is a sensitive (though of course not 'pure') measure of semantic memory. Here, the SD, MCI, and AD groups all generated significantly fewer correct instances than controls in both category domains. Performance on this task is thought to depend on the rapid activation of semantic knowledge of individual objects and the production of their names, plus the ability to organise a search of semantic memory and to keep track of instances already retrieved. As all three types of patients assessed here typically achieve significantly better scores on letter than category fluency (e.g., Rogers, Ivanoiu, Patterson, & Hodges, 2006), it seems unlikely that their deficits in category fluency are mainly attributable to executive dysfunction (e.g., search strategies). Given the growing evidence for attention/executive dysfunction very early in the course of AD (e.g., Amieva et al., 2004; Perry & Hodges, 1999; Pignatti et al., 2005), however, it seems likely that semantic, episodic and attention deficits all contribute to the category fluency deficit for AD and MCI seen here and in previous studies. In contrast, the category fluency deficit in SD may have a more unitary source in a central semantic memory deficit. This is consistent with the finding that the SD patient group were impaired relative to controls and both the MCI and AD patient groups on measures of picture naming, word–picture matching, and picture and word sorting.

On the sorting task, all participant groups were characterised by a pattern of superordinate ≥ basic ≥ subordinate, with the SD patients being impaired at all levels. This is consistent with previous studies investigating the degradation of conceptual knowledge in SD (Crutch & Warrington, 2008; Hodges et al., 1992; Hodges, Patterson, & Tyler, 1994; Lambon Ralph et al., 2007; Patterson & Hodges, 2000; Rogers & Patterson, 2007). Furthermore, the stronger picture > word advantage in the SD group (see Figure 3) is also predictable on the basis, described earlier, of the more systematic semantic mapping between objects and meaning than words and meaning.

The SD cases were impaired on a two-alternative forced choice test of semantic association (PPT) as well as the newer four-alternative 64-item version of this task (CCT). As mentioned in the Introduction, a few previous studies have reported that patients with mild SD are not always impaired relative to controls on the PPT (e.g., Nestor et al., 2006), but the current SD patient sample had reliably lower scores than both the control and MCI groups on both PPT and CCT. Although not reported here, additional correlation analyses confirmed that SD scores on the PPT and CCT were significantly associated with performance on the word–picture matching and the naming tasks, measures commonly reported to estimate severity of semantic degradation (Patterson et al., 2006; Woollams, Lambon Ralph, Plaut, & Patterson, 2007).

The CCT was designed (a) to extend and/or improve on the PPT by taking advantage of the features entering into choice of the 64 items used in the CSM battery (i.e., half living and half manmade objects, matched for familiarity in one subset and age of acquisition in the other, using the same items across different tasks), and (b) to be more difficult than the PPT by virtue of a chance level of performance of .25 rather than .5. It was not possible to analyse differences in the magnitude of the impairment in SD patients relative to controls in these two tasks due to the control group scoring at ceiling on the PPT; therefore the relative sensitivity of the two tasks (PPT vs. CCT) to semantic memory deficits was not directly assessed. Furthermore, although the performance of the MCI and AD patient groups indicated impairments relative to controls on the word version of the PPT but not the CCT, these findings are likely to be influenced by ceiling effects in the control group on the PPT and the inclusion of covariates in the CCT analysis (age at test, years of education). The addition of covariates also appears to account for the lack of significant impairment in the SD group compared to AD patients on the word version of the CCT (i.e., when analysed without covariates, the SD patients are impaired relative to the MCI and AD groups on both the word and picture versions of the CCT). It is possible that, with better matched samples and improved control data, the CCT might prove to be a more sensitive measure of semantic deficits, particularly early in the course of SD. It is, of course, not the only form of receptive test sensitive at an early stage (see for example the use of a synonym judgement task in Jefferies, Patterson, Jones & Lambon Ralph, 2009), but the CCT does have the advantage of being applicable in both verbal and non-verbal format.

A simple test or battery of tests that reliably differentiates MCI and AD from SD would clearly be of value to both clinical and research practice. The relatively small samples of AD and MCI cases assessed here hinders evaluation of the efficacy of the CSM battery, in combination with the background neuropsychological test battery, to classify the performance of individual patients. Instead this study suggests that, despite some semantic memory impairment in AD (e.g., Adlam, Bozeat, Arnold, Watson, & Hodges, 2006; Hodges & Patterson, 1995) and episodic memory difficulties in SD (e.g., Scahill et al., 2005), the two groups can be differentiated when measures of the two types of memory are combined with measures of visuospatial ability.

It is also of interest to note that, despite differences on some tests of episodic and semantic memory, the SD patients did not differ significantly from the MCI or AD groups on MMSE score. Together, these findings further highlight the considerable variability in the extent of neurocognitive impairment among patients with the same overall level of dementia.

In conclusion, some evidence of semantic memory impairment was observed in all patient groups, indicating that the new CSM battery, though sensitive, is not specific and cannot reliably be used *alone* to differentiate MCI and AD from SD. The profile observed across a range of tests, however, including measures of episodic memory and visuospatial abilities, provides a potentially valuable indicator of the type and stage of disease, and at least three semantic memory measures proved to be sensitive to early and subtle semantic memory deficits in both MCI and AD: the category fluency test, the word–picture matching test, and the Pyramids and Palm Trees Test. In addition, the more recently devised measure, the Camel and Cactus Test, can be added to the repertoire of receptive tests of verbal and non-verbal semantic knowledge.

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APPENDIX A

List of stimuli included in the Cambridge Semantic Memory Battery, with associated values of concept familiarity and age of acquisition

Age of Acquisition Matched Set		
Natural kinds	*Familiarity*	*Age of acquisition*
Alligator	1.65	2.95
Camel	2.08	2.75
Chicken	2.42	2.80
Duck	2.75	1.95
Eagle	2.42	3.20
Elephant	2.35	2.05
Kangaroo	1.92	3.05
Monkey	2.58	2.40
Ostrich	1.52	3.80
Owl	2.22	2.45
Peacock	2.05	3.60
Penguin	1.70	3.05
Rhinoceros	1.52	3.30
Swan	1.97	2.50
Tiger	2.10	2.10
Turtle	2.40	3.40
Mean	**2.1**	**2.83**
Artefacts	*Familiarity*	*Age of acquisition*
Axe	2.28	2.95
Brush	3.80	2.30
Candle	3.08	2.80
Comb	4.52	2.10
Envelope	4.12	3.45
Glass	4.78	2.35
Hammer	3.48	2.45
Key	4.85	2.35
Paintbrush	2.78	2.50
Pliers	3.38	4.35
Plug	4.18	2.70
Saw	2.92	2.55
Scissors	3.98	2.65
Screwdriver	3.42	3.45
Spanner	2.72	4.75
Toothbrush	4.62	2.15
Mean	**3.68**	**2.87**

Familiarity Matched Set		
Natural kinds	*Familiarity*	*Age of acquisition*
Apple	3.98	1.70
Banana	3.65	1.80
Cat	4.22	1.50
Cherry	3.38	2.80
Cow	2.42	1.95
Dog	4.60	1.50
Frog	2.48	2.48
Horse	3.55	1.85
Mouse	2.45	2.05
Orange	3.34	1.85
Pear	3.55	2.05
Pineapple	2.95	3.05
Rabbit	2.95	1.85
Squirrel	3.82	2.65
Strawberry	3.32	2.55
Tomato	3.78	2.25
Mean	**3.40**	**2.10**
Artefacts	*Familiarity*	*Age of acquisition*
Aeroplane	3.78	2.30
Barrel	2.02	3.80
Basket	2.18	2.65
Bicycle	3.78	2.40
Bus	4.50	2.20
Dustbin	4.08	–
Helicopter	2.55	3.00
Lorry	4.02	2.65
Motorbike	3.25	3.00
Piano	3.42	2.15
Sledge	2.80	3.10
Stool	3.08	2.35
Suitcase	3.65	3.65
Toaster	4.08	3.45
Train	4.15	4.90
Watering can	2.72	–
Mean	**3.38**	**2.97**