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Re-acquisition of person knowledge in semantic memory disorders

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Semantic memory impairment, from either non-progressive or neurodegenerative brain injury, has a significant impact on day-to-day functioning. Few studies have investigated the best methods for supporting relearning of new semantic knowledge in semantically-impaired individuals, even though these investigations also provide an opportunity to explore how the hippocampal and temporal neocortical systems interact in the acquisition of semantic facts. In the current study, four participants (three who had suffered from herpes simplex viral encephalitis and one with a diagnosis of semantic dementia) were asked to learn new facts about famous people using mnemonic and errorless learning paradigms. Home practice was also encouraged. Training resulted in significant improvements to all participants' naming of the individual and recall of a semantic fact about the famous person. Learning was maintained when home practice ceased. Learning also generalised to naming of a different photograph in three individuals, although generalisation of naming to a different semantic fact was less robust. This study confirms that errorless learning paradigms can be used to help boost naming and semantic knowledge in semantically-impaired individuals. This finding supports theoretical accounts in which different temporal structures are capable of supporting acquisition of new

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semantic facts independently, albeit less efficiently than when both systems are available.

Keywords: Semantic memory; Errorless learning.

INTRODUCTION

Memory impairments are common sequelae of brain injury, causing significant distress and social isolation to patients and their families. While deficits in episodic memory, our ability to encode and retrieve events from the past, is the most common type of memory impaired, patients can also show striking difficulties with semantic memory, our conceptual knowledge about the world. The former is typically associated with damage to structures in the medial temporal lobe, including the hippocampus, perirhinal and entorhinal cortices (Hannula, Tranel, & Cohen, 2006; Holdstock, Mayes, Gong, Roberts, & Kapur, 2005; Lee et al., 2005; Mayes et al., 2004; Yonelinas, 2001), while semantic memory is most often affected after damage to structures within the anterior-lateral temporal neocortex, particularly when involving both hemispheres (Gainotti, 2007; Griffith et al., 2006; Jefferies & Lambon-Ralph, 2006; Levy, Bayley, & Squire, 2004; Rogers et al., 2004; Rogers, Hocking, Mechelli, Patterson, & Price, 2005; Rogers et al., in press; Snowden, Goulding, & Neary, 1989; Thompson et al., 2004; Wilson, 1997). Viral encephalitic illnesses often affect both these brain regions, and therefore some individuals show severe deficits in both episodic and semantic memory after recovering from the initial infection (Hokkanen, Salonen, & Launes, 1996; Kapur, Katifi, el-Zawawi, Sedgwick, & Barker, 1994; Lambon Ralph, Lowe, & Rogers, 2007; Noppeney et al., 2007). In other conditions, such as the neurodegenerative disease, semantic dementia, the predominant cognitive symptom is a progressive deterioration of semantic memory, including loss of knowledge about word meanings, objects, famous people and semantic facts (Hodges, Patterson, Oxbury, & Funnell, 1992; Patterson et al., 2006; Snowden & Neary, 2002; Snowden, Thompson, & Neary, 2004; Thompson et al., 2004). By contrast, day-to-day and visual memory is typically much better preserved (Graham, Simons, Pratt, Patterson, & Hodges, 2000; Graham & Hodges, 1997; Lee, Rahman, Hodges, Sahakian, & Graham, 2003), a pattern that has led some researchers to ask whether such individuals are capable of relearning previously known, but now degraded, semantic information (Graham, Patterson, Pratt, & Hodges, 1999; Snowden & Neary, 2002).

There are anecdotal reports that seem to imply semantic learning in semantic dementia. For example, Snowden and Neary (2002) report one patient who learned the names of potential buyers during a house sale, only to forget this information once the sale had been completed. The first systematic investigation of this issue was a single-case study by Funnell (1995): the patient was able to reacquire the names of six vegetables (names that she would have easily produced prior to the onset of her illness) when she practised with names and written descriptions. Graham and colleagues (1999) used daily practice of words and pictures to test whether a case, DM, would show improved performance on category fluency tasks after training. After two weeks practice, DM performed similarly to control participants on the category fluency task, despite being unable to produce virtually any exemplars prior to training. DM also showed evidence of improved word production on other tasks, such as naming, but not on measures of comprehension such as word-picture matching (Graham, Patterson, Pratt, & Hodges, 2001). DM's improved performance was specific to the items he practised, and even more strikingly, his word production showed a remarkable adherence to the order in which he had practised the items during the two weeks, a pattern the authors interpreted as evidence of rote learning. Once DM stopped practising, performance dropped to just above baseline levels, indicating that the improvements seen in word production could not be maintained without continued training.

Snowden and Neary (2002) reported the findings of retraining in two patients with semantic dementia. The first participant was able to relearn picture names with repeated presentation under errorless learning conditions, with better learning evident when she possessed some residual knowledge about those stimuli. Learning was maintained over a two-week period, but declined by four weeks. A second semantic dementia patient also successfully reacquired vocabulary, learning that was facilitated by the incorporation of personal experiences with the trained stimuli to help with training. Interestingly, her learning was extremely context dependent: performance deteriorated when learning was assessed in a randomised, non-trained order, a pattern similar to that implied by DM's structured and inflexible approach to category fluency (Graham et al., 1999). In a more recent study, focusing on naming, Jokel and colleagues (Jokel, Rochon, & Leonard, 2006) replicated the findings of previous studies showing improvements in naming in a single case of semantic dementia (AK) after practice with pictures, names and personal and general semantic information about objects. Interestingly, Jokel et al. also contrasted learning for concepts for which AK had partial knowledge prior to training, compared to those items that she could not name or comprehend. Providing empirical support for anecdotal reports in previous papers, AK seemed to show better production at all tested time points for those items she could still comprehend, a pattern that implies that residual semantic knowledge about concepts may be beneficial when participants are required to integrate new semantic information with pre-existing concepts.

These studies imply that while semantic learning is possible after loss of conceptual knowledge it comes with certain limitations. In most patients, learning was quite rapid, but it was also context-dependent and required regular input or practice, otherwise performance declined quickly. Residual semantic knowledge about the items, or alternatively regular interaction or experience with these stimuli, seemed beneficial (Graham, Lambon Ralph, & Hodges, 1997; Snowden, Griffiths, & Neary, 1994; Westmacott, Black, Freedman, & Moscovitch, 2004), as was a structured practice order, with a rich and varied set of material that resulted in the co-activation of semantic and phonological representations. That said, even these did not typically result in generalisation across stimuli and vocabulary. Although not rigorously tested in the three published papers, the most effective method seemed to be an errorless learning strategy, a type of rehabilitation that has been used successfully in amnesic individuals (Baddeley & Wilson, 1994; Evans et al., 2000; Hunkin, Squires, Parkin, & Tidy, 1998; Page, Wilson, Sheil, Carter, & Norris, 2006; Squires, Hunkin, & Parkin, 1997; Tailby & Haslam, 2003; Wilson, Baddeley, Evans, & Sheil, 1994), aged populations (Kessels & De Haan, 2003, although see Anderson & Craik, 2006), aphasic cases (Fillingham, Hodgson, Sage, Lambon Ralph, 2003; Fillingham, Sage, & Lambon Ralph, 2006) and in Alzheimer's disease (Clare, Wilson, Breen, & Hodges, 1999; Clare et al., 2000; Clare, Wilson, Carter, Roth, & Hodges, 2002; Haslam, Gilroy, Black, & Beesley, 2006; Metzler-Baddeley & Snowden, 2005; Ruis & Kessels, 2005). To explain the pattern of learning seen in semantic dementia, in which knowledge seems so context-bound and reliant upon repeated practice, it has been suggested that remaining functionality in hippocampal structures, which are less affected early in the disease, support the reacquisition of forgotten semantic facts, although it remains to be explained why learning – while rapid – still seems abnormal compared to that seen in normal healthy control individuals.

While there is a significant literature on the nature of the episodic memory impairment in individuals with non-progressive memory difficulties, there is less documented on the ability of these patients to acquire or relearn new semantic information or associations, although early suggestions were that this was typically poor (Baddeley, 1984; Cermack & O'Connor, 1983; Gabrieli, Cohen, & Corkin, 1988; Rozin, 1976; Verfaellie, Reiss, & Roth, 1995). For example, Gabrieli and colleagues (1988) found no evidence of vocabulary learning in amnesic patients (see also Dopkins, Kovner, & Goldmeier, 1990); and when there is evidence of some learning (associating a coloured pen with a new verbal label), it rarely generalises beyond the studied item (Grossman & Carey, 1987).

When individuals do acquire new memories, the mechanisms by which this occurs and the neuroanatomical structures that support such learning are hotly debated, with most researchers concluding that the methods used to encourage new learning are critically important (e.g., the use of an errorless approach, Anderson & Craik, 2006; Tailby & Haslam, 2003; Wilson et al., 1994). In addition, better learning is typically seen in participants with some residual episodic capacity, in particular individuals with preservation of familiarity-based memory (Baddeley, Vargha-Khadem, & Mishkin, 2001; Bayley & Squire, 2002). For example, recent studies in patients with developmental amnesia, who have hippocampal damage after hypoxic-ischaemic episodes early in life, show relative sparing of semantic and recognition memory in the context of significant impairments in delayed recall tasks (Baddeley et al., 2001; Gadian et al., 2000; Mishkin, Vargha-Khadem, & Gadian, 1998; Vargha-Khadem et al., 1997). These individuals typically develop good language skills and appear to acquire new factual information about the world (Baddeley et al., 2001; Vargha-Khadem et al., 1997). In a systematic investigation of semantic learning in one developmental case (Jon), Baddeley and colleagues (2001) demonstrated learning of novel information presented via newsreels, even when measured using free recall. Thus, in contrast to semantic dementia patients, learning in these developmental amnesia patients suggests that semantic material can be acquired independently of the hippocampus, especially when individuals have relative preservation of non-hippocampal medial temporal lobe structures that might support aspects of familiarity-based memory, such as item or recognition memory (Baddeley et al., 2001; McKenna & Gerhand, 2002). Furthermore, this semantic information seems relatively detailed, is available for flexible use, and is not necessarily significantly different from that seen in age-matched control participants.

Critically, however, even profound episodic memory loss, encompassing all types of episodic memory (i.e., both recall and recognition), does not seem to completely preclude the acquisition of new semantic information (Bayley & Squire, 2002; Hamann & Squire, 1995; Kitchener, Hodges, & McCarthy, 1998; O'Kane, Kensinger, & Corkin, 2004; Shotko et al., 2004; Van der Linden, Meulemans, & Lorrain, 1994; Van der Linden et al., 2001; Verfaellie & O'Connor, 2000). For example, two recent studies in the profoundly amnesic patient, HM, reported semantic learning about people who had become famous since his injury (O'Kane et al., 2004) and on a crossword puzzle task (Shotko et al., 2004). Similarly, Kitchener, and colleagues (1998) reported a single case who was densely amnesic but who showed some knowledge of post-morbid famous people, public events and new vocabulary, although this was most typically seen on tasks of recognition (familiarity judgement) rather than on identification and naming. Westmacott and Moscovitch (2001; see in addition Bayley & Squire, 2002) also documented acquisition of new factual information in densely amnesic individuals, although like Kitchener et al.'s case, learning was typically inflexible, implicit (not easily available for conscious recollection) and slow. Even when studies utilise errorless learning, in which the production of errors during learning trials is minimised (Baddeley & Wilson, 1994; Clare et al., 1999; Fillingham et al., 2003; Theone & Glisky, 1995), learning is clearly abnormal. A large number of learning trials are required and the information learnt by the participant is generally hyper-specific, in the sense that small changes to retrieval questions results in a drop in performance (Bayley & Squire, 2002; Stark, Stark, & Gordon, 2005). Notably, however, introduction of variability within a semantic re-learning paradigm, such as the use of a set of semantically similar sentences in which a non-essential component of the sentence is varied (e.g., a verb), can facilitate semantic learning, helping an amnesic individual learn at a more conceptual level (Stark et al., 2005). These findings have been interpreted as evidence that temporal neocortical structures, with absent or reduced support from the medial temporal lobe, can, with sufficient repetition, support new learning, but that this occurs in a nonconscious manner, rather akin to perceptual learning (Bayley & Squire, 2002). The learning is highly context-dependent, rather similar to that seen in semantic dementia, and affected by changes between study and test.

Learning is also typically much better for items about which the individual still possesses some semantic knowledge. For example, Swales and Johnson (1992) investigated naming and the ability to retrieve semantic facts about concepts (e.g., Trafalgar Square and the term "Yuppie") in a semantically impaired participant recovering from herpes simplex viral encephalitis (HSVE). Rehearsal of picture–name pairs, plus information about the items, improved picture naming and the provision of correct pieces of information, with learning facilitated when the patient possessed residual knowledge about the stimuli being presented. The authors propose that the retraining – which had particularly benefited previously known semantic information – boosted access to information that was still at least partially available (see also McKenna & Gerhand, 2002). Similarly, Francis and colleagues report that NE, a young woman with prosopagnosia and a loss of factual knowledge about famous people secondary to HSVE (Francis, Riddoch, & Humphreys, 2002), was able to relearn semantic knowledge for previously familiar people with presentation of the face, facts and name of the person. Learning was maintained after a week without practice and learning generalised to different photographs of the same person (Francis et al., 2002). In this case, learning of new semantic information about previously unfamiliar people was also successful.

In summary, therefore, studies in semantic dementia and amnesic individuals with non-progressive disorders indicate that rapid and flexible learning of new semantic facts is dependent upon interactions between structures in the medial temporal lobe and temporal neocortex. Interestingly, damage to either of these structures typically results in a common profile of performance: learning that is inflexible, highly context-dependent and rarely generalisable across semantic exemplars or categories. The only exception to this pattern, to date, are cases with developmental amnesia and relatively selective involvement to the hippocampus, that show evidence of familiarity-based learning that can be used in a more flexible manner (Mishkin et al., 1998). What does seem to differ across groups with involvement of different temporal lobe structures is the rate of learning: preservation or residual functioning of medial temporal lobe structures, as seen in semantic dementia, seems to support faster learning and the acquisition of information that is sufficient to support conscious retrieval. By contrast, complete damage to medial temporal lobe structures results in laborious learning that seems more implicit in nature (Bayley & Squire, 2002).

The conclusions that can be drawn about semantic relearning are somewhat limited by the lack of studies that contrast learning across a series of individuals, and that use the same paradigm to compare patients with damage to different brain regions implicated in new learning. Furthermore, little is known about the best paradigm to boost new semantic learning, to maintain access to newly acquired information over time, and to support generalisation. In the current study, four participants with different degrees of semantic impairment were trained on knowledge of famous people. Three of the subjects had survived HSVE but were left with both episodic and semantic memory impairment. The remaining subject was at a relatively early stage of semantic dementia, with degraded knowledge about common objects and especially about famous people, in the context of less impairment to episodic memory, particularly visual recognition memory. Our aim was to investigate the characteristics of relearning of semantic material in these memory-impaired individuals, as well determining whether similar profiles of learning – as implied by the literature on this topic – would be evident across diseases.

METHOD

Participants

The four participants (RFR, VO, FC and DD) were patients at the Memory Clinic, Addenbrooke's Hospital, Cambridge or the Oliver Zangwill Centre, a regional neurorehabilitation centre. All participants were seen by a neurologist prior to inclusion in the study, and a standard neuropsychological battery was given to each subject to determine their degree of memory impairment, and to screen for other cognitive problems, such as attentional or executive difficulties, that might interfere with learning (see Table 1, and below). All patients were also administered a series of people knowledge

TABLE 1
Performance of four subjects on standardised neuropsychological tests and people knowledge tasks

	RFR	*VO*	*FC*	*DD*
General cognitive				
ACE-R (100)	69	87	66	68
NART-R FSIQ	122	111	98	94
WAIS Digit Span (30)	20	14	13	16
WAIS Similarities (33)	23	18	7	19
WAIS Digit Sym (133)	61	**27**	n.t.	n.t.
Episodic memory				
RMT Words (50)	**31**	**38**	n.t.	44
RMT Faces (50)	**32**	**32**	**25**	**30**
D&P people (36)	**0**	**22**	**15**	22
D&P doors (24)	**2**	**16**	**1**	15
D&P names (24)	**12**	**12**	**3**	**11**
D&P shapes (36)	**7**	**19**	**4**	**18**
WMS3 LM1 (75)	29	39	**15**	44
WMS3 LM2 (50)	**0**	20	**0**	**11**
WMS3 VR1 (104)	**38**	93	**24**	n.t.
WMS3 VR2 (104)	**0**	**27**	**0**	n.t.
Semantic memory				
Pyramids and Palm Trees (52)	49	**48**	**45**	**47**
GNT (30)	22	**9**	**9**	**3**
Category Fluency	15	17	12	**13**
People Knowledge Tests				
People Fluency	12	5	9	4
Graded Faces Test (30)	8	**0**	3	3
Name Face Matching (48)	**21**	**4**	**20**	**16**
Association Names (48)	**19**	**33**	n.t.	n.t.
Association Faces (48)	**19**	**Refused**	**24**	**24**
Perception				
Benton Face Recognition (54)	45	42	42	42
VOSP Cube Analysis (10)	10	10	10	10
VOSP Object Decision (20)	17	19	17	19
Executive				
Verbal Fluency	55	37	25	43
TMT part A (secs)	**150**	37	n.t.	62
TMT part B (secs)	**178**	42	n.t.	46
BADS key search	n.t.	**16**	**11**	**7**
BADS zoo map	n.t.	**12**	**8**	**7**
BADS six elements	n.t.	**6**	**1**	n.t.

Bold indicates impairment according to published norms for standardised tests or according to a cut off of more than two standard deviations below the control mean. Addenbrookes Cognitive Examination–Revised (Mioshi, Dawson, Mitchell, Arnold, & Hodges, 2006), NART-R = National Adult Reading Test–Revised (Nelson, 1991), WAIS = Wechsler Adult Intelligence Scale

(Continued on next page)

(Wechsler, 1981, 1997a), Digit Sym = Digit Symbol subtest from WAIS3, VOSP = Visual Object and Space Perception Battery (Warrington & James, 1991), RMT = Recognition Memory Test (Warrington, 1984), D&P = Doors and People (Baddeley, Emslie, & Nimmo-Smith, 1994), LM = Logical Memory subtest Wechsler Memory Scale–Third Edition (Wechsler, 1997b), VR = Visual Reproduction subtest from WMS3, GNT = Graded Naming Test (McKenna & Warrington, 1983), Name–Face Matching, Association Names and Faces see Thompson et al. (2004), TMT = Trail Making Test (Reitan & Wolfson, 1985), BADS = Behavioural Assessment of the Dysexecutive Syndrome (Wilson, Alderman, Burgess, Emslie, & Evans, 1996), n.t. = not tested. Note: VO, FC and DD were assessed on the WAIS– 3rd Edition. RFR was tested on the WAIS–Revised. RFR's verbal fluency score was taken from McCarthy et al. (2005).

tasks to provide potential items for retraining. This battery is described in detail in the Stimulus Materials section below.

RFR was a 73-year-old, right-handed male who contracted HSVE in 1985. MRI and CT showed evidence of bilateral medial temporal lobe lesions and very severe damage bilaterally to the hippocampal complex (see Figure 1a). There was also extensive damage throughout the anterior and lateral regions of the right temporal lobe. The left anterolateral temporal cortex was relatively spared (McCarthy, Kopelman, & Warrington, 2005). A retired police officer, RFR's premorbid level of intellectual functioning was estimated to have been in the superior range. Neuropsychological testing was conducted on a number of occasions 4, 17 and 18 years post-illness (reported in McCarthy et al., 2005). As can be seen in Table 1, which shows testing across these time periods, episodic memory was severely impaired, regardless of the type of task or method of testing, with semantic memory much less affected. Executive, intellectual and naming abilities were satisfactory. Perceptual skills, including basic face perception, were also intact.

VO was a 45-year-old woman who had contracted HSVE in May 2004. MRI at the time of this study, 2 years post-illness, indicated extensive right anteromedial temporal lobe injury including damage to the entorhinal and perirhinal cortices, amygdala and hippocampus (see Figure 1b). The damage extended posteriorly, but with some intact posterior-inferior temporal lobe. There was also damage to the left anteromedial temporal lobe including the perirhinal cortex, with some involvement of the fusiform gyrus. The left hippocampus appeared relatively intact along the anterior posterior axis. Neuropsychological review was conducted at 6 and 14 months post-illness, with data from both assessments reported in Table 1. Prior to her illness, VO worked as a school nurse and her premorbid level of function was estimated to have been in the high average range. Formal assessment indicated an episodic memory impairment that was more marked for non-verbal material. Semantic memory was also affected, with subjective report of poor recognition and knowledge of previously familiar and famous people. Executive skills and attention were relatively preserved.

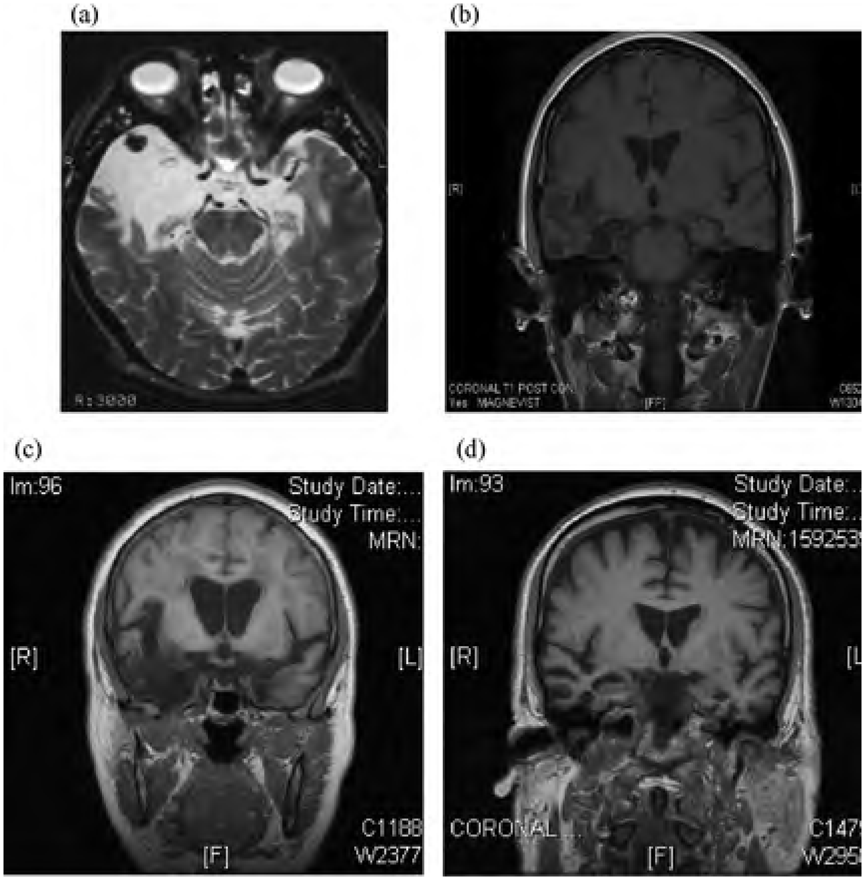

Figure 1. MRI scans for four subjects (a) RFR, (b) VO, (c) FC (d) DD.

FC was a 61-year-old woman who contracted HSVE in December 2003. MRI conducted three years after her illness indicated extensive right anterior, lateral and inferior temporal lobe volume loss which extended to and involved both the amygdala and hippocampus. On the left, there was medial temporal lobe loss which involved the amygdala; although the left hippocampus was not entirely normal, there was relative preservation of this structure, particularly the posterior aspect (see Figure 1c). FC had previously worked in accounts and in traffic control at a local school. Her premorbid level of function was estimated to have been in the average range. Neuropsychological assessment six months post-illness indicated a severe episodic memory impairment for both verbal and non-verbal material (see Table 1). Semantic memory was also somewhat reduced. Although executive abilities were weaker than was likely for her premorbid level of functioning, attention and general intellectual skills remained satisfactory.

DD was a 63-year-old male diagnosed with semantic dementia. MRI at the time of the training programme, four years post-diagnosis, showed bilateral temporal lobe atrophy (see Figure 1d). On the right there was involvement of the entorhinal and perirhinal cortices, which extended into the inferior and middle temporal lobe gyri. The fusiform face area appeared abnormal. There was evidence of right hippocampal volume loss, in addition to some involvement of the amygdala. The right hippocampus was not as markedly involved as other temporal lobe structures. On the left there was evidence of mild to moderate temporal lobe atrophy, including the perirhinal cortex and fusiform gyrus. Damage extended into the hippocampus and amygdala, although these structures were relatively well preserved, particularly posteriorly. DD had worked as a teacher; his premorbid level of intellectual functioning was estimated by the National Adult Reading Test (NART' Nelson, 1991) to have been in the average range, although reading of words with atypical spelling–sound correspondences is perhaps not the best measure of premorbid intelligence in SD (Patterson et al., 2006). Neuropsychological assessment conducted over a period of three and four years after his diagnosis, shown in Table 1, indicated impaired episodic memory for non-verbal material. In contrast, immediate verbal memory was generally intact although this material was forgotten over time. Semantic memory, naming and aspects of executive functioning were poor. Perception was satisfactory.

Stimulus materials

All participants were administered a series of tasks tapping knowledge of famous people, including (1) category fluency, in which the subject was required to generate as many exemplars from each of four categories (politicians/statesmen, actors/television personalities, musicians and sportsmen) as possible in one minute; (2) a confrontation face naming test of graded difficulty (Thompson et al., 2004); (3) a name–face matching test in which the participant was asked to indicate which of 10 pictures of famous people matched a spoken name (Thompson et al., 2004); and (4) two association tests, given in both a face and name format, in which the individual had to choose which one of two people (e.g., Bill Clinton vs. Anthony Hopkins) was associated with another famous person, such as Tony Blair (Thompson et al., 2004).

On the basis of the overall performance of the four participants on these five tasks (scores are provided in Table 1), 10 training stimuli – all very well-known people in the UK – were selected (see Table 2). To ensure that performance could be directly compared across the four subjects, the same cohort of people was selected: Margaret Thatcher, Terry Wogan,

TABLE 2
Performance on five person knowledge tasks for target stimuli

	RFR	*FC*	*VO*	*DD**
Strong knowledge				
Margaret Thatcher	3 (GFT, AN, AF)	4 (GFT, NFM, AN, AF)	3 (CF, NFM category, AN)	3 (CF, GFT, AF)
Terry Wogan	3 (NFM, AN, AF)	2 (GFT category NFM)	2 (AN, NFM category)	0
Partial knowledge				
George Best	1 (NFM)	1 (AF)	2 (NFM category, AN)	1 (AF)
Sebastian Coe	1 (AF)	1 (NFM)	2 (AN, NFM category)	1 (AF)
John Lennon	2 (GFT, AF)	1 (AF)	2 (NFM Category, AN)	1 (NFM)
Elizabeth Taylor	3 (GFT, NFM, AF)	2 (AF, GFT Category)	1 (AN)	1 (GFT category)
Weak knowledge				
Tony Blair	0	1 (GFT Category)	1 (GFT Category)	3 (CF, GFT, NFM)
Camilla Parker-Bowles	2 (NFM, AF)	0	0	0
Dawn French	0	0	0	1 (NFM)
Tim Henman	0	0	1 (NFM Category)	0

GFT = Graded Faces Test (Thompson et al., 2004), AN = Association Names (Thompson et al., 2004), AF = Association Faces (Thompson et al., 2004), NFM = Name–Face Matching Task (Thompson et al., 2004), CF = category fluency task, Category = the subject was able to produce the correct category for the stimulus, e.g., "actor", "sports person", etc. *DD had strong knowledge for Tony Blair and weak knowledge for Terry Wogan.

George Best, Sebastian Coe, John Lennon, Elizabeth Taylor, Tony Blair, Camilla Parker-Bowles, Dawn French and Tim Henman. Furthermore, in order to assess the impact of residual semantic knowledge on relearning, and based on the participants' performance on these tests, we chose four items with weak knowledge, four items with partial knowledge and two items with strong knowledge. As shown in Table 2, strong items were most often correctly named or selected, while weak stimuli were rarely identified or named. Strong items were included as a positive boost to the participants during retraining on items that were no longer as familiar to them. Partial items, considered to have residual semantic knowledge, were named or correctly selected at a level in between that of strong and weak stimuli. While the 10 items used in the training set were identical for all four participants and the division of these 10 items into strong, partial and weak semantic knowledge was the same across the three HSVE participants, it should be noted that there was a swap of two items for case DD (Tony Blair and Terry Wogan).

The stimuli presented during training were black and white photographs of the 10 famous people. In addition, the person's name and a true semantic fact about this individual derived from the Internet and based upon the fame of the person were provided (e.g., Tony Blair - Longest serving Labour Prime Minister). Appendix 1 lists the semantic facts used for each stimulus.

Procedure

Training was conducted using a combination of three methods: a mnemonic, vanishing cues and expanded rehearsal. This combination of techniques was selected as it has been shown to be successful in previous single-case studies involving retraining of people knowledge (Francis et al., 2002; Clare et al., 1999). At the beginning of the training session, the participant was presented with the photograph, the name and the semantic fact. A mnemonic was then generated with the subject, incorporating the name and semantic information. The mnemonic was based on a prominent facial feature of the person, as recommended by Francis and colleagues (2002). Further encoding of the stimulus then took place using the vanishing cues paradigm. The photograph was presented together with the name and semantic fact (in written format). Each word of the fact was then removed, followed by a letter of the name. At each point, the subject had to repeat the name and semantic fact with less information than at the preceding point. Subjects were explicitly told not to guess if they did not know. If a "Don't know" response was given, the previous step that contained additional information was presented again until no errors were made. Once the subject was able to state the name and fact with only the presentation of the photograph, expanded rehearsal was undertaken to consolidate this learning. The photograph, name and fact were removed and re-presented after an interval of 10 seconds with the instructions, "What is his/her name?" and "What is he/she famous for?" If the correct response was provided, the interval between removal of the photograph and testing of recall was increased with presentations made at 20, 40, 90 and 180 seconds. Again subjects were told not to guess if they did not know the answer. If a "Don't know" response was given, the interval was halved until a correct response was made. Criterion for success was set at correct recall of the name and fact at five minutes at which point training on the stimulus was stopped.

Recall of the names and semantic facts for all 10 items was assessed at the beginning of each training session (held once weekly), prior to further exposure to any additional failed items (items correctly named during testing were not further trained). Recall of names and facts was also tested prior to the generalisation session, undertaken two weeks after the completion of training, in order to provide a final score for learning as a comparison to generalisation performance. Naming and semantic fact retrieval was tested by presenting the set of 10 photographs one by one and asking the subject the same questions used during training, (e.g., “What is his/her name?” and “What is he/she famous for?”). Participants were told not to guess if they did not know. If free recall was unsuccessful, the subject was provided with the person’s initials and/or the category. For example, “The person’s initials are TB” and/or “He is a politician” for Tony Blair. One or two stimuli were trained at each session until the participant was able to learn all 10 items and produce the name and semantic fact related to each person. The same order of presentation was used for each participant. Daily home practice was conducted between sessions using photographs of the stimuli that the participants had successfully learned in the previous session(s). Carers were advised to present the photograph with the training instructions, such that if a “Don’t know” response was given, the subject was provided with the person’s initials and category. If the participant was still unable to provide an appropriate response, the correct name and semantic fact were provided.

At the completion of training, generalisation was assessed via three tasks presented in the following order (interspersed by a few minutes distraction): (1) naming of a different photograph of the same person; (2) naming to definition in which the subject was asked to identify the trained stimulus from presentation of a semantic fact that was different from the trained fact (see Appendix 2); and (3) a category fluency task for people. Generalisation was assessed on two occasions: on the first, the three generalisation tasks were given with stimuli presented in the same order as used during the training phase; on the second, two weeks later, the three tasks were administered with stimuli presented in a different order to test for the context specificity of any new learning.

Finally, maintenance of new learning was assessed. Home practice was stopped on five of the 10 stimuli, while allowing the participant to continue to practise with photographs and semantic facts about the remaining five items (practised set). Maintenance was assessed by presentation of the training stimuli two weeks after the second generalisation session, which itself was four weeks after the completion of training. For RFR and FC, each five-item set of stimuli was a mix of one strong, two partial and two weak exemplars. For VO the no practice set was a mix of three weak and two partial exemplars and for DD, the no practice set was composed of three partial and two weak exemplars.

Scoring and statistical analysis

Each subject served as his/her own control, in a within subject design. Training results were obtained by scoring correct naming and correct recall of the semantic fact for each of the 10 stimuli at the beginning of each training session and at the start of the first generalisation session, post-training measure. A point was awarded for each correct item, with a maximum score of 10. Similarly, for the generalisation to a different photograph, the naming to definition task and maintenance components of the study, a correct answer was given a point, with a maximum score of 10. Naming and semantic fact scores were assessed using two measures: (1) free recall of the name and semantic fact and (2) a combined score of free and cued recall of the name and semantic fact. This allowed us to determine whether there was partial learning that could support cued recall in the circumstances in which free recall was poor. Category fluency – used as a measure of generalisation – was scored as the total of target names produced, but also provided an opportunity to determine whether learning of exemplars from a particular semantic category (e.g., the politicians, Tony Blair and Margaret Thatcher) would benefit the retrieval of other, non-trained, exemplars from that category (e.g., Gordon Brown, Winston Churchill, etc.).

Where possible, data were analysed individually using a Wilcoxon signed rank test (Siegel & Castellen, 1988), providing a means to undertake statistical comparison between scores obtained on different components of training. Comparisons included (1) baseline compared to post-training naming (free recall and free plus cued recall measures analysed separately), (2) baseline versus post-training semantic fact retrieval (free recall and free plus cued recall analysed separately), (3) post-training performance versus generalisation for both naming and semantic fact retrieval, (4) baseline versus post-training category fluency, as measured at both generalisation sessions, and (5) comparison of performance on generalisation sessions with scores obtained after a delay, a measure of maintenance.

RESULTS

Training was successfully given to all four participants, with minimal errors occurring during training with vanishing cues. Expanded rehearsal trials did result in occasional "Don't know" responses that necessitated further repetition and reduction of the time interval between presentation of exemplars and recall by the patient. All participants, however, were eventually able to recall all stimuli at five minutes, both name and semantic fact, even if this learning did not always persist to the next training session.

The total number of training sessions required for each participant to learn all 10 names (as evidenced by correct production of the name and semantic fact at the time of training, but not necessarily correct naming in the subsequent test phase) ranged from eight (FC) to five (DD), with RFR requiring seven and VO six sessions, respectively. Figure 2 shows the performance of each individual patient (RFR, VO, FC and DD, respectively) on naming of the

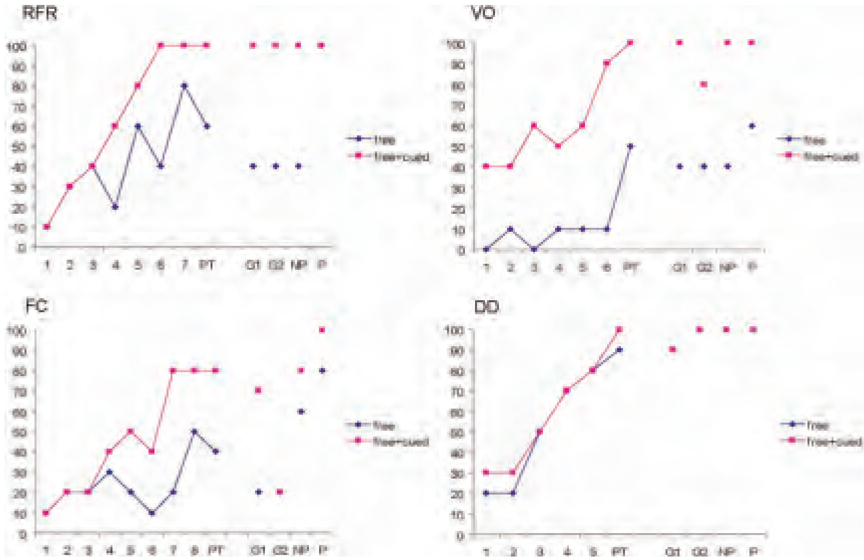

Figure 2. Learning, generalisation and maintenance of name. PT = Post-training, G = Generalisation session, 1 = Generalisation assessed in trained order, 2 = Generalisation assessed in non-trained order, NP = Items not practised prior to maintenance session, P = Items practised prior to maintenance session.

famous person over the training sessions and the post-training measure (obtained two weeks after training prior to the first generalisation test). Figure 3 summarises this information for baseline, post-training, generalisation (same order), generalisation (different order) and maintenance in order to allow more direct comparison across patients. Correct naming is reported in two separate ways on the figures: (1) a score for correct free recall and (2) a combined score reflecting items successful in either free or cued recall.

Considering free recall, while training improved naming without a cue in all four participants, only the case with semantic dementia showed learning of virtually all stimuli names (correctly naming nine out of 10 famous people) after five training sessions. RFR managed free recall of the names of eight individuals at the seventh training session, although performance declined to six by the beginning of the first generalisation session two weeks later. VO and FC only managed free recall of the names of four and five famous people after six and eight training sessions, respectively. Strikingly, while cued recall was not necessary to boost the performance of the patient (DD) with semantic dementia, (see Figure 2 and Figure 3), all three HSVE participants needed cues to achieve perfect or near-perfect naming (see Figure 3).

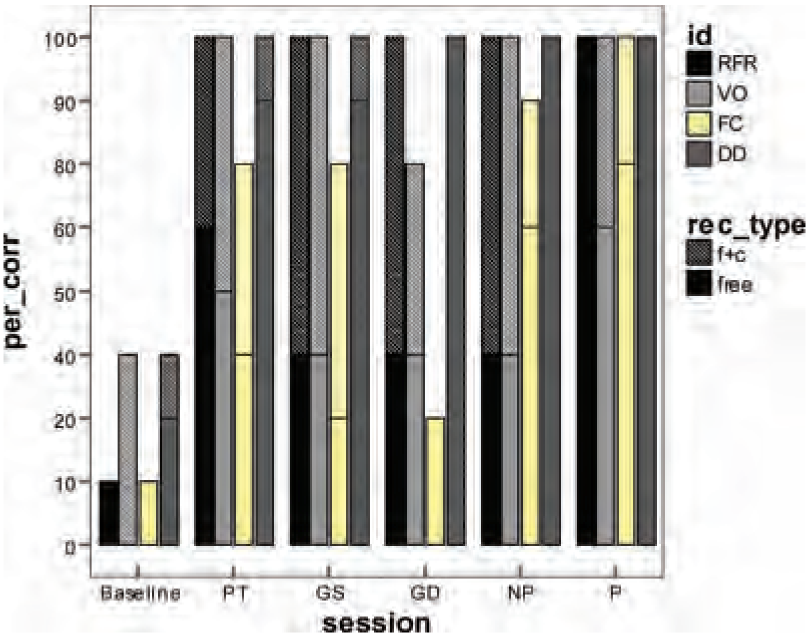

Figure 3. Free and cued recall of name across sessions. per_corr = Percent correct, rec_type = Recall type, PT = Post-training session, GS = Generalisation session tested in trained order, GD = Generalisation tested in non-trained order, NP = Not practised prior to maintenance session, P = Practised prior to maintenance session.

Statistical comparison of performance at baseline and after training (post-training score) confirmed that all participants showed significantly better naming after learning, both for a simple free recall measure and using a combined free and cued recall score (Wilcoxon signed-rank test, $Z = 2.0–3.0$, $p = .025–.003$).

We also assessed learning with two other measures. Prior to training in each session, the participant would be initially presented with all 10 items and asked to name them and provide the appropriate semantic fact. This procedure provided a measure of spontaneous naming and recall for all items ($n = 10$) for each training session (described above). Subsequently, one or two items not named by the participant would be trained until the participant was successful in naming and recall at an interval of 5 minutes. Our first additional measurement, therefore, assessed successful production of the name or fact for all items once they had been trained (e.g., how successful was training in supporting continued naming of an item over subsequent training sessions). More specifically, once a participant had successfully named or recalled a semantic fact after being trained on this by the experimenter did they then always produce this item appropriately at the beginning of each training session? The second measure collated responses when the participant produced the name of an item and recalled the appropriate semantic fact spontaneously subsequent to training. In the situation where training has led to good consolidation of semantic information, there will be no difference in these two measures. If training does not result in better subsequent performance, however, this measure allows us to determine whether spontaneous naming or recall after repeated training is sufficient to support good performance on subsequent sessions (i.e., does naming of an item or recall of a fact persist once it has been spontaneously named by the participant).

For naming of the famous person, both these measures produced a similar pattern. Using the most liberal measure (i.e., accurate naming either by free or cued recall), very few items were lost from the patient's repertoire once the item had been successfully trained, with RFR producing the correct name 100% of the time (a total of 38 responses), VO 91% of the time (over a total of 32 responses), FC 84% (39 responses) and DD 100% of the time (30 possible responses). Taking into account the pattern once the participants themselves produced the item, most patients' scores did not change (not surprisingly given the strong likelihood of accurate naming immediately after training), although FC's score improved to 94% (total of 36 responses).

Figure 3 shows the extent of generalisation of naming to different photographs of the same famous people (when items were presented in the same order or a different order to that used in training). Focusing on the best overall measure of performance – the combined free and cued recall scores – all participants showed similar levels of performance on the same order generalisation task as obtained on the post-training measure (no statistical differences were seen between scores), confirming that their ability to produce the name generalised to a different exemplar of the famous person. While RFR and DD showed no influence of a change in order (still accurately naming all 10 individuals), the performance of VO and, to a much greater extent, that of FC was affected by this contextual change. FC, while naming correctly seven famous people when different photographs were presented in the trained order (albeit predominantly from cues), was only able to name two of these individuals when a different presentation order was adopted. This difference between the two conditions was statistically significant (Wilcoxon rank sum test, post-training vs. generalisation, $Z = 2.5$, $p = .014$).

A final component of the relearning paradigm assessed maintenance over time of re-acquired semantic information. Figure 3 shows maintenance of practised and non-practised items (five in each), and reveals that in all four participants, performance after a two week delay was similar to that obtained at the end of final training session and to the generalisation condition using different photographs in the same order. Three of the participants were still able to name all 10 famous individuals, either entirely by free recall (DD, the case with semantic dementia) or via a combination of free recall and cues (RFR and VO). Case FC managed to name nine famous people (5/5 practised and 4/5 non-practised), a score that reflected an improvement in free recall from her performance on the post-training and generalisation sessions, with a statistically significant difference seen in the comparison between generalisation to a different order and maintenance score (Wilcoxon rank sum test, $Z = 2.6$, $p = .008$). There was thus little evidence that a lack of practice, at least over the short period utilised here, influenced performance: all items maintained a robust impact of learning across time.

A second test of learning was production of a semantic fact about the 10 famous people after training. Figure 4 shows the performance of RFR, VO, FC and DD, respectively, on this part of the test, again with scores separated according to free vs. free plus cued recall (see also Figure 5 for a summary allowing more direct comparison across cases). The best overall performer on this task was DD, the case with semantic dementia (see Figure 5). Despite being able to produce only two semantic facts freely, and four when provided with a cue, at the start of training (see Figure 4), after five training sessions DD succeeded in free recall of all 10 semantic facts

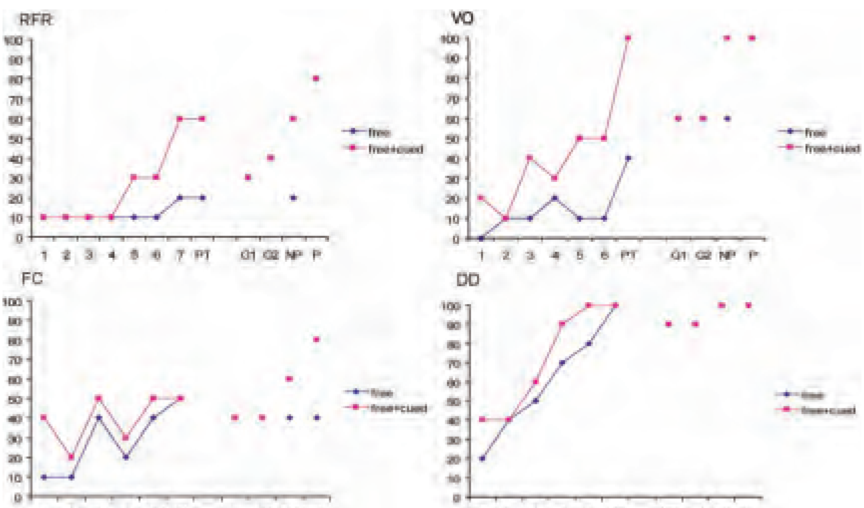

Figure 4. Learning, generalisation and maintenance of fact. PT = Post-training, G = Generalisation session, 1 = Generalisation assessed in trained order, 2 = Generalisation assessed in non-trained order, NP = Items not practised prior to maintenance session, P = Items practised prior to maintenance session.

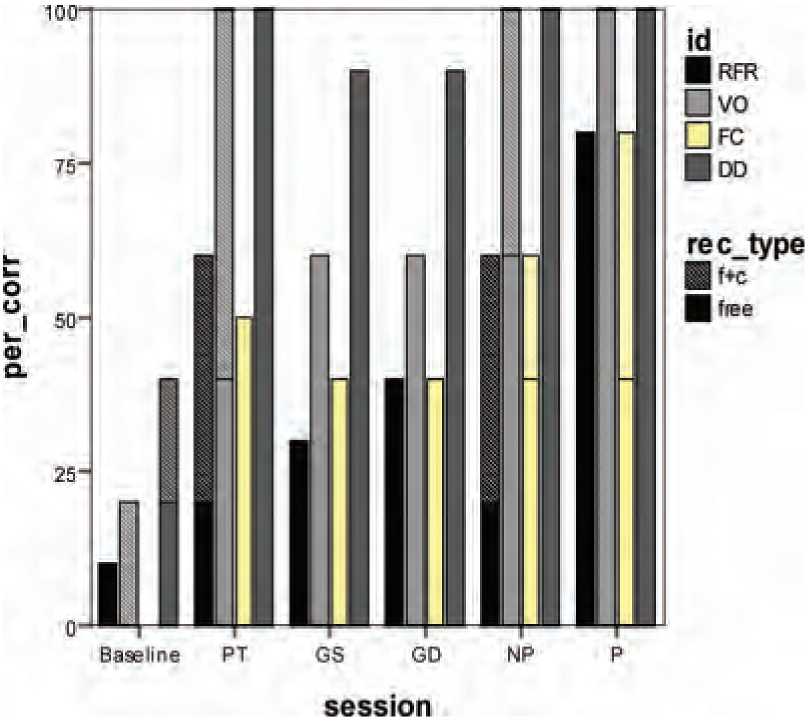

Figure 5. Free and cued recall of semantic fact across sessions. per_corr = Percent correct, rec_type = Recall type, PT = Post-training session, GS = Generalisation session tested in trained order, GD = Generalisation tested in non-trained order, NP = Not practised prior to maintenance session, P = Practised prior to maintenance session.

(Wilcoxon rank sum test, baseline vs. post-training free recall score, $Z = 2.8$, $p = .005$). Furthermore, learning of these semantic facts facilitated performance on the naming to definition task (from both a trained and non-trained order) in which DD was required to produce the name of the famous person when provided with a different semantic fact (no statistical difference between post-training score and generalisation). As with naming, recall of the semantic facts was maintained even in the absence of practice (again there was no statistically significant difference between scores obtained after training and in the maintenance condition). Consistent with this pattern, and similar to his performance in naming, DD's ability to produce the semantic facts was extremely robust across training: all responses subsequent to training were correct in free recall.

Considering the three individuals with HSVE: similar to their naming performance, learning of semantic facts as measured by free recall was poor, ranging from two to five facts after six to eight training sessions (see Figures 4 and 5). When cues were provided, performance improved significantly for VO, who was able to recall 10/10 semantic facts after six training sessions, although six required a cue (Wilcoxon rank sum test, baseline vs. post-training score, free recall, $Z = 2.0$, $p = .04$; free and cued recall, $Z = 2.9$, $p = .005$). RFR also benefited from cuing, albeit to a lesser extent than VO, managing to recall 6/10 semantic facts after seven training sessions, four of which required a cue (Wilcoxon rank sum test, baseline vs. post-training score, free recall, non-significant, free and cued recall, $Z = 2.2$, $p = .025$). FC showed some evidence of improvement with training if measured using free recall (Wilcoxon rank sum test, baseline vs. post-training score, $Z = 2.0$, $p = .046$), but there was no significant difference in her free and cued recall scores across these two conditions, with recall of only one more semantic fact than at initial training (5/10). As with naming it was possible to obtain two further measures of learning ability by (1) collating the number of responses correctly produced once an item had been trained (successful production at an interval of 5 minutes) and (2) assessing the number of responses successfully retrieved once the participant had produced the fact correctly in response to the name. Even the use of a liberal measure incorporating successful free and cued recall highlights clear difficulties with maintaining responses after training. RFR managed to produce the semantic facts only 26% of the time once an item was trained, VO 78% and FC only 55%. Notably, however, once the patients themselves had spontaneously produced the semantic fact in response to the photograph, they were quite likely to be able to continue to produce it appropriately in subsequent sessions: RFR 71%, VO 86% and FC 80%.

Although performance on the semantic facts did not benefit from training as much as did naming, it is notable that any improvement generalised to the naming to definitions task in all participants (see Figures 4 and 5), although there was a significant drop in performance between VO's post-training score (for free and cued recall combined) and those obtained on the two generalisation measures (Wilcoxon rank sum, post-training measure vs. generalisation, both Zs $= 2.0$, $p = .046$). Despite a two week gap, performance was maintained to the same level as obtained at post-training in all participants, regardless of practice; and in the two cases who did not perform at ceiling (RFR and FC), performance improved marginally (both patients now scoring 7/10 as measured by a combination of free and cued recall on both practised and non-practised items).

Despite the strong generalisation and maintenance effects seen in all participants in the ability to name these 10 famous people from photographs and definitions, and in free and cued recall of trained semantic facts, there was less evidence that this newly learnt semantic information could be used effectively to bolster performance on a less constrained semantic task in which there were no cues provided (e.g., category fluency). Table 3 shows the overall performance of the four individuals on category fluency before training and when tested at the two generalisation sessions (separated by two weeks). Considering the three HSVE cases first, while all three showed a numerical improvement after training (ranging from one to four extra items produced from the trained set), these differences were not significant in RFR and FC as measured using a Wilcoxon sign-rank test. In the case of VO, while she only produced one more item after training when tested in the first generalisation session, this improved to four more (a total of 5/10) at the second generalisation, a significant difference (Wilcoxon rank-sum test, $Z = 2.0$, $p = .046$). Like VO, the patient with semantic dementia, DD, showed significantly better performance on category fluency after training, producing five (first generalisation session) and four (second generalisation session) more items over and above the two names he was able to provide prior to learning (both measures significant, Wilcoxon rank-sum test, both $Zs \leq 2.2$, $p = .025$). In terms of performance on non-target items, Tables 3 and 4 confirm little evidence of generalisation, although it is interesting to note that RFR and FC, but not

TABLE 3
Category fluency performance on trained stimuli before and after training (at generalisation sessions)

	RFR			*VO*			*FC*			*DD**		
	Before	*After*		*Before*	*After*		*Before*	*After*		*Before*	*After*	
S	1	1	1	1	1	1	1	0	0	1	1	1
S	0	0	0	0	0	0	0	0	0	0	1	0
P	0	0	0	0	0	0	0	0	1	0	1	0
P	0	0	0	0	0	1	0	1	1	0	0	1
P	0	1	0	0	1	1	0	0	0	0	1	0
P	0	1	0	0	0	0	0	0	0	0	0	1
W	0	0	1	0	0	1	0	1	0	1	1	1
W	0	0	0	0	0	0	0	0	0	0	0	0
W	0	0	0	0	0	0	0	0	1	0	1	1
W	0	0	0	0	0	1	0	1	0	0	1	1
Total	1	3	2	1	2	5	1	3	3	2	7	6
Additional non-target responses												
	10	15	13	5	3	4	9	11	4	2	1	2
Overall total	11	18	15	6	5	9	10	14	7	4	8	8

S = Strong knowledge, P = Partial knowledge, W = weak knowledge, 0 = no response, 1 = correct name production. *Two items were swapped for DD on the basis of semantic knowledge (see Table 2).

TABLE 4
All category fluency responses (verbatim) before and after training (at generalisation sessions)

RFR			*VO*			*FC*			*DD**		
Before	*After*		*Before*	*After*		*Before*	*After*		*Before*	*After*	
Churchill	Churchill	Churchill	George Bush	**Thatcher**	**Tony Blair**	**Thatcher**	**Tony Blair**	Gordon Brown	**Tony Blair**	**Tony Blair**	**Blair**
Thatcher	**Thatcher**	**Thatcher**	**Thatcher**	**John Lennon**	**Thatcher**	Winston Churchill	Winston Churchill	Rex Harrison	**Thatcher**	**Thatcher**	**Thatcher**
Bevin	Heath	Atlee	Marilyn Monroe	Elvis Presley	Trevor McDonald	Ted Heath	Ted Heath	**Terry Wogan**	Winston Churchill	**Dawn French**	**Dawn French**
Marilyn Monroe	Wilson	**Blair**	Elvis Presley	John Otway	**John Lennon**	Marlon Brando	Wilson	Cilla Black	Beckham	**Terry Wogan**	**Elizabeth Taylor**
Kirk Douglas	Disraeli	Dean Martin	John Otway	John McEnroe	Elvis Presley	Marilyn Monroe	Queen	Frank Sinatra		**John Lennon**	Cliff Richard
Billy Wright	Hitler	Marilyn Monroe	Willie Barrett		John Otway	Elvis Presley	Frank Skinner	**Sebastian Coe**		ABBA	Beckham
Ted Dexter	Chamberlain	Jane Russell			Willie Barret	Cliff Richard	Jane Fonda	**George Best**		**Tim Henman**	**Tim Henman**

(Table continued)

TABLE 4
Continued

RFR			*VO*		*FC*		*DD**		
Before	*After*		*Before*	*After*	*Before*	*After*	*Before*	*After*	
Joe Louis	**Elizabeth Taylor**	Ron Coleman		**Tim Henman**	Tommy Steele	Bob Hope		**George Best**	**Sebastian Coe**
	Dirk Bogard	Dirk Bogard		**Sebastian Coe**	Bobby Moore	Frank Sinatra			
	Humphrey Bogart	Bing Crosby				Cliff Richard			
	John Lennon	Eddie Calvert				Elvis Presley			
	McCartney	Dennis Compton				Tommy Steele			
	Ringo Starr	Stanley Matthews				**Sebastian Coe**			
	Bingb Crosby								
	Frank Sinatra								
	Joe Louis								
	Stan Matthews								

Responses are only those exemplars that are famous people. Bold = trained stimuli.

VO or DD, showed a marginal improvement in category fluency (when tested prior to the first, but not the second, generalisation session). Trained stimuli may have facilitated production of previously known exemplars for RFR with retrieval of semantically related items (e.g., other members of the Beatles and politicians); however there was little evidence of such facilitation for other subjects.

A key question in our study was how learning would be influenced by residual semantic knowledge, which is why the items used in our 10 exemplar training set were categorised as strong ($n = 2$), partial ($n = 4$) and weak ($n = 4$), according to the performance of the patients on a set of famous people tasks (see Table 2). Although this was a small sample set, difference scores (partial minus weak) were calculated for each individual across each training session (including the post-training session) in order to evaluate this factor. In learning of a famous name (as measured by the free plus cued recall scores), there was little evidence of a consistent effect of semantic knowledge (i.e., a positive score in favour of the partially known > weak items). Out of a total of six possible training sessions in DD, only two sessions (numbers 1 and 2) were positive, reflecting naming of one more partial than

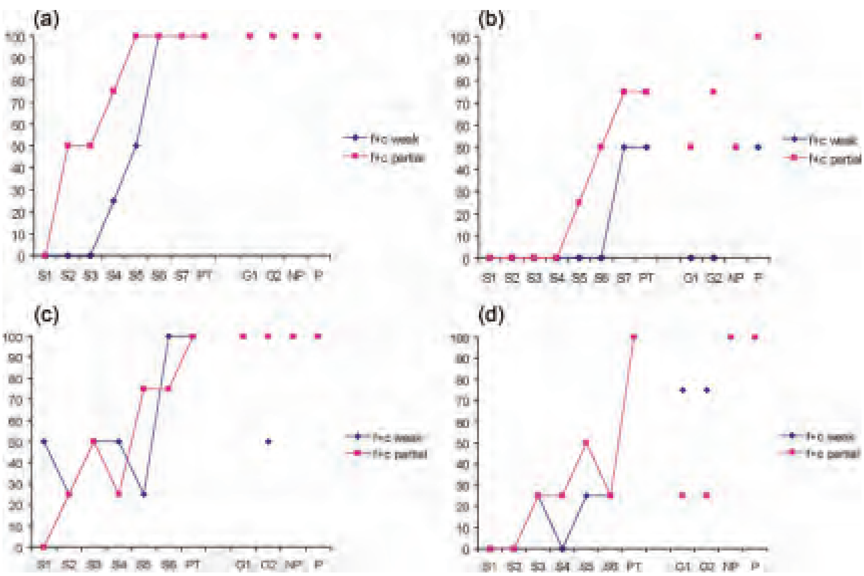

Figure 6. (a) RFR: Free and cued recall of name for items with weak and partial knowledge, (b) RFR: free and cued recall of fact for items with weak and partial knowledge, (c) VO: free and cued recall of name for items with weak and partial knowledge (d) VO: free and cued recall for items with weak and partial knowledge. f+c= Free and cued recall, G = Generalisation session, 1 = Generalisation assessed in trained order, 2 = Generalisation assessed in non-trained order, NP = Items not practised prior to maintenance session, P = Items practised prior to maintenance session.

weak items. In VO, only one out of seven sessions was positive, and in FC, no sessions (out of a possible nine) were positive. A similar pattern was seen in these individuals for retrieval of semantic facts. The exception to this was RFR, who showed attenuated semantic learning for the partially known items, compared to weaker semantic concepts, both over the training sessions and during generalisation and maintenance. Interestingly, this effect seemed most evident when there was increased demand placed on production, such as in free recall (see Figure 7) of the name versus free and cued recall (see Figure 6 for the latter), and in the retrieval of a linguistically demanding semantic fact. For example, out of 12 possible opportunities (reflecting all training, generalisation and maintenance sessions), seven showed an advantage for partial over weak semantic stimuli in free recall compared to four in free and cued recall. In the successful retrieval of semantic facts, 4/12 sessions revealed better performance by RFR on partial compared to weak stimuli on free recall, and 7/12 for free and cued recall. Figure 6(a) and (b) illustrate this profile by showing RFR's performance on free and cued recall (combined score) for the four weak items and four partially known exemplars for naming and semantic fact recall, respectively. For contrast, the profile from VO is also shown in Figure 6(c) and (d).

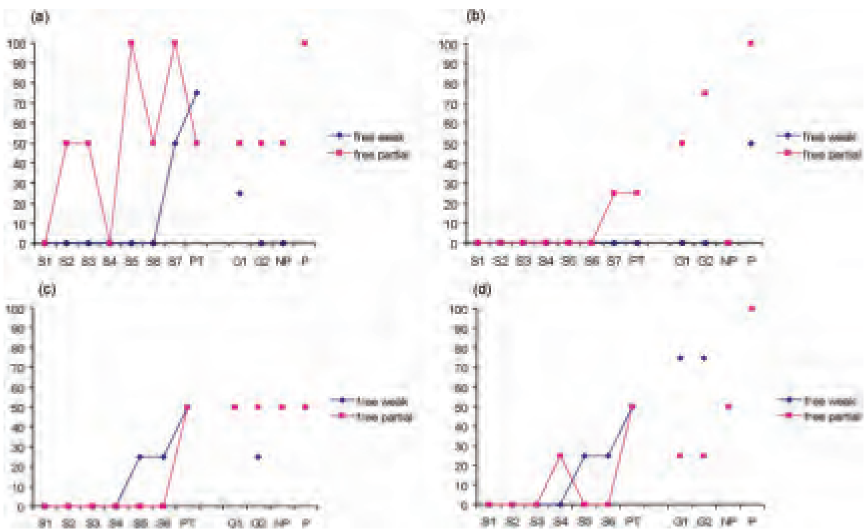

Figure 7. (a) RFR: Free recall of name for items with weak and partial knowledge, (b) RFR: Free recall of fact for items with weak and partial knowledge, (c) VO: Free recall of name for items with weak and partial knowledge, (d) VO: Free recall for items with weak and partial knowledge. G = Generalisation session, 1 = Generalisation assessed in trained order, 2 = Generalisation assessed in non-trained order, NP = Items not practised prior to maintenance session, P = Items practised prior to maintenance session.

DISCUSSION

Four participants with significant deficits in their semantic knowledge about famous people, as measured using a battery of famous people tasks (Thompson et al., 2004), were asked to learn previously known famous individuals using a mnemonic, vanishing cues and expanded rehearsal techniques. In order to draw inferences about semantic relearning that were consistent across patients, and to allow a comparison across learning in HSVE and semantic dementia, we trained the individuals on the same set of stimuli. Furthermore, using information from performance on the famous people test battery given prior to training, it was possible to investigate the impact of residual semantic knowledge on learning by contrasting items that were still partially known to the participants, as measured by either accurate production of the name of the famous person or successful performance on a face–name matching or a semantic association test, with famous individuals that the participants were unable to name or to identify from the face and/or name.

Consistent with the existing literature on the successful use of errorless learning techniques in amnesic participants (Baddeley & Wilson, 1994; Evans et al., 2000; Page et al., 2006; Tailby & Haslam, 2003), including semantic relearning (Francis et al., 2002; Stark et al., 2005), our four participants benefited from training, showing clear improvements in both the ability to name a famous person from a photograph and in recall of a single semantic fact about each of the 10 famous people used in the training set. Notably, however, this improvement could not be characterised as rapid, as it required a significant number of training sessions, particularly in the HSVE individuals. Neither can it be considered complete, as the three HSVE cases demonstrated only modest gains in free recall, with all individuals showing better naming when a cue (the person’s initials and/or a semantic category) was provided. The case with semantic dementia, on the other hand, learned more quickly and achieved good free recall.

A similar pattern was evident for learning of the semantic facts, although overall for the HSVE cases, performance was weaker here, even with cues. This is not surprising given that learning a semantic fact about an individual requires remembering and associating more linguistic entities than required for a name, as well as binding together these words into a coherent semantic concept. The poorer performance, and the less impressive training effect, presumably reflects these additional task demands, and highlights how hard it can be for amnesic individuals to acquire new semantic information of any complexity. Once again DD performed well on this task (see Figure 5), and even more impressively, this knowledge generalised to naming when the experimenter provided a new semantic fact (both when a trained or non-trained order of presentation was adopted).

Although DD outperformed all other participants in both the naming and semantic fact conditions, it is notable that the ability to generalise beyond the training situation was not unique to him, at least in some respects. All participants showed evidence of generalisation, as measured by an ability to name the famous person from a different photograph or when a context change (different order) was introduced. Furthermore, although learning of the semantic facts in the HSVE patients was not particularly good, any information that was acquired with training again seemed to generalise to the extent that the participants were able to produce some or all of the famous names when provided with new semantic facts about them.

It is clear, however, that the extent of generalisation, even within the context of simple naming, was limited. Performance on the category fluency task, which requires a flexible strategic approach to semantic search, and in which no specific cues are provided to aid performance, was not significantly better after training in RFR and FC, although VO's score did improve when tested in the second, but not the first, generalisation session. Again, DD, the individual with semantic dementia, performed best of the four participants, producing the names of four to five more famous people at the first and second generalisation sessions, respectively. This latter finding is consistent with the study by Graham et al. (1999) in which a case with semantic dementia, DM, showed striking improvements in category fluency with practice, even performing similarly to control participants after the training period.

The findings here extend this study by showing that improvements in category fluency can be demonstrated even in the situation where training did not utilise this task as part of the protocol. Notably, however, DD's improvement in category fluency was not as spectacular as that seen in DM, a result that could be due to differences in a number of factors, such as (1) training protocol: in particular, the number of items studied during training; (2) patient: while DM had predominantly left-sided involvement at testing, DD had more right-temporal atrophy and was also at an altogether milder stage of disease than DM; and (3) the semantic category or specificity: while DM was tested on objects and general semantic categories (e.g., cars, newspapers) that he was likely to encounter frequently in every-day life, DD was trained on famous people who might not crop up often in his current experience. The fact that both these cases showed such strong and relatively rapid effects of learning provides convergent evidence that the differences seen across the two diseases contrasted here reflect unique effects of different clinical diseases. It is important to note, however, that semantic dementia is a progressive condition, and that it is not currently known whether similarly good learning would be demonstrable in a patient with a more severe semantic impairment.

Our findings are consistent with other single-case studies in the literature (O'Kane et al., 2004; Verfaellie & O'Connor, 2000; Westmacott &

Moscovitch, 2001) but expand these investigations by allowing conclusions to be drawn across a group of participants trained on the same set of items, as well as providing a means of contrasting how damage to different parts of the temporal lobe may influence learning. As mentioned in the Introduction, studies in individuals with both progressive semantic deficits, as in the case of semantic dementia, and non-progressive memory impairment, as in HSVE, suggest that rapid and generalisable learning of new semantic information is dependent upon key interactions between brain regions within the medial temporal lobe and temporal neocortex. Damage to either of these brain areas typically leads to inflexible and context-dependent acquisition, although the speed of learning and the conscious accessibility of this information can be differentially affected (Bayley & Squire, 2002; O'Kane et al., 2004; Stark et al., 2005; Westmacott & Moscovitch, 2001). Broadly consistent with these conclusions, our HSVE group, with particular involvement of antero-medial temporal lobe structures, learnt slowly, were particularly dependent upon cues and did not generalise to an untrained task that required more flexible semantic processing (category fluency). One notable difference between our cases, however, and others that have been reported in the literature (e.g., Bayley & Squire, 2002; Stark et al., 2005) is that the learning did not seem to be completely hyper-specific or context-dependent. First, although generalisation to a completely different task (category fluency) was not strikingly good, most participants did show some generalisation of learning when tested in two different context changes: (1) naming or recall of a semantic fact to a different photograph of the famous person and (2) naming or recall of a semantic fact when the order of the stimuli was changed.

The finding of some flexibility in the semantic information acquired by two of the HSVE patients was somewhat surprising given previous studies (Stark et al., 2005; Westmacott & Moscovitch, 2001; although see O'Kane et al., 2004), and at first glance it seems challenging to the view that learning in profoundly amnesic individuals is more akin to non-declarative memory, more specifically perceptual learning (Bayley & Squire, 2002). One plausible explanation for this pattern is that the degree to which the HSVE individuals could utilise their newly acquired semantic information in a flexible manner relates to their residual episodic memory functioning (i.e., better episodic memory equals faster learning and more flexibility). This view would predict that RFR and VO might have some residual functioning of non-hippocampal medial temporal structures, such as those preserved in individuals with developmental amnesia (Gadian et al., 2000; Martins, Guillery-Girard, Jambaque, Dulac, & Eustache, 2006), allowing them to support better learning and generalisation of knowledge across contextual changes. Considering Table 1, however, there is little evidence that recognition memory, or even immediate recall, is significantly better in RFR and VO than in FC, with all three individuals showing similar levels of amnesia. Residual episodic memory could, however, explain why DD, the case with semantic dementia, showed such good learning and generalisation: his recognition memory, particularly for verbal compared to visual stimuli (a profile that presumably reflects his greater right-sided atrophy), was significantly better than that seen in the HSVE cases. Furthermore, this explanation cannot easily account for the differential learning effects seen across patients and condition (naming versus semantic fact learning). While RFR is the best HSVE performer for naming (as measured by his 60% post-training score) and FC the worst (40% correct), the opposite pattern is seen in semantic fact recall (RFR post-training score, 20%, FC, 50%).

Our study confirms that errorless learning techniques are useful in the rehabilitation of memory impairments (Baddeley & Wilson, 1994; Clare et al., 1999, 2000, 2002; Fillingham et al., 2006; Haslam, Gilroy, Black, & Beesley, 2006; Page et al., 2006; Tailby & Haslam, 2003), including the treatment of semantic memory deficits (McKenna & Gerhand, 2002; Stark et al., 2005). Here, as suggested by Francis and colleagues (2002) and Clare et al. (1999), semantic material was retrained using a mnemonic incorporating semantic information, followed by vanishing cues and expanded rehearsal. These techniques were utilised as they involved active participation by the individual patient in the encoding and consolidation of material, a method that has been highlighted as key to obtaining successful learning with errorless methods (see Tailby & Haslam, 2003, for more details). While learning was certainly not normal in any of our patients, it was heartening to see that the techniques used could help train patients on a small set of names and facts that might be useful to them (i.e., the names of family and friends, golf partners and so on). The current study did not, however, investigate which combination of error reduction techniques was the most important for successful re-learning, and future investigation of this issue would be useful, particularly if these studies also had the aim of reducing the amount of time required in the retraining of each stimulus. In a recent investigation in healthy adults, Hodder and colleagues (Hodder, Haslam, & Yates, in press) found that, while a combination of spaced retrieval and errorless learning was a better rehabilitative approach than trial and error, spaced retrieval by itself was the better technique. These results need to be extended, however, to amnesic individuals in order to determine the best method to maximise learning and maintenance of new information, particularly in the domain of semantic memory.

A criticism of errorless learning is that it reduces the natural variation that occurs across learning trials and thus lessens the opportunity for flexible application of new learning. This issue may be particularly pertinent to the retraining of semantic information, as this should, by definition, be context free, and our study, in which items were trained in a similar order and with no variation in stimuli provided across learning trials, may provide a false picture of the level of generalisation possible in amnesic individuals with

HSVE. Other researchers, most notably Stark et al. (2005), have proposed that varying the non-essential features of the stimulus may facilitate subsequent generalisation of learning. In an elegant study, a profoundly amnesic individual, TE, was tested on learning and generalisation of three-word sentences. A novel manipulation in the experiment was the introduction of variance during training, allowing testing of TE's ability to learn and generalise when he was trained on semantically similar sentences (variance condition: train frightened kangaroo, train scared kangaroo, train startled kangaroo) versus repetitions of the same sentence (no-variance condition: shepherd ate apple). While TE recalled more items in the studied compared to the non-studied conditions in both the variance and no-variance conditions, his ability to produce the target "kangaroo" to a novel non-trained sentence that had not been seen at study was better when variation had been introduced during training. Interestingly, despite TE's ability to generalise when provided with different, but related, training sentences, his learning did not seem to be consciously available, as measured by a non-significant difference between his confidence ratings and reaction times for correct versus incorrect answers. In addition, TE often said that he did not know the correct answer prior to providing it, a pattern that was also seen in the HSVE patient, EP, described by Bayley and Squire (2002). Our study, unfortunately, cannot address this issue in our patients as they were not asked to rate how confident they were in their responses.

Stark and colleagues' (2005) study, therefore, suggests that temporal neocortical regions can support the acquisition of semantic knowledge in a more flexible manner than previously thought possible, but perhaps only in the situation where modifications to errorless learning paradigms are used that encourage the comparison of different semantic concepts that have broadly similar meanings or inferences. It remains possible, therefore, that the patients reported here might show greater generalisation if variation was introduced in training, and it remains to be tested whether the results from TE would extend to other patients, and also to visual stimuli, such as a face or object or to learning associations between faces and names.

Our patient with semantic dementia, in whom degraded conceptual knowledge was associated with progressive damage to anterior and inferior temporal lobe regions with less complete involvement of medial temporal lobe regions, showed a profile of performance similar to the small number of reported semantic dementia cases in the literature (Funnell, 1995; Graham et al., 1999; Jokel et al., 2006; Snowden & Neary, 2002). DD learnt more rapidly than the HSVE cases, but notably did require a number of training sessions. Differences between DD and the HSVE cases emerged, however, from (1) the comparison between free and cued recall with DD showing learning that transferred to free recall, with little requirement for the provision of cues, and (2) the generalisation of his learning to category fluency.

DD also showed good maintenance of new learning, a pattern that was also reported by Jokel et al. (2006) in their semantic dementia case, AK, and seen to some extent in one of the cases reported by Snowden and Neary (2002). By contrast, in Graham et al.'s (1999) patient, DM, rapid learning was followed by an equally rapid loss of information unless the practice schedule was maintained. To explain the pattern of rapid forgetting in semantic dementia, it has been proposed that it is the particular nature of the learning that makes new memories particularly vulnerable to rapid decay (Graham et al., 1999). More specifically, if the new memories in semantic dementia are dependent upon residual functioning of structures within the medial temporal lobe, constant rehearsal or practice may be necessary to prevent these memories from being overwritten by new experiences (Graham et al., 1999; Meeter & Murre, 2004; Murre, Graham, & Hodges, 2001).

While it is generally agreed that continued practice with stimuli, particularly when there is already partial knowledge of these items, is beneficial in semantic dementia, it is not clear why patients show different degrees of forgetting. Given the short delay periods used here, we do not know whether the information maintained over the two-week period would have been sustained over a longer follow-up interval. Results from previous studies, in which forgetting consistently occurred in semantic dementia, albeit at different rates, seem to imply that DD may have shown a greater loss of knowledge over a longer follow-up interval than the other HSVE participants, but to date no study has undertaken this comparison. As an aside, it is interesting to note that one of the HSVE cases, FC, was tested at 12 months and at this point still showed evidence of preserved learning of the names taught during training. More specifically, differences in speed of learning – reflecting the role of different regions within the temporal lobe critical for the acquisition of new facts and events – may also translate into differences in rates of forgetting (i.e., faster relearning leads to faster loss, while slow learning may lead to more robust memories in the long-term).

Providing some evidence consistent with this hypothesis are studies in Alzheimer's disease, in which pathology affects medial temporal lobe regions more than temporal neocortical structures, and consequently episodic memory more than semantic memory, at least early in the disease (Graham et al., 1997; Simons et al., 2002). Studies using errorless learning techniques have shown that cases can maintain retrieval of personal names over periods as long as two years (Clare et al., 1999, 2000, 2002, although see Ruis & Kessels, 2005). For example, Clare et al. (2000) studied six participants with Alzheimer's disease using personally designed interventions involving errorless learning. Three of these cases were trained on the names of either personal friends or famous people, and errorless learning resulted in a dramatic improvement in naming, a pattern that was present six months later. Perhaps most strikingly, one of these cases was followed-up over two years by Clare and colleagues (2002). VJ, after training on the names of 11 members of his social club, performed at ceiling at one, three, six and nine months (Clare et al., 1999). After nine months, he agreed not to practise with the photographs, yet showed minimal decline in his naming of these individuals after a year (with a mean score of 80% correct) and 71% even after 2 years. Further studies that measure learning and rates of forgetting more systematically in individuals with different aetiologies that result in semantic impairment would be illuminating, providing both clinical information about the limitations of training and theoretical insights about how different temporal lobe regions contribute to re-acquisition and storage of semantic knowledge.

In summary, we have shown re-learning of semantic information in participants with serious impairments in knowledge of famous people. All four cases showed improved naming and recall of semantic facts after training and some evidence of generalisation and maintenance of performance after a delay. Subtle differences between individuals, both across diseases (semantic dementia versus HSVE) and within aetiology (HSVE participants) were evident, although a similar pattern of laborious and relatively inflexible learning was seen broadly across cases. In support of theoretical accounts that distinguish between slow and fast cortical learning systems (McClelland, McNaughton, & O'Reilly, 1995), the HSVE group showed a greater reliance upon cueing to support semantic retrieval, a pattern predicted by a slow neocortical learning system that was functioning in the absence of the hippocampus. Cues were less necessary, however, in the case with semantic dementia, who showed near perfect performance on both learning and generalisation trials both for naming and recall of a semantic fact. While a reasonable explanation for this profile is learning supported by a partially functioning hippocampus, it is notable that this patient still required a number of learning trials to support performance, a pattern that implies – at least with verbal stimuli – a form of learning that differs from the normal in quality as well as quantity.

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APPENDIX 1

Trained semantic fact

Tony Blair: Longest serving Labour Prime Minister

George Best: 1960s Manchester United football player

Terry Wogan: Irish presenter BBC Radio 2

Dawn French: English comedienne *Vicar of Dibley*

Sebastian Coe: Athlete won four Olympic gold medals

Camilla Parker-Bowles: Prince Charles' wife after Diana

John Lennon: Beatles singer/songwriter was assassinated

Margaret Thatcher: First female British Prime Minister

Tim Henman: England's number one tennis player

Elizabeth Taylor: Hollywood actress married seven times.

APPENDIX 2

Naming to definition task used to assess generalisation of learning

Tony Blair: Leader of the Labour party since 1994

George Best: British footballer also infamous for his drinking, liver transplant

Terry Wogan: TV presenter, hosts the Eurovision song contest

Dawn French: TV personality, teamed with Jennifer Saunders

Sebastian Coe: The only man to win 1500 metre Olympic event twice

Camilla Parker Bowles: Long-time partner of current heir to the throne

John Lennon: Musician who wrote "Imagine" and "Strawberry Fields Forever"

Margaret Thatcher: She won three consecutive general elections for the Tory Party

Tim Henman: First British tennis player since 1970s to reach Wimbledon semi-finals

Elizabeth Taylor: Film star who married Richard Burton twice.