Neuropsychology
2009, Vol. 23, No. 2, 144–157

DOI:10.1037/a0014447

Remote Semantic Memory in Patients With Korsakoff's Syndrome and Herpes Encephalitis

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Performance of patients with Korsakoff's syndrome and herpes encephalitis was compared on a retrograde amnesia (RA) test, asking subjects to recall and recognize the definitions of words that had come into the language at different time periods. Performance was also compared on a related test in which participants were asked to produce the words to definitions they were given in free recall and cued recall versions. It was hypothesized that, if the temporal gradient in remote memory results from a shift of information from episodic to semantic memory, then there should be a temporal gradient on these tasks, possibly steeper (i.e., greater relative sparing of early memories) in the patients in the Korsakoff group than in the herpes encephalitis group, who have widespread temporal lobe damage. Furthermore, in comparing semantic and episodic remote memory tests, consolidation theory would predict uniform temporal gradients across such tasks, whereas multiple trace theory would predict a differential pattern. The results showed that patients with Korsakoff's syndrome and patients with herpes encephalitis were significantly impaired across all time periods on the vocabulary tests, with only minimal evidence of temporal gradients, relative to healthy participants, and there was no evidence of a differential pattern of impairment between the two patient groups. Comparison with performance on measures of episodic retrograde amnesia, in which there was a differential pattern of temporal gradient, suggests that the relative preservation of early episodic remote memories in patients with Korsakoff's syndrome does not result from an episodic-to-semantic shift in the quality with which memories are stored. These findings are discussed in relation to existing theories of RA and to the patients' underlying patterns of neuropathology.

Keywords: amnesia, retrograde, semantic, vocabulary, episodic

There is increasing evidence, both from single case reports and group studies, that neurological retrograde amnesia (RA) cannot be thought of as a unitary disorder (e.g., Barr, Goldberg, Wasserstein, & Novelly, 1990; Kapur, 1999; Kopelman, 2002; Kopelman, Stanhope, & Kingsley, 1999; O'Connor, Butters, Milliotis, Eslinger, & Cermak, 1992; Moscovitch et al., 2006; Verfaellie, Reiss, & Roth, 1995b). Temporally graded RAs extending back several decades (i.e., relative sparing of early memories) are a common feature of patients with the alcoholic Korsakoff's syndrome, which primarily affects the diencephalon, usually with concomitant frontal lobe atrophy (Colchester et al., 2001; Jernigan, Schafer, Butters, & Cermak, 1991). Lesions restricted to structures within the medial temporal lobe, while having severe effects on anterograde memory, have sometimes been reported to produce a relatively brief RA extending back only a few years before the onset of illness (Bayley, Gold, Hopkins, & Squire, 2005; Bayley, Hopkins, & Squire, 2003; Bright et al., 2006; Kopelman, 2000, 2002), but other investigators have found a temporally extensive loss across several decades of autobiographical memories (Cipolotti et al., 2001; Moscovitch, Nadel, Winocur, Gilboa, & Rosenbaum, 2006; Nadel & Moscovitch, 1997) or of remote spatial/topographical information (Maguire, Nannery, & Spiers, 2006). Where damage extends beyond the medial temporal lobes to include to lateral temporal cortex, an extensive retrograde amnesia for autobiographical or semantic memories (often with a "gentle" temporal gradient) is usually observed (Bright et al., 2006; Fama, Marsh, & Sullivan, 2004; Kopelman, 1989; Kopelman et al., 1999; Verfaellie, Croce, & Milberg, 1995a). Some investigations have emphasized the role of frontal atrophy in contributing to remote memory impairment (Kopelman et al., 2003), whereas others have emphasized the importance of the lateral temporal regions (Bayley et al., 2005; Bright et al., 2006) or the posterior cortical regions (Fama et al., 2004).

Remote Episodic Versus Semantic Memory

There is evidence that the temporal pattern of retrograde memory loss may differ with respect to the types of information stored. Whereas distant memories may lose temporal and spatial context through a process of repeated rehearsal and forgetting, recent memories may be more closely tied to spatial and temporal context. Cermak (1984) hypothesized that the "episodic" nature of recent memories renders them more susceptible to damage in the limbic system, whereas "older" memories are stored in a more semantic form, which protects them from damage to limbic-diencephalic circuits. Consistent with this theory, a number of studies

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reported severe episodic memory loss in the face of relative preservation of semantic memory (Cermak & O'Connor, 1983; Gabrieli, Cohen, & Corkin, 1988; Kitchener, Hodges, & McCarthy, 1998; O'Connor et al., 1992; Westmacott & Moscovitch, 2001, 2002). An implicit assumption of Cermak's theory is that episodic memory function is important for the long-term acquisition of semantic knowledge. However, recent studies have suggested that new vocabulary and facts can be learned to a very limited extent, even in the presence of a very severe episodic memory deficit (e.g., Bayley & Squire, 2002; McCarthy, Kopelman, & Warrington, 2005; van der Linden, Meulemans, & Lorrain, 1994; Verfaellie, Koseff, Alexander, 2000; Westmacott & Moscovitch, 2001, 2002).

Consolidation Versus Multiple Trace Theory

Consolidation theory predicts uniform temporal gradients across different types of (episodic and semantic) material (e.g., Alvarez & Squire, 1994; Meeter & Murre, 2004), whereas multiple trace theory predicts a steeper gradient for semantic than episodic memories (Moscovitch et al., 2006; Nadel & Moscovitch, 1997; Westmacott & Moscovitch, 2002). According to multiple trace theory, older memories are more resistant to hippocampal damage because, through reactivation and rehearsal, they are associated with a greater number of memory traces, whereas new memories have fewer traces or representations, resulting in a temporally graded RA. Moreover, the temporal gradient for remote personal semantic memories and for public information will be steeper than that for episodic memories, because this type of knowledge can eventually be retrieved independently of hippocampal involvement (Viskontas, McAndrews, & Moscovitch, 2000, 2002); that is, there will be more sparing of early semantic knowledge than of early episodic memories. It seems likely that, if this theory is correct, the same should apply for more purely semantic information such as words and concepts that have come into the language at different times. In summary, both consolidation and multiple trace theory predict that remote semantic memories will show a temporal gradient. However, they differ with respect to episodic memories, consolidation theory predicting a temporal gradient (with no differentiation between the two types of memory), and multiple trace theory predicting a flatter gradient for episodic memories than for semantic memories.

Remote Semantic Memory

Verfaellie et al. (1995b) investigated premorbidly acquired semantic memory in patients with Korsakoff's Syndrome, using (as stimuli) words that had entered common usage at known times across a 25-year period. An impairment was seen in patients in the Korsakoff group compared with alcoholic controls on recall testing, with a temporal gradient indicating better recall of words that entered the dictionary at distant relative to recent periods. The patients in the Korsakoff group showed a disproportionate deficit for recall relative to recognition performance, and the authors suggested that their impairment might lie in a controlled search and retrieval deficit for semantic information. In a further study of a patient who had suffered herpes encephalitis (SS), Verfaellie et al. (1995a) found a severe impairment that extended back at least 15 years prior to the onset of amnesia. The patient was also tested on his memory for words that entered the language post amnesia-onset, and here his performance was even more impaired. The fact that SS was no longer able to acquire new word meanings (despite his verbal facility) was consistent with a key role for episodic memory in the acquisition of novel semantic information. Although direct comparisons were not made in these studies between performance on semantic and episodic remote memory, Verfaellie et al. (1995a) concluded that continued rehearsal may strengthen both episodic and semantic memories in parallel.

Subsequent case studies of vocabulary retrieval have investigated patients with relatively focal hippocampal/medial temporal pathology and/or patients with more widespread temporal pathology (McCarthy et al., 2005; Westmacott & Moscovitch, 2002). Together, these studies indicated that semantic memories may be mediated primarily by the temporal neocortex and can survive extensive hippocampal damage once a process of "cohesion" (short-term consolidation) is completed.

Present Investigation

In this study, we examine the extent to which semantic memory is affected in retrograde amnesia in a comparison of patients with herpes encephalitis, patients with Korsakoff's syndrome, and with healthy controls. The temporal gradient and extensiveness of semantic memory loss in RA was investigated, together with comparisons of recall/recognition and free/cued recall conditions. The study examined three predictions:

(1) If differences in the severity of retrograde semantic impairment relate specifically to the extent of lateral temporal lobe damage, a more extensive remote memory loss on semantic tasks, and a flatter temporal gradient, will be seen in patients with herpes encephalitis patients, relative to patients with Korsakoff's syndrome, because the former group is more likely to show extensive (infero-lateral) temporal lobe damage.

(2) If the semantic memory impairment is primarily one of retrieval rather than storage, the patient groups should show a disproportionate benefit from recognition or cued conditions, relative to free recall, compared with healthy participants. By contrast, if the patients in the Korsakoff group have an impairment primarily of retrieval, and the patients with herpes primarily of storage, there should be differential benefits of recognition/cueing across the patient groups.

(3) If semantic and episodic information are similarly dependent on the medial temporal lobes for a time-limited period, as Squire and colleagues have argued (Bayley et al., 2003, 2005; Manns, Hopkins, & Squire, 2003; MacKinnon & Squire, 1989), amnesic patients will show broadly similar temporal gradients across different aspects of episodic and semantic remote memory. By contrast, multiple trace theory (Moscovitch et al., 2006; Nadel & Moscovitch, 1997) predicts a steeper temporal gradient for semantic than episodic memory loss (i.e., greater sparing of early semantic memories) resulting from medial temporal or thalamic pathology. However, Westmacott and Moscovitch's (2002) finding in semantic dementia (where there is generally severe atrophy of left temporal cortex) suggests that patients with herpes encephalitis might also show a flat gradient for semantic memories, since these patients have

widespread damage to those left temporal lobe neocortical structures thought to mediate vocabulary and semantic knowledge.

Overview and Participant Groups

Three different studies are reported in this article. The first involved a reanalysis of the Verfaellie et al. (1995b) findings in alcoholic patients with Korsakoff's syndrome in an experiment involving recall and recognition of word meanings, and comparison with findings in new groups of patients with herpes encephalitis and controls. The second study was an investigation of the free recall and cued recall of words from definitions in alcoholic patients with Korsakoff's syndrome and patients with herpes. The third study involved a reanalysis of autobiographical incident and personal semantic memory test scores from a previously published study of diencephalic and temporal lobe lesion groups (Kopelman et al., 1999) to show the findings for subgroups of alcoholic patients with Korsakoff's syndrome and patients with herpes encephalitis. The findings from these Korsakoff and herpes subgroups had not previously been published before, and are presented here for comparison with the findings from the vocabulary studies. Table 1 shows the overlap of participant groups across the investigations, mean age, background neuropsychological test scores, and the number of participants who underwent either a nonquantified computed tomography (CT) or magnetic resonance imaging (MRI) brain scan or a quantified MRI brain scan. In our experience, there is always a substantial attrition rate in patients with Korsakoff's syndrome from investigation to investigation, and Table 1 shows that, whereas 8 out of 9 patients with herpes were the same across all 3 studies, only 2 patients with Korsakoff's syndrome in Study 2 were the same as those who had taken part (on an earlier occasion) in Study 3. Obviously, the U.S. patients with Korsakoff's syndrome did not overlap with those in the United Kingdom, but we have no reason to suppose that the patients with Korsakoff's syndrome in Study 1 differed in any important respect from those in Study 2 (mean verbal IQ = 96.2 ± 13.6 vs. 99.3 ± 17.0; Wechsler Memory Scale–Revised (WMS-R) general index = 83.7 ± 14.9 vs. 72.7 ± 19.6; delayed index = 57.2 ± 4.5 vs. 66.7 ± 21.1; attention/concentration = 99.3 ± 11.7 vs. 95.7 ± 13.6). Two groups of controls were employed in the U.S. investigation—a group of participants with histories of chronic alcoholism, whose findings are listed in Table 1, and an age-matched nonalcoholic control group, but there were no significant differences in overall level of performance between these two control groups on either recall ($t(10) = 1.18$, *ns*) or recognition memory ($t(10) = 1.69$, *ns*) for the word definitions in Study 1. It will also be seen that the U.S. controls matched the U.K. controls in Study 1 in terms of WMS-R indices.

Table 1 also shows that WAIS–R Verbal IQ and/or National Adult Reading Test–Revised (NART-R) estimated premorbid IQ scores were available, and that these scores were closely similar across all these participant groups. There was no evidence of dementia in any of the patient groups. The WMS-R general and delayed memory indexes indicate that there was severe impairment in both patient groups relative to the controls. In Study 2, the control groups were assessed on WMS-R immediate and delayed logical memory and the Kendrick Object Learning Test (Kendrick, 1985), and the patient groups were impaired on these two measures. In Study 1, the general memory deficit was more pronounced in the patients with herpes relative to patients with Korsakoff's syndrome, $F(1, 12) = 7.17$, $p < .05$, but there was no significant difference on delayed memory, $F(1, 12) = 1.13$, *ns*, where the mean Korsakoff score was in fact lower than that of the herpes group. There were no significant patient group differences on any of these measures in Studies 2 and 3 ($p > .2$ in all cases).

Finally, Table 1 indicates that all patients with Korsakoff's syndrome and herpes encephalitis in these investigations had undergone a clinical CT or MRI brain scan with findings consistent with their diagnoses. Some of these patients (particularly those in Study 3, as indicated in Table 1) also participated in detailed quantified structural MRI investigations, the findings of which have been reported elsewhere (Colchester et al., 2001; Kopelman et al., 2001, 2003). Colchester et al. (2001) reported that left, right, and total (bilateral) medial temporal, parahippocampal, and hippocampal volumes were significantly reduced in 9 patients with herpes encephalitis , relative to controls, but that 11 patients with Korsakoff's syndrome did not differ significantly from the controls on any of these measurements. Similarly, left, right, and total anterolateral temporal lobe volumes (determined by subtracting hippocampal and parahippocampal volume from whole temporal lobe volume for each hemisphere) were significantly reduced in the herpes encephalitis patients, relative controls, but there were no differences between Korsakoff and control group volumes. By contrast, patients with Korsakoff's syndrome showed reduced thalamic volumes, relative to controls, whereas the patients with herpes encephalitis did not differ significantly from controls in this regard. In addition, the patients with Korsakoff's syndrome and the patients with herpes encephalitis both showed significant reduction in frontal volumes, but there were no significant differences between these two patient groups in this regard.

Comparison by visual inspection of participants' nonquantified CT and MRI brain images with the quantified MRI brain scans from other participants did not indicate any important differences between these subgroups.

Study 1: Recall/Recognition

The first study compared patients with herpes encephalitis and patients with Korsakoff's syndrome on recall and recognition versions of Verfaellie et al.'s. (1995a) test. This involved a reanalysis of Verfaellie et al.'s. (1995b) Korsakoff's findings.

Method

Materials. In the study of patients with Korsakoff's syndrome and their controls, the stimuli consisted of 82 words that could be traced back to when they first entered common usage (Verfaellie et al., 1995a, 1995b) with the assistance of a number of dictionaries (Gabrieli et al., 1988). The stimuli were grouped according to the 5-year period in which they first entered the language (i.e., 1955/1959, 1960/1964, to 1985/1990). Twelve words were selected for each period except the most recent, for which only 10 words were found. Verfaellie et al. (1995a, 1995b) also included 12 words that had entered the vocabulary before 1920 as a baseline measure, but performance on these words did not differ between patients and controls and they were not included in the present investigation. The majority of the words chosen by Verfaellie et al. (1995a,

Table 1
Participants and Background Neuropsychological Test Scores in the Three Studies

	Study 1				Study 2				Study 3		
	Cs	Ks	HEs	Cs	Cs	Ks	HEs	Cs	Cs	Ks	HEs
Where tested	United States	United States	United Kingdom	United Kingdom	United Kingdom	United Kingdom	United Kingdom	United Kingdom	United Kingdom	United Kingdom	United Kingdom
N	6	6	8	6	8	8	8	8	20[a]	13	9
Overlap with Experiment 1	—	—	—	—	0	0	8	0	0	0	8
Overlap with Experiment 2	0	0	8	0	—	—	—	—	0	2	8
Overlap with Experiment 3	0	0	8	0	0	2	8	0	—	—	—
Mean age	57.0 ± 3.6	62.0 ± 6.7	46.5 ± 14.5	46.3 ± 11.4	51.1 ± 7.7	51.1 ± 7.2	48.7 ± 14.9	49.5 ± 14.5	45.8 ± 17.3	55.4 ± 8.1 4	6.1 ± 14.6
NART-R IQ	—	—	109.3 ± 9.1	107.0 ± 14.8	107.3 ± 10.4	106.5 ± 11.9	109.3 ± 9.1	111.4 ± 6.5	104.3 ± 14.4	107.8 ± 12.5 10	3.3 ± 11.6
WAIS-R Vb IQ	99.0 ± 6.4	96.2 ± 13.6	96.4 ± 13.4	105.3 ± 15.5	—	99.3 ± 17.0	96.4 ± 13.4	—	99.1 ± 14.2	101.0 ± 16.0 9	6.0 ± 9.8
WAIS-R F-S IQ	—	—	97.3 ± 13.8	—	—	—	97.3 ± 13.8	—	102.1 ± 15.4	97.4 ± 14.2 9	6.9 ± 12.9
WMS-R General	104.0 ± 8.7	83.7 ± 14.9	63.8 ± 12.9	105.3 ± 14.5	—	72.7 ± 19.6	63.8 ± 12.9	—	103.1 ± 16.4	66.6 ± 19.9 6	5.6 ± 14.7
Delayed	105.0 ± 7.7	57.2 ± 4.5	62.9 ± 14.4	102.0 ± 20.0	—	66.7 ± 21.1	62.9 ± 12.4	—	105.2 ± 19.0	59.3 ± 15.2 6	5.0 ± 13.3
Attention/ concentration	106.0 ± 14.4	99.3 ± 11.7	88.9 ± 19.3	100.0 ± 13.6	—	95.7 ± 13.6	88.9 ± 19.3	—	100.1 ± 12.0	92.1 ± 14.1 8	6.4 ± 19.5
FAS Total	—	37.3 ± 24.6	34.2 ± 12.9	41.5 ± 12.5	40.3 ± 7.4	24.0 ± 9.9	34.2 ± 12.9	49.0 ± 10.4	40.3 ± 13.7	29.0 ± 14.0 3	6.3 ± 13.7
Logical Mem Immed	—	—	—	—	9.9 ± 2.4	6.0 ± 2.2	4.6 ± 1.1	9.0 ± 2.2	—	—	—
Delayed	—	—	—	—	6.6 ± 1.8	1.1 ± 1.0	2.0 ± 2.2	7.6 ± 1.8	—		
KOLT Total	—	—	—	—	39.1 ± 5.1	17.0 ± 7.0	21.2 ± 12.1	9.0 ± 15.9	—	—	—
MRI Quantified	0	0	8	0	0	2	8	0	10	13	9
CT/MRI Nonquantified	0	6	0	0	0	6	0	0	0	0	0
CT/MRI Total	0	6	8	0	0	8	8	0	10	13	9

Note. CT = computed tomography; MRI = magnetic resonance imaging; Cs = controls; Ks = Korsakoff's syndrome patients; HEs = herpes encephalitis patients; NART–R = National Adult Reading Test–Revised; FAS = FAS verbal fluency score; KOLT = Kendrick Object Learning Test; WAIS–R = Wechsler Adult Intelligence Scale–Revised; WMS–R = Wechsler Memory Scale–Revised.
[a] Not included in statistical analyses.

1995b) were also adopted for the herpes study. However, given that the set was devised for an American sample, some changes were necessary for administration to British participants. A pilot questionnaire indicated 19 unsuitable words and 7 replacements were introduced (using the *Oxford Dictionary of New Words*), leaving a total set of 70 words and definitions. The stimuli were grouped, as in the Korsakoff study, into seven 5-year periods from 1955 to 1990, with 10 words in each 5-year block.

Although the words were selected according to their having entered the language between 1955 and 1990, scoring was carried out with reference to the date of onset of each patient's amnesia to ensure that the test was truly of "retrograde" amnesia. For this analysis, in accordance with Verfaellie et al. (1995b), we used data from the 25 years (5 $\times$ 5-year blocks) preceding the onset of the amnesia, since all patients yielded data for a period extending back at least 25 years preonset. An identical procedure was used in the patients in the herpes group. Scores for words that originated in the 5 years before the onset of amnesia formed the most recent datapoint. The next datapoint was comprised of words that had entered the language between 5 and 10 years before onset of amnesia, and so forth This procedure resulted in a total of 5 data points, extending back 25 years. In the case of healthy controls, scoring was in terms of 5 year "blocks" preceding the date of testing. With the exception of a few of the stimuli used (as described earlier), the tasks undertaken by the patients in the Korsakoff and herpes groups were identical. In addition, in subgroups consisting of older patients (>40) of recent onset (<40 months), we also examined the results across the full 35-year sampling period preonset in comparison with age-matched controls. We included these additional statistics to ensure that the sampled period extended as far back as early adulthood for these patients and controls.

Knowledge of the word meanings was assessed in a free recall condition, followed by a recognition condition. In the recall task, words were individually presented and the participant asked to define each word to the best of his or her ability. If a clear and accurate response was made, two points were awarded (e.g., sitcom: "an abbreviation for situation comedy"... "a representation of a normal situation where the amusing aspects are emphasized"). To qualify for one point, an understanding of the context in which the word is used had to be demonstrated, even though clear understanding of meaning was missing (e.g., sitcom: "an amusing TV program"). A zero score was awarded if the response bore no relation to the actual definition (e.g., sitcom: "a communications device"). For the recognition task, each of the words was followed by the target definition along with three plausible, but unrelated, distracter items. As an example, the following items were provided for the word "Frisbee":

(a) A small sample of a product given away for free in order to encourage people to buy the full-priced product at a later date.
(b) A Hair style.
(c) A small plastic disk that may be thrown through the air for recreation.
(d) A refrigerator that maintains temperatures below zero degrees centigrade to freeze perishable goods.

The position of the correct definition varied among trials and was counterbalanced across the conditions. Recognition responses were scored as correct or incorrect, with overall performance expressed as a proportion of total items.

Procedure. The two conditions were presented during successive sessions. In the first session, participants were presented with the recall test, whereby each word was presented visually (on a flash card) and was read aloud to the subject. Participants were asked to define or explain each word as best they could. Incomplete definitions were probed further by asking the participant to "tell me more." In the recognition condition, the word and each definition were presented visually together, and the participant was requested to choose the most accurate definition. Guessing was encouraged if a response was not forthcoming.

Results

Performance in patients with Korsakoff's syndrome. Figure 1 (left panel) shows the comparison of patients with Korsakoff's syndrome recall scores with those of alcoholic controls. These data have been reanalyzed from Verfaellie et al. (1995b) and are presented in terms of the number of years preceding the onset of each patient's amnesia that the word first occurred. In the control participants, the data are presented simply in terms of the number of years ago that a word first originated. For each analysis we have included the partial eta-squared (η^2) statistic as a measure of effect size (the proportion of variability [plus error] in the dependent variable that is explained by the independent variable). There were significant main effects of Period, $F(4, 40) = 3.73$, $p < .05$, partial $\eta^2 = .27$, and Group, $F(1, 10) = 8.17$, $p < .05$, partial $\eta^2 = .45$, but the Group $\times$ Period interaction was not significant, $F(4, 40) = 1.04$, *ns*, partial $\eta^2 = .09$). However, when we compared the 2 most recent decades with the 2 most distant decades, there was a near-significant interaction, $F(1, 10) = 4.83$, $p < .06$. This pattern is consistent with Verfaellie et al.'s (1995b) observations. Finally, we also examined 2 patients with Korsakoff's syndrome and 2 control patients over the full 35-year period preonset; in this case the group by time-period interaction was not significant, $F(6, 12) = 0.96$.

Recognition scores (Figure 1, middle panel) did not differ across the 5 time-periods, $F(3, 25) = 1.80$, *ns*, partial $\eta^2 = .15$, but there was a significant main effect of Group, $F(1, 10) = 6.41$, $p < .05$, partial $\eta^2 = .39$. A significant Group $\times$ Period interaction effect, $F(4, 40) = 2.99$, $p < .05$, partial $\eta^2 = .23$; consistent with Verfaellie et al.'s [1995b] finding, reflected a tendency for the patients with Korsakoff's syndrome to show relative preservation of recognition memory for words from more distant periods, compared with more recent words. There was a highly significant heterogeneity of variance across conditions in this analysis ($p = .0004$), and, after adjusting the degrees of freedom to control for this, this interaction remained only of borderline significance, $F(3, 25) = 2.99$, $p = .06$. In the subgroups for which analysis was possible across 35 years preonset, this interaction was not significant, $F(6, 12) = 2.04$.

To examine whether one of the groups showed a greater discrepancy between recall and recognition performance as a function of time-period, recall scores were subtracted from recognition scores (Figure 1, righthand panel). All effects were nonsignificant: time period: $F(4, 40) = 1.86$, *ns*, partial $\eta^2 = .16$; Group: $F(1, 10) = 2.56$, *ns*, partial $\eta^2 = .20$; Group $\times$ Time-Period interaction: $F(4, 40) = 0.95$, *ns*, partial $\eta^2 = .09$.

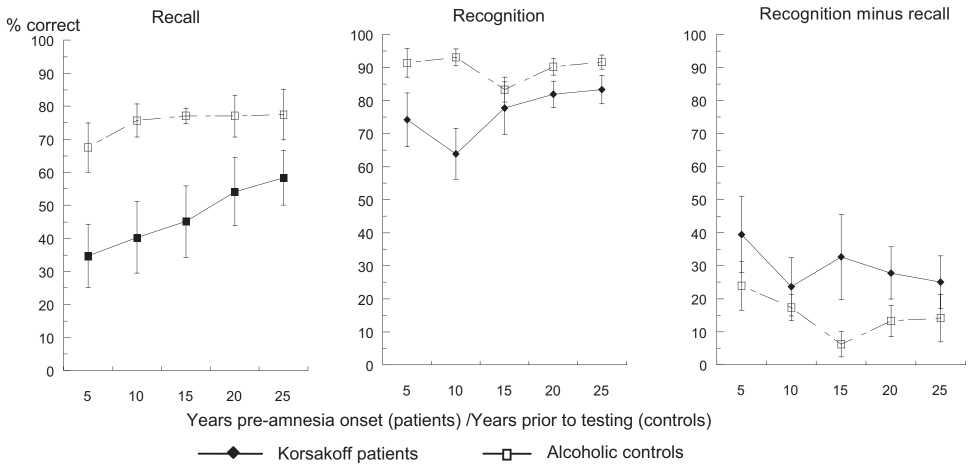

Figure 1. Study 1. Charts showing recall, recognition, and recognition minus recall scores (with *SE* bars) in patients with Korsakoff's syndrome and alcoholic controls for words entering the vocabulary during a period of 25 years prior to the onset of amnesia (grouped by 5-year intervals).

Performance in patients with herpes. Figure 2 (lefthand panel) shows that controls demonstrated better recall performance than patients with herpes. There was a significant main effect of Group, $F(1, 12) = 17.29$, $p < .01$, partial $\eta^2 = .59$, but not of Time Period, $F(4, 48) = 1.82$, *ns*, partial $\eta^2 = .13$, and there was no significant Group × Time Period interaction, $F(4, 48) = 1.00$, partial $\eta^2 = .08$. In a further analysis of 3 patients with herpes and 3 controls across 35 years preonset, the group by time-period interaction was not significant, $F(6, 24) = 0.26$. On recognition performance (Figure 2, middle panel), the main effect of Group was of only marginal significance, $F(1, 12) = 3.31$, $p < .10$, partial $\eta^2 = .09$, with the controls again performing better than the herpes group. There was no significant effect of Time Period, $F(4, 48) = 0.95$, *ns,* partial $\eta^2 = .07$), and the Group × Time Period interaction effect was again not significant, $F(4, 48) = 0.83$, *ns*, partial $\eta^2 = .06$, with both groups showing a fairly consistent level of recognition performance across all time periods. Comparing recognition in 3 patients with herpes and 3 control preonset, the group by time period interaction was not significant, $F(6, 24) = 0.93$.

The patients with herpes showed a wider discrepancy between recognition and recall memory scores than their control group (Figure 2, righthand panel), and this main effect of Group was statistically significant, $F(1, 10) = 22.51$, $p < .01$, partial $\eta^2 = .65$. There was no significant Group × Time Period interaction, $F(4, 48) = 1.58$, partial $\eta^2 = .12$, indicating again that the Group difference was not influenced by the duration of time between acquisition of particular words and the onset of amnesia.

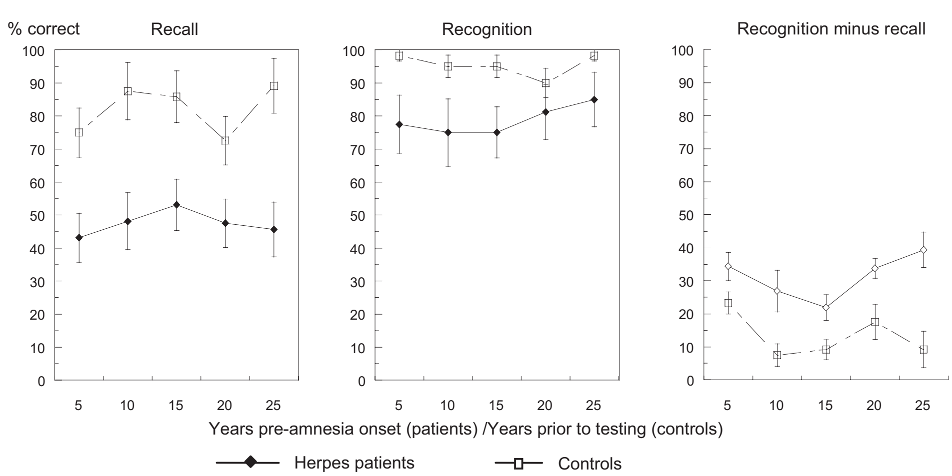

Figure 2. Study 1. Charts showing recall, recognition, and recognition minus recall scores (with *SE* bars) in patients with herpes encephalitis and controls for words entering the vocabulary during a period of 25 years prior to the onset of amnesia (grouped by 5-year intervals).

Comparison of patients in the Herpes and Korsakoff groups. We first compared background measures (memory and frontal/executive function) and the experimental (recall and recognition) test scores in the two control groups (Korsakoff controls, herpes controls): all control group comparisons were nonsignificant. Second, we compared the performance of the two control groups (Korsakoff controls, herpes controls) on the recall and recognition versions of the vocabulary task: there were no significant differences, and Figure 5 (upper row) shows that similar vocabulary test scores were obtained in these control groups across all the tasks. Having done this, we compared the performance of the patient groups: had the controls differed on these measures, the legitimacy of a direct comparison between the patient groups would have been questionable.

An analysis of variance, carried out on recall scores in patients with Korsakoff's syndrome and patients with herpes (Figure 5, upper row) demonstrated similar performance across Groups on recall, $F(1, 12) = 0.01$, *ns*, partial $\eta^2 = .00$, and recognition ($F(1, 12) = 0.07$, *ns*, partial $\eta^2 = .01$, with no significant Group $\times$ Time Period interaction effects for recall, $F(4, 48) = 1.84$, *ns*, partial η^2 .13, or recognition, $F(4, 48) = 0.59$, *ns*, partial $\eta^2 = .05$. A comparison of 2 patients with Korsakoff's syndrome and 3 with herpes across 35 years preonset also failed to give significant interactions on either recall, $F(6, 18) = 0.78$ or recognition, $F(6, 18) = 0.23$. Comparing the two patient groups, the size of the recognition minus recall discrepancy across the 25-year period did not differ significantly across the Group, $F(1, 12) = 0.04$, *ns*, partial $\eta^2 = .00$ and Group $\times$ Time Period $F(4, 48) = 2.18$, *ns*, partial $\eta^2 = .15$, comparisons. In summary, the pattern of performance across the 25-year sampling period in the two patient groups was statistically indistinguishable.

To control for putative age differences in the patient groups, two subgroups of 4 patients with Korsakoff's syndrome (mean age $= 59.5 \pm 6.5$) and 4 patients with herpes (mean age $= 57.75 \pm 10.2$) were compared. On recall, there were no significant differences between these subgroups in terms of either the main Group effect (F $(1, 6) = 0.39$, *ns*) or Group $\times$ Period interaction (F $(4, 24) = 0.81$, *ns*). Likewise, on recognition within these age-matched groups, there was no significant main effect of Group (F $(1, 6) = 0.54$, *ns*) or Group $\times$ Time-Period interaction (F $(4, 24) = 0.62$, *ns*).

Finally, we calculated Pearson correlation coefficients in the small subgroup of patients ($N = 8$) for whom volumetric data were available to determine whether recall or recognition performance was correlated with volume reduction in one or more brain regions (e.g., medial temporal, anterolateral temporal, overall temporal, or frontal). In this small subgroup, correlations between recall or recognition and the three temporal lobe volumes were all nonsignificant ($p > .2$).

Discussion

The performance of patients with Korsakoff's syndrome and patients with herpes encephalitis in Study 1 appears to contradict the view that semantic memory is intact in amnesia (Cermak, 1984; Warrington & Weiskrantz, 1982) and to be consistent with other investigations showing extensive retrograde memory impairment on vocabulary tests (e.g., McCarthy et al., 2005; Verfaellie et al., 1995a, 2000, 1995b). Relative to their controls, both patient groups demonstrated significantly impaired recall performance for premorbidly acquired "new" vocabulary. This performance deficit also held true on recognition testing, although it was of only marginal significance in the herpes group (possibly because of a ceiling effect in the controls). There were no significant Korsakoff versus herpes differences in terms of either recall or recognition memory across the 25-year period, and the patient groups did not differ significantly in terms of recognition minus recall difference scores.

A primary reason for choosing vocabulary words in the current study (as in earlier investigations) was to maximize the involvement of semantic memory in task performance. Nevertheless, it is plausible that more recent words might be more associated with the spatial and temporal context in which they were encountered than older words are, that is, more dependent on episodic memory. However, the finding that amnesic patients' performance was significantly poorer than controls' for words spanning across three decades (with no evidence of a temporal gradient) argues strongly that remote and recent semantic memory are indeed affected in amnesia.

Study 2: Free Recall/Cued Recall

The second study compared patients with Korsakoff's syndrome and patients with herpes encephalitis on free and cued recall versions of the test, in which words were given to definitions instead of definitions to words. The purpose of the study was to corroborate the findings described earlier and to examine whether the deficit in the patient groups was more likely to reflect a problem in accessing (retrieving) the target words, rather than in storing them, by use of a cueing procedure.

Method

Procedure. The same 70 target words that were administered to the patients with herpes in Study 1 were used in the present task. Correct definitions were drawn up and presented to the subjects verbally. For the free recall condition, the participants were requested to think of the most appropriate word to match each definition. Whenever a participant did not respond for several seconds or appeared to forget the definition, it was read out loud once more. All responses were recorded, and no feedback given concerning the accuracy of the response. In the cued recall condition, the definition was orally presented again at the same time as a visual presentation on a "flash" card, which was a cue for the target word. The cue remained until a response was given. The participants were instructed to respond with the word they thought would fit the definition and cue or with the first relevant word that entered their minds. For single target words, the cue comprised the first two letters followed by a horizontal underscore line for each subsequent letter. For two-word targets, the first letter of each word was presented. For example, the cues for "microwave" and "compact disk" were presented as follows:

Microwave: MI_ _ _ _ _ _ _

Compact disk: C_ _ _ _ _ _ D_ _ _

All responses were recorded, and no feedback or further prompts were provided. Both free recall and cued recall conditions took place during the same session, with free recall presented first. No information about the cued recall condition was provided until the free recall condition had been completed.

During free recall, no time limit for a response was set, with the next item presented once a response was given or if the participant decided that he or she could not provide a possible answer. In cued recall, if no response was forthcoming, an attempt to facilitate a response was made by repeating on one occasion that the word(s) began with the letters shown on the card. No further cues or prompts were provided.

Scoring was carried out in the same manner as Study 1, that is, with reference to the date of onset of each patient's amnesia to ensure that the test was of "retrograde" amnesia. The procedure, therefore, resulted in a total of 5 data points, extending back 25 years. However, we again report the results across 35 years preonset in subgroups consisting of older patients (>40 years) of recent onset (<40 months) in comparison with age-matched controls.

Results

Performance in patients with Korsakoff's syndrome. Mean scores of patients with Korsakoff's syndrome and their controls are plotted in Figure 3 (left panel). The analysis of free recall across the 5 periods demonstrated a significant effect of Group, $F(1, 14) = 21.57$, $p < .001$, partial $\eta^2 = .62$, but not Time Period, $F(4, 56) = 1.72$, *ns*, partial $\eta^2 = .11$). There was a marginal Group × Period interaction, $F(4, 56) = 2.08$, $p < .10$, partial $\eta^2 = .13$, such that patients with Korsakoff's syndrome showed a trend for poorer free recall of recent compared with older words. Comparing 6 patients with Korsakoff's syndrome with 6 controls across 35 years preonset, this interaction was not significant, $F(6, 60) = 1.32$.

Cued recall scores differed across groups (Figure 3, middle panel), with the patients with Korsakoff's syndrome scoring more poorly than their controls at all periods, $F(1, 14) = 11.75$, $p < .01$, partial $\eta^2 = .46$. There was also a main effect of Period, better scores being shown for words which had entered common usage in remote, relative to recent, periods, $F(4, 56) = 6.62$, $p < .01$, partial $\eta^2 = .32$. The Group × Period interaction effect was not significant, $F(4, 56) = 1.64$, *ns*, partial $\eta^2 = .11$). On the analysis of 35 years preonset, this interaction was again not significant, $F(6, 60) = 1.15$.

The difference between cued and free recall (Figure 3, right panel) varied by Period (a wider discrepancy for more remote periods), $F(4, 56) = 3.96$, $p < .01$, partial $\eta^2 = .22$, but there was no significant main effect of Group, $F(1, 14) = 0.23$, *ns*, partial $\eta^2 = .02$, nor a significant Group × Period interaction, $F(4, 56) = 1.49$, N.S., partial $\eta^2 = .10$.

Performance in patients with herpes. Mean scores are presented in Figure 4. On free recall (left panel), controls performed better than the patients, $F(1, 14) = 17.92$, $p < .01$, partial $\eta^2 = .56$. The Group × Period interaction was not significant, $F(4, 56) = 0.72$, *ns*, partial $\eta^2 = .05$. On comparison of 3 patients with herpes and 6 control participants across 35 years preonset, this interaction was again not significant, $F(6, 42) = 1.58$.

On cued recall there were significant main effects of Group, $F(1, 14) = 17.47$, $p < .01$, partial $\eta^2 = .56$; Period, $F(4, 56) = 4.22$, $p < .01$, partial $\eta^2 = .23$; and also a significant Group × Period interaction, $F(4, 56) = 2.83$, $p < .05$, partial $\eta^2 = .17$. The controls performed better than the patients with herpes, but the patients showed relative sparing for words from the more remote periods. However, in the analysis of 3 patients with herpes and 6 controls across 35 years preonset, the Group × Period was not significant, $F(6, 42) = 1.58$.

The magnitude of the discrepancy between cued and free recall scores was closely similar across the Groups, $F(1, 14) = 2.81$, *ns*, partial $\eta^2 = .17$; and the Period and Group × Period effects were also nonsignificant, $F(4, 56) = 2.05$, *ns*, partial $\eta^2 = .13$; $F(4, 56) = 0.48$, *ns*, partial $\eta^2 = .03$.

Comparison of Korsakoff and patients with herpes. To check the validity of making comparisons across the patients in the herpes and Korsakoff groups, scores in their respective two control groups were compared. No group differences were found on background measures (memory and frontal/executive function). Figure 5 (middle row) shows that similar vocabulary

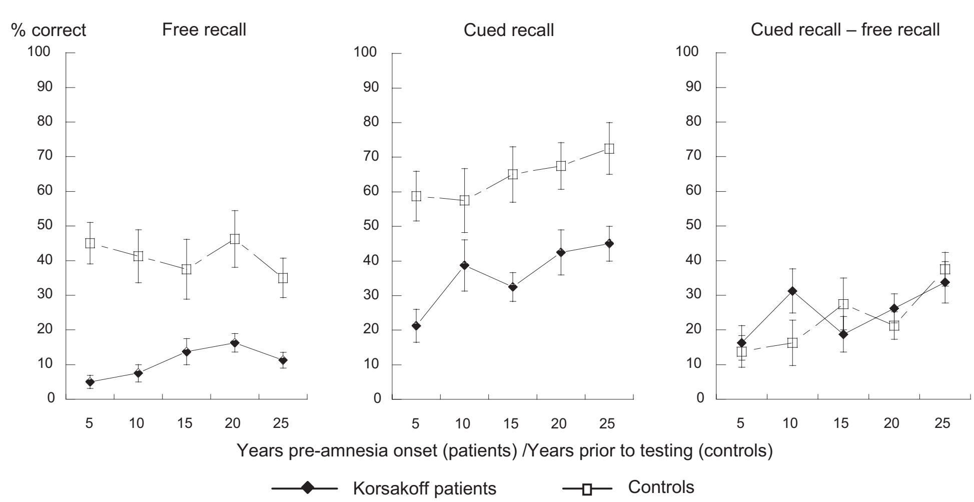

Figure 3. Study 2. Charts showing free recall, cued recall, and cued minus free recall scores (with *SE* bars) in patients with Korsakoff's syndrome and controls for words entering the vocabulary during a period of 25 years prior to the onset of amnesia (grouped by 5-year intervals).

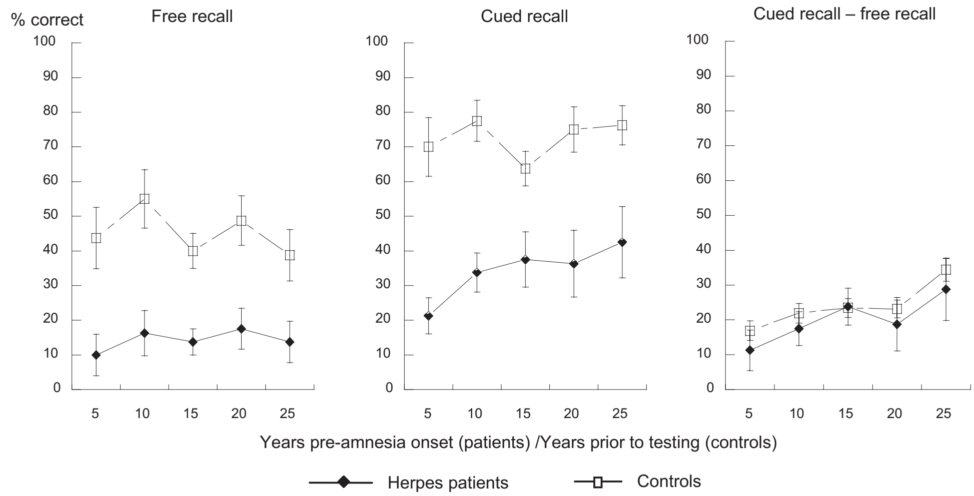

Figure 4. Study 2. Charts showing free recall, cued recall, and cued minus free recall scores (with *SE* bars) in patients with herpes and controls for words entering the vocabulary during a period of 25 years prior to the onset of amnesia (grouped by 5-year intervals).

test scores were demonstrated across the two control groups in all task conditions. Given these overlapping scores in the two control groups, a direct comparison of the patients with Korsakoff's syndrome and patients with herpes was undertaken.

Recall performance did not differ significantly across the two patient groups, $F(1, 14) = 0.63$, *ns*, partial $\eta^2 = .04$. There was also no Group × Period interaction, $F(2, 32) = 0.48$, *ns*, partial $\eta^2 = .03$. This interaction was also not significant when 6 patients with Korsakoff's syndrome were compared with 3 patients with herpes across 35 years preonset, $F(6, 42) = 0.70$.

The analysis of cued recall showed a significant main effect of Period, $F(4, 56) = 10.11$, $p < .001$, partial $\eta^2 = .42$, but not of patient Group, $F(1, 14) = 0.04$, *ns*, partial $\eta^2 = .00$. The Group × Period interaction was also not significant, $F(4, 56) = 0.71$, *ns*, partial $\eta^2 = .05$, and this was also the case when comparing the subgroups across 35 years preonset, $F(6, 42) = 1.06$. The discrepancy between free and cued recall varied by Period, $F(4, 56) = 2.65$, $p < .05$, partial $\eta^2 = .16$, but there were no significant differences between the two patient Groups, $F(1, 14) = 1.05$, *ns*, partial $\eta^2 = .07$, nor was there any significant Group × Period interaction effect, $F(4, 56) = 0.76$, *ns*, partial $\eta^2 = .05$.

Age-matched comparisons were carried out in 5 patients with Korsakoff's syndrome (mean age = 47.6 ± 7.0) and 5 patients with herpes encephalitis (mean age = 47.2 ± 9.5). On free recall, there was no significant main effect of group in these age-matched subgroups ($F = 0.29$, *ns*) or Group × Period interaction ($F = 1.60$, *ns*). Likewise on cued recall, there was no main effect of Group ($F = 0.09$, *ns*) or Group × Period interaction ($F = 0.27$, *ns*).

Finally, we calculated Pearson correlation coefficients for all patients for whom we had volumetric data (herpes and Korsakoff) to determine whether free or cued recall performance appeared to be related to frontal or temporal lobe integrity. In the small group for whom quantitative MRI data were available ($N = 11$), all correlations between recall or recognition and the three temporal lobe volumes were nonsignificant.

Discussion

On free recall and cued recall, patients with Korsakoff's syndrome and patients with herpes encephalitis were significantly impaired compared with healthy participants. In both cases, somewhat better performance was achieved for those items drawn from the more remote periods, but comparison with healthy participants did not reveal a statistically significant temporal gradient except for the herpes group on cued recall. In keeping with these findings, cued minus free recall scores did not differ significantly, and the overall temporal profile on all measures was equivalent in both patient groups. In short, this finding (in keeping with the equivalent recognition minus recall finding in Study 1) did not provide support for the view that the problem was simply in "low-level" retrieval processes.

These overall results are consistent with the findings in Study 1, the clear deficits in both free recall and cued recall measures in the two patient groups (compared with healthy participants) contradicting the hypothesis of preserved semantic memory in amnesia. Furthermore, the extent of overlap in both patient groups on all measures is inconsistent with the view that remote memory deficits arising from extensive temporal lobe damage can be dissociated from those arising from damage to diencephalic and frontal regions. Instead, the findings might suggest that retrieval of these definitions-to-words involves a distributed network which includes temporal, frontal and diencephalic regions. This view is consistent with the findings of studies emphasizing the interconnection of these structures in episodic memory (e.g., Aggleton & Brown, 1999; Aggleton & Saunders, 1997; Kopelman, 1997; Warrington & Weiskrantz, 1982).

Study 3: Comparison of Vocabulary With Autobiographical and Other Remote Memory Tests

To make comparisons between RA for semantic and episodic or personal semantic memories, we report previously unpublished analyses from the Kopelman et al. (1999) data set. These participants had been tested on the autobiographical incidents and per-

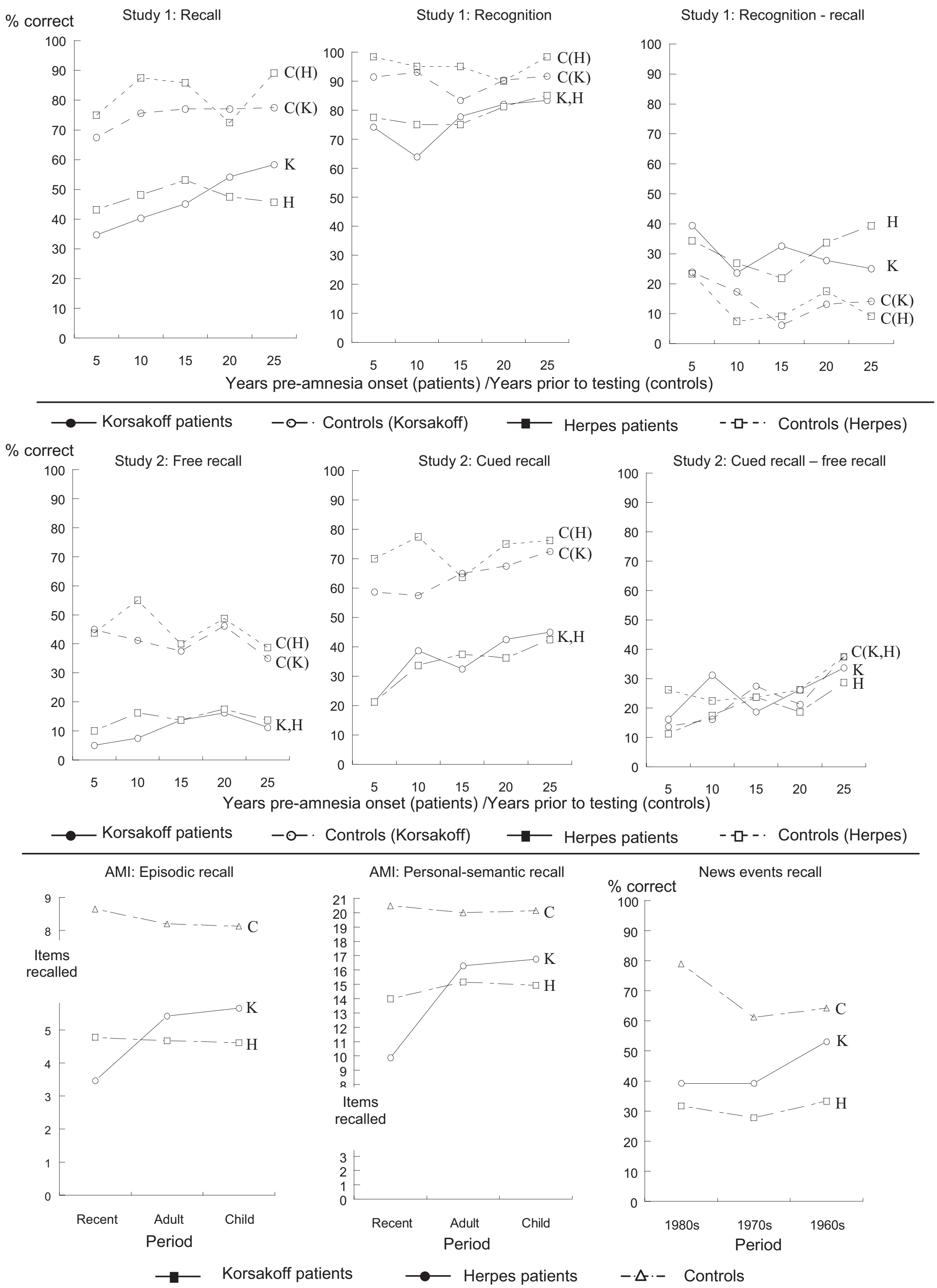

Figure 5. Charts showing data for studies 1 and 2 (top two rows) together with performance on the Autobiographical Memory Interview (AMI) for recall of autobiographical (episodic) incidents and personal-semantic facts, plus Famous News Events recall (bottom row). K = Korsakoff; K(C) = controls (Korsakoff); H = herpes; H(C) = controls (herpes); C = controls.

sonal semantic schedules from the Autobiographical Memory Interview (AMI) (Kopelman et al., 1989), and recall and recognition versions of a Famous News Events test. The data had previously been published in terms of "diencephalic" and "temporal lobe" groups, which contained patients other than just Korsakoff and herpes groups, respectively (Kopelman et al., 1999). Here, the findings from the patients with Korsakoff's syndrome and patients with herpes encephalitis are presented in isolation.

The AMI is a semistructured interview, in which patients are probed for facts (e.g., addresses, names of friends) and specific incidents or events that occurred in each of three time-periods: "childhood," "young adult," and "recent." In the Famous News Events recall test, participants were shown 30 pictures of "famous" events, 10 for each decade from the 1960s to the 1980s (randomly distributed within the test) and were asked to identify each event. No points were awarded for a simple description of the picture without any evidence of having identified the event.

Results

Figure 5 presents the temporal profile of memory loss for vocabulary words from studies 1 and 2 in the upper and middle rows, respectively. Figure 5, bottom row, gives the comparable findings for recall of autobiographical incidents (left panel), personal semantic facts (middle panel), and recall of news events (right panel) in patients with Korsakoff's syndrome and those with herpes encephalitis.

On the measures of vocabulary retrieval, there were no significant Group by Period interactions between the patients in the Korsakoff and herpes groups, who performed at a similarly impaired level (Figure 5, upper two rows), and this was also the case when subgroups of the patients were compared across 35 years preonset. On the basis that the two control groups did not differ significantly on any of these measures, we then merged the two control groups and reran the analyses comparing the two patient groups with this single control group. There were no significant interaction effects on either recall, $F(8, 92) = 1.47$ or recognition, $F(8, 92) = 1.66$ in Experiment 1, nor on free recall, $F(8, 116) = 1.24$ or cued recall, $F(8, 116) = 1.36$ in Study 2.

By contrast, on the measures of autobiographical incident and personal semantic fact recall, there were significant differences in temporal gradient when comparing these Korsakoff and herpes groups, (Figure 5, bottom row): there was relative sparing of early memories in the Korsakoff group relative to the herpes group both for autobiographical incidents, $F(2, 40) = 4.62$, $p < .05$, partial $\eta^2 = .19$, and in the recall of personal semantic facts, $F(2, 40) = 3.77$, $p < .05$, partial $\eta^2 = .16$. While the Korsakoff group showed a definite gradient, the patients with herpes exhibited a virtually "flat" curve, and Figure 5 shows that this difference in temporal gradient resulted entirely from a difference in the Korsakoff group's performance between the "early adult" years and the "recent" period. When healthy controls were also included in the analyses, there were main effects of group: episodic/autobiographical incidents, $F(2, 39) = 21.83$, $p < .001$, partial $\eta^2 = 0.53$; personal semantic memory, $F(2, 39) = 37.0$ $p < .001$, partial $\eta^2 = 0.65$. There were also significant Group by Time Period interaction effects: episodic/autobiographical incidents, $F(4, 78) = 6.81$ $p < .001$, partial $\eta^2 = 0.26$; personal semantic memory, $F(4, 78) = 7.96$ $p < .001$, partial $\eta^2 = 0.29$.

On news event recall, there was no significant Group × Period interaction, $F(2, 40) = 1.77$, *ns*, partial $\eta^2 = .08$; and, although the patients with herpes manifested lower scores for all periods than the patients with Korsakoff's syndrome, the main effect of Group was not significant, $F = (1,20) = 1.44$, *ns*, partial $\eta^2 = .07$.

Because the mean ages in these two patients samples were reasonably well matched (Korsakoff = 55.4 ± 8.1; herpes encephalitis = 49.1 ± 12.2), further analysis in terms of age-matched subgroups was not carried out.

Discussion

Although retrograde amnesia can lead to severe episodic and semantic memory deficits, the present comparison indicates differences in the temporal gradient of memory loss across these domains. Patients with Korsakoff's syndrome and patients with herpes encephalitis had not differed significantly in terms of temporal gradient on our semantic (vocabulary) tasks, when group by time-period interactions were sought on analyses of variance (ANOVAs) over the preonset 25 years or (in subgroups) 35 years. On the other hand, the patients in the Korsakoff group showed a significantly steeper temporal gradient (relative sparing of earlier memories) than did the herpes group where the information was personally relevant (autobiographical incidents or personal semantic facts). This discrepancy between performance on the vocabulary tests and the autobiographical measures cannot be explained in terms of the periods covered in the different tasks. Although the autobiographical memory test taps memories as far back as childhood, the steeper temporal gradient in the patients in the Korsakoff group arose in comparing performance across the early adult/recent periods. On the vocabulary tests, both patient groups showed equivalent performance across these periods, whether the comparisons were based on a 25-year or 35-year preonset sampling period.

General Discussion

Although the present experiments were carried out on different (but overlapping) groups of patients, which might limit the interpretation of the findings, and there was heterogeneity in the extent of the lesions and limited availability of quantified MRI data, each respective group (controls, patients with Korsakoff's syndrome, patients with herpes encephalitis) showed similar performance on background neuropsychological tests across the three experiments (see Table 1). Taken together, the present findings do not support the theory proposed by Cermak (1984), and by Butters and Cermak (1986), that the relative preservation of remote information reflects a shift from episodic to semantic memory systems. Findings in our two main experiments (definitions-to-words; words-to-definitions) were highly consistent in that they indicated that, throughout the sampling period extending back 25 to 35 years preonset, patients' performance was very poor relative to that of healthy participants. As previously argued by Verfaellie et al. (1995a, 1995b), this theory assumes relatively intact remote semantic memories, and this is inconsistent with a memory deficit for words extending across all time-periods.

The damage incurred in patients with herpes encephalitis and the alcoholic Korsakoff's syndrome has been shown to result in a pattern of semantic memory loss that is similar in a number of respects despite disproportionately severe medial and anterolateral temporal lobe damage in the patients with herpes on our MRI measures. Recall of semantic information was severely affected in both patient groups, and the two groups showed equivalent levels of overall performance on the tasks, before and after age-matching. Moreover, in both patient groups, there was only minor evidence of a temporal gradient in the pattern of memory loss for vocabulary words over the 25-year period before the onset of the patients' amnesia. In patients with Korsakoff's syndrome, the gradient was significantly steeper than that found in healthy participants only when the earliest 2 decades were compared with the most recent 2 decades on recall testing in Study 1 (as Verfaellie et al., 1995b, had found) but not in terms of Group by Time Period interaction effects across either 25 or 35 years preonset. On recognition testing, there was a significant group by time-period interaction in Study 1 but, after correction for heterogeneity of variance, this effect did not reach conventional criteria for statistical significance. In patients with herpes encephalitis the temporal profile of scores differed from healthy participants' only on the cued-recall test. No significant group differences were observed in the direct comparisons of patients with Korsakoff's syndrome and patients with herpes encephalitis in either study, before or after controlling for age and whether the analysis was across 25 or 35 years preonset. This pattern cannot easily by ascribed to stimulus-related factors, such as retrieval difficulty of vocabulary items across the different time-periods, because an analysis of recall scores in the control groups showed no effects of period for Study 1, $F(4, 20) = 0.61$, *ns*, or Study 2, $F(4, 28) = 1.24$, *ns*. Thus, in contradiction to our first hypothesis, the herpes and Korsakoff groups did not differ significantly in either the severity or temporal gradient of their remote semantic memory impairment.

There was also minimal support for our second hypothesis: To the extent that the semantic memory impairment is primarily one of simple retrieval, the patient groups should show a disproportionate benefit on recognition or cued conditions, relative to free recall, compared with healthy participants. Both patient groups tended to perform better on the recognition/cued versions of the tasks than on free recall, but only in the herpes group on recognition testing in Study 1 was that benefit significantly greater than the equivalent gain seen in healthy participants, so that the case for a "low-level" retrieval deficit was not supported. Furthermore, there was no difference between patients with Korsakoff's syndrome and patients with herpes encephalitis in the extent to which they benefited from recognition/cued versions of the tasks, a finding which is inconsistent with the notion that patients with Korsakoff's syndrome have an impairment primarily of low level retrieval.

Finally, the findings also raise questions for both consolidation and multiple trace theories, which predict preserved remote semantic memories following focal medial temporal and (by extension) focal diencephalic pathology. Consolidation theory predicts equivalent temporal gradients in the retrieval of episodic and semantic memory, whereas multiple trace theory claims that remote semantic memories will remain relatively normal following medial temporal damage (Nadel & Moscovitch, 1997; Westmacott & Moscovitch, 2002). Even where there is additional temporal neocortical damage, multiple trace theory would suggest that remote semantic knowledge is likely to show a steeper gradient than remote episodic/autobiographical memories (Nadel, Samsonovich, Ryan, & Moscovitch, 2000; Viskontis et al., 2000). Our patients did not have damage confined to the medial temporal lobes but, nevertheless, these theoretical claims do not fit with the present findings.

Patients with herpes encephalitis showed a relatively "flat" temporal gradient across all the semantic and episodic memory tasks (see Figure 5), a finding that is broadly consistent with Westmacott and Moscovitch's (2002) result for vocabulary words in semantic dementia. We postulate that the patients with herpes' impairment on the vocabulary task results from their extensive (left) temporal lobe pathology and atrophy and, consequently, this finding does not conflict with reports of more limited retrograde amnesia on semantic tasks in patients with pathology largely confined to the medial temporal lobes (KC in Westmacott & Moscovitch, 2002; Manns et al., 2003; Rosenbaum et al., 2005; Steinvorth, Levine, & Corkin, 2005).

By contrast, patients with Korsakoff's syndrome showed a striking temporal gradient in the recall of autobiographical incidents and personal semantic facts (i.e., relative sparing of earlier autobiographical memories), but this pattern of relatively preserved early memory was not reliably shown on any of the versions of the vocabulary tasks. The difference between the Korsakoff group's remote episodic and semantic memory temporal gradients (i.e., the relative sparing of their early episodic memories) did not result from any difference in the time-periods covered, because the steeper gradient on the episodic/autobiographical tasks occurred between the "early adult" and "recent" time-periods, which were amply covered in the vocabulary tests. The relatively "flat" gradient on the vocabulary task was an unexpected finding that is not easily accommodated by multiple trace theory. The patients with Korsakoff's syndrome in our series had minor, nonsignificant temporal lobe volume changes (Colchester et al., 2001). However, they did show varying degrees of frontal atrophy (Colchester et al., 2001), and their impairment on the vocabulary tasks may relate to their frontal damage and disruption "upstream" in frontal-temporal lobe circuits affecting some aspect of controlled search and retrieval processes (compare Verfaellie et al., 1995b).

In summary, on these remote semantic memory tasks, patients with Korsakoff's syndrome and patients with herpes encephalitis were impaired across all time-periods, including words acquired long before the onset of amnesia, in itself an important finding. Furthermore, there was only weak evidence of a temporal gradient in either group, nor was there any differential pattern of impairment between these two patient groups. By contrast, on measures of episodic (autobiographical and personal semantic) remote memory, patients with Korsakoff's syndrome, but not patients with herpes encephalitis showed clear evidence of a temporal gradient (relative preservation of early memories), manifest as a difference between the "early adult" and "recent" time periods. This pattern is inconsistent with the hypothesis of an episodic-to-semantic shift in the quality with which memories are stored, and it is also inconsistent with the predictions of both multiple trace and consolidation theory. Each of these theories would have predicted relative sparing of early semantic memories. In the patients with herpes encephalitis the loss of early vocabulary presumably relates to their widespread structural damage in the left temporal lobe, as has been suggested before (Verfaellie et al., 1995a; Westmacott, Leach, Freedman, & Moscovitch, 2001). However, the patients with Korsakoff's syndrome in our series had only minor, nonsignificant temporal lobe volume changes, but they did show varying degrees of frontal atrophy (Colchester et al., 2001). Hence, their impairment on the vocabulary tasks may have a different underlying basis from that of the patients with herpes, presumably related to their fronto-diencephalic damage and disruption "upstream" in frontal-temporal lobe circuits. A potential interpretation of this would be in terms of Verfaellie et al.'s. (1995b) suggestion of a deficit in the controlled search and retrieval of semantic information in patients with Korsakoff's syndrome, which, because "higher-order" cannot be overcome by simple recognition memory or cueing procedures.

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Received July 30, 2008
Revision received August 4, 2008
Accepted August 4, 2008 ■

Correction to Fortier et al. (2008)

In the article "Delay Discrimination and Reversal Eyeblink Classical Conditioning in Abstinent Chronic Alcoholics," by Catherine Brawn Fortier, Elizabeth M. Steffen, Ginette LaFleche, Jonathan R. Venne, John F. Disterhoft, and Regina E. McGlinchey (*Neuropsychology*, 2008, Vol. 22, No. 2, pp. 196–208), the lifetime drinking data listed in Table 1 on p. 198 was not correctly calculated and underestimated lifetime exposure to alcohol. The corrected lifetime variables from that table appear below.

Table 1. Drinking characteristics of the abstinent alcoholic group. Lifetime Drinking History (LDH) (Skinner & Sheu, 1982) is designed to aggregate all drinking phases across the lifespan. Therefore this instrument assesses all time periods (not just phases of heavy drinking) in which a participant reported using alcohol regardless of quantity of use.

	LDH Lifetime Measures	
	Total Lifetime Drinks	Total Lifetime Drinks (g/kg)*
ALC001	7680	1532
ALC002	39112	6825
ALC003	9115	2597
ALC004	62640	9189
ALC005	170694	32949
ALC006	29974	5315
ALC007	66498	9447
ALC008	17338	3973
ALC009	7200	1657
ALC010	24989	3887
ALC011	13070	3918
ALC012	227556	50433
ALC013	67440	12194
ALC014	9556	1773

*adjusted for weight

DOI: 10.1037/a0015035