Serial position and temporal cue effects in multiple sclerosis: Two subtypes of defective memory mechanisms

CAROL ARMSTRONG,* KRIS ONISHI, KEITH ROBINSON, MARK D'ESPOSITO, HEIDI THOMPSON, ABDOLMOHAMMAD ROSTAMI and MURRAY GROSSMAN

Department of Neurology, University of Pennsylvania Medical Center, Philadelphia, PA 19104-4283, U.S.A.

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Abstract—Neurocognitive studies of multiple sclerosis (MS) have identified a robust long-term memory deficit. We hypothesized that this is due in part to the limited representation and use of serial order information. MS patients and controls were studied with a supraspan list learning procedure with post-encoding retrieval and recognition trials. MS patients demonstrated post-encoding negative recency with normal recognition, and word order recall was impaired. These findings appear to be in part to difficulty using temporal order cues in long-term memory. Two dissociable memory deficits were identified, suggesting that there are at least two neurocognitive mechanisms underlying memory impairment in MS. Copyright © 1996 Elsevier Science Ltd.

Key Words: multiple sclerosis; memory; temporal or ordinal coding; serial position.

Introduction

The cognitive impairments accompanying multiple sclerosis (MS) most frequently include memory complaints. A memory impairment is found in 40–60% of MS patients [13, 15]. Free recall is impaired on measures of long-term memory. By comparison, performance on tests of the short-term store is usually normal, including normal recency effects [17, cf. 35, 37]. Although MS patients perform at a generally lower level on supraspan word list indices, multi-trial learning curves including serial position analyses and correlation of memory performance with other cognitive measures have not revealed whether the long-term memory impairment in MS is due to difficulty with encoding, retrieval, or some other cognitive impairment [17, 22]. The purpose of this study is to investigate the bases for long-term memory difficulty in MS.

Whereas some controversy remains about whether encoding or retrieval is impaired in MS patients, most evidence indicates retrieval failure. Evidence of failed long-term memory recall caused by a retrieval deficit has been demonstrated in several studies [12, 35, 36, 42]. The claims of long-term memory retrieval failure come from the findings that recognition and forgetting rates are often not impaired [21, 35, 37], although this has not been a universal finding [17, 28]. However, some authors have suggested that acquisition is defective in MS, largely based on measures of accuracy in recall [10, 12, 17, 22, 42]. In contrast, other authors have provided evidence that semantic encoding is intact in MS patients [4, 7, 35].

We examined MS patients' abilities to learn a supraspan list of words, and then to retain the words over two interference conditions. We sought to learn whether MS patients are failing to learn supraspan word lists during five-trial list learning, and hypothesize that performance over five-trial learning will demonstrate a learning deficit. We propose that a defective retrieval process is the most parsimonious explanation of memory impairment in most MS patients. The basis for this proposition comes from serial position theories for list recall. Recall of a supraspan list does not only reflect short-term memory capacities and long-term retrieval dynamics are also thought to be involved [45]. During learning trials, the list portion which has been recalled least well in MS patients has been the middle list portion. Middle list recall occurs last and is associated with the lowest probability
of recall. Whitten [45] has argued that output interference theories can explain serial position phenomenon. Thus, through the build-up of lexical processing, the result of recalling earlier items may increase interference and decrease the likelihood of recalling later items. Recency items escape this fate by being associated with ordinal cues which support later retrieval of a list's terminal items [24, 25], and rehearsal of list words is thought to support recall of initial words [32]. If the memory processing of MS subjects is most vulnerable to failure of retrieval mechanisms, then difficulty recalling the middle list portion during learning trials should occur. Normal encoding will be demonstrated in part by the finding of normal recall of terminal list words in MS. Previous studies in MS of semantic encoding, as well as typically normal recency, suggest that MS subjects are able to encode terminal words into long-term storage [17, 37]. We will further test the proposition that patients have the capacity to encode words, by directly comparing patients' recall of words learning trials with their post-encoding recall. We will correlate subjects' recall of the list during learning trials with post-encoding recall, and hypothesize that MS patients will demonstrate normal transferability of words into the long-term store, even in a subgroup who fail to recall adequately. This finding would suggest that long-term memory encoding had occurred.

We will also examine post-encoding serial position retrieval effects for evidence that patients have failed to retrieve the words. Recall of terminal words in list learning tasks after a delay, and negative recency in particular, have been associated with failure of retrieval of temporal and semantic attributes [2, 6, 8, 31, 44]. Temporal coding theories propose that an item is associated with information about its relative temporal position [46], or its item-to-item ordinal relationship [41]. In studies of groups of non-neurologically impaired subjects, failure to retrieve the terminal words from lists could be induced after successful learning of the terminal words. Despite efforts to preclude the temporal coding of the terminal words, these words were found to be coded with temporal attributes [24, 31, 45]. Some evidence of a temporal coding deficit in MS comes from Beatty and Monson's [3] finding of impaired recency discrimination of words in MS patients who were able to recognize the previously presented words. Since there is evidence that MS patients are able to represent mentally semantic attributes of words [7], we predict that the major memory impairment in MS will be in the retrieval of temporal attributes of the words. We hypothesize that MS patients will not demonstrate failed temporal activation during the learning trials, and will use ordinal cues (e.g., serial order chaining) normally during this phase.

Furthermore, if retrieval processes account for the primary memory impairment in MS, then the patients' performance on the recognition condition should be unimpaired. However, because free recall is more dependent on retrieval associations than is recognition, a failure to recall items and their associations along with normal recognition could still occur in the presence of a failure to encode or store the inter-item associations. This is because whereas free recall is dependent on the retrieval of associations between list items, recognition can be made based on a familiarity decision only [16]. We will examine the retention of ordinal association cues used in free recall during learning trials and later in free recall during long-term memory retrieval, to understand whether these association cues have been maintained. We will also examine subjects' discrimination of targets from related distracters during recognition, for evidence of degradation of the store of target associations. If association cues have degraded, then patients may falsely recognize the semantically, phonologically and temporally related non-target words.

Methods

Subjects

We tested 67 patients with clinically definite multiple sclerosis (MS) [34] who were recruited from the Comprehensive Multiple Sclerosis Center in the Department of Neurology at the University of Pennsylvania. This group consisted of 45 patients with symptom histories characteristic of a relapsing-remitting (RR) course, and 22 with a chronic-progressive (CP) course. All patients were clinically stable at the time of testing. We did not analyse the CP and RR groups separately because preliminary analyses indicated that the CP and RR groups did not differ in the memory indices used in this study, and lack of significant differences were maintained when we covaried these variables for duration of disease and disability rating score. The summary measure of five-trial learning was not different between the groups [F(1,61) = 0.03, ns], and covarying for Kurtzke's [18] Extended Disability Rating Scale score and duration of disease still resulted in no significant group difference [F(2,61) = 1.74, ns]. Group differences were also not significant for recall after the distracter list [F(1,61) = 1.69, ns] nor when covarying for disability rating score and duration [F(2,61) = 1.89, ns].

The MS group was matched for age and education with 22 normal control subjects. The mean age of the 67 MS patients was 38.6 years (S.D. = 8.3) and of the 22 normal subjects was 38.3 years (S.D. = 12.6) [t(87) = 0.13, ns]. Patients had a mean of 14.6 years of education (S.D. = 2.8), whereas the control group had a mean of 15.1 years (S.D. = 2.6) [t(87) = 0.84, ns]. Normal subjects were comprised of the family members of patients as well as community volunteers.

Procedures

The Rey Auditory Verbal Learning Test [38], supplemented with a recognition procedure [20], was administered to all subjects. A target list of 15 familiar, semantically unrelated nouns was read at an interstimulus interval of 1.0 sec, followed by free recall (T1). No orientation instructions were given at any time during the test except to inform subjects that they were not required to recall the words in the order given. Subjects were allowed unlimited periods for recall, so that subjects with a long latency of recall were not penalized. The list was read four additional times in the same manner, each followed by free recall (T2–T5). Immediately after the recall of the fifth learning trial, another list of 15 words (distracter list) was read, followed
by free recall. This measure was not included in the analysis as it was used only to disrupt memory by limiting rehearsal of the target list. Free recall of the target list (T6) was obtained after recall of the distracter list. Subjects were then asked to listen to a list of 50 words, which included the target list, the distracter list, 10 word foils which were high-frequency associates of the same semantic categories as the target words (e.g. "foil = "teacher", target = "school"), and 10 word foils which were phonologically similar to target list words (e.g., "mouse" = foil, "house" = target). Recognition judgement was indicated by a "yes" or "no" response to each word, indicating the patient's belief about the word's target group membership. A final free recall of the target list was required 30 min later (T7). The intervening period was filled with visuospatial perceptual tasks.

Data analysis

The following indices of memory were used in analyses of both free recall and recognition:

Hit rate (HR). Hit rate calculations are useful for estimating learning over multiple recall trials of a list. This measure was used to reflect learning retrieval because the frequency of retrieval during the learning process is thought to be more sensitive to the likelihood of later retrieval than raw score. Furthermore, it was used as a summary measure of five-trial learning, for correlations with post-encoding recall and recognition scores. Learning of each word on the target list was calculated as:

$$\frac{A + 0.5}{P + 1}$$

[39], where A is the incidence of actual recall of a word over the five trials, and P is the total possible recall. For example, if a subject recalled a word on four of five trials, the hit rate would be

$$\frac{4 + 0.5}{5 + 1} = 0.75.$$

Whole list hit rates were derived by calculating the mean of the hit rates for the 15 words, and serial third analyses used the mean hit rate for the five words in each list third. Hit rates were not used for post-encoding recall trials, where a single recall attempt occurred after the post-distracter condition, and after the post-delay condition. Hit rate, as a measure of the likelihood of the next retrieval, reflects the probability of previous retrieval, and is not appropriate to measure single trial recall.

Signal detection indices of the two-high threshold model [39] including discrimination and response bias, were calculated to analyse the hit rate and false alarm rate of the recognition responses.

Serial position recall. The list was divided into three equal segments (five words each), representing the initial, middle third, and terminal portions. Following Watkins' [43] test of this way of identifying serial positions, we tested our measure of recency by comparing it to the method developed by Tulving and Colotla [40], which calculates the distance of word order from the original presentation order. We calculated serial third scores in both ways, and calculated group differences, finding that both methods yielded similar results. Both serial third hit rates for all five learning trials, and raw scores for post-encoding trials, were used in analyses.

Correlation of hit rate with T6 and with T7. Hit rates from individual words, list total and serial third totals were correlated respectively with individual words, list totals, and serial third totals of T6 (post-distracter free recall) and T7 (delayed free recall). These correlations represented the retention of words which had been learned.

Chaining. As a measure of the use of ordinal cues for retrieval, we used a simple method to count the ordered linking of words that is based on theories that words can be temporally chained by various mechanisms [19]. We counted the number of order links between consecutive pairs of the five words in each third of the list. Links were constrained by their unidirectional relationship. Using a simplified formula derived from Lewandowskii and Murdock's method for measuring retrieval of serial order [19], we measured occurrences of Jn preceded by Jn-1, where J is a serial third of the list, and n represents each of the five words within J; n-1 is counted when the subject recalls the preceding word (within the serial third) correctly, for a maximum of four points. For example, when the five words from the first serial third are recalled in the order, 1, 2, 4, 3, 5, we count 1 order link, for the first and second words recalled in order.

Results

Learning and recall

The mean hit rate (of 15 word hit rates) represents a retrieval-sensitive measure of overall learning over the five trials.* As expected, the MS group performed poorly [mean = 0.66, S.D. = 0.12] compared to normal controls [mean = 0.74, S.D. = 0.09; t(87) = 2.77, P < 0.007]. Confirmation of this result is evidenced by the finding of a significant main effect for group in a group X (five) trials design for the raw number of words recalled [F(1, 87) = 7.65, P < 0.007]. Thus, replicating other studies of list learning in MS, patients performed less well overall than normal subjects.

We then tested serial position effects on hit rates with a group X serial position (initial, middle, terminal words) analysis of variance (ANOVA). The significant main effect for group [F(1, 87) = 7.65, P < 0.007] and group by serial position interaction effect [F(2, 174) = 4.24, P < 0.02] are shown in Fig. 1A. Learning of the middle third averaged across five trials was impaired in the MS group compared to controls [t(87) = 3.50, P < 0.0007], and 16/67 (24%) MS patients obtained z scores of -1.65

* We examined whether MS patients demonstrated recall patterns which deviated from the normal distribution of recall over five trials. For example, we were concerned that an individual may recall half the words very well and half the words very poorly, which would result in the same mean hit rate as that resulting from recalling all the words only moderately well. For each individual we tabulated the occurrence of recall (0 or 1) for each word across the five learning trials. We then tested the similarity of the distributions (for MS and control groups) of these accumulated occurrences with a rank order correlation coefficient of the percentage of subjects in each group at each recall level. Recall levels ranged from no words recalled in five trials to five words recalled in five trials. The rank order distributions of the MS and control subjects' hit rates for each word over all trials were identical (r = 1). Both groups recalled the fewest list items at the lowest hit rates, and the most list items at the highest hit rates (percentages are presented to account for differences in group sizes). Thus, MS patients were not different from controls in that they were able to recall more words at the higher hit rates than at the lower hit rates.
or less, differing from control subjects’ performance at least at the $P < 0.05$ level of significance. Initial and terminal third hit rates did not differ statistically from that of the normal group (initial third $t(87) = 1.54$, ns; terminal third $t(87) = 1.76$, ns). MS patients’ learning was impaired only on recall of the middle words in the list.

In order to examine how much information learned from the first five trials was maintained at the post-encoding retrieval trials, we correlated the mean hit rate with total word retrieval at T6 (post-interference trial), and with total word retrieval at T7 (delayed retrieval trial). Both MS and normal groups demonstrated significant correlations of total mean hit rate with T6 retrieval [MS patients $r = 0.83$, $P < 0.001$; control subjects $r = 0.72$, $P < 0.001$]. The test of significant differences between correlations from independent populations revealed that there was no significant difference between the two coefficients [$z = 1.07$, ns]. A similar pattern was found for correlation of mean hit rate with T7 retrieval [MS patients $r = 0.84$, $P < 0.001$; control subjects $r = 0.80$, $P < 0.001$; $z = 0.47$, ns]. Thus, patients and control subjects tend to maintain a similar amount of information post-interference compared to their learning trials.

These group analyses indicated that MS patients can use their learning in multiple trials to transfer information into a long-term store at a similar proportion to the control group. We sought to determine whether a subgroup of MS patients who were impaired in learning the words, could transfer words into long-term storage, based on correlation of hit rate from the first five trials and T6 recall. We divided the MS patients into poor performers ($n = 15$) on the learning trials (defined as performance of $z < -1.65$, $P < 0.05$ on the total recall on three of the five learning trials, using the normal cohort as the criterion) and compared them with good performers ($n = 18$) (defined as no trial at $z < 0$) and middle performers ($n = 34$) (the balance of MS patients). All MS performance subgroups demonstrated significant correlations (at least at the $P < 0.01$ level) of T6 recall with hit rate (bad performers $r = 0.63$, middle performers $r = 0.52$, good performers $r = 0.57$). Thus, all MS patients, regardless of learning ability during the first five trials, are able to transfer the learned words into long-term memory stores for retrieval at post-encoding trials.

The above findings suggest that MS patients, even those with defective learning, are able to transfer the
words they had learned after five trials, to long-term memory (T6 and T7). We then investigated specific questions of post-encoding retrieval. In our group of 67 MS patients, T6 retrieval of the words was significantly impaired overall, compared to controls \([t(87) = 4.94, P < 0.0001]\). We observed that recall of the terminal third differed significantly from the control group, demonstrating negative recency \([t(87) = 4.94, P < 0.0000]\) (Fig. 1B). Retrieval of the middle third was also impaired \([t(87) = 2.75, P < 0.008]\), although this is not surprising because patients’ learning of the middle portion throughout the five trials was impaired. Using z score analyses, individual analyses show that 22/67 (33%) MS patients were impaired at least at the \(P < 0.05\) level at T6 retrieval of words from the middle third of the list, and 28/67 (42%) were impaired at the same level on T6 recall of words from the terminal third of the list. The primacy effect was similar in both MS patients and normal subjects \([t(87) = 1.72, ns]\). These relative serial position patterns were also significant in the final retrieval at T7 \([t(87) = 1.67, ns; \text{middle third } t(87) = 2.59, P < 0.01; \text{recency effect } t(87) = 3.13, P < 0.003]\) (Fig. 1C). Furthermore, total list recall at T6 and T7 was similar or showed a slight hypermnesia effect as expected \((T6 = 9.78 \text{ words}, T7 = 10.46 \text{ words})\).

There were no group differences in recognition of any serial portion of the list as tested with a group (2) by serial position (3) design \([F(2,174) = 0.07, ns]\) (Fig. 1D), nor were patients impaired in total list hit rate \([t(1,87)= 1.37, ns]\). The terminal third words were located in a long-term memory store as revealed by the MS patients’ normal recognition of these words \([MS \text{ mean words recognized } = 4.55, \text{ S.D.} = 0.82, \text{ control mean } = 4.82, \text{ S.D.} = 0.50; t(87) = 1.43, ns]\). Even the middle third, which MS patients had failed to learn and retrieve by free recall, was recognized normally \([MS \text{ mean words recognized } = 4.61, \text{ S.D.} = 0.83; \text{ control mean } = 4.86; \text{ S.D.} = 0.35; t(87) = 1.37, ns]\).

However, a significant difference between the groups in discrimination (Pr) was found for the total recognition list \([t = 2.05, P < 0.05]\). The slight elevation in the patients’ false alarm rate (FAR) combining all foils \([t = 1.86, P < 0.07]\) without significant response bias \([Br; t = 0.26, ns]\) suggests that patients may have had a mild difficulty in discriminating the targets from other words in memory. Multivariate comparisons of the semantic foils, phonological foils, and recently presented distracter words in the FAR, Pr and Br, however, revealed no interaction effects. These results on recognition versus recall suggest that the memory impairment in MS is primarily caused by a retrieval deficit; MS patients fail to retrieve under free recall conditions, although the words were accessed and discriminated in recognition processes.

Summary. Learning and recall of a supraspan list over five trials is impaired in MS, although the ability to transfer a proportionate amount to the long-term store was not different from normal subjects. The decrement in list learning is explained by impaired middle list recall. During post-interference retrieval, MS patients differed in their retrieval during the five learning trials, by failing to retrieve the terminal portion of the list. This pattern of negative recency retrieval persisted at the 30 min delayed recall trial (T7) as well. Recognition of the total list and all serial thirds was not significantly different from the normal control group, nor were the interference effects found.

Temporal and ordinal effects in retrieval

In an analysis of the subjects’ free recall of the serial order of the words, we examined whether they spontaneously retrieved words in the order in which they had been presented. On the five learning trials, the MS subgroup chained words similarly to control subjects at each learning trial, as revealed in a group \(\times\) trial ANOVA \([F(1,87) = 1.88, ns]\). A group \(\times\) serial position ANOVA of summed chaining scores for all five learning trials revealed a significant main effect for group \([F(1,87) = 6.06, P < 0.02]\), but not a serial position \([F(2,174) = 0.46, ns]\) nor interaction effect \([F(2,174) = 0.46, ns]\). However, because we had an \textit{a priori} interest in how temporal order effects during recall of the terminal third of learning trials related to later recall, we analysed serial position chaining across the five learning trials. The MS patients were impaired only in middle list chaining \([\text{initial portion } t(1,87) = 1.80, ns; \text{middle portion } t(1,87) = 2.70, P < 0.008; \text{terminal portion } t(1,87) = 1.37, ns]\). The group effect most likely reflected MS patients’ overall lower learning level.

We autoregressed recall of the serial position thirds of the five learning trials onto the recall of the serial position thirds at T6 to examine whether certain trials were more predictive than others of the MS group’s retrieval. We used a least squares linear regression equation with the total score for T6 recall as the dependent variable, and the total scores on each of the five learning trials as the predictor variables. The group effect for overall slopes was significant only for the terminal third \([F(6,77) = 3.03, P < 0.01; \text{initial third } F = 1.43, ns; \text{middle third } F = 1.00, ns]\). Normal subjects showed no significant weighting of trial, but the MS patients demonstrated an effect for trial \([F(5,61) = 4.72, P < 0.001]\), and a coefficient of 0.67 for the last learning trial (T5) \([r = 3.63, P < 0.009]\) for prediction of recall of the terminal words. MS patients were more reliant on the most recent recall of the list for their post-encoding (T6) retrieval.

Selective defects in chaining emerged strongly during long-term memory recall. A group \(\times\) serial position (3) analysis of this chaining effect at T6 (Fig. 2) demonstrated a generally weaker chaining effect in MS \([F(1,87) = 10.11, P < 0.002]\), and a significant main effect for serial position \([F(2,174) = 14.46, P < 0.0001]\). Although the group by serial position interaction only approached an accepted level of significance \([F(2,174) = 2.34, P < 0.10]\), we examined chaining effects
for each serial position separately to test whether patients were impaired in their serial processing during T6 retrieval of the terminal list words. MS patients showed abnormally little chaining of the terminal portion of the list at T6 \(t(87) = 3.81, P < 0.003\). The initial and middle portions failed to reach Bonferroni corrected levels of significant difference from controls. Thus, while the MS group were relatively poor at retrieving the middle and terminal thirds of the list, they were impaired in chaining the terminal portion only. The chaining effect was also found in serial third recall at T7; the group \((2) \times \) serial position \((3)\) interaction was significant \(F(2,174) = 3.12, P < 0.05\), and the MS group's chaining of the terminal portion was again impaired compared to that of the control group \(t(87) = 2.06, P < 0.05\), whereas initial and middle list chaining did not differ from controls. Within group comparisons of the chaining of T6 and T7 showed a trend in MS patients towards increasing retrieval of serial word order (chaining) during terminal third recall at T7 compared to terminal third recall at T6 \(t(66) = 1.84, P < 0.07\), whereas there were no differences in degree of chaining between other serial positions. In addition, the mean percentage recalled of the terminal third of T6 was 55.8 and of T7 was 60.6, whereas total list percentage recalled at T6 was 65.2 and at T7 was 69.8. Normal subjects did not show significantly different chaining of any portion of the list between T6 and T7. The chaining effect was thus found only for terminal words, and there is no evidence of consolidation failure at T7.

Summary. The relative spontaneously ordered recall of words during the learning trials was no different across serial portions of the list, although group differences were found in chaining which probably reflect the overall reduced recall capacity of MS patients. Regression analyses demonstrated that MS patients' recall of only the terminal third portion of the list on the last learning trial predicted T6 terminal third retrieval, suggesting that long-term recall accuracy was relatively dependent on the most recent list exposure. Although both the middle and terminal portions had been poorly recalled at T6, the long-term memory chaining effect was found only for the terminal words. No further degradation of chaining occurred at T7.

Discussion

Our findings associate difficulty retrieving ordinal attributes of words with post-encoding negative recency in MS. We found negative recency during spontaneous retrieval at post-encoding trials, but normal recognition of the terminal words. Our results suggest that terminal words are recalled normally during learning trials, that the words can be placed in a long-term store, but that difficulty representing temporal order attributes of these words traces disrupts retrieval from the long-term store. Together with the observations that all portions of the list were recognized normally, our findings suggest disruption of retrieval processes in the long-term memory impairments in MS.

Evidence of long-term memory retrieval impairment in MS was found in both group and individual analyses. Two subtypes of impaired recall were found: a greater proportion of MS patients demonstrated defective post-encoding retrieval than a middle list learning-recall deficit \((42\% \text{ versus } 24\%)\). Although these two recall patterns were found in group analyses, and although serial position theory suggests that retrieval processes may be involved in middle list recall, we do not think that impaired middle list recall during learning trials and T6 negative recency simply represent a range of severity of recall difficulty in MS. The patients with middle list learning failure and those who have terminal third retrieval failure were dissociated in the majority of the patients. Of the patients who demonstrated one or the other type of memory impairment by our criteria, 42% demonstrated negative recency only, 22% failed to learn the middle list only, and 36% had both patterns of memory impairment. The relative infrequency of middle list learning in MS could represent a more severe retrieval failure, but in that case there should be more overlap between the patients who had impaired middle list recall and those who demonstrated negative recency. Recall of initial and terminal list items is more robust \([45]\), so failure of a small subset of MS patients to learn middle list may be a common effect of impaired lexical retrieval. However, if this is the explanation, then a greater proportion of our patients should have been impaired in middle list recall. The pat-
tern which was more frequent in our MS group was
defective retrieval of terminal list words at post-encoding,
an uncommon finding which is induced in normal sub-
jects only when temporal coding has been disrupted. The
implication is that different cognitive functions in
retrieval may represent fully or partially dissociated neu-
ral systems involved in retrieval.

Recency effects in long-term memory could also be
explained by level of processing [26]. Furthermore, sem-
antic attributes are more effective than temporal in sup-
porting later retrieval [2], so the role of semantic encoding in
MS remains an issue. Whereas levels of processing predict
post-encoding retrieval [9], it does so by re-
ferencing the elaboration of stimuli during encoding. But
there is little evidence for a defect in MS patients’ ability
to encode information perceptually or semantically. Car-
roll et al. [7] found that MS patients were as sensitive as
control subjects to deep semantic encoding of namable
pictures, although their reaction times were slower over-
all. Beatty et al. [4] also reported evidence of normal
representation of semantic structures in MS. The findings
of Carroll [7], Mayes and Mclvor [26] and Whitten [44]
suggest that terminal word retrieval would be facilitated
by deep semantic encoding of words, and in fact, this
may help to explain their normal recency recall during
learning trials in our and other studies of MS. Evidence
for normal levels of processing, and normal recognition
of all list portions, suggests that impaired semantic enco-
ding is not the explanation for our MS patients’ recall
difficulties. Accurate recognition can occur in patients
who have encoding and storage deficits, such as amnesics
[33], but not when targets must be discriminated from
other items [16, 33]. A difficulty in discriminating targets
from non-targets could indicate disruption of memory
storage at the level of associative cues. Our patients’ FAR
rate was only marginally elevated, and there was little
evidence of an interference effect from the semantic and
phonological foils or the recently presented distracter list.

Cognitive theories of serial position recall appear to
account for our findings. Serial order effects are com-
monly found in the long-term memory free recall para-
digm [45] in which stimuli are presented in a set order,
whereas subjects are instructed to recall items in any order
they want. Whereas the recency effect is often thought to
be an effect of short-term memory [32], there are several
lines of evidence that a recency effect in long-term mem-
ory is related to retrieval processes, and is disassociated
from short-term storage [1, 5, 24, 41, 44, 45]. Aldridge
and Farrell [1] instructed normal subjects to learn five
words lists with either visual or auditory presentation.
Each list was comprised of seven triads of common, four-
letter monosyllabic nouns. Before and after each word
trid, subjects counted backward by sevens for 20 sec.
Even under these conditions, striking recency effects were
found in both modalities. Others have also demonstrated
robust long-term recency effects by introducing complex
stimuli and/or filled delays which disrupt the rehearsal of
the list items [5, 41, 45]. Whitten [45] produced reliable
long-term memory recency effects despite altering the
order in which subjects retrieved the three serial portions
of the list.

Long-term memory recency effects are thought to be
the result, in part, of temporal coding of terminal words.
Maskarinec and Brown [25] reliably produced a positive
recency effect in the learning of lists whose length could
be anticipated, and suggested that recency was supported
by implicit temporal order cues. Marmurek [24] dis-
tinguished among the cues used to access recency and
pre-recency items, and suggested that recency items are
retrieved on the basis of automatically encoded ordinal
attributes. Marmurek [24] also demonstrated that sub-
jects spontaneously encoded and used ordinal attributes
for long-term memory retrieval of terminal items in a
list. Semantically weighted processing appears to support
temporal and ordinal coding in long term memory [26,
31], is more effective than temporal in supporting retrieval
[2], and can eliminate negative recency [44]. The retrieval
of terminal words has thus been related to both semantic
and temporal cues, and suggests that the difficulty in
retrieving terminal words at later recall in MS could be
explained in part by inadequate activation of both of
these attribute systems.

Negative recency has been demonstrated by normal
subjects in post-encoding free recall and recognition tasks
[2, 23, 44]. Marmurek [24] also found that negative
recency emerged when ordinal cues lost their dis-
tinctiveness for recency items, and explained negative
recency as a contrast in the activation of ordinal cues at
initial and final recall. Both Whitten [45] and Marmurek
[24] proposed that negative recency at post-encoding
retrieval reflects a problem in access to ordinal infor-
mation which is spontaneously encoded, used for later
retrieval, yet which deteriorates at a faster rate than the
perceptual or semantic information based upon which an
item is stored. Delayed recall negative recency is depen-
dent on the successful temporal encoding of terminal list
words at an earlier recall [11, 24].

Serial position theory has posited that terminal words
are learned by ordinal and semantic cues, and the absence
of semantic encoding deficits in MS provides additional
evidence that impaired use of ordinal cues may be respon-
sible for the negative recency we found. MS patients used
ordinal cues normally to recall terminal words, but we
suggest that these cues were less available during post-
encoding retrieval. However, chaining did not worsen
over time, suggesting that there was no weakening of the
store of ordinal word associate cues. Our MS patients
displayed a particular difficulty in using temporal or ordi-
nal cues for long-term memory retrieval. The absence of
a temporal order effect in long-term memory retrieval
was strongest in recency recall, and suggests that patients
did not access the temporal cues formed during learning
of the terminal words (found to be normal across T1–T5)
when reconstructing the terminal words at later recall
trials. While we cannot completely rule-out a deficit in
their long-term store of association cues, we found no
evidence of forgetting, which would suggest a consolidation impairment and thus, a deficit in storage processes. We speculate that negative recency and the related defect in chaining may represent, in MS, a delayed or impaired ability to reactivate information on temporal relationships or the individual temporal attributes to each word, in order to retrieve information stored in long-term memory.

Another explanation for the memory deficit in MS has been that other cognitive deficits may contribute to long-term memory encoding deficits in MS. For example, defective recency discrimination has been reported in MS patients [3]. Recency discrimination has been associated with frontally mediated memory impairment in the absence of general memory loss [27]. However, the similarity between temporal judgment and the use of temporal relationship information to order retrieval of words is not clear. In the studies of temporal discrimination in patients with otherwise normal recognition, subjects are required to recognize the order in which two events had occurred. Free recall tasks require active regeneration of the stimuli and their attributes, which makes direct comparisons between temporal discrimination and ordered free recall tasks difficult.

An alternative explanation is that the defect in post-encoding retrieval found in our MS group represents a defect in their implicit memory system. A clear example of the role of temporal cues in implicit memory is from Whitten [45] who reported that a recency effect emerged even when normal subjects were instructed to recall the initial or middle third of lists first, which reoriented their definition of recency. He proposed that the formation of temporal attributes, possibly at an implicit level, was needed for the robust recency effect to emerge, as subjects were instructed to label other portions of the list as the terminal portion. Access to implicit temporal attributes may be damaged in MS. We may question whether the temporal cueing demonstrated on list learning tasks is a function of a central processor which interprets information semantically, an automatic function which establishes semantic records without conscious recognition as Moscovitch and Umilta' [30] have proposed, or a type of unitization characterized by item association with linear, temporally-defined cues. The patients' abilities to establish temporal-to-semantic links demonstrated during list learning indicates that temporally-defined cues were established and used to support semantic recall. The failure to activate the temporal cues only during the conditions which were supported exclusively by retrieval mechanisms implicates the role of interpretive central-system structures. The failure to retrieve because of impaired temporal order activation may occur in the process of evaluating the output of memory searches, or in the process of using output information to guide later mnemonic searches [29].

We must caution that confirmation of the finding of impaired temporal attribute retrieval in MS depends on replication of this study, and use of experimental methods to measure temporal coding and retrieval. The theoretical relationship of memory for temporal order attributes and implicit memory needs to be examined in studies which compare performances on explicit and implicit paradigms, and temporal and semantic attribute retrieval directly. Also, our MS patients were a part of a cohort who sought services from a neurology clinic, and thus may represent the more severe end of the spectrum of neurocognitive deficit in MS. Finally, the finding of retrieval impairment to the exclusion of storage deficits remains tentative, if only because of the marginally significant overall FAR rate in the MS group. Closer examination of their semantic encoding processes is needed.

The two types of memory impairment identified in our MS patients may contribute to the current notion that long-term memory retrieval is supported by multiple cognitive processes which Moscovitch has referred to as "working with memory" [29]. The differential breakdown of memory processes in MS would not have occurred if memory retrieval was dependent on activation of a single associative process, and their, at least partial, dissociation may reveal separate neural systems. Functional neuro-imaging of these separate memory processes, as Grasby et al. have accomplished [14], may contribute to our knowledge of memory retrieval in normal functioning brains.

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