



Delayed recognition memory in Parkinson's disease: a role for working memory?

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Received 3 June 1997; accepted 25 May 1998

Abstract

Immediate and delayed recognition memory for words was examined in a sample of 16 non-demented patients with Parkinson's disease and 16 normal control participants of equivalent age and educational attainment. The patients, relative to control participants, had intact immediate but impaired delayed recognition memory performance. Patients were also impaired on tests of free and cued recall, working memory and a measure of psychomotor processing speed. Processing speed was a significant covariate for delayed recognition, free and cued recall and working memory performance, but not for immediate recognition performance. These results suggest that the same cognitive processes which support performance on tests of recall and working memory also support performance on tests of delayed recognition. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Cognition and basal ganglia; Fronto-striatal memory system

1. Introduction

Non-demented patients with Parkinson's disease (PD) show a variable pattern of performance on tests of declarative memory. In many studies, they are intact on recognition memory tests [6, 16, 20, 31, 55], but impaired on tests of recall [6, 16, 20, 57–59], recall of temporal order [10, 20, 42, 56, 63], recollection of source [59] and self-ordered pointing [20, 40]. The precise pattern of memory ability and disability varies across studies, probably due to variations in disease severity, treatment and other factors (e.g. Ref. [40]). Many studies, however, report a dissociation between intact recognition and impaired recall of items, order or source.

The frequent dissociation between intact and impaired performance on declarative memory tests in PD patients contrasts with that of patients with amnesia or Alzheimer's disease in whom performance on all tests of declarative memory is impaired (e.g. Refs. [11, 54]). The dissociation of performance on different declarative memory tests in PD is, however, similar to that seen in patients with focal frontal-lobe lesions (e.g. Refs. [21, 26, 27, 37, 39, 41]) or other degenerative striatal diseases,

such as Gilles de la Tourette syndrome [55] and Huntington's disease [50]. The frontal-lobes and striatum are highly interconnected [1] and the common pattern of impaired recall and intact recognition in patients with damage to these structures suggest that the integrity of a fronto-striatal neural system is essential for recall but not for recognition.

It has been hypothesized that the pattern of declarative memory test performance in PD is due to impairments in the cognitive processes which support the development and utilization of strategic operations [20]. Strategic operations require the manipulation of information in declarative memory, rather than simply verifying the presence of information in declarative memory. In this regard, recognition memory tests require minimal strategic operations because the participant is simply required to verify, from among foils and recently presented targets, which stimuli had been previously encountered. The determinant of performance is a non-strategic operation of externally guided search of memory. In contrast, recall tests do not require verification of externally presented targets and foil, but rather require the reconstruction of the study episode. Thus, recall tests place a great demand upon strategic operations because the participant must develop an internally generated strategy to guide memory search.

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An important mediator of internally guided memory processes is working memory [22]. Working memory is a limited-capacity psychological system that is used to temporarily store and transform information in a goal-directed manner [64]. It is a multicomponent system variously conceptualized as comprising a central executor [2], or executors [22, 66], with associated buffer storage systems for speech-based information (the phonological loop) and visuo-spatial information (visuo-spatial sketch pad).

The limitations of working memory are thought to be due to constraints on how much information can be maintained in each of its component parts. The capacity of the buffer storage systems is operationalized as performance on tests measuring span in speech-based (e.g. digit span) and visuo-spatial (e.g. Corsi block span) domains. In most studies, the buffer storage components of working memory are minimally affected in patients with PD (e.g. Refs. [16, 20]). Therefore, the deficit in PD appears to be due to impairments of executive components of working memory.

Besides capacity constraints, another important factor in working memory efficiency is the speed with which operations are accomplished. Because working memory requires simultaneous and synchronized processing and storage of information, decrements in psychomotor processing speed may disrupt the parallel processes required for successful performance. Salthouse [43] has employed the analogy of a central processing unit (CPU) of a computer to explain the effects of slowed psychomotor processing speed on other aspects of cognition: if the CPU is running at a slower rate, programs will not run efficiently or may not run at all because the commands of the program will not run in a synchronized fashion. In humans, one of the first results of this disrupted synchronization may be impaired executive working-memory performance.

There is strong evidence for an interdependence between psychomotor processing speed and working memory. High intercorrelation between tests of psychomotor processing speed and working memory in aged samples, as well as a linear decline in performance on these tests across the lifespan have been reported [43, 45]. In addition, statistical control of the effects of processing speed normalizes working memory tests scores between elderly and young control participants [44]. A similar relationship between psychomotor processing speed and working memory has been found in patients with PD [52, 53].

Perhaps, then, declarative memory performance in PD does not depend upon the type of test per se (e.g. recall or recognition), but rather upon the working memory demands of a given test. PD patients may fail declarative memory tests that place demands upon their limited working memory capacity. Recall tasks may stress both speed and capacity of executive working-memory. There-

fore, these tasks regularly exceed the working memory capacity of PD patients and result in poor performance.

One strategic factor that aids recall is semantic organization. People recall previously studied words better when study lists are semantically organized, i.e. recall is superior when semantically related words are presented sequentially than when these words are randomly distributed throughout the study list. Recall is worst when semantically unrelated words are used [28].

Patients with PD do not show the same benefit as normal control (NC) participants on recall memory tests when semantically related words are used as study items. One study investigated recall and two-choice recognition memory for study lists consisting of multiple exemplars from different categories in a sample of unmedicated PD patients and age- and education-matched NC participants [20]. The PD patients were impaired on recall performance but unimpaired on recognition performance. Their recall performance was marked by reduced semantic clustering, suggesting that the patients were impaired in their ability to utilize a strategy of limiting the search of declarative memory to the relevant categories.

In contrast to recall performance, semantic organization has little or no effect on immediate recognition performance [4, 5, 28]. Semantic organization, however, does effect delayed recognition performance [34]. The magnitude of semantic organization facilitation increases as the study-test delay increases [33]. Thus, the same semantic organizational factors that influence immediate recall also influence delayed but not immediate recognition. This suggests that immediate recall and delayed recognition share a common dependence upon strategic processes that, in turn, are working memory-dependent.

An additional finding from the study that found decreased semantic clustering in PD patients [20] was that the same patients were also impaired on other declarative memory tests that require strategic operations for successful performance, namely recall of temporal order and self-ordered pointing. Scores on these strategic memory tests were significantly correlated with recall performance and with a measure of working memory capacity. The authors suggested that the impairment in strategic memory operations in PD was the result of reduced working memory capacity (see also [7, 57, 65]).

In the present study we assessed recall memory, immediate recognition memory and delayed recognition memory for words derived from semantically related categories in a sample of non-demented patients with PD and age- and education-matched control participants. We sought to test the hypothesis that immediate recall and delayed recognition of semantically organized words share a common dependence upon strategic processes that, in turn, is working memory dependent. Therefore, we hypothesized that PD patients, who have impairments in executive working-memory, would not be able to take

Table 1
Demographic information for Parkinson's disease (PD) and normal control (NC) participants. (mean \pm S.D.)

Variable	Group	
	PD	NC
Age (years)	68.56 (4.91)	69.19 (5.66)
Education (years)	14.80 (1.74)	14.81 (1.94)
Mini-mental status score	28.81 (0.83)	29.33 (0.82)

advantage of the organizational aspects of the study words and would show decreased performance on these measures. Furthermore, we hypothesized that psychomotor processing speed would be a significant covariate of recall and delayed recognition performance, but not of immediate recognition performance.

2. Methods

2.1. Participants

2.1.1. PD participants

Sixteen participants with PD were selected from the Rush-Presbyterian-St. Luke's Medical Center Movement Disorder's Clinic. Each met core assessment protocol for intercerebral transplantation (CAPIT) criteria for the diagnosis of PD [30]. The criteria include the presence of at least two of the following clinical signs: resting tremor, cogwheel rigidity, bradykinesia and postural reflex impairment; with either resting tremor or bradykinesia as one of the two signs. Patients were not demented according to mental status testing [17], and had mild to moderate PD severity [Hoehn and Yahr stages: II ($n=4$), III ($n=12$); [24]]. All patients were receiving anti-parkinsonian medications in the form of levodopa/carbidopa replacement therapy and deprenyl.

2.1.2. NC participants

Sixteen NC participants were matched to the PD group by age and education and were recruited from friends and relatives of the patient participants, community volunteers and from volunteer members of the hospital staff. The number of participants was chosen for two reasons. First, in a prior study we found that this number of participants yielded reliable differences in working and strategic memory performance [20]. Second, this number of participants allowed for complete counterbalancing of study and test material. The PD and NC groups did not differ significantly in regards to age, education or mental status performance (Table 1).

3. Material and methods

3.1. Tests of recall memory

3.1.1. Word-list free and cued recall

One set of stimulus words was used for the word-list recall test and the immediate and delayed word-list recognition tests described below. The stimuli consisted of 216 words: 12 exemplars from each of 9 man-made (e.g. furniture) and 9 naturally occurring (e.g. weather phenomena) categories [3]. Exemplars were not among the 10 most frequently produced ones for their category, but they had been listed by at least 9 of the 442 Battig and Montague's participants.

Six 36-word core lists were constructed, each containing 6 exemplars from each of 3 man-made categories and 6 exemplars from 3 naturally occurring categories. Across all participants the 6, 36-word lists were used equally often as study and test items for recall and as targets and foils for the immediate and delayed recognition tests. Across forms, exemplars in lists were counterbalanced with respect to test-type (recall/immediate/delayed recognition) and item-type (target/foil).

For each participant, one study list, containing 36 exemplars, was used for the recall phase and two study lists, each containing 36 exemplars, were combined and used for the immediate and delayed recognition phases of the experiment. Exemplars in each study list were pseudorandomly organized into blocks, with the constraint that no more than 3 exemplars from the same category appeared in succession. Each exemplar was presented in lowercase letters, using the same type font.

Participants always performed the free-recall phase first followed by the cued-recall phase. This order of test was chosen so as to not bias performance on the free-recall task. The immediate recognition phase followed the cued-recall phase and the delayed recognition phase followed the immediate recognition phase after an approximate 30 min delay. All materials were presented on an Apple Macintosh Powerbook computer using Psychlab software program. In both the recall and recognition study phases, a dot signaling the appearance of one exemplar would appear on the screen for 250 ms. Then, after a 250 ms delay, the study exemplar would appear in the center of the screen and the participant was instructed to read it aloud. After a 2 s exposure the experimenter advanced the program to the next word. Immediately following each of the 2 study phases, an array of 28 single digit arithmetic problems, followed by an array of 14 double digit arithmetic problems were displayed on the computer monitor. The participant was instructed to complete as many arithmetic problems as they could within 30 s.

In the recall test phase, participants were instructed to recall as many of the study exemplars as they could (free-

recall). Then, participants were given category cues corresponding to studied exemplars, and were again instructed to recall as many exemplars within each category (cued-recall). Oral responses were recorded by the experimenter on score sheets so that participants who forgot what they had said could review their responses.

3.2. Test of working memory

3.2.1. Listening span test

This measure of verbal working memory was taken from Salthouse and Babcock [45] and assesses the capacity of the executive working-memory system. Participants were instructed to listen to simple sentences, to immediately afterward select from among three choices the correct answer to a question about the sentence and to remember the last word from each sentence for later recall. Participants were told that the questions had to be answered correctly. The number of sentences presented on each trial increased successively from one to seven, with three trials presented at each series length. The sentences were 6 to 10 words long. The final word from each sentence was one or two syllables, common enough to be found in a children's dictionary [49] and appeared only once as a final word in the sentences. The question and answer alternatives for each sentence did not contain the final word of the sentence.

Participants were provided an answer booklet in which they marked their answers. Participants heard each sentence read aloud by the examiner at a normal speaking rate (e.g. "the boy ran with the dog"). Participants then selected one of three alternatives in response to a question about the sentence (e.g. "who ran? —boy; —man; —girl"). After selecting the answer for the question about each sentence in a trial, participants were asked to turn the page and orally report the last word of each sentence, in the order they had been presented. Only trials on which the participant provided correct answers to the multiple-choice questions were counted. The span score (maximum = 7) was the maximum number of sentences for which a participant recalled all final words of the sentences in the correct order for at least two of the three trials. Participants were given as much time as they required to produce their answers.

3.2.2. Digit ordering test

This measure of verbal working memory was taken from Cooper and colleagues [10] and assesses the capacity of executive working-memory. Participants were instructed to listen to seven single-digit numbers orally presented in random order and repeat them to the examiner in ascending order. Thus, if the participant was presented with the series 7-3-4-2-0-9-1, they had to repeat the series as 0-1-2-3-4-7-9. Digits were presented at the rate of approximately one digit per second. Fifteen series of digits were presented. Scoring awarded 1 point for

each digit placed in the correct order that maintained an ascending sequence. Responses that were not part of the presented sequence, but maintained ascending order were tolerated but not considered in scoring. If a participant reported more than 7 digits, only the first 7 digits were considered. Thus, the maximum attainable score was 105 points.

3.3. Test of psychomotor processing speed

3.3.1. Symbol digit modalities test (SDMT) oral version

The SDMT [51] is a test of psychomotor processing speed. Participants were presented with a "key" consisting of 9 simple geometric designs (e.g. a plus sign, a circle, an inverted T) with each design matched to a unique digit from 1 to 9. The test form consisted of a series of the 9 designs and the participant's task was to identify the corresponding number for each design according to the key. The key was available to the participant throughout the task. Participants were instructed to perform the task quickly but accurately. They were allowed 90 s to complete as many targets as possible. The score was the number of correctly completed targets in the allotted time. The oral version of this test was chosen because it is minimally affected by motoric slowing per se. In this version, participants verbally reported their answer to the examiner as opposed to writing their answer on the test form. The examiner recorded the participant's response on a separate answer form.

3.4. Word-list recognition tests

3.4.1. Immediate recognition

Stimuli for the immediate recognition test were the alternate forms from those used in the word-list recall and cued recall. Immediately following presentation of the 72 item recognition study list, participants completed a 30-s distractor task (simple arithmetic problems). In the immediate recognition test phase, participants were presented with 2 exemplars from the same category; one study exemplar and a corresponding exemplar that served as a foil. Position of the study exemplar (i.e. the left or right item) was counterbalanced for each list. The participant was asked to identify the study exemplar. Upon completion of the immediate recognition test, participants performed a series of non-verbal tasks which took approximately 30 min.

3.4.2. Delayed recognition

In the delayed recognition test phase, participants attempted to select studied exemplars from the two-alternative forced choice items. The delay between study list presentation and recognition test was approximately 30 min. In all other respects, the procedure for the delayed recognition test was identical to that used for the immediate recognition test. The immediate and delayed rec-

ognition scores were the number of words from the study list correctly recognized.

3.5. Data analysis

Participant demographic data were compared using unpaired, two-tailed *t*-tests. Group differences on the dependent measures were first compared using a multivariate analysis of variance (MANOVA), with examination of univariate analysis of variance (ANOVA) results for individual memory tests. This approach was chosen to minimize inflation of Type I error due to multiple comparisons. The effect of covarying psychomotor processing speed on the memory tests was assessed using separate univariate analyses of co-variance (ANCOVAs). Significance level was set at $\alpha < 0.05$ for all analyses.

4. Results

4.1. Group differences on dependent measures

MANOVA results indicated that the dataset met the assumptions of multicollinearity ($X^2 = 49.01$, $df = 15$, $p < 0.001$) and homogeneity of variance–covariance matrices (Box's $M = 54.89$, $F[28, 3136] = 1.46$, $p > 0.05$). Using Hotellings test, the combined dependent measures were significantly different among the groups ($F[7, 24] = 2.60$, $p < 0.05$). Examination of univariate ANOVA results revealed significant decrements in performance for the PD group compared to the NC group for free-recall ($F[1, 30] = 5.70$, $p < 0.05$), cued-recall ($F[1, 30] = 4.89$, $p < 0.05$), delayed recognition ($F[1, 30] = 4.24$, $p < 0.05$), listening span ($F[1, 30] = 4.20$, $p < 0.05$) and digit ordering ($F[1, 30] = 9.02$, $p < 0.01$). The PD group correctly completed

fewer targets on the SDMT oral version than the NC group, although the difference was not significant ($F[1, 30] = 1.98$, $p = 0.169$). The PD and NC group performed similarly on immediate recognition ($F[1, 30] < 1$). Both the PD and NC groups' scores differed significantly from perfect performance on immediate recognition, indicating they were not at ceiling (PD: $t(15) = 4.87$, $p < 0.001$; NC: $t(15) = 6.06$, $p < 0.001$) (Table 2).

4.2. Effects of covarying psychomotor processing speed on memory tests

Psychomotor processing speed, as measured by the SDMT oral version, significantly covaried with tests of free recall ($F[1, 29] = 14.29$, $p < 0.001$), cued recall ($F[1, 29] = 13.43$, $p < 0.001$), delayed recognition ($F[1, 29] = 7.28$, $p < 0.05$), listening span ($F[1, 29] = 5.39$, $p < 0.05$) and digit ordering ($F[1, 29] = 6.57$, $p < 0.05$). Psychomotor processing speed did not, however, covary with immediate recognition ($F[1, 29] < 1$). Once the effects of psychomotor processing speed were removed from the analysis, the main effect of group was no longer significant for free recall ($F[1, 29] = 3.42$, $p = 0.08$), cued recall ($F[1, 29] = 2.74$, $p = 0.11$), delayed recognition ($F[1, 29] = 2.46$, $p = 0.13$), listening span ($F[1, 29] = 2.56$, $p = 0.12$), or digit ordering ($F[1, 29] = 1.96$, $p = 0.17$). Table 3 presents the observed and covariate adjusted means for these variables.

5. Discussion

When recognition memory was tested immediately after study, PD patients and control participants performed comparably. The introduction of a 30 min delay

Table 2
Mean test scores (M) and standard deviation (S.D.) of Parkinson's disease (PD) and normal control (NC) groups

Measures	PD		NC	
	M	S.D.	M	S.D.
Recall memory tests				
Free recall (maximum = 36)	6.69	3.34	9.94	4.30*
Cued recall (maximum = 36)	7.94	3.62	11.56	5.47*
Working memory tests				
Listening span (maximum = 7)	1.81	0.91	2.44	0.81*
Digit ordering (maximum = 105)	74.19	10.29	85.56	8.14*
Psychomotor processing speed test				
Symbol digit modalities test (maximum = 110)	40.25	12.52	45.81	9.64
Recognition memory tests				
Immediate recognition (maximum = 36)	32.06	3.24	32.81	2.11
Delayed recognition (maximum = 36)	28.56	4.70	31.43	3.01*

* $p < 0.05$.

Table 3
Observed mean test scores and predicted mean test scores of Parkinson's disease (PD) and normal control (NC) groups after covarying for psychomotor processing speed

Test	PD		NC	
	observed	predicted	observed	predicted
Recall memory tests				
Free recall	6.69	7.18	9.94	9.45
Cued recall	7.94	8.52	11.56	10.98
Working memory tests				
Listening span	1.81	1.88	2.44	2.37
Digit ordering	74.19	76.73	85.56	84.84
Recognition memory test				
Delayed recognition	28.56	28.94	31.43	31.06

between study and recognition test of semantically organized word-lists, however, hindered performance in PD patients. The deficit in delayed recognition memory performance was not due to differences in the study lists, because equivalent and counterbalanced word lists were used. Nor was the difference in performance due to a truncation of variability in the NC group (i.e. ceiling effect). Therefore, PD patients had a selective impairment in delayed, but not immediate, recognition memory.

The PD patients were also impaired on tests of free recall and cued recall of equivalent word lists and executive working-memory. Statistical control of the effects of psychomotor processing speed, an important component of working memory processing [20, 44, 52, 53], accounted for a significant portion of the variance of the patients' performance on delayed recognition, free recall, cued recall and executive working-memory, but not on immediate recognition. This suggests that delayed, but not immediate, recognition tests share processing demands with working memory tests and free recall tests. These findings are discussed below in terms of the relationship between neuropathological changes and working memory processes in PD.

Parkinson's disease is characterized by a dysfunction of dopamine systems that compromise motoric and cognitive functions [10, 25]. Three systems of dopaminergic functioning are impaired in PD. First, damage to the nigral-striatal dopamine system [25] reduces frontal-lobe input from the striatum via thalamocortical pathways [1]. Second, degeneration of dopamine producing cells in the ventral tegmental area results in a decrease of direct dopamine transport to limbic and frontal regions in PD [48]. Third, there is evidence for degeneration of dopamine receptors in the frontal lobes in PD [61]. The degree of dopamine loss is related to disease severity, with more advanced patients showing greater dopamine depletion in the striatum and nigra [62].

Dopaminergic functioning has a direct effect upon executive working-memory functioning. Single-cell recordings of monkey frontal-lobes have shown decreased activity during delayed ocular response (an analog measure to human working memory) under conditions of dopamine antagonism [8, 46] and increased activity under conditions of dopamine agonism [47]. Pharmacologic studies in humans have reported facilitative effects of systemic dopamine administration on tests of working memory in healthy young and aged participants [32, 38] as well as patient with PD [9]. Currently, there is insufficient evidence to decompose the individual contributions of frontal-lobe and striatal dopamine function to working memory performance.

Although less severe than in PD, there is a similar decline in dopaminergic function in normal aging [18]. Healthy aged individuals experience an estimated 4 to 10%-per-decade loss of dopamine producing cells [15, 36], presynaptic dopamine terminals [60] and post-synaptic dopamine binding [35, 60, 67]. Behaviorally, healthy aged participants also evidence impairments in executive working-memory [44, 45], recall relative to recognition [12], and delayed relative to immediate recognition [14] compared to healthy younger participants.

Thus, convergent evidence suggests a decrease in striatal and frontal-lobe dopamine functional activity in PD and, to a lesser extent, in healthy aging. This reduced fronto-striatal dopamine functioning may impair the speed of working memory, which in turn, impairs performance on declarative memory task that require strategic operations for successful performance. Therefore, the dissociation in declarative memory performance between immediate recall and recognition in PD is not based on the type of test per se, but rather on the greater processing demands recall places upon executive working-memory. When the task demands of a recognition test are modified so as to increase dependence upon executive

working-memory, such as by introducing a delay between study and recognition test, patients with PD evidence impaired recognition.

Acknowledgements

This research was supported by grants from the National Institute on Aging (AG09466-06) and the Office of Naval Research (N00014-92-J-184).

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