Retrograde Amnesia in Parkinson's Disease

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ABSTRACT: Retrograde amnesia was assessed in demented and non-demented Parkinson's patients using a test of remote memory spanning the years from 1920-1979. Results indicated that the demented patients 1) scored significantly below normal controls and 2) had equal impairment for all time periods. This pattern was like that seen in other dementing illnesses (i.e., Huntington's and Alzheimer's diseases), but different from that in amnesic disorders, such as Korsakoff's syndrome. The data, therefore, suggest qualitative differences in pattern of remote memory loss between the dementias and amnesic syndromes.

RÉSUMÉ: Nous avons étudié l'amnésie rétrograde chez des patients Parkinsoniens déments ou non-déments en utilisant un test de la mémoire ancienne des années 1920-1979. Les patients déments 1) étaient inférieurs aux témoins normaux 2) étaient atteints également pour toutes les périodes testées. Ce pattern est semblable à celui des autres maladies démentielles (Huntington et Alzheimer) mais différent des désordres anmésiques comme le Korsakoff.

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Distinct patterns of retrograde amnesia have been identified in neurological disease. Retrograde amnesia may be relatively short, extending from minutes to several years or long, spanning many decades. The amnesic syndromes occurring after head injury (Whitty and Zangwill, 1977), electroconvulsive therapy (Squire, 1975; Squire et al., 1975), and in the well studied cases H.M. (Scoville and Milner, 1957; Milner et al., 1978) and N.A. (Teuber et al., 1968; Squire and Cohen, 1982), are typical of the former pattern, whereas prolonged periods of remote memory loss are seen in Korsakoff's syndrome (Seltzer and Benson, 1974; Marslen-Wilson and Teuber, 1975; Albert et al., 1979; Squire and Cohen, 1982;) and the dementias (Albert et al., 1981; Wilson et al., 1981). Prolonged retrograde amnesia has been categorized into two patterns showing: (1) a temporal gradient with relative sparing of more remote memories, and (2) no gradient with equal loss of memories for all time periods (Butters and Alberta, 1982). Long retrograde amnesia characterized by a temporal gradient has been found in amnesic disorders, such as Korsakoff's syndrome, but not in dementia (Albert et al., 1981; Wilson et al., 1981). Since the only dementing illnesses that have been evaluated for remote memory loss are Huntington's disease (Albert et al., 1981) and Alzheimer's disease (Wilson et al., 1981), the present study was undertaken to determine whether retrograde amnesia also occurs in the dementia of Parkinson's disease (PD), and if so, whether the pattern is like that of the other dementias or whether it resembles that of the amnesic syndrome.

Because PD may occur with or without dementia, the Parkinson patients in this study were separated into demented and non-demented subgroups on the basis of their performance on the Dementia Rating Scale (DRS) (Coblentz et al., 1973). This test correlates well with the Wechsler Adult Intelligence Scale ($r = 0.75$), is relatively easy to administer and is useful for the identification of cognitive impairment. The DRS measures cognitive function along the parameters of attention, perseveration, constructional ability, conceptualization and memory. An independent measure of problem solving ability (Laine and Butters, 1982) was obtained to confirm that the "demented" patients, who formed the major focus of this study, were in fact cognitively impaired as predicted by their DRS scores.

Retrograde amnesia was measured using the Famous Faces Test developed by Albert et al. (1979). This test involves the recall of famous people from their photographs, taken during the period from 1920 to 1979.

Patients

Twenty-two patients with PD and a pool of 32 normal controls (NCs) participated in this study. There were eight demented (DPD) and 14 non-demented (NDPD) Parkinson patients. The DRS criterion for dementia was based upon normative data obtained in 14 NCs. Only those Parkinson patients (PDs) falling outside the range of scores obtained by the NCs (135-144) were classified as being demented (Table 1). This strict criterion,

Table 1: Profile of Parkinson's and Normal Control Subjects

	Age (years)	Education (years)	Duration of disease (years)	Severity Rating (max = 25)	Dementia Rating Scale (max = 144)	Beck Depression Inventory	Boston Naming Test (max = 85)
DPDs*							
Mean	64.5	11.3	7.9	11.3	124.6	7.0	63.0†
S.D.	5.7	2.4	3.8	3.3	8.7	3.3	5.3
N	8	8	8	8	8	8	8
NDPDs**							
Mean	63.5	13.7	7.5	8.6	140.0	7.6	76.0
S.D.	6.3	3.3	4.0	2.6	2.9	4.8	7.6
N	14	14	14	14	14	14	14
Normal Controls							
Mean	64.0	12.6	—	—	140.7	5.3	76.2
S.D.	5.3	1.8	—	—	3.0	3.1	5.7
N	32	32	—	—	14	14	14

 * Demented Parkinson's Disease Patients
 ** Non-Demented Parkinson's Disease Patients
 † Significantly different from NDPDs (p < 0.001) and normal controls (p < 0.001)

which did not allow for any overlap between the NCs and the DPDs, was chosen to help insure that a truly demented subgroup of Parkinson patients was identified for assessment of retrograde amnesia. Such a strict criterion might have produced some false negatives with respect to the diagnosis of dementia among the NDPDs. However, this would not be expected to affect the findings in the DPDs, who are the main focus of this study.

Table 1 summarizes the age, education, duration and severity of illness, performance on the Beck Depression Inventory (BDI) (Beck et al., 1961) and scores on the Boston Naming Test (BNT) (Kaplan et al., 1976). Severity was assessed by rating rigidity, tremor, bradykinesia, gait, abnormal involuntary movements and general impairment on a four-point scale, with 4 representing maximal deficit (Lieberman, 1974). The group differences in age, education, duration and severity of disease were not significant. The BNT showed that the DPDs obtained an average score that was significantly below that of the NDPDs and NCs. However, the naming problem in the DPDs was very mild since their BNT scores were still within normal limits, according to published data (Borod et al., 1980). The mean BDI scores were all in the non-depressed range (i.e. < 10), indicating that depression was not a factor in test performance during this study. All patients were receiving treatment for their Parkinson's disease. The drugs taken by the DPDs included Sinemet [N = 8], anticholinergics [N = 3], bromocriptine [N = 1] and amantadine [N = 2]. In the NDPD group, the drugs included Sinemet [N = 13], anticholinergics [N = 7], bromocriptine [N = 1] and amantadine [N = 7].

The NCs were all non-hospitalized volunteers and had no evidence of neurological disease. Since the entire battery of tests was not given to all of the NCs, the number of NCs will be noted for each test. Each sample of NCs was matched for age and education to the Parkinson patients.

PROCEDURE

Confirmation of Cognitive Impairment in Demented Patients

The Object Identification Test, given to test the validity of using the DRS to diagnose dementia, is a version of the popular game, Twenty Questions. It was administered to the DPDs, NDPDs and 14 NCs, and was carried out as previously described by Laine and Butters (1982). Forty-two black and white line drawings of common objects were arranged on a 21 × 28 cm page in a 6 × 7 matrix. Each object was drawn within a 3 × 5 cm cell. After correctly identifying all items, the subject was told that the examiner was thinking of one of the objects on the page. The subject was instructed that the task was to discover this object by asking questions to which a "yes" or "no" answer can be given. It was stressed that the idea behind the task was for the object to be found with as few questions as possible. There was no time limit set on each question. The questions asked in attempting to identify the target object were classified according to the following criteria:

1. **Constraint seeking** (any question referring to two or more pictures, e.g., "Is it a tool?").
2. **Hypothesis scanning** (any question testing a specific hypothesis, e.g., "Is it the hammer?").
3. **Pseudoconstraint** (any question disguised in the form of a constraint seeking question, but in fact referring only to a single object, e.g., "Does it have sails?").

The most effective way of solving the problem is to use constraint seeking questions until only a few (e.g., two) alternatives remain to be eliminated. At this point, hypothesis scanning questions should be applied. Three consecutive problems were given. Using the appropriate sequence of constraint seeking and hypothesis scanning questions, a given problem could be solved in five or six questions. However, there were some subjects who were able to solve the problems with fewer questions because of a lucky guess. Therefore, in scoring the test, the number of specific hypothesis scanning and pseudoconstraints among only the first three questions were used as the measure of problem solving impairment. Choosing a higher limit would have resulted in too few patients for data analysis.

Test of Retrograde Memory

Retrograde amnesia was assessed using the Famous Faces Test developed by Albert et al. (1979) and was administered as previously described. The following description is taken almost

verbatim from Albert et al. (1979). One hundred and eighty photographs of famous individuals from the 1920s to the 1970s were used in this task. The photographs were divided into six decade groups, with an average of 25 pictures in each group (the number of photographs in each group was not equal). An individual was assigned to the decade in which he or she first became well known to the public at large.

The photographs were presented in a pseudorandom order, with the first face from the 1920's, the second from the 1930's, etc. The task was sufficiently complex that none of the subjects perceived this organization of item presentation. Each photograph was presented individually, and the subject was merely asked, "Do you know who this is?" When a subject failed to respond correctly, a set of phonemic cues was given alternately with a set of semantic cues; i.e., a set of phonemic cues was used after the first incorrect answer, a set of semantic cues was used after the second incorrect answer, etc. For example, for "Marlon Brando", the phonemic cues would have been, "the first name starts with an 'm'; it sounds like 'm'. The last name begins with 'b'; it sounds like 'br'." If the next photograph was one of Elvis Presley, the semantic cues would have been "He was a singer. He sang rock and roll. He first became popular in the 1950s."

However, if a patient clearly indicated that he recognized the photograph, a phonemic cue was given even when the sequence called for a semantic cue. This was done because a semantic cue would not only have been redundant, but also because a phonemic cue would have helped prevent a possible incorrect response due to mild anomic difficulties. If a patient failed to identify a photograph after this cueing procedure, the examiner proceeded to the next photograph in the battery. Each subject's performance could be judged in two ways: first by the number of correct identifications given spontaneously (i.e., without cues), and then by the number correct with cues. In this study, only the number correct with cues were analyzed. This was done to provide the DPDs with every assistance possible, especially with respect to their mild naming problem.

Twenty-one normal controls were administered the Famous Faces Test.

RESULTS

Performance scores on all tests were analyzed by analysis of variance (ANOVA).

Object Identification Test

Figure 1 shows the mean number of pseudoconstraint and hypothesis scanning questions asked by the DPDs, NDPDs and NCs on the first three questions of each trial. All subjects solving one of the problems with three questions or less were excluded from analysis (for reasons previously explained). As expected, the DPDs were significantly impaired. A 3 × 3 (trials × groups) ANOVA showed that there was a significant group difference [F(2,28) = 6.563, p = 0.005]. There was neither a significant main effect for trials, nor a significant group × trials interaction. Collapsing across trials, subsequent between-group comparisons indicated that the DPDs were significantly impaired relative to both the NDPDs [t(16) = 2.721, p = 0.02] and the NCs [t(16) = 2.983, p = 0.009].
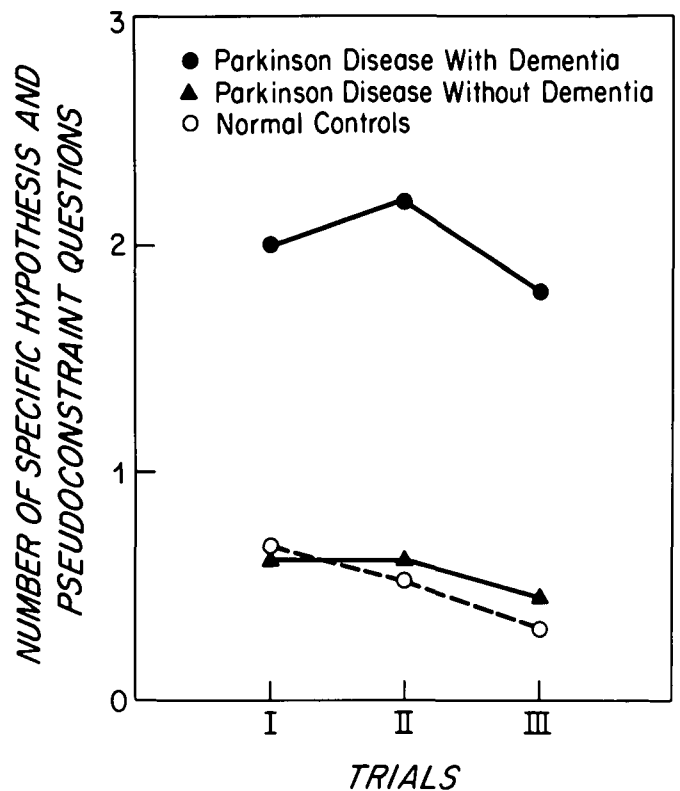

Figure 1 — Mean number of specific hypothesis questions and pseudoconstraints among the first three questions in the Object Identification Test.

Famous Faces Test

On the Famous Faces Test, only the decades from 1930 to 1970 were analyzed. The 1920s were omitted from statistical analysis because many PDs were under age 10 during this period. The 1970s, on the other hand, were omitted since the majority of patients developed their disease during this decade. Thus, any amnesia for this period would be largely anterograde, rather than retrograde.

Figure 2 gives the mean percentages of faces correctly recalled (with cues) by the DPDs, NDPDs and NCs. Three sets of planned comparisons, using analyses of variance, were conducted: 1) DPDs vs. NCs; 2) NDPDs vs. NCs; and 3) DPDs vs. NDPDs.

1) *DPDs vs. NCs*

The DPDs had significantly lower scores than did the NCs [F(1,27) = 5.664, p = 0.03]. The groups × decades interaction was not significant, indicating that the group differences were approximately equal across each decade. There was a significant difference in overall performance across decades which was due to poorer recall for faces from the 1950s and 1960s compared to the 1930s and 1940s (p < 0.001, all comparisons).

2) *NDPDs vs. NCs*

The NDPDs did not differ from the NCs. The groups × decades interaction was also not significant. A significant difference in performance across decades [F(3,99) = 17.795, p < 0.001] reflected the fact that the NDPDs and NCs scored highest on items from the 1930s and 1940s, relative to those from the 1950s and 1960s (p < 0.001, all comparisons).

3) *DPDs vs. NDPDs*

The DPDs and NDPDs did not differ significantly in over-all performance. The DPDs did, however, show significant impair-

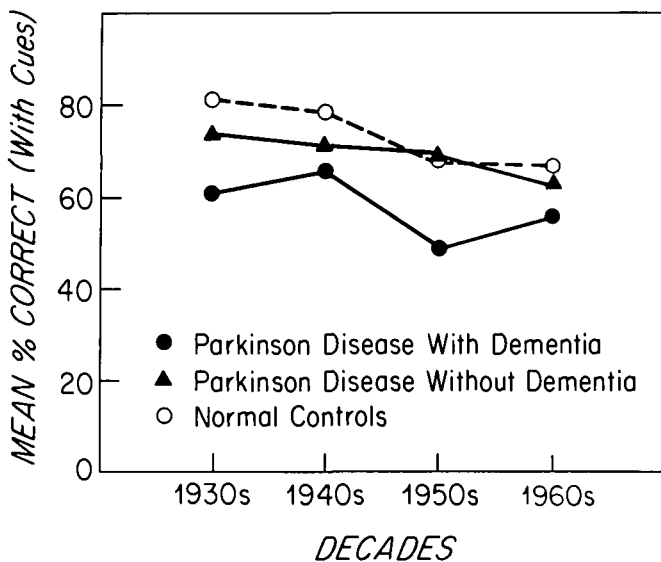ment, relative to the NDPDs, for one of the decades, the 1950s [t(20) = 2.244, p = 0.04].

Figure 2 — Performance of demented and non-demented Parkinson's patients and normal controls on Famous Faces Test.

DISCUSSION

Although Parkinson's disease consists of both demented and non-demented forms, the present study was primarily concerned with the assessment of remote memory loss in the demented type. Since the Dementia Rating Scale criterion for identifying this group was somewhat arbitrary, confirmation that the "demented" subjects were in fact cognitively impaired was sought using an independent measure of problem solving ability. The results indicated that "demented" patients did have impaired cognitive functions.

The results of this study not only show that significant retrograde amnesia occurs in the dementia of Parkinson's disease, but that the pattern of remote memory loss is equal across all time periods. The absence of a temporal gradient demonstrates that remote memory loss in Parkinson's disease follows the same pattern that has been found in the dementias of Huntington's disease (Albert et al., 1981) and Alzheimer's disease (Wilson et al., 1981) and that it is different from the profile of amnesia in Korsakoff's syndrome (Squire and Cohen, 1982), thus supporting the view that there may be a predictable difference in remote memory pattern between the dementias and amnesic syndromes.

The finding that the demented and non-demented Parkinson's patients did not differ in overall performance on the Famous Faces Test indicates that some of the latter patients may have had early signs of memory loss. These "non-demented" patients were probably not identified as having significant cognitive impairment by the Dementia Rating Scale because of the very strict criterion used for the diagnosis of dementia. It should be noted, however, that the demented group did show significant impairment relative to the non-demented patients on recalling faces from one of the decades, the 1950s. This difference probably reflects the greater difficulty of these items, compared to those from other decades. Support for this statement comes from the fact that the demented patients performed poorest on items

from the 1950s, and also from the observation that the NCs had their greatest difficulty recalling faces from the 1950s and 1960s.

With respect to the dementias of Parkinson's disease, Alzheimer's disease and Huntington's disease, it is not known whether the similar patterns of retrograde amnesia reflect a common underlying disturbance, or whether there are different abnormal processes in each disorder which are producing the same clinical picture. For Parkinson's disease and Alzheimer's disease, recent anatomical data have shown that both disorders are characterized by neurofibrillary tangles, senile plaques (Boller et al., 1980) and loss of cholinergic neurons in the nucleus basalis of Meynert (Whitehouse et al., 1981, 1982, 1983). This raises the question of a common mechanism underlying the cognitive impairment, and therefore, the remote memory loss in both disorders. These anatomical similarities between Parkinson's disease and Alzheimer's disease, however, do not extend to Huntington's disease, making it unlikely that a single pathophysiological mechanism accounts for retrograde amnesia across all three types of dementia.

In the amnesic disorder of Korsakoff's syndrome, the site of lesion implicated in the pathogenesis of the memory loss in the dorsomedial nucleus of the thalamus (Victor et al., 1971). As in the case of the dementias, the mechanism by which the anatomical deficits might account for the retrograde amnesia in the amnesic syndrome still remains to be discovered.

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