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Object Location Learning and Non-Spatial Working Memory of Patients With Parkinson's Disease May Be Preserved in "Real Life" Situations

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Summary

The presence of a spatial memory deficit in Parkinson's disease (PD) is still a matter of discussion. Nineteen PD patients and 16 controls were given two spatial tests and a non-spatial task. First, the subject was led into a room containing 4 objects and had 10 s to memorize their location. After being led outside, the subject had to place icons representing the objects on a map of the room. Differences between the real and estimated locations were evaluated. Afterwards, the subject had to choose a map showing the correct arrangement of objects from 4 alternatives. Locations of some objects were changed before the second test. The subject had 10 s to detect these changes. One point was given for each change or its absence detected. In the non-spatial working memory task, 8 cards of different shapes were used. The subject had to select a different card each time while the cards were shuffled between choices. Errors consisted of selecting previously chosen cards. The means of the above measures for both groups were compared. Absence of any significant differences suggests that PD patients perform well in "real life" memory tests in contrast to similar computerized tests.

Key words

Parkinson's disease – Object location learning – Non-spatial working memory – Recall – Recognition

Introduction

Parkinson's disease (PD) is a neuro-degenerative disorder characterized by well-known motor symptoms – rigidity, akinesia and tremor. However, it is not only the motor system which is affected by this disorder. Isolated cognitive deficits concerning speech and language, visuospatial functions, memory and executive functions were also described in PD (Dubois *et al.* 1991). While speech, executive functions and verbal memory are frequently impaired (Lees and Smith 1983, Owen *et al.* 1992, Breen 1993, Buytenhuijs *et al.* 1994), the evidence for a visuospatial deficit in PD is by no means unequivocal (Brown and Marsden 1986). Similarly, the results concerning spatial memory are rather controversial.

Morris *et al.* (1988) and Owen *et al.* (1992) used two computer tasks for studying short-term spatial memory and spatial working memory in PD patients. The short-term spatial memory task was a computerized version of the Corsi block span test. Morris *et al.* (1988) found that PD patients could perform both tasks. In the study of Owen *et al.* (1992) medicated PD patients were divided into two subgroups with mild and severe motor symptoms. While the performance of the short-term spatial memory task was impaired only in the latter subgroup, both subgroups showed deficits in spatial working

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memory. These results concerning spatial working memory were later confirmed in a study where two similar subgroups of PD patients were tested (Owen *et al.* 1993).

All the stimuli in the above mentioned tests of short-term spatial memory and spatial working memory (Morris *et al.* 1988, Owen *et al.* 1992, 1993) were simple and identical, their location on the computer screen being the only variable. Sahakian *et al.* (1988) tested PD patients using a more complex spatial memory task which involved visuospatial associative learning. In this computerized test, subjects had to learn up to 8 pattern-location associations. In general, PD patients were not able to remember as many associations as control subjects. Pillon *et al.* (1996) used a visuospatial learning test where locations of 16 pictures in a matrix had to be remembered. Again, PD patients were found to be defective in the performance of this task.

In the study of Cooper and Sagar (1993), subjects were asked to recall the spatial locations of 20 line drawings on a similar matrix. The testing was performed under two conditions: incidental spatial recall was assessed after the subjects had been told to estimate the sizes of the drawings, while intentional spatial recall was tested after the subjects had been instructed to remember their locations. PD patients showed impairment under the latter condition but their incidental spatial recall performance was similar to that of control subjects. These results suggest that PD subjects may perform well even in quite difficult spatial tasks.

The outcomes of the above studies are often conflicting. However, these studies do have something in common, namely that they all used either computer tasks or matrices with drawings. The minimal motor component of such tasks is clearly an advantage; on the other hand, subjects are expected to solve novel and unusual situations when completing them. This may be rather difficult for patients suffering from impairment of executive functions which is quite common in PD (Lees and Smith 1983, Owen *et al.* 1992). In the present study, object location learning was tested in an experimental situation which was designed to resemble everyday problems related to spatial memory. The design of the tasks minimalized the engagement of executive functions. According to our hypothesis that visuospatial learning is impaired in PD only when the task requires executive components, we expected the PD patients to perform similarly to control subjects in these tasks.

Recall and recognition performance is often compared in studies concerning memory of PD patients. As for verbal memory in PD patients, impaired free recall often contrasts with preserved recognition (Lees and Smith 1983, Breen 1993, Buytenhuijs *et al.* 1994). Appollonio *et al.* (1994) reported the same pattern of impairment when studying memory for pictorial stimuli in PD patients. However, many findings suggest that the "impaired recall – unimpaired recognition" pattern may not be characteristic of spatial memory in PD at all: both preserved spatial recall (Cooper and Sagar 1993) and impaired spatial recognition (Sahakian *et al.* 1988, Owen *et al.* 1993, Pillon *et al.* 1996, 1997) were described.

Following the spatial memory tests, a non-spatial working memory task was employed in the present study. Being both non-spatial and non-verbal, it differs from most working memory tests used in PD subjects by other authors. It bears some resemblance to the subject-ordered pointing task introduced by Petrides and Milner (1982) which was found to be sensitive to frontal lobe damage. PD patients were also shown to be defective in performing this task (Gotham *et al.* 1988).

The methods used in the present study are part of a battery of tests developed in our laboratory by Bohbot *et al.* (1994). The motor demands of all tasks were kept to a minimum and the time taken by the subjects to solve the problems was not limited.

Methods

Patients and control subjects

Nineteen patients with mild to moderate PD stages 1 to 3 according to Hoehn and Yahr (1967) were investigated. Their mean age was 61.4 years (S.D. 9.0), the mean duration of their previous education was 13.8 years (S.D. 3.9). There were 13 males and 6 females in the patient group. Mean disease duration was 7.9 years (S.D. 5.6). All patients were on stable antiparkinsonian medication, 14 of them were treated with levodopa (mean daily dose of 610 mg, range 200–1250 mg).

The control group consisted of 16 volunteers who had never suffered from any neurological problems and were matched for age, education and sex to the patient group.

Subjects showing signs of dementia or depression were not included in the study. The inclusion criteria were based on the scores in the Mini-Mental State Examination (MMSE) (Folstein *et al.* 1975) (24 points or more out of 30) and in the short version of the Geriatric Depression Scale (Yesavage *et al.* 1983) (9 points or less out of 15), respectively. The motor status of PD patients was assessed according to the Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn *et al.* 1987). All subjects except for one control person were right-handed. Informed consent was obtained from all of them prior to the testing.

Test 1: Object location recall and recognition

This task was designed as a memory test for several objects and their different spatial locations. The 3x3 m^2 testing room, where the objects were located, had no windows (but it was illuminated sufficiently by two ceiling lamps) and contained no other spatial cues except for a sink and a radiator. This room represented a novel environment for all the subjects.

Before the test started, a map of the testing room was shown to the subject with the following instructions: "You will be led into this room in a while and you will see four objects there – a kettle, a stand, a flowerpot and a briefcase. You will have 10 seconds to memorize their locations. After this time is over, you will be led out of the room again and asked to mark the object locations on this map with stickers representing different objects (object icons). You do not have to pay attention to the sink and the radiator in the testing room."

After the recall phase of the test took place according to the above mentioned instructions and after the subject had placed all the four object icons on the map of the testing room, this map was taken away by the examiner. The recall performance was evaluated in the following way: the coordinates of the object icons placed on the map by each subject were measured and translated into real space coordinates. The error was measured by the distance between the real location and the estimated location of the objects.

The recognition phase followed immediately. The subject was given four maps of the testing room (A, B, C and D) showing symbols of the four objects in different locations and was asked to choose the one which corresponded to the real situation (Fig. 1). (Four different arrangements of the objects in the testing room corresponding to the maps A, B, C and D were used. One of these arrangements was assigned to each subject before testing so that each of the variants was used approximately in the same number of subjects).

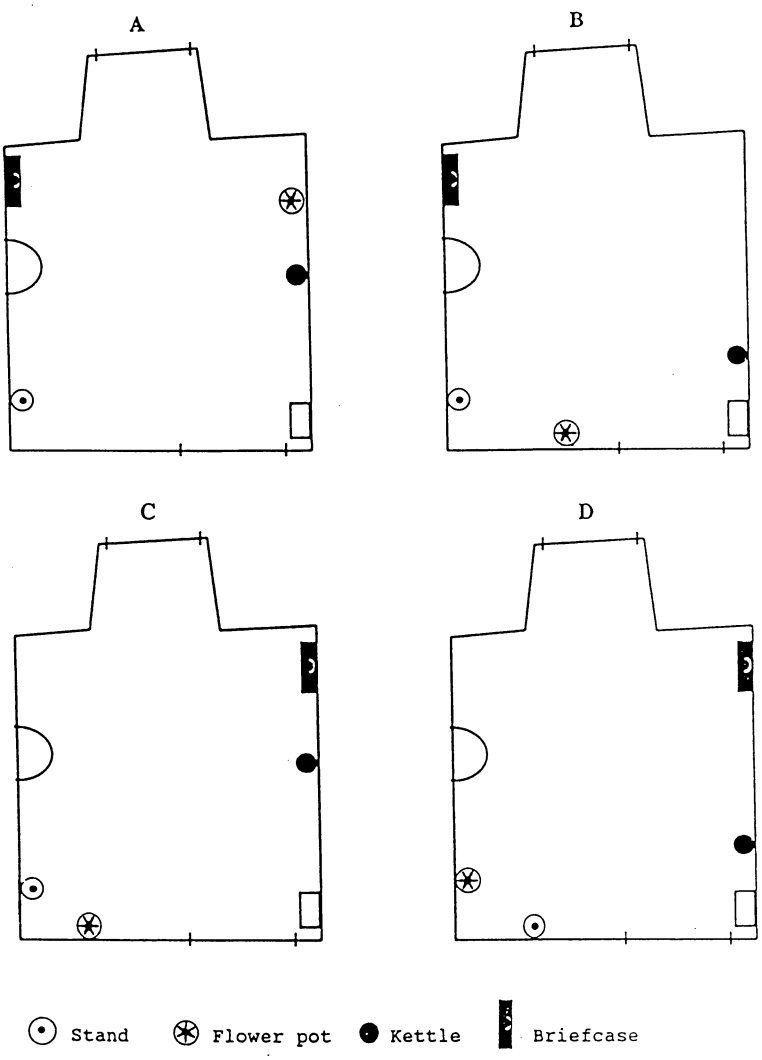

Fig. 1. *Object location recall and recognition tasks. Maps A, B, C, D show four different arrangements of the objects in the testing room.*

Test 2: Object location – Novelty detection

Before giving instructions for this task, some changes were made in the testing room (in the absence of the subject) according to a previously designed scheme. Different schemes of comparable complexity were used for different subjects. In general, one of the objects was left in the original position, one was displaced and the positions of the remaining 2 objects were switched (Fig. 2).

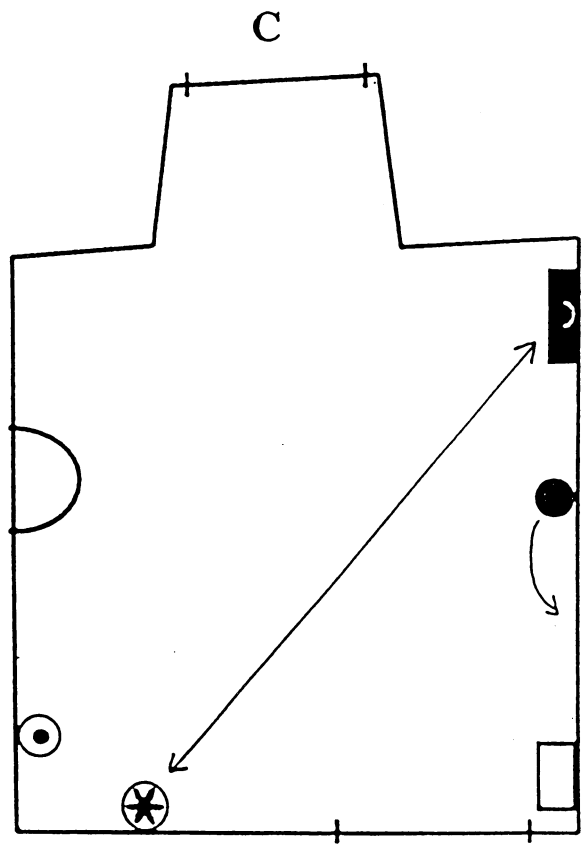

Fig. 2. *An example of changes made in the testing room before the object location – novelty detection task. In this case, the object arrangement of Fig. 1C was changed in the following way: the briefcase and the flowerpot were switched, the kettle was displaced and the stand was left in the original position.*

The subject was given the following instructions: "You will enter the testing room again and you will have 10 seconds to see if any changes have taken place there. Please do not comment on anything while looking into the room. You will be asked questions concerning each of the 4 objects later". After being led out of the testing room, the subject was questioned as follows (the number of points assigned to the subject for correct answers in each of the parameters is given in the parentheses):

"Was there any change in the testing room?" When the answer was YES, the questioning continued:

"Did the briefcase change position?" The same question was asked for the kettle, the stand and the flowerpot.

(Parameter "CHANGE": 1 point for each correct answer; maximum = 4 points).

"Was there a switch in the positions of two of the objects?" When the subject answered YES, another question was asked: "Which objects were switched?" (Parameter "SWITCH": 1 point for each of the switched objects which was correctly identified; maximum = 2 points).

In case that all the questions were answered correctly, 4 and 2 points were assigned to the subject in the parameters "CHANGE" and "SWITCH", respectively. Even after achieving 4 points in the first parameter, the subject could still attain 0 points in the second. This happened if he or she had noticed that three objects had changed place but failed to notice the switch.

Test 3: Non-spatial working memory task

This task was described in detail by Bohbot *et al.* (1997). Eight cards of different shapes were used. They were placed side by side on a 68 x 50 cm table so that they did not overlap. Each card was made of a piece of cardboard folded in half and was numbered from 1 to 8 (each card had a different number). The subject, sitting in front of the table, was told to choose one of the cards, open it, read the number inside and put it back on the table. After the subject had been asked to turn by 180° with the chair (not to see the table), the cards were shuffled and their spatial arrangement was changed. Then the subject was instructed to choose another card, different from the previous one. It was explained that the aim of the test is to open successively all of the 8 cards (while repeating the same procedure as described above) without choosing any card more than once. The subject was advised not to use any strategy such as choosing cards according to their size from the largest to the smallest or *vice versa*. It was stressed that there's no need to remember the numbers inscribed in the cards.

The task was terminated after the subject had succeeded in opening each of the 8 cards or after a limit of 16 choices was reached. Errors consisted of choosing the previously selected cards. Three parameters were considered in the statistical analysis: the number of errors within the first 8 choices (Err. / 8 ch.), the total number of errors (Total Err.) and the total number of choices (Total n. ch.).

A typical experimental session lasted 40–60 min. All the PD patients exhibited their optimal motor functions during the testing.

Table 1. Memory performance of PD patients and control subjects

A. Object location recall and recognition

Distances	PD patients	Control subjects
Briefcase	902.9±240.8	446.8±171.4
Stand	600.1±179.4	458.8±146.3
Kettle	666.4±158.0	526.0±143.2
Flowerpot	776.2±195.8	872.9±248.1
Total	2945.6±460.9	2304.4±590.3

Data are means±S.E.M. Distances in mm between the real and the estimated locations of different objects.

B. Object location – Novelty detection

Parameter	PD patients	Control subjects
Change	3.2±0.2	3.1±0.3
Switch	1.4±0.2	1.3±0.2

Change (max. = 4 points): 1 point for each correct answer to the following questions: "Did the briefcase change position?", etc. (The same question was asked for the stand, the kettle and the flowerpot). Switch (max. = 2 points): 1 point for each of the switched objects which was correctly identified.

C. Non-spatial working memory task

	PD patients	Control subjects
Err. / 8 ch	1.7±0.2	1.4±0.2
Total Err.	4.8±0.7	5.0±0.8
Total n. ch.	12.6±0.7	12.8±0.8

Err. / 8 ch. = number of errors within the first 8 choices, Total Err. = total number of errors, Total n. ch. = total number of choices.

Results

Test 1

The recall phase: For each of the 4 objects, an error was evaluated as the distance between its real and estimated location. The total error (of each subject) was defined as a sum of these 4 "partial" errors. Mean errors concerning different objects and mean total errors were calculated for the group of PD patients and for the control group (Table 1A). Two-tailed t-tests were used to compare these 5-error parameters in both groups. The difference between the two groups did not attain statistical significance in any of the parameters (briefcase: $t(33)=1.45$, $P=0.157$; stand: $t(33)=0.58$, $P=0.567$; kettle: $t(33)=0.63$, $P=0.533$; flowerpot: $t(33)=-0.30$, $P=0.765$; total: $t(33)=0.84$, $P=0.405$).

The recognition phase: All the PD patients succeeded in choosing the correct map of the testing room (the one showing the correct placement of all objects) while 4 control subjects did not. The Fisher exact probability test showed that the above difference was statistically significant ($P<0.05$).

Test 2

The mean values of 2 parameters calculated for the PD patient group and for the control group (Table 1B) were compared using two-tailed t-tests. No statistically significant differences were found ("CHANGE": $t(33)=0.42$, $P=0.680$; "SWITCH": $t(33)=0.62$, $P=0.538$).

Test 3

The differences between the two groups (Table 1C) again failed to reach statistical significance (Err./8 ch.: $t(33)=1.14$, $P=0.261$; Total Err.: $t(33)=-0.15$, $P=0.885$; Total n.ch.: $t(33)=-0.24$, $P=0.816$).

Correlation between the results of the PD patients and their motor status

In the group of PD patients, Pearson product moment correlations between the values of different parameters used in all three experimental tasks and the UPDRS scores were evaluated. The same was done for the values of every experimental parameter and the scores achieved in the short version of Geriatric Depression Scale. None of the investigated correlations was statistically significant except for that between the UPDRS and Geriatric Depression Scale scores themselves. This correlation was significantly positive ($r=0.6106$).

Discussion

Two spatial memory tests requiring subjects to remember four object-location associations were administered to non-demented medicated patients suffering from mild to moderate PD. Their performance was similar to that of control subjects in both tests.

The present findings contrast with the results of Pillon *et al.* (1996) who administered a visuospatial learning test to a similar group of medicated PD patients. In this test, subjects were required to learn as many as 16 picture-location associations which were presented in groups of four in the encoding phase, one group after another. The PD patients showed normal

encoding but had impaired recall and recognition of the picture locations. In another study, Pillon *et al.* (1997) hypothesized that PD patients would perform better in this task if all the stimuli were presented simultaneously at encoding. This hypothesis was recently confirmed (Pillon *et al.* 1998). The good performance of PD patients in our first object location task could thus be partly explained by the fact that the presentation of all stimuli in this task was simultaneous.

Obviously, the number of object-location associations was much lower in our study than in that of Pillon *et al.* (1996). However, subjects in the present study had to estimate distances and to translate the real coordinates of different objects mentally to their coordinates on a map, while in the study of Pillon *et al.* (1996) they just had to remember spatial locations of pictures within a given matrix. It should also be noted that the number of locations to be remembered is only one of many factors influencing the performance of PD patients.

Sahakian *et al.* (1988) reported impaired recognition of 5 'target' locations in medicated PD subjects who were at similar stages of the disease as patients in the present study. In their computerized spatial recognition task, subjects had to learn these 'target' locations at which a white square was sequentially presented and they had to distinguish them from 'distractor' locations later. Provided that PD patients performed well in the recognition phase of our first object location task, it seems that learning of object-location associations may sometimes be easier than learning of locations represented by identical stimuli. For example, knowledge of two object-location associations could help the subject in our recognition task to select the right map of the testing room without remembering the locations of the remaining objects.

Following the spatial recall and recognition assessment, the ability to detect changes in the spatial arrangement of the objects was tested with the object location – novelty detection task in the present study. The questions concerning possible changes which the subjects had to answer ("Did the briefcase change place?", etc.) could be criticized as being too simple; they could only be answered by "yes" or "no" with the exception of the last one ("Which objects were switched?") and no precise description of the changes was required. If the subjects guessed when answering the questions, they would just perform at chance level and their mean score on the parameter "CHANGE" (1 point for a correct answer concerning each of the 4 objects; maximum = 4 points) would be 2.0 = 4 x 0.5. However, the mean scores achieved by the PD patients and the control subjects in this parameter were 3.2 (S.E.M. 0.2) and 3.1 (S.E.M. 0.3), respectively. It can be concluded that both groups performed above the chance level and, in general, did use their knowledge of the original locations of different objects when solving this task.

Neither the spatial memory tests, nor the non-spatial working memory task revealed any deficit concerning the performance of PD patients in our study. On the other hand, Owen *et al.* (1992, 1993) found medicated patients with mild to severe PD to be impaired when solving a computerized spatial working memory task. These findings support the hypothesis of Bradley *et al.* (1989) that the visuospatial subsystem of working memory is specifically impaired in PD. However, the spatial working memory task used by Owen *et al.* (1992, 1993) was probably more difficult than our non-spatial task. It involved repetitive searches for 'tokens' through 4, 6, or 8 'boxes' on the computer screen. A single token was hidden inside one of the boxes at any occasion and no box was used to hide a token more than once. During this task, subjects had to remember not only which boxes they had opened previously but also in which boxes the tokens had been found in preceding tests. Morris *et al.* (1988) reported normal performance of medicated patients with mild to moderate PD using an earlier version of this spatial working memory test which Owen *et al.* (1992) considered to be less demanding. It must be stressed that the hypothesis of Bradley *et al.* (1989) about working memory in PD is not generally accepted. Dubois *et al.* (1991) suggested that it was questionable because it was based on a comparison of a visuospatial and a verbal task which, again, were not of comparable difficulty.

Gotham *et al.* (1988) tested PD patients on and off levodopa treatment on a subject-ordered pointing task. Only patients on levodopa showed significant impairment during this task in comparison with control subjects. It was suggested that levodopa was responsible for the deterioration of their performance. Provided that our non-spatial working memory task resembles the subject-ordered pointing task, this conclusion is not supported by the present study. However, the mean daily dose of levodopa was lower in our group of PD patients than in the study of Gotham *et al.* (1988) and not all patients in our group were on levodopa treatment.

No significant correlations between the performance of PD patients in any of the tasks and their UPDRS scores were found in the present study. Taking into consideration that they performed similarly to control subjects in all the tasks, this fact is not surprising. Pillon *et al.* (1996) also failed to find any significant correlation between visuospatial recall performance of PD patients and their motor disability. On the other hand, Taylor *et al.* (1986) and Sahakian *et al.* (1988) found spatial memory scores of PD subjects to correlate significantly with disease severity. Owen *et al.* (1992) emphasized, however, that if any relationship between the motor symptoms and the performance in cognitive tasks existed in PD, it was not a direct one. In

our study, the only significant correlation was that between the UPDRS and Geriatric Depression Scale scores. This finding is in agreement with Owen *et al.* (1993).

In summary, the performance of medicated patients with mild to moderate PD was shown to be normal in our tests of object location learning and non-spatial working memory. The spatial tasks used in the present study, unlike many computer and "matrix" tasks, resemble spatial problems one may encounter in real life. Their results are thus possibly less contaminated by the decreased ability of PD patients to deal with novel situations. Furthermore, the "real life" nature of our spatial tasks might have influenced the performance of the PD patients in these tasks in a positive way. We believe that for a person who moves with difficulty (like these patients) it is very important to be able to estimate distances correctly and to consider how much time or how many steps it would take to reach any object. This fact may partly explain why the performance of PD patients in our object location recognition task was even better than that of control subjects.

The results of the present study are quite encouraging for both patients and neurologists; they suggest that non-demented PD subjects can solve common memory-related problems as well as other individuals of their age.

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