Working memory in medicated patients with Parkinson’s disease: the central executive seems to work

Nathalie Fournet, Olivier Moreaud, Jean-Luc Roulin, Bernadette Naegle, Jacques Pellat

Abstract

Objective—To determine whether a deficit of the central executive can explain the attentional deficits of patients with Parkinson’s disease.

Methods—Fifteen patients with idiopathic Parkinson’s disease and 15 controls were given a dual task paradigm minimising motor demands and combining verbal, visual, or spatial span with two conditions of articulatory suppression.

Results—Although the spans were systematically lower in medicated parkinsonian patients than in controls, suggesting a decrease of central processing resources, there was no direct evidence for a deficit of the central executive.

Conclusions—A deficit of the central executive either is not an inevitable feature of the disease, or is dependent on the nature of task (visuomotor vs cognitive), or is corrected by dopaminergic medication.

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Keywords: Parkinson’s disease; working memory; attention; frontal lobe

Numerous tasks requiring intact frontal lobe function are impaired in Parkinson’s disease. However, different studies have given conflicting results. According to Brown and Marsden, one way to account for these discrepancies is to postulate that patients with Parkinson’s disease are impaired only in tasks that rely on internally guided behaviour, whereas they perform far better on more automatic and externally cued tasks. The same authors suggested that this impairment could be explained by a decrease in attentional resource allocation, secondary to a dysfunction of a central system supervising cognitive functioning. This central system could be the supervisory attentional system of Norman and Shallice’s model, or the central executive component of Baddeley’s working memory model.

In a direct test of their hypothesis, Brown and Marsden found that patients with Parkinson’s disease were impaired compared with normal subjects on a double task paradigm combining a cued version of the Stroop task with simultaneous random number generation. In the authors’ opinion, these results were consistent with a depletion in attentional resource allocation. However, because of the predominant verbal nature of the two tasks employed, structural interference might have led to the impairment. Furthermore, random number generation seemed to be more difficult in patients with Parkinson’s disease. It then becomes difficult to know if impaired performance on a double task follows from task difficulty or from a specific deficit in resource allocation supplied by the central executive.

Recently, Dalrymple-Alford et al used a tracking/digit span dual task paradigm. The performance of medicated patients with Parkinson’s disease and controls was adjusted to prevent the consequences of a general information processing problem. The two tasks employed were different in nature (verbal for digit span, visuomotor for tracking), thus making separate demands on the two subsystems of the working memory model, without structural interference. The results were a decline in performance on the tracking task in patients with Parkinson’s disease, evident only when digit sequences were recalled simultaneously. Although the authors assumed that their results were strongly in favour of a deficit in the functioning of the central executive, they did not eliminate an effect of worse learning of the tracking task by patients with Parkinson’s disease. Indeed, the tracking task exerts a strong motor demand, and some studies found evidence for an impairment of patients with Parkinson’s disease on visuomotor procedural learning tasks. Other studies, however, suggested that a deficit was evident only in demented parkinsonian patients. Furthermore, as far as recall of digits was not affected by simultaneous concurrent performance of the tracking task, a deficit of the visuospatial subsystem could account, in part, for the results. There is some evidence for such a deficit, but definitive data are lacking.

To specify the nature of working memory deficits in Parkinson’s disease, we devised a dual task paradigm minimising motor demands. Verbal and visuospatial aspects—namely, the phonological loop and the visual spatial sketchpad—were evaluated separately. The span method was used: word span for the phonological loop, visual and spatial spans for the visual spatial sketchpad. The same method was used while performing a verbal interference (articulatory suppression). Articulatory suppression interferes with the functioning of the articulatory loop (structural interference), so that a double task combining verbal span and articulatory suppression is not pertinent to
test the central executive.12 To place heavier demands on the central executive, the attentional cost of the articulatory suppression was varied. A deficit in the functioning of the central executive in patients with Parkinson's disease would then result in a more pronounced effect (lower spans) of higher cost interference than in controls. A specific task designed to disrupt the functioning of the visual spatial sketchpad still does not exist. To mobilise the capacities of the central executive, we decided to perform simultaneously visual or spatial span with articulatory suppression. In this case, articulatory suppression was supposed to place a general attentional load, requiring more attentional resources from the central executive. If a deficit of the central executive exists in patients with Parkinson's disease, this double task should lead to a larger decrease of spans than in normal subjects.

Methods

SUBJECTS

Fifteen patients with idiopathic Parkinson's disease and 15 volunteer controls matched for age, educational level, and verbal IQ13 were tested. Subjects with clinical evidence of dementia, history of stroke, head injury, meningitis, neurosurgical intervention, and alcoholism or drug consumption were excluded. All patients with Parkinson's disease were diagnosed by a neurologist. There were nine men and six women. The mean duration of the disease was 8.0 (SD 4.8) years. The severity of the disease was rated with the score in the motor part of the unified Parkinson's disease rating scale (UPDRS)14 (mean score = 21.8 (SD 11.7)), and the Hoehn and Yahr scale.15 Two patients were classified as Hoehn and Yahr stage I, 12 as stage II, and one as stage III. At the time of testing, all patients were taking levodopa with a decarboxylase inhibitor; 11 patients were taking a dopamine agonist (bromocriptine or piribedil); and one patient was taking selegiline. The mean age of patients and controls was, respectively, 66-1 (SD 8.2) and 66-6 (SD 11-5); the mean number of years of education 9-7 (SD 4-1) and 10-3 (SD 3-7); and the mean verbal IQ13 111-1 (SD 13-4) and 114-5 (SD 12-4). All subjects gave informed consent.

PROCEDURE

Subjects were seated in front of the screen of a microcomputer (AMSTRAD PC 1512; size of the screen 255 mm \( \times \) 205 mm). The distance from eye to screen was about 60 cm. For the verbal span, words of two syllables were presented sequentially on the screen at a rate of one word every 700 ms. Each word was seen for 800 ms. Subjects were instructed to read them silently and to keep them in the memory. After a four second delay, a question mark appeared on the screen. At this time the subjects were to recall as many words as they could. The number of words was progressively increased and spans were assessed using the methodology of the Wechsler adult intelligence scale (WAIS).16 Three successive trials were made. The span in each trial was the maximal number of items recalled, minus 0.5 if the subject recalled this maximal number after having failed once. The final span was the average of the three spans obtained. The words were chosen randomly from a list of 18 French words.

A computerised test, based on those of Wilson et al17 and Phillips and Christie,18 was developed to assess visual span. The computer used and the position of the subjects were the same as those for verbal span. Stimuli were patterns composed of a matrix of boxes. The boxes might be either filled (white) or empty (black). The first pattern presented was simply made up of two boxes, one of which was filled. Pattern complexity was increased in stages, two boxes at a time \((2 \times 2, 2 \times 3, 2 \times 4, 3 \times 4 \ldots \text{matrix})\), half of the boxes being randomly filled at each level of complexity. The boxes filled simultaneously. The pattern was presented for three seconds. The same pattern was presented again four seconds after the end of the first presentation, but one box that was previously filled was now empty. The subject had to touch the missing box with a pointer. Visual span was the number of filled boxes at the highest level of complexity at which the subject produced a correct response. The methodology of the WAIS19 was used and three successive trials were made.

Spatial span was assessed by remembering locations of boxes that sequentially filled a 5 \( \times \) 5 matrix on the screen of the computer. Each box was filled for 1-5 seconds, and then emptied, before the next box was filled. After four seconds, the subject was asked to repeat the sequence by touching the boxes of an empty matrix with a pointer. The simple level of difficulty was a sequence of one box. The sequence was gradually increased up to a maximum of eight boxes. As previously, three trials were made and the same notation was employed. This task is a modification of the block tapping test.10 The corresponding task consisted of articulatory suppression. To increase the attentional demand made on the central executive, two conditions of articulatory suppression were devised. The first condition was to repeat aloud the phoneme “da”. The second condition, supposed to be more attention demanding, consisted of counting aloud upwards in threes from a number (between 1 and 9) given by the experimenter immediately after the items were presented. The same tasks as previously described were employed, except that articulatory suppression was performed during the delay between presentation and recall of the items. Each subject was given the whole experimental condition, and the order of the tasks was balanced as a function of the nature of the interference. For each condition of interference, the verbal span was measured first, then visual span, and finally spatial span.

DATA ANALYSIS

Analysis of mean spans in the tasks was carried out by analysis of variance (ANOVA). When significant effects or interactions were found,
Mean verbal, spatial, and visual mean spans (SD) of patients with Parkinson’s disease and control subjects as a function of interference conditions

<table>
<thead>
<tr>
<th>Patients with Parkinson’s disease</th>
<th>Control subject</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Verbal spans:</strong></td>
<td></td>
</tr>
<tr>
<td>Without interference</td>
<td>4-4 (0-9)</td>
</tr>
<tr>
<td>“Counting upwards in threes”</td>
<td>4-4 (1-2)</td>
</tr>
<tr>
<td><strong>Spatial spans:</strong></td>
<td></td>
</tr>
<tr>
<td>Without interference</td>
<td>4-3 (0-7)</td>
</tr>
<tr>
<td>“Counting upwards in threes”</td>
<td>3-7 (0-9)</td>
</tr>
<tr>
<td><strong>Visual spans:</strong></td>
<td></td>
</tr>
<tr>
<td>Without interference</td>
<td>9-1 (2-6)</td>
</tr>
<tr>
<td>“Counting upwards in threes”</td>
<td>5-4 (2-2)</td>
</tr>
</tbody>
</table>

Further post hoc comparisons were carried out to elucidate the nature of the effect.

**Results**

The table gives the mean spans for both groups.

**COMPARISON OF MEAN SPANS BETWEEN THE TWO GROUPS**

Patients with Parkinson’s disease performed, on the whole, worse than control subjects: there were significant group effects for the verbal (F (1-28) = 7-19; P < 0-05), the spatial (F (1-28) = 13-4; P < 0-01), and the visual tasks (F (1-28) = 22-4; P < 0-01).

**EFFECT OF AN ATTENTIONAL LOAD IN THE VERBAL SPAN TASK**

There was a significant main effect of interference (F (2-56) = 36-55; P < 0-01). Verbal spans were significantly lower with interference than without it (comparison between the without interference condition with the two interference conditions: F (1-28) = 77-72; P < 0-01). As expected, the supposedly more demanding interference task (counting upwards in threes) led to lower performances (comparison between the two interference conditions: F (1-28) = 14-83; P < 0-01). There was no group × interference interaction (F (2-56) = 0-75; NS): the decrease in the performance throughout the interference conditions was the same for both groups.

**EFFECT OF AN ATTENTIONAL LOAD IN THE VISUAL AND SPATIAL SPAN TASKS**

A main effect of interference was present (spatial task: F (2-56) = 18-02; P < 0-01; visual task: F (2-56) = 39-07; P < 0-01) with a significant difference between the two interference conditions (spatial task: F (1-28) = 5-24; P < 0-05; visual task: F (1-28) = 23-34; P < 0-01). Furthermore, the interference conditions showed a significant effect compared with the no interference condition (spatial task: F (1-28) = 30-4; P < 0-01; visual task: F (1-28) = 57-24; P < 0-01). Once again, the group × interference interaction was not significant (spatial task: F (2-56) = 0-026; NS; visual task: F (2-56) = 1-87; NS); the decrease in performance along the interference conditions was the same for both groups, for spatial and visual tasks.

**Discussion**

Medicated patients with Parkinson’s disease were not significantly impaired compared with controls, when a span task was combined with an articulatory suppression. The results were the same, whatever the nature of the span task (verbal, visual, or spatial). The reproducibility of results within these different modalities strongly supports this absence of impairment. Moreover, we showed that articulatory suppression was attentionally demanding. The second condition of interference (counting upwards in threes) was more demanding than the first condition (repetition of “dada”). A dysfunction of the central executive in patients with Parkinson’s disease would have inevitably resulted in greater effects of higher cost interference than in controls. This was not the case, even when the test induced structural interference (verbal span task with articulatory suppression). These results suggest that the central executive seems to work well enough to perform the tasks. Before discussing this hypothesis, we must consider four alternative explanations. Firstly, control subjects and patients with Parkinson’s disease could have a comparable dysfunction of the central executive. Indeed, such a deficit has been shown with aging.20 We did not compare the performance of our controls with young healthy subjects, so that this hypothesis remains open. However, the previous studies by Brown and Marsden6 and Dalrymple-Alford et al,9 who tested subjects comparable in age and years of education with ours, did not show any impairment in old controls.

An alternative assumes that the double task that we designed is not sensitive enough to detect a dysfunction of the central executive. Indeed, if our double task paradigm is inspired by Baddeley’s model,1 it is not strictly comparable with the tasks previously employed to assess the central executive in patients with Parkinson’s disease6 or Alzheimer-type demented patients.21 Nevertheless, we clearly showed that the two conditions of interference used were sufficiently demanding, even when performed simultaneously with spatial or visual span tasks—that is, when no structural interference was expected. In Baddeley’s model, this type of dual task cannot be achieved if the central executive does not function well. However, basal levels of impairment were not reached by all patients with Parkinson’s disease when counting by threes in the span tasks, so that we cannot rule out the fact that our interference tasks are not demanding enough to detect a dysfunction of the central executive.

As a third possibility, the fact that at least some patients might have reached basal levels, potentially masks a greater impairment, and may not permit detection of an impairment of the central executive.

A fourth possibility is that patients with Parkinson’s disease could have used strategies different from controls to perform the interference tasks. Patients with Parkinson’s disease possibly found it more difficult to repeat “dada” or count upwards, so that they may
have adopted a strategy that would minimise the influence of these tasks on memory load. Unfortunately, we did not measure the performance of patients on secondary tasks. Thus, we do not know exactly if they performed as well as or worse than controls, although, subjectively, it did not seem to us that patients had difficulty repeating “dada” or counting upward in threes. Moreover, it would be very surprising if the same decrease of spans in patients with Parkinson’s disease and controls could be a consequence of this sole strategy.

Despite these drawbacks, our results challenge the fact that a deficit of the central executive is an inevitable feature of Parkinson’s disease. They disagree to some extent with the results of D’Alimont-Allford and colleagues, who tested a similar population of medicated patients with Parkinson’s disease. Comparable in both studies is the fact that a cognitive task span does not seem to be affected more by the simultaneous performance of a concurrent task in patients with Parkinson’s disease than in controls. The studies differ in that we were unable to find direct evidence for a dysfunction of the central executive in our patients. However, we used an experimental task that minimised the motor demand. This point is worth discussing: if we do not take into account a possible deficit of procedural learning of visuomotor tasks in parkinsonian patients, it may suggest that the dysfunction of the central executive is evident only for some kinds of performance, and not for others. The results of Baddeley et al. in Alzheimer-type demented patients, seem to support this view: these patients, who do not usually present with a deficit of procedural learning, had their performance on tracking similarly altered by concurrent performance of a span task. Further studies, combining different types of dual tasks on different populations, are needed to clarify this suggestion. Perhaps they will show different profiles of impairment, and more crucially, will allow us to describe more accurately the functions subserved by the central executive.

It is important to consider the role of dopaminergic medication. Our patients were all taking dopaminergic drugs. We did not test them when off medication (due to the long duration of the experiments), but it could be hypothesised that the presence of dopamine improved a possible dysfunction of the central executive (the same way as it improves some frontal lobe tasks in parkinsonian patients). Another important result of our study is that our patients with Parkinson’s disease had consistently lower spans than controls, whatever the modality, even when no interference was performed. Previous studies usually did not find reduced verbal span in parkinsonian patients. A few studies assessed visual and spatial spans with a methodology almost comparable with ours. They reported deficits only in non-medicating patients with Parkinson’s disease, or in medicated patients with severe forms of the disease (Hoehn and Yahr stages III and IV). No deficit was found in mild or moderate forms (Hoehn and Yahr stages I and II). For example, in these studies, spatial spans of patients with mild or moderate forms were about 5, and those of non-medicating patients, or medicated patients with severe forms, about 4 or less (exactly as in our patients, when no interference was performed). The major difference between these studies, apart from the fact that we placed a delay between the presentation and the recall of the items, we deliberately chose to perform articulatory suppression during a delay between the presentation and the recall of the items, because, by this means, the only processes disrupted were those involved in the maintenance of information in memory. If we had performed articulatory suppression during the presentation of the items, encoding would have been modified, so that it would have been impossible to know if the decrease of spans was a consequence of a deficit of working memory processes, or of a disruption of other processes (for example, perceptual). Delayed-response deficits have been shown in Parkinson’s disease. Such a delay may possibly be responsible for the low spans found in our controls too. Delayed response deficits can be considered to result from a deficit of keeping in memory a stimulus that has been taken away from perception, a process called working memory by some authors. In Baddeley’s framework, this deficit cannot be interpreted as a dysfunction of the central executive, because the subsystems can maintain the information during the delay, refreshing it with rehearsal. As we did not test our patients without delay, we cannot eliminate a dysfunction of the subsystems. As far as we know, the role of the phonological loop has not been accurately tested in Parkinson’s disease, but a dysfunction of the visual spatial sketchpad is suspected. Whatever the explanation for these results, the span tasks without interference seem more difficult for patients with Parkinson’s disease than for controls. Even if this difficulty is the consequence of a disruption of the central executive, because the subsystems can maintain the information during the delay, we have no direct evidence that it results from a deficit of the central executive. Indeed, if that was the case, we can hypothesise that interference would have resulted in much lower performances in parkinsonian patients. We are then left with results difficult to interpret with Baddeley’s model. More work is needed to understand whether our results are the consequences of experimental drawbacks, or express a reality that would need a repecification of the model.

In conclusion, using a double task paradigm minimising motor demands, we were unable to find any evidence for an impairment of the central executive in medicated patients with Parkinson’s disease. Although the methodology could be improved, our study suggests that the impairment of the central executive, either is not an inevitable feature of the disease, or is dependent on the nature of the task (visuomotor vs cognitive), or is corrected by dopaminergic medication. Some of our results would confirm the effect of the delay during the maintenance of the material, need further classification to allow a better under-
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