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Are central executive functions working in patients with focal frontal lesions?

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Abstract

The aim of this study was to examine the hypothesis of a link between frontal cortex and two executive functions in working memory: the capacity to perform a dual task and the ability to inhibit irrelevant information. A dual task designed to assess the capacity to perform storage and processing simultaneously and a directed forgetting task designed to assess the capacity to actively inhibit no-longer relevant information were administered to a group of patients with focal frontal lesions and to a group of control participants. The results revealed that despite showing reduced short-term storage, frontal patients performed the dual task and inhibited the no-longer relevant information as well as control participants. These findings suggest that not all-executive processes are exclusively sustained by the frontal cortex [Quart J Exp Psychol 9 (1996) 5; Curr Opin Neurobiol 10 (2000) 195; Neuropsychology (1994) 544; The Cognitive Neuropsychology of Alzheimer-type dementia. Oxford, New York: Oxford University Press, 1996].

Keywords: Central executive; Working memory; Inhibition; Dual task; Frontal

1. Introduction

The term working memory [14] refers to a system involved in the short-term maintenance and manipulation of information necessary for the performance of complex cognitive tasks. The model proposed by Baddeley [9] includes two slave systems ensuring temporary storage of information, the phonological loop and the visuospatial system, and an attentional system, the central executive (CE). Baddeley suggested that the CE is essentially equivalent to the Supervisory Attentional System (SAS), which is needed in novel or problematic situations, such as planning future actions and decision-making [43]. One important characteristic of the SAS is its non-unitary nature [48–54]. Baddeley [10] also distinguished between different CE functions, among which the ability to select and manipulate information in long-term memory, to select relevant information while rejecting (inhibiting) irrelevant material, and to coordinate two or more concurrent activities.

In a recent review of the neuroimaging studies on working memory, Smith and Jonides [56] showed that short-term storage (on the order of seconds) for verbal materials depends on frontal areas such as Broca (Brodmann area (BA) 44) and the left supplementary and premotor areas (BA 6). D'Esposito et al. [26] showed that other frontal areas (BA 9, 45, 46) might also be involved in short-term storage. However, although storage processes (the phonological loop and the visuospatial sketchpad) have been investigated from a neuropsychological point of view in numerous studies, the CE has received little attention in comparison. This led Smith and Jonides [56] to suggest that the 'highest priority is to turn now further attention to executive processes and their implementation in the frontal cortex' (p. 1660).

Empirical evidence from neuroimaging studies (e.g. [23,44]) and from studies with brain-damaged patients [21,25,39,45] supports the involvement of the frontal cortex (i.e. dorsolateral frontal areas, BA 9 and 46 and anterior cingulus, BA 24) in executive processes such as coordinating a dual task and inhibition. The picture is not that straightforward however, and the univocal relation between these functions and the frontal cortex is still debated. With regard to the ability to perform concurrent tasks, Frisk and Milner [30] did not observe any impairment in patients who had undergone frontal lobectomies, and neither did Vilkki et al. [61] in patients with focal frontal lobe lesions following surgery for excision of tumors. Also, in the last study looking at the effect of focal frontal lesions on performance in dual task situations, Baddeley et al. [13] showed that whilst frontal patients with signs of dysexecutive syndrome

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(DS) presented poor dual task performance, frontal patients with no such DS signs did not (see also [3]). Finally, two recent neuroimaging studies show that dual task performance is not specifically supported by prefrontal activation [1,15]. With regard to the ability to inhibit irrelevant information, recent neuropsychological studies also failed to show impaired performance in patients with focal frontal damage in classical tests of inhibition such as the Wisconsin card sorting test (e.g. [4,5]) and the Stroop test (e.g. [2]), and recent neuroimaging studies have shown widely distributed cortical activation in inhibitory tasks [31,32].

It appears that relations between dual task performance, inhibition and the frontal cortex are not yet clearly understood and are in need of further study. There can be several possible reasons for the inconsistencies observed between studies on dual tasks involving frontal patients, for example, different methods of administration of the tasks and measures, different aetiologies of the lesions, discrepancies in the criteria used to select patients and variability of the time lag between the onset of the lesions and the testing phase. As for inhibition, despite the increasing interest that this concept has attracted in cognitive psychology (e.g. [20]) and its proposed role in the functioning of the CE, there is as yet no study examining working-memory inhibitory capacities in patients with frontal lesions.

Although classical views of executive functions tend to locate these functions in the frontal cortex [9,35,48,49], more recent views suggest that executive functions might be sustained by a broader cortical neural network rather than by solely the frontal cortex [19,40,41] (see also [8,11,12,29,31,32,61]). In order to contribute to the distinction between these two views, we have limited our research to patients with focal lesions of the frontal lobes, and have attempted to characterize the lesion location and extent as well as possible in naturally occurring (with the possible exception of traumatic brain injury) lesions in human patients. Indeed, only patients with frontal lesions not extending to other cerebral areas (in contrast to the patients examined in the studies that mainly support Shallice and coworkers view, i.e. [16,17,48]) were considered in our study (also see [8,57,58]).

The aim of this study was to explore further the hypothetical link between the frontal cortex and the ability to perform two concurrent activities and to inhibit no-longer relevant information in working memory. The first was assessed by using the computation span task [47]. This task allows comparing recall in a simple condition in which maintenance only is required with recall in a dual condition in which both maintenance and information processing are required. The ability to inhibit no-longer relevant information was assessed by using a short-term directed forgetting task [46], which taps the capacity to recall some information and actively inhibit other that was initially processed but subsequently became irrelevant. Two methodological issues received particular attention in the current study: the type of lesions considered, which had to be limited to the frontal lobe, and the stability of the clinical state (see [61], for the importance of this factor).

If an unequivocal link between executive functions and the frontal cortex does exist (the frontal cortex is the necessary and 'sufficient' region for all the executive functions), patients with focal frontal damage should be impaired in the capacity to undertake simultaneously storage and processing and in the ability to inhibit no-longer relevant information. However, if, as recently suggested by Baddeley [11,12], Carpenter et al. [19] and Morris [40,41] (also see [8]), executive functions are sustained by parts of the brain other than the frontal cortex, patients with focal frontal lesions could present with some executive functions spared.

2. Experiment

2.1. Participants

Patients with possible (or putative) frontal lesions were screened by neurologists in five French-speaking Belgian hospitals. The instructions concerning the selection criteria emphasized that a CT scan and/or MRI should confirm the frontal lesion. Only patients with lesions strictly restricted to the frontal lobe could be included in the study. Any hint of lesion in regions other than the frontal lobe led to the exclusion of the patient from the study. Other restrictions were that participants had to be younger than 55 and could not present any antecedent of alcohol or drug abuse, or of any psychiatric disorder. Finally, patients were only included if examined at least 5 weeks after the occurrence of the lesion, or, in the case of neurosurgical patients, the date of surgery.

Under these conditions, among the 43 patients referred to us as 'frontal' patients, only 13 were included in the study. Four patients had cerebral vascular accidents: two due to anterior communicating artery aneurysm (F3 and F10), one due to anterior cerebral artery aneurysm (F7) and one of unknown origin (F11). Seven patients had traumatic brain injury: five due to motor vehicle accidents (F1, F4, F5, F6 and F14) and two due to falls (F2 and F8). Finally, two patients had been operated for excision of an astrocitomas (F12 and F15). Six patients had a left-sided lesion, four a right-sided lesion and three a bilateral lesion. Location of lesions is shown in Fig. 1a and b. These illustrations reproduce the last radiographic examination undertaken prior to the testing. The affected regions were identified using the methodology of Damasio and Damasio [22] with the help of an experienced neurologist working blind to the purpose of the study.

Damasio and Damasio's [22] methodology comprises two main steps. The first consists in transposing the lesion from the CT scan or MRI scan into a set of detailed anatomical templates (Damasio and Damasio [22] p. 207–17). The second step consists in identifying the region damaged (e.g. 'F07' or prefrontal region) and to translate it into the Brodmann nomenclature with reference to the key codes

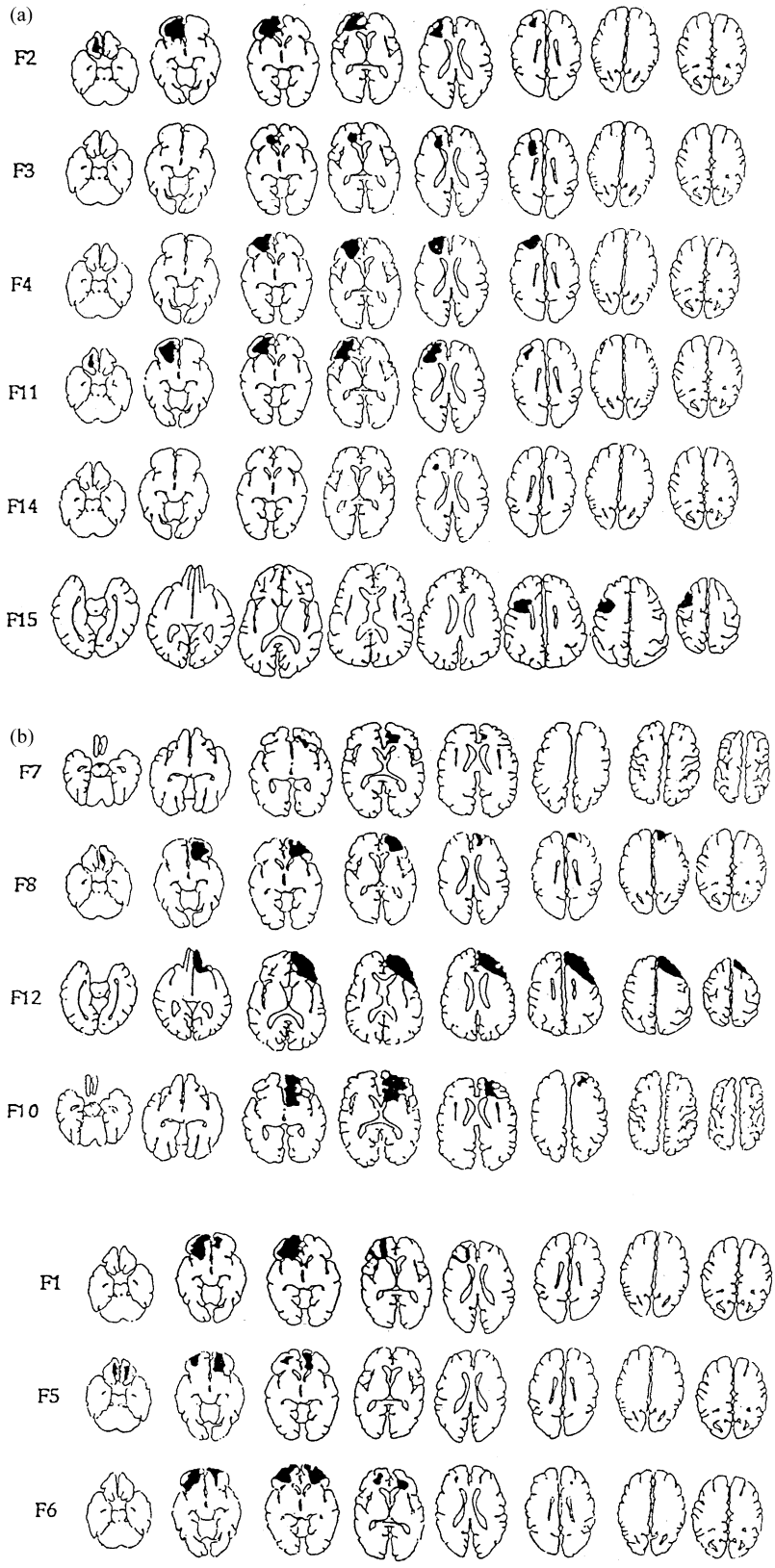

Fig. 1. Reconstruction of (a) left frontal; (b) right and bilateral frontal lesions based on CT scan and magnetic resonance scans. For each patient, the horizontal cuts, from left to right, go from most inferior to most superior.

Table 1
Identification of the lesion locations[a]

Patient	Left region														Right region													
	F01	F02	F03	F04	F05	F06	F07	F08	F09	F10	F11	F12	F13	F14	F01	F02	F03	F04	F05	F06	F07	F08	F09	F10	F11	F12	F13	F14
F1	X			X		X	X		X			X		X	X						X					X		X
F2	X			X		X	X		X		X	X		X													
F3	X			X			X		X					X													
F4	X			X			X		X			X		X													
F5	X					X	X				X	X		X	X			X		X					X	X		X
F6				X		X	X		X									X		X	X		X					X
F7															X			X		X			X			X		X
F8															X			X		X	X		X			X		X
F10															X			X		X	X	X	X					X
F11	X			X		X	X	X	X		X	X		X														
F12															X			X		X	X	X	X	X	X	X		
F14									X																			
F15							X	X		X																		

[a] Correspondence between Damasio and Damasio [22] codes and Brodmann areas is: median aspect: F01, anterior cingular gyrus [23]; F02, posterior cingular gyrus [22,30]; F03, supplementary motor area [6]; F04, prefrontal area [8–10]; F05, rolandic region [1–4]; lateral aspect: F06, frontal operculum [43,44]; F07, prefrontal region [8,9,45]; F08, premotor region [6] and rolandic region [1–4]; F09, paraventricular; F10, supraventricular area; orbital aspect: F11, anterior [10]; F12, posterior [11–13,46]; F13, basal forebrain; F14, subventricular area.

Table 2
Age and duration of education (in years) of participants[a]

Participant	Age		Education	
	Frontal	Control	Frontal	Control
F1, C1	19	19	11	12
F2, C2	54	51	9	9
F3, C3	51	52	16	17
F4, C4	40	40	16	16
F5, C5	18	18	10	10
F6, C6	19	19	11	12
F7, C7	43	41	12	12
F8, C8	21	20	15	14
F10, C10	23	24	11	12
F11, C11	38	39	16	16
F12, C12	51	50	8	8
F14, C14	21	21	9	9
F15, C15	34	33	10	12

[a] F corresponds to frontal patients and C to control participants.

provided on p. 219 of Damasio and Damasio [22] (e.g. 'BA 8, 9, 46', see Table 1).

The standard Damasio and Damasio [22] procedure for the analysis of CT and MRI was applied to our study as follows (see p. 143–7 of Damasio and Damasio [22]).

The set of best-fitting templates was first chosen on the basis of the angle of incidence in which CT or MRI scans were obtained. The lesion was then charted on the templates at every level at which it occurred. Subsequently, an appropriate "in-register" transparency containing anatomical cells representing neural "areas of interest" in both gray and white matter structures was superimposed over the template in order to establish the anatomical areas damaged.

The results of this analysis were then filled in as a hard-copy visual record (see Fig. 1a and b) and keyed in Table 1 to the codes mentioned (e.g. 'F07' or prefrontal region corresponds to 'BA 8, 9, 46').

Frontal patients were examined after a post-surgery period long enough to avoid the presence of a "mass effect" [1] often observed when patients are examined in the acute period. The mean delay between the occurrence of the lesion and the neuropsychological evaluation was of 179.8 days (range = 39–467), the mean delay between the occurrence of the lesion and the latest radiographic examination was 99.9 days (range = 1–467) and the mean delay between the radiographic examination and testing was 84.18 days (range = 1–215). Patients were not on anticonvulsant medication at the time of testing.

Frontal patients were matched to control participants on the basis of their individual age, sex, type and duration of education (see Table 2). Patients, all males, were 33.2 (S.D. = 13.75) years old and had 11.8 (S.D. = 2.9) years of education. Control participants were 32.8 (S.D. = 13.2) years old and had 12.23 (S.D. = 0.8) years of education. A one-way analysis of variance confirmed that the two groups were correctly matched in terms of age ($F(1, 12) = 1.35$; $P = 0.268$) and years of education ($F(1, 12) = 3.26$; $P = 0.1$).

All participants volunteered and gave their informed consent.

Table 3
Mattis dementia rating scale: results for each subscale[a]

	Frontal	Control
Attention	36.4 (0.9)	36.9 (0.3)
Initiation	33.2 (4.8)	36.4 (1.7)
Construction	6 (0)	6 (0)
Concepts	35.5 (5.1)	36.8 (1.9)
Memory	24 (1.5)	24.9 (0.6)

[a] Standard deviations in brackets.

The global cognitive profile was evaluated by means of the Mattis dementia rating scale (DRS) [38]. The mean overall score was significantly lower for frontal patients ($M = 135$; S.D. = 9.62) than for control participants ($M = 141$; S.D. = 2.6) ($F(1, 12) = 6.8$; $P < 0.05$). The analysis of the different subscales (Table 3) revealed significant differences in the attention ($F(1, 12) = 6.255$; $P < 0.05$) and initiation subscales ($F(1, 12) = 8.094$; $P < .05$). This profile of performance is characteristic of that generally observed in other studies examining frontal patients (e.g. [55]).

2.2. Materials, procedure and scoring

2.2.1. Computation span task

To evaluate the capacity to undertake two tasks simultaneously, we adapted the dual task method used by Salthouse and Babcock [47]. The materials comprised a series of cards on each of which was presented an arithmetic problem without the solution (see Fig. 2). The second number in each arithmetic problem was framed and the solution was replaced by a question mark. The arithmetic problems were all sums ($X + Y$) or differences ($X - Y$) between two one-digit numbers (excluding 0). The values of the digits were further restricted as follows. Y was different from the solution and different from the digit framed in the next problem. Finally, the solution of each problem was always a number between 1 and 18. The number of arithmetic problems presented on each trial increased successively from two to nine, with three trials presented for each series length. Testing discontinued when two trials were failed at a particular series length.

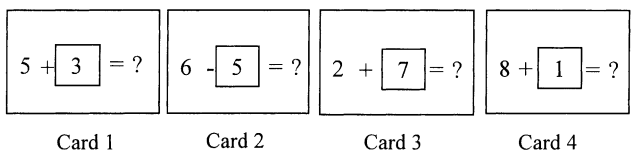

Fig. 2. Example of a series of four cards presented for the span four at the computation span task.

[1] Canavan et al. [18] found, for example, that important DS symptoms observed in brain-damaged patients examined in the acute period disappeared after the post-operative period. This indicated that the DS were the consequence of some diffuse brain damage observed in the acute period rather than the consequence of a focal frontal brain lesion.

Two conditions were compared: one in which participants were required to remember the digits framed but not to solve the problems (simple span condition), and a second in which they were required to remember the digits while solving the problems. In the simple condition, the cards were presented at the rate of 1 s and participants had to remember the framed digits in order. At the end of the series a blue "recall" card was presented and participants had to recall the series of digits. In the computation span (dual task), the cards were presented at a rate of one every 3 s and participants had to solve the arithmetic problems and give the solution aloud while remembering the framed digit from each problem. When the blue "recall" card appeared at the end of the series, participants had to recall the series of framed digits.

Two scores were considered in both the simple and dual conditions. The span was designated as the highest number of target items recalled correctly (all items recalled in original order) on at least two of the three trials for a particular sequence length. In the dual condition, recall of digits was considered only when the solution to the arithmetical problem was correct. A second score, less restrictive, was obtained by assigning one point for each digit correctly recalled and then adding the number of items correctly recalled across the experiment.

2.2.2. Directed forgetting

In order to evaluate the ability to actively inhibit no-longer relevant information in working memory, the procedure of Reed [46] was adapted. There were three experimental conditions, with the following sequence of events occurring in each trial: (a) presentation of the material to be remembered (one or two trigrams of consonants presented on cards for 2 s each, for example 'DRG'), (b) an interpolated activity (reading aloud strings of numbers for 10 s), and (c) serial recall. In the 'single-item' condition (control condition), a single trigram was presented for retention. Participants were then required to read strings of numbers aloud (interpolated activity) before recalling the trigram in its correct order. In the 'interference' condition, an additional (interfering) trigram was presented for retention immediately after the first one. Participants had to recall both trigrams at the end of the interpolated task in the order of their presentation. In the 'directed forgetting' condition, two trigrams were presented consecutively, as in the interference condition. However, immediately after the presentation of the second trigram, a card was displayed for 500 ms with the inscription 'to be forgotten', which prompted participants to forget the second trigram since they would not be required to recall it later. Participants were asked to recall the three letters of the trigrams in strict serial order after the 10 s of the interpolated activity and were allowed to take as long as they needed to respond. Three practice trials, one per condition, were presented prior to the beginning of the task. Participants were then presented with 30 trials, 10 per experimental condition, presented in the same pre-established random order for all participants.

Table 4
Mean recall (span and number of correctly recalled items) for simple and dual tasks in the computation span[a]

	Frontal	Control
Simple span	5.3 (1.4)	6.8 (2.2)
Dual span	2.9 (1.4)	4.8 (2.2)
Simple score	48.8 (23.6)	83.1 (45.6)
Dual score	15.4 (14.9)	41.1 (30.7)

[a] Standard deviations in brackets.

Participants' responses were scored following Reed's criterion [46] by assigning one point for each letter recalled (regardless of its serial position within the trigram) and an additional point when this letter was recalled in its correct serial position (maximum score in each condition was therefore 60). In the interference condition, only the first trigram was scored. Inhibitory capacity was measured by the difference in recall performance between the single-item and directed forgetting conditions (directed forgetting cost) [37]. Sensitivity to interference was measured by the difference in performance between the single-item and interference conditions.

3. Results

The results are presented for each task separately.

3.1. Computation span

The mean span and mean number of correctly recalled items are presented in Table 4.[2] A 2 (group) × 2 (type of span) ANOVA for repeated measures performed on the span measure revealed a significant main effect of group ($F(1, 11) = 5.584$; $P < 0.05$), showing that frontal patients presented lower recall performance than control participants. There was also a significant effect of the type of span ($F(1, 11) = 92.172$; $P < 0.0001$), revealing that the performance in the computation span (dual condition) was weaker than in the simple span. There was no significant interaction between these two factors ($F(1, 11) = 0.25$; $P = 0.627$). An ANOVA on the number of correctly recalled items revealed the same pattern of results. There were significant main effects of group ($F(1, 11) = 5.962$; $P < 0.05$) and type of span ($F(1, 11) = 63.502$; $P < 0.0001$), but again there was no significant interaction between these two factors ($F(1, 11) = 0.627$; $P = 0.445$).

In conclusion, patients with focal frontal lobe lesions presented impaired performance compared to control participants, but to a similar extent for the simple and computation spans.

[2] One patient (F5) and his control participant (C5) could not be administered this task.

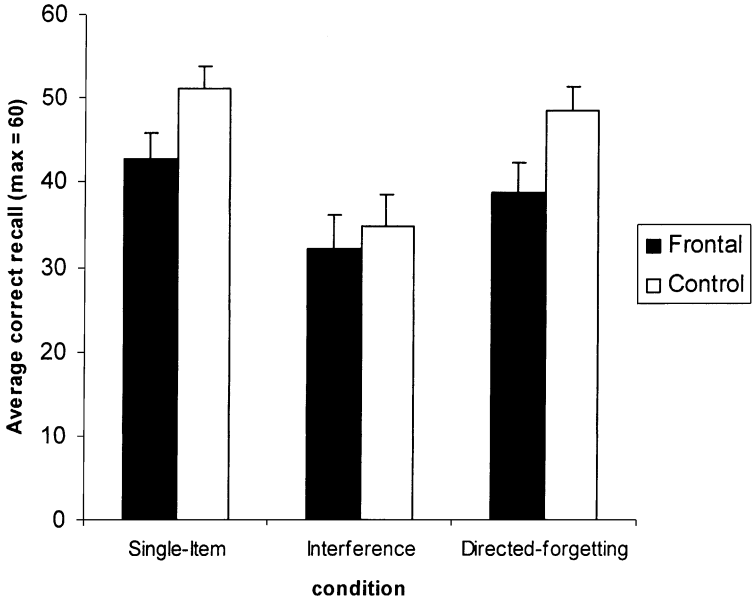

Fig. 3. Mean correct performance in the directed forgetting task by condition. Error bars illustrate standard errors.

3.2. Directed forgetting

The mean recall performance in the single-item, interference and directed forgetting conditions is shown in Fig. 3. A 2 (group) × 3 (conditions) ANOVA for repeated measures revealed a significant main effect of group ($F(1, 12) = 4.506$; $P < 0.05$) indicating that frontal patients recalled fewer items than control participants. The effect of condition was also significant ($F(2, 24) = 27.355$; $P < 0.0001$). Newman–Keuls post-hoc comparisons revealed that, for both groups, performance in the interference condition was lower than performance in both the single-item condition ($P < 0.001$), and the directed forgetting condition ($P < 0.05$). No difference was found between the single-item and directed forgetting conditions ($P > 0.05$). The interaction between group and condition was not significant ($F(2, 24) = 2.461$; $P = 0.107$). Directed forgetting cost indices (single-item minus directed forgetting) were calculated for the frontal patients (mean = 3.9; S.D. = 10.1) and the control participants (mean = 2.6; S.D. = 6.7), and revealed no difference between groups ($F(1, 12) = 0.238$; $P = 0.634$). Intrusion errors, that is, the recall of consonants of the second trigram as items of the first, were analyzed in order to obtain an additional measure of the capacity to suppress the no-longer relevant information. The mean number of intrusions was 1.46 (S.D. = 1.6) for the frontal patients and 1.6 (S.D. = 1) for the control participants in the interference condition, and 0.62 (S.D. = 1.6) for the frontal patients and 1.54 (S.D. = 2.1) for the control participants in the directed forgetting condition. Given the rarity of such errors, no statistical test could be carried out. One can note, however, that the number of intrusions was equivalent for both groups in the interference condition and that the difference in the number of intrusions in the directed forgetting condition was in favor of the frontal patients.

In sum, patients with focal frontal lesions showed an overall lower recall performance in the short-term directed forgetting task, but this deficit did not interact with condition. Thus, their efficiency in inhibiting the no-longer relevant information was as good as that of control participants (as confirmed by the equivalent directed forgetting cost indices [37]) and sensitivity to interference was equivalent for both groups.

4. Discussion

The purpose of the present study was to examine to what extent a group of patients with lesions restricted to the frontal cortex present deficits in two working memory tasks expected to implicate the CE [9]. The executive functions investigated were the capacity to perform two tasks simultaneously, evaluated by the computation span task [47] and the ability to suppress no-longer relevant information, evaluated by a directed forgetting task [46]. Special care was taken with regard to two methodological aspects: the type of lesion, which had to be restricted to the frontal cortex, and the stability of the clinical state, i.e. patients had to be examined at least 5 weeks after the occurrence of the lesion. Furthermore, the majority of our patients ($n = 11$) presented a lesion of the dorsolateral frontal lobe, hypothesized to be importantly involved in executive functions (see Table 1 for specific location of lesions in our patients).

In the computation task, the results revealed that patients with focal frontal lesions showed lower recall in both the simple and dual conditions. This result is consistent with

the studies showing that short-term storage of verbal information depends on frontal regions such as Broca's area (BA 44), the ventral cortex (BA 45) and the left premotor cortex (BA 6) [25,56]. Contrary to what is predicted by the hypothesis of a unequivocal link between frontal cortex and dual task management, the results also showed that the decrement in recall induced by dual tasking was equivalent in patients with focal frontal lesions and control participants. Thus, patients and control participants were comparable in their ability to undertake storage and processing simultaneously. This result is in agreement with those of Frisk and Milner [30] and Vilkki et al. [61]. It is also compatible with the observation by Baddeley et al. [13] (also see [3]) that only frontal patients with behavioral signs of DS present impaired performance in dual tasks since our patients did not show any clinical sign of DS (e.g. behavioral disinhibition). What is needed to explain is the paradox observed between the findings from D'Esposito et al.'s [23] neuroimaging study showing specific frontal activations (dorsolateral prefrontal cortex) during dual task management and studies such as the current one (and [30,61]) showing no deficit of dual task performance in patients with lesions of this area. In this vein, a recent neuroimaging study of working memory by Klingberg [34] shows that the prefrontal region is activated during both single working memory and dual working memory tasks. Therefore, contrary to the study by D'Esposito et al. [23], no specific prefrontal activation during the dual task was observed in this study. As Klingberg argued, it is possible that in D'Esposito et al.'s study, the prefrontal activation during the dual task was simply due to the increase in working memory demand occurring during the simultaneous performance of two non-working memory single tasks. For example, the stimulus processing or response in one task must be delayed while the other task is given priority, thus inducing a working memory requirement. It may thus be possible that performing working memory induces the activation of prefrontal areas as has been shown in several studies (e.g. [25,34,56]), but there is not yet evidence to presuppose any prefrontal areas specific to dual task performance 'per se' (see [1,15], for similar results).

The directed forgetting task administered in the current study required the maintenance of information no-longer available in the environment during an interval occupied by a secondary task. Additionally, in the directed forgetting condition participants had to actively suppress the no-longer relevant trigram that had been presented. Our data showed that although frontal patients were globally impaired in the capacity to maintain the relevant information, they could inhibit the no-longer relevant information just as well as control participants. Again, the deficit observed in recall is consistent with the numerous studies showing the implication of the frontal cortex in short-term storage of verbal information (see [25,56] for reviews). It is also consistent with the observation by D'Esposito and Postle [25] that the frontal cortex is necessary for some rehearsal processes (also see [56]). The current results do not support however, the hypothesis of the frontal cortex as the exclusive neural substrate of inhibitory mechanisms.

In conclusion, our results show that whilst patients with lesions restricted to frontal regions evaluated in a stable period present impaired short-term storage, they also show normal performance in measures of executive processes such as the capacity to undertake two tasks simultaneously and the capacity to inhibit no-longer relevant information. It could be argued that the lower recall performance observed in both conditions of the computation span might have been influenced by an executive aspect of this task. Actually, given the characteristics of the type of material, even the simple condition differs from a classical span task: participants have to select the information to be remembered (digit in the frame) and reject the irrelevant information (rest of the string). Therefore, correct recall in this task might depend on short-term storage capacity as well as on the inhibition of the concurrent irrelevant information. However, an executive deficit is not likely to account for the results observed. Indeed, it seems implausible that the low level of interference induced by the irrelevant information in the computation span (the to-be-remembered numbers were framed) led to such a pronounced difference between groups whereas the much more powerful manipulations of interference (dual compared to simple conditions in the computation span and interference and directed forgetting conditions compared to single-item in the directed forgetting task) revealed no particular group differences.

The literature provides little information about the question of the necessity of bilateral lesions to impair cognitive inhibition and dual task in working memory and the few neuroimaging studies of these functions have yielded contradictory findings. Whereas D'Esposito et al. [23] and Klingberg [34] found greater activation of the right cortex during dual task, Bunge et al. [15] found a left dominance. From four neuroimaging studies investigating the areas activated by inhibition tasks, three revealed a right hemispheric dominance [31,32,60] and one left prefrontal activation [33]. It might be possible that unilateral lesions (which were the majority in our study) would not be sufficient to impair inhibition and dual task management. In this context, studies of brain damage and stroke recovery suggest an increasing ability to recruit regions that are contralateral or adjacent to the lesioned area [42,59]. This dynamic organization of cortical functions could also apply to inhibition and dual task management. In a modest attempt to assess the effect of bilateral frontal lesions, we analyzed the individual performance of the two patients of our study with bilateral lesions of BA 9/46. We considered patients' performance 'impaired' when beyond the interval defined by the mean value of the control group $\pm$ 2 S.D. and below the lowest performance in the control group. The analysis revealed that no patient showed an increased dual task decrement or any impairment of the inhibitory measures (performance on the directed forgetting condition, directed forgetting cost or intrusion errors). This of course may not represent the entirety of patients with

bilateral frontal lesions. To tackle this question more directly, further studies should involve the comparison of patients with bilateral and unilateral frontal lesions. Large groups are needed to address these questions (bilaterality and laterality) and this type of research can only be considered in multicenter studies involving multiple research teams and hospitals. Finally, we should note that, although the hypothesis that bifrontal lesions are necessary to impair dual task and inhibition mechanisms in working memory is yet to be tested, the evidence described in the recent literature [8,19,40,41,61] suggests that the hypothesis of more distributed neural network as an alternative for the neural substrate of inhibition and dual task management deserves further investigation.

Measures were taken in the present study to minimize the potential influence of mass effects on executive functions ([18,36,61], i.e. as Vilkki et al., we intended to control for the acuteness of the injury by testing patients outside the time period following immediately the onset of the lesion). The fact that we found no deficit of dual task or inhibition in our frontal patients when tested well after a potential "mass effect" converges with the results of other studies [18,36,61] in which DS symptoms were found to disappear after some post-operative period. In this vein our results, together with those of Vilkki et al. and Canavan et al. provide additional support to the suggestion that more cerebral regions than frontal sustain executive functions.

The dissociation observed in patients with frontal lesions between short-term storage and executive processes in working memory is important for the hypotheses concerning the neural substrate of executive functions. As a whole, the current results suggest that not all executive functions are uniquely sustained by the frontal cortex. This finding provides additional support to the hypothesis that some executive functions may be sustained by a distributed cortical neural network rather than by a unique frontal region [11,12,19,32,34,40,41] (see also [6,8,24,31,32,61]). Although the frontal cortex must be involved in executive functions (see for example [8] for some executive deficits in patients with focal frontal lesions examined in a stable period), the current findings suggest that it cannot serve, on its own, as the CE of the brain. It rather must play a role in a distributed set of neural networks concerned with executive functions [24,62]. This idea is also supported in the study by Foster et al. [29] in which performance of normal elderly participants on executive tests correlated more strongly with global cerebral measures than with frontal regional measures.

We should note that it might be possible that some further recovery had happened in three of our patients who received a MRI or CT scan less than 2 months after the lesion. Strictly speaking, if this were the case, this could have contributed to some extent to the good performance on dual task and inhibition of our patients as a group. In this vein, further studies excluding this possibility would provide stronger evidence in supporting our results.

We cannot exclude the possibility that some invisible (below the threshold detection of CT or MRI scans) microscopic pathology in non-frontal sites existed in our patients with traumatic brain injury. However, it must be clarified that this possibility is irrelevant to our central argument. Indeed, our argument is that the good performance on executive tasks in working memory does not depend necessarily upon having an intact prefrontal cortex. Our results show that patients with frontal lesions are able to perform executive processes (dual task and inhibition) in working memory as well as normal participants, in spite of their reduced short-term storage. Since we are drawing attention to the intact performance of these patients on key executive processes of working memory, hypothetical extra-frontal damage is not relevant to our main argument.

A possible limitation of our study might be the small number of participants, which is a consequence of the rarity [3] of patients with lesions restricted to the frontal cortex. It might be argued that this could lead to insufficient statistical power to detect significant differences in executive measures. This is not likely to be the case for three reasons, however. First, significant differences between our patients and control participants were observed for several measures (MDRS and short-term memory capacity in both working memory tasks). Insufficient statistical power should have masked such differences. Second, if the frontal cortex is necessary and sufficient to perform executive processing, a unique lesion of that area should affect performance in tests of executive functions. Despite the fact that the majority of our patients presented lesions in BA 24, 9 and 46 (see Table 1), which are hypothesized to be particularly important for executive functions [26,56], none of them exhibited significant deficits in such tests when analyzed using a single-case approach. Third, it would be difficult to argue that the frontal cortex is the unique area responsible, for example, for the inhibitory mechanisms involved in directed forgetting when studies with similar sample sizes found deficits in a directed forgetting task with temporal patients (e.g. [28]). Altogether, it seems unlikely that a lack of statistical power is responsible for the good performance of our patients on inhibition and dual task.

As described in the introduction, Baddeley [10–12] suggests that the CE is a fractionable system with multiple independent functions. There is indeed strong neuropsychological evidence supporting this view [27,48–54]. Additionally, in a recent study [7], we have shown that performance on executive tasks (Hayling and Brixton tests) conceived in the theoretical framework of Norman and Shallice [43] do not correlate in a group of elderly and/or young participants once processing speed has been carried out. In this context, we should note that although the executive processes involved in our tasks (inhibition and coordination of storage and processing) do not seem to be impaired in patients with focal

[3] It should be noted that 4 years were needed to accumulate 13 patients for this study.

frontal lesions, other executive processes (e.g. more active manipulation of information in working memory) could be disrupted. Moreover, it remains to be solved whether those patients present a deficit of executive functions when the amount of information to be held in working memory is, contrary to the current study, close to and beyond the span of the participant.

Further research should be conducted in order to break down the CE component of working memory and investigate the neural substrate of its different executive functions. In this vein, it might be likely that some executive functions were sustained by a diffuse cortical (and subcortical) neural network and other by more localized areas.

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