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Working memory after severe traumatic brain injury

CLAIRE VALLAT-AZOUVI,[1,2,4] THOMAS WEBER,[1,3] LUDOVIC LEGRAND,[1,3]
AND PHILIPPE AZOUVI[2,3,4]

[1]Antenne UEROS-UGECAM Hôpital Raymond Poincaré, Garches, France
[2]INSERM U 731, Paris, France
[3]Service de Médecine Physique et de Réadaptation, Université de Versailles Saint Quentin;
AP-HP, Hôpital Raymond Poincaré, Garches, France
[4]Université Paris 6, Faculté de Médecine, Laboratoire de Physiologie et Physiopathologie de la Motricité, Paris

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Abstract

The aim of the present study was to assess the functioning of the different subsystems of working memory after severe traumatic brain injury (TBI). A total of 30 patients with severe chronic TBI and 28 controls received a comprehensive assessment of working memory addressing the phonological loop (forward and backward digit span; word length and phonological similarity effects), the visuospatial sketchpad (forward and backward visual spans), and the central executive (tasks requiring simultaneous storage and processing of information, dual-task processing, working memory updating). Results showed that there were only marginal group differences regarding the functioning of the two slave systems, whereas patients with severe TBI performed significantly poorer than controls on most central executive tasks, particularly on those requiring a high level of controlled processing. These results suggest that severe TBI is associated with an impairment of executive aspects of working memory. The anatomic substrate of this impairment remains to be elucidated. It might be related to a defective activation of a distributed network, including the dorsolateral prefrontal cortex. (*JINS*, 2007, *13*, 770–780.)

Keywords: Head injury, Executive functions, Attention, Divided attention, Central executive, Short-term memory

INTRODUCTION

Working memory is as a system used for both storage and manipulation of information, hence playing a central role in complex cognitive abilities, such as problem solving, planning, language, and more globally in nonroutine tasks (Baddeley, 1986). According to the Baddeley and Hitch model, working memory is assumed to be divided into three subsystems (Baddeley, 1986, 1998; Baddeley & Hitch, 1974). The central executive is an attentional control system, whereas the phonological loop and the visuospatial sketchpad are two modality-specific slave systems, responsible for storage and rehearsal of verbal and visuospatial information, respectively. The central executive functions to coordinate and schedule mental operations. It has a limited capacity and also serves as an interface between the two slave systems. The central executive is assumed to be similar to the supervisory attentional system (Norman & Shallice, 1980; Shallice & Burgess, 1996). The phonological loop is responsible for processing and maintenance of verbal information. This system comprises two components: the phonological store in which representations of verbal material are held, and a subvocal rehearsal mechanism that serves to refresh the contents of the phonological store. The visuospatial sketchpad is devoted to the processing of visual and spatial information. Although this component has received less attention, it is currently assumed to comprise two components: a "passive" visual store and an active mechanism to refresh the contents of the visuospatial store. More recently, Baddeley (2000) proposed to include a fourth component to the model, namely the episodic buffer, which is assumed to be a limited capacity system serving as an interface between working memory and long-term memory. However, the functions and the methods of investigating the episodic buffer are debated, and it cannot yet be assessed in routine clinical practice.

To our knowledge, there has been to date no systematic study of the different components of working memory in adults with chronic severe traumatic brain injury (TBI). However, several studies suggested an impairment of the

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Correspondence and reprint requests to: Philippe Azouvi, Service de Médecine Physique et de Réadaptation, Hôpital Raymond Poincaré, Garches, 92380 France. E-mail: philippe.azouvi@rcp.aphp.fr

central executive system. Early studies found that severe TBI patients performed poorly on a backward digit span task (Brooks, 1975) or on the Brown–Peterson paradigm of short-term memory with interference (Stuss et al., 1985). A few individual case-reports of TBI patients suffering from a selective impairment of the central executive have been reported (Allain et al., 2001; Van der Linden et al., 1992). Dual-task processing is usually considered as one of the key functions of the central executive. There is quite a large amount of studies in the literature that focused on dual-task performance after severe TBI. As recently suggested, it seems actually that the degree of impairment of divided attention after TBI is largely task-dependent (Leclercq & Azouvi, 2002; Park et al., 1999). Several studies found that TBI patients perform normally on divided attention tasks that can be carried out relatively automatically, although they are impaired relative to controls in more complex tasks, performed under high time-pressure, including substantial working memory load, or requiring executive control (Brouwer et al., 1989, 2001, 2002; Mangels et al., 2002; McDowell et al., 1997; Park et al., 1999; Spikman et al., 1996; Stablum et al., 1994; Veltman et al., 1996; Vilkki et al., 1996; Withaar, 2000). Similar results were found in divided attention studies performed in our department (Azouvi et al., 1996, 2004; Leclercq et al., 2000). The suggestion that deficits in divided attention after TBI are task-dependent is also in accordance with a meta-analysis carried out by Park et al. (1999), who found that the severity of the dual-task decrement varied considerably from one study to another (range, .03 to 1.28). Although slowed information processing seems sufficient to explain a divided attention deficit in simple and relatively automatic dual tasks, additional impairment emerges in more complex tasks. Other studies, using different experimental tasks, such as the *n*-back task, or the Paced Auditory Serial Addition Test also found evidence for an impairment of working memory after TBI (Bublak et al., 2000; Christodoulou et al., 2001; McAllister et al., 2004; Perlstein et al., 2004). Moreover, recent studies demonstrated working memory deficits in children with severe TBI (Chapman et al., 2005; Levin et al., 2002, 2004).

The aim of the present study was to test the assumption of an impairment of the central executive system of working memory after severe TBI. For this purpose, chronic severe TBI patients and a control group were given a wide range of tasks assessing the different subsystems of working memory.

METHODS

Participants

Thirty patients were included in this study. They all had sustained a severe TBI, as defined by a score of 8 or less on the Glasgow Coma Scale (GCS; Teasdale & Jennett, 1974) within the first 24 hours and before sedation. They had been consecutively referred for assessment and/or follow-up to a specialized postacute community reentry program. They were compared with 28 healthy controls. Patients were not included in the study in cases of severe behavioral, motor, or visual deficits that could interfere with experimental tasks. Patients and controls were free of any pre-existing neurological or psychiatric condition, including substance abuse. The main demographic and injury severity characteristics of the patient and the control groups are displayed on Table 1. The two groups did not significantly differ in terms of age. Educational level tended to be lower and sex ratio (% male) higher in the patient group, but these differences did not reach statistical significance (both $p > .05$). Brain injury was due to a high velocity impact due to motor vehicle accident in the great majority of cases ($n = 28$, 93.3%), to a fall in one case, and to an assault in one case. Injury severity data [worst Day-1 GCS score and/or post-traumatic amnesia (PTA) duration] were available in all patients but five (16.6%). The GCS score was obtained retrospectively in 19 (63.3%) cases from acute medical charts. PTA duration could be estimated in 21 cases (70%) with a questionnaire on first reliable postinjury souvenirs (McMillan et al., 1996). All these patients had a PTA duration of 7 days or more. PTA lasted 30 days or more in 14 of 21 patients (66.6%), suggesting that the majority of patients sustained an extremely severe TBI, according to the classification by Jennett and Teasdale (1981). In the five cases where neither GCS nor PTA were available, decision of inclusion in the study was based on information provided by the family indicating that these patients had prolonged coma and PTA durations, suggesting that they sustained a severe or very severe injury. Patients were in a chronic stage, at least 1 year after injury. Time since injury ranged from 14 to 202 months, and the median was 32 months. The global level of disability at the time of the study was assessed with the Glasgow Outcome Scale (GOS; Jennett & Bond, 1975). The majority ($n = 18$, 60.0%) were classified in the Moderate Disability category, eight patients (26.6%) were in the Severe Disability and only four (13.3%) in the Good Recovery category. Acute neuroimaging data were available in 22 (73.3%) patients. The majority showed signs of diffuse injury, either isolated ($n = 9$), or in combination with various types of focal lesions ($n = 4$). Focal lesions, when present, pre-

Table 1. Demographic and injury severity characteristics of the TBI and the control groups

	TBI ($n = 30$)	Controls ($n = 28$)
Sex ratio (n (%) male)	23 (76.6%)	14 (50.0%)
Age (years)	29.0 (6.9)	30.7 (8.0)
Years of education	11.7 (2.3)	12.1 (2.9)
Time since injury (months)	51.5 (43.6)	
GCS ($n = 19$)	5.2 (1.7)	
PTA duration (days) ($n = 21$)	65.5 (58.2)	

Note. Data on injury severity were not available for all patients. Data are mean (*SD*). TBI = traumatic brain injury.

dominated, as expected, in the prefrontal areas ($n = 7$). Subjects were informed of the experimental aim of the study and gave their consent to participate. Data included in this article were obtained in compliance with the Helsinki Declaration.

Tasks

The tasks used in this study were designed to address the different subsystems of working memory. Subjects performed the tasks in the same order.

Digit spans

Both forward and backward digit spans were assessed. Five trials were given for each span length, starting with two digits, with a maximal length of nine digits. Digits were presented at the rate of one per second. The numbers were read aloud by the examiner. The test ended when the subject failed the five consecutive trials for a given length. The measures were the percentage of correct responses out of five trials for each span length, and the best span length successfully achieved on at least one trial.

Phonological loop

The *phonological store* was tested using the phonological similarity effect (Baddeley, 1986). This effect is defined as a poorer performance for short-term recall of phonologically similar letters (such as t, p, b, v), as compared with phonologically dissimilar letters (such as r, m, l, s). Consonant letters were read aloud by the examiner at a 1-s rate, starting with two letters, the maximum length being six for phonologically similar letters and eight for phonologically dissimilar letters. The *subvocal rehearsal process* was assessed using the word-length effect, with short (mono- and bisyllabic) and long (quadrisyllabic) words. The word-length effect is defined as a higher span for short words (Baddeley, 1986), due to the subvocal rehearsal process. Words were read aloud by the examiner at a 1-s rate, starting with two words, the maximum length being six for long words and eight for short words. Word frequency usage was controlled and was similar for short and long words. Subjects were asked to recall the items exactly in the same order. The scores, both for letters and words, were the percentage of correct responses out of four trials at each span length, and the best span length successfully achieved on at least one trial.

Visuospatial sketchpad: Visuospatial spans

Forward and backward visuospatial spans were assessed using a procedure similar to the Corsi Block-tapping test (Lezak, 1995). It consisted of nine white 2-cm cubes fastened in a random order to a blackboard. The examiner taped the blocks in a prearranged sequence at a 1-s rate, then the subjects attempted to copy this tapping pattern, in the same or in the reverse order. Like for digit spans, five trials were given for each span length, starting with two items, with a maximal length of nine items. The test ended when the subject failed the five consecutive trials for a given length. The measures were the percentage of correct responses out of five trials for each span length, and the best span length successfully achieved on at least one trial.

Central executive system

Given the complex and heterogeneous nature of the central executive (Baddeley, 2002), different tasks were designed to address three of its main different functions, namely: the ability to deal with the simultaneous storage and processing of information in working memory; dual-task processing; working memory updating.

Storage and processing of information

One of the key functions of the central executive is to deal with situations requiring both storage and processing of information in working memory. Four experimental tasks were used to address this ability. All these tasks required subjects to store information in a short-term store to be able to recall it after a short delay, and simultaneously to carry out some other cognitive task. Two tasks used a paradigm of short-term memory with interference, both in the verbal and in the visual modality (Brown–Peterson paradigm; Brown, 1958; Peterson & Peterson, 1959). The two other tasks were an arithmetic span and a reading span, both combining storage (of digits or of words) and processing (mental calculation in the former, reading in the latter).

Brown–Peterson paradigm, verbal modality. Subjects were asked to recall consonant trigrams after 3 delays (5, 10, or 20 s) with or without an interfering task. The interfering tasks served as a distractor, preventing subvocal rehearsal of material. Consonants were read aloud by the examiner at a 1-s rate. Three interfering tasks of increasing complexity were used, in the following order, after the no-distractor condition. The more elementary was a sensorimotor task in which the subject was asked to touch on the subject's own hand a finger at the same place and immediately after it has been touched by the examiner. The second interfering task was articulatory suppression, the subject being asked to repeat sounds such as "ba" at approximately a 1-s rate. The last, more demanding distractor was mental calculation, consisting of simple additions or subtractions that were read aloud by the examiner. Five trigrams were given for each delay and for each condition, and the score was the percentage of correct responses.

Brown–Peterson paradigm, visual modality. The Corsi board was used again. At each trial, the examiner tapped two blocks in a predetermined order. Subjects were required to repeat the same sequence after three delays (5, 10, or 20 s), first without distractor, then with an interfering task. The interfering task was designed to tap visuospatial functions: subjects were asked to reproduce manual postures made by the examiner.

Arithmetic span. Sequences of simple arithmetic calculations (either additions or subtractions) were read aloud by the examiner. Subjects had to solve each operation and, at the end of a given sequence, they were required to recall in the correct order the second number of each operation. There were two trials at each sequence length (range, 2–5). The measures were the percentage of correct responses out of two trials for each span length, and the best sequence length successfully achieved on at least one trial.

Reading span. Subjects were asked to read aloud series of two to eight sentences, and to recall afterward the last word of each sentence (Daneman & Carpenter, 1980). Three trials were given at each span length (range, 2–5). The measures were the percentage of correct responses out of three trials for each span length, and the best span length successfully achieved on at least one trial.

Dual-task processing

The procedure was similar to that proposed by Baddeley and colleagues (Baddeley et al., 1997; Greene et al., 1995). Subjects combined crossing out a chain of boxes with repeating span-length sequences of random digits read out by the examiner. As a first step, each subject's forward digit span was determined, by presenting three sequences of digits at each length. The highest level at which performance was perfect was selected and then used during a 2-min session during which each subject's recall was immediately followed by the presentation of another sequence at that length. Performance was measured as the percentage correct in 2-min. The box-crossing task consisted of a total of 160 1-cm^2 boxes joined with lines and arranged along a winding path, printed on an A4 sheet of paper. Then, subjects were asked to perform both tasks concurrently.

Updating working memory

A running span paradigm was used (Morris & Jones, 1990). Subjects were asked to recall the n last digits of a list of n, $n+2$, $n+4$ or $n+6$ digits read aloud by the examiner at a 1-s rate. Subjects were not informed of the length of each list before presentation, and the lists (five for each length) were presented in a pseudorandom order. The number of items to recall (n) was adapted individually, and corresponded for each subject to the last level successfully achieved for backward digit span. This task required the ability to update working memory, that is, modifying the current status of representation of schema in memory to accommodate new input. The measures were the percentage of correct responses out of five trials for each span length. In addition, an updating span was computed, defined as the best number of updates successfully achieved on at least one trial (i.e., if a subject was able to recall the last n digits of a list of $n+4$ digits, but failed with n+6 digits, the subject's updating span was set at 4).

Data Analysis

Performance, as defined as the percentage of correct responses under each experimental condition has been analyzed using repeated-measures analyses of variance (ANOVA). To minimize type I error on multiple comparisons, the p level was arbitrarily set at .01. In addition, effect-sizes (*mean* and 95% confidence interval) of the main experimental findings have been computed by using the following formula: mean performance of the control group minus mean performance of the TBI group divided by the total standard deviation.

RESULTS

Digit Spans

Repeated-measures ANOVAs were used. The percentage of correct responses for each span length was the dependent variable, and there was one between-subject factor (patients *vs*. controls) and two within-subject factors (task: forward *vs*. backward; span length: 2–8). The main effect of group was not significant [$F(1.56) = 4.01$; $p = .05$], although there was a trend for a slightly poorer performance in the patient group, for both forward and backward digit span (Figure 1). As shown on Table 2, effect-sizes of the effect of TBI on forward and digit spans were small (.23 and .29, respectively). The two other main effects (span length and task condition) were significant, as expected (both p's $<$ .0001), due to a poorer performance for longer span length and for backward span. Group × span length and group × task interactions were not significant ($p > .1$).

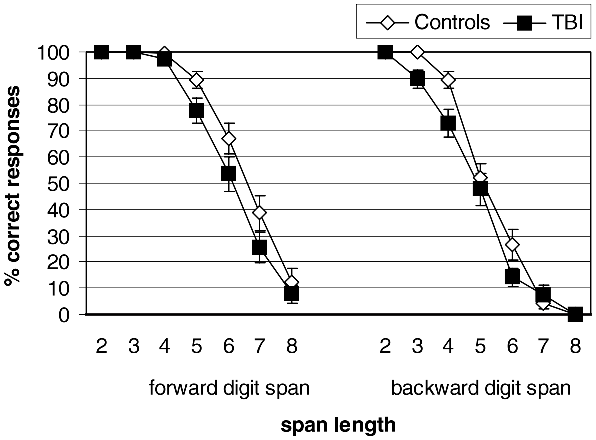

Fig. 1. Digit span. Mean (± 1 *SE*) percentage correct responses at each span length.

Table 2. Verbal short-term memory: digit span and phonological loop

	TBI (n = 30)		Controls (n = 28)		Effect-size	
	M	*SD*	*M*	*SD*	*M*	95% CI
Digit span (f)	6.37	1.13	6.61	.99	.23	−.05/.50
Digit span (b)	5.00	1.02	5.29	.94	.29	.04/.54
Letter span (sim)	4.90	1.35	5.68	.67	.69	.39/.98
Letter span (dissim)	5.53	1.72	6.39	.96	.59	.22/.97
Word span (short)	5.10	1.40	5.79	.74	.59	.28/.89
Word span (long)	3.70	.95	4.00	.61	.37	.16/.58

Note. The table shows the performance of the traumatic brain injury (TBI) and the control group (*mean* and *SD*) and the effect-size and the 95% confidence interval (CI) of between-group differences. Performance for span measures refers to the best span length successfully achieved on at least one trial. f = forward; b = backward; sim = phonologically similar; dissim = phonologically dissimilar.

Phonological Loop

Phonological store

A repeated-measures ANOVA was conducted on the letter span task, with the percentage of correct responses for each span length as dependent variable, one between-subject factor (group), and two within-subject factors (phonological similarity: similar *vs*. dissimilar; span length: 2–6). The main effect of group was significant [$F(1,56) = 18.06$; $p < .0001$], due to a poorer performance in the patient group. The main effect of phonological similarity was significant [$F(1,56) = 7.45$; $p < .01$], due to a poorer performance for similar letters, as expected. The interaction of interest here was the group × phonological similarity interaction, which was not significant [$F(1,56) = .81$; $p > .1$], suggesting that the phonological similarity effect did not differ in both groups (Figure 2). These results were supported by estimates of effect-sizes (Table 2), showing that the effect of TBI on letter span was of comparable moderate amplitude for similar and dissimilar letters (.69 and .59, respectively).

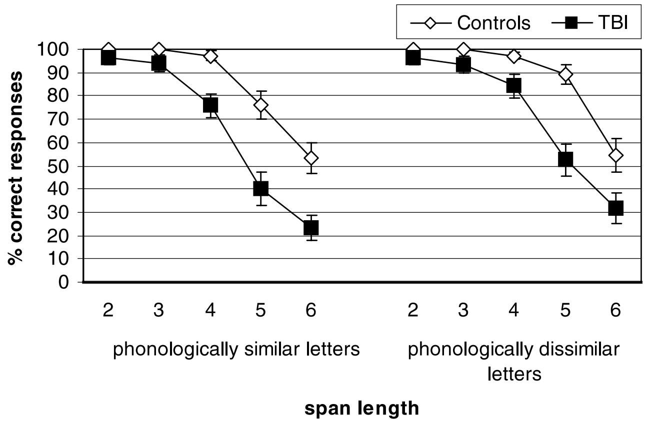

Fig. 2. Letter span. Mean (± 1 *SE*) percentage correct responses at each span length.

Subvocal rehearsal process

A repeated-measures ANOVA was conducted on the word span task, with the percentage of correct responses for each span length as dependent variable, one between-subject factor (group), and two within-subject factors (word length; span length: 2–6). The main effect of group was significant [$F(1,56) = 7.60$; $p < .01$], due to a poorer performance in the patient group. The main effect of word length was significant also, due to a poorer performance for long words, as expected [$F(1,56) = 368.5$; $p < .0001$]. The interactions of interest here were the group × word length interaction that was statistically significant [$F(1,56) = 8.9$; $p < .01$], and the triple group × word length × span length interaction that did not reach significance [$F(4,224) = 3.30$; $p = .012$]. The significant group × word length interaction was due to a relatively poorer performance in the patient group, as compared with controls, for short words, whereas the two groups did not differ for long words span (Figure 3). To further investigate this interaction, a word length effect was computed, as the ratio between performance for short and long words. The word length effect was significantly higher in the control than in the patient group [mean scores respectively: 1.8, $SD = .7$; 1.4, $SD = .7$; $F(1,56) = 4.03$; $p < .05$]. These results were supported by estimates of effect-sizes (Table 2), showing that the effect of TBI was higher on short-word as compared with long-word span (.59 and .37, respectively).

Visuospatial Sketchpad: Visuospatial Spans

A repeated-measures ANOVA was used. The percentage of correct responses for each span length was the dependent variable, with one between-subject factor (patients *vs*. controls) and two within-subject factors (task: forward *vs*. backward; span length: 2–7). There was no significant main effect of group [$F(1,56) = 1.14$; $p > .1$], indicating a normal performance in the TBI group. This negative result was

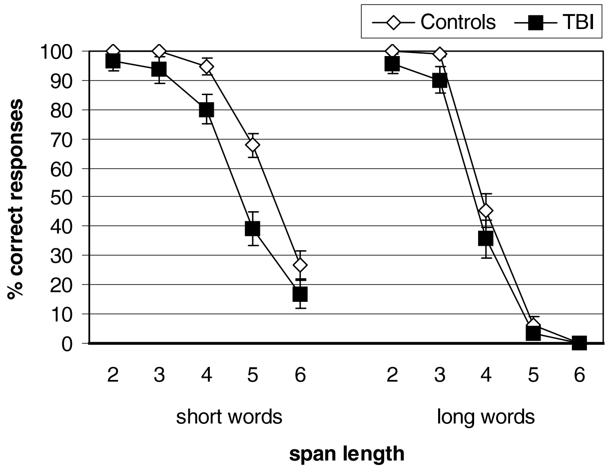

Fig. 3. Word span. Mean (± 1 *SE*) percentage correct responses at each span length.

Table 3. Visuospatial sketchpad

	TBI ($n = 30$)		Controls ($n = 28$)		Effect-size	
	M	*SD*	*M*	*SD*	*M*	95% CI
Visuospatial span (f)	5.97	.81	5.86	.71	−.14	−.34/.05
Visuospatial span (b)	5.37	.96	5.29	.71	−.10	−.31/.12

Note. The table shows the performance of the traumatic brain injury (TBI) and the control group (*mean* and *SD*) and the effect-size and the 95% confidence interval (CI) of between-group differences. Performance refers to the best span length successfully achieved on at least one trial. f = forward; b = backward.

further supported by measures of effect-sizes, shown on Table 3, that were close to 0, both for forward and backward spans (−.14 and −.10, respectively).

Central executive system

Storage and processing of information

Brown–Peterson paradigm, verbal modality. A repeated-measures ANOVA was used, with the percentage of correct responses as dependent variable, one between-subject factor (group), and two within-subject factors (interfering task: no interference, motor task, articulatory suppression, mental calculation; recall delay: 5, 10, 20 s). A significant main effect of group was found, due to a poorer performance in the patient group [$F(1,56) = 30.67$; $p < .0001$]. The two other main effects were also significant, as expected [interfering task: $F(3,168) = 98.92$, $p < .0001$; recall delay: $F(2,112) = 17.08$, $p < .0001$]. The interactions of interest here were the group × interfering task that was significant [$F(3,168) = 25.66$; $p < .0001$] and the triple group × interfering task × recall delay interactions, which did not reach statistical significance [$F(6,336) = 2.48$; $p = .02$]. These results were due to a disproportionately poorer performance in the patient group as compared with controls for the more demanding conditions (Figure 4). This effect was supported by measures of effect-sizes showing that TBI had large-sized effects on performance under demanding conditions (articulatory suppression: 1.14; mental calculation: 1.23), whereas there were only medium-sized effects under easiest conditions (.43 and .59; Table 4).

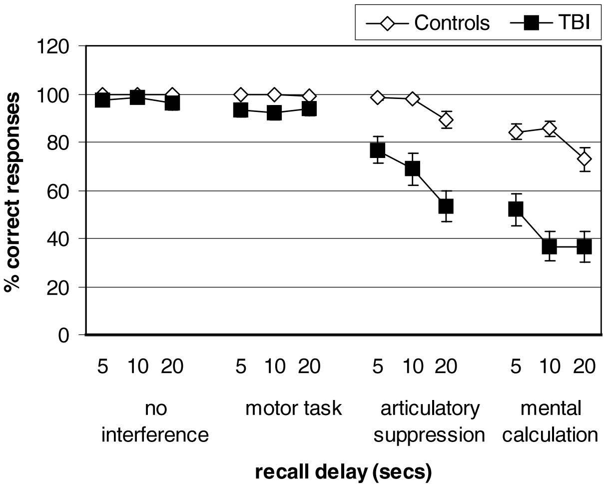

Fig. 4. Brown–Peterson task, verbal modality. Mean (± 1 *SE*) percentage correct responses for the three recall delays (5, 10, 20 s) for each experimental condition.

Brown–Peterson paradigm, visual modality. The same design as with the verbal Brown–Peterson task was used

Table 4. Central executive system

	TBI ($n = 30$)		Controls ($n = 28$)		Effect-size	
	M	*SD*	*M*	*SD*	*M*	95% CI
BP (verbal) no interference	97.33	8.51	100.00	.00	.43	−1.17/2.03
BP (verbal) motor task	93.11	15.01	99.76	1.26	.59	−2.30/3.49
BP (verbal) articulatory	66.22	28.50	95.24	5.98	1.14	−5.39/7.67
BP (verbal) calculation	41.78	32.66	80.95	13.42	1.23	−6.98/9.44
BP (visual) no interference	96.67	18.26	100.00	.00	.25	−3.13/3.63
BP (visual) with interference	75.18	22.41	96.73	3.65	1.11	−3.91/6.12
Arithmetic span	2.25	1.25	2.76	1.01	.45	.11/.78
Reading span	3.07	.91	4.00	1.19	.82	.52/1.11
Dual-task (mu)	93.20	23.51	91.26	14.60	−.10	−5.16/4.96
Updating	1.53	2.15	3.79	1.57	1.03	.46/1.59

Note. The table shows the performance of the traumatic brain injury (TBI) and the control group (*mean* and *SD*) and the effect-size and the 95% confidence interval (CI) of between-group differences. For the Brown–Peterson (BP) tasks, performance refers to the mean percentage of correct responses across the three delay intervals under each condition. For arithmetic and reading spans, performance refers to the best span length successfully achieved on at least one trial; for dual-task, performance refers to the combined *mu* score (see text); for updating task, performance refers to the best number of updates successfully achieved on at least one trial.

for statistical analysis. Main effects and double and triple interactions were all statistically significant [main effect of group: $F(1,55) = 12.91, p < .001$; interfering task: $F(1,55) = 52.32$, $p < .0001$; recall delay: $F(3,165) = 29.11$, $p < .0001$; group × interfering task: $F(1,55) = 28.59, p < .0001$; group × interfering task × delay: $F(3,165) = 15.17$, $p < .0001$]. These results were due to a disproportionately poorer performance in the patient group in the interfering task condition, particularly for the longer recall delay (Figure 5). Accordingly, a large-sized effect was found under interference (1.11) as opposed to a small-sized effect without interference (.25; Table 4).

Arithmetic span. This task proved to be very difficult, both for patients and controls, with a floor effect starting at span length 3 (more than 50% of subjects obtained a score of 0). So, only the easiest condition (span length = 2) has been analyzed, using nonparametric tests due to the distribution of scores. Patients performed significantly poorer than controls (mean scores respectively: 70.0, $SD = 37.7$; 96.0, $SD = 13.8$; Mann–Whitney test: $U = 154.5$, tied $p < .01$). Measures of effect-size showed a medium-size effect (.45; Table 4).

Reading span. A repeated-measures ANOVA was conducted, with the percentage of correct responses for each span length as dependent variable, one between-subject factor (group), and one within-subject factors (number of sentences: 2–5). There was a significant main effect of group [$F(1,56) = 20.4$; $p < .0001$], a significant main effect of number of sentences [$F(3,168) = 297.0$; $p < .0001$], and a significant group × number of sentences interaction [$F(3,168) = 7.9$; $p < .0001$]. Patients' performance was similar to that of controls under the easiest condition (two sentences), but significantly dropped for longer span lengths (Figure 6). The effect of TBI on the reading span was relatively large (effect-size: .82; Table 4).

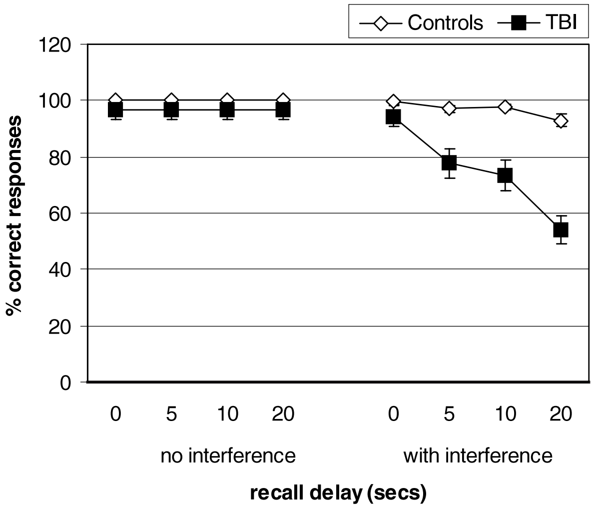

Fig. 5. Brown–Peterson task, visual modality. Mean (± 1 *SE*) percentage correct responses for the four recall delays (0, 5, 10, and 20 s) without and with interfering task.

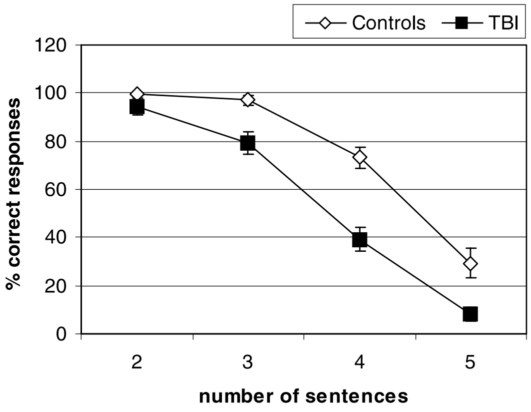

Fig. 6. Reading span. Mean (± 1 *SE*) percentage correct responses as a function of the number of sentences presented.

Dual task processing

As a first step, performance on each one of the two tasks was assessed separately. The number of boxes crossed out is shown on Figure 7 (upper part). Analysis indicated a significant main effect of group [$F(1,55) = 26.5$; $p < .0001$] and of condition [$F(1,55) = 310.8$; $p < .0001$], but the

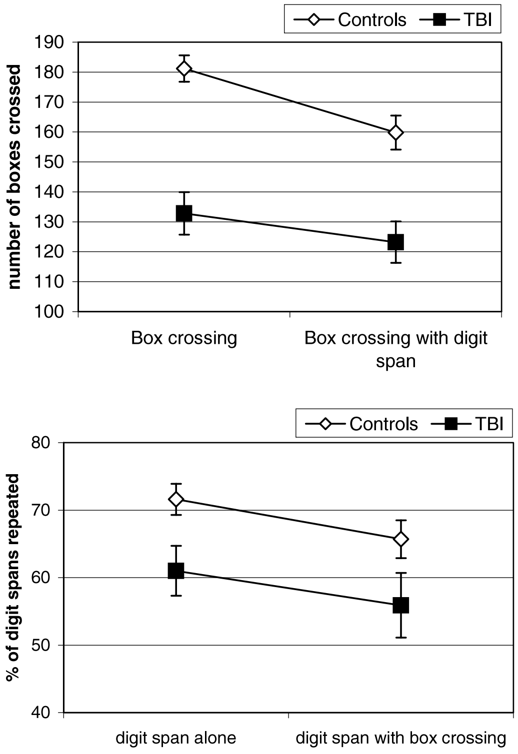

Fig. 7. Dual-task performance. Upper part: mean (± 1 *SE*) number of boxes crossed out; lower part: mean (± 1 *SE*) percentage of digit spans repeated.

interaction was not significant [$F(1,54) = 4.6$; $p = .04$]. Indeed, contrary to expectations, visual inspection of data (cf. Figure 7, upper part) showed that there was actually a trend for a greater dual-task decrement of performance in the control group (who nevertheless performed better than patients under both conditions). The number of digit-span sequences attempted with and without box-crossing is shown on Figure 7 (lower part). There was no significant main effect of group [$F(1,54) = 5.4$; $p = .02$], nor of condition [single *vs*. dual task, $F(1,54) = 4.3$, $p = .04$], nor any significant group × condition interaction [$F(1,54) = .2$; $p > .1$]. In addition, as suggested by Baddeley and colleagues (1997, 2001), a combined score was computed to assess the dual-task decrement across the two tasks. The combined *mu* score was defined as follows: $mu = [1 - (pm + pt)/2] \times 100$, where *pm* is the proportional loss of memory (digit span) performance under the dual-task condition, and *pt* the proportional loss in tracking score. A score of 100 indicates no decrement, whereas a score of <100 suggests impaired performance as a result of combining the two tasks. The *mu* score was not significantly different in the patient ($mean = 93.2$; $SD = 23.5$) and in the control group [$mean = 91.3$; $SD = 14.6$; $F(1,54) = .12$; $p > .1$; Table 4].

Updating working memory

This task proved to be quite difficult for patients. Surprisingly, at the *n*-level, corresponding to the individually adjusted digit span length, thus requiring no updating, only 13 (43.3%) patients obtained an optimal performance (80% or more correct responses), as compared with 25 (90%) control subjects. With longer series, requiring working memory updating, performance decreased dramatically in the patient group. Under the $n+2$ level, 18 patients (60%) *versus* 5 controls (17.8%) obtained a null performance (0% correct responses), and under the $n+4$ level, 25 patients (83.3%) *versus* 10 controls (35.7%) also obtained a null performance. Consequently, only the *n* and $n+2$ levels were subjected to statistical analysis, using nonparametric methods (Mann–Whitney test) due to the distribution of performance. The differences between groups was statistically significant under both conditions (*n*-level: $U = 168.5$, tied $p < .0001$; $n+2$ level: $U = 177.0$, tied $p < .0001$). As indicated on Table 4, the mean updating span was 1.5 in the TBI group, whereas it was 3.8 for controls, with a large effect-size (1.03).

DISCUSSION

The objective of the present study was to assess the different components of working memory in patients with a severe chronic (> 1 year) TBI. The tasks were designed to tap, as selectively as possible, the main functions of working memory, according to the model proposed by Baddeley and colleagues (Baddeley, 1986, 1998; Baddeley & Hitch, 1974).

Regarding the two slave systems, after correction for multiple comparisons, patients did not show any statistically significant deficit for digit and visuospatial spans (neither forward nor backward). Effect-sizes of TBI were small (.23–.29) for digit spans and close to 0 for visual spans. However, it should be underlined that even though behavioral performance was essentially the same between groups, the mental effort required by the tasks and, hence, the cerebral substrate, might differ. For example, McAllister et al. (1999) found that mild TBI patients performed on an *n*-back task at the same level as controls while demonstrating different patterns of activation on functional magnetic resonance imaging (fMRI).

The functioning of the phonological loop was tested with the phonological similarity effect and was not significantly impaired in the patient group. The subvocal rehearsal process was assessed using the word length effect and was significantly lower in patients with TBI. These results may suggest an impairment of the subvocal rehearsal process in patients with severe TBI. However, recent data suggest that the word length effect, like the phonological similarity effect, may also depend, at least in part, on strategies used by the subject and, hence, on the central executive system (Logie et al., 1996).

The main group differences were found with central executive tasks. Three main functions of the central executive were addressed in the present study: the ability to simultaneously store and process information (either verbal or visual), dual-task processing, and working memory updating. The Brown–Peterson paradigm requires subjects to hold information in a short-term store while in the same time completing more or less demanding interfering tasks. Results showed a dramatic decrease of performance of patients with TBI under interference, both in the verbal and the visual modality. In addition, patients also performed significantly poorer than controls in arithmetic span and reading span tasks, which both also require the ability to simultaneously store and process information.

By contrast, the lack of any significant impairment in the span plus box-crossing dual-task may seem surprising. This task had previously been found sensitive to central executive dysfunctions in patients with Alzheimer's disease (Baddeley et al., 2001). This was the only central executive task correctly performed by patients with TBI in the present study. As discussed earlier (see Introduction section), previous literature on dual-task processing after severe TBI suggests that TBI patients' ability to perform two tasks simultaneously depends on the executive demand (or working memory load) of the tasks at hand (Park et al., 1999). For example, in a previous study, severe TBI patients were asked to perform simultaneously random generation and a card sorting test of different complexity levels (Azouvi et al., 1996). Results showed that the dual-task decrement of performance increased with the complexity of the card sorting task. A meta-analysis showed that TBI patients are impaired on divided attention when the tasks require controlled processing, but not when the tasks can be carried out relatively automatically (Park et al., 1999). It could be assumed that the dual-task that was used in the present study did not put a sufficient load on executive control. Indeed, the task was performed without time pressure, and the box-crossing subtask is a relatively simple visuomotor task, that can be processed relatively automatically. These different data are consistent with the view that the performance of patients with severe TBI is task-dependent. In addition, it should be noted that the dual-task decrement surprisingly tended to be higher in the control group. Such paradoxically high performance by patients with severe TBI on executive tasks performed without time-pressure had been occasionally reported in previous research (Ponsford & Kinsella, 1992). This effect might be related to coping mechanisms, associated with a higher level of motivation or mental effort in the patient group.

The last central executive task used in the present study was working memory updating. The ability to update information in working memory has been found to be an independent function of the central executive (Miyake et al., 2000). Subjects were asked to recall the *n* last digits of a list without being informed of the length of each list before presentation. Patients performed poorly on that task, with a large effect-size (1.03). However, surprisingly, patients' performance appeared to be significantly impaired even under the easiest, *n*-level condition, which actually required no updating. This finding suggests that the expectation of a possible updating was sufficient to produce a significant interference for patients with TBI.

In summary, patients with a chronic severe TBI performed poorly on a wide range of tasks assessing the different components of working memory, mainly on central executive tasks requiring a high level of controlled processing. Effect-sizes for central executive tasks ranged from −.10 for a task with minimal load (span plus box-crossing), to 1.23 for the more demanding condition of short-term memory with interference (Brown–Peterson). These data are in accordance with previous studies, using different experimental tasks, showing that TBI patients performed poorly on dual-tasks with high executive demands (Azouvi et al., 2004), on the Brown–Peterson paradigm (Stuss et al., 1985), or on *n*-back tasks (Perlstein et al., 2004). Whether these impairments reflect specific or generalized deficits remains a matter of debate. Specific impairments of distinct subcomponents of working memory, such as the subvocal rehearsal process and some, but not all, functions of the central executive, seem rather unlikely. Patients' performance seems to be more plausibly explained in terms of a generalized nonspecific impairment of higher-level, executive aspects of working memory. This impairment could be related to a reduction of available resources within the central executive of working memory, which would limit patients' ability to deal with complex, resource-demanding tasks.

A few limitations should be acknowledged. The first one is related to the selection criteria. Patients were attendees in a community reentry program. In this regard, it is not surprising that the majority (60%) fell in the Moderate Disability category, according to the GOS (Jennett & Bond, 1975). Indeed, patients in the Good Recovery and in the Severe Disability categories are less likely to be referred to such programs. Whether the present findings apply to patients with less severe injury or at the opposite with very severe residual disability remains to be investigated. The second limitation comes from the variability of time since injury. However, most patients were examined between 1 and 4 years after injury. This timing is representative of patients referred to a community reentry program. The third limitation comes from the recruitment strategy of control subjects, that, for practical reasons, only included healthy, uninjured subjects. This strategy raises the question of the intervention of confounding factors, such as risk factors predisposing to injury, or nonspecific posttraumatic stress disorder. However, whereas such factors may be a major source of bias in studies on mild TBI, it can be assumed that they have a more limited impact in studies of patients with severe and very severe TBI.

The anatomic substrate of working memory impairment after TBI remains to be elucidated. Unfortunately, only limited brain imaging data were available in the present study, which did not permit any reliable clinical–anatomic correlations. Available evidence from previous functional neuroimaging studies suggests that working memory circuitry mainly involves the bilateral prefrontal cortex for storage and executive components, and the bilateral parietal and cingulate cortex for attentional functions (Collette & van der Linden, 2002). As recently suggested (McAllister et al., 2004), these regions that are critical for working memory are particularly vulnerable to the effects of TBI. A few recent studies found altered activation in a distributed network of working-memory–related brain regions after TBI, including the dorsolateral prefrontal cortex. A positron emission tomography study (Fontaine et al., 1999) found that cognitive and behavioral impairments of severe TBI patients were related to a hypoactivity in the dorsolateral prefrontal cortex and in the cingulate gyrus. A defective activation of the dorsolateral prefrontal cortex was also found in an fMRI study of severe TBI patients during performance of a planning task, the Tower of London (Cazalis et al., 2006). A recent study used fMRI to assess brain activation during a modified version of the Paced Auditory Serial Addition Test in nine patients (Christodoulou et al., 2001). Results showed that patients with TBI made more errors than controls and that they displayed a pattern of cerebral activation that was more regionally dispersed and more lateralized to the right hemisphere. In two fMRI studies of patients with mild TBI at an acute stage, a modification of the pattern of activation of frontoparietal areas was found during a working memory task (*n*-back; although patients did not differ from controls in terms of performance; McAllister et al., 1999, 2001). A visual *n*-back task was also used in a very recent behavioral and fMRI study (Perlstein et al., 2004). These authors found that patients with moderate and severe TBI performed poorer than controls or patients with mild TBI, but only at higher working memory load levels (two-back and three-back conditions). The fMRI results showed that moderate-to-severe

TBI patients had an altered load-related activity in a distributed network, including the dorsolateral prefrontal cortex and Broca's area (Perlstein et al., 2004).

In conclusion, the present study extends findings from previous studies suggesting that severe TBI is associated with an impairment of executive aspects of working memory. Specific tasks were used to assess in a systematic way the different components of Baddeley's (1986) working memory model. The results support the assumption that central executive tasks are most sensitive to the effect of TBI. Patients' pattern of performance seems to be better explained by a nonspecific reduction of processing resources within working memory. Such deficits may have a clinically significant impact on community and vocational reintegration of individuals with severe TBI. However, there has been to date only little research on rehabilitation of working memory after TBI or other neurological conditions such as stroke or children with attention deficit hyperactivity disorder (Cicerone, 2002; Klingberg et al., 2005; Vallat et al., 2005). The results of the present study should encourage the realization of controlled trials of rehabilitation of the central executive of working memory after severe TBI.

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