Journal of the International Neuropsychological Society (2006), **12**, 510–518.

DOI: 10.1017/S1355617706060668

Differential disruptions of working memory components in schizophrenia in an object–location binding task using the suppression paradigm

PIERRE SALAMÉ, FRANCK BURGLEN, AND JEAN-MARIE DANION
INSERM, Département de Psychiatrie, Hôpitaux Universitaires, Strasbourg Cedex, France

(RECEIVED January 14, 2005; FINAL REVISION March 10, 2006; ACCEPTED March 13, 2006)

Abstract

Patients with schizophrenia exhibit normal memory for separate objects or locations but are disproportionately impaired when the items must be bound for later recognition in a working memory (WM) setting (Burglen et al., 2004). This study aimed at further evaluating the contribution of each WM component to the patients' binding deficit, using selective articulatory, visuospatial, and executive suppression tasks. In the object–location binding task used, a trial comprised the successive presentation of three drawings of familiar objects and of three spatial locations in a grid, either separately (i.e., objects alone or locations alone) or bound (i.e., object+location), and required a recognition test following an 8-s delay. In the suppression modalities, suppression was continuous from presentation to test. A total of 22 patients with schizophrenia and 24 healthy controls participated. The results confirmed the binding deficit in patients' performance in the baseline modality where no suppression was required. They also showed that patients were particularly disrupted when suppression was visuospatial. This last finding extends the specific visuospatial vulnerability in schizophrenia to the operations of binding. (*JINS*, 2006, *12*, 510–518.)

Keywords: On-line processing, Articulatory, Visuospatial, Executive, Interference, Episode

INTRODUCTION

Working memory (WM) is a constellation comprising two slave systems that are specialized in handling the processes of temporary storage and on-line maintenance of verbal (articulatory loop) and visuospatial (visuospatial sketchpad) material and that operate under the control of the central executive acting as a general attentional system (Baddeley, 1986). It is also accepted now that, whereas the functioning of the articulatory loop is relatively preserved in patients with schizophrenia (Clare et al., 1993; McKenna et al., 1990; Salamé et al., 1998; Tamlyn et al., 1992), there have been reports of pronounced cognitive impairments extending to the visuospatial and certain aspects of the executive components of WM (reviewed in Keefe, 2000), and it has been suggested that the visuospatial deficit may be an effective endophenotypic marker for schizophrenia (Glahn et al., 2003). In addition, while the verbal, visuospatial, and executive abilities have been assessed using a variety of span and executive tasks, the mechanism whereby distinct features of an event could be bound together to create a new temporary representation, or episode, in WM, and its effectiveness in schizophrenia have been the subject of very little study. Recent research addressed this issue using an object–location WM binding task initially devised by Mitchell and colleagues (Mitchell et al., 2000), consisting of the sequential presentation of three drawings of familiar objects in different cells of a 3×3 grid, followed by a 8-s blank delay and a recognition test. The binding condition involved recognizing whether an object+location cue pair had been presented together (bound) or separately (i.e., the object and location belonged to distinct pairs within the same trial). The results showed that patients' performance was preserved in the features condition (i.e., objects alone or locations alone) but disproportionately reduced in the binding condition when compared to healthy controls. Correct response times were also longer in the binding condition than in the features alone and longer for lure than target

Note: The data provided in this study have been partly matter of a university thesis presented by Franck Burglen.

Correspondence and reprint requests to: Pierre Salamé, INSERM Unité 666 Physiopathologie clinique et expérimentale de la schizophrénie, Département de Psychiatrie, Hôpitaux Universitaires, 67091 Strasbourg Cedex, France. E-mail: salame@alsace.u-strasbg.fr

trials. Taken together, these findings suggested that performance in the object–location binding task is defective in patients with schizophrenia (Burglen et al., 2004). Using a change detection paradigm (Luck & Vogel, 1997), Gold et al. (2003) found an opposite result and concluded that feature binding was normal in patients with schizophrenia. The discrepancy between the two conclusions might actually stem from conceptual and methodological differences between the studies. In the task by Gold et al., the same stimuli (rectangles with different orientations and colors) were displayed very briefly (up to 500 ms) at both presentation and test, and the lure trials only differed by one feature. According to Wheeler and Treisman (2002), the change detection task and the whole-display technique are likely to tap some form of perceptual distraction, rather than reflect binding in WM (see Wheeler & Treisman, 2002, for more details). At best, therefore, it might be the case that the change detection and object–location tasks would tap two distinct forms of perceptual and WM binding, the former being preserved and the latter disrupted in patients with schizophrenia. However, the reasons for the disruption in patients remain unknown, and they are one of the issues the present study attempted to address.

The fractionation of WM into distinct subcomponents benefited considerably from use of the suppression technique (Murray, 1968), which involves performing a secondary, redundant, task while at the same time carrying out a primary cognitive task (i.e., serial recall). The assumption is that, if carrying out both tasks simultaneously were to result in reduced performance in the primary task, this reduction would indicate that the tasks involved the same underlying cognitive mechanism. Conversely, a lack of disruptive effect would point to the distinctiveness of the mechanisms subtending the primary and secondary tasks (see Baddeley, 1986; Baddeley & Hitch, 1974).

Therefore, articulatory, visuospatial, and executive suppression modalities were used to identify the likely cause of the patients' impairments in the object–location binding task. It was hypothesized that if the binding operations involved the visuospatial and executive components of WM, pronounced impairments in patients' performances should be found under visuospatial and executive suppressions.

MATERIALS AND METHODS

Participants

A total of 47 participants matched in age and education took part in the study: 23 patients with schizophrenia and 24 healthy controls. One patient refused to carry out the executive suppression task, so the data of that patient were excluded from the analyses, reducing the patients' sample size to 22. All were outpatients who met Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (American Psychiatric Association, 1994) criteria for schizophrenia (paranoid, $N = 19$; residual, $N = 2$; deficitary, $N = 1$) as determined by consensus of the current treating psychiatrist and two senior psychiatrists belonging to the research team. None had a history of traumatic brain injury, epilepsy, substance abuse, other diagnosable neurological conditions, or organic mental disorders, nor were they being treated with antidepressants, benzodiazepines, or lithium. All were clinically stabilized at the time of testing.

Twenty-four controls were also recruited. None had a history of alcoholism, drug abuse, neurological or psychiatric illness, and none were taking any drugs. The demographic and clinical characteristics of the two samples are presented in Table 1.

The research was carried out in accordance with the Helsinki Declaration; the Strasbourg Consultative Committee for the Protection of Human Subjects in Biomedical Research approved the study. Each participant signed an informed consent form before the experiment and received financial compensation for taking part.

Table 1. Demographic and clinical characteristics (mean ± SE) of the patients with schizophrenia and healthy controls

	Patients ($n = 22$)	Controls ($n = 24$)	t_{44}	p
Gender ratio (F/M)	10/12	13/11		
Age (yr)	37.05 ± 1.58	37.63 ± 0.93	<1	NS
Education	11.64 ± 0.58	12.50 ± 0.29	<1	NS
IQ (Wechsler, 1981)	90.58 ± 2.90	98.04 ± 2.13	2.07	<.05
BPRS	38.27 ± 2.42	N/A		
SAPS	22.09 ± 3.41	N/A		
SANS	23.41 ± 3.42	N/A		
Medication				
Typical/atypical neuroleptic	9/13	N/A		
Chlorpromazine equivalent (mg) (Woods, 2003)	216.35 ± 21.63	N/A		
Antiparkinsonian	7	N/A		

Note. IQ, intelligence quotient; BPRS, Brief Psychiatric Rating Scale; SAPS, Scale for the Assessment of Positive Symptoms; SANS, Scale for the Assessment of Negative Symptoms; NS, not significant; N/A, not applicable.

https://doi.org/10.1017/S1355617706060668 Published online by Cambridge University Press

Binding Task

This task was borrowed from Mitchell et al. (2000) and assessed participants' ability to remember drawings of common objects, or their locations, or objects together with their locations (see Mitchell et al., 2000, for a figure depicting the task). A trial consisted of the presentation of three successive drawings (Snodgrass & Vanderwart, 1980) of familiar objects (i.e., trumpet, bell, airplane) that appeared in a 3 × 3 grid. Mitchell et al. colored the drawings to discriminate between the presentation and test phases of the task. In the presentation phase, each of the three colored drawings was presented in a different cell for 1 s. All cells apart from the middle one were used for stimulus presentation. After 8 s, the word "Test" was displayed briefly and the participants were probed for their memory for Object only, Location only, or Object+Location (Combination), using a Yes/No recognition procedure. In the Object condition, the probe consisted of a black and white (B/W) drawing presented in the center cell of the grid, and the participant had to decide whether it corresponded to one of the objects presented during the trial. In the Location condition, the probe was a big black dot presented in any of the cells in the grid except the middle one, and the participant had to decide whether that particular cell had been occupied by an object during the trial. In the Combination condition, the probe consisted of a B/W object presented in any cell except the middle one, and the participant had to decide if it was presented in its correct location. A "target" was an object, or location, or object+location that had been presented in the trial (i.e., a "studied" item from that trial). For the Object and Location conditions, a "lure" was an item not presented during the current trial, although it would have been presented during previous trials since the objects and locations were repeated across trials. In the Combination condition, a lure was an object that had been presented during the same trial but was located in a grid cell that, during the trial, had been occupied by another object, that is lures consisted of presented but re-paired objects and locations. During each trial, subjects responded by pressing the appropriate keys with the index and middle fingers of their preferred hand.

Suppression Modalities

In addition to a baseline, no distracter modality, suppression modalities consisted of articulatory, visuospatial, and executive suppression.

Articulatory suppression

The participant was asked to count out loud from 1 to 4 continuously at a rate of 3–4 digits/s.

Visuospatial suppression

This task was borrowed from Logie et al. (1990) and involved asking participants to visualize an 8 lines × 3 columns matrix. They then heard a series of instructions, to fill or leave blank each of the cells of the imagined matrix, starting from the top left-hand corner. The filled cells made a capital letter, which the participant was required to identify and name. For example, after successive "fill, fill, fill; fill, blank, fill; fill, blank, fill; fill, fill, fill; fill, blank, fill; fill, blank, fill; fill, blank, fill; and fill, blank, fill" statements participants would eventually respond by naming the letter "A". The letters "A, B, C, D, E, F, G, H, P, S, and U" were selected from the full 26-letter alphabet to keep guessing before the end of the associated instructions to a minimum, and they were presented in random order during the test.

Executive suppression

This task consisted of counting backwards in threes, out loud, starting from a random three-digit number provided by the experimenter at the start of each trial. Each participant practiced this task before the beginning of the experiment. Participants were instructed to maintain a constant rate while performing the suppression tasks.

Procedure

Each participant was tested in three distinct sessions, starting with the binding task and ending with the IQ measures. The first session of testing with the binding task started with a detailed overview of the task, followed by practice trials. The Object, Location, and Combination conditions were always practiced in this order. Each condition was first practiced in baseline (no suppression), then, depending on the experimental counterbalancing design, a given modality of suppression was explained. For instance, a participant required to carry out a session in articulatory suppression practiced this modality first alone, then simultaneously with the binding task in Object, then in Location, then in Combination. This practice pattern was repeated in the next session for another modality of suppression (i.e., executive suppression), and then again in the third session. Each condition in each modality comprised two alternating target and lure practice trials. After a practice session followed by a short break, testing sessions always started with 12 trials in baseline (blocks of 6 target and 6 lure trials of each Object, Location, and Combination condition, in random order), followed by a block of 16 trials in each condition (in a counterbalanced order) with the same suppression modality, then 12 new trials in baseline. Thus, each condition comprised 24 trials in baseline and 16 in each suppression modality, with equal numbers of target and lure trials. Each trial lasted 18 s, which meant that each whole block lasted approximately 5 min. Within any one session, two different orders of conditions were counterbalanced across participants in each group. Half the participants started with the Object condition and the other half with Location. Thus, none started the experiment with the Combination condition. In short, in any given session, all conditions were tested in the same suppression modality and consecutive sessions were carried out at weekly intervals.

https://doi.org/10.1017/S1355617706060668 Published online by Cambridge University Press

With regard to the suppression modalities, the participant was required to start suppression (letter imagining, counting forward or backward) 2 s before the onset of each trial, and suppression was continuous until the word "Test" was displayed. In baseline, there was no secondary task and the delay was unfilled. A thorough screening of the initial participants' practice data revealed no counting errors, sudden breaks in rhythm, or consistent slowing. Consequently, data from the articulatory and executive suppression tasks were not recorded; however, the number of letters incorrectly recognized in the visuospatial suppression task was recorded for subsequent analyses.

Data Analysis

The practice trials were discarded from the analyses, and test data were analyzed using Statistica 6.0. Analyses of accuracy were first carried out on Hit–False Alarm (H-FA) and d' scores. Subsequent detailed analyses were based on d' scores only, however, which point to the ability to discriminate between signal (targets) and noise (lures) stimuli. H-FA scores were first converted into arcsines. Before calculating d' scores, raw proportion values of 1 and 0 Hits and False Alarms, respectively, were corrected following Macmillan and Creelman's suggestion (Macmillan & Creelman, 1991; a constant equal to $1/2n$ where n is the adjusted mean based on the total number of trials in any given condition, i.e., 18). The comparisons involved analyses of variance that included group (Schizophrenia *vs*. Controls) as a between-subject factor and conditions (Object, Location, Combination) and suppression modalities (baseline, articulatory, visuospatial, executive) as within-subject factors. The same model of analysis was used to examine data from the visuospatial suppression task. *Post hoc* analyses addressed two distinct aims. One-way F tests evaluated between-group differences (pairs of means) at the level of each condition (i.e., Object, Location, Combination). Newman–Keul's (N-K) tests evaluated differences between means of the three conditions in each modality separately (i.e., baseline, articulatory suppression, visuospatial suppression, executive suppression). In all comparisons, the alpha level was set at 0.05.

RESULTS

Binding Task

The mean scores for H-FA in each group, condition, and modality of suppression are presented in Table 2a and b, respectively. Overall analysis of variance of H-FA scores that included all modalities of suppression and conditions revealed a main effect of group ($F_{1,44} = 23.44$; $p < .0001$), condition ($F_{2,88} = 141.69$; $p < .0001$), suppression ($F_{3,132} = 124.98$; $p < .0001$), and significant suppression × group ($F_{3,132} = 3.15$; $p < .03$), condition × suppression ($F_{6,264} = 4.40$; $p < .0004$), and condition × suppression × group ($F_{6,264} = 3.31$; $p < .004$) interactions. A comparable pattern

Table 2a,b. Mean ± SE of the proportions of Hits (H) and False Alarms (FA) as a function of condition and modality of suppression in patients with schizophrenia and healthy controls

	Object				Location				Combination			
	N	AS	VS	ES	N	AS	VS	ES	N	AS	VS	ES
						(2a) H						
Patients with schizophrenia	0.94 ± 0.02	0.67 ± 0.05	0.47 ± 0.05	0.50 ± 0.04	0.91 ± 0.02	0.89 ± 0.05	0.57 ± 0.06	0.77 ± 0.04	0.81 ± 0.03	0.63 ± 0.04	0.44 ± 0.05	0.57 ± 0.04
Healthy controls	0.99 ± 0.01	0.83 ± 0.04	0.63 ± 0.04	0.54 ± 0.05	0.96 ± 0.01	0.96 ± 0.01	0.85 ± 0.03	0.86 ± 0.04	0.94 ± 0.02	0.79 ± 0.04	0.55 ± 0.04	0.58 ± 0.04
						(2b) FA						
Patients with schizophrenia	0.02 ± 0.01	0.10 ± 0.02	0.18 ± 0.04	0.18 ± 0.03	0.03 ± 0.01	0.05 ± 0.02	0.24 ± 0.04	0.24 ± 0.04	0.15 ± 0.02	0.32 ± 0.04	0.36 ± 0.05	0.38 ± 0.05
Healthy controls	0.01 ± 0.01	0.10 ± 0.03	0.10 ± 0.02	0.13 ± 0.03	0.02 ± 0.01	0.04 ± 0.01	0.13 ± 0.04	0.18 ± 0.05	0.05 ± 0.01	0.21 ± 0.04	0.29 ± 0.04	0.38 ± 0.05

Note. N, baseline; AS, articulatory suppression; VS, visuospatial suppression; ES, executive suppression.

https://doi.org/10.1017/S1355617706060668 Published online by Cambridge University Press

of results was obtained in the analysis of d' scores. It revealed a main effect of group ($F_{1,44} = 24.37$; $p < .0001$), with patients' performance lower than that of controls (Patients, 1.69 ± 0.09; Controls, 2.30 ± 0.09). It also showed main effects of condition ($F_{2,88} = 141.90$; $p < .0001$) and suppression ($F_{3,132} = 150.34$; $p < .0001$). There were also significant condition × suppression ($F_{6,264} = 7.48$; $p < .0001$) and condition × suppression × group ($F_{6,264} = 4.30$; $p < .002$) interactions. Subsequent analyses examined each suppression modality separately as a function of the groups and conditions to disentangle the terms of the interaction.

In baseline (Fig. 1A), the analysis showed an effect of group ($F_{1,44} = 20.09$; $p < .0001$), indicating lower performance in patients than in healthy controls. There was also an effect of condition ($F_{2,88} = 35.79$; $p < .0001$) and a significant condition × group interaction ($F_{2,88} = 9.37$; $p < .0003$). In patients, the analysis showed an effect of condition ($F_{2,42} = 33.85$; $p < .0001$) and subsequent N-K test revealed that performances in Object and Location were comparable ($p < .37$) and both conditions were significantly better than Combination ($p < .0002$). In controls, a broadly comparable pattern of results emerged. There was an effect of condition ($F_{2,46} = 6.34$; $p < .004$), and the N-K test showed that performance in Combination was significantly lower than in Object ($p < .003$). Between-groups comparisons showed that patients d' scores were disproportionately lower than those of controls in Combination ($F_{1,44} = 22.84$; $p < .0003$) and Object ($F_{1,44} = 8.19$; $p < .007$). No significant difference was found between groups in Location ($F_{1,44} = 2.77$; $p < .11$), however.

Articulatory suppression (Fig. 1B)

In the articulatory suppression modality, the analysis revealed an effect of group ($F_{1,44} = 6.93$; $p < .02$) and condition ($F_{2,88} = 63.61$; $p < .0001$), and the group × condition interaction failed to reach statistical significance ($F_{2,88} = 2.93$; $p < .06$). Patients did not perform as well as controls (Patients, 2.00 ± 0.16; Controls, 2.60 ± 0.16), and the N-K test indicated that Location was better than Object, which in turn was better than Combination ($p < .0002$ in each comparison).

Visuospatial suppression (Fig. 1C)

The analysis showed an effect of group ($F_{1,44} = 25.20$; $p < .0001$) and condition ($F_{2,88} = 33.04$; $p < .0001$), and the group × condition interaction was also significant ($F_{2,88} = 4.18$; $p < .02$). In patients, the analysis showed a significant effect of condition ($F_{2,42} = 7.35$; $p < .002$) and a subsequent N-K test revealed that performance in Object and Location did not differ from each other ($p < .79$), and that both conditions were significantly better than Combination ($p < .003$). In controls, the analysis showed an effect of condition ($F_{2,46} = 33.16$; $p < .0001$) and the N-K test revealed that all three conditions differed significantly from each other ($p < .0002$ or better). Between-group comparisons showed that patients' performance was disproportionately lower than that of controls in Object ($F_{1,44} = 10.17$; $p < .003$), Location ($F_{1,44} = 23.00$; $p < .0001$), and Combination ($F_{1,44} = 4.61$; $p < .04$). In comparison with controls, patients, therefore, appear to have been heavily disrupted when required to carry out the visuospatial suppression task in all three conditions of the binding task.

Executive suppression (Fig. 1D)

The analysis showed a main effect of group ($F_{1,44} = 4.60$; $p < .04$) and condition ($F_{2,88} = 30.89$; $p < .0001$), and no interaction ($F_{2,88} = 1.21$; $p < .31$). The N-K test showed that all three conditions differed significantly from each other ($p < .002$ or better), with overall performance being the highest in Location and lowest in Combination. Although patients' performance in the binding task was statistically lower than that of healthy controls under executive suppression, none of the between-group comparisons proved significant in any experimental condition.

Visuospatial Suppression Secondary Task

The analysis that considered the number of errors (max = 16) in each group and condition showed a main effect of group (Schizophrenia, 7.79 ± 0.40; Controls, 4.68 ± 0.40; $F_{1,44} = 13.20$; $p < .01$), no effect of condition (Object, 6.52 ± 0.56; Location, 6.09 ± 0.58; Combination, 5.89 ± 0.46; $F_{2,88} = 1.24$; $p < .30$) and no interaction ($F_{2,88} < 1$). These results indicate that patients were less efficient than healthy controls at correctly identifying the letters described by successive "fill" and "blank" statements; however, their accuracy was similarly reduced in all three conditions of the binding task.

Additional Analyses

Because the two groups differed in terms of IQ, the possibility that this independent variable might have influenced participants' performance could not be ruled out. To confirm this question, an analysis of covariance that included IQ as covariate was carried out. The results failed to show any interaction of IQ with either group ($F_{1,42} < 1$), condition ($F_{2,84} < 1$), or suppression ($F_{3,126} = 1.14$; $p < .34$) factor. For the sake of consistency, a comparable analysis that considered educational level as covariate was also carried out, and produced similar results. There was no clear sign, therefore, that these independent factors influenced performance in the binding task.

In the patients' group, an additional set of correlational computations was carried out to examine the potential influence of the clinical symptomatology and medication on performance. Correlations were computed between the Brief Psychiatric Rating Scale, subscale and total Scale for the Assessment of Positive Symptoms and Scale for the Assessment of Negative Symptoms scores, and performance in each condition of the task in the baseline modality. A significance threshold was set at $p < .01$ to take into account

https://doi.org/10.1017/S1355617706060668 Published online by Cambridge University Press

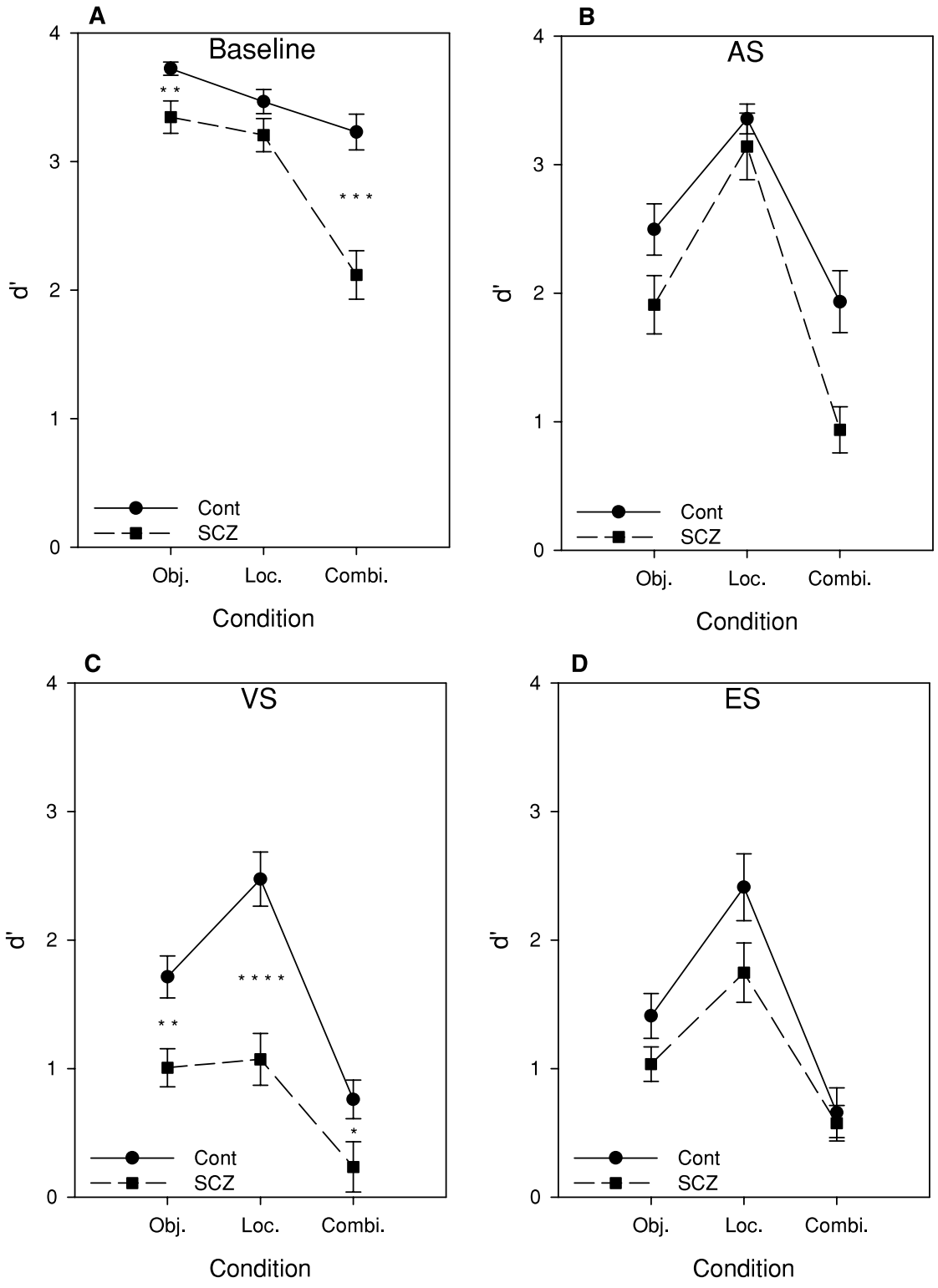

Fig. 1. Mean ± SE of *d′* scores as a function of condition in baseline (A), articulatory (B), visuospatial (C) and central executive (D) suppression modalities in patients with schizophrenia (SCZ) and healthy controls (Cont). Obj., Object; Loc., Location; Combi., Combination. *$p < .05$; **$p < .01$; ***$p < .001$; ****$p < .0001$

the multiplicity of computations. No significant correlation emerged. Finally, there was no significant correlation between the neuroleptic dose (chlorpromazine equivalent) and performance in the whole group of patients.

DISCUSSION

This study explored the contributions of each WM component to the binding operations by examining the respective

https://doi.org/10.1017/S1355617706060668 Published online by Cambridge University Press

effects of articulatory, visuospatial, and executive suppressions on recognition in an object–location binding task. The performances of two groups of participants, schizophrenia and control, were assessed. In baseline, whereas patients' memory for separate objects or locations was preserved, it was disproportionately reduced when the distinct features were to be bound and maintained in WM for later recognition. This result replicates the one obtained previously with the same task (Burglen et al., 2004). A similar result was obtained in a later work (Leiderman & Strejilevich, 2004). Their task assessed memory for a single object and a single location presented visually first separately and then combined. Recognition was tested following two delays (5 and 30 s) filled with a complex secondary task where participants were presented with a series of numbers and asked to detect any breaks in the normal order of sequence. For instance, in the sequence 13 − 14 − 15 − 17 . . . , they were required to detect that 16 is missing. Patients with schizophrenia were disproportionately impaired in the combined state, as opposed to object or location alone, a result interpreted by the authors as defective dual-task ability (Leiderman & Strejilevich, 2004). However, this result is interpreted (dual-task or binding), the actual locus of the impairment on WM components remained unclear, because the detection task is likely to tap each of the visuospatial sketch pad (visual identification), phonological loop (verbal coding), and executive (counting and updating) components of WM simultaneously.

In our study, the choice of suppression tasks was dictated by two major requirements, (1) to devise tasks that were reasonably selective so as to address primarily the verbal, visuospatial, and executive components of WM, and (2) to ensure full compatibility of the selected tasks with the output modality (i.e., key presses) of the main binding task. Thus, any suppression task had to require an oral output, which in turn was likely to reduce its selectivity. With regard to the articulatory and executive suppression tasks, both involved the phonological and central executive components of WM, albeit to different extents. The wide-ranging literature available on forward and backward digit spans on normals and neuropsychological patients (see Lezak, 1995) strongly suggests that counting backwards in threes requires far more central executive resources and mental arithmetic ability than iterative counting from 1 to 4, which involves an overlearned verbal skill and a minimal executive demand, if any. Concerning visuospatial suppression, the task capitalizes on maintaining in visuospatial WM a progressively growing mental representation of an unpredictable pattern; the subject must maintain the sequential "fill/blank" descriptions and wait for the last oral statements order to identify the targeted letter and respond accordingly. In this sense, it could be assumed that the task depends primarily on the storage of visuospatial information, although the involvement of executive processes in this task is far from negligible.

The results showed that, although articulatory suppression disrupted performance in all three conditions, the effect was similar in both groups since no significant group × condition interaction was obtained. This finding suggests, in line with previous reports (Elvevag et al., 2002; Salamé et al., 1998), that the functioning of the phonological loop of WM is qualitatively preserved in schizophrenia. With regard to executive suppression, a complex pattern was obtained. Overall, patients performed worse than controls, but the analysis failed to show a group × condition interaction, and no specific differences between groups were observed, in apparent contrast to what is generally described in the relevant literature (i.e., Andreasen et al., 1998; Keefe, 2000). It is plausible to think that these somewhat negative results might actually be due to the great difficulty of the secondary task of counting backwards in threes, which might have caused a performance drop to floor level in both groups, thus considerably minimizing the sensitivity of the object–location binding task. Future research should explore the effects of executive suppression using a more tractable secondary counting task so that the executive contribution of WM to object–location binding can be better assessed. Of the three suppression modalities, the visuospatial one caused the clearest impairments and interactions. The performance of patients was lower than that of controls in each condition of the binding task, and as hypothesized, the most drastic reduction was observed when their memory for spatial locations was tested (Fig. 1C). This reduction would seem to reflect a specific propensity of patients to show impaired performance when faced with processing visuospatial material in WM settings. As it stands, this assumption is not new, insofar as the visuospatial memory deficit in schizophrenia has been well evidenced in the relevant literature for the past 20 years (i.e., Aleman et al., 1999; Fleming et al., 1997; Fraser et al., 2004; Heinrichs & Zakzanis, 1998; Kolb & Whishaw, 1983; O'Donnell et al., 1996; Park & Holzman, 1992; Rabinowicz et al., 1996; see also Pelletier et al., 2005, for a meta-analysis). However, little is known about the underlying mechanism of this impairment, and various explanations such as a reduced processing speed in WM (i.e., Brebion et al., 1998; Salamé et al., 1998; Schatz, 1998) or response initiation (i.e., Nathanieljames et al., 1996) have been proposed. Unfortunately, none of these explanations can tell us, unequivocally, why the disproportionate deficit was confined to the visuospatial suppression, particularly in the location condition of the task. It has also been suggested that the patients' reduced ability to inhibit irrelevant information, or reduced "cognitive inhibition" (Beech et al., 1989), could explain the intrusive thoughts (Waters et al., 2003) and memory deficits of reality monitoring (Brebion et al., 1996), as well as the patients' failure to bind content and context (source and temporal) information in long-term memory settings (Waters et al., 2004). It might be tempting to extend the inhibition explanation to binding in WM, to explain the patients' reduced performance, providing it is further assumed that such an inhibition deficit is not general but specific to the processing of visuospatial information in WM. Thus, the precise reasons for the defective mechanism in visuospatial WM have yet to be identified, and further research is clearly needed to attempt to

fractionate the global concept of inhibition into more tractable subcomponents, so that the WM impairments in schizophrenia can be better explained. Nonetheless, our findings are new on two counts. First, they extend the range of the cognitive deficits in schizophrenia to the operations of object–location binding in WM, which so far has only been partially documented. Second, patients' impaired performance under visuospatial suppression suggests that the link between drawings of familiar objects and spatial locations in pairs relies on a visuospatial code, and, therefore, provides a neuropsychological contribution to the understanding of cognitive operations involved in object–location binding in WM.

With regard to neuroleptic intake and whether it can explain patients' reduced performance, the results failed to show any significant correlation between the neuroleptic dose taken by the patients and their performance in the binding task. However, although the impact of medication cannot be ruled out completely, two meta-analyses (Aleman et al., 1999; Heinrichs and Zakzanis, 1998) that examined this specific issue concluded that cognitive functions are not significantly influenced by medication. Our current results are in line with this suggestion.

In conclusion, the suppression paradigm allowed us to highlight the greater patients' deficit of visuospatial processing in WM that extends to the operations of binding. One of the study's limitations is that, in requiring that subjects recognize drawings of familiar objects that could be verbally and visuospatially coded, the object–location binding task bears an ecological advantage but does not allow for a generalization of the proposed interpretation. Due to the involvement of the binding operations in everyday life in creating temporary episodes, future research should consider the effects of suppression modalities of moderate difficulty in binding tasks involving simple verbal material, such as letters, presented in spatial locations. Such further research would have the potential to force participants to rely on specific coding strategies, allowing, therefore, for a better understanding of the level of involvement of the WM components in binding, and of their respective disruption in patients with schizophrenia.

REFERENCES

Aleman, A., Hijman, R., Dehaan, E.H.F., & Kahn, R.S. (1999). Memory impairment in schizophrenia: A meta-analysis. *American Journal of Psychiatry*, *156*, 1358–1366.

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (pp. 273–290). Washington, DC: American Psychiatric Association Press.

Andreasen, N.C., Paradiso, S., & Oleary, D.S. (1998). "Cognitive dysmetria" as an integrative theory of schizophrenia: A dysfunction in cortical subcortical-cerebellar circuitry? *Schizophrenia Bulletin*, *24*, 203–218.

Baddeley, A.D. (1986). *Working memory*. Oxford: Oxford University Press.

Baddeley, A.D. & Hitch, G.J. (1974). Working memory. In G. Bower (Ed.), *The psychology of learning and motivation: Advances in research and theory*. Vol. VIII (pp. 47–90). New York: Academic Press.

Beech, A., Powell, T., McWilliam, J., & Claridge, G. (1989). Evidence of reduced 'cognitive inhibition' in schizophrenia. *British Journal of Clinical Psychology*, *28*, 109–116.

Brebion, G., Amador, X.F., Smith, M.J., & Gorman, J.M. (1998). Memory impairment and schizophrenia: The role of processing speed. *Schizophrenia Research*, *30*, 31–39.

Brebion, G., Smith, M.J., Gorman, J.M., & Amador, X.F. (1996). Reality monitoring failure in schizophrenia: The role of selective attention. *Schizophrenia Research*, *22*, 173–180.

Burglen, F., Marczewski, P., Mitchell, K.J., Van der Linden, M., Johnson, M.K., Danion, J.-M., & Salamé, P. (2004). Impaired performance in a working memory binding task in patients with schizophrenia. *Psychiatry Research*, *125*, 247–255.

Clare, L., McKenna, P.J., Mortimer, A.M., & Baddeley, A.D. (1993). Memory in schizophrenia: What is impaired and what is preserved? *Neuropsychologia*, *31*, 1225–1241.

Elvevag, B., Weinberger, D.R., & Goldberg, T.E. (2002). The phonological similarity effect in short-term memory serial recall in schizophrenia. *Psychiatry Research*, *112*, 77–81.

Fleming, K., Goldberg, T.E., Binks, S., Randolph, C., Gold, J.M., & Weinberger, D.R. (1997). Visuospatial working memory in patients with schizophrenia. *Biological Psychiatry*, *41*, 43–49.

Fraser, D., Park, S., Clark, G., Yohanna, D., & Houk, J.C. (2004). Spatial serial order processing in schizophrenia. *Schizophrenia Research*, *70*, 203–213.

Glahn, D.C., Therman, S., Manninen, M., Huttunen, M., Kaprio, J., Lonnqvist, J., & Cannon, T.D. (2003). Spatial working memory as an endophenotype for schizophrenia. *Biological Psychiatry*, *53*, 624–626.

Gold, J.M., Wilk, C.M., McMahon, R.P., Buchanan, R.W., & Luck, S.J. (2003). Working memory for visual features and conjunctions in schizophrenia. *Journal of Abnormal Psychology*, *112*, 61–71.

Heinrichs, R.W. & Zakzanis, K.K. (1998). Neurocognitive deficit in schizophrenia: A quantitative review of the evidence. *Neuropsychology*, *12*, 426–445.

Keefe, R.S.E. (2000). Working memory dysfunction and its relevance to schizophrenia. In T. Sharma & P.D. Harvey (Eds.), *Cognition in schizophrenia* (pp. 16–50). Oxford: Oxford University Press.

Kolb, B. & Whishaw, I.Q. (1983). Performance of schizophrenic patients on tests sensitive to left of right frontal, temporal, or parietal function in neurological patients. *Journal of Nervous and Mental Disease*, *171*, 435–443.

Leiderman, E.A. & Strejilevich, S.A. (2004). Visuospatial deficits in schizophrenia: Central executive and memory subsystems impairments. *Schizophrenia Research*, *68*, 217–223.

Lezak, M.D. (1995). *Neuropsychological assessment*. (3rd ed.). Oxford: Oxford University Press.

Logie, R.H., Zucco, G.M., & Baddeley, A.D. (1990). Interference with visual short-term memory. *Acta Psychologica*, *75*, 55–74.

Luck, S.J. & Vogel, E.K. (1997). The capacity of visual working memory for features and conjunctions. *Nature*, *390*, 279–281.

Macmillan, N.A. & Creelman, C.D. (1991). *Detection theory: A user's guide*. Cambridge: Cambridge University Press.

McKenna, P.J., Tamlyn, D., Lund, C.E., Mortimer, A.M., Hammond, S., & Baddeley, A.D. (1990). Amnesic syndrome in schizophrenia. *Psychological Medicine*, *20*, 967–972.

Mitchell, K.J., Johnson, M.K., Raye, C.L., Mather, M., & D'Esposito, M. (2000). Aging and reflective processes of work-

ing memory: Binding and test load deficits. *Psychology and Aging*, *15*, 527–541.

Murray, D.J. (1968). Articulation and acoustic confusability in short-term memory. *Journal of Experimental Psychology*, *78*, 679–684.

Nathanieljames, D.A., Brown, R., & Ron, M.A. (1996). Memory impairment in schizophrenia: Its relationship to executive function. *Schizophrenia Research*, *21*, 85–96.

O'Donnell, B.F., Swearer, J.M., Smith, L.T., Nestor, P.G., Shenton, M.E., & Mccarley, R.W. (1996). Selective deficits in visual perception and recognition in schizophrenia. *American Journal of Psychiatry*, *153*, 687–692.

Park, S. & Holzman, P.S. (1992). Schizophrenics show spatial working memory deficits. *Archives of General Psychiatry*, *49*, 975–982.

Pelletier, M., Achim, A.M., Montoya, A., Lal, S., & Lepage, M. (2005). Cognitive and clinical moderators of recognition memory in schizophrenia: A meta-analysis. *Schizophrenia Research*, *74*, 233–252.

Rabinowicz, E.F., Opler, L.A., Owen, D.R., & Knight, R.A. (1996). Dot enumeration perceptual organization task (DEPOT): Evidence for a short-term visual memory deficit in schizophrenia. *Journal of Abnormal Psychology*, *105*, 336–348.

Salamé, P., Danion, J.-M., Peretti, C.S., & Cuervo, C. (1998). The state of functioning of working memory in schizophrenia. *Schizophrenia Research*, *30*, 11–29.

Snodgrass, J.G. & Vanderwart, M. (1980). A standardized set of 260 pictures: Norms for name agreement, image agreement, familiarity, and visual complexity. *Journal of Experimental Psychology—Human Learning*, *6*, 174–215.

Schatz, J. (1998). Cognitive processing efficiency in schizophrenia: Generalized vs. domain specific deficits. *Schizophrenia Research*, *30*, 41–49.

Tamlyn, D., McKenna, P.J., Mortimer, A.M., Lund, C.E., Hammond, S., & Baddeley, A.D. (1992). Memory impairment in schizophrenia: Its extent, affiliations and neuropsychological character. *Psychological Medicine*, *22*, 101–115.

Wechsler, D. (1981). *Manual for the Wechsler Adult Intelligence Scale*. New York: Psychological Corporation.

Wheeler, M.E. & Treisman, A.M. (2002). Binding in short-term visual memory. *Journal of Experimental Psychology—General*, *131*, 48–64.

Waters, F.A.V., Badcock, J.C., Maybery, M.T., & Michie, P.T. (2003). Inhibition in schizophrenia: Association with auditory hallucinations. *Schizophrenia Research*, *62*, 275–280.

Waters, F.A.V., Maybery, M.T., Badcock, J.C., & Michie, P.T. (2004). Context memory and binding in schizophrenia. *Schizophrenia Research*, *68*, 119–125.

Woods, S.W. (2003). Chlorpromazine equivalent doses for the newer atypical antipsychotics. *Journal of Clinical Psychiatry*, *64*, 663–667.