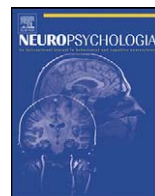




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Visuo-perceptual organization and working memory in patients with schizophrenia

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ABSTRACT

We explore the mechanisms sub-tending the re-organization and memorization of visual information by studying how these mechanisms fail in patients with schizophrenia. Several studies have suggested that patients have difficulties in organizing information in perception and memory. We explore to what extent prompting patients to group items influences memory performance. We distinguish automatic grouping from top-down grouping processes, which are especially involved in re-organizing information. The main task was to memorize pairs of figures. Following manipulation of proximity, pairs of figures were part of the same perceptual group (within-group pair, formed on the basis of automatic grouping) or belonged to different groups (between-group pairs, re-grouped through top-down processes). Prior to the memory task, subjects ran a perception task prompting them to prioritize either within-group or between-group pairs. Unlike patients, controls globally benefited from grouping by proximity in the memory task. In addition, the results showed that prioritizing between-group pairs had a deleterious effect in patients, but with a large decrement in memory performance in the case of within-group rather than between-group figures. This occurred despite preserved focalization on within-group figures, as shown by eye-movement recordings. The suggestion is that when patients are prompted to re-group separate items, they can do so, but the benefit derived from automatic grouping is then not only lost but also reversed. This suggests re-organizing visual information not only involves re-grouping separate items but also integrating these new groups in a unified representation, which is impaired in patients with schizophrenia.

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1. Introduction

Our perception and memorization of our environment involve conflicting abilities, maintaining a perceptual stability while still being able to navigate flexibly between elements and mentally create new links between items. We explore these abilities by studying how they are disrupted in pathologies like schizophrenia. We test for two possibilities in patients: an impaired ability to create links between items-to-be-remembered, or an impaired ability to integrate new links in a unified representation. We argue that the latter might result in a loss of perceptual stability by disrupting representations stemming from automatic grouping.

Patients with schizophrenia are known to display an impaired organization of information, in both visual perception (Giersch & Rhein, 2008; Silverstein et al., 2006; Uhlhaas, Phillips, & Silverstein, 2005; van Assche & Giersch, in press) and memory (Burglen et al.,

2004; Danion, Huron, Vidailhet, & Berna, 2007; Danion, Rizzo, & Bruant, 1999; Diaz-Asper, Malley, Genderson, Apud, & Ellevåg, 2008; Ellevåg, Fisher, Weickert, Weinberger, & Goldberg, 2004; Huron et al., 1995; Lepage et al., 2006; Luck, Buchy, Lepage, & Danion, 2009; Luck, Montoya, et al., 2009; Rizzo, Danion, van der Linden, & Grangé, 1996a; Rizzo, Danion, van der Linden, Grangé, & Rohmer, 1996b; Waters, Maybery, Badcock, & Michie, 2004). However, these impairments might be due to different types of mechanisms, since organizing information involves both automatic and controlled processes, the latter being based on attentional top-down mechanisms (Beck & Palmer, 2002; Palmer & Beck, 2007). What is more, both types of grouping are required all the time, even though they are not accessible to introspection. To illustrate their roles, let us consider the task of grocery shopping. In a store, identical items are usually arranged in stacks or piles. These items are thus grouped and segregated automatically, according to both proximity and similarity. When customers want to choose between different piles of the same fruit (e.g. tangerines of different origins), they have to select single items from each pile to compare them and decide which suits them best. At the same time, the customer is still able to

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perceive each individual item as being part of its pile. Local/global processing alone cannot account for this ability. Local processing allows single items to be considered individually while, at the same time, global processing provides the means to consider piles of fruit. Mentally re-grouping two items from different piles occurs at an intermediate level of processing, between local and global processing. It enables individuals to segregate items at the same time as re-grouping them, and apparently effortlessly. The question is how this conflict is resolved. Do subjects oscillate between two conflicting representations or do they build a representation including both types of grouping? If they oscillate between different, conflicting representations, it would mean that when their attention is focused on one kind of grouping, the conflicting representation is suppressed. While this clearly does happen in some instances, like with the Necker cube (Bruno, 2005), such perceptual multistability is not usually experienced in occasions like the one described above. The rarity of multistable experiences suggests that newly formed groups coexist with those deriving from automatic grouping, at least in healthy subjects, e.g. the two independent piles would coexist along with the pairs of items belonging to different piles. It would mean that access to groups deriving from automatic grouping should be preserved in all cases. This could be important, since this kind of grouping makes it possible to access the identity of the objects in our environment. Preserved access to groups resulting from automatic grouping would then help with maintaining a sense of perceptual stability. In patients with schizophrenia, on the other hand, the experience of stability appears to be disrupted. Patients frequently describe a fragmented visual environment: 'Everything I see is split up. It's like a photograph that's torn in bits and put together again' (Chapman, 1966). Several explanations have been put forward to explain these impairments. Here we explore the hypothesis that patients have a difficulty integrating different types of grouping in a coherent and stable perception.

1.1. Visual perception, attention, and schizophrenia

Some studies have suggested that automatic grouping is impaired in patients (Kéri, Kelemen, & Benedek, 2009; Kurylo, Pasternak, Silipo, Javitt, & Butler, 2007). However, when information organization is unambiguous, patients usually benefit from grouping to a similar degree as controls (Carr, Dewis, & Lewin, 1998; Chey & Holzman, 1997; Gabrovska, Laws, Sinclair, & McKenna, 2002; Giersch & Rhein, 2008; Herzog, Kopmann, & Brand, 2004; Uhlhaas, Phillips, & Silverstein, 2005; van Assche & Giersch, *in press*). In particular, we used a task in which subjects had to search for a pair of two identical targets among distracters. Proximity or the presence of connectors defined pairs of objects (Fig. 1A), and the target pair was either within the same group (Fig. 1, A2) or in different groups (Fig. 1, A3). In this task, stabilized patients benefited to the same extent as controls from grouping by both proximity and connectors (Giersch & Rhein, 2008; van Assche & Giersch, *in press*). Furthermore, they were able to focus on groups derived from automatic grouping when the task prompted them to do so. Patients performance was impaired, however, in the case of targets that were not part of the same group insofar as, unlike controls, they were unable to focus selectively on separate object. We suggested that patients failed to build an internal representation of unrelated figures. It is unclear, however, to what extent patients can build such representations when the task forces them to do so, and what happens if they do. If patients can mentally bind separate items together, are they able to maintain this link together with the groups resulting from automatic grouping? If not, what happens to the groups that stem from automatic grouping? Do the patients replace the representations deriving from automatic grouping (the piles) with those deriving from top-down grouping (the pair of tangerines)? This would entail an unusual suppression

of representations stemming from automatic grouping, and would mean the visual environment lacked stability. In the present study, we tested this hypothesis with the help of a memory task that involved memorizing two types of pairs of figures, namely pairs resulting from automatic grouping, and pairs composed of separate figures. In memory, as in perception, grouping is expected to improve performance (Campo et al., 2010; Luck, Foucher, Offerlin-Meyer, Lepage, & Danion, 2008; Luck & Vogel, 1997; Olson & Jiang, 2002; Prabhakaran, Narayanan, Zhao, & Gabrieli, 2000; Wu, Chen, Li, Han, & Zhang, 2007). We wanted to know whether patients (1) benefit from automatic grouping, (2) are able to memorize pairs of unrelated figures, and, if so, (3) whether or not the advantage usually brought by automatic grouping is then lost or reversed.

1.2. The paradigm and the predictions

One originality of the paradigm is to measure grouping both in visual perception and in memory. In the visual perception task, subjects have to detect a pair of identical figures among distracters, with the figures part (or not) of the same group. It is typically easier to detect the pair of target figures when they are part of the same group rather than belonging to different groups. Automatic grouping thus yields a response time and accuracy advantage in the task, and grouping is evaluated by measuring the performance difference observed when target figures belong to the same group, as compared to when they belong to different groups (Beck & Palmer, 2002). In the present study, we use grouping by proximity. The same figures are used in both the perception and memory tasks, and there is the same manipulation of proximity. In the memory task subjects have to memorize the relative spatial position of three figures, which requires them to retain two types of pairs, one resulting from automatic grouping (two figures that belong to the same pair) and the other one based on top-down grouping (two figures belonging to different pairs) (Fig. 1B). In addition, manipulation of attention demands during the visual perception blocks provides the means of prompting subjects to focus on either pairs of objects grouped by proximity or, on the contrary, ungrouped objects. So that the impact of this incentive on memorization can be assessed, each perception block is followed by a memory block (Fig. 1C).

We expected that a focalization on either objects grouped by proximity or on separate objects during perception would be carried forward to the following memory block. Since the memory blocks are all equivalent to each other in terms of attention conditions, a difference in performance across memory blocks can only be attributed to the prioritization bias induced during the visual perception blocks.

If patients mainly have difficulty establishing links between separate items (i.e. top-down grouping), then memory performance should be selectively impaired in this type of trials. If, however, patients are able to build representations of separate figures but have difficulty maintaining newly formed links together with links derived from automatic grouping, then the benefit of automatic grouping would not only be lost but even be reversed.

2. Methods

2.1. Subjects

Participants were the same as in Giersch and Rhein (2008): for the sake of simplicity, the perception task results have been reported separately from the memory results. Three patients and their matched controls were taken out of the analysis, because their performance in the memory task failed to exceed chance level. The 27 remaining outpatients were 9 women and 18 men (mean age 34.4 years SD 8.8; mean level of education 11.7 SD 1.8). Controls were individually matched with patients on gender, level of education, and age, and in respect of these characteristics did not differ from patients (9 women and 18 men, mean age 33.8 years SD 8, mean level of education 11.9 SD 1.8, $F_s < 1$). The project had the approval of local ethics committee. Informed written consent was obtained from each patient and control

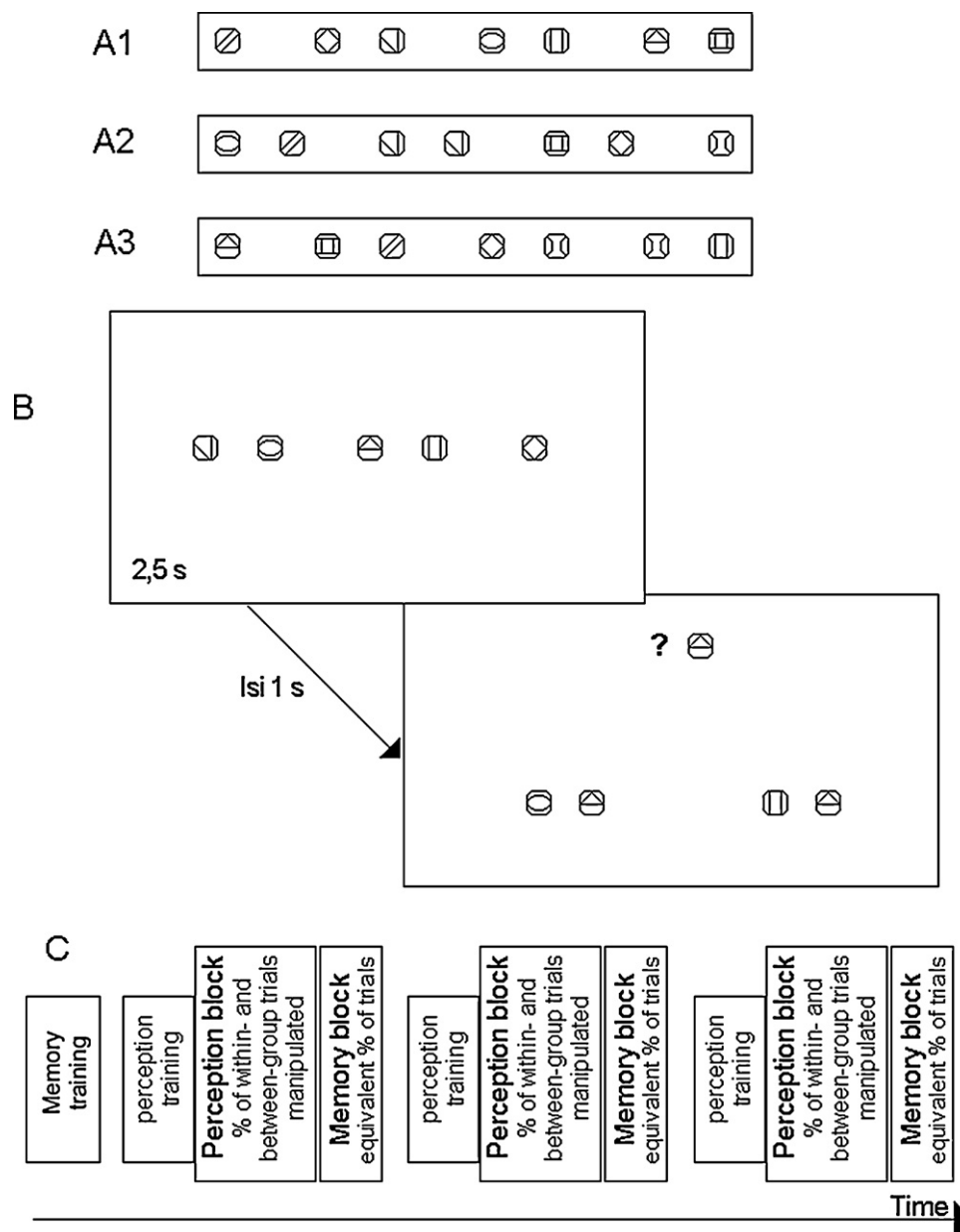


Fig. 1. (A) Illustration of the experimental conditions in the visual perception task in Giersch and Rhein (2008), with examples in (A1) the target absent condition (all figures are different), (A2) the within-group condition (there are two identical figures within the same group), and (A3) the between-group condition (the two identical figures belonging to two different groups). (B) Illustration of the experimental setting for the memory task. Five figures are displayed for 2.5 s. After a 1 s time-lag, the middle figure reappears with a question mark alongside it, and subjects are asked to retrieve the figure previously displayed in the position of the question mark. They must answer by choosing between two alternatives shown at the bottom of the screen and hitting a right or left response key accordingly. In the example, the correct response is on the left, and represents a between-group target. (C) Illustration of the experimental design. The protocol started with a training block for the memory task, to avoid any interruption between the visual perception and memory blocks and to preserve the influence of the prioritization induced during the perception block. During this training phase, proximity between figures was not manipulated. Subjects performed two blocks of 16 trials, and their performance in the second block was used to gauge baseline performance. Subjects finally performed perception and memory blocks successively. Three memory blocks had been created, and were randomly associated with visual perception blocks (reference block, 75% within-group or 75% between-group) with equal frequency across subjects.

subject before the study, in accordance with the recommendations of the Helsinki Declaration. All subjects had normal or corrected-to-normal visual acuity.

Psychiatric diagnoses of the patients with schizophrenia were established by a senior psychiatrist and fulfilled the criteria for schizophrenia laid down in the Diagnostic and Statistical Manual of Mental Disorders (4th ed.; American Psychiatric Association, 1994). The mean scores for the PANSS (Positive and Negative Syndrome Scale; Kay, Fiszbein, & Opler, 1987) were 16.2 (SD 5.7) for the positive sub-scale, 19.4 (SD 7.6) for the negative sub-scale, and 40.2 (SD 14.8) for the global sub-scale. The mean total score for the PANSS was 76 (SD 25).

The mean age at onset of schizophrenia symptoms was 23.4 years (SD = 5.2), the mean disease duration was 11.3 years (SD = 6.6), and the mean number of hospitalizations was 2.4 (SD = 1.4). Twenty-five patients were receiving long-term antipsychotic treatment, administered in a standard dose (mean dose = 200 mg/day

of chlorpromazine or chlorpromazine equivalents, SD = 142). Seven were being treated with typical neuroleptics, and eighteen with atypical neuroleptics. Six were also receiving antiparkinsonian treatment, either trihexyphenidyl (mean dose 5.6 mg/day, SD 3.1) or tropatepine (10 mg in all cases). Two patients were not receiving any treatment.

2.2. Equipment

The experiment was first run on a Pentium3 PC with no recording of eye movements, with 16 patients and their matched controls. Late acquisition of an eye tracker (50 Hz video eyetracker, Cambridge Research System) meant we could record eye movements only in a second stage involving 11 patients and their matched controls. The same experiment was then run on a Pentium4 PC equipped with a Cam-

bridge Research System (Rochester, Kent, UK) visual stimulus generator (ViSaGe), and programmed with matlab and the ViSaGe software library. Visual signals were presented on a 120 Hz Enzo visual display monitor (resolution 1024 × 768) and participants responded by hitting one of two keys interfaced with the computer. The eyetracker was mounted on a rigid headrest incorporating the camera, illumination and optics. The output from the eyetracker was recorded via the ADC input of the Cambridge Research System visual stimulus generator which also controls the visual display.

2.3. Stimuli

Our paradigm derived from a study by Beck and Palmer (2002). We made two main changes to their procedure. First, because we needed a series of different figures to test we drew geometrical features within rounded squares (Fig. 1A). Second, to make the perception and the memory task more similar we used a yes–no procedure and included target-absent trials: in both tasks, there were thus trials in which all the figures were different.

A total of eight different figures were used throughout the tasks, but only a subset of 5–7 figures was used in each trial, depending on the task and condition. Each figure ($0.7^\circ \times 0.7^\circ$ of visual angle) was defined by black outlines against a gray background. In each trial, figures were displayed on the screen in a horizontal row. The space left between figures varied, to define pairs of figures and one singleton. Within-group figures belonged to the same pair and were separated by a spacing of 1.1° of visual angle (Fig. 1, A2). Between-group figures belonged to different pairs and were separated by a spacing of 2.1° of visual angle (Fig. 1, A3). The singleton was on the right or left side in equal proportions of the trials. This randomization ensured subjects could not predict where the pairs were located; to focus on either within- or between-group pairs, they first had to process and group figures.

2.4. Procedure

2.4.1. Visual perception task

In the visual perception task, participants had to decide whether or not a series of seven figures displayed on the screen included a pair of identical figures. In half of the trials, all the figures were different (target absent, see Fig. 1, A1), whereas, in the other half, two adjacent figures were identical (target present; see Fig. 1, A2 and A3). The display remained on the screen until the subjects responded. They were instructed to hit a right or left response key according to whether targets were present or absent, respectively. Subjects were asked to give their answer as quickly and as accurately as possible. A 300 ms sound emitted after the response had been given denoted a wrong answer. Trials including mistakes were not repeated and in such cases the reaction times (RT) were not included in the statistical analysis (see Giersch & Rhein, 2008 for more details).

As in the original paper by Beck and Palmer (2002), the probability that the two identical figures belonged to the same or different groups of figures was manipulated. In one block (referred to hereafter as the ‘75% between-group’ block), they belonged to the same group in 25% of the target-present trials and to different groups in 75% of the target-present-trials. These trials are expected to prompt subjects to prioritize between-group pairs. In the reference block, targets belonged equally frequently to the same group or different groups. As there is no prioritization, this block is considered neutral. In the third block (the ‘75% within-group’ block), targets belonged to the same group in 75% of the target-present trials, resulting in an incentive to prioritize within-group pairs. As in the original study, the participants were explicitly informed about this manipulation. The order of the three experimental blocks was randomized between subjects. After a 24-trial training phase, each perceptual block included 96 target-absent trials and 96 target-present trials. The minimal number of trials per condition was 24.

In each experimental block, the figures were displayed the same number of times in each possible location. All eight figures were used equally often as targets, both within pairs and between pairs.

2.4.2. Memory task

In the memory task, five figures were used instead of seven to limit task complexity but, other than that, perception and memory trials were displayed in an identical fashion. The initial display comprised two pairs of two figures and one singleton. The whole display subtended 10° of visual angle. Subjects were instructed to attend to the three central figures and to memorize them. The five figures were displayed for 2.5 s. After 1 s time-lag during which the screen remained blank, one of the three middle figures, the reference figure, was displayed with a question mark to the right or left. The subjects’ task was to decide which figure in the initial display had been replaced in terms of its position by the reference figure and a distractor (Fig. 1B). One pair consisted of the reference figure and the target, displayed in the same relative position as in the initial display, but with a spatial separation of 0.8° of visual angle, whereas the other pair consisted of the reference figure and a distractor (Fig. 1B). In the initial display the distractor, like the target, had been located next to the reference figure, but on the opposite side. Subjects were instructed to respond by hitting the response key on the same side as the target figure, as quickly and as accurately as possible. No feed-back was given on response accuracy.

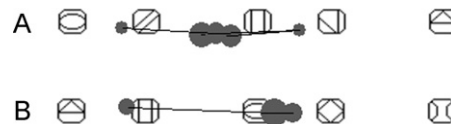


Fig. 2. Illustration of two typical ocular pathways during the study phase of the memory task. The example on the top (A) illustrates a focalization on between-group regions (by a control subject), whereas the example on the bottom (B) illustrates a focalization on within-group regions (by a patient). These examples are derived from the same conditions, in this case after a perception block prompting subjects to prioritize between-group pairs.

The reference and the target figures could belong to the same pair of figures (within-group target) or two different pairs (between-group target). Figures located in the far left or righthand positions were not taken into account. In 32 trials, the reference figure was in the middle. The targets were within-group in 16 trials and between-group in 16 trials. To prevent subjects from concentrating exclusively on the middle figure, thus making the task too easy, 8 filler trials were included, where the reference was one of the figures flanking the central figure. In those trials, however, the question mark always took the place of the central figure. In this way, the task could always be performed correctly as long as the three central figures were memorized.

The experimental design is illustrated in Fig. 1C.

2.5. Eye movement analysis

The aim of the eye movement analysis was to ascertain whether memory performance was related to the duration of the visual exploration of within-group and between-group pairs. Since the middle figure belongs to both types of pairs, we restricted the analysis to the exploration of the figures on either side of the middle one, and to the exploration of the space in between these figures and the middle one (Fig. 2). These figures and spaces were labelled ‘regions of interest’, and the cumulated fixation duration for these regions was computed across trials, with durations below 200 ms and above 1000 ms excluded from the computation (similar results were observed with a criterion of 100 ms for fixation durations) (Manor & Gordon, 2003). The first 150 ms of the recordings was discarded, as a voluntary saccade was not possible before 150 ms.

3. Results

Results in the visual perception task are described elsewhere (Giersch & Rhein, 2008), and were found to be equivalent for the 54 subjects included in the present study. Most importantly, patients benefited from grouping by proximity to the same extent as controls (+7.2% and 216 ms in controls vs. +7.4% and 260 ms in patients). Statistical interaction with the group was not significant ($F_{s[1,52]} < 3.5$, ns). We shall therefore focus on the memory results.

For the sake of simplicity only results on errors are presented. There was an absence of effect on both RT and the speed/accuracy trade-off.

Baseline memory performances were recorded at the beginning of the protocol, when proximity was not manipulated. Patients were significantly less accurate than controls in this baseline task, with a 29% error rate for controls vs. 38% for patients ($F_{[1,58]} = 5$, $p < .05$).

In the experimental memory task we conducted an ANOVA with repeated measures and distinguished results according to the type of visual perception task preceding the memory test. There were thus two within-group variables. One was the type of prioritization resulting from the visual perception block, i.e. (1) prioritization of between-group pairs (75% between-group block), (2) no prioritization (reference block), and (3) prioritization of within-group pairs (75% within-group block). The second variable was the type of pairs to be memorized, either within-group or between-group targets. Since the bias induced during the visual perception blocks was expected to continue on during the memory block, we hypothesized that it could induce behaviour modifications not only during the first visual perception block but also afterwards, throughout the experiment. Hence, we took into account the possible influence of the order of the visual perception blocks by analyzing

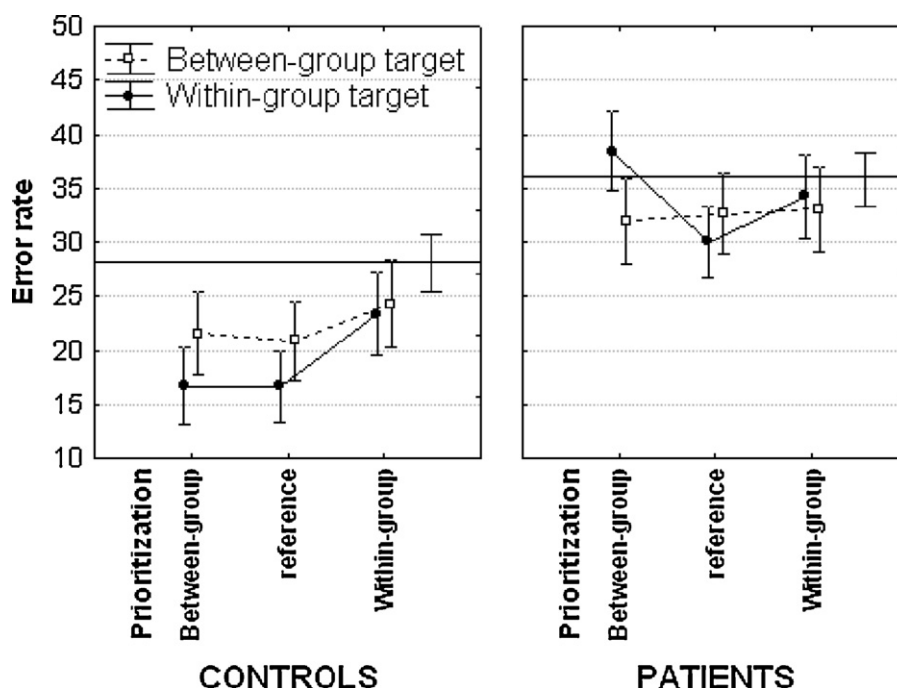


Fig. 3. Illustration of the memory task performance (mean error rate averaged over subjects with standard errors), for within-group targets (continuous line) vs. between-group targets (dashed line), in controls (left) and patients (right), as a function of the type of visual perception block (prompting to prioritize between-group trials – 75% between-group, reference, and prompting to prioritize within-group trials – 75% within-group). Baseline performance is represented by the horizontal continuous performance (with a standard error bar). Data is averaged across the first block type.

results as a function of the first experimental block type. The following effects were considered: Group (patients vs. controls); Target type (within-group vs. between-group target); Prioritization (75%, 50%, 25% between group); First block type (75%, 50%, 25% between group).

The global ANOVA showed a main effect of Group, with patients making 12.8% more errors than controls ($F[1,48] = 7.3, p < .01$). There was also a significant interaction between Group and Target type ($F[1,48] = 6.3, p < .05$). Sub-analyses were conducted within each group (controls and patients), first to compare within-group and between-group trials, and second to compare each condition with baseline. The difference between within-group and between-group targets was significant in controls ($F[1,24] = 14, p < .001$, Fig. 3 left panel), but not in patients ($F < 1$, Fig. 3, right panel). Controls reduced their error rate by 9.5% from baseline to within-group trials ($F[1,24] = 6.1, p < .05$), whereas patients reduced theirs by only 2% ($F < 1$). There were no significant improvements in either group for between-group trials relative to baseline ($F_s < 1$).

The global ANOVA also showed a significant quadruple interaction between Group, Target type, Prioritization and First block type ($F[4,96] = 3.6, p < .01$). Subsequent analyses showed that performance varied with the Prioritization in both groups, and additionally with the order of presentation of the visual perception blocks in controls. The effect of the first block type was observed only in controls, with a significant interaction between Target type, Prioritization and First block type ($F[4,48] = 3.1, p < .05$). This interaction was not significant in patients ($F[4,48] = 1.8, ns$). The impact of the first block type in controls is illustrated in Fig. 4. Detailed results are given according to Prioritization type. For each Prioritization type, we conducted analyses of variance with Target type and First block type as within-group variables. These analyses were performed with Group as between-group variable, and in each group separately in the case of a significant interaction with Group. Since results were not significantly different in the case of neutral or within-group prioritization, and for simplicity's sake, results have been pooled across these two conditions.

3.1. Neutral or within-group prioritization

After neutral or within-group prioritization, the result patterns differed significantly in controls and patients, as revealed by the triple interaction between Group, Target type and First block type ($F[2,48] = 7.1, p < .005$)¹. Subsequent analyses were conducted in each group separately.

In controls, the advantage for within-group relative to between-group targets varied with the order of the visual perception blocks, as suggested by a significant interaction between Target type and First block type, $F[2,24] = 3.9, p < .05$. After the reference block and after the 75% within-group perception block, the within-group advantage was larger when controls started the protocol with a block prompting them to prioritize within-group pairs (advantage of 10%, Fig. 4 right panel) than when they started with a reference block (advantage of 0.9%, Fig. 4 middle panel) or a block prompting them to prioritize between-group pairs (disadvantage of 2.5%, Fig. 4 left panel). These results are consistent with the idea that prioritizing within-group pairs during perception leads to an advantage in memorizing within-group figures.

In patients, there was no global advantage for within-group trials over between-group trials after either the reference or the 75% within-group perception blocks (Fig. 3, right panel). Furthermore, this was observed irrespective of the first block type (global advantage of only 0.4%, $F < 1$, data not shown).

3.2. Between-group prioritization

After the 75% between-group perception block, Target type interacted significantly with the group (controls vs. patients): $F[1,48] = 8.3, p < .01$.

¹ The graphs suggest an increase in error rates for within-group trials when the memory block follows within-group prioritization as compared to when it follows a reference block. However, this increase did not yield any significant effect in the global analyses, and will require further exploration.

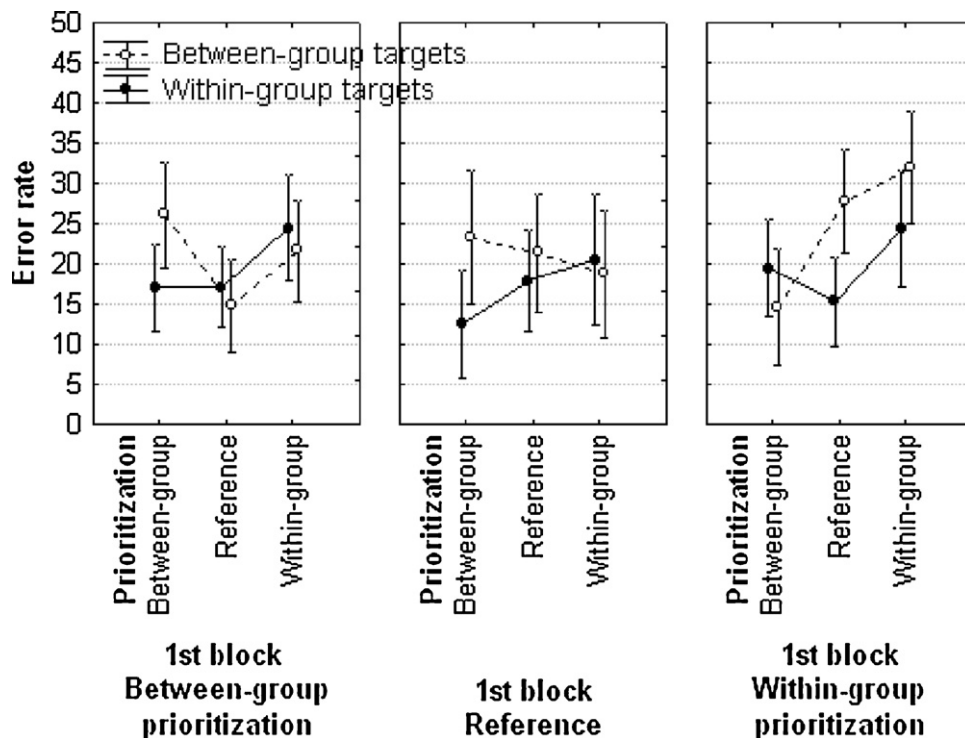


Fig. 4. Illustration of the controls' memory task performance (mean error rate averaged over subjects with standard errors), for within-group targets (continuous line) vs. between-group targets (dashed line), as a function of the type of visual perception block (prompting to prioritize between-group trials – 75% between-group, reference, and prompting to prioritize within-group trials – 75% within-group), and of the first block type (75% between-group on the left, reference in the middle, and 75% within-group on the right panel).

In controls, there was a significant advantage for within-group trials, which varied according to the First block type, as suggested by a significant interaction between Target type and First block type, $F[2,24] = 3.6$, $p < .05$. The influence of the first block in controls is the mirror image of the effect observed after the other perception blocks. This time, the advantage for within-group pairs was paradoxically larger when controls started the protocol with the block prompting them to prioritize between-group pairs (9%, Fig. 4 left panel) or with the reference block (10.7%, Fig. 4 middle panel), rather than with the 75% within-group perception block (disadvantage of 4.8%, Fig. 4 right panel). This means that subjects re-focused on within-group pairs after being prompted to prioritize between-group pairs, except when they started the protocol with a perception block prompting them to prioritize within-group pairs.

In patients, the advantage for within-group trials was reversed following the incentive to prioritize between-group pairs. There was a significant advantage for between-group as compared to within-group trials (by 6.5%, $F[1,24] = 4.8$, $p < .05$, Fig. 3 right panel), but no significant effect of First block type ($F < 1$, data not shown). Thus, in patients, a significant increase in the error rate was observed for within-group trials, relative to their performances after reference and 75% within-group perception blocks ($F[2,48] = 3.2$, $p < .05$).

3.3. Eye movement analysis

We conducted an ANOVA with Group (patients vs. controls) as between-group variable and region type (within-group vs. between-group target) as within-group variable. It showed a significant interaction between the two variables, $F[1,20] = 5.9$, $p < .05$. The effect of region type was then analyzed in each group separately. In controls, the cumulated exploration duration was longer for between-group regions (1789 ms) than for within-group regions (1215 ms), $F[1,10] = 16.5$, $p < .005$, whereas in patients it did not differ between between-group regions (1475 ms) and within-

group regions (1336 ms), $F[1,10] = 1.6$, ns . These effects did not vary significantly across blocks, and similar results were observed after a perception block prompting subjects to prioritize between-group pairs (examples shown in Fig. 2 are drawn from this condition).

3.4. Relationship with demographic and clinical variables

Correlations with clinical evaluations revealed two negative correlations with performance, and especially with the memory deterioration observed in the within-group condition after subjects were prompted to prioritize between-group pairs. In this particular condition, the error rate for within-group trials relative to baseline decreased with (1) the gravity of negative symptoms, as evaluated using the negative subscale of the PANSS ($r = -0.46$, $N = 27$, $p < .05$), and (2) the gravity of global symptoms as evaluated using the global subscale of the PANSS ($r = -0.4$, $p < .05$). In other words, the less symptomatic patients were those who saw their error rate increase the most in terms of memory for within-group pairs after a perception block prompting them to prioritize between-group pairs. Irrespective of the first block type, results were similar for the patients when account was taken of the various demographic and clinical variables ($F_s < 2$). There was no significant effect or correlation between chlorpromazine equivalents and performance levels.

4. Discussion

Controls benefited from grouping by proximity in the memory task, which is consistent with the literature. In patients, however, there was a dissociation between the visual perception and memory results. Patients benefited from grouping by proximity during the visual perception to the same extent as controls, and, during the study phase of the memory task, explored within-group regions for at least as long as controls. Despite this, and unlike con-

trols, they did not benefit from binding in memory, showing no significant improvements relative to baseline. Moreover, the prioritization of between-group pairs during the visual perception task was especially deleterious for memorization of pairs grouped by proximity in patients. In other words, creating new links to bind separate items together does not help patients to memorize such pairs better, and even induces difficulties regarding pairs that were grouped automatically and which are remembered more easily by controls. The fact that the difficulties concerned within-group rather than between-group trials suggests that when patients are prompted to give priority to considering between-group pairs, these between-group representations replace within-group representations, instead of coexisting with them. The main difficulty for the patients would thus concern their ability to make conflicting representations coexist, rather than to create new links between items. However, there are several alternatives that need to be considered first.

4.1. *Impact of reduced short-term memory span?*

It might have been the case that patients chose to encode two figures instead of three, especially as their short-term memory span is reduced (Brown et al., 2007; Fleming et al., 1997; Salamé, Danion, Peretti, & Cuervo, 1998; Strauss, Bohannon, Stephens, & Pauker, 1984). When prompted to prioritize between-group pairs, they would have encoded the two figures making up the between-group pair, and neglected the third. This would explain the disadvantage for within-group pairs after the block prompting them to prioritize between-group regions. Several results would appear to invalidate this interpretation, however. Patients should have been at chance level for within-group trials, which was not the case. Second, there should have been an advantage for within-group trials after the block prompting subjects to prioritize within-group pairs, which was not the case either. Moreover, the recording of eye movements showed that patients steadily explored within-group regions whatever the experimental block. It seems likely therefore that patients performed the task as instructed and tried to memorize three figures.

4.2. *Impact of fragile binding by proximity?*

A second possible explanation was that the patients' results are due to fragile binding by proximity (Kurylo et al., 2007). Even if binding by proximity is preserved in the visual perception task (Giersch & Rhein, 2008), memory may require grouping to be more stabilized than in visual perception. Indeed, it has been proposed that attention is required to reinforce binding between elements (Cinél & Humphreys, 2006). This might be more critical for the memory task (Elsley & Parmentier, 2009; Hollingworth & Henderson, 2002; Sperling, 1960; Wendelken, Bunge, & Carter, 2008). Studies conducted by Wheeler and Treisman (2002) do suggest that memorizing bound information requires more attention than simply perceiving the same information. However, fragile binding in memory is unlikely to explain the whole pattern of results reported here. The main effect of binding is to provide an advantage over conditions where to-be-memorized items are separate. Loss of the binding benefit should produce equal performance in within-group, between-group and neutral trials, with everything other than the presence or absence of proximity between figures being equal across conditions. However, what happens in fact is that the advantage for within-group trials is not only lost in patients, but also actually reversed, with performance for within-group trials worse than for between-group trials. These results cannot be explained by a difficulty in within-group binding alone. We suggest they are related rather to a difficulty in maintaining both types of representations in a non-mutually exclusive fashion.

All in all, the present results suggest that controls and patients deal differently with the need to encode both figures grouped by proximity and separated figures. They show complex adaptations in controls (see Fig. 4), who appear to adjust their priorities between the perception and memory blocks. This can be explained by the fact that the proportion of within-group and between-group trials changes from the perception to the memory block. It is striking that when between-group prioritization is maximal during perception blocks controls appear to re-focus on within-group trials (left-most panel Fig. 4, when the perception block prompts subjects to prioritize between-group pairs and when they start the protocol with this block). Most importantly, in spite of these adaptations, controls show no disadvantage for within-group trials relative to between-group trials. It is as if their priority is to maintain the link provided by automatic grouping by proximity. In patients, this pattern of results is reversed. They display impaired performance for within-group pairs after perception blocks prompting them to prioritize between-group pairs. It is as if, instead of avoiding the risk of losing the advantage for within-group pairs, they try to avoid the risk of being unable to memorize between-group pairs. It is the effort put into memorizing between-group pairs that might explain the disadvantage for within-group pairs, which is never observed in controls. This is supported by the results showing that it is the patients with fewer symptoms who are most impaired in respect of the within-group trials. From the results it would seem those with less symptoms are the most likely to try to overcome their difficulties with between-group pairs by establishing new links between separate items. They would then replace the representations of within-group figures by representations of between-group figures, because, for them, the two types of representations are mutually exclusive. This would finally lead to impaired performance in within-group trials. Patients with the most symptoms, on the other hand, would be less prone to adapt their strategies across blocks, especially given the difficulty of the task. An easier task would be a helpful way of checking whether the results can be generalized to patients with more symptoms.

4.3. *Impairment in memory or in top-down grouping?*

What remains unclear is whether the effects observed in the present study are selectively related to memory impairments. This is plausible given the suggestion that binding in memory, and especially in long-term memory, is impaired in patients (Danion et al., 1999, 2007; Diaz-Asper et al., 2008; Huron et al., 1995; Lepage et al., 2006; Luck, Montoya, et al., 2009; Rizzo, Danion, van der Linden, & Grangé, 1996; Rizzo, Danion, van der Linden, Grangé, et al., 1996; Waters et al., 2004). It might also be true for working memory, although the results available are mixed (Burglen et al., 2004; Gold, Wilk, McMahon, Buchanan, & Luck, 2003; Luck, Buchy, et al., 2009; Luck, Montoya, et al., 2009; Luck et al., 2008). At first sight, an effect specific to memory is supported by the dissociation that exists between the results observed in perception and memory. It might be noted, however, that an effect similar to the one described here was observed in patients during a perception task (Giersch & van Assche, 2010), in which once again they had to detect two identical targets. Throughout the trial they fixated a central fixation point, which forced them to plan their exploration instead of sweeping across the stimuli. Once again an impairment was found in patients for within-group targets when between-group pairs were prioritized, suggesting that this effect can occur independently of memory mechanisms. The relationships between the mechanisms at work in perception and memory require further investigation before definitive conclusions can be drawn. Meanwhile, it should be noted that our results suggest impaired binding in memory varies according to attention conditions.

An effect of psychotropic drugs cannot be ruled out completely, despite the lack of any correlation with chlorpromazine equivalents. However, it is worth noting that impairments have been observed in siblings of patients with schizophrenia when tested for visuo-spatial short-term memory (Kéri, Kelemen, Benedek, & Janka, 2001) and visual scanning behaviour (Loughland, Williams, & Harris, 2004). This indicates that impairments related to the mechanisms at study in the present work are observed independently of drug intake. In any case, the results would still be relevant, from the point of view of their fundamental implications, insofar as they suggest that creating new links between items is not enough to be able to reorganize information and maintain these new links in memory. It appears that a necessity for processing the environment in a flexible way while maintaining a sense of that environment's stability is that the new links must, in addition, be integrated with existing representations.

These results also have implications for cognitive remediation. They suggest that the effects of prompting patients to attend to separate objects can be more deleterious than positive, since their performance in relation to automatically bound objects can then worsen. This effect disappeared, however, when there was no longer any incentive to prioritize between-group pairs. Further studies now need to explore to what extent patients can improve their performance with the help of longer or more explicit learning procedures. Meanwhile, the present results suggest that incentives to establish links between items should be used with caution.

In conclusion, the present results show that patients with schizophrenia can lose the advantage provided by grouping by proximity, at least in memory, and suggest this might be related to a difficulty with maintaining additional representations of separate items. Re-organizing information might be easy in controls, but would involve the constraint of maintaining a sense of coherence and stability, i.e. a preservation of existing representations. This would be impaired in patients. This hypothesis offers a potential explanation for the contradictory findings described in the literature and may also account for the sense of fragmentation reported by patients.

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