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Episodic Memory and Impairment of an Early Encoding Process in Schizophrenia

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Investigations of memory impairment in schizophrenia have frequently revealed a strategic processing deficit at encoding. The authors studied an early encoding process, refreshing (in this case, thinking of a stimulus that has just-previously been presented), and its impact on recognition memory in schizophrenia. Following simultaneous presentation of three words or a single word in the top, middle, or bottom position of the screen, 25 patients with schizophrenia and 25 control participants saw and read a new word (read condition), or a word presented on the previous screen (repeat condition), or saw a dot indicating that they should think of and say the last word to have appeared in that position (refresh condition). Later, on a surprise test, participants were asked to recognize words seen previously and give a Remember, Know, or Guess response according to whether they recognized each on the basis of conscious recollection, familiarity, or guessing. The cognitive operation of refreshing was impaired in schizophrenia: patients were slower on 1-word trials and less accurate on 3-word trials to refresh a word, and their Remember responses did not benefit from refreshing.

Keywords: encoding, episodic memory, recollection, schizophrenia, Remember/Know procedure

Episodic memory, that is, the ability to remember past events, is dramatically impaired in schizophrenia (Aleman, Hijman, de Haan, & Kahn, 1999; Cirillo & Seidman, 2003; Danion, Huron, Vidailhet, & Berna, 2007). This impairment has critical consequences for the everyday life of patients and thus plays a major role in their difficulties with social integration (Green, 1996; Green, Kern, Braff, & Mintz, 2000). For instance, it reduces patients' ability to use past experiences to adjust ongoing behavior. Remediating this memory impairment is essential but cannot be achieved without understanding its functional mechanisms and identifying impaired elementary processes that might be specifically targeted later by remediation techniques.

Tulving (1985) characterized episodic memory as a memory system that allows people to reexperience past events by mentally reliving them. This experience of recollecting details of a particular event is different from the feeling of knowing that an event has taken place but without recollecting the details of the event. Tulving (1985) proposed the Remember-Know procedure to investigate this difference in subjective experience. During a recognition memory task, participants are asked to make a Remember response if recognition is accompanied by the conscious recollection of some specific feature of the item's presentation (where it was, what they thought, etc.) and a Know response if recognition is associated only with a feeling of familiarity.

Huron, Danion, and their colleagues used this procedure in patients with schizophrenia (reviewed in Danion & Huron, 2007) and found impairment in Remember but not in Know responses. This impairment is particularly marked when patients are required to bind separate components of events to form a coherent, relational memory representation, for example, target information and its source (Danion, Rizzo, & Bruant, 1999), semantic associations between words (Huron et al., 1995), or perceptual and semantic characteristics of pictures (Huron, Danion, Rizzo, Killofer, & Damiens, 2003). On the whole, these findings suggest that the impairment in the subjective experience of remembering in schizophrenia results from patients' impaired ability to deploy an efficient strategy at encoding to construct a memory representation that can later trigger conscious recollection.

Ranganath, Cohen, and Brozinsky (2005) demonstrated that initial encoding processes of working memory can be distinguished from working memory maintenance processes. Ranganath et al. (2005) suggested that one type of early encoding process is *refreshing* (Johnson, 1992; Johnson, Reeder, Raye, & Mitchell, 2002; Raye, Johnson, Mitchell, Reeder & Greene, 2002). They also suggested that such early processes help transform a sensory representation into an internal representation and contribute disproportionately to successful long-term memory formation over and above maintenance processing later in a working memory delay.

Refreshing is an elementary reflective process that consists of thinking of an event that has just been experienced and is no longer externally present, but the representation of which is still active. The result of refreshing is to briefly augment or extend the activity of this representation (Johnson, Mitchell, Raye, D'Esposito & Johnson, 2007). Thus, refreshing is one of the attentional processes whereby a temporary perceptual representation in iconic memory can be transformed into a more stable, working memory representation that can be maintained for a longer period and can facilitate subsequent long-term memory (e.g., Johnson et al., 2002). Refreshing can be operationally and neurally distinguished from

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other working memory processes, such as rehearsal, which refers to the active, cyclic repetition of information, usually subvocally, over several seconds (Johnson et al., 2005; Raye et al., 2007) and from processes by which information that is no longer active is revived from long-term memory (reactivation and retrieval). Behavioral and fMRI studies of refreshing in young and older, normal adults have identified a frontal region (BA9) associated with refreshing in young adults (Johnson et al., 2005; Raye et al., 2002), provided behavioral evidence of a refresh deficit in older adults associated with less refresh-related activation in BA9 (Johnson, Mitchell, Raye, & Greene, 2004), and shown that refreshing benefits long-term memory for young but not older adults and that this long-term memory benefit is related to refresh-related activity in BA9 (Johnson et al., 2004). Together, these findings provide evidence that refreshing is a component process of cognition that can be studied in itself and that plays a critical role in long-term remembering when it is engaged at encoding.

We used an experimental procedure developed by Johnson, Reeder, Raye, and Mitchell (2002) to investigate the refresh process in schizophrenia (Grillon et al., 2005). Verbal response times were measured when participants read a new word, read a word immediately again, or refreshed a word just after it was no longer present. This first phase was followed by a surprise recognition memory test in which participants were asked to recognize the words they had seen before and to give Remember, Know, or Guess responses according to whether they recognized words on the basis of conscious recollection, familiarity, or guessing (Gardiner, Java, & Richardson-Klavehn,1996; Tulving, 1985).[1] Patients were slower than controls to say a word only in the refresh condition in which they had to think back to the just-seen word to say it aloud, but were not slower than controls in the read and the repeat conditions in which they had to read a word for the first or second time. This increase in response times of patients occurred under experimental conditions in which neither patients nor controls made any errors because saying a just-seen word aloud is an easy task. Therefore, this result suggests that the process of refreshing may suffer some disruption in schizophrenia. It is interesting to note that Remember responses benefited from refreshing, compared with reading an item once, to the same extent in patients as in controls. Moreover, unlike the reduced levels of Remember responses typically shown in schizophrenia (review in Danion & Huron, 2007), the difference between the proportions of Remember responses in patients and controls was not significant.

In this first study, words were presented individually in the center of the screen. However, experiences rarely occur in isolation and in the same place; instead, they often are part of a more complex context and less predictable in time and place. Investigating whether remembering still benefits from refreshing when an item is presented in an unexpected part of the screen or displayed along with other items is critical to understanding the impairment of episodic memory in schizophrenia.

In a previous study (Grillon, Johnson, Krebs, & Huron, 2008) in healthy students, we compared the original refresh paradigm in which single words always occurred in the middle of the screen with a modified version of the paradigm in which critical words were presented alone in the top, middle, or bottom position of the screen. There was a loss of benefit in remembering from perceiving an item twice when attention was divided between locations rather than focused on the center of the screen. However, Remember responses still benefited from refreshing regardless of whether the word always occurred in the center of the screen or not. Taken together, these findings provide evidence that under certain circumstances the processes involved at encoding are vulnerable to divided attention between locations and thus less likely to form a representation that will be detailed enough to later prompt a Remember response. In Grillon et al. (2008), we also compared refreshing a single perceived item (1-word trials) with refreshing one of three just perceived items (3-words trials) in healthy students. Compared to reading, the time to refresh a word increased dramatically from 1-word to 3-words trials. In addition, the benefit in remembering from refreshing observed on 1-word trials disappeared when students had to refresh an item that was initially displayed along with two others (3-words trials). Taken together, these findings suggest that increasing the number of active representations during refreshing is associated with a cost for the initial operation of refreshing and for the long term-memory benefit from refreshing.

Here, we compare the speed and the accuracy of the operation of refreshing and its impact on Remember/Know responses between patients with schizophrenia and normal controls when the word to be refreshed is (A) presented in one of three different *locations* of the screen (in contrast to our earlier study of schizophrenia patients were items always occurred in the center), and (B) when participants have to refresh one from among three just perceived *items* compared to refreshing a single item that was just perceived. This study should provide evidence about whether the more demanding conditions investigated here will result in an impairment in the formation of mental representations from refreshing: patients with schizophrenia might be slower and/or less accurate to refresh a word and less likely to show increased conscious recollection associated with refreshing.

Because Grillon et al. (2005) reported impairment of the refresh process in schizophrenia, we hypothesized that patients with schizophrenia would benefit less than controls when a representation was refreshed versus read under conditions of divided attention between locations: refreshing versus reading one word that can be presented in the top, middle, or bottom position of the screen. If this is the case, we should observe a greater beneficial effect of refreshing versus simply reading a word on Remember responses on 1-word trials in normal controls but not in patients.

Since a greater vulnerability to interference in working memory has been reported in schizophrenia (Stevens, Donegan, Anderson, Goldman-Rakic, & Wexler, 2000), we hypothesize that patients will be slower or less accurate than controls in refreshing a word among three active items. In contrast, as Remember responses of healthy students did not benefit from refreshing on 3-word trials in Grillon et al. (2008)'s study, we did not except any differences in Remember responses between patients and controls when the word to refresh was initially displayed along with two others.

[1] Gardiner et al. (1996) introduced a third category of responses (Guess responses) to take into account guessing and to obtain purer measures of familiarity by Know responses.

Method

Participants

Twenty-five patients (17 men, 8 women) comprising 14 outpatients and 11 inpatients participated in the study. Their mean age was 30.6 (SD = 6.8) years, and their mean educational level was 13.3 (SD = 2.44) years. Their mean duration of illness was 8.8 (SD = 7.34) years; their mean total duration of hospitalization was 28.4 (SD = 49.3) weeks; and their mean number of hospitalizations was 3.3 (SD = 2.5). All patients fulfilled the *DSM–IV* criteria for schizophrenia as determined by consensus of the current treating psychiatrist and two senior psychiatrists belonging to the research team. Psychiatric symptoms were assessed by means of the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962; mean score = 46, SD = 11.84) and by the Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein, & Opler, 1987; mean negative = 35 ± 1.4; mean positive = 20 ± 9.9; mean disorganized = 12 ± 2.8; mean general = 41 ± 8.5; mean total = 96 ± 16.9). Patients with histories of traumatic brain injury, epilepsy, alcohol and substance abuse, or other diagnosed neurological conditions were excluded from the study. Patients were clinically stable on maintenance antipsychotic medication exclusively (5 on conventional neuroleptics and 20 on atypical antipsychotics; mean chlorpromazine equivalent dose = 596 ± 349 mg/day).

Twenty-five control participants (17 men, 8 women) were matched with the 25 patients for sex, age, and educational level. The controls had no history of alcoholism, drug abuse, or neurological or psychiatric illness and did not take any drugs. Their mean age was 28.6 (SD = 6.8) years, and their mean educational level was 14.1 (SD = 2) years. The groups did not differ significantly in age, $F(1, 48) = 0.99$, $p = .32$, or education, $F(1, 48) = 1.96$, $p = .17$. The mean IQ as assessed with a short form of the Wechsler Adult Intelligence Scale—Revised (Crawford, Allan, & Jack, 1992) was significantly lower in patients (m = 100.9, SD = 19.1) than in control subjects (m = 112.7, SD = 17.1, $F(1, 48) = 5.11$, $p = .03$). All participants provided informed written consent.

Materials

A set of 288, two-syllable, common unrelated French words, each comprised of four to 10 letters, with a mean word frequency of 47.00 per million, was selected from the Brulex database (Content, Mousty, & Radeau, 1990) and randomly divided into 16 subsets of 18 words each, which did not differ in terms of either their mean frequency or mean number of letters ($F < 1$). Each subset was counterbalanced such that each word was presented equally often as a read target, a refresh target, a repeat target, a distractor, and a new word in the recognition task.

Procedure

Phase 1. During Phase 1, on the first computer screen of each trial, either three words were presented simultaneously in a column for 4500ms (54 trials) or a single word was presented in one of the three locations (top, middle, or bottom) for 1500ms (54 trials). Then, 500ms later, participants saw (for 3000 ms) a screen showing a single, new word in one of the three locations (*read* condition), a just-seen word in the same location as before (*repeat* condition), or a single dot in one of the three locations (*refresh* condition). They were instructed to read the words, from the top to the bottom of the screen, aloud as quickly and accurately as possible. In the refresh condition, the dot signaled them to think back and to say aloud the word that had appeared in that position on the previous screen. Response times were collected via a voice key. A practice session of 24 trials preceded the test phase to check whether participants were able to read efficiently and had correctly understood the instructions of Phase 1. In the test phase, there were 18 trials of each type (read, repeat, or refresh, crossed with 1 or 3 prior words) pseudo randomly intermixed (see Figure 1).

Phase 2. Ten minutes after the end of the Phase 1, participants performed a surprise recognition task consisting of 144 items (the 108 targets presented in phase 1 and 36 completely new items). They were asked to identify (read, refreshed, and repeated) words from Phase 1 by pressing a Yes or No button. If the response was Yes, they were asked to make a Remember, Know, or Guess judgment. They gave a Remember response if they could recollect some aspect of the word event in Phase 1, a Know response if they knew but without any conscious recollection that the word had appeared in Phase 1, and a Guess response for words that elicited neither the experience of remembering, or knowing, but which they thought may have appeared in Phase 1.

During the 10-min interval separating phases 1 and 2, participants were given oral and then typed instructions regarding the general test procedure, and Remember, Know, and Guess responses. They were informed that they could refer to the typed instructions during the test phase as often as they needed to. Some examples from everyday life were described and participants were

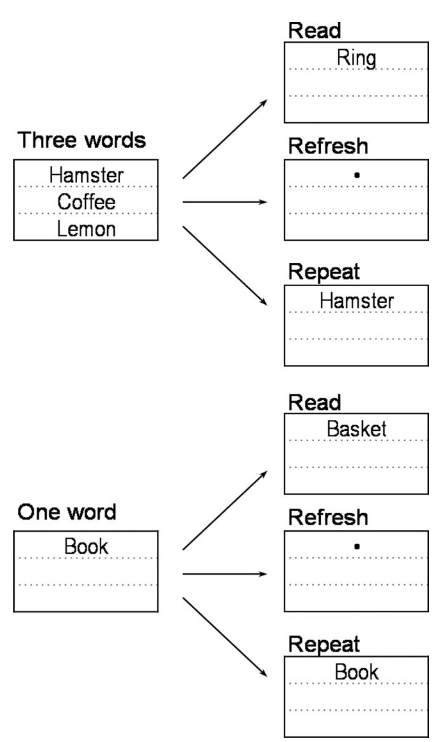

Figure 1. Procedure in Phase 1.

asked whether they would choose a Remember, Know, or Guess response for each instance. Corrections were made by the investigator when necessary. In addition, all participants took a practice test including 18 items, 12 of which were presented during the practice session of Phase 1 and 6 of which were new items. For each item, participants were asked whether they recognized it as having been presented previously or not. When they recognized an item, they were asked to select a Remember, Know, or Guess response. At the end of the practice test, they were asked to explain each response to check that they had correctly interpreted the instructions.

Data Analysis

Trials in which participants gave a word from an incorrect position ($M = 4.22\%$, 2.00% of the total critical responses for patients and controls, respectively) or did not pronounce any word ($M = = 1.77\%$, 0.88% of the total critical responses for patients and controls, respectively) were excluded for mean responses times and recognition scores analyses and responses were considered as errors for accuracy analyses.

For Phase 1, mean response times (RT) and accuracy, that is the proportion of trials in which a correct word was pronounced, were computed separately for read, refresh, and repeat conditions for 1-word trials and for 3-word trials. These normally distributed variables were subjected to analyses of variance (ANOVAs) on repeated measures with Group (patients, controls) as a between-subjects factor, and Condition (read, refresh, repeat) and Number of items (1, 3) as within subject factors.

For Phase 2, proportions of Yes, Remember, Know, and Guess responses were calculated separately for read, refresh, and repeat conditions for 1-word trials and for 3-word trials by dividing the number of responses given during Phase 2 (test) by the number of correct responses during Phase 1 (encoding). Corrected proportions were obtained by subtracting false recognition of new items from correct recognition of critical items (see Table 1).[2] These corrected proportions were subjected to an analysis of variance (ANOVA) with Group, Condition, Number of Items, and Response type (Remember, Know, Guess) as factors.

Alpha level was set at $p < .05$. Whenever the result was significant, post hoc analyses (Fisher LSD) were carried out to localize differences and Cohen's d were computed to measure effect sizes.

Results

Phase 1: Encoding Task

Figure 2 shows response times (RTs) for correct responses (left) and error rates (right) in Phase 1. For the RTs, there were significant Condition, $F(2, 96) = 146.31$, $p < .0001$, Number, $F(1, 48) = 240.01$, $p < .0001$, and Group, $F(1, 48) = 15.95$, $p = .0002$, effects, as well as significant interactions between Number and Condition, $F(2, 96) = 73.01$, $p < .001$, and between Number, Condition, and Group, $F(2, 96) = 2.9$, $p = .05$. Interactions between Condition and Group, $F(2, 96) = 0.46$, $p = .63$, or between Number and Group, $F(1, 48) = 1.29$, $p = .26$, were not significant. Subsequent analyses showed that patients were slower than controls in the refresh condition on 1-word trials ($t = 2.28$, $p = .027$, $d = 1.75$) whereas RTs in the other conditions were not significantly different between patients and controls ($ts < 1.76$, $ps > .09$, $ds < 1.05$). In addition, for 1-word trials, patients, but not controls, were slower in the refresh condition than in the read condition ($t = 3.37$, $p < .001$, $d = 0.78$ vs. $t = 0.7$, $p = .48$, $d = 0.15$), whereas, for 3-word trials, both patients and controls were slower to refresh than to read a word ($t = 8.5$, $p < .0001$, $d = 1.34$ and $t = 9.24$, $p < .0001$, $d = 1.66$, in patients and controls, respectively). Patients and controls displayed equivalent repetition priming effects (faster response times in the repeat than in the read condition) for both 1 and 3-word trials, respectively (patients: $t = 3.35$, $p = .001$, $d = 0.53$, and $t = 2.87$, $p < .0001$, $d = 0.88$; controls: $t = 5.25$, $p < .001$, $d = 1.51$, and $t = 2.83$, $p = .005$, $d = 0.49$).

Accuracy, is defined as the proportion of trials in which a correct word was pronounced. This excluded trials where 1 of 3 words had to be refreshed and participants either gave a word from an incorrect position (mean rates = 4.22% of trials in patients; mean rates = 2% of trials in controls) or pronounced no word (mean rates = 1.77% of trials in patients; mean rates = 0.88% of trials in controls. There were also significant Number, $F(1, 48) = 15.75$, $p = .0002$, and Condition, $F(2, 96) = 18.47$, $p < .0001$, effects; a significant Condition × Number interaction, $F(2, 96) = 19.95$, $p < .001$; and a close-to-significant Group × Condition × Number interaction, $F(2, 96) = 2.56$, $p = .08$. To further understand this marginal three-way interaction, we conducted Tukey's tests to compare all pairs of means.[3] These subsequent analyses revealed that patients were less accurate than controls ($t = 3.75$, $p = .021$, $d = 0.44$) when refreshing a word from 3-word trials. Other comparisons were not significant ($ts < 0.01$, $ps > .99$, $ds < 0.28$).

To summarize the results of phase 1: patients were slower than controls only when they had to refresh a word that had been presented alone (1-word trials) and less accurate than controls when they had to refresh a word that had been presented with two others (3-words trials).

Phase 2: Recognition Task (see Table 1)

One control participant was excluded from these analyses because for an unknown technical dysfunction, his responses were not recorded by Psyscope during the memory task.

An ANOVA on corrected recognition scores showed the following significant effects: Group, $F(1, 47) = 9.62$, $p = .003$; Response type, $F(2, 94) = 16.01$, $p < .001$; Condition × Number, $F(2, 94) = 5.61$, $p = .005$; and Group × Condition × Number × Response type, $F(4, 188) = 2.68$, $p = .03$. The group effect reflected lower recognition scores in patients than controls. Separate analyses were conducted for each response type to analyze the interactions.

An ANOVA on Remember responses showed a significant Group effect, $F(1, 47) = 4.35$, $p = .04$, with patients giving fewer Remember responses than controls, and a significant Condition × Number, $F(2, 94) = 3.34$, $p = .04$, interaction, and a significant Group × Condition × Number interaction, $F(2, 94) = 4.15$, $p = .01$. There were no significant effects of Condition, F(2,

[2] Analyses on uncorrected recognition scores have also been carried out and led to the same conclusions as those on corrected scores.

[3] It has to be noted that the Tukey's test can be performed regardless of the results of the overall ANOVA.

Table 1
Mean (SD) Proportions of Corrected Recognition Scores and Remember, Know, and Guess Responses, According to Group, Condition, and Number

Group	Patients with schizophrenia							Control subjects						
Condition	Read		Refresh		Repeat			Read		Refresh		Repeat		
Number	1	3	1	3	1	3	New	1	3	1	3	1	2	New
Yes	0.34 (0.18)	0.38 (0.19)	0.37* (0.23)	0.34 (0.20)	0.37* (0.23)	0.34 (0.20)	0.24 (0.16)	0.47 (0.15)	0.51 (0.18)	0.52* (0.18)	0.51 (0.17)	0.57* (0.13)	0.48 (0.17)	0.14 (0.12)
Remember	0.18 (0.17)	0.18 (0.19)	0.18 (0.18)	0.17 (0.22)	0.18 (0.18)	0.17 (0.22)	0.07 (0.11)	0.26 (0.18)	0.29 (0.22)	0.32* (0.20)	0.25 (0.20)	0.32* (0.22)	0.22 (0.20)	0.03 (0.05)
Know	0.13 (0.13)	0.13 (0.15)	0.13 (0.15)	0.12 (0.13)	0.13 (0.15)	0.12 (0.13)	0.08 (0.08)	0.1 (0.20)	0.16 (0.15)	0.18 (0.16)	0.20 (0.19)	0.20 (0.18)	0.21 (0.18)	0.06 (0.08)
Guess	0.04 (0.08)	0.08 (0.12)	0.07 (0.11)	0.05 (0.12)	0.07 (0.11)	0.05 (0.12)	0.09 (0.08)	0.03 (0.11)	0.06 (0.12)	0.02 (0.09)	0.05 (0.13)	0.05 (0.13)	0.05 (0.11)	0.06 (0.07)

* Significant differences ($p < .05$) in comparison with responses for read words.

94) = 0.19, p = .82, Number, $F(1, 47) = 1.52$, p = .22, Number × Group, $F(1, 47) = 3.78$, p = .06, or Condition × Group, $F(2, 94) = 0.38$, p = .68. Subsequent analyses revealed more Remember responses in 1-word trials for refreshed (t = 2.33, p = .022, d = 0.45) and for repeated (t = 2.25, p = .027, d = 0.46) words than for read words in controls but not in patients (t = 0.91, p = .36, d = 0.19, for refreshed, t = 0.1, p = .92, d = 0.02, for repeated in comparison with read words).

ANOVAs on Know and Guess responses showed no Group, $F(1, 47) = 2.02$, p = .16, and $F(1, 47) = 0.41$, p = .52, Number, $F(1, 46) = 0.44$, p = .50 and $F(1, 47) = 3.17$, p = .08, or Condition, $F(2, 94) = 1.37$, p = .26 and $F(2, 94) = 0.15$, p = .86, effects and no significant interactions, $Fs < 1.91$, $ps > .16$.

To summarize, patients were less likely to give a Remember response than controls and the beneficial effect on Remember responses from refreshing versus reading a word was observed in controls but not patients on 1-word trials. Remember responses did not benefit from refreshing on 3-word trials either in patients or in controls.

Secondary Analyses

Patients were matched with control participants for sex, age, and education level, but not for IQ. This raises the question of whether the pattern of results observed in patients is related to IQ. To investigate this issue, we excluded from the analysis the two patients with the lowest IQ and the two control subjects with the highest IQ. Secondary analyses were conducted on subgroups that did not differ in IQ, $F(1, 44) = 1.68$, p = .20. They displayed exactly the same results as analyses carried out on the entire group for both mean RT, accuracy rate in Phase1, and recognition scores. This indicates that differences in response pattern of the whole group of patients compared with controls did not result from differences in IQ.

Response times and recognition memory performance were not significantly correlated with measures of psychiatric symptoms from the BPRS or PANSS nor with drug dose ($ps > .10$).

Discussion

As expected, our results confirm that the cognitive operation of refreshing, in this case thinking of a just-seen word, is impaired in schizophrenia. Consistent with our previous study (Grillon et al., 2005), patients, compared to controls, were particularly slow to refresh a word that had been presented alone. A new finding in the present study was that patients were also less accurate than controls to refresh one of three active items.

This pattern of results cannot be explained in terms of a speed/accuracy trade-off because in the 3-word condition patients were both slower and less accurate than controls. Moreover, response times of patients for trials in which an incorrect word was spoken (*mean RT* = 1191ms) were not faster than for successful trials (*mean RT* = 1043ms). Also, because saying a just-seen single word is a particularly easy task, as reflected by the absence of errors in both groups, it seems unlikely that patients were induced on single-item refresh trials to be especially cautious, as they might be for more complex response-time tasks. The lack of benefit in Remember responses for patients from refreshing on 1-word trials suggests that on this simple task, patients may activate fewer features of the items, resulting in more shallow encodings.

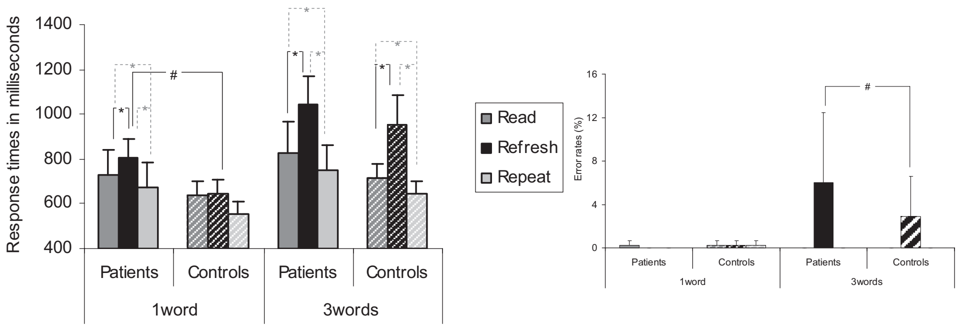

Figure 2. On the left, mean response times in Phase 1; on the right, error rates in Phase 1. * Significant differences ($p < .05$) between conditions obtained by the analyses of variance with Group, Condition, and Number as factors. # Significant differences ($p < .05$) between groups obtained by the analyses of variance with Group, Condition, and Number as factors.

It could be argued that the poorer performance during Phase 1 of patients with schizophrenia in the refresh condition might reflect in part an impairment in task switching ability, a well-established deficit among people with schizophrenia (Karayanidis et al., 2006; Kieffaber et al., 2006; Meiran, Levine, Meiran, & Henik, 2000). However, we previously showed that switching from a repeat or read trial to a refresh trial was not associated with longer response times than when refresh trials followed refresh trials either in patients with schizophrenia or in controls (Grillon et al., 2005). We also showed no differences in response times or memory performance for single words following 1-word or 3-word trials in healthy students (Grillon et al., 2008). Because these findings argue against a switching cost from reading (or repeating) to refreshing or from 3-word trials to 1-word trials, it is unlikely to account for the performance of patients with schizophrenia in the refresh condition.

There may be several explanations for the impaired ability of patients to accurately refresh an item on 3-word trials. Impaired performance in long-term memory and working memory has been reported in schizophrenia when the task required binding objects to their location (Burglen et al., 2004; Rizzo, Danion, Van der Linden, & Grange, 1996). In the present experiment, on 3-word trials, the target to be refreshed was indicated with a location cue. Therefore, refreshing an item from a 3-word set requires that items are bound to their locations, whereas reading a word (as in the *read* and *repeat* conditions) does not. This suggests that poorer binding of item and spatial information may have contributed to the refresh deficit in patients.[4] If this is true, then the ability to create a new representation by linking distinct features of an event would be disrupted from the very earliest phases of encoding. Another possibility is that the process of refreshing may be more vulnerable in patients than in controls to interference from multiple active representations. Schizophrenia patients are more vulnerable than controls to interference in working memory, for example, proactive interference from stimuli from prior trials (Stevens et al., 2000) . Compared to a single refresh condition, selective refreshing is associated with greater activation of the anterior cingulate cortex (Johnson et al., 2005), an area thought to be involved in conflict detection (Botvinick, Cohen, & Carter, 2004), and for which there is some evidence of dysfunction in schizophrenia (Dehaene et al., 2003). It is interesting to note that in a similar refresh study that compared old normal adults with young normal adults, Raye et al. (2008) showed that increasing the number of active representations impaired performance of older adults not only when they had to refresh a word but also when they had to read a word for the second time. A preserved performance in repetition together with a spared priming effect on 3-words trials suggest that in contrast with older adults, patients with schizophrenia experience interference from activated representations only during reflection (refresh trials) but not during perception (repeat trials).

As predicted, patients with schizophrenia were not only particularly slow to refresh a word presented alone but also impaired in their ability to later consciously recollect it. Since patients were as accurate in refreshing a word as controls on 1-word trials, the lack of benefit from refreshing in long-term memory performance cannot be explained by a decrease in accuracy in working memory performance. This result provides evidence that the impairment of the operation of refreshing can have consequences at the working memory level by increasing the response time of patients to think back to a just-seen word and to say it aloud and at the long term memory level by reducing the level of Remember responses. This result sheds a different light on previous findings that suggested that dorsolateral prefrontal cortex deficits contributed to both working memory and long-term memory disturbances in schizophrenia (Barch, Csernansky, Conturo, & Snyder, 2002).

Although the decrease in Remembering on 1-word trials in patients is consistent with evidence of reduced levels of Remember responses reported in schizophrenia (reviewed in Danion & Huron, 2007), this result is at variance with our previous study (Grillon et al., 2005) where refreshing increased remember responses to the same extent in patients as in controls. This difference may stem from differences between the two studies in the way single words

[4] It has to be noted that on 1-word trials, the dot signaled participants that they had to refresh a just-seen word whereas on 3-word trials the dot signaled participants that they had to refresh (rather than read or repeat) a word and the location of the dot indicated which word from the 3-word set they had to refresh.

were presented. In the Grillon et al. (2005)'s study, single words always occurred in the center of the screen whereas in the present study they were displayed at the top, in the center, or at the bottom. This particular presentation, chosen because half the trials involved three words, might entail a disproportionate cost in patients with schizophrenia by spreading their attention across the screen. Perception studies have shown that if attention is paid to a larger area, performance at any single location can suffer. Mizuno, Umilta, and Sartori (1998) suggested that the ability to adjust the size of the attentional focus from a larger to a smaller area in order to increase processing efficiency is impaired in schizophrenia. Thus, in patients, refreshing might fail to form a representation in working memory that is sufficiently stable, cohesive, or detailed to later support conscious recollection from just-seen information since this information has not been efficiently processed at a perceptual level.

This interpretation is consistent with the fact that the Remember responses of patients with schizophrenia, unlike those of controls, did not benefit in the present study from having a single word repeated perceptually whereas in Grillon et al. (2005) the beneficial effect of perceptual repetition was observed in both patients and controls. However, in the present study, patients with schizophrenia still showed a preserved repetition priming effect equal to controls. These findings suggest that some processing differences between patients and controls occurred during the stimulus displays where the item was perceptually present not at the automatic early stage of visual processing, but at a later stage of processing.

Results from 3-word trials showed that, even in controls, the impact of refreshing on Remember responses depended on the number of items presented at encoding: Remember responses of both groups did not benefit from refreshing one from among three active items. All participants were significantly slower at refreshing on 3-word trials than on 1-word trials. This suggests that when more representations are active, foregrounding a mental representation of one of these may be more demanding for both controls and patients and may result in a less stable, cohesive, or detailed representation that is less likely later to trigger a conscious recollection of the event.

In conclusion, our study provides evidence of an impaired ability in schizophrenia to transform perceived verbal information into a long-term memory representation by refreshing it. This impairment of an early encoding process is associated with episodic memory impairment even for a single item when patients are required to distribute attention across locations. This could be particularly debilitating for patients with schizophrenia in their daily lives since, in everyday situations, refreshing typically occurs in an environment where information can occur in many locations and multiples items of information may be momentarily active simultaneously. These findings suggest developing new therapeutic approaches targeted at remediating this disrupted process. For instance, patients might be trained to refresh items initially presented among others to improve their working memory performance under these conditions. Alternatively, patients could be trained to exploit spared processes. For instance, they could be instructed to isolate each item that they need to remember by writing it in the center of a piece of paper before refreshing it, in order to increase the likelihood of later recollecting it.

Finally, it is important to determine whether refreshing is also impaired for nonverbal stimuli. It would be informative to conduct neuroimaging studies in patients with schizophrenia similar those that have been conducted with healthy participants (Johnson, Raye, Mitchell, Greene, & Anderson, 2003; Johnson et al., 2005; Johnson et al., 2007) to investigate the neural correlates of refreshing in patients with schizophrenia as a function of the type of material processed (words, abstract colored patterns, line drawings of objects, and photographs of people or places).

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