Perceptual priming in schizophrenia evaluated by word fragment and word stem completion

María José Soler a⁎, Juan Carlos Ruiz a, Martín Vargas b, Carmen Dasí a, Inma Fuentes a

a Faculty of Psychology, University of Valencia, Spain
b Department of Psychiatry, “Complejo Asistencial” of Segovia, Spain

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A B S T R A C T

Implicit memory seems to be preserved in schizophrenia as a whole, but dissociations between conceptual and perceptual tasks and between accuracy and reaction time measures have appeared. The present research has revealed some methodological limitations in many studies to date that are focused on the study of perceptual implicit memory in schizophrenic patients using accuracy measures. The review of these studies revealed that limitations are related to an inadequate definition of performance and priming measures, a lack of control over the characteristics of the stimuli, and the absence of information on the experimental procedures used in data collection. Moreover, the task used in these studies is word stem completion, a task that makes use of perceptual and conceptual processes. In the experiment reported here we use a pure perceptual implicit task and stimuli selected from a normative database to measure perceptual implicit memory in schizophrenic patients. Their performance was compared with that of normal participants. Thirty-two schizophrenic patients and 30 healthy control participants were administered a word fragment completion task. Direct comparison between the two groups yielded similar results in priming, suggesting that perceptual implicit memory is preserved in schizophrenia.

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1. Introduction

Cognitive impairment is recognized as one of the most reliably distinguishing features of schizophrenia. Some quantitative reviews of the existing literature based on comparative studies with healthy controls indicate that memory is one of the principal deficits in people with a diagnosis of schizophrenia. The majority of these people scored lower than normal when memory functioning was assessed by explicit objective tests (e.g., recall tasks) (Heinrichs and Zarkonis, 1998; Fioravanti et al., 2005), and they obtained similar scores when memory was evaluated using implicit memory tasks (e.g., lexical decision) (Spinheim et al., 2004; Gold et al., 2009).

Cognitive psychologists refer to conscious awareness of memory as explicit memory and implicit memory as memory without awareness. In the first case the individual is aware of the retrieval process but not in the second. Graf and Schacter (1985) stated that, “implicit memory is revealed when performance in a task is facilitated in the absence of conscious recollection”. As a consequence, implicit memory is assessed by tasks in which instructions do not make reference to the context of the learning episode. In other words, a past experience with the episode facilitates its processing without a conscious recollection of the past experience itself. This facilitation is due to a phenomenon referred to as priming (Graf and Schacter, 1985).

Although implicit memory appears to be preserved in schizophrenia as a whole, some studies have indicated dissociations between different implicit tasks (Kreher et al., 2009). These tasks can vary in a continuum going from those requiring more perceptual information (data-driven tests) like the word-fragment completion task, to those requiring knowledge of meaning (conceptually driven tests) like the category exemplar generation task.

Recent research using factor-analysis techniques have provided strong support for the multidimensional nature of implicit memory (Mitchell et al., 1998; Bruss and Mitchell, 2009). In line with the proposals of memory systems and transfer-appropriate processing frameworks (Tulving, 1995; Roediger et al., 1999), Bruss and Mitchell’s (2009) results identify two implicit memory forms: perceptual implicit memory, assessed using tasks like word-fragment completion, and conceptual implicit memory, assessed using tasks like category exemplar generation.

Studies that have used tasks to test conceptual implicit memory have shown that patients with schizophrenia are unimpaired in both category instance generation and word identification tasks (e.g. Schwartz et al., 1993), but they are significantly less accurate on the category verification task compared to controls (Rossell and David, 2006). In the case of perceptual implicit memory, differences between patients and controls have emerged from two lines of research. The first line, extensively explored, concerns performance based on reaction time measures and the second with performance based on accuracy measures.
The vast majority of studies have followed the first line using the semantic priming paradigm via tasks like lexical decision or word naming. In these tasks a word (prime), which may or may not be semantically related to a string of letters (target), is briefly shown. After a short interval, the string, that may or may not be a word, is presented, and the subject has to decide if it is a word or a non-word (lexical decision task) or has to read it as quickly as possible (word naming task). Pomarol-Clotet et al. (2008) carried out a meta-analysis of over 30 studies using these tasks and could not provide evidence of altered semantic priming in schizophrenia as a whole. However, some of these studies have yielded conflicting results. For example, when the comparison is made between patients with thought disorder and normal controls, there is increased semantic priming (Kreher et al., 2009). In addition, the deficit of attention that characterizes schizophrenia could produce a slowness of processing that may also explain these conflicting results. Alternatively, accuracy measures could provide results uninfluenced by slowness of processing when implicit memory is assessed.

The study of perceptual implicit memory using accuracy measures has been performed using different tasks, like word-fragment completion (WFC) and word-stem completion (WSC), that should include two steps following Graf and Schacter’s (1985) definition of implicit memory. In the first step, participants are asked to perform a task on a group of words (e.g. judge a word’s familiarity) to force them to process the words without any explicit instruction to learn the words. In the second step, participants have to complete as many word-fragments (or stems) as possible. These fragments have been obtained by deleting some letters from words processed in the first step or by adding new ones. In both tasks, the difference between the proportion of correct completions of new words and words previously processed, or priming, is taken as the measure of implicit memory (Tulving et al., 1982).

Studies with schizophrenia patients using these tasks have not been extensively reviewed. For this reason we have made a systematic review of studies published in the period from 1990 to 2010 that compare performance between patients with schizophrenia and controls, in WFC or WSC tasks. We only found a small group of 14 studies. All of them reported data on WSC, but they varied considerably in methodological aspects and yielded conflicting results. No studies using WFC were found.

In some studies the first stage in the experimental design was an explicit learning of words (Gras-Vincendon et al., 1994; Brebion et al., 1997; Kazes et al., 1999; Linscott and Knight, 2001; Balsa and Fernández, 2002). Or there was no first stage (Marvel et al., 2004). The studies also differed in the operational definition of the dependent variable used to measure implicit memory. Only four studies reported priming percentage data from patients with schizophrenia (Randolph et al., 1993; Bazin and Perruchet, 1996; Perry et al., 2000; Kern et al., 2010). In contrast, most of the published studies define the dependent variable as the number of completions of processed words that appeared in the first phase of the task or use other definitions. In the studies of Clare et al. (1993), Brebion et al. (1997), and Ruiz-Vargas et al. (2005), the authors defined priming as the number of word-stems correctly completed divided by the total number of word-stems in the list. They did not include new stimuli in the second stage of the task. Bressi et al. (1998), and Schmandt et al. (1992) measured implicit priming in a similar way, based on the number of stems completed that appeared in the first phase of the task.

In addition, many of the studies share a lack of control of relevant variables related to the characteristics of the stimuli that contribute to priming in these tasks (Soler et al., 2006). When word-fragments or word-stems are used, variables associated to the words from which the fragments or stems are constructed, and also to the fragment itself, should be controlled because they contribute to priming. Available evidence (Erickson et al., 1987; Olofsson and Nyberg, 1992; Dasí et al., 2004) has shown that two factors account for variance in priming: a lexical factor representing accessibility to a lexical representation in memory, and a perceptual factor representing the perceptual information present in the fragment. The first factor is associated with the variables: number of meanings, frequency and familiarity of the word; and the second with the variables: number of letters given in the fragment, ratio of given letters to blanks and first and/or last letters given. Additionally, the estimation of priming should be made using normative data (Soler et al., 2006). In most research studies that use implicit tests, the proportion of correct completions of fragments whose words were not previously processed is considered to be the baseline of the participant’s performance. And, in turn, is the reference value used to calculate priming. However, this procedure is a controversial issue in research because completion difficulty may vary considerably between fragments, introducing a great variability in the probabilities of correct completions within the set of fragments (Shaw, 1997; Ostergaard, 1998). As a consequence, the priming effect may be overestimated or underestimated. These potential problems could be controlled using fragments with a known difficulty that should be obtained from normative controlled studies, as is done with variables such as frequency or familiarity when verbal material is used in human memory experimental studies. However, the studies that we have reviewed have not been carried out in this way and the different patterns of observed results could be due to the absence of control over the factors listed above.

Finally, our review has shown that all the experiments used WSC tasks. In the past some research (Roediger et al., 1992) considered that WFC and WSC measure a similar form of perceptual memory, but recent research suggests that a “word-stem may invoke both conceptual and perceptual processes” (Bruss and Mitchell, 2005, p. 185). With this in mind, it seems reasonable to explore implicit memory in schizophrenia using a task free of conceptual components.

To sum up, the review provides two conclusions. Firstly, only four studies have an adequate design to measure implicit memory in accordance with the classical priming definition, and these four used a WSC task. Secondly, they yield conflicting results. Randolph et al. (1993) and Kern et al. (2010) concluded that patients exhibit impaired implicit memory, but Bazin and Perruchet (1996) and Perry et al. (2000) concluded that implicit memory was not impaired in patients with schizophrenia.

Therefore, the necessity to explore implicit memory in schizophrenia with a more methodologically sound approach is evident. To this end, we have designed an experiment to compare patients with schizophrenia with healthy participants on implicit memory using a WFC task because we wanted to use a pure measure of perceptual implicit memory. The Bruss and Mitchell (2009) study revealed that one of the tasks making unique use of perceptual processes was WFC. Furthermore, the selection of the fragments used in the task was made from a normative database with the purpose of having control over the lexical and perceptual factors that determine fragment completion probability. This information is available in a normative database for Spanish word-fragments (Dasí et al., 2004, 2007; Soler et al., 2009).

2. Method

2.1. Participants

All the participants were recruited from the population of schizophrenia outpatients at the Psychiatric Services, Health Assistance Center, Zamora (Spain). The inclusion criteria were as follows: (1) DSM-IV diagnosis of schizophrenia or schizoaffective disorder according to the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-1) (First et al., 2001). A psychiatrist performed the diagnostic interviews as part of the ordinary routines at the assistance center. (2) IQ above 70; (3) no substance abuse or dependence; (4) no organic cerebral diseases; and (5) to be in a stable phase of illness. A total of 32 patients, aged between 20 and 55, met the inclusion criteria and completed the assessment and the word-fragment task. The antipsychotic medication in the previous 3 months was stable for all patients. All patients were given the Spanish version (Peralta and Cuesta, 1994) of the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) as an index of symptom severity and the Global Assessment of Functioning (GAF) (American Psychiatric Association, 2000) to evaluate functioning. The PANSS has 30 items grouped in three scales that measure positive, negative and general psychopathology. The GAF gives an index on a scale from 1 to 100 that integrates three different dimensions: psychological, social and occupational function.

Intellectual function in all participants was assessed using a reduced version of the Wechsler Adult Intelligence Scale (WAIS-III) (Byler et al., 2000) that includes these...
The word-fragments were selected from the Soler et al. norms (2009). This database includes normative data of 269 one-solution Spanish word-fragments and provides information about relevant variables to the fragments: difficulty of completion or probability of correct fragment completion, priming index or capacity of an item to be primed, number of letters given in the fragment, first and/or last letter given, ratio of letters to blanks. There are also variables relative to the corresponding target words: familiarity, frequency, number of meanings, activation and valence. Two lists of 28 word-fragments were selected. The first contained low difficulty word-fragments and the second high difficulty word-fragments. In both lists the items were low frequency (2–25 per million), and had no significant differences in the indices contained in the norms, except in the case of priming because low difficulty word-fragments have low priming values and high difficulty word-fragments have high priming values (see Table 2). These two initial lists were combined to create two lists (A and B) containing high and low difficulty word-fragments. Half of the words in list A were randomly selected from the low difficulty list and the other half from the high difficulty list. The remaining word-fragments formed list B.

The WFC test was administered individually. The test had two phases. In the first phase, participants were required to judge their knowledge of 28 words on a scale anchored by: 1 known and 3 unknown, using a rating sheet. Half of the participants received list A as a rated list (studied word-fragments) and the other half list B. Following this phase, participants were given a filler task for a 5 minute period. They had to write first word that came to mind with the missing letters indicated by underscores (e.g. w_r__). Participants were instructed to write on a sheet the first word that came to mind to successfully complete the fragment. No explicit reference was made to the previously rated list. Twenty-eight of the word-fragments could be completed with the words from the rated list, and 28 with the remaining target words of the other list (non-studied word-fragments). Studied and non-studied word-fragments were presented randomly.

2.3. Data analysis

Statistical analyses were conducted on performance measures and priming, comparing groups, study conditions and difficulty of the fragments using ANOVAs.

### Table 1

Demographic and clinical characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Patient group (n = 32)</th>
<th>Control group (n = 30)</th>
<th>Test</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, M (S.D.)</td>
<td>39.59 (9.28)</td>
<td>40.27 (5.58)</td>
<td>t = −0.35</td>
<td>0.729</td>
</tr>
<tr>
<td>Gender, n (% male)</td>
<td>22 (68.75)</td>
<td>19 (60.31)</td>
<td>χ² = 0.20</td>
<td>0.652</td>
</tr>
<tr>
<td>Education in years, M (S.D.)</td>
<td>9.56 (2.11)</td>
<td>10.80 (2.71)</td>
<td>t = −2.00</td>
<td>0.051</td>
</tr>
<tr>
<td>IQ, M (S.D.)</td>
<td>77.09 (13.31)</td>
<td>77.0 (13.31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of illness (years since diagnosis), M (S.D.)</td>
<td>16.63 (10.57)</td>
<td>105.93 (8.10)</td>
<td>t = 6.56*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Antipsychotic medication, n (%)</td>
<td>First-generation 9 (28.13)</td>
<td>First and second generations 14 (43.75)</td>
<td>9 (28.13)</td>
<td></td>
</tr>
<tr>
<td>PANSS-general</td>
<td>23.06 (8.46)</td>
<td>26.00 (7.93)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANSS-negative</td>
<td>9.09 (3.79)</td>
<td>9.09 (3.79)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANSS-total</td>
<td>48.06 (17.82)</td>
<td>49.66 (13.55)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PANSS, Positive and Negative Syndrome Scale; GAF, Global Assessment Functioning.

a d.f. = 60.
b d.f. = 1.

c F(1,60) = 11.08, P < 0.001.
d F(1,60) = 456.32, P < 0.001.
e F(1,60) = 271.85, P < 0.001.
f F(1,60) = 447.10, P < 0.001.
g F(1,60) = 11.08, P < 0.001.
h F(1,60) = 456.32, P < 0.001.

The core dependent variables in the WFC test were the percentages of correctly completed fragments and priming. Implicit memory or priming was calculated subtracting the percentage of correct, non-studied, completed word-fragments from the percentage of correct, studied, completed word-fragments.

### Table 2

Word-fragments means and S.D. in the normative indices.

<table>
<thead>
<tr>
<th>Index</th>
<th>Low difficulty list</th>
<th>High difficulty list</th>
<th>r²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty</td>
<td>0.82 (0.08)</td>
<td>0.33 (0.11)</td>
<td>19.12</td>
<td>0.001</td>
</tr>
<tr>
<td>Priming</td>
<td>0.12 (0.07)</td>
<td>0.32 (0.14)</td>
<td>6.56</td>
<td>0.001</td>
</tr>
<tr>
<td>Familiarity</td>
<td>4.90 (1.11)</td>
<td>4.50 (1.24)</td>
<td>1.26</td>
<td>0.213</td>
</tr>
<tr>
<td>Frequency</td>
<td>11.14 (7.52)</td>
<td>11.12 (7.20)</td>
<td>0.01</td>
<td>0.991</td>
</tr>
<tr>
<td>Number of meanings</td>
<td>3.71 (2.09)</td>
<td>4.50 (2.90)</td>
<td>1.16</td>
<td>0.250</td>
</tr>
<tr>
<td>Number of letters given</td>
<td>3.50 (0.51)</td>
<td>3.46 (0.58)</td>
<td>0.25</td>
<td>0.807</td>
</tr>
<tr>
<td>First and/or last letters given</td>
<td>1.36 (0.56)</td>
<td>1.07 (0.60)</td>
<td>1.84</td>
<td>0.072</td>
</tr>
<tr>
<td>Ratio of letters to blanks</td>
<td>1.50 (0.37)</td>
<td>1.36 (0.42)</td>
<td>1.35</td>
<td>0.182</td>
</tr>
<tr>
<td>Activation</td>
<td>4.87 (1.07)</td>
<td>4.71 (1.10)</td>
<td>0.56</td>
<td>0.581</td>
</tr>
<tr>
<td>Valence</td>
<td>4.95 (1.39)</td>
<td>5.38 (1.34)</td>
<td>1.16</td>
<td>0.249</td>
</tr>
</tbody>
</table>

a d.f. = 54.

The two groups did not differ on any of the demographic variables, but the difference was nearly significant in years of education. To explore whether years of education influenced the study findings, we ran parallel analyses including and excluding education as a covariate. However, its inclusion as a covariate did not alter any results. Therefore, we report the results of analyses that do not include education as a covariate.

3. Results

The two groups did not differ on any of the demographic variables, but the difference was nearly significant in years of education. To explore whether years of education influenced the study findings, we ran parallel analyses including and excluding education as a covariate. However, its inclusion as a covariate did not alter any results. Therefore, we report the results of analyses that do not include education as a covariate.

3.1. Performance

Performance (see Table 3), the proportion of correctly completed fragments, was analyzed with a 2×2×2 mixed ANOVA, with group as a between-subject factor and with both study conditions (fragments from studied/non-studied words) and difficulty (high/low) as within-subject factors. Results showed significant differences between groups [F(1,60) = 11.08, P < 0.001]. Schizophrenia patients' performance was below that of control participants. Study condition was also significant [F(1,60) = 271.85, P < 0.001]. The proportion of correctly completed word-fragments was higher in fragments corresponding to words previously processed than in fragments corresponding to words not previously processed. The third analyzed factor, word-fragment difficulty, was also significant [F(1,60) = 456.32, P < 0.001]. Performance on high difficulty fragments was worse than on low difficulty fragments. The ANOVA also revealed a significant interaction effect between group and study conditions [F(1,60) = 7.06, P < 0.01]. Simple effects follow-up analyses indicated that patients with schizophrenia [F(1,31) = 232.34, P < 0.001] and healthy controls [F(1,29) = 77.37, P < 0.0001] completed more studied than non-studied word-fragments, reflecting the effect of intact implicit memory. Simple effects also showed significant differences between the two groups on non-studied fragments [F(1,60) = 15.97, P < 0.001]. Control participants completed more non-studied fragments than patients with schizophrenia. But there were no significant differences between healthy controls and patients in the studied fragment condition [F(1,60) = 2.80, P = 0.099]. No other significant interaction was observed.

<table>
<thead>
<tr>
<th></th>
<th>Studied words</th>
<th>Non-studied words</th>
<th>Total</th>
<th>Priming</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>S.D.</td>
<td>Mean</td>
<td>S.D.</td>
</tr>
<tr>
<td>Patients (n = 32)</td>
<td>72.54</td>
<td>14.09</td>
<td>40.74</td>
<td>14.05</td>
</tr>
<tr>
<td>Controls (n = 30)</td>
<td>77.86</td>
<td>10.50</td>
<td>54.88</td>
<td>13.80</td>
</tr>
</tbody>
</table>
In summary, global performance in the WFC task indicates that patients with schizophrenia perform significantly below healthy control participants when fragments have not been previously processed. Patients' performance is 14.14% below that of control participants (Cohen's $d$ effect size = 0.91). This pattern appears to be independent from the difficulty of the fragments: 13.61% for high difficulty fragments (Cohen's $d$ effect size = 0.78) and 14.67% for low difficulty fragments (Cohen's $d$ effect size = 0.76). However, patients with schizophrenia perform at the same level as control participants when word-fragments correspond to previously processed words.

### 3.2. Priming

A two-way mixed ANOVA was carried out on priming, the difference in performance between studied and non-studied words, to determine whether priming was different in the groups and whether difficulty has an effect on priming. The ANOVA revealed a significant group effect ($F(1,60) = 7.07, P<0.01$), but the fragment difficulty effect and the interaction between group and difficulty were not significant. Priming was significantly worse in healthy controls than in patients (see Table 3). These quantities of priming are similar to the magnitudes observed in other previous studies (Ruiz et al., 2007). The higher priming in the patient group appears because their performance is lower than that of control participants in the non-studied fragments. As a consequence, their benefit after the study phase is around 9% greater (Cohen's $d$ effect size = 0.64).

### 4. Discussion

The main interest of the present study was to determine if implicit memory is preserved in patients with schizophrenia. Although literature usually presents implicit memory as a non-impaired cognitive function in schizophrenia, the multiplicity of tasks used to measure it and the different underlying perceptual and conceptual memory processes that they make use of, have yielded contradictory results.

The primary finding in our study was that perceptual implicit memory is preserved in patients with schizophrenia. Patients with schizophrenia showed a significant priming effect supporting the hypothesis that these patients have an intact implicit memory. Furthermore, their priming is within the range of priming values reported in other normative studies based on hundreds of healthy control participants (Soler et al., 2009).

Despite the comparable results in implicit memory in both groups, the performance of patients with schizophrenia is about 14% below that of control participants in the percentage of completions when fragments had not been previously processed. This initial lower performance could be associated to a general intellectual impairment and to the attention deficit that characterizes schizophrenia. Previous studies have shown a significant positive correlation between intellectual function and execution on fragments not previously processed. Ruiz et al. (2007) compared two groups of patients with schizophrenia, one with an IQ above 85 and the other below 85, in a word-fragment completion implicit memory test. Differences between the two groups appeared in the proportion of completed fragments from previously unprocessed words. This measure was the only one that correlated significantly with IQ. Our study has replicated this result; the patients group IQ was 87.69 and the correlation between this variable and performance on non-studied fragments was significant ($r = 0.45; p = 0.01$). The correlation was also significant in the case of studied fragments ($r = 0.55; p = 0.001$).

However, it should be emphasized that this lower starting level of performance reaches a level similar to that of control participants when the fragments are previously processed. The previous non-explicit processing of the words seems to be enough to compensate for the initial deficit and this suggests that implicit memory capacities in schizophrenia should be considered in the development of cognitive rehabilitation programs.

There are two reasons to consider that our results are relevant. Firstly, they have been obtained by controlling all the critical variables involved in the experimental design in this type of task. The prior studies have an inadequate control over relevant indices of the stimuli, words and fragments, like frequency and difficulty. In our experiment, one of the variables manipulated to determine its influence on subjects' performance was fragment difficulty, whereas word frequency was matched. Our findings supported the expected results showing that in both groups performance was worse in fragments of higher rather than lower difficulty. Secondly, although the standard task used in all the reviewed studies is WSC, our results were obtained using WFC, an implicit task that uniquely taps perceptual processes (Bruss and Mitchell, 2009). Our review revealed that all the experimental research that focused on the study of implicit memory using accuracy measures was performed with different modalities of WSC. However this task has some limitations when it comes to studying implicit memory.

While word-stem is often classified as a data-driven task in which the stems evoke the perceptual identification record of the target, several results have shown that there need not necessarily be a perceptual relation between prime and target to elicit priming. For example, priming has been obtained with homophone word primes and stem targets (Ruецk and Mathew, 1999) with associate word primes and stem targets (McKone and Murphy, 2000), or with auditory word primes and visual stem targets (Blum and Yonelinas, 2001). Moreover, Bruss and Mitchell’s (2009) study using factor analysis on data from 11 memory tasks, showed that four factors, related with explicit memory (episodic and semantic) and implicit memory (conceptual and perceptual) accounted for 60.7% of the variance. In this study the word-stem task did not load in any of the four factors. These authors concluded that word-stem “appears to tap unique processes or systems, processes that show almost no statistical relationship with the perceptual or conceptual processes tapped by the other implicit measures used” (Bruss and Mitchell, 2009, p. 182). As a consequence this task complexity should be considered when it is used in the study of implicit memory because it could explain conflicting findings like for example those of Randolph et al. (1993) and Bazin and Perruchet (1996). Although their studies use experiments that, in accordance with the operational definition of priming used in our review are clearly well designed, they nonetheless have obtained conflicting results.

In short, it was important to test perceptual implicit memory with a less complex task, one that was able to make use of only perceptual processes. Hence we used a word-fragment task and the results have confirmed that perceptual implicit memory is preserved in patients with schizophrenia. However, future studies on perceptual or conceptual implicit memory in schizophrenia could be carried out to compare performance in word-stem and word-fragment completion.

### Conflict of interest

The authors have no conflict of interest.

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