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# Executive Functions Influence on Memory Process in Patients with Paranoid Schizophrenia and Bipolar Disorders with and without Psychotic Symptoms. A Pilot Study

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**Abstract.** The objective of the present study was to evaluate whether declarative memory deficits are related to executive function deficits (EF), since they could be a consequence of a poor organization of the material to memorize. This interaction between both cognitive processes can be studied simultaneously in a single task such as the Test of Memory Strategies (TSM). 23 patients with paranoid schizophrenic disorder, 11 with bipolar disorder with psychotic symptoms, 13 with bipolar disorder without psychotic symptoms and 15 healthy subjects were evaluated with the TSM; with the memory test Texts A and B (subtest of the Barcelona neuropsychological assessment battery), which assesses short-term and immediate recall without the influence of EF; and with the Trail Making Test (TMT): Part A (sustained attention) and Part B (executive control). The patients groups and the control group showed an improvement in memory performance across each of the TSM conditions. However, this facilitating effect of the strategies differed among the groups (the patients with higher EF deficits showed less improvement). Regarding these results, we conclude that this cognitive process cannot be independent of EF. However, due to the pilot nature of this study, it would be recommended to replicate these findings in new studies.

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The interrelation between executive functions (EF) and memory, and how it could explain the observed deficits in both cognitive domains in several pathologies, has been widely acknowledged in the literature. Since deficits in memory and EF are well established as characteristics of bipolar disorder and schizophrenia (Amann et al., 2012) is of interest for us, study the characteristic cognitive impairment of these two processes in individuals affected from bipolar (Amann et al., Bora et al., 2010; Martínez-Arán et al., 2001; Robinson et al., 2006; 2012) and schizophrenic disorders (Amann et al., 2012; Balanzá-Martínez & Tabarés-Seisdedos, 2009). Such impairment influences patients' performance on neuropsychological assessment, rendering it difficult to distinguish whether the typical underperformance in memory tests is a by-product of other impairments e.g., EF. This, in turn, ultimately biases the intervention and rehabilitation provided to the individual. It seems thus necessary to understand the interplay between these processes in order to gain better understanding of the disorders and to design appropriate interventions.

EF comprise a series of cognitive processes related to goal formulation and planning, as well as to effective coordination and execution of the pertinent behaviours. This supervisory role of EF includes the generation of strategies to code and retain information. These strategies in turn maximize working memory (i.e., a storage wherein information is maintained actively and temporarily so that the individual can manipulate it, Baddeley,

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2000; 2002; Logie, 2003) by easing the organization, search, selection, and verification of information stored (Yubero et al., 2011; Shimamura, 2000; 2002). Therefore, there is an association between EF and working. This association could imply that impairments observed in the latter related to executive dysfunctions might arise due to problems in the generation of appropriate strategies to store information, rather than with the information itself. Such an approach could be taken to understand the impairments observed in patients with bipolar (Bora et al., 2008; Caixeta et al., 2017; Thompson et al., 2006) and schizophrenic disorders (Berberian et al., 2009, 2016; Trapp et al., 2017; Wonguppara et al., 2015). Studies employing neuroimaging techniques have found evidence supporting the idea that both processes would be related via certain areas in the dorsolateral prefrontal cortex (Major et al., 2015). These brain areas are highly involved in working memory (Baddeley, 1996; Fuster, 2009; Koechlin et al., 1999; Manoach et al., 1997; Smith & Jonides, 1999) and their dysfunction could explain the associated cognitive impairments in schizophrenia and bipolar disorder (Konopaske et al., 2014; Perlstein et al., 2001).

The interplay between impairments in EF and memory in these populations had been proposed before: Gjerde (1983) suggested that the performance on memory tasks of patients with schizophrenia could be improved if they were given an organisational aid of the input. Likewise, Vázquez et al. (1989) attributed the underperformance on memory tasks of schizophrenia patients to a poor organization of the material employed, arguing that an inappropriate codification of information was central to the memory deficits of this population (Hartman et al., 2003; Lencz et al., 2003; Tek et al., 2002). The same reasoning has been applied to patients with bipolar disorder (e.g., Robinson et al., 2006).

### *Evaluation of the Influence of Executive Function on Memory: The Test of Memory Strategies (TMS)*

Given this situation, it is interesting to consider the objective of using a parametric task capable of evaluating both EF and memory. The Test of Memory Strategies (TSM; Yubero et al., 2011) has five declarative memory tasks, which are presented with gradually increasing strategies for storing information such that the need of control by EF is less necessary as the test progresses. This is based on the idea that memory tasks depend on the organisation of the information to be stored (Logan et al., 2002; Maestú et al., 2003; Savage et al., 2001). One of the roles performed by EF is the generation of appropriate strategies in situations wherein information is ambiguous and non-structured (Maestú et al., 2003; Savage et al., 2001), so that in situations wherein strategies for codification are given, memory performance should be better than when no strategies are given. The test, therefore, allows the researcher to assess whether the impairment relies on primary memory itself (e.g., retrieval of information) or on problems coding information because the individual is incapable of generating effective strategies.

Yubero et al. (2011) employed the TMS to study the effect of providing strategies on the declarative memory performance of individuals with healthy and pathological aging. The gradual reduction in the requirements to generate strategies to memorise the elements of the task diminished the negative effect that healthy aging usually has on neuropsychological memory tasks. This allowed the authors to differentiate between healthy and pathological aging. Therefore, the main characteristic of the TMS (i.e., the gradual input of strategies to code information) makes it a tool capable of discriminating between problems in executive functioning that impair memory and problems in memory itself.

In this study we have tried to test the following hypothesis: If deficits in memory in patients with schizophrenia and bipolar disorder are cause by deficits in EF, then both groups should improve their performance as they progress through the TMS given the gradual need of less executive function input. This in turn would mean that the crucial problem in these populations is the lack of capacity of generating effective strategies to codify and thus maintain and retrieve information.

## Method

### *Participants*

62 participants were distributed in four groups: Patients suffering from schizophrenia subtype paranoid ($N$ = 23 / mean age = 39.56 / mean age with the disorder = 15.43/ male = 15, female = 8 / Primary school = 5, Secondary school = 16, Diploma = 2); patients with bipolar disorder without psychotic symptomatology ($N$ = 13 / mean age = 44.61 / mean age with the disorder = 15 / male = 3, female = 10 / Primary school= 3, Secondary school = 8, Diploma = 1, College = 1); patients with bipolar disorder with psychotic symptomatology ($N$ = 11 / mean age = 45.27 / mean age with the disorder = 12.5 / male = 4, female =7 / Primary school = 3, Secondary school = 7, College = 1); and a control group of participants without pathologies ($N$ =15 / mean age = 36 / male = 10, female = 5 / Secondary school = 8, Diploma = 2, College = 5). Patients were recruited from the Short-Term Hospitalization Unit from the following hospital; Hospital D. Rafael Lafora (Madrid), Fundacion Hospital de Alcorcon (Alcorcon, Madrid), Hospital Gregorio Marañón (Madrid), and Complejo

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Asistencial Benito Memni (Ciempozuelos, Madrid). Participation was voluntary and informed consent was given prior to participation. Participants for experimental groups (i.e., patients with schizophrenia and bipolar disorder) were chosen following the criteria from the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM–IV–TR; American Psychiatric Association [APA], 2002). The control group was assessed via an open interview. Exclusion criteria for control group assessed whether participants had reading and/or writing impairments. Furthermore, participants did not have any prior diagnoses of mental or neurological illness, did not consume drugs, whether they were familiar with the tests employed, and if they had any sensorial and/or motor deficits that could interfere with the performance of the tasks. Each patient's medical history was examined to decide whether they met the inclusion or exclusion criteria. All patients presented an optimal response to their corresponding medications and were euthymic at the time of the evaluation.

A evaluation of the executive function of the subjects was also made through the Trail Making Test, Parts A & B (Reitan, 1958; Reitan & Wolfson, 1985), (mean in seconds/standard error): Schizophrenia subtype paranoid: Part A: 75.61/9.11; Part B: 153.48/13.42 / Patients with bipolar disorder without psychotic symptomatology: Part A: 73.54/22.43; Part B: 109.00/20.53 / Patients with bipolar disorder with psychotic symptomatology: Part A: 67.45/9.09; Part B: 139.82/22.13 / Control group: Part A: 34.87/2.90; Part B: 77.00/7.70. The Bonferroni contrasts showed differences between the control group and the group of schizophrenics and bipolar with psychosis, not detecting any other difference between the groups. This data is in favor of studies that indicate that bipolar patients with psychosis have a worse cognitive performance in neuropsychological tests (Cavanagh et al., 2002; Clark et al., 2002) similar to that of schizophrenia.

### *Instruments*

TMS was developed to assess declarative memory via five lists comprising ten low-, medium- and high-frequency words (Algarabel, 1996) randomly distributed in each trial. The evaluator reads each list at a pace of a word every two seconds. Both the instructions and the lists incrementally increase in their external organisation, thereby, fewer self-generated memory strategies are required to perform the same task (i.e., memorize ten words). TMS assess auditory attention, incidental memory (immediate recall) and participants' abilities to develop consciously relationships and semantic categories – skills related to executive functioning. The five lists are distributed and organized in the following manner:

(i) TMS–1: Consists on an incidental-learning task, which includes a list of ten words unrelated semantically and/or phonologically. Participants are not aware that it is a memory task. The instructions given by the evaluator are: "Now I am going to read you a series of words. I need you to pay attention because you will be asked afterwards". In this first list the evaluator shall not say the aim of the task (i.e., the posterior recall of words). In case the participant asks about the goal, the evaluator should answer "The aim will be explained afterwards, by now pay as much attention as possible to the words".

(ii) TMS–2: This is an explicit learning task involving a new list of ten words unrelated semantically or phonetically. This time, participants are aware that they are performing a memory task. The evaluator will explain to them: "Now I am going to read a list of words, I want you to pay attention as you will have to recall as many as possible afterwards".

(iii) TMS–3: This time, the words comprising the list are semantically distributed in two categories: Trees and furniture. Words are presented randomly with semantical categories mixed. Participants should not be told about the existence of these categories. Instructions are as follows: "Now I am going to read you a list of words, I want you to pay attention as you will have to recall as many as possible afterwards".

**Table 1.** *Characteristics of the Sample*

| | *N* | Age (years) | Mean duration of illness (years) | Female | Male |
|---|---|---|---|---|---|
| Controls (C) | 15 (24.%) | 36 | - | 5 (33.3%) | 10 (66.7%) |
| Patients with schizophrenia (SZ) | 23 (37.1%) | 39.56 | 15.43 | 8 (34.8%) | 15 (65.2%) |
| Patients with bipolar disorder and psychotic symptomatology (BPD) | 11 (17.7%) | 45.27 | 12.5 | 7 (63.6%) | 4 (36.4%) |
| Patients with bipolar disorder (BD) | 13 (21.0%) | 44.61 | 15 | 10 (76.9%) | 3 (23.1%) |
| Total | 62 (100%) | 40.77 | 11 | 30 (48.4%) | 32 (51.6%) |

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(iv) TMS–4: As in TMS–3, ten words are distributed in two different semantic categories: Means of transportation and colours. Yet, in TMS–4 these categories are not mixed when presenting the words: The first five words belong to the former category, and the five last, to the latter. Once again, participants are not warned about the existence of these categories. The evaluator's instructions are: "I am going to read a list of words, I want you to pay attention as you will have to recall as many as possible afterwards".

(v) TMS–5: The words on the final list are also presented in two, non-mixed, semantical categories: The first five belong to that of sports, and the last five to vegetables. Contrary to previous lists, participants are warned in the instructions about this distribution: "Now I am going to read you a series of words. These words have been distributed in two semantic categories, I want you to pay attention as you will be later asked to recall as many as possible." If needed, evaluator would explain the participant what is meant by semantic category.

Likewise, memory was assessed with the neuropsychological test Text Memory Test A and B (TMT; *Test Barcelona;* Peña-Casanova, 1990) to assess short-term memory and immediate recall without the influence of EF. This was done to analyse to what extent impairments on memory can explain the performance on the TMS. The Text Memory Test assesses immediate recall and short-term memory. This test comprises two texts that differ in the amount of information they contain and the familiarity of individuals to them. Therefore, Text B is more difficult to memorise, and thus requires more effort from the subject. The subject's task is to repeat each text once is read to them. 1 point is given if the subject recalls a fragment perfectly, and 0.5 if the subject recalls something similar to the original fragment. The total score for Text A is 9 points, and 14 points for Text B. Both TMS and TMT were administered in Spanish by the same evaluator within a single session.

A baseline measure of FE was also taken with the Trail Making Test (Reitan, 1958; Reitan & Wolfson, 1985) has two parts called A and B. It is a timed test and the goal is to complete the tests accurately and as quickly as possible. Form A: The subject must join a series of dots numbered from 1 to 25 in the shortest possible time. Form B: The subject must join a series of numbers by inserting the letters of the alphabet (1–A–2–B–3–C…) like this until reaching 1 to 13. If a mistake is made, the administrator must inform the person immediately and move the pencil back to the last correct circle. Part A is a good measure of sustained attention and Part B is sensitive to executive functioning (Arbuthnott & Frank, 2000).

Procedure: We processed first by passing the TMT (trail making test) Forms A and B, then the text memory test and then, after a rest period of about 15 minutes, the TMS.

### *Data Analyses*

#### *Test of Memory Strategies*

The TMS was measured using the number of recalled items in each condition. We fitted the data in two linear models. To check that data met ANOVA assumptions, Levene test of homogeneity, Mauchly spherecity test, and a contrast for the interaction between factor and covariable were run.

The first model included group as a between-group factor and scores in each list of the TMS as within-groups factor. Descriptive statistics (Table 2) showed a right-skewed distribution of scores. However, these scores were not transformed given the robustness of linear models against slight deviations. This first model met the homogeneity assumption (the smallest significance in Levene test was for scores from TMS4, $p = .074$), but not the sphericity assumption, $\chi^2(9)=23.99$; $p < .01$,

**Table 2.** *Descriptive Statistics for Each List of the Test of Memory Strategies per Group*

| List TMS | M | SD |
|---|---|---|
| Control | | |
| 1 | 3.80 | 1.37 |
| 2 | 5.00 | 1.07 |
| 3 | 6.47 | 1.41 |
| 4 | 8.33 | 1.05 |
| 5 | 7.80 | 1.26 |
| Patients with schizophrenia (SZ) | | |
| 1 | 2.04 | 0.98 |
| 2 | 3.43 | 1.38 |
| 3 | 4.35 | 1.75 |
| 4 | 5.83 | 2.04 |
| 5 | 4.91 | 2.31 |
| Patients with bipolar disorder and psychotic symptomatology (BPD) | | |
| 1 | 2.09 | 1.30 |
| 2 | 3.82 | 1.54 |
| 3 | 4.82 | 1.47 |
| 4 | 6.36 | 2.66 |
| 5 | 5.73 | 2.24 |
| Patients with bipolar disorder (BD) | | |
| 1 | 2.54 | 1.66 |
| 2 | 3.92 | 1.66 |
| 3 | 5.38 | 1.89 |
| 4 | 6.38 | 1.89 |
| 5 | 6.08 | 2.22 |

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and thus a Greenhouse-Geisser correction was applied ($\varepsilon = 0.81$).

The second model was nested in the first one and included scores on TMT as a covariate variable. As what happened with the first model, homogeneity was met (smallest significance $p = .097$) but not sphericity, $\chi^2(9) = 23.04$; $p < .01$, so Greenhouse-Geisser correction was applied ($\varepsilon = 0.81$).

Effect size is reported as partial eta square ($\eta_p^2$). Post-hoc Bonferroni comparisons were run for significant effects of a variable.

## Results

### *Test of Memory Strategies*

Table 2 depicts descriptive statistics of scores on each list of the TMS per group. Means and standard deviations match what was expected. The distribution of means shows an expected trend: recalled items increase as memory strategies were provided (Figure 1 Left), except for TMS5 where in performance is worse than in TMS4 for both experimental and control groups following Yubero et al. (2011). This trend could be attributed to either instructions or the words employed and suggests a review of both.

Analysis of the first model showed a significant effect for group, $F(3, 58) = 8.82$; $p < .001$; $\eta_p^2 = .31$, and for conditions of the TMS, $F(3.23, 187.83) = 101.45$; $p < .001$; $\eta_p^2 = .63$, but not for the interaction between the two, $F(9.71, 187.83) = 0.73$; $p = .692$; $\eta_p^2 = .03$. Bonferroni comparisons for groups showed two distinctive groups: one formed by the control group, whose scores were significantly better than those of the experimental groups ($p < .001$ for patients with schizophrenia, $p < .05$ for patients with bipolar disorder without psychosis, and $p < .001$ for patients with bipolar disorder with psychosis); and a second group formed for experimental groups, with no significant differences among them. The same comparison for conditions of the TMS showed significant differences among all of them, even for those including the TMS–5 condition.

The second model's homogeneity of the slopes was tested with the interaction of the covariate with the measurements from TMS, which yielded a non-significant result, $F(3.25, 185.72) = 1.34$; $p = .254$. An ANCOVA showed significant differences between levels of the TMS, $F(3.25, 185.72 = 4.80$; $p < .01$; $\eta_p^2 = .08$; but not for group, $F(3.57) = 1.45$; $p = .238$; $\eta_p^2 = .07$; nor the interaction, $F(9.77, 185.72) = 0.55$; $\eta_p^2 = .02$. In line with the previous Bonferroni comparisons, there were significant differences among all levels of the TMS.

Figure 1 depicts the influence of memory on participants' performance. The left side of the picture shows the means of each group on the TMS, with the control group performing the best. The right side of the picture depicts the estimated means when memory influence is removed. This picture shows that performance on the TMS is similar for all groups, thus all groups show a similar trend of improvement when given memory strategies. This can be regarded as a proof that memory deficits, and not deficits in executive functioning, lead to worse performance on memory tasks in participants with pathologies.

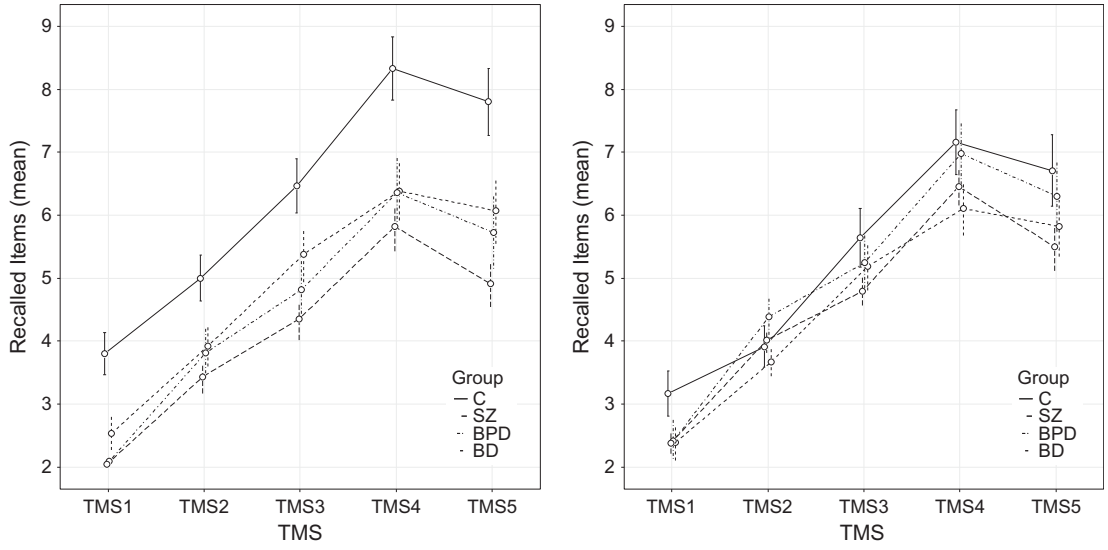


**Figure 1.** Recalled Items in Test of Memory Strategies per Group

*Note.* Means and confidence intervals (95%) for each list of the Test of Memory Strategies per group (C: Control, SZ: Patients with schizophrenia, BPD: Patients with bipolar disorder and psychotic symptomatology, and BD: Patients with bipolar disorder), when effects of memory are removed (right), and when they are not (left).

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### *Test of Memory Strategies and Test of Memory Strategies (TMS)*

The deficits observed in memory in patients with schizophrenia and bipolar disorder have been hypothesized to be attributable to deficits in executive functioning, given the interplay between both cognitive processes. To test this hypothesis, we employed the Test of Memory Strategies (TMS), which assesses the impact of different forms of coding information on memory. To assess memory performance, the Text Memory Test A and B (TMT) was employed (Table 3). A control group and 3 experimental groups, comprised by patients with these disorders, took the test and their performance was compared. After subtracting from their scores, the variance explained by memory, we found that performance on the task improved in a similar fashion for both the pathological and the control group. This finding suggests that in the group with pathology, the main difference in performance is due to previous deficits in executive functions, evidenced by the improvement achieved when executive process were minimized progressively in Conditions 3, 4 and 5 of the TMS. In addition, patients in this sample were able to detect the organization of the material and taking advantage of the strategies given by the organization of the material.

## Discussion

This finding is due to the test employed, which requires both EF and general memory processes in order to take it. In this study, the control group showed a higher number of words recalled at the beginning of the task. This is because they showed no memory impairments and good executive function abilities. Therefore, the starting point of each group with or without pathology was different. These results follow previous literature (e.g., Abellán-Martínez et al., 2019; Fernandes et al., 2018; Yubero et al, 2011;): studies on patients with Amnesic Mild Cognitive Impairment, Multidomain Mild Cognitive Impairment, Vascular Cognitive Impairment and Elderly with Depression found that each group improved their performance across TMS conditions. This benefit was similar across groups in the current study. Differences in the total score were explained by the authors as reflecting a previous executive disorder in the initial conditions of the TMS in the vascular and depressive participants. However, the MCI patients showed a primary episodic memory impairment with a slight improvement when executive functions demands were minimized. In this study the psychiatric population showed a clear improvement on memory test performance when the material was progressively organized, with a similar pattern than that found in Yubero et al. (2011) in vascular and depressive patients.

Overall, the current study highlights that patients with schizophrenia and bipolar disorder were as able as control groups to detect and employ the strategies provided throughout the test to code and memorise the items. This is relevant given that deficits in executive functions and memory are key aspects of daily life of patients with schizophrenia (Amann et al., 2012; Balanzá-Martínez & Tabarés-Seisdedos, 2009) and bipolar disorder (Amann et al., 2012; Bora et al., 2008; Martínez-Arán et al., 2001; Robinson et al., 2006).

**Table 3.** *Performance of Patients and Control Subjects on the Text Memory Test A and B (TMT, Test Barcelona) of Immediate Recall*

| | | | | 95% CI | |
|---|---|---|---|---|---|
| Text Memory | *N* | *M* | *SE* | *LL* | *UL* |
| Text Memory A | | | | | |
| Control | 15 | 0.74 | 0.05 | 0.65 | 0.84 |
| Schizophrenia (SZ) | 23 | 0.58 | 0.04 | 0.50 | 0.66 |
| Bipolar disorder (BD) | 13 | 0.70 | 0.05 | 0.60 | 0.80 |
| Bipolar disorder and psychosis (BPD) | 11 | 0.55 | 0.06 | 0.43 | 0.66 |
| Total | 62 | 0.64 | 0.20 | 0.59 | 0.69 |
| Text Memory B | | | | | |
| Control | 15 | 0.63 | 0.04 | 0.55 | 0.72 |
| Schizophrenia (SZ) | 23 | 0.28 | 0.03 | 0.21 | 0.35 |
| Bipolar disorder (BD) | 13 | 0.43 | 0.05 | 0.34 | 0.52 |
| Bipolar disorder and psychosis (BPD) | 11 | 0.31 | 0.05 | 0.21 | 0.40 |
| Total | 62 | 0.40 | 0.22 | 0.35 | 0.45 |

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Results for the current study show that those populations would benefit significantly from the use of external context facilitators and elements of organisation in tasks. In this sense, the patients herein tested were capable of following the external organization of the material improving their ability to memorize the items proposed. This could improve the development of guides and programmes tailored to these populations, so that they include precise and individualised instructions or organizing the context to improve the patients' daily lives, especially in situations wherein episodic memory is involved.

The effect of decreasing the mean of correct answers in the last condition of the TMS test for all the groups evaluated has also been observed when the TMS was applied to other populations: Elderly population (96 subjects with a mean age of 75.2 years) that comprised controls (subjects with normal ageing), Mild-Multidomain Cognitive Impairment, Mild-Amnesic Cognitive Impairment, Vascular Cognitive Impairment and elderly affected by major depressive disorder (Yubero et al., 2011). Which would indicate a misalignment in the design of the final test condition. This could be due to two different causes: 1) That the words of test 4 are easier to memorize than those of 5. Although the characteristics of imaginability, frequency, etc. have been homogenized of the words it is possible that a bias in any of these senses will escape in our original design. A review of the words included seems necessary for future studies; 2) on the other hand, it is possible that making the subject aware of the organization of the material, either produces a greater load on their working memory, making learning difficult, or that being aware of the organization does not improve performance. The combination of these two interpretations could justify the loss of linearity between conditions 4 and 5.

TSM was done for a simultaneous evaluation of cognitive processes and was used with subjects with dementias. This is the first time it is applied in a clinical population with psychotic symptoms. Given its character as a pilot study, there are some limitations in the present study. The size of the samples (access to subjects, especially those affected by bipolar disorder was not easy, so it would be advisable to replicate our findings in new studies with larger samples), the lack of more cognitive and clinical measures before the application of the test and a follow-up. Within the TSM test we can consider a more comprehensive control of linguistic aspects such as the articulatory difficulty of words or the number of syllables of each word. However, given the small number of subjects due to the pilot nature of this study, it would be recommended that these findings be replicated in new studies with larger samples.

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