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Efficacy of cognitive rehabilitation of attention, executive functions, and working memory in psychotic disorders: A systematic review

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Cognitive impairment is a core aspect of schizophrenia. Studies have postulated that it is the basis of the disease as evidenced by its independent and persistent quality and its relation to prognosis. Research on cognitive deficits in psychotic disorders has led to the development of intervention strategies for the cognitive rehabilitation of these patients. Attention, working memory, and executive functions are among the most widely affected functions and are closely related to the functionality of these patients. This work aims to study the effectiveness of cognitive rehabilitation targeting attention, executive functions, and working memory in people diagnosed with a psychotic disorder (mostly schizophrenia).

An exhaustive search in PubMed and PsycINFO was conducted up to January 2016. All research papers that were included studied a therapeutic technique to improve one or more of the aforementioned functions in patients over age 16 years diagnosed with psychotic disorder. Studies with methodological diversity were included, which were afterwards organized by levels of evidence. Thirty-four papers were studied, from which we can conclude that cognitive rehabilitation of the aforementioned cognitive functions brings about improvements in cognition. As a result of the influence of cognitive rehabilitation on other variables such as social functioning and symptoms of the disease, the results are promising.

Keywords: Cognitive rehabilitation, Attention, Executive functions, Working memory, Psychosis, Systematic review

Actas Esp Psiquiatr 2017;45(2):167-78

Eficacia de la rehabilitación cognitiva de la atención, funciones ejecutivas y memoria operativa en los trastornos psicóticos. Revisión sistemática

Los déficits cognitivos se consideran una parte primaria de la esquizofrenia y se postula que puedan estar en la base de la enfermedad dado su carácter independiente, persistente y determinante en el pronóstico. Paralelamente al desarrollo de los estudios de investigación sobre los déficits cognitivos en los trastornos psicóticos, se han ido desarrollando estrategias de intervención para la rehabilitación cognitiva de estos pacientes. La atención, la memoria operativa y las funciones ejecutivas están entre las funciones más afectadas, y se encuentran íntimamente relacionadas con la funcionalidad de estos pacientes. El objetivo de este trabajo fue estudiar la eficacia de la rehabilitación cognitiva de la atención, funciones ejecutivas y memoria operativa en personas diagnosticadas de trastorno psicótico (principalmente la esquizofrenia).

Para ello se realizó una búsqueda electrónica exhaustiva en las bases de datos PubMed y PsycINFO hasta enero de 2016 y se seleccionaron los artículos que estudiaban una técnica terapéutica orientada a la mejoría de una o varias de las funciones mencionadas, en pacientes mayores de 16 años diagnosticados de trastorno psicótico. Se seleccionaron estudios con diversidad metodológica que posteriormente se organizaron según su nivel de evidencia. Finalmente se estudiaron 34 artículos de los que se puede extraer que la rehabilitación de las funciones mencionadas produce mejoras a nivel cognitivo. En cuanto a su influencia sobre otras variables como el funcionamiento social y la sintomatología, los resultados son promisorios.

Palabras clave: Rehabilitación cognitiva, Atención, Funciones ejecutivas, Memoria operativa, Psicosis, Revisión sistemática

INTRODUCTION

Currently, over 80% of patients diagnosed with schizophrenia present with associated cognitive dysfunction¹. When compared to healthy subjects, these patients have cognitive deficits of between 1 and 2 standard deviations across different domains, including memory, language, attention, motor functions and visuospatial skills¹⁻³. Indeed, studies that predate the publication of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) advocated the inclusion of criteria on cognitive deficit when diagnosing schizophrenia, although this measure has not been enacted due to a lack of consensus on which criteria to include¹. Though there is no concrete cognitive profile for schizophrenia, studies have produced comparable findings on the severity of impairments in different neuropsychological domains. Perception, memory (recognition), naming, and visuospatial abilities show mild to moderate impairment, while executive functions, attention span, and processing speed are severely impaired (over 2 standard deviations below the healthy control group)^{4,5}. Attention, memory, and executive functions have traditionally been the most widely studied as well as the most severely impaired cognitive domains in schizophrenic patients⁶. Abnormalities have been described in both first-episode psychosis⁷ and in chronic patients⁸. These abnormalities are therefore present in the early stages of the disease and persist despite treatment.

Of all the symptoms of schizophrenia, cognitive deterioration has received the least attention for its study and diagnosis. However, these symptoms are now becoming recognized as a factor in poor rehabilitative outcomes in some patients despite the absence of psychotic symptoms, and it is currently believed these symptoms must be included in the treatment approach. Green⁹ ushered in a change in way schizophrenia is understood, showing that cognitive impairments have a definitive influence on the daily lives of patients with the disease. The findings published by Green⁹⁻¹¹ conclude that neurocognitive abnormalities more accurately predict social competence in schizophrenia patients than the positive and negative symptoms of the disease, explaining between 20% and 60% of variance in functional prognosis.

It is currently believed that neuropsychological symptoms may be at the root of the disease, given the fact that they are primary, independent, persistent, and play a determining role in prognosis¹².

Attentional impairments –with attention taken to be a cognitive function that enables individuals to remain in an alert state in order to process information, direct this processing toward concrete stimuli, provide continued responses, select from a number of choices, alternate between different tasks or focus on one source of input at a time¹³– and deficits

in executive functions –a series of cognitive processes including anticipation, choice of objectives, planning, choice of conduct, self-regulation, self-control, and reinforcement¹⁴– are associated with several symptoms of schizophrenia such as negative symptoms and social and emotional deficits¹² and formal thought disorder, related to a deficit in executing functions of discourse editing and planning¹⁵. Also, working memory is closely linked to executive function, and some classification systems consider working memory to be an executive function in itself. Working memory is usually defined as the ability to maintain and manipulate information over short periods of time, and for this reason is not a mere short-term repository but rather a function that relies on other processes^{16,17}. There is a clear deficit in all modalities of working memory which appears to be more related to an executive dysfunction than to the ability to store memory⁴ and primarily affects coding, retrieval, and executive control^{16,18}.

The clear cognitive impairment caused by schizophrenia and its impact on patient functioning and quality of life explain the existence of cognitive rehabilitation programs included in treatment approaches for psychotic disorders. Drug treatments have been shown to be effective for treating the psychotic symptoms of the disease, and particularly positive symptoms; drugs, however, have poor effectiveness in treating the cognitive symptoms¹⁹. Psychosis treatments have evolved from a model focused primarily on symptom relief to a “recovery” model, where the aims are improving patient quality of life and functioning. Cognitive rehabilitation plays a key role in recovery-based approaches. The overall aim of this paper is to assess the effectiveness of cognitive rehabilitation targeting attentional capacity, executive functions, and working memory for individuals diagnosed with psychotic disorders, particularly schizophrenia.

METHODS

Study selection criteria

The criteria used to select the studies included in this work appear in Table 1.

Study identification method

The electronic databases PubMed and PsycINFO were used as primary sources. In cases where full texts were not available in the aforementioned databases, searches were performed using ProQuest, ScienceDirect, Google Scholar, and ResearchGate; in some cases, direct contact was made with the principle investigators of the articles. The strategies used when searching the literature are included in Table 2.

Table 1	Search criteria
Criteria	Operational definition
Object of study	An action or therapeutic technique oriented to the improvement of attention and /or executive functions and /or operative memory in psychotic patients
Population	Patients over 16 years-old diagnosed with psychotic disorder, without comorbid neurological condition
Type of study	Original scientific paper, indexed in PubMed or PsycInfo database before January 2016
Type of design	Clinical trials (randomized or not), other experimental designs with test-retest measures and at least two groups (experimental and control, or two or more experimental groups), quasi-experimental designs of a single group with test-retest measures, and designs of a single subject or case studies

Following an initial search, a second-level search was performed of the bibliographic references appearing in a number of key recent reviews²⁰⁻²² and meta-analyses²³ in cases where the titles of these referenced works were relevant to our study objective. The secondary search was carried out using the same inclusion criteria as the first.

Data collection and analysis

Once the search had been carried out in the two databases, duplicate results were eliminated and all abstracts were reviewed to determine whether the texts met the eligibility criteria. The PEDro scale was applied to all papers included in the final selection to evaluate their methodological quality. This scale was created to assess the internal validity and statistical soundness of clinical trials, and its reliability has been studied previously²⁴ (Table 3).

Articles were categorized by level of evidence based on the PEDro scale score as well as other criteria appearing in Table 4, as indicated in a recently published set of guidelines for neurorehabilitation in acquired brain injury²⁵. As in the guide used as a reference, each level of evidence was also assigned a value for strength of recommendation. These values were assigned based on the international system of the National Health and Medical Research Council, which assesses recommendation strength based on the methodological reliability of the source of the empirical evidence (Table 4).

RESULTS

Of the 399 references that resulted from the searches, 34 articles were selected: 30 from the initial search and 4 from the second. The following subsection contains a

Table 2	Search strategy	
	PsycInfo	PubMed
Search	<i>("schizophrenia" OR "psychosis" OR "psychotic") AND ("cognitive remediation" or "cognitive training" OR "cognitive rehabilitation" OR "neuropsychological rehabilitation" OR "neuropsychological intervention" or "neuropsychological training" OR "neurocognitive enhancement") AND ("attention" OR "executive function" OR "working memory")</i>	<i>(("schizophrenia" OR "psychosis" OR "psychotic"[Title/Abstract])) AND ("cognitive remediation" OR "cognitive training" OR "cognitive rehabilitation" OR "neuropsychological rehabilitation" OR "neuropsychological intervention" OR "neuropsychological training" OR "neurocognitive enhancement"[Title/Abstract])) AND ("attention" OR "executive function" OR "working memory" [Title/Abstract])</i>
Filters	- Abstract	- Title/Abstract- Humans
Last entry	27/01/2016	27/01/2016
Number of references	186	213

Table 3		PE德罗 criteria
Criterion	Criterion description	
Eligibility criteria	Eligibility criteria were specified (the source of subjects and a list of criteria used to determine who was eligible to participate in the study)	
Random allocation	Allocation to groups was randomized. In crossover design studies, the order of initiation of treatments or experimental conditions is randomized	
Concealed allocation	The person who determined if a subject was eligible for inclusion in the trial was unaware, when this decision was made, of which group the subject would be allocated	
Similar baseline	Experimental groups showed similar values in outcome and prognostic variables at baseline	
Blinding of all subjects	Subjects in the study did not know which group they had been allocated and they were unable to distinguish between the treatments applied to different groups	
Blinding of all therapists	Therapists in the study were blinded to the group they had been allocated and they were unable to distinguish between the treatments applied to different groups	
Blinding of all assessors	All study investigators (at least those who evaluated at least one outcome measure) did not know which group the subject had been allocated to. In trials in which key outcomes are self-reported (eg, visual analogue scale, pain diary), the assessor is considered to be blind if the subject was blind	
Measures of at least 85% of the subjects	Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	
Analysis by "intention to treat"	All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by "intention to treat"	
Between-group comparisons	The results of between-group statistical comparisons are reported for at least one key outcome	
Measures of variability	The study provides both point measures and measures of variability for at least one key outcome	

detailed description of the selection process (Figure 1) and the articles included.

Description of the studies selected

Attention

We found 10 studies in which specific cognitive training was the only method used for treatment of attention deficits in patients diagnosed with a psychotic disorder.

- Evidence level IIa / Strength of recommendation B

Results surpassing those of the comparison group were found in only 2 of the 6 studies. Silverstein et al.²⁶ found

improved attention span in a group of chronic patients who were refractory to therapeutic measures designed to develop social competence. These patients received molding-based behavioral intervention using immediate reinforcement while they participated in a social competence program. The group improved their level of attention (i.e., focus, attention span, active and appropriate participation) during an intervention targeting social competence. As a result, the participants had a higher number and level of social skills compared to the control group (social-competence training without a specific focus on attention). However, it is worth noting that in this study, attention was measured during the study rather than after its completion. The study by Medalia et al.²⁷ used attention training based on the Orientation Remediation Module (ORM)²⁸ in

Table 4		Assessment of level of evidence	
Level of evidence	Grades of recommendation	Characteristics of the study	
I	A	<ul style="list-style-type: none"> - Randomized Clinical Trial (RCT) and PEDro ≥ 6 - Quasi-randomized Clinical Trial and PEDro ≥ 6 	
IIa	B	<ul style="list-style-type: none"> - Randomized Clinical Trial (RCT) and PEDro < 6 - Quasi-randomized Clinical Trial and PEDro < 6 - Designs that include test-retest measures, with non-randomized control group, and whose smallest experimental group is $N > 29$ - Multiple-baseline randomized crossover design, whose smallest experimental group is $N > 29$ 	
IIb	C	<ul style="list-style-type: none"> - Designs that include test-retest measures, with non-randomized control group, and whose smallest experimental group is $N < 30$ - Randomized cross-over design with multiple baseline, whose smallest experimental group is $N < 30$ 	
III	D	<ul style="list-style-type: none"> - Non-randomized cross-over design with multiple baseline - Single case studies 	

Adapted from Fundación Reintegra. Guía Clínica de Neuro- Rehabilitación en Daño Cerebral Adquirido. Oviedo: IMSERSO; 2013.

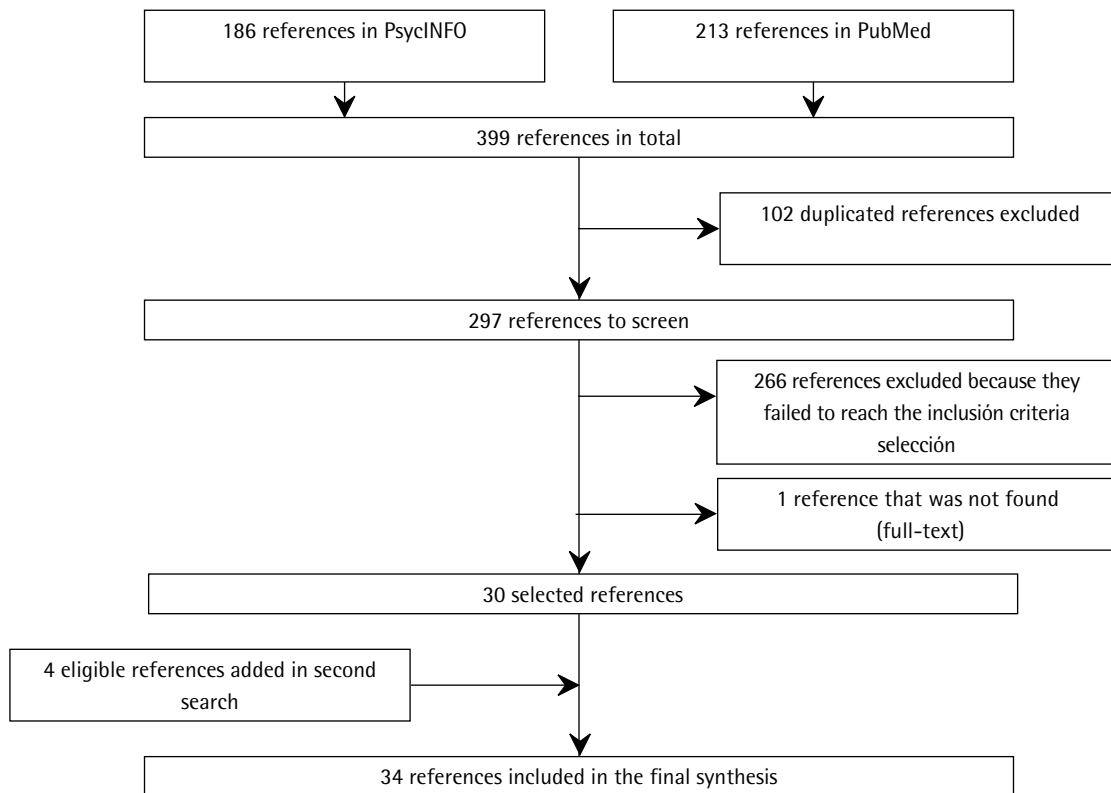


Figure 1 Flowchart. Summarizes the selection of the articles included in this literature

inpatients. After a 6-week training program was completed, the experimental group showed statistically significant improvements beyond those of the control group in the attentional task Continuous Performance Test (CPT).

Two studies in which evidence of improvements was detected failed to demonstrate improvement beyond that of the control group. Specifically, Brown et al. found that the improved attention functioning in the group that underwent Attention Process Training (APT) was not greater than the improvements seen in the participants who received individual occupational therapy. Also, neither of the two interventions was effective in treating difficulties related to problem solving²⁹. Hermanutz and Gestrick³⁰ obtained similar results when they compared the efficacy of a cognitive program based on the acquisition of skills such as communication and social competence by providing a group of acute patients with specific, computer-assisted attention training. Patients from both treatment groups showed improved control over distractions when carrying out tasks as measured by reaction time; the results of these patients were similar to those of a group of healthy controls.

Two studies found a total lack of improvement. The study by López-Luengo and Vázquez³¹ on subjective perception of improvement among patients after having completed an APT cognitive training program failed to find subjective or objective improvements in attention. In addition, no improvements were found following a brief, computer-assisted cognitive training program for attention in a group of patients attending a day facility³².

Some of the studies described above have included variables outside of cognitive parameters. The effect of attention training on self-esteem and quality of life has been subject of study²⁹. Although certain improvements were found, these were immaterial when compared to the group undergoing occupational therapy. The symptoms of schizophrenia were assessed by Medalia et al.²⁷ revealing positive results.

- Evidence level IIb / Strength of recommendation C

In the outpatient study performed by Field et al.³³ improvements in attention achieved through a game-based computer-assisted program were no different than those produced using a graphic-based therapy system. This study does not mention the type of attention therapy administered, though it does make reference to the short treatment period (6 one-hour sessions over a three-week period).

- Evidence level III / Strength of recommendation D

Single-case studies have demonstrated the efficacy of

individual interventions.

Hatashita-Wong and Silverstein³⁴ described the effects of an intervention based on the classical paradigm of dichotic listening in a 36-year-old patient diagnosed with paranoid schizophrenia with multiple auditory hallucinations that had caused impaired functioning. Selective listening over a 25-session, 8-week period resulted in progressive improvement in task completion and in a number of aspects of daily living. However, the treatment failed to lower the frequency and intensity of hallucinations in the patient.

Satisfactory results were also achieved when four inpatients underwent a shaping intervention within a psychiatric rehabilitation unit, revealing acceptable attention span while on task, although no reduction in symptoms was seen³⁵.

For their part, Bell et al.³⁶ studied learning curves in a 40-hour visual attention training carried out in a group of chronic patients who had undergone prior cognitive therapy, finding improved attention.

Executive functions / working memory

There were found 5 studies in which interventions targeted patients' working memory or executive functions.

- Evidence level I / Strength of recommendation A

Medalia, Revheim and Casey³⁷ studied the efficacy of a computer-assisted problem-solving program performed twice weekly (25 minutes per session) over a 5-week period. The patients who participated in the study had been diagnosed with schizophrenia or schizoaffective disorder and had memory deficits and difficulties with problem solving. The patients were randomly assigned to either a problem-solving group (i.e., planning, organization, and deductive reasoning), to a memory-training group, or to a group of controls. Those who underwent the 10-session training program in problem solving showed a substantially greater improvement in problem-solving skills when compared to the members of the other two groups. These improvements were manifested in direct measures of problem-solving performance in daily life as well as the WAIS-III comprehension scale.

- Evidence level III / Strength of recommendation D

Beginning with one patient and later in a small group of outpatients, Davalos et al.^{38,39} carried out a test of a specific 20-session training program for executive functions focusing on planning, self-regulation, and problem-solving. In the case study, the patient's score improved in all neuropsychological measures applied, and the results revealed a change in activities of daily

living, with the patient acquiring competences that allowed them to live semi-independently. The group results showed that 60% of participants achieved normal scores for executive functions despite the fact that only 20% had a normal score at baseline. A significant clinical change was observed in 40% of the measures used, that is, two subtests of the Behavioural Assessment of Disexecutive Syndrome Scale (BADSD), the Trail Making Test (TMT-part B), and the Dysexecutive Questionnaire (DEX).

One of the two papers we found that specifically dealt with working memory, was a case study in which the primary aim was to rehabilitate three of the functions of working memory: storage and manipulation of information, updating, and the monitoring of dual tasks⁴⁰. Patients were shown three different reorganization strategies: dual coding (verbal and visual), serial processing, and speed reduction. These strategies were taught in order to consolidate coding before the processing of information, thus reducing the mental load placed on the central executive functions. Upon the completion of the training program, the patients presented improved updating and planning functions. Improvements were also found in processing load and flexibility (which were not affected at baseline) but not in verbal episodic memory. The negative symptoms and subjective complaints of cognitive impairment were reduced, although the patients' self-esteem and positive symptomatology remained unchanged.

In the other study that specifically targeted working memory⁴¹, it was found that following 8 weeks (approximately 20 hours) of training of schizophrenic patients' working memory using an online program and telephone-based psychoeducational support, patients experienced improved cognitive performance in working memory, though these results were not seen in overall cognitive functioning.

Several functions

There were found 19 studies in which interventions targeted patients' attention span, working memory, and executive functions together.

- Evidence level I / Strength of recommendation A

9 studies met the criteria for inclusion in this group. Seven of them studied the effectiveness of the Cognitive Remediation Therapy (CRT) program initially developed by Delahunty and Morice⁴². This program, which aims to rehabilitate attention span and executive functions, consists of 40 one-to-one sessions held at least three times weekly.

Drake et al.⁴³ used a computerized version based on this

program over a 12-week period in patients diagnosed with first-episode schizophrenia. They failed to find statistically significant differences in cognition, psychotic symptoms, depression, self-esteem, and time to relapse or admission when compared to a control group which was treated with "social contact." Although statistically significant differences were found in executive function, these improvements were not sustained during follow-up (42 weeks). Other studies have found improvements in various cognitive functions, such as executive function and memory assessed immediately after the treatment⁴⁴ or 6 months after treatment⁴⁵, in working memory and cognitive flexibility⁴⁶, in cognitive flexibility and visual memory⁴⁷ or in verbal working memory and attention/vigilance, but not in reasoning or problem solving⁴⁸.

Additionally, the cost-effectiveness of this type of intervention has been subject of study. Wykes et al.⁴⁹ found lasting effects on improvements in working memory; these effects also predicted improved social functioning. These benefits in working memory only caused a minimal increase in costs when compared to traditional approaches. In a later work, Patel et al.⁴⁶ failed to find evidence of changes in social functioning in patients with cognitive and social-functioning difficulties, and no evidence indicated that cognitive remediation therapy had long-term cost-saving potential. Wykes et al.⁴⁷ found improvements in social functioning, though only in cases where improvements in cognitive flexibility were above a certain threshold. The authors found no improvements in symptomatology, though they did detect improvements in self-esteem. Penadés et al.⁴⁵ found changes in social functioning in a group of outpatients under the age of 55 at the conclusion of treatment and at 6 months of follow-up.

Changes in the brain caused by therapy are another variable currently being studied. In a study that included a group of 30 patients with schizophrenia, Penadés et al.⁴⁴ found an increase in the brain network and white matter integrity in the corpus callosum. Statistically significant correlations were also found between these structural and functional changes and cognitive improvement.

Garrido et al.⁵⁰ assessed the effectiveness of another computer-assisted cognitive remediation (CACR) program. The aim of this program is to train attention span, working memory, and executive functions (reasoning and problem-solving). The treatment comprised 48 one-hour sessions over a 6-month period. At 6 months of follow-up, the experimental group exhibited statistically significant improvements over the control group in terms of working memory, reasoning, problem-solving, and processing speed, but not in attention span or verbal learning. Significant improvements were also ob-

served in quality of life and self-esteem.

In a recent multi-center study that included 130 patients with chronic schizophrenia to study the effects of computer-assisted training on attention span, working memory, and executive functions (FesKits Program), a statistically significant improvement was found in participants' performance of the tasks for which they had been trained. However, these improvements did not translate into statistically significant changes in neuropsychological function when this variable was measured before and after the intervention; additionally, no change was found in daily functioning⁵¹.

- Evidence level IIa / Strength of recommendation B

There were found 7 studies that fit this criterion. Wykes et al.⁵² studied changes to the brain following CRT intervention; similar to the study by Panadés et al.⁴⁴, the authors observed a statistically significant increase in brain activity in the areas associated with working memory -primarily in frontal areas- accompanied by improved performance in working memory. Haut et al.⁵³ also found a relation between increased activity in areas such as the dorsolateral prefrontal cortex, the anterior cingulate cortex, and the frontopolar cortex, noting improved cognitive function following a training regimen intended to improve attention span and cognitive memory. Vianin et al.⁵⁴ found increased executive functioning in Broca's area and improved performance on tasks evaluating executive functions after the RECOS training program was performed. The RECOS program targets selective attention, verbal memory, visuospatial attention, working memory, reasoning, and processing speed.

As in other studies, the results of treatments show varying effects on social functioning and quality of life. After a CRT program was carried out in a group of patients, Reeder et al.⁵⁵ found improvements in verbal working memory, but not in other factors such as response inhibition speed or stimulus-driven responding. Although working memory was significantly associated with social functioning and symptom severity, the changes observed in this factor did not predict functional changes. In a later paper, Reeder et al.⁵⁶ found that schema generation was the only cognitive variable studied that predicted improvement in social functioning, whether the subjects had undergone CRT or not. In another study, 50 hours of cognitive training brought about improvements in verbal memory and cognitive control, and these improvements were sustained at 6-month follow-up⁵⁷. A more intensive treatment calling for 30 additional hours of training in visual processing and 20 hours devoted to cognitive control was necessary to produce gains in processing

speed and overall cognition. The cognitive improvements that resulted from the treatment were associated with functional improvements at 6-month follow-up. A shorter (13 sessions) computer-assisted intervention consisting of simple, repetitive tasks to train attention span and visual and verbal working memory was carried out in a sample of Chinese patients diagnosed with a psychotic disorder found improvements in the Clinical Global Impression rating scale, in social functioning, and in the symptoms of the disease⁵⁸.

Varying results have also been obtained from studies that have aimed to account for the influence of cognitive intervention on symptoms. While Byrne et al.⁵⁸ found improvements in both the positive and negative symptoms of the disease, Fisher et al.⁵⁷ and Vianin et al.⁵⁴ failed to detect changes in symptoms as a result of the intervention.

- Evidence level IIb / Strength of recommendation C

We found one study within this group. La Paglia et al.⁵⁹ used a virtual reality environment structured by hierarchical sequences of tasks taking place in four different virtual settings to train patients' sustained, divided, and selective attention, as well as executive function. At the conclusion of the ten 90-minute sessions, both the experimental and control groups exhibited improved performance in divided attention, although only those patients who had been exposed to the virtual reality environment showed improved planning capacity.

- Evidence level III / Strength of recommendation D

The studies with the lowest level of evidence also analyzed the efficacy of CRT. Ghirasim et al.⁶⁰ found improvements in cognition and in positive and negative symptoms when studying a sample of Romanian patients after they had undergone a 6-month intervention. Wykes et al.⁶¹ studied the influence of CRT on job performance. Their results revealed improvements in working memory and cognitive flexibility following a 13-week treatment period, although at 25 weeks of follow-up the only statistically significant improvements were those seen in cognitive flexibility. On the other hand, improvements in planning were observed during follow-up, and this was the only variable shown to be associated with improved quality of work.

CONCLUSIONS

Though not uniform, the findings of the different studies allow us to conclude that training in cognitive function brings about cognitive improvements in patients diagnosed with a psychotic disorder. Contrasting with this general

statement, the areas in which cognitive improvement is evidenced tend to vary from study to study, and there is scant evidence on the long-term maintenance of these gains. Most studies have assessed post-treatment improvements or those evidenced at 6-month follow-up, and no longitudinal studies lasting more than 6 months have been performed.

Studies that only target attention have produced the poorest results. These results are not altogether surprising if we take into account the fact that the other interventions also have a collateral effect on attention span, especially in programs held over longer time periods.

Secondary benefits have been found in numerous areas, although the results are varied in this aspect. The most widely studied aspects are positive and negative symptoms and social functioning. A large number of studies have failed to find results indicating a statistically significant change when assessing the influence of cognitive rehabilitation on the symptoms of the disease. Concerning social functioning, though it is known that cognitive impairment is the best predictor of functioning in patients with a psychotic disorder¹¹, improved performance on cognitive tasks has not always translated into improved social functioning, which should be the ultimate goal of the intervention. Some studies argue that a certain threshold of improvement must be passed for there to be notable changes in functional aspects⁴⁷. It follows from this that the ideal scenario would be for the clinician to assess the patient before the patient enters the program, as this would guarantee a minimum performance, which can be manifested in functional improvements. It would also be beneficial to identify those aspects of training that are associated with the most significant cognitive changes. The most consistent results have been obtained in studies that assess changes to the brain following cognitive intervention, and these have found a statistically significant increase in brain activation in areas associated with executive functions.

Comprehensive approaches have been found to be most effective⁶². These studies have been excluded from the present review, however, as our intent was to pinpoint the specific role played by cognitive treatment within the areas described. Despite this effect, however, the data studied also suggest that the most complex interventions produce the best results.

There is great variety in the intervention methods, which complicates even further the task of synthesizing the results from different studies. No conclusions can be reached on the optimal intensity or duration of the intervention. In addition, we have found greater uniformity in the type of strategies employed: most of the interventions include tasks of increasing complexity, error-free learning, upscaling, and intensive practice.

Overall, the results from the interventions cannot be easily extrapolated, as they do not include tasks that lend

themselves to generalizations; rather, the studies opt for approaches such as identifying reinforcers of learning in the natural environment or using situations that closely resemble those encountered in real contexts⁶.

Most studies are centered on schizophrenia rather than other psychotic disorders; however, there are studies that include heterogeneous patient samples (e.g., schizophrenia, bipolar disorder, unspecified psychotic disorder), thus introducing a substantial methodological limitation. Most of the subjects included in the studies reviewed are patients with long-term illness. It would be useful to have data on which patients stand to benefit the most from neurocognitive treatment and then identify possible predictors of individual response⁶³. Some papers have already done so^{23,64-66}, and it is important for there to be more studies along these lines. It is of prime interest for both researchers as well as clinicians to identify possible predictors of intervention effectiveness, as treatment efficacy largely depends on appropriate patient selection.

Regarding the limitations of this study, it is worth noting the great disparity in the methodological quality of the research reviewed. On the one hand, this variability may have skewed the results, while on the other, our procedure allowed us to include a higher number of studies. The level of methodological rigor in the studies is average. Most of the papers with a high level of evidence (I) are the ones that assessed the CRT program. The oldest studies are generally those that analyze one function, and these have the lowest level of methodological quality. It is worth noting, however, the importance of case studies. In accordance with the criteria of the National Health and Medical Research Council guidelines, which consider case studies to have some of the lowest levels of evidence (level D), in our paper these have been assigned an evidence level of III. Case studies have long been a fundamentally important source of knowledge within the field of neuropsychology⁶⁷⁻⁶⁹, and despite the fact that they are considered to be the least able to generate robust empirical evidence, in recent years they have become increasingly important⁷⁰. Another limitation of our work is the "artificial" distinction made between cognitive functions, although one of the primary aims of our research was to study the individual contribution made by each form of cognitive training.

In conclusion, we can state that cognitive rehabilitation has a promising impact on attention, working memory, and executive functions. Type-A recommendations can be made for the CRT intervention program as well as for specific training of executive functions using training initiatives for planning, organization, and deductive reasoning; type-B recommendations can be made concerning interventions in attention that use the ORM model and behavioral interventions using shaping techniques for attention span; type-C recommendations can be made for attention and

executive-function training that is based on virtual reality, and type-D recommendations for training that uses dichotic listening and approaches that target specific components of working memory in isolation.

It is important to highlight the problems currently facing attempts to extrapolate results within this field given the methodological limitations of many of the studies analyzed and the variability in the different intervention formats.

Research must shed light on the ideal timing for interventions, indicating which are the most effective strategies for each type of patient according to the stage of disease, the time from onset, cognitive level, among others. Future studies should also aim to shed light on whether individual treatments based on specific neuropsychological examinations are better than the more commonly used group-based treatments.

Despite the unresolved issues and the recent creation of multiple specific programs for cognitive rehabilitation of schizophrenia, there has not been a significant increase in the output of scientific studies on the matter. In fact, of all the papers published in the last year, only two have met the inclusion criteria used for our review. While it is true that advances are being made in the study of cognitive rehabilitation of psychosis in the form of consensus-based assessment and treatment models for schizophrenia, there is still work to be done in exploring the characteristics and possibilities of the most effective treatments as well as their clinical and social impact.

CONFLICT OF INTEREST.

The authors declare that they have no conflicts of interest.

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