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A Systematic Review of Cognitive Training for Schizophrenia in Developing Countries

Livia Maria Martins Pontes* and Hélio Elkis

[1]*Department and Institute of Psychiatry, University of São Paulo Medical School, Brazil*

[2]*Department and Institute of Psychiatry, University of São Paulo Medical General Hospital, Brazil*

***Corresponding Author:** Livia Maria Martins Pontes, Department and Institute of Psychiatry, University of São Paulo Medical School, Rua Ovídio Pires de Campos, Brazil.

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Abstract

The majority of programmes created to improve cognitive difficulties in schizophrenia were developed in Europe and the United States. To our knowledge, very few studies on this area were conducted in developing nations. We conducted a systematic review of the literature in search for studies on cognitive training in schizophrenia in developing countries and discussed the possible difficulties involved in this type of research. Seven different databases were searched for studies on cognitive training in schizophrenia in developing nations. Only 5 studies were found. The main difficulties in conducting this type of research identified by us involve low budget, a lack of necessary infrastructure (trained professionals to deliver the intervention and to carry out assessments, cost of training programmes and availability of space), hurdles to publishing results in larger indexed journals. Despite all the difficulties encountered, we believe it is important that more programmes to treat cognitive deficits in schizophrenia are created in developing countries, as they can be adapted to the cultural differences and different needs of these nations. We also believe cognitive training can be constructed in a low cost manner, requiring minimal infrastructure, adequate to developing nations' reality.

Keywords: *schizophrenia; cognition; rehabilitation; training; developing countries*

Introduction

Schizophrenia is one of the most costly illnesses in the world [1]. Among the many factors involved with its cost, cognitive deficits also play a role. Impairments in cognition affect functionality and domains affected include independent living, social skills, self-care and work abilities [2-6]. These, in turn, lead to an increased burden in families and on governments, as patients are unable to continue working or to look for competitive employment, rehospitalisation rates are high [7] and many end up claiming for sickness/disability benefits at an early age [8]. The literature has indicated that the magnitude of cognitive deficits in schizophrenia is an important limiting factor that prevents patients from fully benefiting from psychosocial rehabilitation programmes such as social skills training, vocational rehabilitation, daily living activities [3,9,10]. Thus, the importance of interventions for improving cognition in schizophrenia is made clear.

Studies focusing on techniques to improve cognitive functioning in schizophrenia started around 1970 [11]. Two initial studies [12,13] used behavioural procedures, reinforcement and self-instructional training, and reported positive outcomes. Nevertheless, these initial studies aimed to test theories about cognitive deficits in schizophrenia, as did other laboratory studies [14-16]. These latter ones characteristically employed only one training strategy, specifically developed to a certain task, usually a neuropsychological test, and were very short in duration. Their aim was also to investigate the possibility of improvement in cognitive performance, but the gains were limited to the task trained and not transferred to other tasks or daily life. It was not until 1990 that researches started to concentrate on treatments to improve cognition in schizophrenia [11].

Different treatment programmes have been created and a study identified and reviewed eight treatment approaches [17], differentiating them between approaches to improve cognition and compensatory approaches. Encouraging results were reported.

Several meta-analyses and reviews [18-23] pointed to mixed results on the efficacy of improving cognitive performance in schizophrenia. Various aspects are highlighted as contributing the variability in results: heterogeneity in samples (patients with different degrees of symptoms and duration of the disorder), different kinds of medication, great variability in assessment and outcome measures and treatment aspects (computerized vs. non-computerized, individuals vs. groups, presence vs. non presence of a therapist in computerized programmes, cognitive training as part of a larger rehabilitation programme, number of sessions needed, differences in underlying theories, use of monetary reinforcement [18-23].

The two main guidelines on treatments for this population, the Schizophrenia Patient Outcomes Research Team (PORT) [24] in the USA, and the National Institute for Health and Clinical Excellence (NICE) [25] in the UK, do not recommend cognitive training for schizophrenia arguing that

1. Still there is not enough clinical evidence to justify its adoption in the public health system
2. It is difficult to identify key elements to treatment as there is great variation in programmes
3. Rigorous clinical trials are still a minority and present mixed results.

Conversely, a recent large meta-analysis [26] point out that efficacy does not seem to be related to methodological rigour, as even the most rigorous studies presented only small to moderate effect sizes. Additionally, there seems to be no relationships between the results and aspects of treatment (type of approach used, computerized programmes vs. paper and pencil programmes) and positive and lasting effects on cognitive and psychosocial functioning were found.

The vast majority of studies in this field were developed and conducted in Europe and the United States. Although the prevalence of schizophrenia seems to be similar in developed and developing countries, most people who suffer from this disorder live in developing countries [27] and it is estimated that around 25 [28] to 41.7 [29] million people are affected by schizophrenia in low and middle income countries (LAMIC). The lack of studies on psychosocial interventions in LAMIC have been reported, regarding many mental health conditions [30-32]. However, no studies seem to have concentrated on strategies to improve cognition in people who suffer from schizophrenia in LAMIC. Hence, some important questions seem to arise: whether programmes developed in high income countries would be suitable for LAMIC and whether any treatment programmes developed in LAMIC differ from those of high income countries. In order to try to answer these questions we conducted a systematic review of the literature in this field in order to identify the creation of possible treatment programmes and research developed in these nations. We then discuss the difficulties involved in this kind of research and hope to motivate more mental health professionals to get involved.

Methods

We searched PubMed/Medline, Psychinfo, Scielo, Scopus, Embase/Ovid, LILACS and Cochrane Systematic Review databases for studies on cognitive training in schizophrenia in developing countries. The search was performed using the following terms: "cognitive training OR cognitive rehabilitation OR neuropsychological training OR neuropsychological rehabilitation OR cognitive remediation OR cognitive remediation therapy AND schizophrenia AND low middle income countries OR LAMIC OR LMIC OR developing countries". These terms were searched on the title/abstract and topic of studies. Although our aim was to find clinical trials in developing nations, in order to avoid missing relevant studies, no limits were set regarding date of publication or type of study. As LILACS is a database of the scientific literature of Latin America and the Caribbean, additionally to the search using the mentioned terms, we conducted an additional search removing the terms low middle income countries, LMIC and LAMIC. This was done to ensure no papers would be missed. This review has not been registered.

This search was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [33], and a complete PRISMA checklist has been filled out.

PRISMA guidelines also recommends using the acronym PICOS (patient, intervention, comparator, outcome, study design) to list important aspects in a systematic review [33]. Thus, in our search, P refers to schizophrenia; I refers to cognitive training and its known variants in the literature (cognitive rehabilitation, cognitive remediation, cognitive remediation therapy, neuropsychological rehabilitation, neuropsychological training); C is any form of control group (e.g. treatment as usual) or placebo group or absent in observational studies; O is cognitive performance; and S refers to experimental studies, quasi-experimental studies, observational studies, case studies, series of cases or longitudinal studies.

Eligibility criteria

Initially, 273 papers were found. All titles were read to check for relevance to this review and if the title was not clear, the abstract was also read. If a study appeared in more than one database, it was considered only once.

The following inclusion criteria were adopted: studies written in English, Portuguese or Spanish; researches on treatments to improve cognitive functions in schizophrenia; experimental studies; quasi-experimental studies; observational studies; case studies; series of cases; longitudinal studies.

Manuscripts were excluded if they: included other mental health conditions (e.g. bipolar disorder, depression, psychotic depression); did not involve some form of cognitive training (e.g. studies on pharmacological treatment, prevalence, demographic or neuropsychological profiles etc.) or included other types of psychosocial rehabilitation that did not primarily focus on the improvement of cognition (social skills training, skills training); were not conducted in developing countries; editorials, reviews and letter to the editors.

The PRISMA flow diagram (Figure 1) illustrates the search strategy and numbers of studies included and excluded.

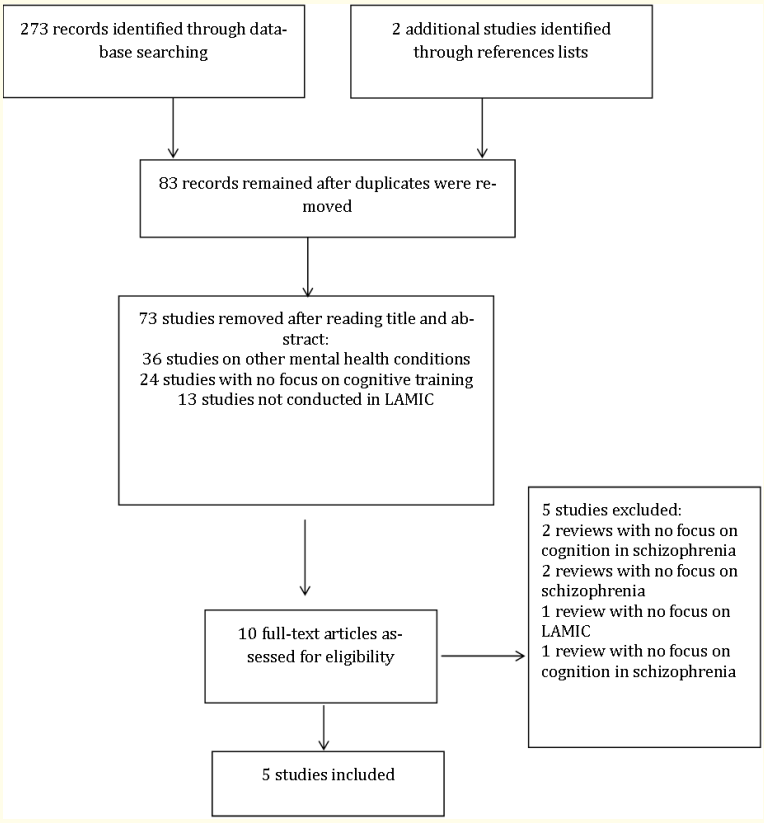

Figure 1: *Prisma flow diagram.*

Results

Only 10 studies matched these inclusion criteria and were read in it's entirely. Only five of these studies [34-38] reported cognitive training conducted in developing countries (Table 1). The remaining were reviews that either addressed many different aspects of schizophrenia and mentioned developing nations very briefly [27], addressed the efficacy of treatment interventions for various mental health conditions in developing countries [39] with no focus on cognition in schizophrenia, reviewed treatment interventions for many mental health conditions in children and teenagers in developing nations [30], or reviewed both pharmacological and psychosocial interventions for children and adolescents with schizophrenia but with no focus on LAMIC [40]. A specific review on psychosocial rehabilitation in LAMIC was also found [31], but it did not mention any studies on interventions to improve cognitive performance in schizophrenia.

Finally, the reference lists of the review studies were hand searched for further studies. Two extra papers were found [29,41]. Among these papers, one describes interventions that combine medication and psycho-education for schizophrenia in LAMIC, but with no reference to cognitive training [29]. Another, conducted in Mexico, investigates psycho-education and social skills training programmes for schizophrenia, with no focus on improving cognitive performance [41].

Study	Design	Objective	Intervention	Sample
da Costa & de Carvalho, 2004[33]	Observational/qualitative	Exploratory	Virtual reality programme	4
Zimmer., *et al*. 2006[34]	Observational/qualitative	Pilot	IPT	22
Zimmer., *et al*. 2007[35]	RCT	Efficacy	IPT (adapted version) + psycho education	54
Pereira and Pereira 2009[36]	Observational/qualitative	Exploratory	Flower arrangements	4
Bio and Gattaz 2011[37]	RCT	Efficacy	Supported employment	112
IPT: Integrated Psychological Therapy				

Table 1: *Characteristics of studies.*

One study conducted in Brazil [34] reports the development of a virtual reality programme for cognitive training of diverse conditions derived from brain damage. The programme acceptability was qualitatively tested among four patients with schizophrenia. The assessment was qualitative (direct observation) and involved the use of a questionnaire developed by the authors. Patients could have contact with the programme during four sessions, but one of the patients did not complete all four sessions. Results provide an indication that the programme had a good acceptability among patients and that the activities were enjoyable and motivating. Nevertheless, there were no measures of cognitive performance, so this aspect could not be assessed. Some difficulties encountered were described: hardware of virtual reality is expensive in developing nations and difficult to find and there is a scarcity of tools to help the development of such programmes.

A qualitative research[35] conducted in a sample of three centres in the South of Brazil shed light on very important aspects about the use and adaptation of a programme developed in Europe (Integrated Psychological Therapy - IPT) to a Brazilian population. Patients were asked their opinion about the treatment and stimulated to describe difficulties in doing activities. Analyses were conducted based on the transcripts of patients' interviews. Main barriers appointed by patients involved repetition of activities, rendering them monotonous; difficulties in doing activities that involved writing (despite all participants being literate in Portuguese); lack of practical use of some of the tasks; need to receive more information about the disorder (psychoeducation). Nevertheless, some activities were rated as enjoyable and positive by the patients. This research enabled the authors to continue investigating the adaptation of this programme to the Brazilian population.

A randomized controlled trial was then conducted [36], in which reading and writing activities and two sub-programmes (cognitive differentiation and verbal communication) were removed from the intervention and psycho education was introduced. 54 patients were randomized in an experimental group (EG) and a control group (CG). The EG received 12 weeks of training using the adapted

Integrated Psychological Therapy (IPT) programme and the control group received treatment as usual. Results indicated an improvement favouring the EG in some aspects of cognition, social adjustment and quality of life. Although the initiative and effort in conducting this study is commendable, only three cognitive domains were assessed (working memory, attention and concentration) through two instruments (Mini Mental State Examination and Word Recall Test). These are very brief instruments and a more comprehensive assessment of cognition is recommended. Replication of the study using different control conditions is also necessary to match groups for professional interaction time, as the interaction with the therapist in the EG might have also contributed to the gains observed.

Another qualitative study [37] investigated the effect of a Flower Workshop on four patients with schizophrenia. It was conducted in a Center for Psychosocial Care (CAPS), in the city of Ribeirão Preto, in the state of São Paulo, Brazil. The programme consisted of initial physical relaxation exercises, construction of vases using a choice of low cost materials, preparation of flower arrangements and a social interaction activity, consisting of verbalisations to other group members about feelings, memories and ideas during the preparation of the arrangements. Although the authors report positive effects over cognition, there were no formal assessment measures. Despite the fact that this programme does show promising effects on socialisation and maybe even cognition, it was not developed specifically for people with schizophrenia. We believe this is an important factor to be taken into account when developing interventions for schizophrenia, as specific aspects of cognition have been reported as a feature of the disorder and need to be specifically targeted.

An innovative research conducted in Brazil studied the effects of vocational rehabilitation on cognition in a sample of 57 stable outpatients with schizophrenia, in comparison to a waiting list condition (n = 55) [38]. It was found that six months of an internship programme improved some aspects of cognition (set shifting, inhibitory control, judgment and critics abilities, concept formation and flexibility), negative symptoms and quality of life, in comparison to the control group. To our knowledge, this seems to be the first large study conducted in a developing nation that used a very structured methodology (randomized, controlled trial) to assess an intervention to improve cognition in a sample of patients with schizophrenia. However, no specific cognitive training or stimulation was used prior or during the internship. Participants only received guidance from the employer regarding the adequate performance of the job. This may indicate that some form of social re-insertion (as a supported internship) and feeling productive may have a positive impact on cognition of people with schizophrenia.

Discussion

Return over investments in mental health treatments are usually measured by improvements in health and the cost-effectiveness of interventions. Occasionally non-health benefits (increases in employment and productivity) are also considered [39].

Although LAMIC decide where to invest their budget based mainly on competing public health needs, factors such as the economic consequences of not investing need to be taken into account [39]. It is known that the difficulties in cognition in schizophrenia prevent patients in finding and keeping jobs, increasing the burden on families and also on the State, if we consider the high proportion of patients that seek for sickness benefits at an early age [8]. Reports indicate that investments in mental health disorders in developing nations can be as cost-effective as treatments for other chronic conditions such as HIV, prevention of hypertension and glycaemic control for diabetes [39]. Furthermore, it has also been reported that limited and poor quality outpatient services can lead to hospital readmissions [42]. A programme of cognitive training to people with schizophrenia may reduce hospital readmissions and can be beneficial in helping patients find or return to work, as it has been demonstrated that such programmes contribute to a decrease in symptoms [1]. This, in turn, can help reduce the overall burden of the disease.

It seems that studies conducted in a specific country are more likely to generate changes in clinical practice in that country than research from high income countries [43]. However, the simple repetition of activities such as handicraft work, or selling of cooked food or handicraft, without a structured environment and underlying rationale, does little to contribute to the psychosocial rehabilitation of the severely mentally ill [32] and specifically to the cognition of people with schizophrenia. The objectives of psychosocial rehabilitation programmes need to include helping patients achieve a good level of independent functioning, reducing stigma, improving social abilities and decreasing iatrogeny [32]. As described by the clinical trials, reviews and meta-analysis aforementioned, the improvement of cognitive deficits in schizophrenia do contribute to all these objectives.

Diverse aspects need to be taken into account when conducting research in the field of schizophrenia in developing countries. One of the problems faced by researchers is the difficulty in having a good sample size. Patients and family members are not always motivated to come to treatment centres, are not always aware of the importance of such interventions [31], and attrition rates are often high [28]. It has been reported that the course of this illness seems to be less severe in developing countries than in developed countries. Although the mechanisms for this are not clear, it is hypothesised that differences in socio-cultural aspects such as the central role of the family and beliefs about the development of mental illness might play a role [27]. This is an indicator that involving families in clinical trials could help improve patients' adherence to interventions. Most people suffering from severe mental illness in LAMIC live with their families [31,32], who are often responsible for taking patients to treatment centres. In this view, it seems that expanding family members' and also patients' information about the symptoms of schizophrenia in general, and sensitizing them to the importance and advantages of treating cognitive deficits could be beneficial. This could be done through psychoeducation. The benefits of adding psychoeducation to a cognitive training programme have been demonstrated in a study conducted in Latin America [36] and it highlights the importance of adapting a programme developed in a high income nation to the culture of a developing nation.

Another obstacle to the development of such interventions in LAMIC is the lack of qualified mental health professionals [28,30-32]. With a scarcity of qualified professionals to deliver pharmacological treatment, most people with schizophrenia in LAMIC receive little pharmacological care or no treatment at all [28]. Thus, it seems even more challenging to target the issue of enhancing the work force to treat cognitive deficits in these patients. However, this type of treatment is of no lesser importance. In order to tackle this barrier, it has been suggested that non-specialist health professionals could be trained to deliver psychosocial interventions [30,32].

Added to that, many cognitive training programmes created in developed countries require the use of computers [17,26], increasing the costs of treatment. A low level of computer literacy in LAMIC [44] adds to the difficulties in using computerised programmes. A recent report about research priorities for a developing nation (Brazil) [45] recommends the development of interventions that do not require expensive technology or highly specialised professionals. Another recommendation is that interventions should be conducted in groups, as not only it is more cost-effective, but it can aide addressing social skills difficulties [45], another important area of impairment in schizophrenia.

Our own experience in conducting a pilot study on cognitive training for schizophrenia patients in a developing country (Brazil) has also indicated additional hurdles. However, it is important to stress that these aspects are based on observations and cannot be extrapolated to other LAMIC. We identified that restricted budgets, difficulties in obtaining financial support and scarce infra-structure in public hospitals can be important barriers when conducting clinical trials in LAMIC. Public hospitals are frequently working to full capacity and it is not infrequent that professionals have to compete for treatment rooms to be able to conduct interventions. Methodologically rigorous studies (i.e. double-blind randomized controlled trials) require the help of a professional team in order to meet the requirements for masking and to minimize biases. It is hard enough to direct any budget and find grants to this type of study, let alone seek for additional remuneration for the professionals involved. The professionals who do decide to get involved seem to do it on the basis of their own personal interest in the research but need to keep regular full-time paid jobs to support themselves. Consequently, they can dedicate a very limited amount of time every week.

All these factors only add to the importance in developing and adapting psychosocial rehabilitation programmes to developing countries [27,36]. Recently, a training programme for the treatment of attention and memory difficulties in schizophrenia has been developed by our group in Brazil [46,47]. It seems that this programme can help address some of the difficulties in research in this field, as it can be delivered in groups, is easy to administer and requires very little infra-structure (a room to fit 6 or 7 people, a large table and chairs), indicating it can be cost-effective, and it is adapted to cultural aspects in Latin America. The training incorporates aspects of evidence-based programmes created in developed countries, but it is adapted to the reality and budget of a developing country. It is a paper-based intervention and it deploys easily accessible and inexpensive materials. Different professionals in the mental health field could be easily trained to apply such programme. Nevertheless, studies with good sample sizes are still needed to confirm its efficacy [47].

A treatment intervention for LAMIC needs to be affordable, feasible, acceptable and evidence-based [28]. Our treatment programme is affordable, feasible and acceptable, but we do need to build a larger evidence base to confirm its efficacy and be able to sensitize policy makers about its importance [47].

Our review indicates the paucity of data in LAMIC in the field of cognitive training in schizophrenia, but some limitations have to be addressed. One limitation of our review is the difficulty in conducting a search using the terms mentioned above and the name of each low and middle income country, as some clinical trials might have gone undetected. Also, it is possible that studies were missed due to the lack of indexation of LAMIC journals in major databases, as it has been reported that LAMIC publications correspond to only 5% of indexed publications [48]. Additionally, we cannot rule out the possibility that more research on this area has been conducted in developing countries but might be unpublished, as barriers to the publications of mental health research on low and middle income countries have also been reported [45]. Nonetheless we tried to minimize these limitations as much as possible, by hand searching reference lists of the review papers.

Conclusion

Despite variations in results, the efforts invested in studies conducted in developed countries provide a good indication of viable ways to develop a programme of cognitive training for schizophrenia, as well as aspects that require special attention and others that should be avoided.

Considering all the already mentioned consequences of cognitive deficits in schizophrenia, including economic related problems of not treating them (difficulties in entering or re-entering the job market and the burden to families and the pension system, rates of hospital admissions and re-admissions) and the exacerbation of such problems in developing countries, there is a pressing need for more studies conducted in these nations for the treatment of cognitive deficits in schizophrenia.

It has also been considered that more investment in psychosocial interventions for mental health in LAMIC are needed, not only to inform policy makers, but it could also indicate to richer nations that low-cost technologies and strategies can provide efficacious results [28].

Differences in culture, public health systems and budgets between developed and developing nations make necessary that more programmes directed to the amelioration of cognition in schizophrenia are created specifically to LAMIC.

We do believe interventions for treating cognitive deficits in schizophrenia can be developed in a low cost manner, with minimal infrastructure demands and it can be delivered by different mental health professionals, thus, in accordance with the reality of LAMIC. Nonetheless, studies with good sample sizes and methodologically sound are necessary to verify programmes efficacy and also warrant publication. We urge more mental health professionals to get involved in this area of research.

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