Chapter 3

Cognitive Impairment in Schizophrenia: Description and Cognitive Familiar Endophenotypes. A Review of the Literature

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Additional information is available at the end of the chapter

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Abstract

The presence of cognitive deficits in schizophrenia is a fact widely confirmed by a more than abundant literature. The existence of these deficits cannot be ignored, given their presence even with stabilized symptoms and their proven correlation with the functioning of the subject. The following chapter focuses on describing the main affected cognitive domains most frequently described in this pathology, mutually before and after the appearance of the clinical signs, as well as reviewing the presence of these affected domains in first-degree relatives of these patients. The existence of these deficits in relatives reveals that these alterations can not only be considered as markers of heritability and risk for the development of the pathology, but that their ignorance, in the family context, is also related to an important stain in the perception of the quotidian aspects, in the healthy interaction between relatives and an impact on the overall functionality of the subject.

Keywords: cognitive impairment, schizophrenia, cognitive endophenotype, family, psychosis

1. Introduction: cognitive impairment in schizophrenic disorder

There is considerable evidence of the presence of cognitive deficits in schizophrenic disorder that are unfavorably correlated to the daily functioning of these patients [1]. These dysfunctions are present before the beginning of the psychotic symptomatology [2]. Cognitive déficits in schizophrenia affect most of cognitive functions and are especially relevant in: memory and learning; abstraction and executive functions; processing speed and attention [3–7].

It is important to point out that there are similar cognitive impairments, in much lower intensity, in close relatives, and these deficits can be considered as potential cognitive endophenotype markers of the disorder [8–13]. From this data, it can be accepted that, in many cases, the effect of these alterations, potentially, may be affecting the functioning of any family nucleus and not only the patient or relative at risk of developing disease.

These data show the existence of a biological basis, despite the undeniable influence of environmental factors on the development and course of both pathologies. In this sense, the DSMIV-TR [14] notes that: *"Although numerous data suggest the importance of genetic factors in the etiology of schizophrenia, the existence of a substantial discrepancy in the frequency of monozygotic twins also indicates the importance of environmental factors"*.

As expected, this cognitive dysfunction has influence in the main aspects of daily life [15]. Respecting the family point of view, there is also a great ignorance of the existence and influence of these cognitive symptoms present in the affected relatives. In general, it is suggested that the psychoeducational programs made for this subject directed to family members provide them with an important first step. These programs provides means in order to understand these factors, which make an important stain in their overall functioning, and therefore, in the daily life of these patients [16–19]. On the other hand, it is important to point out that the same patients do not usually present insight of their deficits, and when they do, although they are usually associated with higher levels of adherence to treatment, they also tend to do so with a loss of self-confidence [20]. This fact indicates that family interventions in the education of cognitive aspects should not only stay there and should also involve a research for solutions of family support in other ways. At this point, it cannot be ignored the effect on the family dynamics of the probable presence (even being slight) of these deficits in any of the relatives of the affected subjects. Their awareness and identification are important in order to carry out a family intervention.

2. Cognitive deficit in schizophrenia

One of the main recently advances of the concept of schizophrenia has been the confirmation that this disorder is primarily associated to cognitive deficits, do not being a consequence to symptoms or drugs [21]. Nevertheless, the idea that cognitive domains played a fundamental role in this disorder was not so recent. Since the first descriptions of schizophrenia, which was known under the Dementia praecox label, the aspects related to what it is now understood as cognitive deficit were considered as central symptoms of the picture. Besides the essential idea of Bleuler was that the core of schizophrenia, its fundamental symptoms, was the fragmentation of the thought process and delusions and hallucinations were accessory symptoms, a consequence of the main process [22, 23]. It has also been shown that this cognitive deficit has not only been described in long-standing schizophrenic patients [24], but is also present in patients with a first psychotic episode [25–27], in remission [28], in patients without antipsychotic medication [21, 29] and even in studies in high-risk subjects [30] and in close relatives and healthy patients with schizophrenia [12].

It is estimated that among 61–78% of patients with schizophrenia manifest a significant level of cognitive deficit [1] reaching between 1 and 2 standard deviations below the control

groups of the same age [6, 31]. These cognitive deficits seem independent of positive symptoms [32] and are maintained throughout the course of the disease.

Although some early investigations [33] showed that about 27% of schizophrenic patients, after neuropsychological evaluation, could not be considered deficit, in fact, it has been proven that they would continue to present neuropsychological deficit compared to healthy subjects, even matching IQ measurements [34]. This group of patients, without supposed deterioration, would show high levels of premorbid functioning, but once the disease was diagnosed, this would be considerably lower [35]. In addition, discordant monozygotic twin comparisons for schizophrenia suggest that almost all affected twins perform worse on cognitive tests than their unaffected twin [36]. In this sense, it can be safely talked about cognitive deficits in schizophrenic patients although, in any case, it is very likely that their cognitive performance is below than what was expected in the absence of disease. It is also interesting to mention that several authors have found a worse performance in tasks of work memory (especially in visual) and in learning verbal tests and free memories in unaffected monozygotic twin brothers and, even a lesser degree, in not affected dizygotic twin brothers against controls [37–40].

It is interesting to point out that many patients have a lack of awareness of cognitive dysfunction. Those who are better aware of their deficits are not associated with a lower use of treatment, nor with a lesser deterioration of executive function. But they do have better results in the rehabilitation of some cognitive domains, in adherence to treatment and in their functional capacity [41, 42].

The neurocognitive dysfunction affects the ability to perform activities of daily living, impairs the ability to solve social problems [15, 16] and has proved to be the better predictor of reincorporation to activities in social and community settings [43, 44] and, especially, in terms of work rehabilitation and maintenance works [45–48]. These data review the importance of cognitive domains as a reliable scale of clinical improvement [15, 49–52] and, as is to be expected, the degree of cognitive impairment implies a worse adjustment in the quality of life of these patients [52–54]. Some authors also consider cognitive functions as an integral part of the concept of resistance to treatment [55]. On the other hand, several studies emphasize the importance and efficacy of cognitive rehabilitation treatments in early stages of psychosis [56, 57].

As expected with these data, the cognitive alteration in schizophrenia is the current focus of attention for the research of therapeutic strategies, both pharmacological and psychological. Regarding the interventions on cognitive domains, the pharmacological treatment, although it has offered certain results, has not been very encouraging [58], however studies using cognitive stimulation (training in executive skills, memory and other cognitive processes) have achieved more hopeful data [59–62].

2.1. Cognitive domains affected

Patients with schizophrenia have, comparing with healthy subjects, problems in performing almost all conventional neuropsychological tests. The most widely affected functions are executive tasks. Memory and attention, in their different modalities, are not the only ones affected, but it is these domains that stand out especially about a generalized cognitive

dysfunction. The functions relatively preserved in schizophrenia are usually verbal knowledge and linguistic comprehension and naming. Cognitive functioning in schizophrenia is considered a primary or essential characteristic of the disorder [15, 63], so that schizophrenia is now considered to be a complex disorder whose base is fundamentally neurocognitive [64, 65]. For a review of the characteristics of these disturbances see **Table 1**.

2.2. Description of the disturbance in the affected domains

In general, it can concluded that the meta-analysis by Schaefer *et al* [69] would indicate that patients with schizophrenia would present important alterations in: Attention, especially in sustained attention and interference control; significant deficits in the operational memory (maintenance of information and manipulation) and important alterations in long-term memory. However, the implicit memory, specifically the so-called procedural memory, related to the ability to learn psychomotor skills, would be relatively preserved [73] and the recognition of verbal material was not as altered as the delayed memory. They presented important alterations in the different components of the executive functions such as cognitive flexibility and planning and serious alterations in the speed of processing.

Going in dept. the studies of executive functions in schizophrenic patients, these tend to describe a greater presence of persistent responses. The Wisconsin card sorting test [74] indicates that these patients tend to have a low number of categories achieved and many persistent responses, which can be seen as a deficit of cognitive flexibility [75]. This inability to select the relevant information and reject the irrelevant has also been documented using tasks such as the Stroop test [76–78] or the Tower of Hanoi [79].

This inability to inhibit response (which would affect to planning and organizing actions, persist in an activity and find novel solutions) is present, to a greater or lesser degree, in these patients, even in the case of not showing up serious dysfunctions in attention capacity and operative memory (necessary for an adequate executive functioning) [52, 70].

Regarding to memory in schizophrenia, it is common to see studies showing general alterations in all memory processes. It shows that there is poor performance in declarative (explicit) memory, short-term and long-term memory, intentional learning, operational memory, semantic memory and priming. However, non-declarative memory (implicit) seems be less affected and procedural memory seems to be preserved [80, 81].

Some authors have considered that the alteration of autobiographical memory [82] as well as in prospective memory (the ability to remember the performance of planned actions in the future) [83] and the memory of the source (of the contextual aspects of the information: Where, when, etc.) [84] are the product of a general deficit, especially related to a reduced executive function [70].

The studies of working memory in schizophrenia reflect the existence of deficits in the capacity of storage/apprehension [85], although it is considered if such storage difficulties could be linked to alterations in the process of coding the information (more related to the executive function),

Balanzá-Martínez and Tabarés-Seisdedos [66] highlight the following aspects:

- They affect significantly the majority of patients.
- On a generalized cognitive impairment, the most intense deficits are linked to memory, attention and executive functions.
- They are not secondary to psychotropic drugs, institutionalization or symptoms, although they may be related to negative symptoms.
- They are very stable during the evolution of the disorder.
- They are present since the first episode, even in the premorbid stages.
- They are also present in healthy patients relatives (cognitive endophenotypes) [67, 68].
- They are indicators of functional prognosis.
- Nowadays, they constitute a therapeutic objective.

The meta-analysis conducted by Shaefer *et al.* [69] concluded:

- There is evidence of a broad cognitive deterioration in schizophrenia, which can be considered moderate to severe compared to control subjects in all the neurocognitive measures studied.
- The cognitive deficits are somewhat greater in the domains of processing speed and episodic memory.
- Studies of diverse world regions in which a study of cognition is carried out present very few differences to each other.
- The studies showed higher percentages of involvement in male patients.
- The cognitive deterioration does not keep too much relation with the majority of the measures of symptomatology, something in contrast with the studies that highlight moderate but statistically reliable associations between cognition and negative or disorganized symptoms [32].
- Interestingly, they found no significant relationship between the duration of the disorder and cognitive decline.

Crespo, Rodriguez-Sanchez, Barbas-Calvo, Duarte-Armolea and González-Blanch [70] clarify that the existence of these deficits (to a much lesser degree) is not exclusive to patients and is often found within first-degree family members. Considering the affected domains and controlling medication variables, it can be considered:

- Attention: Difficulty to inhibit irrelevant information. Presence of these deficits in both patients and their children (higher than controls and young subjects at high risk for affective disorders).
- Executive functions: Difficulties in the use of problem solving strategies, self-control and supervision of own behavior. In first-degree patient's relatives, there have been problems in verbal fluency, inhibition of an arrogant response pattern or tasks with a change in cognitive function.
- Working memory: Deficit in the storage capacity of information (verbal and spatial) and also emphasize the role of working memory as an essential element for the processing of information, which malfunction compromises the execution of other cognitive systems. It is interesting to complete it with the study of Guimon, Padani, Lutz, Eack, Thermenos and Keshavan [71] about how emotional distracters impacted more on their performance in working memory tasks than in control subjects. Also note that Botero *et al.* [72] tested performance on tasks involving verbal work memory and the results were lower in subjects with schizophrenia and their relatives that in the controls of the community.
- Memory: Deficits to remember are present, to a lesser degree, in healthy relatives of patients. These memory deficits are aggravated by attention problems, working memory and coding difficulties.
- Speed of processing: Indicate a slowdown that affects other cognitive domains.
- Psychomotor functioning: Significant psychomotor slowdown even in first episode patients and, to a lesser degree, in parents of patients.

Table 1. Presence of cognitive disturbance in schizophrenia and first grade relatives.

rather than in processes related to the actual maintenance of the information. Authors such as Sharma and Antonova [86] and Brebion *et al*. [87] consider that schizophrenic patients did not use the properties/facilities of the material to be memorized in learning (for example, grouping it by categories or sequences) because they presented problems when are making complex coding strategies (based on the characteristics of the information). Although, these alterations in coding could be secondary related to the generalized slowdown in processing speed [88]. It is also point out that deficits in working memory could be due to errors in the search, maintenance and manipulation of information.

2.3. MATRICS study (measurement and treatment research to improve cognition in schizophrenia) of the National Institute of Mental Health (NIMH). The cognitive search in schizophrenia

One of the most important study projects of cognition in schizophrenia comes from the National Institute of Mental Health (NIMH) in the United States. The MATRICS initiative, Measurement and Treatment Research to Improve Cognition in Schizophrenia, is a program whose initial objective was to provide data that facilitated the development of drugs that improve the deficits presented in cognition in schizophrenia [89, 90] and that adopted as an initial objective the identification of the domains of cognitive effects in schizophrenia as well as the development of a battery for their evaluation.

The MATRICS project [91, 92] pointed out seven cognitive scopes in which patients with schizophrenia presented critical deficits: Speed of processing, attention/vigilance, working memory, learning and verbal memory, learning and visual memory, reasoning and problem a solving, and, a domain that was often ignored in many studies, social cognition.

2.4. Social cognition and schizophrenia

It is interesting to emphasize the relevance that social cognition has achieved in schizophrenia. This comes, among other sources, from the evidence that relates social cognition to social functioning [15, 93, 94] as well as for its mediating role between neurocognition and social functioning [95, 96].

Although there is no generalized consensus on the domains that make up social cognition, most authors identify five domains: Emotional processing, theory of mind, social perception, social knowledge and attribution style [97]. Even if the domains of emotional processing (perception and handling of emotions), and of theory of mind are usually cited as the most affected in schizophrenia, it can be accepted, based on the investigations carried out, that there is a mishandling of all of them on some of these patients [98].

Considering the meta-analyses of Chan *et al.* [99] and Savla *et al*. [100] it is indicated that people with schizophrenia present serious and generalized deficits in social cognition, especially in perception of emotions. More specifically, they show important difficulties in the perception of facial emotions as well as in the identification and discrimination of different emotions compared to undiagnosed controls. Difficulties in the processing of emotions were also observed in emotional prosody, that is, in the emotional tone of the voice. This alteration

is found in early stages of the disorder [101]. They also found that people with schizophrenia have major alterations in the theory of mind. In general, they also found alterations, although to a lesser extent to the previous ones, in social perception (ability to identify roles, social norms and social context as well as social knowledge that refers to the conscience of roles, norms and objectives that characterize social situations and direct interactions) [102]. However, Savla *et al*. [100] did not find significant differences in attribution biases between people with schizophrenia and non-diagnosed controls.

Regarding the presence of alterations in social cognition in relatives of patients, it is usually noted that patients score significantly worse in all domains of social cognition evaluated compared to controls and in the attribution style domain compared to family members [103].

In the Mondragón-Maya *et al*. review [104] point out that consistent discoveries on deficits in the theory of mind have been reported in family members of patients with schizophrenia compared to control subjects. In this sense, two meta-analyzes have reported effects (from modest to moderate) on alterations of the theory of the mind in unaffected relatives [105, 106].

Moreover, Mondragón-Maya *et al*. [104] consider that studies of the other fields of social cognition in family members offer more scarce and inconsistent results, requiring further investigation. Cella *et al.* [107] and the meta-analysis of Lavoie *et al*. [106] reported moderate déficits in social perception in relatives of schizophrenia versus controls. However, later, Lavoie *et al*. [108] did not find that parents of patients with schizophrenia showed worse performance than controls in social perception tasks. Regarding attribution style, Rodríguez *et al*. [103] reported that there were no deficits in the unaffected relatives of patients with schizophrenia. Studies on emotional processing in unaffected family members of patients with schizophrenia are also scarce. Despite this, some studies have reported worse performance of their relatives to identify emotions compared to controls [109]. The meta-analysis of Lavoie *et al*. [106] found a moderate deficit in emotional processing of unaffected family members, especially in tasks of emotional identification. However, this result is not completely generalize and needs further investigation, since it focuses on emotional identification skills, more than other components of emotional processing, such as emotional regulation [104].

2.5. Clinical status and cognition

It is important to emphasize that these deficits are not a direct consequence of pharmacological treatment, nor of the institutionalization situation or other factors such as lack of motivation or distractibility due to psychotic symptoms [3]. Cognitive deficits in schizophrenia affect the majority of cognitive functions [6], but they are especially marked in executive functions and memory [3, 4]. This cognitive deficit is presented with autonomy of positive and negative symptoms, even when there is a greater association with this latter ones [63, 110].

The systematic review of Dominguez *et al*. [32] (58 studies, 5009 individuals) shows a relation between the psychopathological dimensions of psychosis (negative, positive, disorganized and depressive) and measures of neurocognitive impairment in subjects with non-bipolar psychosis. The results showed that negative and disorganized symptoms are significantly but modestly associated with cognitive deficits. The positive and depressive dimensions

were not associated with neurocognitive measures. The patterns of association between these dimensions were stable in all neurocognitive domains and were independent of age, sex and chronicity of the disease. In addition, significantly high correlations were found for the negative dimension in relation to verbal fluency and in the disorganized dimension for reasoning/problem solving and attention.

2.6. Origin of cognitive deficit and family endophenotypes

Traditionally, two hypotheses about this disease have been considered [111]: The neurodevelopmental hypothesis, which considers that schizophrenia would come from an early disorder of brain development, which would be present in a relatively silent way during childhood, and that it would begin to exacerbate during adolescence and the beginning of adulthood with cerebral maturation [112, 113]. The neurodegenerative hypothesis indicates the existence of an active pathological process associated with periods of exacerbation, due to the neurotoxicity of acute psychosis, which would explain the progressive deterioration observed in these patients in the first years of the disorder. The evidence points out that although there is an alteration in neurodevelopment in schizophrenia [2, 111, 114, 115], but neither can be ignored that there are progressive brain changes in the appearance of psychotic crises not always associated with treatment [111].

There is evidence which shows that these cognitive disorders are prior to the onset of psychotic symptoms and the diagnosis of the disorder [114] and even seem to indicate that, the subjects who will suffer from schizophrenia, already in the 7–13 years of age, obtain lower scores in neurocognitive tests compared to subjects who did not develop it. These scores will remain relatively stable until descending significantly between 13 and 38 years [2]. These data would be in favor of the authors who suggest that these dysfunctions are significant and central to the disorder [116] and close to the neurodevelopmental hypothesis [112].

Similar cognitive alterations are also found, but to a lesser extent, in first-degree relatives of schizophrenia [8–10] and in people at risk for the disorder [8, 117]. This fact suggests that cognitive alterations may represent the expression of genetic vulnerability to schizophrenia and may be endophenotype for psychosis [118]. Other studies have indicated functional dysfunctions in brain regions (medial prefrontal cortex, posterior cingulate cortex, and superior temporal gyrus) in both non-psychotic patients and first-degree relatives and healthy controls [119, 120].

The alteration of executive functions in schizophrenia has come to be proposed as a phenotypic marker of the disease. Not surprisingly, studies with first-degree relatives of these patients have shown that they share some of these executive deficits [70].

Also note that the heritability of schizophrenia is high and family studies indicate that first-degree relatives of patients with schizophrenia have a seven times greater risk of developing the disease compared to individuals who do not have an affected family member [121].

2.7. Some considerations from interventions from the family

Antipsychotic drugs, although essential in the treatment of the disease, have a limited capacity to improve the general cognitive functioning of patients with schizophrenia. Numerous

studies agree that including psychosocial treatments of psychoeducation, family intervention, skills training and cognitive interventions for long periods (a year or more), produce a greater functional improvement especially in patients of first psychotic episodes which can be only obtained with drugs [122–127].

As previously pointed out, in general the data suggest that many subjects affected by schizophrenia are poor assessors of their own cognition [19, 128, 129] and its daily functioning. In this line, it is important to indicate that, in the study by Poletti *et al*. [19] noted that close relatives of patients also have great difficulties in recognizing the presence of cognitive deficits in their affected relatives and they usually interpret them as a product of their personality, attitude, lack of interest or motivation, instead of understanding that they are due to the disorder. In addition, it should be remembered that the relatives of patients with schizophrenia also present more neuropsychological alterations than the control subjects [130], such deficits could represent an important difficulty to identify some symptoms of schizophrenia that can be present in the family.

It is also important to remember that knowing the biological and genetic origins of mental disorders does not help reduce social distances or avoid stereotypes. (In fact, Angermeyer *et al.* [131] found the opposite. They describe they were related to an even stronger rejection). In family interventions of patients with schizophrenia, although the lack of knowledge the parents is linked to a poor vision of the patient on their deficits and on their awareness of disease, [132] these must go further. The study by Macgregor *et al* [133] concludes that it should not be focused only on giving information and observing compliance with treatment, but also on other parental factors such as better cognitive performance (since there is an association between cognitive performance of parents -especially in executive functioning and verbal comprehension - and the perception of the illness of their children [18]), daily contact, a lower attitude of rejection are associated with better patients awareness of their disorder. Therefore, they conclude, that these factors should be included in specific programs aimed at caregivers, including cognitive intervention aimed at improving the cognitive flexibility of parents. In general Macgregor *et al.* [17] support the introduction of cognitive remediation techniques in family interventions. The objective would be to reduce the cognitive biases of healthy first-degree relatives. The perception of the patient and parents is an essential step on the road towards a good prognosis of the disorder.

It should be noted that, within family influences, not all are reduced to the simple knowledge of the symptoms. At this point, one of the most accepted hypotheses is that high levels of expressed emotion (EE) in front of a sick family member can lead patients to feel more ashamed and less open to self-understanding about their disorder [133]. This hypothesis underlies the idea of the influence that the development of the parent–child relationship implies [134]. Commonly, family therapy is recommended to reduce stressful family interactions and increase support, this, joined to cognitive training exercises are interventions that not only improve the well-being and functioning of patients, but also, even during the prodromal phase [135], can promote resiliency to stress, which has the potential to prevent the appearance of psychotic episodes [136].

Other family aspects to consider are the ones pointing out by Raffard *et al*. [18] in their study: In the prodromal phase of psychosis, patients often show nonspecific symptoms, such as anxiety and depression, social deterioration, drug abuse or alcohol, which are not interpreted

as possible symptoms of a major condition [137] and are associated with behavior typical of adolescence [138]. If a young individual is labeled as "sick" or "psychotic" is always a source of anguish [139, 140] and a potential risk of stigma [141], which can lead to maladaptive coping such as denial, avoidance and difficulties [142, 143]. The presence of cognitive deficits in patient and parents, can lead both to the difficulty to receive corrective feedback from professionals and to affect the ability to adequately judge the psychotic experiences of their children, which can lead parents to use coping strategies "avoidant" (as denial/disengagement) instead of more "approximation" strategies (such as seeking social support, reinterpretation, acceptance).

As already mentioned, there are programs of psychoeducation of cognitive symptoms for family members of schizophrenia and numerous intervention programs of cognitive symptoms in schizophrenia [59–62]. But nowadays, there are hardly any specific programs focused on cognitive intervention since the same family. Among the very few family intervention programs we can mention the Family-Directed Cognitive Adaptation (FCA). This program is designed to teach patients and family members the neurocognitive problems associated with schizophrenia; how to develop compensation strategies to minimize their impact on family and daily functioning; and teach families how to implement adaptive strategies to solve problems [144, 145].

In a first application of the program to a patient who lived with his mother [144], these authors, in addition to cognitive problems, also found a situation of abandonment of activities (friends, leisure), sedentary life, absence of social life beyond of family members, dull mood, poor diet, side effects of drugs and a family activity limited to doing small household chores (often incompletely, although the evaluations revealed a capacity to do tasks preserved, he used to leave them in the hands of his mother, including medication and calls to the doctor). In spite of everything, patient and family could take an active role in solving problems and generate practical objectives. They were taught what cognitive skills were and then strategies for adapting them in daily life (some of them already used list of "things to do" to avoid frequent forgetting of the patient). Then the best and worst preserved domains were observed (the latter: verbal memory, processing speed and executive function) and a series of strategies were introduced to overcome these difficulties (such as: using notes and reminders, dividing goals into smaller steps and maintaining short and simple communication …). An identification and problem solving format was applied (similar to that used in behavioral family therapy programs [146]) to prioritize goals (take care of food, make calls, medication …) and specific strategies aimed at addressing these barriers (lists of foods, use of agendas, summarize what is heard and ask for clarification of what was not understood, exercise …) and cognitive-behavioral technique to see the evidence for and against beliefs and concerns (this technique also it was used by the mother to test the irrational beliefs of the patient-possible residual symptoms-instead of acting against them fearfully or hostilely. Assertiveness and communication skills programs were also applied, identifying barriers and examining evidences (pros and cons). As the tasks increased, mutual trust improved, the patient was able to do more skills on his own and the burden of the mother decreased, improving the relationship and communication between them.

In a second pilot application of the program to a larger sample [145], the aspects considered most useful by relatives were: "Learning about cognitive deficits related to schizophrenia" and "learning about the specific cognitive strengths and difficulties of my relative" and patients considered: "Learning about my strengths and cognitive difficulties"and "learning strategies to overcome cognitive difficulties". This pilot study suggests that it may have helped family members to better understand the nature of cognitive challenges, which may have reduced feelings of irritation or guilt and with them the family burden. Despite the limitations of this study, it can be affirmed that it was shown that families could be involved in a program designed to teach strategies to reduce the effects of cognitive disabilities on daily living skills. They also suggested some benefits in terms of improved functioning and reduced family burden. Finally, they pointed to the natural and supportive role that relatives play in helping a member(s) with schizophrenia to have more control over their life and to progress towards important personal goals.

However, these achievements were not maintained. Although the program was effective during its implementation, it is possible, according to its authors, that 16 sessions are insufficient for families to master the basic fundamentals to implement cognitive adaptations on their own (not in vain, it is usually recommended that cognitive training last more than 1 year); or that the families that would have benefited from the program were gradually reducing participation in reinforcement sessions and did not facilitate the maintenance of the results.

Within other compensatory deficit strategies programs that involve the family exits the 9-months Cognitive Adaptation Training (CAT) [147]. It is especially applied, with the purpose of recovering vocations (work, studies) in first episode patients. Although the results seem promising, they are still pending confirmation in studies of larger samples.

It can be concluded that, in addition to inquiring into the ways of application of specific programs to treat cognitive deficits from the family framework (there are few programs yet, and despite having apparent good results, are still pending on a further study), the simple fact of giving knowledge about the symptomatology of schizophrenia is not always enough for parents to adopt attitudes of understanding towards the symptoms of their children. As pointed out by Friedman-Yakoobian *et al.* [145], rehabilitation and intervention should be oriented to improve the daily needs of each patient and it cannot be ignored the fact that many of these patients live with their families. Even when they live far away, relatives usually get involved in trying to give support (financial, emotional, etc. …) and a common consequence of this is that family members often suffer significant levels of stress, anxiety and caregiver burden. Therefore, we must also address attitudes such as the acceptance and overcoming of defeatist and critical attitudes, which help to avoid the denial of symptoms and improve their perception of the disorder and its daily adjustment. Highlighting that the association between the patient and the vision of the parents depends not only on the biological relationship, but on the frequency of daily contact and, therefore, in the immediate environment, supporting the role of environmental factors play in the perception of the disorder by the patient [133]. In this sense, as Kirkpatrick *et al*. point that [148] it is often forgotten the enormous complexity of schizophrenia and its impact, treatment and social and family functioning by focusing exclusively on psychotic symptoms.

3. Conclusions

Deficits influence in cognitive domains in schizophrenia disorder is something that severely affect the clinic symptomatology as well as in social, labor and familiar adjustment of this patients, been something not to be ignored. Even so, so few familiar intervention programs are focus in explain and give intervention strategies to this deficits from home daily life. To these problems it might be added a big possibility of finding a lower cognitive deficit in some family members without pathology, with what it might be necessary to intervene face to them having a more realistic and adjusted perception of their children illness. With that we wish to avoid that cognitive disrepair might be seem as a personal product, an attitude lack or even a defiance sign [19].

Considering all the presented data about cognitive endophenotypes, it might be understand that a genetic component exits in the pathology, but we cannot erase environmental factors influence. It is not impossible to add changes in the psychosocial patient environment with whom it might improve, not only symptomatology, but it social and labor adjustment. In the other hand, it is already been commented that family might affect negatively in both patient types, frequently because a high expressed emotion [133] affecting patient self – perception and with it, its global functionality.

In this way, it was expected to find that, in general, familiar interactions to resolve problems might seem to be less constructive and more problematic when the family member suffers schizophrenia disorder versus others disorders. Salinger *et al*. [149] recently studied those interactions between parents and their teenage affected children (or at high risk) of psychosis and bipolar disorder. After control variables in the parents as: sex, age, functionality, education. They observed that mothers of psychotic teenagers got a significantly more conflictive and less constructive communication than mothers of bipolar teenagers. The obvious conclusion is that, given that the family environment among adolescents seeking help may be more challenging for families with adolescents with psychosis than in other serious pathologies. These families need a more intensive and focused communication training than would be required for families with adolescents with high-risk for bipolarity or other mood disorders.

In general, research highlights the importance of psychosocial and family factors. These interventions become more important if we take into account works such as Engh *et al.* [20] where he pointed out that an adequate awareness of deficits is related to a good adherence to treatment, but also to a bad perception of self-confidence and self-efficacy. And on the other hand, we cannot ignore that all these aspects will be terribly influenced by the more than frequent stigmatization suffered by these patients and the disastrous consequences of it in their personal perception [139–143]. As can be observed, the intervention of cognitive aspects, although important, must go beyond and in order to ensure their effectiveness, it should be encompassed in other fields closely linked to family interactions according to achieve a greater perception of the effectiveness of the subject, which can lead to greater functional participation as it would be through the promotion of self-esteem, absence of continuous criticism, skill training, daily contact and attitudes of acceptance and coping.

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Conflict of interest

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