Chapter 1

Pharmacotherapy and Cognitive Behavioral Therapy for Patients with Schizophrenia

Stavroula Rakitzi[1,2]*, Polyxeni Georgila[2,3] and Konstantinos Efthimiou[2,4]

[1]Private practice. Ilision 34, 15771, Athens, Greece
[2]Hellenic Society for the training in CBT. Lifelong learning center. (http://cbt.edu.gr/erg/). Gladstonos 10. Kanniggos Square. 10677 Athens, Greece
[3]Psychiatric department for adults at the General hospital G. Gennimatas, Mesogion 154, 11527 Athens, Greece
[4]Institute of Behavioral research and therapy in Athens. http://www.ibrt.gr/edu/ , Eolou 102, 10564 Athens, Greece

*__Corresponding Author:__ Stavroula Rakitzi, Ilision 34 15771 Athens, Greece, Tel: 210 3824669; 6989766935; Fax: 210 3824669; Email: srakitzi@gmail.com

First Published **April 24, 2017**

Abstract

Evidenced based treatments are the treatments of choice for mental health disorders. Schizophrenia is a chronic mental disorder with negative impact on the quality of life of patients with schizophrenia and their families. The main therapy for these people is the pharmacotherapy. Cognitive behavioral therapy and rehabilitation can be implemented as an adjunct therapy to medication. Diagnostic issues are presented. The basic therapeutic goals in the treatment of schizophrenia are presented. The main principles of the pharmacotherapy are discussed. The various treatments in the context of cognitive behavioral therapy and rehabilitation as well as their efficacy are discussed. The Greek experience with the promotion and implementation of the Integrated Psychological Therapy, an evidenced based rehabilitation approach for patients with schizophrenia, is presented. Finally, the results of the above chapter are discussed.

Introduction

Schizophrenia is a chronic and debilitating condition. Patients with schizophrenia experience positive, negative symptoms, cognitive dysfunctions and other mental health problems as co morbidity. The suicidal risk of people with schizophrenia is very high. Schizophrenia is associated with many traumatic moments for the patients and their families. The main therapy for people with schizophrenia is the pharmacotherapy. Cognitive behavioural therapy and various rehabilitation programs present an adjunctive effective and efficacious treatment in combination with the pharmacotherapy.

The implementation of evidenced based treatments in mental health presents today a very important goal. Evidenced based treatments are those who offer a manual for the therapy, which therapeutic goals are specific and for which efficacy and effectiveness studies are available to the scientific community [1].

The cooperation of mental health experts regarding diagnostic issues and the coordination in the therapy is the most important condition in the clinical praxis for patients with schizophrenia and their families.

Diagnosis and Diagnostic Procedure

The diagnostic procedure must be the result of eng cooperation between psychiatrists and clinical psychologist,

in which the clinical interview and adequate psychometric tests strengthen the diagnosis. A period of 3-5 years of vulnerability is appropriate in order to give the diagnosis schizophrenia.

Diagnostic Criteria for Schizophrenia 295.90 (F20.9) (APA, 2013) [2]

A. Two (or more) of the following, each present for a significant portion of time during a 1 -month period (or less if successfully treated). At least one of these must be (1),(2),or (3):

1. Delusions.
2. Hallucinations.
3. Disorganized speech (e.g., frequent derailment or incoherence).
4. Grossly disorganized or catatonic behaviour.
5. Negative symptoms (i.e., diminished emotional expression or avolition).

B. For a significant portion of the time since the onset of the disturbance, level of functioning in one or more major areas, such as work, interpersonal relations, or self-care, is markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, there is failure to achieve expected level of interpersonal, academic, or occupational functioning).

C. Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or by two or more symptoms listed in Criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).

D. Schizoaffective disorder and depressive or bipolar disorder with psychotic features

have been ruled out because either 1) no major depressive or manic episodes have

occurred concurrently with the active-phase symptoms, or 2) if mood episodes have

Occurred during active-phase symptoms, they have been present for a minority of the total duration of the active and residual periods of the illness.

E. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.

F. If there is a history of autism spectrum disorder or a communication disorder of childhood onset, the additional diagnosis of schizophrenia is made only if promi-

nent delusions or hallucinations, in addition to the other required symptoms of schizophrenia, are also present for at least 1 month (or less if successfully treated).

Specify if:

The following course specifiers are only to be used after a 1-year duration of the disorder and if they are not in contradiction to the diagnostic course criteria.

First episode, currently in acute episode: First manifestation of the disorder meeting

the defining diagnostic symptom and time criteria. An acute episode is a time period

in which the symptom criteria are fulfilled.

First episode, currently in partial remission: Partial remission is a period of time

during which an improvement after a previous episode is maintained and in which the

defining criteria of the disorder are only partially fulfilled.

First episode, currently in full remission: Full remission is a period of time after a

previous episode during which no disorder-specific symptoms are present.

Multiple episodes, currently in acute episode: Multiple episodes may be determined

after a minimum of two episodes (i.e., after a first episode, a remission and a

minimum of one relapse).

Multiple episodes, currently in partial remission

Multiple episodes, currently in full remission

Continuous: Symptoms fulfilling the diagnostic symptom criteria of the disorder are remaining for the majority of the illness course, with sub threshold symptom periods being very brief relative to the overall course.

Unspecified

Specify if:

With catatonia (refer to the criteria for catatonia associated with another mental disorder,pp. 119-120, for definition).

Coding note: Use additional code 293.89 (F06.1) catatonia associated with schizophrenia to indicate the presence of the co morbid catatonia.

A differential diagnosis must be made from the following disorders (APA, 2013) [2]:

Major depressive or bipolar disorder with psychotic or catatonic features

- Schizoaffective disorder
- Schizophreniform disorder and brief psychotic disorder
- Delusional disorder
- Schizotypal personality disorder
- Obsessive-compulsive disorder and body dysmorphic disorder
- Posttraumatic stress disorder
- Autism spectrum disorder or communication disorders
- Other mental disorders associated with a psychotic episode.

The following psychometric tests could be administrated, in order to strengthen the diagnosis and the diagnostic procedure:

-Interviews: SKID (Structured Clinical Interview for DSM-IV) [3,4], CIDI (Composite International Diagnostic Interview) [5].

- Tests, which are evaluated from Psychiatrists and Clinical Psychologists: BPRS [6], SANS [7], PANNS [8].

- Tests, who are evaluated from the patients: SCL-90-R [9], Cognitive Assessment of Voices [10] and BAVQ (The Revised Beliefs about Voices Questionnnaire [11].

- Evaluation of cognitive dysfunctions: WAIS (Wechsler Intelligence Scale) [12] and MCCB [13].

It is also important to make a behaviour analysis of the dysfunctional behavioural components of the patients with schizophrenia. This analysis will contribute to the case formulation and to an effective therapeutic plan.

The clinical model that guides treatment in schizophrenia assumes that the experience of psychotic symptoms, hallucinations and delusions is a dynamic interaction between internal and external factors, which contribute to the origins of the disorder and to the maintaining of the symptoms. Dysfunction in the processing of information (hallucinations, delusions) in combination with dysfunctions in the arousal system and its regulation, will result in the disturbances of perception and thought that are characteristic for psychosis. The individual is reactive to these experiences and there is a process of primary and secondary appraisal in which the individual attempts to interpret these experiences, give them meaning and then react to their consequences. This reaction include emotional, behavioural and cognitive elements. Secondary effects such as low mood, anxiety in social situations and the effect of trauma may further compound the situation [14].

Therapeutic Goals

Evidenced based treatments focus on specific therapeutic goals: The positive symptoms, the negative symp-

toms, the cognitive dysfunctions (neurocognition and social cognition) and functional recovery [15,16]. Integrative models [17] present the above therapeutic goals, which are related to each other. The positive symptoms are independent and their remission contributes to functional recovery. The improvement of negative symptoms has a positive impact on neurocognition and social cognition and vice verca. Negative symptoms are possible mediators between neurocognition, social cognition and functional recovery. All this procedure improves the insight towards the disorder, increases the intrinsic motivation and activates the resources of the patients [17]. Treatment resistant schizophrenia presents also a very difficult therapeutic goal [18-20]

The intrinsic motivation [21] present an internal resource for patients with schizophrenia and for the mental health experts. The enhancement of intrinsic motivation with the motivational interviewing [22] is a very important step before every therapeutic procedure, which can increase the possibilities for the participation in an evidenced based treatment in a long term.

Pharmacotherapy

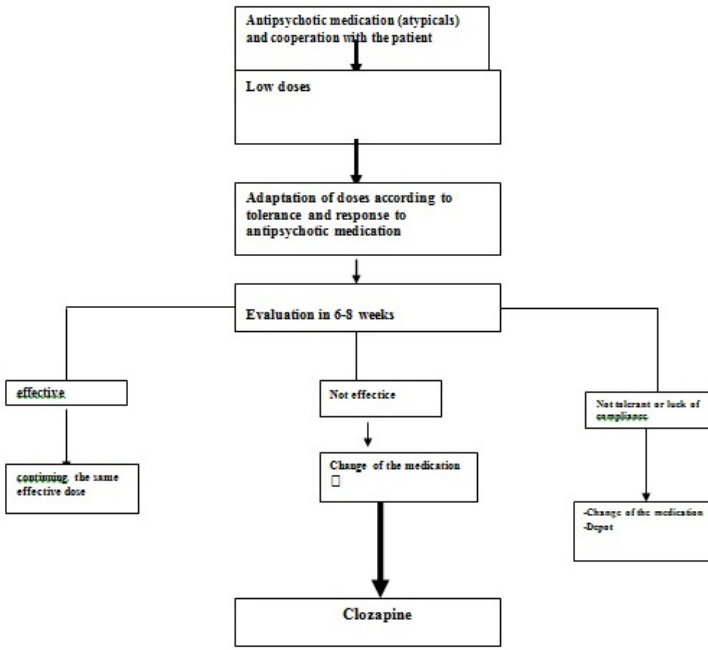
Although a hundred years and more the definition of schizophrenia as a clinical disorder from Kraepelin exists, for several decades has been untreated. For the last 7 decades pharmacotherapy has become the basic and effective

treatment of the psychotic symptoms of the disorder. The effectiveness of the antipsychotic medication has been significantly proved through international multi-centre clinical studies. The development of neurosciences including neuropharmacology has lead during the last decades to more effective and less harmful agents. There are two categories of agents: FGA (Haloperidol) and SGA (all the others).

The implementation of pharmacotherapy is follows basic principles of the Evidenced Based Medicine:

- In time appropriate intervention.
- Administration of appropriate medication (form, dosage, duration) AT the first psychotic episode.
- Maintenance therapy delivery.
- The detection of necessity for a co-administration of other drugs or parallel other treatments.
- Improvement of the efficacy.

There are several algorithms used as strategies as the following:



Algorithm for the first Psychotic Episode [23]

Several factors should be taken into accont in the choice of antipsychotic drug in the first psychotic episode, namely the severity of the episode, the patient's age, sex, the patients cooperativity and his environments, the his-

tory, the existence of a supportive environment, but co-morbidity with somatic and psychiatric diseases [24].

The presence of severe anxiety, psychomotor anxiety, stimulation accompanied by confusion and loss of control of reality creates the need for hospitalization and application of injectable treatment.

The range of therapeutic dosage varies according to the antipsychotic agent:

- Haloperidol (6-20 mg)
- Risperidone (4-6 mg)
- Olanzapine (10-20 mg)
- Sertindole (12-20 mg)
- Quetiapine (400-800 mg)
- Ziprasidone (80-120 mg)
- Aripiprazole (8-16 mg)
- In injectable form available are for hospital use:
- Haloperidol (5 mg)
- Olanzapine (10 mg)
- Ziprasidone (40 mg)
- Aripiprazole (8 mg)

The atypical antipsychotics (SGA) are the treatment of choice in the last decades because of their safest profile.

Positive symptoms (Hallucinations and Delusions) are treated effectively by atypical antipsychotics, while cognitive and negative symptoms have pure improvement [25-27].

We recommend average dosis for antipsychotic medication for the 4-6 weeks decreasing in the maintenance cource of the illness. High dosis increases the likelihood of side effects [28,29].

The compliance to the medication presents a very important goal in psychiatric treatment and should be evaluated frequently and is influenced by the side effects of its medication.

The treatment of side effects of the medication (neurological side effects, metabolic syndrome, cardio toxicity, diabetes, dystonia) is crucial and increases the possibility for higher compliance. Low doses of medication lead to the improvement or remission of the symptomatic and to reducing of the risk of neurological side effects and secondary negative symproms [30,31].

Knowing from compliance studies that a big percentage of patients, 30-50%, don't take their medication, the long acting injection (LAI) administration is the only choice. According to several studies the danger of relapse and hospitalization is three times less from the ones who take the medication p.os.

Treatment resistant patients with schizophrenia (TRS) are 30%. Clozapine is the treatment of choice for these patients. Clozapine affects effectively the suicidality, the hos-

tility and the aggressive behaviour, a fact that may lead to clozapine as first agent. To conclude, the key to successful pharmacotherapy is effectiveness as well as tolerance.

Cognitive Behavioural Therapy (CBT)

Psycho Education

Psycho education can be implemented in groups of in- and outpatients with schizophrenia, who are in remission. The first part of the program focuses on information and the treatment of the disorder. The second part focuses on the coping strategies in the context of the disorder. The third part focuses on the psycho education of the family members, which aims in relapse prevention, in decrease of the guilt and in the improvement of the communication between the family members [32].

Behaviour Family Therapy

The main goals of behaviour family therapy is the improvement of the communication between the family members, the improvement of problem solving and the improvement of the coping of stress and of insight towards the disorder. Families with high expressed emotion can benefit from this intervention [33].

Individual Cognitive Behaviour Therapy

Cognitive Behavioural Therapy for schizophrenia focuses on the treatment of delusions, hallucinations, nega-

tive symptoms and formal thought disorder. It is imperative that the therapeutic relationship be based on warmth and concern; the patient's perception of being supported may determine whether he or she attends the early sessions of treatment. In subsequent stages of therapy, a solid therapeutic relationship will allow the exploration and testing of strongly held and emotionally

charged beliefs. Finally, in the latter stages of treatment, where the work typically focuses on painful longstanding core beliefs and associated experiences, a warm and caring relationship will be instrumental in providing an alternative basis to beliefs regarding interpersonal vulnerability and rejection. So, first and foremost, the success of cognitive therapy for schizophrenia is contingent on the continuity of a warm, respectful, trusting, safe, and accepting therapeutic relationship [34, 35].

Metacognitive Therapy

Metacognition is the ability to form complex ideas about self and others. Deficits in metacognition may be a route cause of dysfunction in schizophrenia. Metacognitively oriented psychotherapy may promote subjective forms of recovery [36-43].

Efficacy of CBT

CBT presents an effective and efficacious psychotherapy for people with schizophrenia [44-51]. The evaluation of the efficacy is an ongoing process in the scientific community.

Rehabilitation

Integrative rehabilitation programs, which improve symptoms, cognitions, social competence and problem solving have encouraging improvements in proximal outcomes (cognition) but also in distal outcomes of psychopathology and psychosocial functioning. The Integrated Psychological Therapy, the Integrated Neurocognitive Therapy, the Cognitive Enhancement Therapy, the Neurocognitive Enhancement Therapy and the Neuropsychological Educational Approach to Cognitive Remediation present evidenced based integrated approaches for individuals with schizophrenia [52].

The IPT Program represents one of the very first comprehensive and manual-driven behaviour therapy group approaches combining interventions of neurocognition (INT), social cognition, social skills and interpersonal problem solving. IPT has been, and continues to be innovative because of different reasons [53]:

-Theoretically, because the therapy concept of IPT was initially based on the underlying assumption that basic deficits in cognitive functioning have a pervasive effect on higher levels of behavioral organization (pervasiveness hypotheses by Brenner, 1986). First of all, a link is made between deficits in neurocognitive functioning and the micro-social level, which describes non-verbal and verbal communication in social interactions. This process refers

to what is now called social cognition. According to the model of pervasiveness, the link is continued to the macro-social level of social functioning [53].

-Clinically, because IPT included new designed and high structured exercises focusing near all of the relevant treatment topics of schizophrenia patients. For example, social cognition were designed and standardized long before these cognitive domains became even defined by other research groups [53].

Moreover, IPT worked as a model for other later developed therapy approaches designed in the USA. Not only the American Psychological Association (APA) [54] recommends IPT as state of the art treatment, it has also been established as a standard approach in many countries, especially in Europe [55].

IPT is divided into 5 subprograms (SP) with increasing levels of complexity. It begins with intervention on neurocognition (SP1: Cognitive Differentiation) and social cognition (SP2: Social Perception), followed by intervention on communication skills (SP3: verbal communication), social skills (SP4) and interpersonal problem-solving skills (SP5). These 5 modular subprograms should be applied sequentially, but they have also been administered separately both in research and practice. A detailed description of the IPT concept is available as a manual [56], which has been translated into 13 languages [57-59].

A detailed description of the IPT concept is available as a manual [58], which has been translated into 13 lan-

guages [56-58]. Over the past 30 years, research groups in 12 countries have evaluated integrated psychological therapy (IPT) in 37 independent studies, including 1632 patients with schizophrenia. These studies on IPT were recently summarized and quatitatively reviewed in meta-analyses [59-61]. IPT revealed significant superior effects compared to Treatment as Usual (TAU), to active control groups in neurocognition, social cognition and functional outcome, as well as in the more distal outcome area of negative symptoms. All these favorable effects were maintained at follow up. The positive results were very robust in respect to cited conditions and setting [59-61].

The IPT concept was expanded in our lab and modified continuously [53]:

-In a first step, the social subprograms of IPT were developed: We designed three new cognitive social skills programs for residential, vocational and recreational rehabilitation (WAF German abbreviation for "Wohnen, Arbeit, Freizeit" [32].

-In a second step, the cognitive part of IPT was expanded and the Integrated Neurocognitive Therapy for the improvement of neurocognition and social cognition was designed [62-64].

The Greek Experience with the Integrated Psychological Therapy

Integrated Psychological Therapy is one of the most evaluated evidenced based programs for individuals with schizophrenia. Our Group (K. Efthimiou, S. Rakitzi, P. Georgila) cooperates since 2005 with Prof Volker Roder, Professor of Clinical Psychology, Head of Therapy Research, University Hospital of Psychiatry in Bern Switzerland. Our Project has two main goals: The promotion and implementation of IPT in the Greek population and the training of psychologist and psychiatrists, who are trained in CBT, in IPT. Our first efficacy IPT study was recently published [65] and our results are in line with the meta analyses of IPT [59-61]. Our IPT training program is offered from the Hellenic Society for the training in CBT. Lifelong learning center in cooperation with the Institute of Behavioral Research and Therapy in Athens Greece. This trainings program includes the training in the 5 Subprograms of IPT and the implementation of IPT in clinical groups under supervision and lasts about one year [66]. The promotion of an evidenced based treatment for people with schizophrenia is very important especially for Greece due to the social and financial crisis the last 7 years.

Conclusions

The main therapy for people with schizophrenia is the biological therapy. CBT and evidenced based rehabilita-

tion are appropriate in combination with biological therapy for a better improvement of positive, negative symptoms, cognitive functions (neurocognition and social cognition) and insight towards the mental disorder [67]. All these factors lead to an improvement of the functional recovery. Effective evidenced based pharmacological and non pharmacological treatments are available for the patients and for the mental health experts. The combination of various evidenced based treatments and their efficacy must be evaluated in the future in longer follow ups. Psycho education, rehabilitation programs for the improvement of neurocognition, social cognition, social competence and problem solving in combination with individual CBT and metacognitive therapy must be implemented in the future in longer follow ups. There are also new trends in CBT for individuals with schizophrenia but their evaluation of efficacy and effectiveness is not satisfied. The evaluation of efficacy is nowadays an ongoing process for these new trends [68]. Treatment resistant schizophrenia presents a very difficult category of patients with schizophrenia, in which a very eng cooperation between the psychiatrists and psychologists is on demand. The above combination of treatments is the treatment of choice for treatment resistant schizophrenia. The integrated Psychological Therapy is one of most evaluated integrated treatment approach for patients with schizophrenia. IPT is well accepted in Greece.

References

1. Roder V, Mueller D. Psychotherapie der Schizophrenie. Spect. Psychiatrie 2008; 1: 26-28.
2. American Psychiatric Association. APA. Diagnostic and Statistical Manual of Mental Disorders, 5th edition. DSM-5. Washington: American Psychiatric Publishing. 2013.
3. First MB, Spitzer RL, Gibbon M, Williams BWC. Structured Clinical Interview for DSM-IV. Axis I: Disorders (SCID-I). Clinical version. User's guide. Arlington: American Psychiatric Publishing. 1997.
4. First MB, Spitzer RL, Gibbon M, Williams BWC, Smith-Benjamin L. Structured Clinical Interview for DSM-IV. Axis II: Personality disorders. (SCID-II). Clinical version. User's guide. Arlington: American Psychiatric Publishing. 1997.
5. Kessler RC, Abelson J, Demler O, Escobar JI, Gibbon M, et al. Clinical calibration of DSM-IV diagnoses in the World Mental Health (WMH) version of the World Health Organization (WHO) Composite International Diagnostic Interview (WMH-CIDI). Int. J. Meth. Psychiatr. Res. 2004; 13: 122-139.
6. Lukoff D, Nuechterlein KH, Ventura J. Manual for expanded Brief Psychiatric Rating Scale (BPRS). Schizophr. Bull. 1986; 12: 594-602.

7. Andreasen NC. Scale for the Assessment of Negative Symptoms (SANS) Iowa City: The university of Iowa. 1983.
8. Kay SR, Opler L. Structrured Clinical Interview for the Positive and Negative Syndrome Scale (SCI-PANNS). Toronto: Multi Health Systems Inc; 1990.
9. Derogatis LR. The SCL-90-R Manual I: Scoring, administration and procedures for the SCL-90R. Baltimore: John Hopkins University School of Medicine Clinical Psychometric Unit. 1977.
10. Chadwick P, Birchwood MJ, Trower P. Cognitive therapy for Delusions, Voices and Paranoia. Chichester: Wiley. 1996.
11. Chadwick P, Lees S, Birchwood MJ. The revised Beliefs About Voices Questionnaire (BAVQ-R). Br. J. Psychiatry. 2000; 177: 229-232.
12. Aster M, Neubauer M, Horn R. Wechsler-Intelligenztest für Erwachsene WIE. Frankfurt: Harcourt Test Services. 2006.
13. Nuechterlein KH, Green MF. Matrics Consensus cognitive battery. MATRICS. Los Angeles: MATRICS Assessment Inc. 2006.
14. Tarrier N. A cognitive behavioural case formulation approach to the treatment of schizophrenia. In: Tarrier N, eds. Case formulation in cognitive

Behaviour Therapy. The treatment of challenging and complex cases. London: Routledge; 2006; 167-187.

15. Kircher T, Gauggel S. Eds. Neuropsychologie der Schizophrenie. Heidelberg: Springer. 2008.
16. Roder V, Medalia A. Eds. Neurocognition and social cognition in Schizophrenia Patients. Basel: Karger. 2010.
17. Mueller DR. Integrierte Neurokognitive Therapie bei Schizophrenie. Psychiatr. Psychother. 2012; 6: 1-16.
18. Kuipers E, Garety P, Fowler D, Freeman D, Dunn G, et al. Cognitive, emotional, and social processes in psychosis: Refining Cognitive Behavioural Therapy for persistent positive symptoms. Schizophr. Bull. 2006; 32: 24-31.
19. Turkington D, Sensky T, Scott J, Barnes TBE, Nur U, et al. A randomized controlled trial of cognitive behavioural therapy for persistent symptoms in schizophrenia: A five year follow up. Schizophr. Res. 2008; 98: 1-7.
20. Freeman D. Improving cognitive treatment for delusions. Schizophr. Res. 2011; 132: 135-139.
21. Medalia A, Choi J. Motivational Enhancements in Schizophrenia. In: Roder V, Medalia A, eds. Neu-

rocognition and Social Cognition in schizophrenia patients. Basel: Karger. 2010; 158-172.

22. Miller WR, Rollnick S. The motivational interviewing. Greek Translation. Athens: Litsas. 2010.
23. Osser DN, Roudsar MJ, Manschreck T. Har. Rev. Psychiatry 2013; 21: 28-45.
24. Buckley PE. Substance abuse and schizophrenia review. I clm Psych. 1998; 59: 26-30.
25. Stroup TS, Lieberman JA, Mc Envoy JP. Effectiveness of olanzapine, quietiapine, risperidon and ziprasidon in patients with chronic schizophrenia. Am. J. Psychiatry. 2001; 158.
26. Bjoerkestam E, Bjoerkestam C, Hjern A, Rentfors J, Boden RA. 5 year diagnostic follow up of 1840 patients after a first episode non-schizophrenic psychosis. Schizophr. Res. 2013; 150: 205-210.
27. Buchanan RW. Persistent negative symptoms. An overview. Schizophr. Bull. 2007; 33: 1013-1022.
28. Sernyak MJ, Leslie DL, Alarcon RD. Association of diabetes mellitus with use of atypical neuroleptics in the treatment of schizophrenia. Am. J. Psychiatry. 2002; 159: 561-566.
29. Suzuki T, Remington C, Benoit M, Mulsant, et al. Treatment resistant schizophrenia and response to antipsychotics. A review. Schizophr. Res. 2011;

133: 54-62.

30. Mackin P, Thomas SHL. Atypical antipsychotic drugs. BMJ. 2011; 342: 1126.
31. Osser DN, Patterson RD. Pharmacotherapy of schizophrenia. Handbook for the treatment of the serioudsly mental ill. Toronto. 1996.
32. Roder V, Zorn P, Andres K, Pfammatter M, Brenner HD. Praxishandbuch der verhaltenstherapeutischen Behandlung schizophrenen Erkrankter. Bern: Huber. 2002.
33. Falloon IRH, Boyd C, McGill C. Family care of schizophrenia. New York: Guilford. 1984.
34. Beck A, Rector N, Stolar N, Grant P. Schizophrenia: Cognitive Theory, Research and Therapy. New York: The Guilford Press. 2009.
35. Grant P, Huh G, Perivoliotis D, Stolar N, Beck A. Randomized Trial to Evaluate the Efficacy of Cognitive Therapy for Low-Functioning Patients With Schizophrenia. Arch. Gen. Psychiatry. 2012; 69: 121-127.
36. Lysaker PH, Beck KD, Carcione A, Procacci M, Salavatore G, et al. Addressing metacognitve capacity for self reflection in the psychotherapy for schizophrenia. A conceptual model of the key tasks and processes. Psychol. Psychoth: Th. Res.

Pract. 2010; 00: 1-13.

37. Lysaker P, Dimaggio G, Buck K, Callaway S, Salvatore G, et al. Poor insight in schizophrenia: links between different forms of metacognition with awareness of symptoms, treatment need and consequences of illness. Compr. Psychiat. 2011; 52: 253-260.

38. Lysaker PH, Erikson MA, Buck B, Buck KD, Olesek K, et al. Salvatore G. Popolo R. Dimaggio G. Metacognition and social function in schizophrenia: Associations over a period of five months. Cogn. Neuropsych. 2011; 16: 241-255.

39. Lysaker PH, McCormick BP, Snethen G, Buck KD, Hamm JA. Metacognition and social function in schizophrenia: Associations of mastery with functional skills competence. Schizophr. Res. 2011; 131: 214-218.

40. Lysaker P, Dimaggio G. Metacognitive capacities for reflexion in schizophrenia: Implications for developing treatments. Schizophr. Bull. 2014; 40: 487-491.

41. Badouna A, Lysaker PH, Rakitzi S. New psychotherapeutic approaches to schizophrenia: Enhancing metacognitive capacities. Cogn. Behav. Res. Ther. 2015; 1: 95-103.

42. Lysaker PH, Roe D. Integrative Psychotherapy for Schizophrenia: Its Potential for a Central Role in Recovery Oriented Treatment. J. Clin. Psychology. 2015.

43. Lysaker P H, Kukla M, Belanger E, White DA, Buck K, et al. Individual Psychotherapy and Changes in Self-Experience in Schizophrenia: A Qualitative Comparison of Patients in Metacognitively Focused and Supportive Psychotherapy. Psychiatry. 2015; 78: 305–316.

44. Wykes T, Steel C, Everitt B, Tarrier N. Cognitive Behavior Therapy for Schizophrenia: Effect Sizes, Clinical Models, and Methodological Rigor. Schizophr. Bull. 2008; 34: 523–537.

45. Tai S, Turkington D. The Evolution of Cognitive Behavior Therapy for Schizophrenia: Current Practice and Recent Developments. Schizophr. Bull. 2009; 35: 865-873.

46. Gottlieb JD, Romeo KH, Penn D, Mueser KT, Chiko BP. Web-based cognitive-behavioral therapy for auditory hallucinations in persons with psychosis: A Pilot study. Schizophr. Res. 2013; 145: 82-87.

47. Morrison AK. Cognitive behavior therapy for people with schizophrenia. Psychiatry. 2009; 6: 32-39.

48. Sommer IEC, Slotema CW. Daskalakis ZJ, Derks EM, Blom JD, et al. The Treatment of Hallucinations in Schizophrenia Spectrum Disorders Schizophr. Bull. 2012; 38: 704–714.

49. Hofmann SG, Asnaani A, Vonk IJJ, Sawyer AT, Fang A. The efficacy of CBT: A review of metaanalyses. Cogn. Ther. Res. 2012; 35: 427-440.

50. Addington J, Lecomte T. Cognitive behaviour therapy for schizophrenia. F1000 Med. Reports. 2012; 4: 6.

51. Burns A N M, Erickson DH, Brenner C A. Cognitive-Behavioural Therapy for Medication-Resistant Psychosis: A Meta-Analytic Review. Psychiatr. Serv. Adv. 2014; 65: 874-880.

52. Roder V, Medalia A. Eds. Neurocognition and social cognition in Schizophrenia Patients. Basel: Karger. 2010.

53. Mueller DH, Benjing VJ, Roder V. Integrated Psychological Therapy program and its further developments: From research to clinical practice. In: Rakitzi S, Georgila P, Efthimiou K, eds. Intervention by schizophrenia. Biological interventions and interventions in the context of CBT. Athens. 2016; 155-170.

54. Hogarty GE, Flesher S. Practice principles of cognitive enhancement therapy for schizophrenia.

Schizophr. Bull. 1999; 25: 693-708.

55. Roder V, Brenner HD, Kienzle N. Integriertes Psychologisches Therapieprogramm bei schizophren Erkrankten. IPT. Weinheim: Beltz. 2008.

56. Efthimiou K, Rakitzi S, Roder V. A cognitive behavioural group therapy program for the improvement of the cognitive and social abilities of patients with schizophrenia. Psychiatriki. 2009; 20: 245-254.

57. Roder V, Brenner HD, Kienzle N, Efthimiou K. The Greek manual of Integrated Psychological Therapy. (I.P.T.). Athens: Scientific Publications. 2007.

58. Roder V, Mueller DR, Brenner HD, Spaulding W. Integrated Psychological Therapy (IPT) for the Treatment of Neurocognition, Social Cognition and Social Competency in Schizophrenia Patients. Seattle: Hogrefe & Huber. 2010.

59. Roder V, Mueller D, Mueser K, Brenner HD. Integrated Psychological Therapy (IPT) for Schizophrenia: Is it effective? Schizophr. Bull. 2006; 32: 81- 93.

60. Roder V, Mueller DR, Schmidt SJ. Effectiveness of Integrated Psychological Therapy (IPT) for schizophrenia patients. Schizophr. Bull. 2011; 37: 71-79.

61. Mueller DR, Schmidt SJ, Roder V. Integrated Psychological Therapy (IPT):effectiveness in schizophrenia inpatient settings related to patients age. Am. J. Geriat. Psychiatry. 2013; 21: 231-241.

62. Roder V, Mueller DR. INT - Integrierte neurokognitive Therapie bei schizophren Erkrankten. Berlin, Heidelberg: Springer. 2013.

63. Mueller DR, Schmidt SJ, Roder V. One-year randomized controlled trial and follow-up of Integrated Neurocognitive Therapy for schizophrenia outpatients. Schizophr. Bull. 2015; 41: 604-616.

64. Mueller DR, Khalesi Z, Benzing V, Castiglione CI, Roder V. Does Integrated Neurocognitive Therapy (INT) reduce severe negative symptoms in schizophrenia outpatients? Schizophr. Res. 2017.

65. Rakitzi S, Georgila P,Efthimiou K, Mueller DR. Efficacy and feasibility of the Integrated Psychological Therapy for outpatients with schizophrenia in Greece: Final results of a RCT. Psychiatry Res. 2016; 242: 137-143.

66. Rakitzi S, Georgila P, Efthimiou K. Edn. Intervention by schizophrenia. Biological interventions and interventions in the context of CBT. Athens: IBRT. 2016.

67. Rakitzi S, Georgila P, Efthimiou K. Insight and re-

habilitation of patients with schizophrenia. J Mem Disord Rehab. 2016; 1: 1002.

68. Rakitzi S, Georgila P. Acceptance and Commitment Therapy as a Part of a Multimodal Rehabilitation for Patients with Schizophrenia. J Psychol Clin Psychiatry. 2015; 3: 00148.