



# Efficacy and feasibility of the Integrated Psychological Therapy for outpatients with schizophrenia in Greece: Final results of a RCT



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## ABSTRACT

The goal of this study was to evaluate the efficacy and the feasibility of cognitive remediation group therapy in patients with schizophrenia in Greece. For this purpose, the cognitive part of the Integrated Psychological Therapy (IPT), focusing on neuro- and social cognition, was compared in a randomized controlled trial (RCT) with treatment as usual (TAU). 48 outpatients took part in the study. IPT groups received 20 biweekly 1-h-therapy sessions. A test-battery was assessed at baseline, after therapy, and at a 3-month follow-up. Regarding cognitive functioning, significant effects favouring IPT were found in working memory and social perception during therapy and at follow-up. No effects could be found in verbal memory and vigilance. Significant effects favoring IPT were found in negative symptoms, in insight and in general symptoms during therapy and at follow-up using the Positive and Negative Syndrome Scale (PANSS). No effects were evident in positive symptoms and in psychosocial functioning. Significant effects favoring TAU were found in the quality of life assessment at follow-up. The study supports evidence for the feasibility and efficacy of IPT in psychiatric care in Greece and it hopefully will initiate the broader use of evidenced-based treatments like IPT in Greek Psychiatry.

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## 1. Introduction

Long-lasting functional deficits represent a challenge in the treatment of schizophrenia patients. 75–90% of all patients with schizophrenia suffer from cognitive deficits (Bell et al., 2013; Fett et al., 2013; Fioravanti et al., 2012; Green et al., 2012; Hovington et al., 2013; Roder and Mueller, 2008; Sachs, 2008; Ventura et al., 2013). A decade ago, the National Institute of Mental Health (NIMH) supported the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) initiative, to stimulate the development of pharmacological agents in treating cognitive deficits in schizophrenia, which are considered to be a core feature of the disorder. The following cognitive domains were initially recognized by MATRICS as being relevant for the treatment of schizophrenia: neurocognition: speed of processing, attention/vigilance, verbal and visual memory and learning, working memory, reasoning and problem solving; social cognition:

emotion processing, social perception, Theory of Mind (ToM), social schema, attribution (Green et al., 2005; Nuechterlein et al., 2004; Nuechterlein and Green, 2006).

According to the NIMH-MATRICS Consensus Statement on Negative Symptoms, negative symptoms are common features for individuals suffering from schizophrenia. They are associated with poor function and quality of life and have been proposed as a separate domain since 1974. Some of the conclusions of the NIMH-MATRICS consensus Statements on negative symptoms are the following: 1. Negative symptoms constitute a distinct therapeutic indication area, 2. Negative symptoms and cognitive impairments represent separate domains 3. Negative symptoms have face validity as disease manifestations, and represent loss or diminution of normal functions (Buchanan, 2007; Kirkpatrick et al., 2006; Kirkpatrick, 2014; Velligan et al., 2014).

Pharmacological agents show only small effects in improving cognitive domains (Leucht et al., 2013; Tandon, 2011). Consequently, psychological therapy approaches become of major interest. Cognitive Remediation therapy (CRT) is the only approach intervening directly in the enhancement of some cognitive functions. Meta-analyses support efficacy of CRT in improving most of the MATRICS domains (Kurtz et al., 2001; Kurtz and Richardson,

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2012; McGurk et al., 2007; Wykes et al., 2011), but generally fail to improve a more distal outcome such as social functioning (McGurk et al., 2007). Integrated approaches combining CRT with other therapy topics seem to be far more successful in improving a more distal outcome (McGurk et al., 2007; Wykes et al., 2011). Cognitive rehabilitation in schizophrenia becomes an even more important treatment, since there is evidence that neurocognitive domains are linked to functional outcome and these connections are strongly mediated by social cognitive functions as well as negative symptoms (Green et al., 2012; Robertson et al., 2014; Schmidt et al., 2011; Strassnig et al., 2015; Ventura et al., 2014).

### 1.1. Integrated Psychological Therapy (IPT)

IPT is a comprehensive manualized group cognitive behavioural therapy approach, integrating interventions on neurocognition, social cognition and social functions in one therapy concept (Roder et al., 2008, 2010). Its conceptualization is based on the assumption that main deficits in cognitive domains have a pervasive effect on higher levels of behavioural organization such as social functioning. 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 (Roder et al., 2008), which has been translated into 13 languages (Efthimiou et al., 2009; Roder et al., 2007, 2010).

Over the past 30 years, research groups in 12 countries have evaluated integrated psychological therapy (IPT) in 37 independent studies, including 1632 schizophrenia patients. These studies on IPT were recently summarized and quantitatively reviewed in meta-analyses (Mueller et al., 2013; Roder et al., 2006, 2011). 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 favourable effects were maintained at follow-up. The positive results were very robust in respect to cited conditions and setting.

In this study, only the cognitive part of IPT (SP1, SP2, and the first two levels of SP3) was conducted. The SP3 aims to train basic communication skills: Hearing, Understanding and React. The first level of SP3 focuses on the precise repetition of sentences and the second level focuses on the repetition of the main meaning of a sentence (Roder et al., 2008, 2010). As a first implementation step, only the cognitive part of IPT was conducted: it is highly structured, easy to handle and needs only a limited time frame.

The aim of the study was to examine the following hypothesis: the IPT group shows better improvement in proximal outcome of neurocognitive and social cognitive functions. Moreover, IPT obtains superior effects in symptom reduction and in psychosocial functioning in comparison to the control group.

## 2. Methods

### 2.1. Study population

The outpatients were recruited from the outpatients department of the Psychiatric Department of the General Hospital “G. Gennimatas” in Athens. All patients, who participated in this project, were initially invited by the Director of the clinic for an interview, in which the research project was presented.

“G. Gennimatas” is one of the largest general hospitals in Greece. It consists from many departments, one of which is the psychiatric department. This psychiatric department contains an inpatient department, an outpatient department, liaison psychiatry and a hostel. Patients are offered psychiatric and psychological-psychotherapeutic treatment. In the past there was no initiative regarding the implementation of an evidenced based rehabilitation program for individuals with schizophrenia for improvement in neurocognition and social cognition. That means that this study is the first implementation of an evidenced based rehabilitation program for improvement of neurocognition and social cognition by individuals with schizophrenia in this department and in a context of a general hospital in Greece.

The advantages and disadvantages of participating in this study were discussed in individual sessions with the patients and their families, separately. The patients have given informed consent to participate in the project. The patients were not paid for participation. It is common in the Greek mental health system care to include families in the therapy of individuals with schizophrenia, when the inter-family relationships are positive. The majority of these patients live with their families these last years of social and economic crisis.

Finally, the study protocol was approved by the Scientific Committee of the General Hospital “G. Gennimatas”. A total of 48 outpatients took part in this study. The following inclusion criteria were used: Diagnosis of schizophrenia according to DSM-IV (American Psychiatric Association, 2004), IQ > 80, patients were between 20 and 50 years, the duration of the disease was more than two years, no excessive substance abuse, no brain disease, and no relapse 2 months before the study entry.

Changes in medications were allowed before the study intake, when necessary. The medication was controlled during the whole therapy at monthly sessions with the psychiatrists of the clinic. The medication did not change at all during the project.

The patients of this study had no experience regarding the participation in individual cognitive behavioural therapy or in an evidenced based rehabilitation program for the improvement of neurocognition, social cognition and symptoms.

### 2.2. Study design

This study summarized a randomized controlled trial (RCT). After a baseline assessment (T1), a randomization procedure took place: Patients were allocated the IPT group as experimental group and treatment as usual (TAU) as the control group using a random drawing of lots by an independent person. The second assessment was carried out after the 10 week intervention. The third and final assessment was carried out at a follow-up of three months after the end of therapy.

TAU was chosen for the control group because there were no additional staff-therapists for another control condition. This study is the first RCT study for the efficacy of IPT in Greece. TAU is recommended as a necessary first step in evaluating the efficacy of IPT.

### 2.3. Therapists

Two therapists led all the IPT groups: A Psychologist was the main therapist and a Psychiatrist was the co-therapist. Both are experienced psychotherapists and well educated in IPT procedure. One blinded rater with an MD degree, not participating in the study, conducted the assessments.

### 2.4. Intervention

The experimental group represents a cognitive remediation approach in a group therapy setting following the cognitive part of

IPT. This consisted completion of the first two subprograms of “Cognitive Differentiation” and “social Perception”, along with the first two levels of the third subprogram “Verbal Communication”. IPT groups received 20 biweekly therapy sessions over 10 weeks, in addition to TAU. Each therapy session lasted 60 min. The duration and frequency of 20 bi-weekly therapy session was chosen in accordance with the guidelines of the authors recommendation for the implementation of the cognitive part of IPT (Roder et al., 2008, 2010, 2011).

TAU is defined as standard medication, case management and individual supportive therapy by a psychiatrist or psychologist. Supportive therapy included non-specific intervention, which helped the outpatients to cope with problems in daily routine. It did not contain specific cognitive behavioural therapy techniques or goals referring to work therapy. TAU was used as a control condition to be compared with the experimental group. The TAU group received the same therapy as IPT regarding the intensity of the therapy. Our 2 comparison groups are in the range of the intensity of treatment of the studies summarized in the meta-analysis on IPT of Roder et al. (2006, 2011). Each of the groups consisted of 8 participants. 3 IPT and 3 TAU groups took part. An attendance rate of less than 50% was defined as drop out and was excluded from the analysis.

## 2.5. Measures

### 2.5.1. Cognition (proximal outcome)

The following standardized assessments of cognitive variables addressing proximal outcome were used in the study. The neurocognitive domain of vigilance/attention was evaluated with the Continuous Performance Test (CPT), which measures selective attention, vigilance or sustained attention and impulsive behaviour (Mass, 2002). Working memory was evaluated with the Letter Number Span (LNS) (Gold et al., 1997; Nuechterlein and Green, 2006) using the Greek translation (Rakitzi, 2007a). The Greek verbal memory Test (VMT) was used to assess verbal memory (Kosmidou, 2002). Finally, the social cognitive domain of social perception was assessed with a Greek translation of the Social Perception Scale (SPS).

The SP2 “social perception” of the IPT improves the ability of the patients to perceive and interpret social situations. The Social Perception Scale was developed to measure social perception, one of the components of social cognition, after the implementation of SP2. The SPS assesses the three main aspects of Social Perception Program of IPT: stimuli identification, interpretation of images, and title assignment. The SPS is an instrument to support the therapists decision, whether the patients are ready for the next subprogram or not. The correlation between pre-test and post-test measurements is high (.96–1.00) (Garcia et al., 2003; Rakitzi, 2007b; Ruiz et al., 2005).

### 2.5.2. Psychopathology (distal outcome)

Positive, negative and general symptoms were assessed using the Greek version of the Positive and Negative Syndrome Scale PANSS (Kay et al., 1987; Lykouras et al., 2005). A well-experienced and blinded rater (M. D. degree) conducted the PANSS interview.

### 2.5.3. Functional outcome (distal outcome)

Quality of life was assessed using the Greek version of the World Health Organization Quality of Life WHOQOL (Ginieri-Coccosis et al., 2003, 2012). Psychosocial functioning was assessed using the Global Assessment and Functioning scale GAF (American Psychiatric Association, 2004). GAF and PANSS were both conducted by the same blinder rater.

### 2.5.4. Data analysis

The SPSS Version 21 has been used for statistical analysis. The General linear model for repeated measurements (GLM) and *t*-test were chosen to treat analysis of the empirical data (Bortz and Döring, 2002). Additionally, effect sizes were calculated using the difference between the mean scores of the comparison groups divided by the pooled standard deviation (Cohen, 1988). The sample size estimation was therefore based on the predicted large effect sizes for GLM for repeated measurements ( $f=0.4$ ) and for *t*-tests ( $d=0.8$ ), and for Pearson correlation coefficient ( $r=0.5$ ) with a generally accepted statistical power of 0.80 at an alpha level of significance of 5% (Cohen, 1988). Effect sizes can be generally categorized into small ( $d=0.2$ ), medium ( $d=0.5$ ), and large ( $d=0.8$ ). However, the sample size is underpowered to identify medium or small effect sizes.

## 3. Results

IPT and the control group each included 24 outpatients with schizophrenia (Fig. 1). 6 patients of the IPT group (25%) and 9 of the control group (37.5%) dropped out (chi-square=0.87,  $p=0.35$ ). The patients who dropped out, did not differ in any patient characteristics or baseline assessments from those who finished the study participation ( $t < 1.5$ ;  $p > 0.14$ ). The reasons for dropping out were low motivation (IPT:  $n=5$ ; TAU:  $n=5$ ) to follow through this project (attendance rate < 50%) or relapse (IPT:  $n=1$ ; TAU:  $n=4$ ).

The two comparison groups are near identical regarding patient characteristics (Table 1). There was no significant difference regarding age, intelligence assessed by Wechsler Adult Intelligence Scale (WAIS, Aster et al., 2006), sex, medication and duration of illness.

Baseline analysis revealed no significant differences in any outcome variable (*T*-test:  $t < 1.6$ ;  $p > 0.13$ ) between the two comparison groups. Regarding proximal outcome, inconsistent results could be found in neurocognitive functions. IPT patients showed significant higher effects in working memory, assessed by LNS, during therapy and highly significant effects during therapy and the follow-up period when compared to the control group. However, the two groups did not differ in verbal memory (VMT) and vigilance (CPT). Regarding social cognition, IPT patients obtained generally highly significant effects in all variables concerning

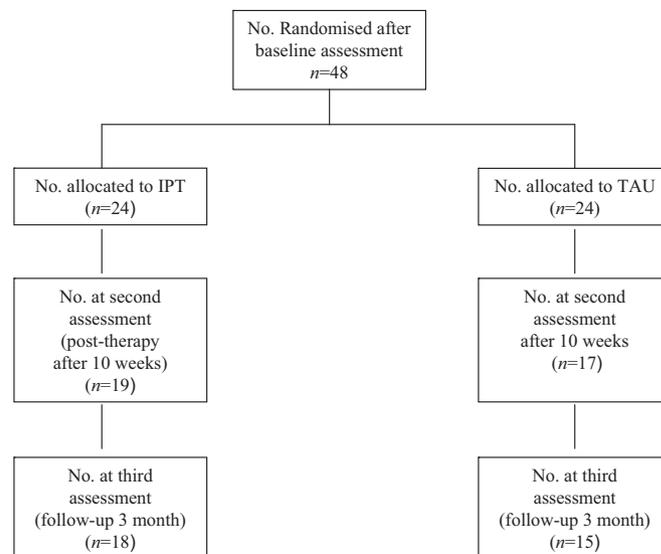


Fig. 1. Consort diagram: Flow diagram of subject progress through phases of the randomized controlled trial for the Integrated Psychological Therapy (IPT) and Treatment As Usual (TAU) group.

**Table 1**  
Patient characteristics (N=48).

	IPT	TAU	<i>t/Chi. Sq</i>	<i>p</i>
	N=24	N=24		
	M (SD)	M (SD)		
Age	31.3 (7.2)	33.8 (6.7)	1.2	0.22
IQ (WAIS <sup>a</sup> )	89.9 (9.4)	89.7 (7.7)	0.0	0.92
Duration of illness	5.4 (1.3)	(5.9) (1.1)	1.4	0.16
Medication (chlorpromazine equivalents)	542.1 (391.1)	512.1 (355.0)	0.28	0.78
Atypical (%)	83.3	83.3	0.0	1.0
Gender (% male)	67	67	0.0	1.0

Note:

<sup>a</sup> Wechsler Adult Intelligence Scale WAIS.

social perception assessed by SPS during therapy as well as during therapy and the follow-up period compared to TAU. These effects were the strongest in social perception and most robust in all assessments.

Regarding more the distal outcome, strong effects of high significance favoring IPT could be found in negative symptoms assessed by PANSS during therapy, and in negative symptoms as well as general symptoms during therapy and the follow-up period. However, no effects could be found relating to positive symptoms (PANSS) and psychosocial functioning as assessed by GAF. The PANSS score of insight showed significant superiority for IPT compared to TAU both after therapy and at the follow-up. In the

assessment of the quality of life (WHOQOL), a significant effect favoring TAU was found at the follow-up (Table 2).

Pearson correlation coefficients between patient characteristics and change scores in outcome (T1–T2; T1–T3) were calculated to identify possible impacts on outcome. Only the duration of illness was significantly associated with an improvement in insight assessed by PANSS during therapy in IPT ( $r=0.49$ ;  $p < 0.04$ ) suggesting that younger patients improved more than the older patients did. However, this effect was not evident at follow up and under TAU condition.

In addition, the calculation of effect sizes ( $d$ ) for the therapy phase (T1–T2) and the therapy and the follow-up phase (T1–T3) between the IPT and the TAU group showed large effect sizes in working memory (LNS) and in social perception (SPS) during therapy, which were still evident at follow-up. Small to medium effect sizes in vigilance (CPT) and verbal memory (VMT) indicate some increased functioning over time strictly favouring IPT compared to TAU. The composite scores of neurocognition (mean of all assessed variables relating to neurocognition) were  $d=0.62$  during therapy and  $d=0.57$  during therapy and the follow up period. Composite scores of all cognitive assessments (neuro- and social cognition) were  $d=1.70$  during therapy and  $d=1.99$  during therapy and the follow up (Table 2).

Regarding more distal outcomes, large effect sizes could only be found in negative symptoms and to a lesser extent also in positive symptoms (PANSS). Effect sizes of the composite score of distal outcome variables were  $d=0.56$  during therapy and  $d=0.42$  during therapy and follow up. Ultimately, the mean effect of all variables reporting the overall therapy outcome, showed a large

**Table 2**  
Proximal and distal outcome: General Linear Model (GLM) for repeated measures and effect sizes ( $d$ ).

		T1	T2	T3	GLM T1-T2		Effect size T1-T2		GLM T1-T2-T3 <sup>a</sup>		Effect size T1-T3
		M (SD)	M (SD)	M (SD)	<i>F</i>	<i>p</i>	<i>d</i>	<i>F</i>	<i>p</i>	<i>d</i> <sup>b</sup>	
<b>Proximal outcome</b>											
CPT <sup>c</sup> commission	IPT	3.3 (4.2)	2.9 (7.6)	1.7 (4.1)	2.4	0.13	0.68	0.39	0.48	0.39	
	TAU	2.5 (3.3)	3.3 (5.0)	3.1 (5.2)							
LNS <sup>d</sup>	IPT	13.1 (4.2)	17.9 (2.4)	17.3 (4.8)	<b>9.0</b>	<b>0.00</b>	0.95	<b>3.5</b>	<b>0.04</b>	0.80	
	TAU	12.4 (4.49)	13.6 (4.9)	12.8 (4.5)							
VMT <sup>e</sup> recognition	IPT	14.1 (1.6)	14.7 (1.2)	14.6 (2.1)	0.4	0.56	0.23	0.6	0.53	0.53	
	TAU	13.1 (1.7)	13.7 (1.5)	12.4 (5.3)							
SPST <sup>f</sup> stimulus	IPT	19.6 (7.3)	41.9 (11.7)	46.3 (10.2)	<b>21.9</b>	<b>0.00</b>	2.64	<b>31.7</b>	<b>0.00</b>	3.89	
	TAU	15.7 (7.2)	16.1 (5.9)	14.0 (8.6)							
SPST interpretation	IPT	6.2 (1.1)	10.2 (1.5)	11.1 (2.2)	<b>27.0</b>	<b>0.00</b>	2.50	<b>15.7</b>	<b>0.00</b>	3.18	
	TAU	5.9 (1.6)	6.3 (1.4)	6.1 (2.9)							
SPST title	IPT	4.1 (2.1)	11.3 (1.0)	10.7 (1.7)	<b>48.6</b>	<b>0.00</b>	3.24	<b>30.3</b>	<b>0.00</b>	3.18	
	TAU	3.4 (2.2)	3.5 (2.8)	3.5 (2.9)							
<b>Distal outcome</b>											
PANSS <sup>g</sup> positive symptoms	IPT	25.9 (6.9)	20.1 (5.2)	17.6 (5.7)	2.9	0.09	0.43	2.6	0.08	0.44	
	TAU	27.5 (6.9)	25.2 (5.0)	21.9 (5.1)							
PANSS negative symptoms	IPT	33.5 (4.5)	26.1 (4.3)	24.0 (4.6)	<b>13.6</b>	<b>0.00</b>	0.89	<b>12.0</b>	<b>0.00</b>	1.21	
	TAU	31.0 (4.3)	30.3 (5.8)	28.9 (4.7)							
PANSS general symptoms	IPT	59.9 (14.3)	45.6 (9.4)	43.9 (13.8)	3.7	0.06	0.62	<b>5.0</b>	<b>0.01</b>	0.75	
	TAU	59.0 (12.6)	55.5 (9.9)	52.2 (13.0)							
PANSS insight	IPT	4.1 (1.2)	2.9 (0.9)	2.6 (0.8)	1.7	0.20	0.62	1.9	0.16	0.57	
	TAU	4.5 (1.2)	4.1 (1.2)	3.6 (1.1)							
GAF <sup>h</sup>	IPT	36.0 (10.9)	44.1 (11.5)	54.3 (11.8)	1.7	0.20	0.28	1.9	0.16	0.50	
	TAU	40.5 (15.8)	43.9 (16.2)	52.5 (17.0)							
WHOQOL <sup>h</sup> (overall)	IPT	13.5 (3.7)	14.8 (3.5)	13.4 (4.4)	0.3	0.60	0.17	<b>4.0</b>	<b>0.03</b>	–0.69	
	TAU	13.7 (4.0)	14.8 (2.2)	16.2 (2.7)							

Note:

<sup>a</sup> GLM pre and post therapy and follow up;<sup>b</sup>  $d$ : Cohen's  $d$  (positive  $d$  scores indicate superiority of the experimental group IPT);<sup>c</sup> Continuous Performance Test;<sup>d</sup> Letter Number Span;<sup>e</sup> Verbal memory Test; <sup>f</sup> Social Perception Test;<sup>f</sup> Positive And Negative Syndrome Scale;<sup>g</sup> Global Assessment and Functioning scale;<sup>h</sup> World Health Organization Quality of Life. Bonferroni correction (Type I error):  $\alpha = 0.004$ .

effect size after therapy favouring IPT ( $d=0.95$ ), that could be maintained at follow-up ( $d=0.97$ ) (Table 2).

#### 4. Discussion

This RCT represents the very first efficacy study of IPT in the Greek population.

This study focused exclusively on the cognitive part of IPT addressing neurocognition and social cognition. Therefore, cognitive functions were defined as proximal outcome. Regarding neurocognition, IPT groups only showed significant effects after therapy in working memory that could be maintained during follow-up, though not in verbal memory and vigilance. The positive effects in working memory are in line with the effects presented by the meta-analysis of Wykes and Spaulding (2011) and Wykes et al. (2011), as well as the meta-analysis of IPT studies (Mueller et al., 2013; Roder et al., 2006, 2011). But the effects in vigilance and verbal memory were contrary to the ones found in the above mentioned meta-analysis. Both found significant medium effects in verbal memory and vigilance. Besides the actual social and financial strain on Greek society, the strict outpatient setting of our study including more functional patients, may explain these results: assessment in CPT had already obtained relatively good functioning at baseline (Suwa et al., 2004). Furthermore, the small sample size may be responsible for the fact that only large effect sizes achieved the statistical level of significance (type 2 error).

Moreover, it has to be mentioned that no explicit intervention on verbal memory is included in the IPT conception and therefore has yet been conducted in the procedure. So far, verbal memory does not represent proximal outcome. On the other hand, the assessment of social perception (Fuentes et al., 2007) was very close to the content of the intervention. In consequence, the improvement of the IPT patients was by far the highest of the whole study. However, the superior effects in social perception, which were maintained during follow up, could be interpreted as the horizontal generalization of the therapy effect. The effect sizes in social perception were much higher compared to the meta-analysis on social cognitive training (Kurtz and Richardson, 2012), but reached the same level as in the evaluation study of SPS (Fuentes et al., 2007).

Regarding more distal outcome variables, IPT intervention significantly reduced negative symptoms, and to a lesser extent also showed reductions in other symptom dimensions after therapy and at follow-up. These effects are superior to those summarized by the meta-analysis of Wykes et al. (2011), where no follow-up effects were evident. In particular, the effect in our study addressing negative symptoms are of some importance in psychiatric care, since it replicates the evidence found in other IPT studies: the cognitive part of IPT group procedure appeared to reduce negative symptoms even more in middle-aged patients, and these effects could be maintained after the end of therapy (Mueller et al., 2013; Roder et al., 2011).

The reduction of negative symptoms through the neuro- and social cognitive part of IPT (i. E. cognitive remediation group approach) is more important in the background of empirically-based mediator models on schizophrenia symptomatology, suggesting that neurocognitive domains are linked to functional outcome. These connections are strongly mediated by social cognitive functions as well as by negative symptoms (Brekke and Nakagami, 2010; Green et al., 2012; Lincoln et al., 2011; Schmidt et al., 2011; Ventura et al., 2013). From a clinical point of view, the reduction of negative symptoms may support a better prognosis and improved social functioning, since negative symptoms are shown to have a negative impact on these issues (Klingberg et al., 2011).

However, no effects favouring IPT could be found in the GAF score and in the quality of life. Since the social subprograms of IPT were deleted from the therapy procedure, these results recommend the implementation of the whole integrated procedure of IPT. In other studies, only the combination of cognitive remediation with other goal-oriented interventions obtained effects in social functioning (McGurk et al., 2007; Wykes et al., 2011). In this study, patients under TAU conditions showed even better self-rating in the overall quality of life, than did IPT patients after the end of the 3 month follow-up period. This may be an artefact of the assessment. On the other hand, it may be linked with the insight of patients into the illness: poor insight has been linked to more negative attitudes toward medication, longer episodes of antipsychotic non-adherence, more frequent hospitalization, greater levels of positive and negative symptoms, lower self-esteem as well as poorer psychosocial function and quality of life (Lysaker et al., 2011). IPT patients significantly increased insight and therefore may also have developed a more realistic view of their own life, which was, in fact, much more pessimistic compared to that of the control groups.

However, in this study we have no data supporting this assumption, due to some limitations to be discussed later. We found only some data supporting an impact of the duration of illness on the improvement in insight in IPT groups during therapy but not at follow-up.

IPT could be implemented for the first time in a context of a psychiatric department of a general hospital in Greece. The co-ordination of the colleagues in this clinic was not always possible. Some psychiatrists were a little bit suspicious about the possibility of proposing the patients to participate in a project like that. The Director of the psychiatric department had tried to increase the motivation of the psychiatrists, in order to refer patients to the project. This study makes such context possible and attractive for further rehabilitation initiatives with IPT and further research regarding the efficacy of IPT.

Some limitations of the study have to be discussed: 1) First of all, the sample was small and only sufficient to discover large effects. The statistically underpowered sample size may have led to type II (Beta) errors: we possibly would have found more significant effects in a larger sample. 2) The follow-up phase of 3 months after the end of therapy may have been too short to really identify stable generalization effects. In comparison, the mean follow-up among IPT studies is more than 8 months (Roder et al., 2011). 3) The inclusion of TAU may have been limited in controlling unspecific group effects of IPT treatment. An active control condition may have helped to identify these effects. However, IPT is a well-evaluated therapy approach. In quantitative reviews, the superiority of goal-oriented intervention of IPT compared to unspecific group therapy, is well documented (Roder et al., 2011). Therefore, TAU is recommended as a necessary first step in evaluating the efficacy of IPT in the Greek population. 4) Regarding the assessments, the much in common MATRICS Consensus Cognitive Battery (MCCB) would have been a more appropriate instrument in measuring cognitive changes in these Greek patients. However to our knowledge, no Greek translation of MCCB is available yet.

5) Regarding more distal outcomes, it is a clear limitation to have assessed social functioning only by GAF. Although GAF is widely used and seems appropriate in samples of stable patients, it may be confused with symptom severity and may not be very sensitive for psychosocial changes (Mueller et al., 2015; Robertson et al., 2013; Startup et al., 2002). Therefore, it would have been useful to include more measures of social functioning. 6) We have only included the cognitive part of IPT in this study. To really benefit from the advantage of IPT as an integrated therapy approach in long-term treatment, it would be important to implement the complete IPT program (Roder et al., 2011).

A further goal of this project was to implement an evidence-based therapy approach such as IPT into Greek health care. In a first step we carried out the cognitive part of IPT procedure representing a cognitive remediation approach in a group setting. After the initial publication of the Greek version of IPT in 2007 (Roder et al., 2007), this study now supports evidence for the feasibility of IPT procedure in patients with schizophrenia in Greece. The relatively low drop out rate and satisfying feedback by patients suggest a positive acceptance of the treatment. It is believed that this study works well as an initiation for new intervention and research possibilities in Greek psychiatric care. Some evidence was found for proximal and distal outcome success for the cognitive part of IPT, relating to cognitive remediation. More importantly, this study supports the feasibility of IPT treatment in Greek health care.

Further RCTs of adequate sample size, together with a longer follow-up plus active control conditions should also be included in the social part of IPT, in order to improve the benefit of evidence-based integrated intervention based on cognitive remediation in IPT procedure. Further RCTs of evidenced based treatments with a larger sample size plus active control groups and longer follow up, are necessary to improve evidenced based psychiatric treatment in Greek health care.

### Conflict of interest

None.

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### References

- American Psychiatric Association, 2004. DSM-IV-TR. Diagnostic criteria. DSM-IV-TR. Litsas, Athens.
- Aster, M., Neubauer, M., Horn, R., 2006. Wechsler-Intelligenztest für Erwachsene WIE. Harcourt Test Services, Frankfurt.
- Bell, M.D., Corbera, S., Johannesen, J.K., Fiszdon, J.M., Wexler, B.E., 2013. Social cognitive impairments and negative symptoms in Schizophrenia: are there subtypes with distinct functional correlates? *Schizophr. Bull.* 39 (1), 186–196.
- Bortz, J., Döring, N., 2002. *Forschungsmethoden und Evaluation für Human- und Sozialwissenschaftler*. Springer, Berlin.
- Brekke, J.S., Nakagami, E., 2010. The relevance of neurocognition and social cognition for outcome and recovery in schizophrenia. In: Roder, V., Medalia, A. (Eds.), *Neurocognition and Social Cognition in Schizophrenia Patients*. Karger, Basel, pp. 23–36.
- Buchanan, R.W., 2007. Persistent negative symptoms in schizophrenia: an overview. *Schizophr. Bull.* 33 (4), 1013–1022.
- Cohen, J., 1988. *Statistical Power Analyses for the Behavioural Sciences*. Erlbaum, Hillsdale, NJ.
- Efthimiou, K., Rakitzi, S., Roder, V., 2009. A cognitive behavioural group therapy program for the improvement of the cognitive and social abilities of patients with schizophrenia. *Psychiatriki* 20, 245–254.
- Fett, A.K.J., Maat, A., GROUP, Investigators, 2013. Social cognitive impairments and psychotic symptoms: what is the nature of their association? *Schizophr. Bull.* 39 (1), 77–85.
- Fioravanti, M., Bianchi, V., Cinti, M.E., 2012. Cognitive deficits in schizophrenia: an updated meta-analysis of the scientific evidence. *BMC Psychiatry* 12 (64), 1–20.
- Fuentes, I., Garcia, S., Ruiz, J.C., Soler, J., Roder, V., 2007. Social perception scale in Schizophrenia. A pilot study. *Int. J. Psychol. Psychol. Ther.* 7 (1), 1–12.
- Garcia, S., Fuentes, I., Ruiz, J.C., Gallach, E., Roder, V., 2003. Application of the IPT in a Spanish sample: evaluation of the "social Perception subprogram". *Int. J. Psychol. Psychol. Ther.* 3 (2), 299–310.
- Ginieri-Coccosis, M., Triantafyllou, E., Antonopoulou, V., Tomaras, V., Christodoulou, G., 2003. The Greek Manual of WHOQOL-100. Vita, Athens.
- Ginieri-Coccosis, M., Triantafyllou, E., Tomaras, V., Soldatos, C., Mavreas, V., Christodoulou, G., 2012. Psychometric properties of WHOQOL-BREF in clinical and healthy Greek populations: Incorporating new culture-relevant items. *Psychiatriki* 23 (2), 130–142.
- Gold, J.M., Carpenter, C., Randolph, C., Goldberg, T.E., Weinberger, D.R., 1997. Auditory working memory and Wisconsin card sorting test performance in Schizophrenia. *Arch. Gen. Psychiatry* 54 (2), 159–165.
- Green, M.F., Bearden, C.E., Cannon, T.D., Fiske, A.P., Helleman, G.S., Horan, W.P., Kee, K., Kern, R.S., Lee, J., Sergi, M.J., Subotnik, K.L., Sugar, C.A., Ventura, J., Yee, C. M., Nuechterlein, K.M., 2012. Social cognition in schizophrenia, part 1: performance across phase of illness. *Schizophr. Bull.* 38 (4), 854–864.
- Green, M.F., Olivier, B., Crawley, J.N., Penn, D.L., Silverstein, S., 2005. Social cognition in schizophrenia: recommendations from the measurement and treatment research to improve cognition in schizophrenia new approaches conference. *Schizophr. Bull.* 31 (4), 882–887.
- Hovington, C.L., Bodnar, M., Joobar, R., Malla, A.K., Lepage, M., 2013. Impairment in verbal memory observed in first episode psychosis patients with persistent negative symptoms. *Schizophr. Res.* 147 (2–3), 223–229.
- Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr. Bull.* 13 (2), 261–276.
- Kirkpatrick, B., Fenton, W.S., Carpenter, W.T., Marder, S.R., 2006. The NIMH-MATRICES consensus statement on negative symptoms. *Schizophr. Bull.* 32 (2), 214–219.
- Kirkpatrick, B., 2014. Progress in the study of negative symptoms. *Schizophr. Bull.* 40 (Suppl. 2), S101–S106.
- Klingberg, S., Wölwer, W., Engel, C., Wittorf, A., Herrlich, J., Meisner, C., Buchkremer, G., Wiedermann, G., 2011. Negative symptoms of schizophrenia as primary target of cognitive behavioral therapy: results of the randomized clinical TONES study. *Schizophr. Bull.* 37 (Suppl. 2), S98–S110.
- Kosmidou, M., 2002. The greek verbal memory Test. In: Stalikas, A., Triliva, S., Roussi, S. (Eds.), *The Psychometric Tests in Greece*. Greek letters, Athens, p. 171.
- Kurtz, M.M., Moberg, P.J., Gur, R.C., 2001. Approaches to remediation of neuropsychological deficits in schizophrenia: a review and meta-analysis. *Neuropsychol. Rev.* 11 (4), 197–210.
- Kurtz, M.M., Richardson, C.L., 2012. Social cognitive training for schizophrenia: a meta-analytic investigation of controlled research. *Schizophr. Bull.* 38 (5), 1092–1104.
- Leucht, S., Cipriani, A., Spineli, L., Mavridis, D., Örey, D., Richter, F., Samara, M., Barbui, C., Engel, R.R., Geddes, J.R., Kissling, W., Stapf, M.P., Lässig, B., Salanti, G., Davis, J.M., 2013. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. *Lancet* 382 (9896), 951–962.
- Lincoln, T., Mehl, S., Kesting, M.L., Rief, W., 2011. Negative symptoms and social cognition: identifying targets for psychological interventions. *Schizophr. Bull.* 37 (Suppl. 2), S23–S32.
- Lykouras, L., Botsis, A., Oulis, P., 2005. *The PANSS Scale*. Scientific Publications, Athens.
- Lysaker, P.H., Dimaggio, G., Buck, K.D., Callaway, S.S., Salvatore, G., Carcione, A., Nicolò, G., Stanghellini, G., 2011. Poor insight in schizophrenia: links between different forms of metacognition with awareness of symptoms, treatment need, and consequences of illness. *Compr. Psychiatry* 52 (3), 253–260.
- Mass, R., 2002. Das Vigilanzparadigma in der Schizophrenieforschung. *Fort. Neurol. Psychiatry* 70 (1), 34–39.
- McGurk, S.R., Twamley, W.T., Sitzer, D.I., McHugo, G.J., Mueser, K.T., 2007. A Meta-analysis of cognitive remediation in schizophrenia. *Am. J. Psychiatry* 164 (12), 1791–1802.
- Mueller, D.R., Schmidt, S.J., Roder, V., 2013. Integrated Psychological Therapy (IPT): effectiveness in schizophrenia inpatient settings related to patients age. *Am. J. Geriatr. Psychiatry* 21 (3), 231–241.
- Mueller, D.R., Schmidt, S.J., Roder, V., 2015. One-year randomized controlled trial and follow-up of Integrated Neurocognitive Therapy for schizophrenia outpatients. *Schizophr. Bull.* 41 (3), 604–616.
- Nuechterlein, K.H., Barch, D.M., Gold, J.M., Goldberg, T.E., Green, M.F., Heaton, R.K., 2004. Identification of separable cognitive factors in schizophrenia. *Schizophr. Res.* 72 (1), 29–39.
- Nuechterlein, K.H., Green, M.F., 2006. *Matrices Consensus cognitive battery. MATRICES. MATRICES Assessment Inc*, Los Angeles.
- Rakitzi, S., 2007a. The Letter Number Span in Greek. Unpublished.
- Rakitzi, S., 2007b. The Social Perception Scale in Greek. Unpublished.
- Robertson, D.A., Hargreaves, A., Kelleher, E.B., Morris, D., Gill, M., Corvin, A., Donohoe, G., 2013. Social dysfunction in schizophrenia: an investigation of the GAF scale's sensitivity to deficits in social cognition. *Schizophr. Res.* 146 (1–3), 363–365.
- Robertson, B.R., Prestia, D., Twamley, E.W., Patterson, T.L., Bowie, C.R., Harvey, P.D., 2014. Social competence versus negative symptoms as predictors of real world social functioning in schizophrenia. *Schizophr. Res.* 160 (1–3), 136–141.
- Roder, V., Brenner, H.D., Kienzle, N., Efthimiou, K., 2007. *The GREeK MANUAL OF Integrated Psychological Therapy*. (I. P. T.). Scientific Publications, Athens.
- Roder, V., Brenner, H.D., Kienzle, N., 2008. *Integriertes Psychologisches Therapieprogramm bei schizophoren Erkrankten. IPT*. Beltz, Weinheim.
- Roder, V., Mueller, D.R., 2008. *Psychotherapie der Schizophrenie*. Spec. Psychiatr. 1, 26–28.
- Roder, V., Mueller, D., Mueser, K., Brenner, H.D., 2006. Integrated Psychological Therapy (IPT) for Schizophrenia: Is it effective? *Schizophr. Bull.* 32 (Suppl. 1), S81–S93.

- Roder, V., Mueller, D.R., Brenner, H.D., Spaulding, W., 2010. Integrated Psychological Therapy (IPT) for the Treatment of Neurocognition, Social Cognition and Social Competency in Schizophrenia Patients. Hogrefe & Huber, Seattle, WA.
- Roder, V., Mueller, D.R., Schmidt, S.J., 2011. Effectiveness of Integrated Psychological Therapy (IPT) for schizophrenia patients. *Schizophr. Bull.* 37 (Suppl. 2), S71–S79.
- Ruiz, J.C., Garcia, S., Fuentes, I., Garcia-Merita, M., 2005. SPS: A scale for the assessment of social perception in schizophrenia. VII International Symposium on Schizophrenia. Bern, Switzerland.
- Sachs, G., 2008. Neurokognition und Schizophrenie. *Spec. Psychiatr.* 1, 16–18.
- Schmidt, S., Mueller, D.R., Roder, V., 2011. Social cognition as a mediator variable between neurocognition and functional outcome in schizophrenia: Empirical review and new results by structural equation modeling. *Schizophr. Bull.* 37 (Suppl. 2), S41–S54.
- Startup, M., Jackson, M.C., Bendix, S., 2002. The concurrent validity of the Global Assessment of Functioning (GAF). *Br. J. Clin. Psychol.* 41 (4), 417–422.
- Strassnig, M.T., Raykov, T., O’Gorman, C., Bowie, C.R., Sabbag, S., Durand, D., Harvey, P.D., 2015. Determinants of different aspects of everyday outcome in schizophrenia: the roles of negative symptoms, cognition and functional capacity. *Schizophr. Res.* 165 (1), 76–82.
- Suwa, H., Matsushima, E., Otha, K., Mori, K., 2004. Attention disorders in schizophrenia. *Psychol. Clin. Neurosci.* 58, 249–256.
- Tandon, R., 2011. Antipsychotics in the treatment of schizophrenia: an overview. *J. Clin. Psychiatry* 72 (Suppl. 1), S4–S8.
- Velligan, D., Maples, N., Roberts, D.L., Medelin, E.M., 2014. Integrated psychosocial treatment for negative symptoms. *Am. J. Psychiatr. Rehab.* 17 (1), 1–19.
- Ventura, J., Subotnik, K.L., Ered, A., Gretchen-Doorly, D., Hellenmann, G.S., Vaskinn, A., Nuechterlein, K.H., 2014. The relationship of attitudinal beliefs to negative symptoms, neurocognition and daily functioning in recent-onset schizophrenia. *Schizophr. Bull.* 40 (6), 1308–1318.
- Ventura, J., Tom, S.R., Jetton, C., Kern, R.S., 2013. Memory functioning and negative symptoms as differential predictors of social problem solving skills in schizophrenia. *Schizophr. Res.* 143 (2–3), 307–311.
- Wykes, T., Huddy, V., Cellard, C., McGurk, S.R., Czobor, P., 2011. A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. *Am. J. Psychiatry* 168 (5), 472–485.
- Wykes, T., Spaulding, W.D., 2011. Thinking about cognitive remediation therapy – what works and could we do better? *Schizophr. Bull.* 37 (Suppl. 2), S80–S90.