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Integrated Psychological Therapy (IPT) for Schizophrenia: Is It Effective?

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Against the background of evidence-based treatments for schizophrenia, nowadays the implementation of specific cognitive and behavioral interventions becomes more important in the standard care of these patients. Over the past 25 years, research groups in 9 countries have carried out 30 independent evaluations of Integrated Psychological Therapy (IPT), a group program that combines neurocognitive and social cognitive interventions with social skills approaches for schizophrenic patients. The aim of the present study was to evaluate the effectiveness of IPT under varying treatment and research conditions in academic and nonacademic sites. In a first step, all 30 published IPT studies with the participation of 1393 schizophrenic patients were included in the meta-analysis. In a second step, only high-quality studies (HQS) (7 studies including 362 patients) were selected and analyzed to check whether they confirmed the results of the first step. Positive mean effect sizes favoring IPT over control groups (placebo-attention conditions, standard care) were found for all dependent variables, including symptoms, psychosocial functioning, and neurocognition. Moreover, the superiority of IPT continued to increase during an average follow-up period of 8.1 months. IPT obtained similarly favorable effects across the different outcome domains, assessment formats (expert ratings, self-reports, and psychological tests), settings (inpatient vs outpatient and academic vs nonacademic), and phases of treatment (acute vs chronic). The HQS confirmed the results of the complete sample. The analysis indicates that IPT is an effective rehabilitation approach for schizophrenia that is robust across a wide range of patients and treatment conditions.

Key words: schizophrenia/cognitive behavior therapy/neurocognitive remediation/meta-analysis

Introduction

Until recently, the treatment of schizophrenia was grounded in pharmacotherapy with conventional antipsychotics, nonspecific social rehabilitation, and supportive or insight-oriented psychotherapy. However, over the past 2 decades, there has been a sea change in treatment philosophy and technology for schizophrenia, as exemplified by the following advances: (1) a paradigm shift in the locus of treatment from the hospital to the community,[1–3] including the development of the Assertive Community Treatment model[4] for ensuring continuity of care for severely ill and difficult to engage patients; (2) the focus on work as a rehabilitation goal and the validation of the supported employment model for improving employment outcomes[5]; (3) the development of atypical neuroleptics with a more benign side effect profile[6–8]; (4) an improved understanding of the role of neurocognitive and social cognitive deficits as mediators of functional and community outcomes[9–21]; and (5) a growing body of evidence demonstrating the efficacy of specifically targeted, standardized, predominantly cognitive-behavioral interventions.[22–29] This last group of approaches can be divided into 4 groups based on their respective objectives as follows[25,30,31]: (1) family therapy approaches, (2) social skills and problem-solving training, (3) neurocognitive remediation, and (4) cognitive behavior therapy (CBT) to reduce persistent positive symptoms.

The preponderance of research on the specifically targeted interventions listed above focuses on a single treatment approach. An exception to this is the Integrated Psychological Therapy (IPT), which combines neurocognitive remediation with training in social cognition, social skills, and problem solving.[31–33] This review explicates the IPT model and summarizes research conducted on it over the past 25 years.

IPT

IPT is a group-based CBT program for schizophrenia that integrates neurocognitive and social cognitive remediation with psychosocial rehabilitation. IPT is based on the underlying assumption that basic deficits in neurocognitive functioning have a pervasive effect on higher levels of behavioral organization, including social skills and social and independent functioning.[9,34–36] Based

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on this, successful psychosocial rehabilitation requires remediation of both underlying neurocognitive impairments and related social cognitive deficits, as well as building social, self-care, and vocational skills. IPT strives to integrate neurocognitive with psychosocial rehabilitation in a systematic, manualized fashion with the end goal of improved social competence. IPT is organized into 5 subprograms (figure 1). As the later subprograms build on the earlier ones, they are taught sequentially, beginning with neurocognition and social cognition, and followed by communication and social skills, and then problem-solving skills. The first subprogram primarily targets basic impairments in neurocognition (eg, attention, verbal memory, cognitive flexibility, concept formation). Remediation of neurocognitive deficits in IPT differs from conventional computer-based training approaches that emphasize repetitive training (rehearsal learning) of so-called "cold" cognitions in that specific interactive exercises are practiced through engaging group exercises, where patients learn alternative strategies for achieving individual goals (strategy learning).[27] The second subprogram addresses deficits in social cognition (eg, social and emotional perception, emotional expression). The fourth and fifth subprograms focus on building patients' social competence through practice of interpersonal skills (eg, role plays) and group-based problem-solving exercises. The third subprogram serves as a bridge between the first 2 and last 2 subprograms by focusing on neurocognitive skills that directly impact on interpersonal communication, such as verbal fluency and executive functioning. The specific targeted goals for each individual subprogram depend on each patient's deficits and strengths and the functional outcomes that are the focus of treatment.[31]

In order to capitalize on advances made in understanding and rehabilitation of social cognition, and social and problem-solving behavior, the original IPT model was modified to include Emotional Management Therapy[37,38] together with specific skills training programs to address vocational, residential skills, and recreational topics.[39–41] Because IPT was one of the first systematic, comprehensive, and manualized treatment approaches for schizophrenia, it has been wide adopted, especially in Europe. The German edition of the IPT manual is in its fifth printing,[31] and has been translated into 10 languages. Furthermore, a growing body of research has been conducted to evaluate the effects of IPT, but no comprehensive reviews of this literature have been published. Therefore, the time is ripe for a review.

Methods

Over the past 25 years, research groups in 9 countries have conducted 30 studies investigating IPT or a combination of several IPT subprograms, with a total sample (TS) of 1393 patients with schizophrenia (diagnosed according to International Classification of Diseases or Diagnostic and Statistical Manual of Mental Disorders). All study investigators were in contact with the IPT research group in Bern, Switzerland, which supervised some of them in treatment procedure. An additional literature search of IPT studies independent of language in international data sources (e.g., Medline, WebSPIRS) using the key words "schizophrenia," "IPT," "behavior therapy," or "cognitive therapy" found to no further IPT studies. With no exception, all 30 IPT studies were included in the analysis. Sample size, patient characteristics, state of illness, design, setting, and site conditions were extracted independently by 2 of us each, and differences were resolved by consensus after review. In 2 of the studies under review, IPT was compared with standard care (pharmacotherapy and social therapy) and with a placebo-attention condition (nonspecific group activity). In 11 studies, IPT was compared with standard care, in 10 studies with a placebo-attention condition, and in 2 studies, IPT was used as a control condition compared with another treatment approach. Five studies had no control group. These studies are summarized in table 1.

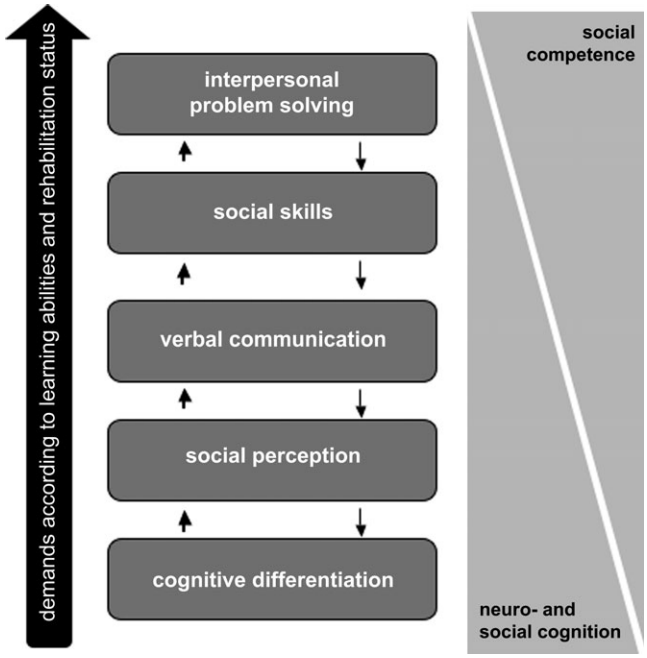

Fig. 1. Integrated Psychological Therapy (IPT) for schizophrenia.

IPT has been provided to patients at different stages of their illness (eg, immediately following the postacute phase of a symptom exacerbation, in stabilized patients exhibiting continuing or residual symptoms between episodes) in a variety of different locations (eg, inpatient and outpatient settings in academic and nonacademic institutions). The characteristics of these studies vary in terms of sample size and design; in 25 studies (83.3%), a controlled

Table 1. Thirty Independent Integrated Psychological Therapy (IPT) Studies ($N = 1393$)

Source	Country	Intervention	*N*	Setting	State of Illness	Center
Brenner et al[42,43]	Germany	IPT	43	Inpatient	Symptom stabilized	Academic
Brenner et al[44]	Germany	SP4 or SP2	28	Inpatient	Symptom stabilized	Academic
Stramke and Hodel[45]	Switzerland	SP2	18	Inpatient	Symptom stabilized	Academic
Bender et al[46]	Germany	SP1 + 2	28	Inpatient	Symptom stabilized	Nonacademic
Brenner et al[43]	Germany	IPT	18	Outpatient	Symptom stabilized	Nonacademic
Hermanutz and Gestrich[47]	Germany	IPT	64	Inpatient	Postacute	Nonacademic
Kraemer et al[48]	Germany	SP1 + 2 + CC	30	Inpatient	Symptom stabilized	Mix
Roder et al[49]	Switzerland	IPT	17	Inpatient	Symptom stabilized	Nonacademic
Funke et al[50]	Germany	SP1 + 2	24	Inpatient	Symptom stabilized	Nonacademic
Heim et al[51]	Germany	SP1–3	65	Inpatient	Symptom stabilized	Nonacademic
Peter et al[52,53]	Germany	SP1–3	83	Inpatient	Postacute	Academic
Kraemer et al[54]	Germany	SP1 + 2 vs SP4	43	Inpatient	Symptom stabilized	Academic
Olbrich and Mussgay[55]	Germany	SP1	30	Inpatient	Postacute	Academic
Roder[56]	Switzerland	SP1	18	Inpatient	Symptom stabilized	Nonacademic
Schüttler et al[57] and Blumenthal et al[58]	Germany	SP1–4	95	Inpatient	Postacute	Nonacademic
Hubmann et al[59]	Germany	SP4 + Token	21	Inpatient	Symptom stabilized	Nonacademic
Gaag van der[60]	The Netherlands	SP1 + 2	42	Inpatient	Symptom stabilized	Nonacademic
Takai et al[61]	Japan	IPT	34	Inpatient	Symptom stabilized	Mix
Theilemann[62]	Germany	IPT	45	Inpatient	Postacute	Nonacademic
Hodel[63]	Switzerland	IPT	21	Inpatient	Symptom stabilized	Academic
Spaulding et al[64]	USA	SP1–3 + SST	91	Inpatient	Symptom stabilized	Academic
Roder et al[65]	Switzerland	SP4	143	Mix	Symptom stabilized	Mix
Vallina-Fernandez et al[66]	Spain	SP2–4 + PE	35	Outpatient	Symptom stabilized	Nonacademic
Vauth et al[67]	Switzerland	SP4 + 5	57	Inpatient	Postacute	Academic
Vita et al[68]	Italy	IPT	86	Outpatient	Symptom stabilized	Nonacademic
Briand et al[69,70]	Canada	IPT + EMT	90	Mix	Mix	Mix
Penadés et al[71]	Spain	SP1 + 2	37	Outpatient	Symptom stabilized	Academic
García et al[72]	Spain	SP2	23	Outpatient	Symptom stabilized	Nonacademic
Lewis et al[73]	USA	SP1–3	38	Outpatient	Symptom stabilized	Nonacademic
Ueland and Rund[74]	Norway	SP1 + 2 + PE	26	Inpatients[a]	Postacute	Academic

Note: IPT, Complete IPT (subprogram [SP] 1–5); SP, IPT subprograms: cognitive differentiation (SP1), social perception (SP2), verbal communication (SP3), social skills (SP4), interpersonal problem solving (SP5); CC, cognitive coping strategies according to Meichenbaum[75]; Token, Token Economy Program; SST, Social Skills Training according to Liberman et al[76]; PE, psychoeducation; EMT, Emotional Management Training according to Hodel et al.[37]
[a]Adolescent; symptom stabilized, stabilized residual state.

design was used, while in 16 of these studies (64%), patients were randomized to IPT or another treatment. In 24 studies (80%), expert ratings of outcome were conducted, with blind ratings obtained in 8 (26.7%) studies. The heterogeneity of the scientific quality of studies on IPT can be attributed to changing therapy settings and designs over the 25-year period during which the research was conducted. For example, earlier studies tended to have smaller sample sizes, were less likely to employ a randomized controlled trial design, and provided a higher frequency of therapy sessions in predominantly inpatient settings (Spearman's correlation, 1-tailed: $r > .30$, $P < .05$, K studies ≥ 28).

We conducted a meta-analysis in order to evaluate the effectiveness of IPT in adults with schizophrenia (age > 18 years) when applied under varying clinical conditions. The only study[74] including adolescents is reviewed separately. In order to cover the full spectrum of different treatment conditions, in the first step, all 30 IPT studies were included. Of special interest are (1) the global therapy

effect, defined as the mean of all assessed outcome variables referring to documented symptom dimensions, neurocognitive and social functioning, quality of life, well being, and treatment satisfaction at the end of therapy and at follow-up; (2) separate symptom dimensions and functional impairments, including neurocognition (attention, memory, executive functioning), psychopathology (negative and positive symptoms), and psychosocial functioning (social and role functioning, self-care, occupational skills); (3) singular tests used in different studies to control the comparability of the assessments addressing different symptom and functional domains; (4) moderators of treatment response, including patient characteristics (eg, gender), setting (eg, inpatient/outpatient), and site conditions (eg, academic and nonacademic sites); and (5) predictors of outcome defined as the influence on outcome by moderating variables of patient characteristics and setting.

In the second step, we evaluated whether methodological rigor of the studies contributed to the observed effects by comparing the results of the complete sample of IPT studies with those of a subset of 7 rigorously controlled studies.[50,55,58,60,62,64,66] Rigorously controlled studies were defined as those which employed a controlled study design including randomization of patients to different treatment groups, fixed dosage of neuroloptics or statistically controlled change of medication, clearly stated blind ratings, and complete explication of data for the different dimensions of symptoms and functional domains that were assessed.

Data Analysis

To determine the extent of change in patients across the different control conditions, effect sizes (ESs) within the comparison groups were first calculated: ES = $(M_{pre} - M_{post\ or\ follow\text{-}up}) / SD_{pre\ of\ pooled\ groups}$.[77] As clinical studies have indicated higher ESs for patients in placebo-attention conditions than for patients receiving standard treatment,[64,78] these 2 types of control groups were dealt with separately. In addition, between groups ES were calculated according to Cohen's *d*.[79] ES can generally be categorized as small (0.2), medium (0.5), or large (0.8).[79] The possible influence of unequal sample sizes and SEs between the studies was statistically controlled by using a fixed effects model in which the ES of each study was weighted by its inverse variance (ES_w, d_w).[80] The homogeneity of variance of the ES of the individual studies was tested by calculating Hedges's Q_W.[81] To measure the significance of the weighted ES, the confidence interval and *z* transformation of the ES were used.[80] Differences between groups were evaluated by calculating Hedges's Q_B.[81] In order to weigh the strength of the findings against the possibility of publication bias toward more favorable results (ie, the "file drawer problem"), we calculated the number of unpublished studies with no effects that would be needed to negate the overall positive results of the published studies.[82] Finally, predictors of outcome were evaluated by calculating nonparametric Spearman's correlation coefficients.

Table 2. Patient Characteristics ($K = 29$ Studies)

	Mean	95% Confidence Interval
Gender: % male	68.0	$61.8 < \delta < 74.2$
Age, y	35.0	$32.9 < \delta < 37.0$
IQ	92.0	$87.6 < \delta < 96.4$
Duration of hospitalization, mo	77.9	$40.2 < \delta < 115.6$
Number of hospitalizations	3.9	$3.6 < \delta < 4.2$
Duration of illness, y	10.2	$8.1 < \delta < 12.3$
Daily dose of antipsychotics (chlorpromazine values)[a]	876.9	$364.2 < \delta < 1389.6$

[a]$K = 8$ studies.

Results

The patient characteristics of the entire sample comprising 1367 adult patients in 29 studies are displayed in table 2. As a result of the different phases of patient rehabilitation in each study, the duration of illness and hospitalization is heterogeneous. All studies provided pharmacological treatment for patients, and 8 studies provided information on the daily dosage of antipsychotics.

Therapy Setting and Dropout Rate

The mean treatment period was 17.2 weeks (95% confidence interval, CI, 11.8–22.6 weeks) or 49.3 hours (95% CI, 37.5–61.1). The mean number of therapy sessions was 44.4 (95% CI, 37.7–54.0) with a mean frequency of 3.2 sessions a week (95% CI, 2.7–3.7). In 14 studies (48.3%), the professional qualifications of the therapist were stated. In 13 of these studies (92.8%), primarily cognitive-behavioral–trained psychologists were involved, and in 5 studies (35.7%), psychiatrists trained in IPT participated as therapists. Fifteen studies (52%) indicated the dropout rate from the treatment period, and five of these (33.3%) also provided information on dropout from the entire study including follow-up (treatment and follow-up phase). The average dropout rate during the treatment period was 14.7% (95% CI, 7.8–21.6), and during the entire trial, it was 15.6% (95% CI, 0.2–31.0).

Effect of IPT on Global Therapy Outcome

IPT had significantly higher ESs (ES_w) compared with both control conditions for changes from baseline to the posttreatment assessment ($Q_B = 12.59$, $df = 2$, $P < .01$, 1-tailed) (table 3). Placebo-attention conditions

Table 3. Effect Sizes (ESs) Within the Integrated Psychological Therapy (IPT) Group, Placebo-Attention Condition, and Standard Care: Global Therapy Effect, Functioning Domains, and Measures

	IPT						Placebo Attention Condition						Standard Care					
	K	*N*	ES	ES_w (95% CI)	*Z*	Q_W	*K*	*N*	ES	ES_w (95% CI)	*Z*	Q_W	*K*	*N*	ES	ES_w (95% CI)	*Z*	Q_W
Global therapy effect																		
Treatment phase	27	710	.55	.51 (.40 to .61)	9.40**	10.99	10	202	.21	.24 (.04 to .44)	2.40*	1.79	12	160	.10	.13 (−.09 to .35)	1.12	4.21
Treatment and follow-up phase	8	253	.65	.57 (.39 to .74)	6.23**	6.27	2	36	.16	.15 (−.31 to .62)	0.65	0.00	3	38	−.12	−.07 (−.52 to .38)	−0.30	1.94
Follow-up: M = 8.1 mo																		
Functional impairments and symptom dimensions																		
Neurocognition	23	633	.61	.54 (.43 to .65)	9.41**	18.05	10	202	.18	.17 (−.02 to .37)	1.73	4.06	9	119	.15	.20 (−.05 to .46)	1.55	2.77
Psychosocial functioning	19	530	.43	.41 (.29 to .54)	6.65**	9.59	4	96	.17	.28 (−.01 to .56)	1.91	1.32	9	133	−.01	−.01 (−.25 to .24)	−0.04	3.10
Psychopathology	23	638	.58	.50 (.39 to .61)	8.74**	15.96	7	160	.29	.33 (.11 to .55)	2.94**	1.22	10	145	.18	.21 (−.02 to .44)	1.75	5.39
Positive symptoms	16	424	.42	.46 (.32 to .60)	6.60**	5.94	5	139	.29	.33 (.09 to .56)	2.70**	1.05	8	122	.15	.19 (−.07 to .44)	1.45	2.94
Negative symptoms	10	277	.46	.41 (.24 to .57)	4.75**	11.15	4	109	.21	.25 (−.02 to .51)	1.80	2.27	3	38	.11	.04 (−.41 to .49)	0.16	0.88
Assessment formats																		
Self-ratings	18	498	.55	.51 (.38 to .64)	7.92**	9.58	4	79	.30	.32 (.01 to .63)	1.99*	1.52	7	96	.10	.08 (−.20 to .37)	0.56	3.87
Expert ratings	21	543	.50	.48 (.36 to .60)	7.74**	14.70	6	124	.24	.30 (−.05 to .55)	2.35*	0.69	11	155	.15	.15 (−.07 to .38)	1.35	11.65
Psychological testing	23	633	.57	.52 (.41 to .64)	9.14**	18.39	10	202	.18	.17 (−.02 to .37)	1.73	4.06	9	119	.17	.21 (−.04 to .47)	1.64	2.61
Separate measures																		
d2	11	293	.65	.60 (.43 to .76)	7.01**	19.51	4	66	.16	.18 (−.16 to .52)	1.03	0.38	5	87	.23	.28 (−.02 to .58)	1.85	1.50
GAF	6	152	.72	.59 (.36 to .82)	5.05**	2.20	2	48	.12	.20 (−.20 to .60)	0.96	0.90	4	67	−.06	.00 (−.34 to .34)	−0.01	1.73
BPRS	16	333	.64	.61 (.45 to .77)	7.62**	24.05	4	76	.34	.28 (−.04 to .60)	1.73	0.24	10	145	.25	.29 (.06 to .53)	2.44*	15.53

Note: *K*, number of studies; *N*, number of patients; ES, unweighted effect sizes within the group; ES_w, weighted effect sizes within the group; 95% CI, 95% confidence interval; *Z*, significance statistic within the group; Q_W, homogeneity statistics, χ^2, 1-tailed. $df = K - 3$; d2, Attention Stress Test[83]; GAF, Global Assessment of Functioning Scale (Diagnostic and Statistical Manual of Mental Disorders); BPRS, Brief Psychiatric Rating Scale.[84]
*$P < .05$, **$P < .01$.

Table 4. Effect Sizes (ES) Within the Integrated Psychological Therapy (IPT) Groups and the Subsumed Control Groups (CGs): Global Therapy Effect Controlled by Centers, Treatment Settings, and State of Illness

	IPT						CG					
	K	*N*	ES	ES_w (95% CI)	*Z*	Q_W	*K*	*N*	ES	ES_w (95% CI)	*Z*	Q_W
Centers												
Academic centers	10	258	.63	.56 (.38 to .73)	6.19**	5.43	5	102	.25	.31 (.01 to .61)	2.06*	1.63
Nonacademic centers	13	288	.51	.50 (.34 to .67)	5.92**	2.90	13	230	.09	.14 (−.05 to .32)	1.43	1.85
Multicenters	4	90	.47	.44 (.22 to .66)	3.96**	2.01	2	30	.06	.05 (−.46 to .56)	0.20	0.07
Treatment setting												
Inpatients	20	475	.57	.53 (.40 to .66)	8.07**	9.39	15	287	.14	.20 (.03 to .37)	2.29*	3.81
Outpatients	5	105	.53	.49 (.22 to .77)	3.50**	1.00	5	75	.07	.08 (−.24 to .40)	0.50	0.55
State of illness												
Symptom-stabilized patients	20	446	.57	.52 (.39 to .66)	7.67**	9.39	16	264	.10	.14 (−.04 to .32)	1.57	4.36
Postacute patients	6	174	.51	.50 (.29 to .72)	4.62**	1.34	4	98	.24	.25 (−.03 to .53)	1.73	0.04

Note: CG, placebo-attention conditions and standard care subsumed; *K*, number of studies; *N*, number of patients; ES, unweighted effect sizes within the group; ES_w, weighted effect sizes within the group; 95% CI, 95% confidence interval; *Z*, significance statistic within the group; Q_W, homogeneity statistics; χ^2, 1-tailed. $df = K - 3$; multicenters, predominantly nonacademic centers; symptom-stabilized patients, stabilized residual state.
*$P < .05$, **$P < .01$.

exhibited small ES_w, which significantly differed from zero. These differed only marginally from those of the groups receiving standard treatment ($Q_B = 3.54$, $df = 1$, $P < .1$). The superiority of the IPT group was maintained at a follow-up at an average 8.1 months later ($Q_B = 8.29$, $df = 2$, $P < .05$). The single study with adolescent inpatients[74] found a moderate ES favoring IPT combined with psychoeducation (ES = .59) compared with psychoeducation alone (ES = .41).

Symptom Dimensions and Functional Impairments

There were highly significant improvements for the IPT group in neurocognition, psychopathology, and psychosocial functioning (table 3). With reference to the control conditions, only the placebo-attention group showed significant improvement in psychopathology. A between-group comparison showed a marked superiority of IPT compared with the control conditions—most notably with respect to the neurocognitive domain and psychosocial functioning ($Q_B > 9.34$, $df = 2$, $P < .01$) but not psychopathology ($Q_B = 5.74$, $df = 2$, $P < .1$). When the 2 control conditions were combined, IPT yielded significantly higher symptom reduction ($Q_B = 5.19$, $df = 1$, $P < .05$). The findings pertaining to positive and negative symptoms were similar to those with the combined psychopathology factor.

Assessment Formats

Highly significant improvements were found favoring IPT for all 3 assessment formats as follows: self-report (questionnaire), interview (expert rating by interviewing patient or related person), and psychological testing (paper-pencil or computer-based tests to assess predominantly neurocognitive and social cognitive performance) (table 3). Moreover, the IPT effects for these 3 formats were markedly homogenous ($Q_B = 0.31$, $df = 2$, not significant [NS]). Self-report and interview ratings yielded significant findings in the placebo-attention condition as well. There was a strong correspondence between self- and interview ratings in the IPT group (Spearman's correlation, 2-tailed: $r = .74$, $P < .01$, K studies = 14). Furthermore, the 3 most frequently used assessment instruments (Attention-Stress Test, d2[83]; Brief Psychiatric Rating Scale, BPRS[84]; the Global Assessment of Functioning Scale, GAF) had an average 24% higher weighted effects for the IPT group than the variables subsumed under the 3 domains of functioning. Thus, a significant superiority of IPT vs the 2 control conditions in regard to the BPRS was shown, in contrast to the combined domain of psychopathology ($Q_B = 6.62$, $df = 2$, $P < .05$).

Centers

The possible influences of institutional conditions, treatment settings, or stage of illness on the effects of IPT were evaluated by first combining the 2 control conditions in order to maximize the cell size of the comparison group. The ESs of IPT and the combined control groups are displayed in table 4.

Taken as a whole, the academic center studies yielded slightly larger effects than nonacademic center studies,

with regard to both IPT and to the control groups. IPT had significantly greater improvements in both settings. In academic centers, the control groups also achieved significant improvements during the treatment phase. The 4 multicenter studies with predominantly nonacademic participation had broader variance yield effects and were comparable to the other nonacademic centers. The differences based on institutional conditions were not significant ($Q_B < 1.24$, $df = 2$, NS) for either IPT or the control group.

Treatment Setting

Studies using samples of exclusively inpatients or outpatients both showed highly significant within-group effects for IPT (table 4). When compared with the control group, IPT was significantly better only for inpatients ($Q_B = 9.33$, $df = 1$, $P < .01$) and marginally significantly better for outpatients ($Q_B = 3.65$, $df = 1$, $P < .1$). Although inpatients in the control conditions showed significant improvements during the treatment period, neither IPT nor the control conditions differed with respect to treatment settings ($Q_B < 0.42$, $df = 1$, NS). During the therapy and follow-up periods, IPT inpatients had significantly greater improvements ($K = 4$, follow-up = 10 months; $ES_w = .79$, 95% CI, 0.43–1.16) than IPT outpatients ($K = 2$, follow-up = 7.5 months; $ES_w = .44$, 95% CI, 0.07–0.80). Whereas outpatients maintained the improvements made during therapy at follow-up, inpatients continued to improve during the follow-up period ($Q_B = 8.46$, $df = 1$, $P < .01$). Consistent with the presumed more acute or more severe stage of psychiatric illness in the hospital, inpatients had more pronounced psychopathology on the BPRS[84] ($K = 12$; BPRS total score: mean [SD], 47.8 [8.7]) than outpatients ($K = 4$; BPRS total score: mean [SD], 40.2 [11.8]).

Stage of Illness

IPT showed significant effects for both symptom-stabilized patients and postacute patients (see table 4). No significant effects were found for the control group; postacute patients showed small ES_w, while symptom-stabilized patients showed no effects during the therapy phase. At the beginning of therapy, postacute IPT and control patients exhibited more marked neurocognitive deficits ($K = 4$; d2 standard value[83]: mean [SD], 88.3 [3.5]) than symptom-stabilized patients ($K = 5$; d2 standard value: mean [SD], 101.7 [21.8]). IPT was significantly more effective than the control group only for symptom-stabilized patients ($Q_B = 11.17$, $df = 1$, $P < .01$). The stage of illness had no influence on the efficacy of IPT ($Q_B = 0.02$, $df = 1$, NS). For the posttherapy period, IPT patients whose symptoms were stabilized maintained the effects achieved during therapy at follow-up ($K = 6$, follow-up = 9.7 months; ES = .64, $ES_w = .53$, 95% CI, 0.29–0.77).

IPT Subprograms

In each of the studies, a variety of different IPT subprograms was provided. Twelve studies used the "cognitive differentiation," "social perception," and/or "verbal communication" subprograms (SP-Part I). Five studies only utilized the "social skills" and "interpersonal problem-solving" subprograms (SP-Part II), while 12 studies employed all 5 IPT subprograms (IPT-Complete). All 3 IPT variations showed highly significant global therapy effects during the therapy period (SP-Part I: ES = .58; $ES_w = .58$, 95% CI, 0.39–0.77; SP-Part II: ES = .54; $ES_w = .52$, 95% CI, 0.26–0.78; IPT-Complete: ES = .51; $ES_w = .46$, 95% CI, 0.32–0.61). The medium weighted effects of the 3 IPT variations were homogeneous ($Q_B = 0.92$, $df = 2$, NS).

With respect to the specific domains of functioning, patients receiving SP-Part I attained the highest weighted effects in the neurocognitive domain ($K = 12$; ES = .72; $ES_w = .71$, 95% CI, 0.51–0.90) and the smallest in psychosocial functioning ($K = 7$; ES = .38; $ES_w = .37$, 95% CI, 0.13–0.61) compared with those receiving SP-Part II and IPT-Complete. A between-group comparison of the 3 IPT variations revealed no significant findings with regard to the 3 outcome domains ($Q_B < 4.59$, $df = 2$, NS). In order to evaluate whether the effects at follow-up of providing the complete IPT program were stronger than providing only some of the subprograms, we combined studies that provided only SP-Part I or II and compared them with IPT-Complete. An assessment after a posttherapy follow-up averaging 8.3 months for SP-Part I or II ($K = 3$) and 7.9 months for IPT-Complete ($K = 5$), yielded significant improvements for both groups compared with the baseline. The weighted effects of therapy and of the posttherapy period were 25% higher for IPT-Complete (ES = .74; $ES_w = .60$, 95% CI, 0.39–0.81) than for SP-Part I or II (ES = .50; $ES_w = .48$, 95% CI, 0.13–0.82), although this difference was not statistically significant ($Q_B = 0.35$, $df = 1$, NS).

Predictors of Outcome

The duration of illness was the only independent patient variable that had a negative effect on the global therapy outcome of IPT (mean effect) ($K = 19$, Spearman's correlation, 2-tailed: $r = -.64$, $P < .01$). Patients who had a longer duration of illness tended to benefit less from IPT. In contrast, age and duration of hospitalization had a moderate negative effect on the global therapy outcome in the combined control conditions ($K > 10$, $r < -.50$, $P < .06$). The duration of therapy (in weeks or hours), the number of therapy sessions, or the weekly frequency of therapy sessions did not correlated with the global therapy outcome IPT ($K = 27$, $r < .30$, NS). However, a longer duration of therapy favorably affected improvement in functional outcome ($K = 19$, $r = .47$,

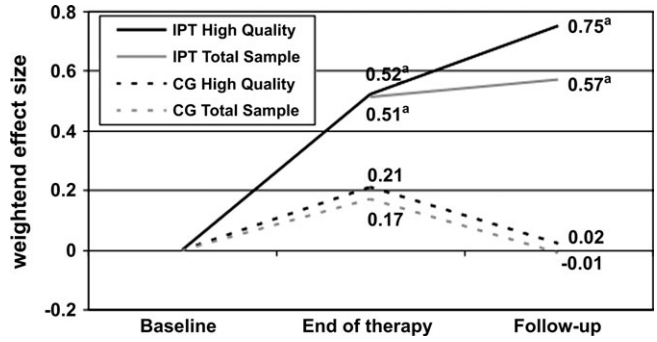

Fig. 2. Mean Weighted Effect sizes of the Total Sample ($K = 29$) and of the High-Quality Studies ($K = 7$) of Integrated Psychological Therapy (IPT) and Control Group (CG). [a]Significant weighted effect size ($Z > 2.58$, $P < .01$).

$P < .05$). Within this context, the study conducted by Takai et al[61] was an exception, inasmuch as it yielded small mean effects (ES = .17) in spite of providing only a single weekly session over more than 1 year of therapy (60 sessions).

The effects of IPT on the specific outcome domains were partially intercorrelated during the therapy period. Improvement in neurocognition was significantly correlated with improvement in psychopathology ($K = 19$, $r = .52$, $P < .05$) and functional outcome ($K = 15$, $r = .51$, $P < .05$). However, the correlation between improvement in psychopathology and functional outcome was not significant ($K = 17$, $r = .08$, NS).

Furthermore, the improvement in global therapy outcome from baseline to follow-up assessment was significantly correlated with improvement from baseline to posttherapy ($K = 8$, $r = .91$, $P < .01$). Changes in the neurocognitive domain ($K = 6$, $r = .89$, $P < .05$) and in psychopathology ($K = 8$, $r = .79$, $P < .05$) during therapy predicted mean follow-up effects. Improvements in these 2 domains also correlated significantly with a lower dropout rate ($K = 11$, $r < -.60$, $P < .05$).

ESs Between Comparison Groups

In calculating ESs (d) between IPT and comparison groups, a subsample of studies including control conditions was selected ($K = 21$; $N = 900$ patients). Patient characteristics and setting did not differ from those of the TS ($K = 29$). The 2 control conditions were combined. In comparison with the control conditions, IPT had significantly stronger global therapy effects during therapy and at follow-up (therapy period: $K = 21$; $d = .40$; $d_w = .36$, 95% CI, 0.23–0.50; therapy and follow-up phase: $K = 6$, $d = .52$; $d_w = .45$, 95% CI, 0.91–0.71).

The superiority of IPT was also evident in the 3 specific outcome domains (neurocognition: $K = 18$; $d = .46$; $d_w = .41$, 95% CI, 0.26–0.55; psychosocial functioning: $K = 13$; $d = .34$; $d_w = .31$, 95% CI, 0.15–0.48; psychopathology: $K = 16$; $d = .31$; $d_w = .31$, 95% CI, 0.16–0.46).

When d_w of the global therapy effect was converted into a correlation coefficient, $r = .20$. This means that according to Rosenthal's Binomial Effect Size Display,[82] an average of 60% of the IPT patients and 40% of the control patients benefited from their respective treatments. To address the issue of publication bias toward positive results, based on Rosenthal[82] we calculated that a minimum of 108 IPT studies showing no effect ($Z = 0$, $P = .05$) would be needed to negate the positive effects of IPT compared with the control group based on this analysis ($K = 21$; $r = .20$, $Z = .89$).

Methodological Rigor of Studies

To eliminate methodological and design-related bias, in a second step we repeated the analyses including only high-quality studies (HQS), as previously defined. In all, 7 studies with a total of 362 patients met these criteria. These studies did not differ from the Total Sample (TS) ($K = 29$) in terms of patient characteristics or therapy setting. Six of these studies recruited inpatients (85.7%) exclusively. Four studies (57.1%) included blind ratings, and three studies (42.9%) had no interview ratings. Three of the studies were confined to IPT subprograms for the neurocognitive and social cognitive domains (subprograms 1–3), while four studies provided the complete IPT program. Five studies compared IPT with a placebo-attention condition, one study compared IPT with standard care, and one study compared IPT with both control conditions. The weighted medium ES for global therapy outcome of IPT and combined control groups of the HQS was similar to that of the TS (figure 2).

The global therapy effect of the HQS and the remaining studies of the TS (non-HQS, $K = 22$) did not differ with respect to the IPT group or the control group ($Q_B < 0.19$, $df = 1$, NS). The superiority of IPT vs the control conditions was statistically significant for the HQS ($Q_B = 4.02$, $df = 1$, $P < .05$), as well as for the TS ($Q_B = 12.66$, $df = 1$, $P < .01$). The effects of the HQS across therapy and the follow-up period were higher than those of the TS but were identical to those of the inpatient subpopulation in the TS because HQS included predominantly inpatients. Once again, the HQS and non-HQS did not differ ($Q_B = 0.81$, $df = 1$, NS). As with the TS (see table 3), the IPT patients in the HQS showed significant improvements in all 3 specific domains: neurocognition ($K = 6$; ES = .52; $ES_w = .48$, 95% CI, 0.27–0.70), psychosocial functioning ($K = 4$; ES = .55; $ES_w = .62$, 95% CI, 0.33–0.92), and psychopathology ($K = 5$; ES = .50; $ES_w = .49$, 95% CI, 0.26–0.72). The HQS and non-HQS did also not differ in the specific domains ($Q_B < 2.37$, $df = 1$, NS).

With respect to the selection criterion of "blind ratings" for the HQS, the comparison between this set of studies and the TS on the interview rating variable is of particular interest. There was no difference in global

therapy outcome based on interviewer ratings of IPT in the HQS compared with the TS of studies ($K = 4$; ES = .49; ES_w = .52, 95% CI, 0.35–0.60). In addition, there was no significant difference between the HQS and the TS in the effects on psychopathology ratings (TS: K = 19; ES = .51; ES_w = .45, 95% CI, 0.33–0.58; HQS: K = 3; ES = .53; ES_w = .49, 95% CI, 0.17–0.81) and on psychosocial functioning (TS: K = 17; ES = .43; ES_w = .45, 95% CI, 0.32–0.58; HQS: K = 4; ES = .55; ES_w = .62, 95% CI, 0.33–0.92).

Discussion

This meta-analysis includes randomized-controlled trials as well as studies under routine psychiatric care, with inpatient and outpatient samples in academic and nonacademic sites. Therefore, the results of this meta-analysis have high generalizability to clinical and nonclinical settings and provide support for the effectiveness of IPT. In comparison with nonspecific group therapy or standard care, IPT yielded significantly higher global therapy effects, which were present both following the completion of therapy and were sustained at follow-up. The results of studies with high methodological quality support the efficacy of IPT and did not differ from the less rigorous studies.

The IPT group therapy approach differs from most other psychosocial treatment approaches to schizophrenia in the integration of neurocognitive and psychosocial rehabilitation methods. In contrast, family intervention, CBT for psychosis, social skills training, and neurocognitive rehabilitation programs have primarily been delivered as nonintegrated, independent programs. Meta-analyses have generally supported the effectiveness of family intervention and CBT for psychosis,[25,26,29,85,86] although the data supporting social skills training and neurocognitive remediation are weaker[27,28,87–89] and are the topic of some debate.[30,90,91] The present findings are of interest considering that the subprograms that comprise IPT focus primarily on neurocognitive remediation and social skills training.

The positive effects of IPT on both neurocognitive functioning and social behaviors reported in the present meta-analysis, in light of the weaker effects of neurocognitive rehabilitation or skills training interventions reported in some other meta-analyses, suggest that the integration of neurocognitive remediation and psychosocial skills training may work synergistically to improve both domains more effectively than either intervention alone. This tentative conclusion is in line with a recent study by Hogarty and colleagues,[92] who found that "cognitive enhancement therapy," which combines computer-based cognitive training exercises with individual and group work on social cognition and psychosocial skills development, had a significant impact on both neurocognitive functioning and psychosocial adjustment.

The studies included in this review covered a wide range of settings, methods, and patient characteristics. In order to understand the implications of the findings, we discuss these issues below.

Assessment Formats

No differences were found between expert ratings by interviews and self-reports. Among the studies included, expert ratings and patient self-assessments were significantly correlated, even within nonblind study designs. Most of the ratings used in IPT studies focus on social behavior and psychopathology. Studies of neurocognitive functioning have generally failed to find a strong association between self-ratings and objective performance in different neurocognitive domains.[93,94] Thus, expert ratings and self-reports may converge more in some areas of functioning, such as social behavior than others, such as neurocognition. In addition, it has been suggested that neurocognition impairment may moderate the relationship between self-ratings and objective ratings of functional behavior.[95]

Outcome Domains and Operationalized Variables

A general finding in the psychosocial rehabilitation field has been that interventions have their greatest effect on the proximal outcomes that are the most immediate focus of intervention.[96,97] This was evident in several IPT studies.[50,72] When compared with the control conditions, the largest effects of IPT were obtained in neurocognitive functioning, which is a major focus of IPT. In particular, the effects of strategy learning imparted by the first IPT subprogram are consistent with the meta-analytic findings for neurocognitive remediation.[27] Moreover, the larger effects of the IPT neurocognitive subprogram compared with other IPT variations on neurocognitive functioning is consistent with this observation. Similarly as might be expected, when the IPT neurocognitive subprogram was used exclusively, the mean effects in functional outcome were smaller compared with the additional or alternative application of the social competence subprogram. These results point to the internal validity of the IPT model and underscore the importance of domain-specific interventions for improving functioning in schizophrenia.

All the IPT variations were also found to have clearly superior effects on functional outcomes compared with control conditions. But in line with other meta-analyses, the IPT effects on psychosocial functioning tend to be smaller than in neurocognition and psychopathology.[23,25,30] Most notably, the measurement of social functioning is problematic and difficult to operationalize in a highly controlled environment such as an inpatient setting,[96,98] where the constituent elements of social behavior may be very different than in less overtly controlled settings.

The maintenance of IPT effects during the follow-up phase is consistent with the integrated model of mutual impact of different levels of neurocognitive and psychosocial skills functioning.[9,11,12] Only those patients who participated in the complete IPT, including the neurocognition, social cognition, and social competence treatment components, continued to improve during the follow-up phase. In addition, a longer treatment duration contributed to greater improvement in functional outcome. In accordance with recent studies,[19,21,71,92,99–106] these results further support the hypothesized generalization of improved neurocognition and social skills to actual social behavior and suggest that improving the distal outcome of social functioning requires the close integration of social and neurocognitive rehabilitation, such as in IPT.

Psychiatric Care Conditions

The impact of IPT was unaffected by patient variables, settings, or site conditions. The mean effects of inpatients and outpatients during the therapy phase are similar to findings reported on other meta-analyses of psychosocial treatments.[23,89] When interpreting the stronger effects for inpatients during the follow-up phase, the more pronounced pathology of this group compared with outpatients must be taken into account. Symptom-stabilized and postacute patients also displayed significant improvements under IPT. At the beginning of therapy, postacute patients exhibited larger selective attention deficits. This finding is supported by an aggregation of empirical findings on neurocognitive deficits (eg, selective attention) during the premorbid and remission phases as well as during acute psychotic episodes.[105] These selective attention deficits may be improved through neurocognitive remediation in IPT, accounting for strong observed effect.

With respect to the other patient variables, only duration of illness predicted lower success in IPT. In contrast, the age and the duration of hospitalization predicted the outcome for the control conditions but not IPT. Considering the small effects of the control interventions, older patients with longer lasting hospitalizations failed to benefit. In comparison, these patients benefited from IPT more than the control conditions. The marginal predictive value of the other patient variables was previously noted by Mojtabai et al.[23] In line with other studies of psychosocial and neurocognitive approaches,[23,27,92] treatment setting had no apparent influence on treatment effects. However, the effects of IPT tended to be stronger for studies carried out in academic centers than nonacademic settings, consistent with other findings,[23] and pointing to the need to conduct "effectiveness" research in nonacademic settings which presumably have higher generalizability to routine clinical settings where most patients receive treatment.[107]

Clinical Implications

During the 1980s, the frequency of IPT group therapy varied between 2 and 5 sessions a week. In recent years, however, a reduced regime of 2 weekly IPT sessions has become accepted as standard. The use of a combination of only some IPT subprograms for homogeneous groups of selected patients based on a behavioral and problem analysis[31] would appear a reasonable, efficient, and cost-effective treatment approach. In cases of more heterogeneous groups of patients with impaired functioning across a broader range of domains, only the application of the complete IPT would appear to produce sustainable effects. Furthermore, the broad scope of IPT, including neurocognitive, social cognitive, and psychosocial components, renders it suitable for patients in various states of illness and with rehabilitation needs spanning the entire spectrum of psychiatric care. Therefore, IPT may be useful in closing the gap between selective neurocognitive or psychosocial interventions and nonspecific rehabilitation approaches in standard care for schizophrenic patients.

Perspectives for Future Research

The findings of the present meta-analysis are naturally subject to limitations of the methods used in the research and the clinical applications of the IPT model. When reviewing the results of the limited number of studies of outpatients and postacute patients, the statistical testing of these studies had only modest power. Hence, further replication studies addressing these limitations are desirable. To date, authoritative statements pertaining to differential treatment indication, which also take the individual course of rehabilitation, the impact of therapeutic variables, and relapse prevention into consideration, are lacking, not least owing to the available data pool. In accordance with the National Institute of Mental Health-Measurement and Treatment Research to Improve Cognition in Schizophrenia initiative,[10,12–17] the coherence of differentiated functional domains during the course of treatment and aftercare of IPT—especially in the domains of neurocognition and social cognition and its relation to functional and community outcome—should be investigated in further controlled trials utilizing adequate sample sizes.

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