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Efficacy of Psychological Therapy in Schizophrenia: Conclusions From Meta-analyses

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Over the past years, evidence for the efficacy of psychological therapies in schizophrenia has been summarized in a series of meta-analyses. The present contribution aims to provide a descriptive survey of the evidence for the efficacy of psychological therapies as derived from these meta-analyses and to supplement them by selected findings from an own recent meta-analysis. Relevant meta-analyses and randomized controlled trials were identified by searching several electronic databases and by hand searching of reference lists. In order to compare the findings of the existing meta-analyses, the reported effect sizes were extracted and transformed into a uniform effect size measure where possible. For the own meta-analysis, weighted mean effect size differences between comparison groups regarding various types of outcomes were estimated. Their significance was tested by confidence intervals, and heterogeneity tests were applied to examine the consistency of the effects. From the available meta-analyses, social skills training, cognitive remediation, psychoeducational coping-oriented interventions with families and relatives, as well as cognitive behavioral therapy of persistent positive symptoms emerge as effective adjuncts to pharmacotherapy. Social skills training consistently effectuates the acquisition of social skills, cognitive remediation leads to short-term improvements in cognitive functioning, family interventions decrease relapse and hospitalization rates, and cognitive behavioral therapy results in a reduction of positive symptoms. These benefits seem to be accompanied by slight improvements in social functioning. However, open questions remain as to the specific therapeutic ingredients, to the synergistic effects, to the indication, as well as to the generalizability of the findings to routine care.

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Introduction

Over the past years a need for supplementary psychological therapies in the treatment of schizophrenia spectrum disorders became apparent for various reasons. For one, pharmacotherapy—commonly considered as cornerstone in the treatment of schizophrenia—has limits. For example, relapse rates in schizophrenia remain substantial even when adherence to prescribed medication is monitored.[1] Furthermore, a considerable number of schizophrenic patients suffer from persistent positive symptoms despite an ongoing medication regimen,[2] and current neuroleptic drugs have little beneficial effect on negative symptoms, residual cognitive impairments, and social functioning.[3] Finally, hospital treatment of schizophrenia has increasingly been replaced by community-based care. Thus, more responsibility for managing the burden of illness-related impairment was passed on to patients and their relatives, who in turn had to develop or improve adequate coping strategies. Therefore, many experts in the field advocate a multimodal treatment approach for schizophrenia.[4]

Most health-care systems, however, are challenged by serious financial constraints. Thus, decisions about what treatment to provide for whom must be based on evidence. Meta-analyses represent a reliable method to establish evidence-based clinical practice. They describe criteria for the selection and evaluation of employed sources, which allows for a replication of their findings. Summarizing data from different studies on the same subject by using a standardized quantified measure provides the possibility to estimate and compare interventions by the magnitude and significance of their effects. Meta-analyses also facilitate the explanation of the variance between the findings of different studies by testing statistical models including moderator variables. In doing so, they increase the statistical power of the original single studies and thereby enhance the validity of their findings.[5] Although problems inherent to this method may compromise the validity of the results (eg, with regard to the inclusion and comparison of

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methodologically heterogeneous or flawed studies), meta-analyses became widely accepted as a primary tool to assess the efficacy of specific treatment approaches.

However, none of the existing meta-analyses summarizing the efficacy of psychological therapies in schizophrenia allows for a comprehensive and comparative review of the effects of psychological interventions. The meta-analysis by Pilling et al[6,7] represents the only systematic quantitative review of randomized controlled trials on the efficacy of different well-defined psychological interventions. Yet, the power to detect the effects on different types of outcome is limited in this meta-analysis due to the small number of included randomized controlled trials. Therefore, we intend to summarize the findings of all meta-analyses published between 1990 and 2005 in order to draw consistent conclusions regarding the effects of different psychological therapy approaches in the treatment of schizophrenia. This summary is supplemented by selected results from an own meta-analysis of randomized controlled trials on the efficacy of psychological therapies in schizophrenia, where these results were suited to add to the findings of the existing meta-analyses.

Materials and Methods

Search

Relevant meta-analyses and randomized trials were identified by searching several electronic databases (PsycINFO; MEDLINE; the Cochrane Schizophrenia Group's Register of Trials; PSYNDEX). The following search algorithm was used to identify randomized controlled trials:

[schizophren* or psychosis or psychotic] and
[(psychological or psychosocial or psychotherapeutic* or supportive or behavio* or cognitive or operant or contingent or social-learning or skills or assertive* or problem-solv* or self-control or self-instruction* or self-management or rational-emotive or psychoeducation* or education* or adherence or compliance or psychoanal* or psychodynamic* or insight-oriented or system* or gestalt or client-centered or person-centered or experiential) near
(psychotherapy or therapy or intervention or treatment or training or rehabilitation or remediation or program* or modification or conditioning)] and
[(random* or controlled or clinical or comparative or empirical or experimental or evaluation or efficacy or outcome or treatment-outcome or prospective or single-blind-method or double-blind-method) near
(study or trial)]

In addition, references of all identified meta-analyses, reviews, and studies were hand searched.

Selection

For reasons of internal validity, the scope of our meta-analysis was limited to randomized controlled trials. All randomized controlled trials published in peer-reviewed journals up to 2005 were selected if they evaluated the impact of a specific psychological intervention compared with standard treatment or with an unspecific psychosocial treatment condition and if they included a homogeneous sample of standardized diagnosed schizophrenic patients and at least one standardized outcome measure. The identified studies were categorized according to the described psychological therapy approach and comparison group. To verify reliability of the selection process and categorization, a second coder reassessed a random sample ($n = 40$) drawn from all studies identified with the search strategy. The inclusion and categorization criteria checklist may be obtained from the authors upon request.

Data Analysis

In order to compare the findings of the existing meta-analyses, we extracted and transformed the reported effect sizes into Hedges *g* effect sizes where possible.

For our own meta-analysis, the data of the single studies were extracted and transformed into effect sizes for different types of outcomes. A mean effect size was calculated if several outcome measures were applied to the same type of outcome in a single study in order to avoid dependent data. Differences in effect sizes between the compared treatment and control conditions were calculated by dividing the mean pre-post difference (or pre–follow-up difference) by the pooled pre-post standard deviations (SDs) (or pre–follow-up SDs) for each condition and outcome variable. These calculations were based on an according-to-protocol analysis. The resulting effect sizes of the experimental and control condition were subtracted from each other. The differences in effect sizes in the individual studies were weighted by the inverse conditional variance and integrated by means of a categorical model of fixed effects. If the indication of means and SDs was missing, the effect sizes were estimated by *F*-, *t*-, *U*- or chi-square tests. In addition, 95% confidence intervals were estimated to test the significance of the effects, and heterogeneity tests were applied to evaluate the consistency of the resulting effect sizes regarding different types of outcomes and different categories of comparisons.

Data analyses were performed using an SPSS software package for calculating effect sizes developed by Rustenbach.[8]

Results

Meta-analyses of Efficacy Studies on Psychological Therapies in Schizophrenia

Between 1990 and 2005, a total of 21 meta-analyses of studies assessing the efficacy of various psychological

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Table 1. Meta-analyses of the Efficacy of Psychological Therapies in Schizophrenia

Therapy Approach	Meta-analysis	Inclusion Criteria	Number of Included Studies
Psychosocial interventions	Mojtabai et al[9]	Controlled studies	106
	Wunderlich et al[10]	Controlled studies	31
Psychodynamic therapy	Malmberg and Fenton[11]	Randomized controlled studies	3
Hypnosis	Izquierdo de Santiago and Kahn[54]	Randomized controlled studies	3
Token economy	McMonagle and Sultana[14]	Randomized controlled studies	3
Social skills training	Pilling et al[6,7]	Randomized controlled studies	9
Cognitive remediation			5
Family interventions			18
Cognitive behavioral therapy			7
Social skills training	Benton and Schroeder[16]	Controlled studies	27
	Corrigan[17]	Observational and controlled studies	73
Cognitive remediation of executive functions (Wisconsin Card Sorting Test)	Kurtz et al[26]	Laboratory and controlled studies	11
Cognitive remediation of attention	Suslow et al[27]	Laboratory and controlled studies	9
Cognitive remediation	Krabbendam and Aleman[28]	Controlled studies	12
	Twamley et al[29]	Controlled studies	17
	Hayes and McGrath[30]	Randomized controlled studies	3
Integrated Psychological Therapy	Müller et al[31]	Controlled studies	28
Family interventions	Pharoah et al[40]	Randomized controlled studies	28
	Pitschel-Walz et al[41]	Controlled studies	25
Cognitive behavioral therapy	Jones et al[58]	Randomized controlled studies	19
Cognitive behavioral therapy of positive symptoms	Tarrier and Wykes[49] and Tarrier[50]	Controlled studies	20
	Gould et al[51]	Controlled studies	7
	Rector and Beck[52]	Controlled studies	7
	Zimmermann et al[53]	Controlled studies	14

therapies in schizophrenia became available (table 1). The most comprehensive of these was conducted by Mojtabai et al.[9] It included a total of 106 studies published between 1966 and 1994 comparing any psychosocial therapy with a control condition. Each study was categorized according to treatment and control condition, respectively, and for each category obtained, a mean effect size was computed. On average, the studies comparing a combination of psychosocial and drug treatment with pharmacotherapy alone yielded an effect size of 0.39 in favor of the combined treatment. This can be interpreted as the magnitude of the additional effect of psychosocial treatment to pharmacotherapy. It indicates that the mean in effect variables between experimental and control conditions differs in 0.39 SDs. This implies that on average a patient receiving combined psychosocial and pharmacological treatment does better than 65% of patients with pharmacological treatment alone. By showing the additional effect of psychosocial treatment approaches to pharmacologic treatment, the meta-analysis by Mojtabai et al[9] provided the first solid empirical basis of the multimodal treatment model. They also provided a comparison between different types of psychosocial interventions.

In a similar way Wunderlich et al[10] compared the effect sizes resulting from different psychosocial therapy approaches. Their meta-analysis included all controlled studies ($n = 31$) published in English or German language between 1955 and 1994 that contrasted a psychosocial experimental condition with a pharmacologically or nonspecifically treated control group.

The meta-analyses by Mojtabai et al and Wunderlich et al thus license a first quantitative evaluation of the comparative efficacy of different psychosocial interventions. However, the specific psychological therapies were not well defined in these meta-analyses. Yet, both analyses demonstrate that psychological interventions designed to reduce disorder-related impairments in cognitive

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functioning or social behavior as well as psychoeducational and behavioral interventions focusing on the coping resources of schizophrenic patients and their relatives achieve significantly larger effects than insight-oriented psychodynamic therapy methods. The lack of evidence for the efficacy of psychodynamic therapies in schizophrenia has also been confirmed by a recent meta-analysis of Malmberg and Fenton.[11] Therefore, the findings of meta-analyses seem to confirm the theoretical assumptions provided by the vulnerability-stress-coping models.[12] These models suggest that favorable outcomes may be expected from psychological approaches that, in combination with neuroleptics, aim to improve the resources of patients and relatives for the management of disorder-related impairments and social strain. Considering these interventions in view of their specific therapeutic content, 4 distinct psychological treatment approaches can be identified on the basis of the available meta-analyses:

1. Training of social skills
2. Cognitive remediation
3. Psychoeducational coping-oriented interventions with families and relatives' groups
4. Cognitive behavioral therapy of positive symptoms.

The theoretical background, the content, as well as the empirically supported efficacy of these approaches will be outlined in the following sections.

Social Skills Training

Schizophrenic patients in general exhibit deficits in social competence that are widely independent of the severity of prevailing symptoms.[13] Poor social competence provokes cliff-hanging, stressful interactions with the social environment and leads to social isolation. In contrast, social competence generates social resources and improves community integration and role functioning. Social competence may, therefore, be viewed as an essential factor in the fragile balance between vulnerability and stressors. Consequently, it is seen as a key factor of outcome and serves as a target for therapeutic interventions.

Institutionalized token economy, based on operant conditioning, was the first psychological intervention focusing the social behavior of psychiatrically disabled persons. Despite the positive effects of token economy on negative symptoms,[14] its significance for the treatment of schizophrenic patients has decreased because the effects did not extend beyond the therapeutic setting and the possibility for contingent reinforcement is limited in community-based care settings. Therefore, social skills training gained an important role in therapeutic efforts to improve social functioning. The training is based on the perspective that social competence is composed of a set of skills allowing to receive, process, and express socially relevant clues. Prototypical sequences of social interactions are broken down into their components. These components are then practiced mostly within group settings by employing techniques derived from operant and social learning theory.

During the 1980s and 1990s, training approaches were tailored to address common problems particularly relevant to schizophrenic patients. The most widely studied skills training approach are the training modules for Social and Independent Living Skills developed by Liberman et al.[15] This training program consists of a series of training modules to practice specific disorder-related social and instrumental skills such as basic conversation, medication management, or community reentry.

Three meta-analyses have explored the efficacy of social skills training in schizophrenia so far. Overall, they show a rather inconsistent pattern of findings (table 2). Their results largely depend on the degree of rigor in the determination of the methodic quality of the individual studies included. The analyses by Benton and Schroeder[16] and by Corrigan[17] also included quasi-experimental studies. They revealed large effect sizes with regard to the acquisition of social skills and assertiveness and small to large effects regarding the reduction of psychopathology and hospitalization rates. In contrast, the meta-analysis by Pilling et al,[7] which included only randomized controlled trials, did not support these findings.

In our meta-analysis, we identified a total of 108 randomized controlled trials on the efficacy of various psychological interventions with schizophrenic patients. Twenty-two of these had to be excluded from further analysis because they could not be assigned unequivocally to a specific psychological therapy approach. Of the remaining 86 randomized controlled trials, 19 evaluated the efficacy of a social skills training approach. The included studies and their assignment to a specific class of psychological therapies as well as the excluded ones are listed in Appendix. To be classified as social skills training, the intervention had to include a range of techniques founded on the operant or social learning theory to enhance social performance such as instructions, modeling, role-play, reinforcement, corrective feedback, and in vivo exercises by homework assignments.

Our meta-analysis confirms a large, homogeneous and enduring effect on the acquisition of social skills by schizophrenic patients as measured in role-play tests and a short-term enhancement of their assertiveness (table 3). In addition, social skills training consistently leads to a moderate but significant and stable improvement in social functioning, slightly reduces general psychopathology, and considerably decreases the hospitalization rate at follow-up. However, the latter finding is based on only 2 randomized controlled trials.

Cognitive Remediation

The vast majority of schizophrenic patients demonstrate poor performance in different aspects of cognitive

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Table 2. Findings of the Meta-analyses Regarding the Effects of Social Skills Training

Meta-analysis	Outcome Variable	Effect Size[a] (95% CI)	Heterogeneity Q[b]
Benton and Schroeder[16]	Skill acquisition	0.76 (0.59 to 93)	13.49 ($P > .90$)
	Skill acquisition (follow-up)	1.13 (0.62 to 1.64)	NR
	Assertiveness	0.69 (0.43 to 95)	13.52 ($P > .10$)
	General psychopathology	0.32 (0.06 to 0.58)	8.87 ($P > .20$)
	Hospitalization (follow-up)	0.47 (0.18 to 0.76)	2.54 ($P > .30$)
Corrigan[17]	Skill acquisition	1.43*	NR
	Skill acquisition (follow-up)	1.40*	NR
	Assertiveness	0.92*	NR
	General psychopathology	1.08*	NR
Pilling et al[7]	Social functioning	Lack of data	
	Relapse	0.17 (−0.14 to 0.46)	3.71 ($P = .29$)

Note: CI, confidence interval; NR, not reported.
[a]Hedges *g*.
[b]Sum of squares.
*t-test, $P < .05$.

processing, most often reported in the domains of processing speed, sustained attention, working memory, verbal learning, executive functioning, and social cognition. 85% of the individuals suffering from schizophrenia score 1.3–2 SDs below the mean of samples drawn from mentally healthy populations. This is equivalent to scoring lower than 90% of healthy controls. Cognitive impairments tend to be relatively stable over the course of the disorder and are apparent even if psychotic symptoms remit. Mild cognitive impairments in schizophrenic patients are also observed before the onset of the disease as well as in a subgroup of their first-degree relatives.[18] This indicates that cognitive impairment in part represents a stable vulnerability marker of schizophrenia.

Most important, certain cognitive dysfunctions clearly have been identified as rate-limiting factors impairing learning in psychosocial therapy and rehabilitation programs, as well as social and vocational functioning.[19] Impairment of long-term verbal memory or sustained attention has been shown to limit the ability to acquire social and instrumental skills. Repeatedly, correlations were identified between impaired executive functioning and long-term verbal memory on the one hand and reduced social and vocational adaptation on the other hand.[20] Therefore, cognitive impairments are now recognized as a core feature of schizophrenia and are considered an important therapeutic target.

Over the past decade, several cognitive training approaches have been developed to improve cognitive

Table 3. Significant and Homogeneous Effects of Social Skills Training Across Various Control Groups

Outcome variable	Number of Included Studies	Number of Included Patients	Effect Size (95% CI)	Heterogeneity Q[a]
Posttreatment				
Skill acquisition	14	688	0.77 (0.62 to 0.93)	16.54 ($P = .22$)
Assertiveness	5	160	0.43 (0.11 to 0.76)	2.63 ($P = .62$)
Social functioning	6	342	0.39 (0.19 to 0.59)	1.22 ($P = .94$)
General psychopathology	8	349	0.23 (0.01 to 0.44)	13.25 ($P = .07$)
Follow-up				
Skill acquisition	6	295	0.52 (0.28 to 0.77)	5.57 ($P = .35$)
Social functioning	3	210	0.32 (0.08 to 0.56)	0.90 ($P = .64$)
Hospitalization	2	110	0.48 (0.11 to 0.86)	0.02 ($P = .89$)

Note: CI, confidence interval.
[a]Sum of squares.

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deficits in schizophrenic patients by means of the following methods.

1. Repetitive exercise of cognitive tasks presented in a computerized or paper and pencil version.
2. Establishing compensatory strategies, which imply the learning of strategies to organize information (eg, categorization), or adaptive strategies, which involve prompts and other aids in the environment (environmental engineering) of the patient such as posting reminders, placing pills, or clothes boxes, etc.
3. Behavioral and didactic learning techniques, such as instructions, positive reinforcement or "errorless learning." Errorless learning is based on the premise that learning is improved in the absence of errors and includes the following components: (1) the task is broken down into a set of hierarchically ordered components, (2) training begins on the simplest component and proceeds stepwise to more complex ones, (3) each component is overlearned through repeated practice, and (4) previously used prompts, cues, and instructions are slowly faded.

These methods have been employed alone or in various combinations in a series of training programs, which are summarized under the terms cognitive remediation or cognitive adaptation. Examples are the cognitive subprograms of the Integrated Psychological Therapy (IPT) developed by Brenner and coworkers,[21] the Cognitive Remediation Therapy (CRT) by Delahunty and Morice,[22] the Neuropsychological Educational Approach to Rehabilitation (NEAR) by Medalia et al,[23] the Cognitive Enhancement Therapy (CET) of Hogarty et al,[24] or the Cognitive Adaptation Training (CAT) by Velligan et al.[25]

A number of laboratory trials have demonstrated change on neurocognitive tests used in training or close parallels. In addition, these studies indicate that various learning strategies differ in their positive effects on different cognitive functions. By now, a series of controlled clinical studies have also been conducted. Clinical investigations have examined the impact of cognitive remediation on functional outcome and neurocognitive measures that are independent of the tasks used in training.

Presently, the studies on the efficacy of cognitive remediation are covered by 6 meta-analyses. Two of them included laboratory and quasi-experimental studies evaluating the efficacy of cognitive training on executive functioning as assessed by the Wisconsin Card Sorting Test (WCST)[26] or attention tasks.[27] Four meta-analyses included controlled clinical trials.[7,28–30] Another meta-analysis evaluated the efficacy of the IPT program.[31] The findings of this analysis will be discussed in detail in a separate contribution to this issue.

Again, findings are inconsistent with respect to the specific cognitive function that is evaluated and the rigor of the inclusion criteria (table 4). Suslow et al[27] show heterogeneous results with regard to improvements in various attention tasks, whereas Kurtz et al[26] demonstrate large effects on the performance in the WCST. The meta-analyses including only randomized controlled clinical trials[7,30] again do not support evidence for the clinical benefit of cognitive remediation. However, the meta-analyses of Krabbendam and Aleman[28] as well as the one of Twamley et al,[29] which also included quasi-experimental clinical trials, demonstrate small to medium effects on general cognitive functioning and indicate a possible transfer of these effects to social functioning.

Our meta-analysis included 19 randomized controlled trials on cognitive remediation. Cognitive remediation was defined as an intervention that focuses on improving cognitive functioning by applying repeated practice of cognitive tasks or by the training of strategies for compensating cognitive impairments.

The findings provide support for the generalization of training effects to attention, executive functioning, memory, and social cognition. It demonstrates small to medium, but robust beneficial effects on these functions (table 5). It also supports the finding of a moderate transfer effect on social functioning and demonstrates small reductions in overall psychopathology and negative symptoms.

Psychoeducational Coping-Oriented Interventions With Families and Relatives' Groups

Over the past decades, psychoeducational interventions with families that focus on the improvement of disorder- and stress-related coping strategies of patients and their relatives have gained particular relevance. The finding of a consistent relation between family interactions characterized by high-expressed emotion and the risk for recidivism was an important trigger for their development.[32] This type of intervention was introduced in various treatment settings including single families,[33–36] multiple family groups[37] and relatives' groups without patients,[38] or bifocal groups with patients and relatives in separate sessions.[39]

Despite some variability as to the treatment setting, the psychoeducational and coping-oriented family interventions share 2 basic features. They usually start with psychoeducation providing information on the disorder based on the vulnerability-stress models to patients and their relatives. Particular emphasis is given to the instruction of patients as regards medication and treatment adherence. In addition, they intend to improve the ability to cope with stressors arising from illness-related symptoms or from the social environment. This is accomplished by means of various cognitive behavioral interventions that aim to improve dealing with early warning signs, problem-solving capacity, and communication skills.

No other psychological treatment approach for schizophrenic patients has been investigated as intensively during recent years. Since the end of the 1970s, a

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Table 4. Findings of the Meta-analyses Regarding the Effects of Cognitive Remediation

Meta-analysis	Outcome Variable	Effect Size[a] (95% CI)	Heterogeneity Q[b]
Kurtz et al[26]	Executive functioning	0.98 (0.80 to 1.16)	17.6 (P = .61)
Suslow et al[27]	Attention	NR	NR
Krabbendam and Aleman[28]	Cognitive functioning	0.45 (0.26 to 0.64)	14.3 (P = .43)
Twamley et al[29]	Cognitive functioning	0.32 (NR)	NR
	Social functioning	0.51 (NR)	NR
	General psychopathology	0.26 (NR)	NR
Hayes and McGrath[30]	Cognitive functioning	Lack of data	
	Social functioning	Lack of data	
	General psychopathology	Lack of data	
Pilling et al[7]	Attention	0.11 (−0.31 to 0.53)	NR
	Verbal memory	0.14 (−0.23 to 0.50)	NR
	Visual memory	0.34 (−0.23 to 0.92)	NR
	Executive functioning	NR	NR
	General psychopathology	0.23 (−0.20 to 0.66)	NR

Note: CI, confidence interval; NR, not reported.
[a]Hedges *g*.
[b]Sum of squares.

considerable number of controlled, longitudinal studies on the efficacy of these approaches have been conducted. The findings of these studies were summarized in 3 meta-analyses,[6,40,41] which consistently demonstrate that schizophrenic patients with relatives taking part in such interventions suffer from significantly fewer relapses and hospitalizations during follow-up (table 6). Pitschel-Walz et al[41] found a 20% average decrease in relapse or hospitalization rates due to these interventions. In addition, psychoeducational family interventions lead to an improvement in the patients' adherence to medication.[6,40] Long-term interventions with families have significantly more impact on relapse and hospitalization rates than short-term interventions with relatives' groups.[6,41]

This is in line with the findings of our meta-analysis, which is based on 31 randomized controlled trials. For an intervention to be classified as a psychoeducational coping-oriented intervention with family or relatives' groups, it had to include psychoeducation and problem solving or crisis management.

The results of our meta-analysis additionally indicate that psychoeducational interventions foster a better knowledge of the disorder among the relatives of the patients and lead to a considerable shift from high- to

Table 5. Significant and Homogeneous Effects of Cognitive Remediation Across Various Control Groups

Outcome Variable (posttreatment)	Number of Included Studies	Number of Included Patients	Effect Size (95% CI)	Heterogeneity Q[a]
Attention	13	539	0.32 (0.15 to 0.49)	7.67 (P = .81)
Memory	12	704	0.36 (0.20 to 0.51)	15.77 (P = .17)
Executive functioning	10	606	0.28 (0.12 to 0.44)	6.24 (P = .72)
Social cognition	3	228	0.40 (0.13 to 0.68)	0.28 (P = .87)
Social functioning	7	306	0.49 (0.27 to 0.70)	10.82 (P = .09)
General psychopathology	9	452	0.20 (0.01 to 0.38)	5.01 (P = .76)
Negative symptoms	9	394	0.24 (0.04 to 0.44)	13.52 (P = .09)

Note: CI, confidence interval.
[a]Sum of squares.

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Table 6. Findings of the Meta-analyses Regarding the Effects of Psychoeducational Interventions With Families or Relatives

Meta-analysis	Outcome Variable	Effect Sizea (95% CI)	Heterogeneity Q^b
Pharoa et al[40]	Relapse (at 12 months follow-up)	0.30 (0.14 to 0.46)	26.40 ($P = .002$)
	Relapse (at 24 months follow-up)	0.26 (0.02 to 0.50)	16.28 ($P = .006$)
	Hospitalization (at 12 months follow-up)	0.15 (−0.08 to 0.38)	9.39 ($P = .15$)
	Hospitalization (at 18 months follow-up)	0.62 (0.31 to 0.94)	0.65 ($P = .72$)
	Days in hospital	Lack of data	
	General psychopathology	NR	NR
	Social functioning	0.78 (0.35 to 1.21)	4.05 ($P = .04$)
	Compliance with medication	0.34 (0.11 to 0.56)	4.19 ($P = .65$)
	Expressed emotion	0.67 (0.29 to 1.04)	6.24 ($P = .04$)
	Burden	Lack of data	
	Quality of life	Lack of data	
Pilling et al[6]	Relapse (first 12 months)	0.25 (0.08 to 0.43)	23.04 ($P < .01$)
	Relapse (1 to 2 years)	0.17 (−0.12 to 0.45)	17.93 ($P < .01$)
	Hospitalization (first 12 months)	0.31 (0.00 to 0.61)	11.79 ($P < .01$)
	Hospitalization (1 to 2 years)	0.28 (0.10 to 0.46)	15.60 ($P < .01$)
	Compliance with medication	0.25 (0.01 to 0.50)	2.48 ($P = .65$)
Pitschel-Walz et al[41]	Relapse and hospitalization (overall)	0.41 (0.28 to 0.56)	3.45 ($P > 0.10$)
	Relapse and hospitalization (during first year)	0.39 (NR)	NR
	Relapse and hospitalization (during second year)	0.52 (NR)	NR
	Relapse and hospitalization (intervention lasting 3 months or less)	0.28 (0.12 to 0.45)	3.85 ($P > .50$)
	Relapse and hospitalization (intervention lasting 9 to 24 months)	0.63 (0.39 to 0.90)	2.73 ($P > .50$)

Note: CI, confidence interval; NR, not reported.
[a]Hedges *g*.
[b]Sum of squares.

low-expressed emotion, a substantial improvement in the social adjustment of the patients, a decline of inpatient treatment, and an overall reduction of psychopathology during the follow-up (table 7).

Cognitive Behavioral Therapy of Positive Symptoms

Despite continuous pharmacological treatment, one fourth to up to one half of all schizophrenic patients suffer from persisting delusions and/or hallucinations.[42] Therefore, cognitive behavioral therapy approaches for the treatment of positive symptoms have gained great attention over the last decade. One reason for this is the increasing importance of cognitive models for the description and understanding of delusions and hallucinations. It is now widely accepted that nonpsychotic and psychotic experiences can be modeled along a continuum. This assumption is supported by the observation that under certain conditions—for example, through hypnosis, sensory deprivation, sleep deprivation, or severe stress—psychotic experiences can be induced in healthy subjects. Cognitive explanatory models are essentially based on the assumption that irrational beliefs, misinterpretations, and misattributions form the foundation of delusions and hallucinations. These misjudgments could originate from impaired social cognition like theory of mind or self-monitoring deficits, which in turn may hamper the discrimination between external stimuli and internal intentions.[43]

These assumptions open up the possibility to apply cognitive therapy methods in the treatment of psychotic symptoms. Presently, groups from England,[42,44,45] Scandinavia,[46] and Australia[47] have elaborated specific therapy models. A key feature of cognitive behavioral therapy for psychosis involves the development of a reasonable, ''normalizing'' explanation of the patients' symptoms. Therapy is based on an analysis of the quality of psychotic symptoms (ie, their frequency, intensity, and duration), their triggering events, and their maintaining conditions. The subjectively presumed consequences of delusions and hallucinations as well as their individual meaning are then targeted by means of cognitive interventions. Cognitive restructuring employs verbal challenge, empirical reality testing, or

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Table 7. Significant and Homogeneous Effects of Psychoeducational Interventions With Families or Relatives Across Various Control Groups

Outcome Variable	Number of Included Studies	Number of Included Patients	Effect Size (95% CI)	Heterogeneity Q^a
Posttreatment				
Relatives' knowledge about the disorder	8	3662	0.39 (0.31 to 0.46)	2.04 ($P = .96$)
Patients' social functioning	6	3362	0.38 (0.30 to 0.46)	2.84 ($P = .72$)
High-expressed emotion	7	284	0.59 (0.36 to 0.83)	3.56 ($P = .74$)
Days in hospital	3	3197	0.27 (0.18 to 0.36)	0.39 ($P = .82$)
Follow-up				
General psychopathology of patients	4	178	0.40 (0.10 to 0.70)	2.10 ($P = .56$)
Days in hospital	2	127	0.71 (0.35 to 1.06)	1.70 ($P = .19$)
6–12 months follow-up				
Relapse	14	3838	0.42 (0.35 to 0.49)	16.58 ($P = .22$)
Hospitalization	13	3789	0.22 (0.14 to 0.29)	12.35 ($P = .42$)
18–24 months follow-up				
Hospitalization	8	445	0.51 (0.32 to 0.70)	6.83 ($P = .45$)

Note: CI, confidence interval.
[a]Sum of squares.

reappraisal. Another aspect of cognitive behavioral therapy for psychosis involves the enhancement of the patient's coping strategies. Cognitive behavioral therapies of positive symptoms are usually tailored to the specific situation of an individual patient and thus are conducted in single therapy settings. Lately, however, group therapy approaches have been conceived and evaluated as well.[48]

The existing set of meta-analyses[49–53] generally demonstrates medium to large effect sizes with regard to the severity of positive symptoms (table 8).

Our meta-analysis underscores this finding. It included 17 randomized controlled trials on the efficacy of interventions targeting positive symptoms by cognitive restructuring methods and coping enhancement strategies.

However, consistent significant effects could only be established in trials on cognitive behavioral therapy of persistent positive symptoms (table 9). Compared with various control groups, cognitive behavioral therapy leads to a substantial decline of psychopathology at posttreatment assessments and attains a substantial and stable decrease of persistent positive symptoms. A

Table 8. Findings of the Meta-analyses Regarding the Effects of Cognitive Behavioral Therapy of Positive Symptoms

Meta-analysis	Outcome Variable	Effect Size[a] (95% CI)	Heterogeneity Q^b
Gould et al[51]	Positive symptoms	0.65 (0.56 to 0.71)	NR
	Positive symptoms (follow-up)	0.93 (NR)	NR
Rector and Beck[52]	Positive symptoms	0.68 (NR)	NR
	Positive symptoms (follow-up)	0.84 (NR)	NR
	Negative symptoms	0.61 (NR)	NR
	Negative symptoms (follow-up)	0.80 (NR)	NR
Tarrier and Wykes[49] and Tarrier[50]	General psychopathology	0.37 (NR)	NR
Zimmermann et al[53]	Positive symptoms	0.35 (0.23 to 0.47)	21.45 ($P > .05$)
	Positive symptoms (3–12 months follow-up)	0.40 (0.24 to 0.57)	12.80 ($P > .05$)
	Positive symptoms (>12 months follow-up)	0.33 (0.14 to 0.51)	2.77 ($P > .05$)

Note: CI, confidence interval; NR, not reported.
[a]Glass' Δ (Gould et al), pre-post effect size differences between cognitive behavioral therapy and supportive therapy (Rector and Beck), and Hedges *g* (Tarrier and Wykes and Tarrier; Zimmernann et al).
[b]Sum of squares.

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Table 9. Significant and Homogeneous Effects of Cognitive Behavioral Therapy of Persistent Positive Symptoms Across Various Control Groups

Outcome Variable	Number of Included Studies	Number of Included Patients	Effect Size (95% CI)	Heterogeneity Q^a
Posttreatment				
General psychopathology	11	477	0.45 (0.27 to 0.62)	7.41 (P = .69)
Positive symptoms	12	486	0.47 (0.29 to 0.65)	7.82 (P = .73)
Hallucinations	6	259	0.34 (0.09 to 0.58)	1.86 (P = .87)
Follow-up				
Positive symptoms	9	335	0.39 (0.17 to 0.61)	4.51 (P = .81)
Delusions	5	196	0.47 (0.18 to 0.75)	2.02 (P = .73)

Note: CI, confidence interval.
[a]Sum of squares.

considerable reduction in the severity of hallucinations is achieved at the time of completion of the therapy, but this gain is lost at follow-up. In contrast, a significant weakening of the impact of persistent delusions cannot be observed until follow-up.

Discussion

It remains difficult to draw consistent conclusions from the existing literature on the efficacy of psychological interventions in the therapy of schizophrenic patients. On the one hand, there is sound evidence for the efficacy of these approaches at a general level, suggesting their implementation into routine care. This evidence is based on numerous studies that have been summarized in a series of meta-analyses over the past 2 decades. On the other hand, several important questions are still awaiting an answer. There are marked discrepancies between the results from meta-analyses in the field that only included randomized controlled trials, compared with those that also allowed for observational or quasi-experimental studies. The methodological quality of the included studies is likely to affect the effect sizes as pointed out by Tarrier and Wykes.[49] There is also some concern about the homogeneity of the therapeutic approaches included in those reviews.

We intended to give an overview of the results from presently available meta-analyses and tried to relate their findings to different specific psychological approaches in the treatment of schizophrenia. In the case of ambiguous results, we complemented them by selected findings from an own recent, but as yet unpublished, meta-analysis. We paid special attention to the methodological homogeneity of the included studies by focusing on randomized controlled trials and to the homogeneity with regard to the contents of the different specific psychological therapy approaches in our meta-analysis. In this way, we also intended to stimulate the discussion on possible fruitful directions of future psychotherapy research in the field.

From the meta-analyses that became available over the past 15 years, 4 distinct strands of psychological therapies for schizophrenic patients have emerged: social skills trainings, cognitive remediation, psychoeducational interventions with families and relatives, and cognitive behavioral therapy of psychotic symptoms. Other approaches still failed to provide a sufficient evidence base (eg, psychodynamic psychotherapy,[11] hypnosis[54]).

For social skills training, significant and consistent positive effects on skills acquisition, assertiveness, social functioning, and general psychopathology—which were only reported by those meta-analyses that also included quasi-experimental and observational studies[16,17]—were confirmed by our own analysis. This is in contrast to the negative findings in the analysis by Pilling et al,[7] who also included only randomized controlled trials. The conflicting results might be explained by the higher number of randomized controlled studies we were able to include.

A crucial question regarding social skills training still remains the transfer of the verifiable gains in social skills to general social adjustment and role fulfillment of schizophrenic patients in their daily living environment. In recent years, training approaches such as the ''Partners in Autonomous Living'' approach or the ''In Vivo Amplified Skills Training'' were developed, which either include relatives or friends of the patient in order to provide opportunities, encourage, and contingently reinforce the patient's use of acquired skills in daily living or where training became an integral part of a case management program.[55] However, the data do not yet allow for a final conclusion regarding the additional benefits from these refined approaches. Moreover, findings indicate that the effects of social skills training on social functioning may be enhanced by an increase in cognitive functioning achieved by cognitive remediation.[56] Thus, further questions arise regarding the synergistic effects of combining social skills training with cognitive remediation or integrating it into the framework of interventions for psychosocial rehabilitation such as supported employment.

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Systematic reviews covering cognitive remediation again reveal differences between the analyses that included only randomized controlled trials and those with less stringent inclusion criteria. Whereas no consistent positive effect of cognitive remediation could be found in the analyses that included only randomized trials, we demonstrated small to medium effects on cognitive functioning for this approach in our own analysis.

Because the available studies on cognitive remediation are based on short periods of observation, the question for the durability of these achievements in cognitive functions cannot be answered. Moreover, the strategies and techniques of the different cognitive remediation approaches vary considerably. Therefore, it may not be justified to summarize them under the same label. For future research there is a clear need to evaluate the functional relevance of specific cognitive profiles for certain instrumental and social requirements of daily life. This may help define the corresponding treatment targets and identify the essential common therapeutic components regarding the strategies and techniques of cognitive remediation that relate to these contents. Because the influence of neurocognition on social functioning seems to be widely mediated by social cognition and other metacognitive parameters, these variables may preferably be taken as a target of cognitive remediation. In addition, future training should place strong emphasis on individual profiles of cognitive deficits as not all schizophrenic patients suffer from the same cognitive impairments. Consideration should also be given to motivational factors because there is some evidence that a patient's level of motivation is associated with a beneficial treatment response.[57]

The efficacy of psychoeducational family interventions in reducing relapse and hospitalization rates bas been empirically established by a large number of studies. Results from our own meta-analysis are well in line with the findings of previous systematic reviews. However, as to their implementation in routine care settings, some questions are still unanswered. There is uncertainty about the (cost-)effectiveness and the most efficient treatment format for these approaches. In addition, there is only limited knowledge about what specific components are effective in these approaches. For example, relapse rates seem to depend strongly on the patients' adherence to prescribed medication. To date, investigations have rarely addressed the issue of whether and to what extent the efficacy of psychoeducational coping-oriented therapy approaches may be mainly the consequence of improved medication compliance. It also remains unclear whether the intended improvements in the coping behavior of patients and their relatives play the supposed pivotal role in the efficacy of these interventions.

With regard to cognitive behavioral therapy of psychotic symptoms, the findings of our own meta-analysis in general support the positive findings at hand. But again, specific therapeutic ingredients within the overall toolbox of cognitive behavioral therapy for positive symptoms still need to be identified. Another unanswered question relates to differential indication of cognitive behavioral therapy because the benefits of approaches that are not specifically directed to a reduction of the severity of positive symptoms have not been clearly demonstrated.[6,58] For example, the application of cognitive behavioral therapy in early intervention programs has not yet proven effective.[47,59,60] Moreover, all the present efficacy studies on cognitive behavioral therapy of positive symptoms excluded a considerable number of patients. One main reason for nonacceptance was the patients' refusal to talk about their symptoms.[61]

Conclusions

The present state of research provides sound evidence for the efficacy of psychological therapy in the treatment of schizophrenia. However, many questions remain unanswered. These relate to the most efficient treatment setting and to the differential indication of the various psychological interventions. Moreover, the specific therapeutic ingredients still have to be identified. Future research must also focus on the synergistic effects of combinations of psychological interventions with pharmacotherapy or psychosocial rehabilitation programs. The present gaps in knowledge hamper the implementation of effective psychological interventions into routine mental health-care settings because they prevent therapy planning from being economically tailored to the specific needs and resources of individual patients. These gaps in knowledge result from a neglect to study the association between therapy processes and treatment outcomes as well as from the prevailing tendency to regard the efficacy of psychological therapy as independent of the general framework of the mental health-care system. Therefore, it seems essential that future psychotherapy research in schizophrenia will focus on process-outcome relations as well as on (cost-)effectiveness of psychological therapy. Otherwise, budgetary constraints may prevent these promising therapeutic approaches from being implemented into standard mental health care.

Appendix

Included Studies

Social Skills Training

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