Integrated Psychological Therapy (IPT): effectiveness in schizophrenia inpatient settings related to patients' age

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Abstract

Objective: Elderly people with schizophrenia often suffer from cognitive impairments, which affect their social functioning. Today, only few therapy approaches for middle-aged and older patients are available. The Integrated Psychological Therapy (IPT) combines neurocognitive and social cognitive interventions with social skills approaches. The aim of this study was to evaluate (1) whether IPT is effective in younger patients (age<40 years) and middle-aged patients (age≥40 years), and (2) whether control conditions (CC: treatment as usual or unspecific group activities) reveal some change in outcome depending on age.

Method: A total of 15 controlled IPT studies with 632 schizophrenia inpatients were included into a standard meta-analytic procedure. Studies were categorized into two age-categories.

Results: Significant medium to high effect sizes (ES) were evident for IPT independent of age on the global cognitive score (mean score of all cognitive variables), on neurocognition, social cognition, social functioning, psychopathology, and on the global therapy effect (mean of all variables). The IPT effects in middle-aged patients were significantly higher on the global cognitive score, on neurocognition and on social cognition compared to younger patients. Opposite results could be observed in CC. Only younger patients participating in the CC showed small but significant ES on these variables, but almost middle-aged control patients did not. However, none of the differences in CC were significant between the two age-categories. A moderator analysis obtained no evidence for a strong impact of IPT variations, therapy setting, patient characteristics and methodological rigor of the research design.

Conclusions: These results support evidence for the efficacy of IPT independent of age. Results further indicate the need of goal-oriented specific psychological interventions for middle-aged and older schizophrenia patients.

There is evidence for a gradual aging of the population in developed countries all over the world, and also an increase of middle-aged and elderly schizophrenia patients.[1] Therefore, research focusing on the impact of the age on schizophrenia features as well as on the successful treatment of these features becomes important. During the last decades, a large bulk of data was published addressing younger people suffering from schizophrenia, but the needs of older schizophrenia patients were often neglected.

Recent reviews of published data on the rehabilitation goals for older people with serious mental illness summarized that poor outcome in social functioning and lower quality of life are strongly associated with social isolation, depression, cognitive impairment, and chronic medical illness.[1,2] The authors concluded that specific interventions are needed with regard to these specific features associated with social functioning and quality of life in older patients. Interventions should enhance social integration and involvement in meaningfulness activities and should diminish depressive symptoms. Another review of empirical data suggests that positive symptoms in schizophrenia patients decrease with age, while negative and depressive symptoms are similar in younger and older adults. Additionally, cognitive impairments tend to increase with age.[3] Therefore, successful interventions on cognitive functions may be a promising treatment target to support the rehabilitation of the primary intervention topics in older schizophrenia patients. In younger, non-geriatric people with schizophrenia, a key issue in understanding and treating the disease is cognitive functioning. Cognition represent the most powerful empirical based predictor of functional recovery.[2,4,5] 75-85% of schizophrenia patients experience long lasting cognitive deficits.[6-7] However, inconsistent data are available whether the research results based on patients in early stages of the illness can be generalized on more geriatric populations.[5, 8-11]

Today, only few evaluated therapy approaches are available for middle-aged and older schizophrenia patients focusing on the defined treatment targets. A recent review[1] identified three social skills therapy approaches (SST) for elderly people with schizophrenia: the Functional Adaptation Skills Training[12] (FAST), Helping Older People Experience Success[13] (HOPES), and the Cognitive Behavioral Social Skills Training[14] (CBSST), which combines SST with cognitive-behavioral therapy. Furthermore, the review includes a work rehabilitation program.[15] All of these approaches improved functioning successfully. Furthermore, two cognitive remediation therapy approaches (CRT) have already been evaluated in samples of middle-aged and older patients: McGurk and Mueser[16] used a computer program (Cogpack, Marker software) in combination with work rehabilitation, and Wykes and colleagues[10] administered the classic cognitive remediation therapy.[17] However, in both studies middle-aged and older patients showed only minimal improvements in cognitive functioning compared to significant improvements in younger schizophrenia patients.

Against this background combined therapeutic interventions targeting deficits in cognition and social functioning integrated in a multidimensional treatment concept – so-called integrated therapy approaches - have received a great deal of interest in recent years. The term integrated points out to the necessity that cognitive remediation therapy should always be embedded in a broad-based treatment concept tailored to the patients` rehabilitative and cognitive resources and deficits. One of the first and broadest evaluated approaches is the Integrated Psychological Therapy (IPT), which combines neurocognitive and social cognitive remediation with therapy of social skills and interpersonal problem solving.

Integrated Psychological Therapy (IPT)

IPT is a manualized cognitive behavioral therapy program for groups of 5-8 schizophrenia patients. Its conceptualization is based on the underlying assumption that basic deficits in cognitive functioning have a pervasive effect on higher levels of behavioral organization such as social skills and social and independent functioning.[4,18]. Therefore, IPT is structured into five subprograms (SP) with increasing levels of complexity that are taught sequentially as a building-block model. It begins with neurocognition (SP1: "Cognitive Differentiation") and social cognition (SP2: "Social Perception"), followed by communication (SP3: "Verbal Communication") and social skills (SP4: "Social Skills") and ends with problem solving skills (SP5: Interpersonal Problem Solving"). A detailed description of the IPT concept was published in a manual and translated into 13 languages.[4] The first study on IPT was carried out in 1980 and the initial German manual was published in 1988.[19-20] Today, the sixth German edition of the IPT manual is available.[21]

METHODS

Over the past 30 years, a large body of research has investigated IPT. Up to now, research groups in 12 countries in North and South America, Europe, and Asia have conducted 36 studies investigating IPT or a combination of IPT subprograms, with a total sample of 1,601 patients with schizophrenia (diagnosed according to ICD or DSM). These studies were reviewed and evaluated by meta-analytic research.[22-25] Study identification and selection was based (a) on individual contacts in supervising IPT procedure by members of our research group, and (b) on extensive standard literature search in international data sources (PsychINFO, Medline, PubMed) using the key words "schizophrenia" or "psychosis" and "IPT" or "Integrated Psychological Therapy" and "therapy" or "training". The studies were heterogeneous with regard to study characteristics: They used different IPT variations and research designs, were applied in inpatient and outpatient settings, in academic and non-academic sites and included patients at different stages of illness and age.

Research aims

The primary aim of this study was to evaluate the impact of patient's age on outcome of IPT intervention. We were particularly interested in the cognitive part of IPT procedure for the following reasons: (a) the initial part of IPT procedure represents a cognitive remediation approach rarely used in the rehabilitation of older schizophrenia patients; (b) due to the rate-limiting factor of cognitive deficits, the initial cognitive remediation is thought as a requirement for positive treatment effects on social functioning. It is therefore defined as the basic mechanism of change in integrated interventions. Regarding the age, studies including older populations relative to the total sample of all IPT studies were conducted exclusively in inpatient settings and did not use active goal-oriented therapy as a control condition. Therefore, in order to compare primary studies with younger patients with those including older patients we intended to select a homogeneous sample with regard to treatment content, setting and design of the large number of different IPT studies.

Study selection

For that purpose, we selected all studies of the available 36 IPT studies, in which (a) the cognitive subprograms or the complete IPT (including the cognitive and social subprograms) were evaluated, (b) the study was conducted in inpatient setting, and (c) IPT was controlled by treatment as usual (TAU) or placebo-attention conditions (unspecific group activities). Studies focusing exclusively on IPT subprograms addressing social competence (K=3 studies), studies in outpatient or mixed setting (K=12), studies using other goal-oriented therapy approaches as control condition (K=6), studies using no control condition (K=5), or studies including adolescent patients (age<18 years; K=1) were excluded. Finally, 15 independent studies on IPT (N=632 inpatients) [26-42] could be included into the meta-analytic procedure. Data related to the age of the participants were based on two resources: on study inclusion and exclusion criteria, and on the mean score (M) and the standard deviation (SD) of the inpatient sample. Against this background, we categorized the mean age of study participants using the median split method. The mean age of patients across the 15 studies was 37.1 years (SD=6.7). The median split method revealed two age-categories characterized by younger adult patients of age <40 years (Range: 28-36 years; K=9 studies; N=493 patients) and near middle-aged patients of age ≥40 years (Range: 40-50 years; K=6; N=139). However, there was no study that included patients with a mean age between 36 and 50 years. This suggests two relatively homogeneous and non-overlapping sub-samples. The mean study sample comprised 42.1 patients. Studies that comprised patients with a mean age <40 years generally consisted of larger samples (N=54.8 participants) than studies with patients' age ≥40 years (N=23.2). All 15 included studies are described in Table 1 in chronological order.

12 studies were conducted in Europe, one in the USA, Japan and Panama. 8 studies evaluated the complete IPT, and 7 studies evaluated the IPT subprograms addressing cognition. The different IPT interventions were equally distributed over the two age-categories. 9 out of 15 studies used RCT design, 6 studies used a quasi-randomized design or did not describe patient allocation.

Insert Table 1 about here

Data analysis

To determine the separate extent of change in adult inpatients across the experimental group (IPT) and the control conditions (TAU; placebo-attention) in both age categories (age<40 years and age ≥40 years), weighted effect sizes (ES) within the four comparison groups (IPT and controls in age<40; IPT and controls in age ≥40 years) were calculated.

Effect sizes (ES) were based on the means (M) of IPT and control group in each study at baseline and post-therapy, and on the pooled standard deviation (SD) at baseline. ES were calculated using the following equations: $ES=(M_{post\text{-}therapy} - M_{baseline}) / SD_{pooled\ baseline}$. Effect sizes can generally be categorized as small (.2), medium (.5), or large (.8).[43] Meta-analytic procedure was conducted using the method of Rustenbach[44] based on Cohen[43] and Hedges and Olkin[45]. Effect sizes were weighted by their inverse variance (d_w). The outcome was classified into the following categories during therapy: global therapy effect (mean of all assessed variables), cognition (composite score: mean of all assessed variables addressing cognition), neurocognition (composite score), social cognition (composite score),

social functioning, psychopathology (composite score), negative symptoms, and positive symptoms. Additionally, the cognitive scores were grouped according to the definitions of the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) initiative supported by NIMH. The members of this initiative yielded consensus on six relatively distinct neurocognitive domains (speed of processing, attention/vigilance, verbal memory, visual memory, working memory, and planning/problem solving) and five social cognitive domains (emotion processing, social perception, Theory of Mind (ToM)) relevant in schizophrenia.[46-47]

If studies included more than one variable of one category, the mean effect size was used. When different outcomes of the same study had been published in more than one article, the results were combined. Effect size categories and study characteristics were rated independently by the authors as well as by a researcher with PhD degree, who was not involved in the study.

We combined the effect sizes using a fixed-effects model. To determine whether the mean effect size of an outcome category was statistically significant, the 95%-confidence interval (CI) of ES_w was used. Lower bond of CI>0 indicates a statistically significant effect on the 5%-level. The heterogeneity of the effect sizes across studies in an outcome domain was evaluated by using the Q statistics.[45] The significance level of Q_w was proved using Chi-Squares values (DF=K-1 studies). When Q statistics indicated a heterogeneous mean ES_w, an integration of the effect sizes into a random-effects size model was conducted.[45] Additionally, Q statistics were used to compare d_w between groups ($Q_{b;}$ DF=K-1 groups).[44] All statistical tests were conducted two-tailed.

To control whether the treatment benefit was affected by moderating factors we hypothesized the following moderators when analyzing the total sample of the 15 included studies: (1) IPT variation (complete IPT vs. cognitive IPT subprograms only); (2) strength of research design (randomized vs. not randomized patient allocation); (3) significant differences in patient characteristics between the two age-categories (e.g., IQ, gender, and age to assure the adequacy of the research design); and (5) significant differences in the therapy setting between the two age categories (e.g., number of sessions, weeks of therapy). If at least 10 studies were available, a meta-regression analysis[44,45] was carried out using the effect size of an outcome as the independent variable and the hypothesized moderators as potential predictors. If a potential moderating factor has been statistically identified by the meta-regression analysis, it was categorized and its influence on outcome of the age-categories was controlled using Q statistics.[44,45]

RESULTS

The patient characteristics of the 15 studies (N=632) are displayed separately for the two age categories (age<40 years; age≥40 years) in Table 2. The patient characteristics age, distribution of gender, duration of hospitalization and duration of illness were all significantly different in the two age-categories. Only the IQ did not differ significantly between the two groups. However, only few studies published data addressing IQ, duration of hospitalization and illness (DF<9).

Insert Table 2 about here

Table 3 shows the setting characteristics used in studies addressing the two age-categories. None of the setting variables was statistically significant between the two age categories, although there is a tendency for longer lasting therapy in the older age-category. The drop-out rate in studies including younger patients was 16.7% (standard deviation SD=20.8) and in studies including middle-aged patients 13.4% (SD=13.6).

Insert Table 3 about here

General outcome

In a first step, all outcome variables were pooled together to generate a mean within-effect size, which corresponds to the global therapy effect of IPT and control group in both age-category settings. Using a fixed-effects model, the medium global therapy effect of IPT was significant during therapy in the younger age category (weighted effect sizes within the group ES_W=.52; 95% confidence interval CI: .39-.65; DF=8 homogeneity Q_w=8.11) as well as in the older age category (ES_W=.57; CI=.30-.84; DF=5; Q_w=8.84). The difference between these two homogeneous IPT effects was not significant (Q_b=.13; DF=1; p=.72). However, the IPT effects were larger than those of the control conditions in both age groups (Q_b>5.75; DF=1; p<.02).
With regard to the control conditions, only studies with younger patients revealed a small but significant effect size (ES_w=.24; CI=.10-.38; DF=8; Q_w=5.75). Studies with almost middle-aged patients showed no effects (ES_w=.04; CI=-.04-.30; DF=5; Q_w=.14). The difference on the global therapy effect between control groups of the two age-categories was not significant (Q_b=2.32; DF=1; p=.13).
The effect sizes on cognitive and social functioning and symptoms within IPT and control groups are summarized in Table 4.

Insert Table 4 about here

Outcome in cognition

With regard to the mean scores of cognitive functions, neurocognition and social cognition, effects for IPT were twice as large in studies including middle-aged patients (high $ES_w \geq .9$) than in studies comprising younger patient samples (moderate $ES_w \leq .59$) (Table 4). These differences were all significant ($Q_b \geq 4.71$; DF=1; p<.03). However, IPT obtained significantly larger effects on these cognitive variables in both age-categories compared to controls ($Q_b \geq 4.09$; DF=1; p<.05). Again, only control patients of the younger age category revealed small, significant effect sizes ($ES_w \geq .23$), while middle-aged patients did not show such effects ($ES_w \leq .19$). These differences were not significant in any of the described variables ($Q_b \leq .52$; DF=1; p>.47).
Dividing the neurocognitive and social cognitive mean scores into cognitive domains defined by MATRICS[46-47] revealed only enough data for the neurocognitive domains of attention/vigilance, memory (pooled data of visual and verbal memory) and executive functions (pooled data working memory and planning/problem solving). To generate social cognitive MATRICS domains, only enough data were available to

pool together a social and emotion perception score. IPT showed significant medium to high effects on all cognitive domains in both age categories ($ES_w \geq .43$). However, the effect size for younger IPT-patients was largely heterogeneous on the cognitive domain of attention ($Q_w=20.91$; DF=7; p<.01). This effect size of younger patients measuring the change in attention remained significant using a random effect size model ($ES_w=.57$; CI=.28-.86). With the exception of the memory score the control groups of younger patients revealed smaller but significant effects on these domains ($ES_w \geq .23$). A comparison of the effects of IPT and the control group in younger patients obtained no significant differences between groups ($Q_b \leq 3.34$; DF=1; p>.06). Pattern of results were different in the near middle-aged patient sample: the older control patients showed no significant changes in any of the cognitive domains defined by MATRICS ($ES_w \leq .2$). Furthermore, IPT effects in the middle-aged category compared to controls were significantly larger on memory, executive functioning and social/emotion perception ($Q_b \leq 5.63$; DF=1; p<.02), but not on attention ($Q_b=2.36$; DF=1; p=.12). Investigating age-related effects in IPT showed significant stronger effects in older IPT-patients compared to younger IPT-patients on executive functioning ($Q_b=7.30$; DF=1; p<.01) and on social/emotion perception ($Q_b=17.85$; DF=1; p<.01), but not in memory and attention ($Q_b \leq .65$; DF=1; p>.42). Regarding the control groups, no statistically significant difference was evident in any of these cognitive domains between the two age-categories ($Q_b \leq 2.88$; DF=1; p>.08).

Outcome in social functioning

IPT showed significant small to medium effects sizes on social functioning in both age-categories ($ES_w \geq .39$). It should be considered that the IPT effects in both age-categories were significantly heterogeneous (younger age category: $Q_w=9.58$; DF=4; p=.05; older age category: $Q_w=11.02$; DF=3; p=.01). The IPT effects were stable on a level of significance using a random-effect model in younger patients ($ES_w=.38$; CI: .17-.59) as well as in middle-aged patients ($ES_w=.66$; CI: .09-1.23). The effects of IPT on social functioning did not differ significantly between the two age-categories ($Q_b=.43$; DF=1; p=.51). Again, only younger patients in the control group revealed a small but significant effect ($ES_w=.2$). This effect was statistically not significantly larger than the one of older control patients ($Q_b=1.24$; DF=1; p=.27). Finally, the effects on social functioning between IPT and controls did not differ in any of the two age-categories ($Q_b \leq 1.34$; DF=1; p>.24).

Outcome in symptoms

IPT showed significant effects in both age-categories on the mean score of psychopathology as well as in reducing positive and negative symptoms ($ES_w \geq .3$). One exception was an insignificant within-effect on negative symptoms of younger IPT-patients ($ES_w=.15$). However, the IPT-effects did not differ significantly between the two age-categories on any of these variables ($Q_b \leq 2.72$; DF=1; p>.09). Again, only younger control patients revealed significant effects on psychopathology ($ES_w=.34$) and positive symptoms ($ES_w=.36$), whereas middle-aged patients showed zero-effect sizes. Moreover, the superiority of younger controls compared to older patients was significant on psychopathology ($Q_b=4.80$; DF=1; p=.03) and positive symptoms ($Q_b=4.37$; DF=1; p=.04). Only very few studies assessed the change in negative symptoms. This should be taken into account when interpreting the following results: IPT revealed only in middle-aged patients statistically significant effects ($ES_w \geq .3$), whereas IPT in younger patient samples and all control conditions did not. Finally,

the IPT-effects did not differ significantly from those of controls on any of the symptom variables in both age-categories ($Q_b \leq 3.80$; DF=1; p>.05). However, there was a trend on the psychopathology score of younger patients (Q_b=3.80; DF=1; p=.051) .

Moderator analysis

IPT groups and control groups were dealt with separately when calculating a meta-regression analysis. We included only effect sizes of outcome as dependent variables and moderator variables in the statistical procedure if data of at least ten studies were available. The following variables were used as moderator variables: IPT variation, strength of research design, age, and gender. Although only few studies provided sufficient information about the IQ-score (K=8 studies), it was also included because of its hypothesized impact. Furthermore, we included all setting variables (duration of therapy, number of sessions) in the analysis although there was no statistical difference among age-categories. In the control groups, none of the described outcome variables was affected by any of the hypothesized moderator variables. In the IPT group, the strongest impact on any outcome variable was found for cognitive outcome (composite score). It was moderated by patients' age (regression coefficient B=.03; Z=2.17; p=.03). Additionally, IPT variation (integrated vs. non-integrated) was identified to moderate cognitive outcome at an almost significant level (B=.25; Z=1.93; p=.06). The strength of research design, gender, IQ, and all setting variables addressing length and intensity of therapy did not have an impact on effect sizes of any outcome variable summarized in Table 3. Consequently, the only identified potential moderator variable besides patients' age at study entry was the factor IPT variation.

The analysis of IPT variations refers to (a) the effects of integrated cognitive remediation therapy combining interventions on neurocognition, social cognition and social competence (complete IPT), and (b) the effects of unidirectional neurocognitive and/or social cognitive remediation therapy including only IPT subprograms addressing cognition (cognitive subprograms). The use of cognitive IPT subprograms showed only significant medium to large effects on cognition for younger patients (K=4; ES_w=.66; CI: .42-.90) as well as for middle-aged patients (K=3; ES_w=1.02; CI: .62-1.42) using a fixed-effect model. The complete IPT obtained a smaller significant medium effect on cognition in younger patients (K=5; ES_w=.48; CI: .32-.64) compared to a significant large effect in middle-aged patients (K=2; ES_w=.84; CI: .11-1.57). None of the presented categories regarding age and IPT variation differed significantly from each other ($Q_b \leq 2.62$; DF=1; p>.11). This does not support evidence of an impact of IPT variations on outcome.

DISCUSSION

This quantitative review supports evidence that IPT is effective on various outcome domains during therapy of younger and near middle-aged inpatients compared to TAU or placebo-attention conditions. Significant effects could be observed on neurocognition and social cognition. To our knowledge, this is one of the very first therapy studies evaluating the outcome of near middle-aged patients in social cognition. In general, middle-aged patients showed higher therapy effects on the cognitive domains. This effect is in opposite to the results of studies evaluating other cognitive remediation approaches for middle-aged and older patients.[10,16] Both of these approaches did not support group dynamics as it is explicitly used in IPT

technology. In contrast to drill and practice exercises within the use of computer programs,[16] IPT puts emphasis on strategy learning tasks, which may have the stronger impact on cognitive functioning.[36] Both authors of the two other studies concluded that cognitive remediation therapy methods have to be adapted to elderly people due to small effects. It should be mentioned that the effects of the two other studies might not be comparable to the results of our analysis due to patients' age. The IPT studies including older patients used in this analysis were characterized by an age category between 40 to 50 years. This does not represent a geriatric population. It can even be discussed whether the older populations' mean age of 44.2 years is in accordance with the definition of middle-aged patients. Accordingly, the discrepancy in outcome with the two cited studies[10,16] may simply be due to age effects. The fact that IPT effects were larger in the older age-category than in the younger one contradicts the results of other studies and is also contrary to clinicians' expectation about practicing cognitive remediation: the older and the more chronic a patient is, the lower his potential for change. One possible explanation of this inconsistency may be the group setting of IPT procedure. Consequently supporting group processes and group dynamics within IPT may represent a powerful mechanism of change. This may especially be the case in the older population. The very broad evaluation of IPT has clearly demonstrated, that a group setting alone is not sufficient to generate adequate effects. Controlling for unspecific group effects, IPT was superior to unspecific group activities on all outcome variables including cognition and social functioning. Unspecific group effects obtained higher effects compared to TAU.[4,22-23] Learning compensation strategies within IPT procedure seems to bypass the diminished benefit of repeated exposure to cognitive tasks in elderly people.[5]

In this study, younger control patients obtained small but significant effects on cognition whereas middle-aged, more chronic patients did not. This result may be due to better psychiatric (standard) treatments for younger patients than for elderly people.[10,16] On the other hand, the results may be influenced by a longer experience of failure in the treatment of older patients, which makes it harder to motivate them by the use of standard treatment tools. At least, there was some evidence that older patients are less treatment motivated in work rehabilitation.[48-49] These results strongly support the recommendation that goal-oriented psychological interventions should be offered to middle-aged and older schizophrenia patients.

Regarding outcome in social functioning, the IPT effects were lower than on cognitive outcome, but still significant and independent of age. These results are in accordance with the effects found for social skills therapy approaches (FAST, HOPES, CBSST).[1] Again, only younger control patients showed some small but significant change, middle-aged patients did not. However, the difference of effects in IPT and control patients regarding age should not be overestimated since it was not significant between groups.

The effects on general symptom reduction and on the positive symptoms were contradictory to the effects on the functional areas: Younger IPT-patients obtained stronger effects compared to middle-aged patients. However, IPT reached level of significance independent of age, as did control groups of younger patients on a lower level. Again, middle-aged control patients showed no effects on symptom reduction. One possible explanation for different IPT effects between age-categories may be derived from another review summarizing the relationship of aging and severity of symptoms in schizophrenia.[3] This study found evidence that positive symptoms decrease with age, while negative symptoms are similar frequent in younger and older patients. Only very few of the included IPT studies assessed negative

symptoms, which influences the validity of the results. However, middle-aged patients showed again stronger effects than did younger patients.

The moderator analysis identified no relevant effect addressing IPT variation due to the limited sample size. It has to be mentioned, that even studies including only the cognitive subprograms of IPT represent some kind of integrated approach since they combine in many parts neurocognitive and social cognitive remediation therapy interventions. The pooled effects of the IPT variation are in line with findings of McGurk and colleagues[50] that combined interventions have superior effects on more distal outcome than unidirectional cognitive interventions.

The therapy duration and intensity of therapy was different in the two age-categories: Younger patients participated more often a week at a therapy session, while the therapy duration of middle-aged patients was longer lasting. In summary, the older population received more therapy, but none of the setting differences among age-categories was statistically significant. And neither the therapy duration nor the therapy intensity could be identified as moderator influencing outcome. Additionally, IQ, gender (percentage of male in the study sample) and the strength of research design had an impact on any of the various domains of outcome. However, due to the partially very small cell sizes in this analysis, the results may not be decisive in negating the impact of these hypothesized moderator variables.

CONCLUSIONS

IPT represents integrated therapy approaches combining interventions on cognition with interventions on other therapy targets. The results of this analysis support evidence for the efficacy of RCTs as well as some effectiveness in clinical trials independent of patients' age. Results indicate that middle-aged patients clearly benefit from the treatment with IPT. Results further indicate the necessity of goal-oriented specific psychological interventions for near middle-aged schizophrenia patients. In opposite to younger control patients, no change in most of the functional domains or symptoms was evident during treatment period for the middle-aged control patients. However, it has to be mentioned that this analysis was exclusively based on the data of inpatient setting not referring to a geriatric population. Up to now, sufficient data of middle-aged or older (out)patients participating in IPT are not available. The generalization of the results to the population of geriatric patients seems to be questionable due to the further development of impairments and symptoms with age in both directions. Another limitation of the analysis is the partially small cell sizes due to the lack of data as well as the completely missing follow-up data for middle-aged patients. Thus, we do not know whether the positive effects during therapy could be maintained at follow-up. However, the analysis of all 36 IPT studies showed that the therapy effects still improved during follow-up.[22-23] Finally, other potentially powerful mediators between cognition and functional outcome are not considered in the analysis, mediators such as motivation[51] or insight (awareness of having a mental illness that requires treatment).[52] And, the analyzed moderator variables in this study - IQ, gender, the duration of treatment – may be influenced by the small sample size. Therefore, further research projects on IPT as well as on general cognitive remediation therapy should be extended to more geriatric populations specifically targeting moderators and mediators in RCT designs including long lasting follow-up assessment.

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TABLE 1. 15 independent IPT studies (N=632)

	Source	Country	Intervention	N	Setting	Mean age at study entry (years)
1)	Brenner et al.[26-27]	Germany	Complete IPT	43	inpatient	33[1]
2)	Stramke et al.[28]	Switzerland	Subprograms	18	inpatient	40[2]
3)	Hermanutz and Gestrich[29]	Germany	Complete IPT	64	inpatient	28[1]
4)	Kraemer et al.[30]	Germany	Subprograms	30	inpatient	46[2]
5)	Roder et al.[31]	Switzerland	Complete IPT	17	inpatient	44[2]
6)	Funke et al.[32]	Germany	Subprograms	28	inpatient	50[2]
7)	Heim et al.[33]	Germany	Subprograms	65	inpatient	35[1]
8)	Olbrich and Mussgay[34]	Germany	Subprograms	30	inpatient	31[1]
9)	Roder[35]	Switzerland	Subprograms	18	inpatient	33[1]
10)	Schüttler et al.[36]; Blumenthal et al.[37]	Germany	Complete IPT	95	inpatient	29[1]
11)	Gaag van der.[38]	The Netherlands	Subprograms	42	inpatient	31[1]
12)	Takai et al.[39]	Japan	Complete IPT	34	inpatient	43[2]
13)	Theilemann.[40]	Germany	Complete IPT	45	inpatient	35[1]
14)	Spaulding et al.[41]	USA	Complete IPT	91	inpatient	36[1]
15)	Alguero[42]	Panama	Complete IPT	12	inpatient	43[2]

N, number of patients
[1]age category<40 years.
[2]age category≥40 years.

TABLE 2. Patient characteristics of the two age categories

	Age<40 years		Age≥40 years		statistics[1]		
	Mean	SD	Mean	SD	DF	t	p
Age (years)	32.3	2.8	44.2	3.3	13	7.6	>.01
Gender: % male	55.3	7.8	74.1	16.1	12	2.9	.01
IQ	97.1	1.6	86.4	10.8	7	1.9	.09
Duration of hospitalization (months)	23.3	23.0	164.4	40.4	8	6.8	>.01
Duration of illness (years)	8.1	2.6	20.1	1.3	7	6.0	>.01

M, mean; SD, standard deviation.

[1]t.test, two-tailed; DF, degree of freedom; t, t-value; p, significance level.

TABLE 3. Setting variables of the two age categories

	Age<40 years		Age≥40 years		statistics[1]		
	Mean	**SD**	**Mean**	**SD**	**DF**	**t**	**p**
Duration of therapy (hours)	40.8	26.0	50.8	26.0	12	.5	.52
Duration of therapy (weeks)	10.1	6.3	24.3	21.3	13	1.5	.17
Weekly number of sessions	4.1	1.1	3.3	1.5	13	1.1	.30
Duration of a session (minutes)	51.8	14.3	64.0	25.9	12	1.0	.36
Total number of sessions	38.3	20.4	58.3	34.0	13	1.4	.17

M, mean; SD, standard deviation.

[1]t.test, two-tailed; DF, degree of freedom; t, t-value; p, significance level.

TABLE 4. Effect sizes (ES) within the IPT group and control group regarding the two age categories

		Age<40 years						Age≥40 years				
		IPT		Control group				IPT		Control group		
	K	ES_w (95% CI)	Q_w	ES_w (95% CI)	Q_w	Q_b	K	ES_w (95% CI)	Q_w	ES_w (95% CI)	Q_w	Q_b
Cognition (mean)	9	.54* (.41-.67)	10.99	.23* (.09-.37)	4.14	10.14*	5	.98* (.63-1.33)	4.47	.12 (-.20-.44)	0.37	12.84*
Neurocogniton	9	.56* (.43-.69)	15.35	.23* (.09-.37)	4.71	11.37*	5	.90* (.56-1.24)	5.79	.10 (-.22-.42)	0.35	11.32*
Attention	8	.54* (40-.68)	20.91*	.11 (.,04-.26)	8.48	1.89[1]	3	.53* (.16-.90)	0.07	.11 (-.28-.50)	1.45	2.36
Memory	7	.52* (.37-.67)	8.85	.36* (.20-.52)	6.91	1.98	4	.65* (.32-.98)	0.39	.07 (-.28-.42)	1.66	5.63*
Executive functions	7	.43* (.28-.58)	5.72	.23* (.07-.39)	2.37	3.34	4	1.05* (.66-1.44)	6.44	.-.05 (-.4-.30)	2.71	14.11*
Social cognition	5	.59* (.42-.76)	3.57	.31* (13-.49)	1.08	4.09*	4	1.43* (1.0-1.86)	0.46	.19 (-.16-.54)	0.51	20.09*
Social/emotion perception	4	.52* (.32-.72)	1.59	.24* (.02-.46)	0.09	3.31	3	1.40*(.94-1.86)	0.26	.20 (-.19-.59)	0.60	15.85*
Social functioning	5	.39* (.22-.56)	9.58*	.20* (.01-.39)	4.58	0.41[1]	4	.48*(.12-.84)	11.02*	.01 (-.31-.33)	0.24	1.34[1]
Psychopathology (mean)	7	.55* (.41-.69)	12.45	.34* (.18-.50)	1.70	3.80	4	.30* (.01-.59)	0.56	.00 (-.30-.30)	0.17	2.03
Positive symptoms	6	.54* (.39-.69)	3.98	.36* (.19-.53)	1.35	2.63	4	.31* (.02-.60)	0.34	.00 (-.30-.30)	0.72	2.16
Negative symptoms	2	.15 (-.08-.38)	1.72	.18 (-.07-.43)	0.56	0.03	3	.36* (.03-.69)	2.15	.08 (-.25-.41)	1.16	1.40

K, number of studies; N, number of patients; ES_w, weighted effect sizes within the group; 95% CI, 95% confidence interval; Q_w, homogeneity statistics, $\chi2$-test, df=K-1; Q_b, homogeneity statistics between IPT and control group in each age category, $\chi2$-test, df=1, [1]based on values of a random effect size model due to heterogeneous Q_w, *p<.05.