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Research paper

The effect of cognition and age on the efficacy of psychotherapy in late-life depression

Bettina Bewernick [a,*], Julijana Buschmann [a], Kathrin Heser [a], Luca Kleineidam [a], Katharina Domschke [b], Moritz Elsaesser [b], Nadine Zehender [b], Melanie Luppa [c], Martin Hellmich [d], Oliver Peters [e], Lutz Froelich [f], Steffi Riedel-Heller [c], Elisabeth Schramm [b], Martin Hautzinger [g], Frank Jessen [h,i,j], Forugh S. Dafsari [h], Michael Wagner [a,i]

[a] Department of Old Age Psychiatry and Cognitive Disorders, University of Bonn, Bonn, Germany
[b] Department of Psychiatry and Psychotherapy, Medical Center, University of Freiburg, Faculty of Medicine, Freiburg, Germany
[c] Institute of Social Medicine, Occupational Health and Public Health, University of Leipzig, Leipzig, Germany
[d] Institute of Medical Statistics and Computational Biology, University of Cologne, Faculty of Medicine, University Hospital Cologne, Cologne, Germany
[e] Department of Psychiatry and Psychotherapy, Charité – Universitätsmedizin Berlin, Campus Benjamin Franklin, Berlin, Germany
[f] Department of Geriatric Psychiatry, Central Institute of Mental Health, Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany
[g] Department of Clinical Psychology and Psychotherapy, Eberhard Karls University, Tuebingen, Germany
[h] Department of Psychiatry and Psychotherapy, University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany
[i] German Center for Neurodegenerative Disease (DZNE), Venusberg-Campus 1, Building 99, Bonn, Germany
[j] Cellular Stress Response in Aging-Associated Diseases (CECAD) Cluster of Excellence, University of Cologne, Faculty of Medicine, University Hospital Cologne, Cologne, Germany

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ABSTRACT

Background: Cognitive impairment is prevalent in older age and in patients with depression, which may limit the efficacy of psychotherapy for late-life depression (LLD). We analyzed the effect of age and baseline cognition on the efficacy of psychotherapy in LLD.

Methods: This secondary analysis of a randomized controlled multicenter study included 213 participants (60–92 years) with moderate to severe depression who had received either supportive psychotherapy (SUI) or an LLD-specific cognitive behavioral therapy (LLD-CBT), both of which led to a substantial reduction in depressive symptoms. We examined the influence of age and baseline cognition, assessed with the CERAD-plus neuropsychological battery, on changes in the Geriatric Depression Scale (GDS) at the end of treatment and at 6-month follow-up. Trial registration at ClinicalTrials.gov (NCT03735576) and DRKS (DRKS00013769).

Findings: Baseline cognition was slightly below norms (<1SD), with 15 % of patients meeting criteria for Mild Cognitive Impairment (MCI). GDS change at the end of treatment was not significantly associated with baseline cognition or MCI status, although additional interaction analyses suggest that, in the SUI group, lower baseline cognitive performance was associated with reduced treatment efficacy at follow-up only. Additionally, we found that higher age predicted a smaller reduction in GDS scores both at end-of-treatment and at follow-up in both treatment groups.

Interpretation: Higher age, but not lower cognitive performance, was associated with reduced psychotherapy efficacy. Thus, age-related factors should be considered in psychotherapy.

1. Introduction

Meta-analyses and reviews have demonstrated that psychological treatments, specifically cognitive behavioral therapy (CBT), are effective in treating depression in older adults (Cuijpers et al., 2006; Peng et al., 2009; Jayasekara et al., 2015). Internationally, psychotherapy is strongly recommended for mild to severe late-life depression by several guidelines (LLD DGPPN et al., 2017; American Psychological Association, 2019; National Institute for Health and Care Excellence (NICE), 2022).

* Corresponding author.
E-mail address: bettina.bewernick@ukbonn.de (B. Bewernick).

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In our recent multicentre study "CBTlate", we investigated the efficacy of psychotherapy in an outpatient LLD population. A total of 251 patients were randomly assigned to either LLD-specific cognitive behavioral therapy (LLD-CBT) or an active supportive psychotherapy group (SUI), based on humanistic approaches and general psychotherapy factors (Dafsari et al., 2019). Patients underwent 15 twice-weekly psychotherapy sessions for eight weeks, following either the LLD-CBT manual or a supportive therapy manual. Therapeutic efficacy was evaluated at the end of treatment and at a 6-month follow-up. We found a substantial reduction in depressive symptoms in both treatment arms at both time points (end-of-treatment: LLD-CBT = 40.4 %, SUI = 36.4 %; follow-up: LLD-CBT = 35.6 %, SUI = 28.6 %, Dafsari et al., 2023).

In a meta-analysis, Tunvirachaisakul et al. (2018) found that higher age was associated with lower treatment response in 50 % of the included studies, which applied a variety of biological and psychological antidepressant treatments. However, the literature on the effects of age on psychotherapy efficacy remains inconsistent (Tanguay-Sela et al., 2022). Additionally, little is known about how specific psychotherapy methods interact with age and other moderators - such as cognitive performance - in affecting treatment response. To our knowledge, no study has yet investigated global cognitive performance as a predictor of response to antidepressant psychotherapy in LLD. However, there is some evidence that people with cognitive disorders might benefit more from specific treatment approaches: In a recent meta-analysis, Orgeta et al. (2022) examined the efficacy of psychotherapy in LLD patients with dementia and found a positive effect of CBT at the end of treatment, but not for supportive therapies. Regarding long-term efficacy, the authors concluded that there were insufficient data available to evaluate long-term effects.

Psychological treatments require cognitive abilities such as memory (Dong et al., 2017) to retain and apply intervention contents, attention to follow the sessions, and executive abilities for planning and organizing behavior – all of which are known to decline slightly with age (Wagner et al., 2018). Depression is also associated with reductions in specific cognitive functions, especially processing speed, memory, and executive functions (Butters et al., 2004; Wagner et al., 2018). Therefore, one might assume that elderly patients' cognitive abilities may influence psychotherapy efficacy.

Studies examining the association between cognition and treatment response in depression are heterogeneous in design, often involve small samples, focus on younger patients, and vary in psychotherapy methods - or even combine psychotherapy with pharmacotherapy (Groves et al., 2018; Tunvirachaisakul et al., 2018). Nonetheless, early evidence suggests that verbal learning and memory are positively associated with the efficacy of CBT (Kundermann et al., 2015; Carter et al., 2018) and SUI (Deckersbach et al., 2018) in younger adults (<60 years) with depression or bipolar disorder.

In LLD treatment, the evidence is more heterogeneous. One study suggests a positive association between executive functioning and CBT efficacy (Dobkin et al., 2012), while two other studies report the opposite: poorer executive functioning predicted better outcomes for both CBT and SUI (Beaudreau et al., 2015; Goodkind et al., 2016).

Whether global cognitive performance and age are independent predictors of psychotherapy efficacy has yet to be investigated. Therefore, in this secondary analysis, we aimed to study the effect of baseline cognitive performance and of age on the reduction of depressive symptoms following psychotherapy (LLD-CBT and SUI). We examined several cognitive aspects: global cognitive performance, specific cognitive functions, and MCI versus non-impaired status and their interaction with treatment type. Additionally, we quantified the predictive effects of age and cognition, as well as their interaction with treatment group, on psychotherapy efficacy at end-of-treatment and follow-up.

2. Methods

2.1. Subjects

A total of 251 subjects participated in the CBTlate study, which compared the efficacy of 15 sessions of twice-weekly LLD-CBT in individuals over 60 years of age with LLD to an active, manualized supportive therapy (SUI) in a multicenter setting. The LLD-CBT intervention is based on a published manual and includes 6 modules reflecting the core structure of CBT (e.g., psychoeducation, development of an individualized cognitive-behavioral model of depression, day structuring, activation), with specific adaptations for older adults, such as life review and the selection, optimization, and compensation (SOC) model (Baltes and Baltes, 1989).

In contrast, SUI employs supportive techniques grounded in humanistic psychotherapy and general psychotherapy factors such as self-reflection, emotional expression and validation, and activation of personal resources and strengths. The SUI manual was also successfully tested in a pilot study with LLD outpatients. For further details, please refer to the Supplementary materials of the main publication (Dafsari et al., 2023, www.karger.com/doi/10.1159/000529445).

Secondary study aims included the identification of predictors and moderators of treatment efficacy (Dafsari et al., 2019). For the current secondary analysis, we used the per-protocol sample (n = 213, Dafsari et al., 2023), consisting of participants without major protocol violations who completed at least nine therapy sessions.

2.2. Measures

The 30-item Geriatric Depression Scale (GDS, range 0–30, higher scores indicating greater symptom severity) was the primary outcome measure (Yesavage and Sheikh, 1986). It is a self-report instrument designed to assess depressive symptoms in older adults. In the CBTlate study, depression was assessed at four time points: baseline (T0), at an intermediate point (5 weeks after randomization and after 50 % of treatment sessions; T1), at end-of-treatment (10 weeks after randomization; T2), and at follow-up (6 months after randomization; T3).

Cognitive data were collected using the original Consortium to Establish a Registry for Alzheimer's Disease (CERAD) neuropsychological battery (Morris et al., 1988). Global cognitive performance was measured using the raw CERAD total score, calculated as the sum of subtest scores for verbal fluency (animals), Boston Naming Test (BNT), word list learning, word list delayed recall, word list recognition, and constructive praxis (Chandler et al., 2005).

Additional subtests included word list discriminability, figural memory, lexical fluency, and the Trail Making Tests A and B (CERAD-plus version). Performance in specific cognitive domains was represented by raw scores from the 12 individual subtests (Schmid et al., 2014).

Z-standardized scores, adjusted for age, sex, and education, based on German normative data (Ehrensperger et al., 2010), were used to compare cognitive performance in the LLD group with normative controls, estimate the prevalence of cognitive impairment, and assess its role in therapeutic outcomes. However, since this normative adjustment controls for age, sex, and education, it does not directly assess whether poorer absolute cognitive abilities relate to psychotherapy efficacy in LLD. Therefore, the main analyses used raw CERAD scores as independent variables and included age, education, and sex as separate covariates. As higher scores (time to completion) indicate worse cognition in the TMT, these scores were inverted before analysis.

Neuropsychological variables were assessed at baseline (T0) and at follow-up (T3). At follow-up, a parallel version of the CERAD word list was used to minimize retest effects. Fig. 1 shows the number of participants of the per-protocol analysis per group at each time point (T0, T2, T3) and the number with available neuropsychological data (NPT). One participant of the LLD-CBT group had no neuropsychological data at

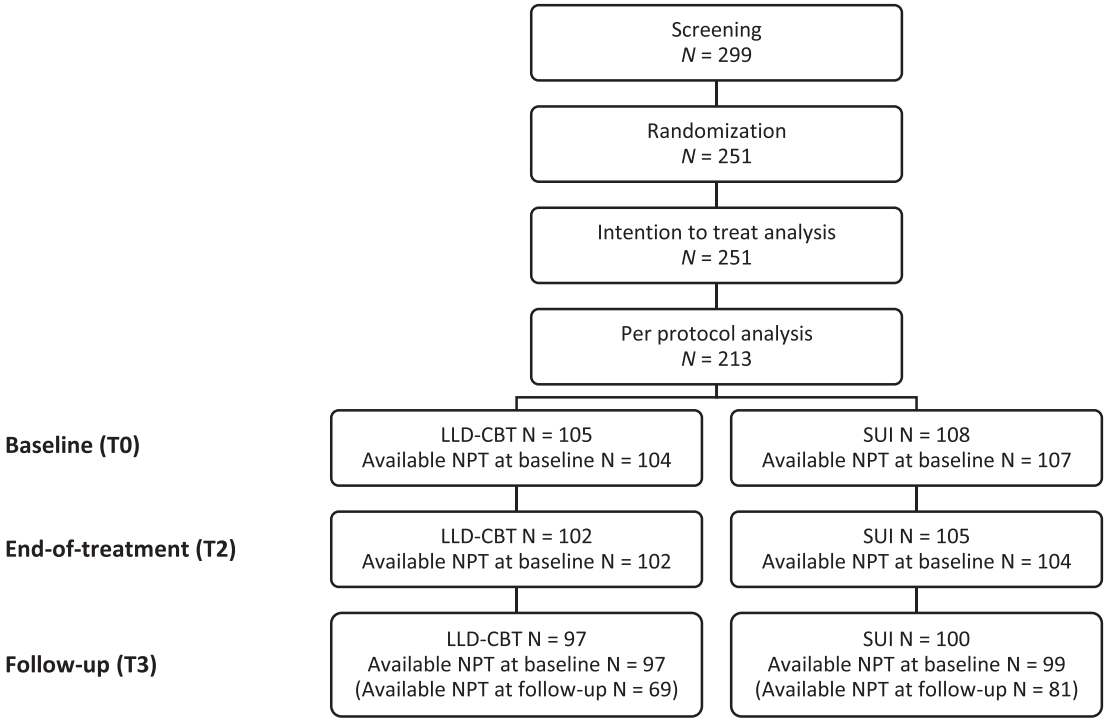

Fig. 1. Flow chart of the per-protocol sample. The current analyses included 212 participants with baseline neuropsychological testing (NPT) who completed treatment assessments at T0, T2 or T3.

baseline. Most missing NPT follow-up data were due to participants declining to undergo the assessment. Since we only analyzed baseline cognitive scores, missing follow-up NPT data did not reduce our sample size.

In addition to analyzing cognitive performance quantitatively, we used a categorical approach to examine whether participants with MCI showed different treatment response. MCI was defined according to Mistridis et al. (2015), using a base-rate method that adjusts for the frequency of low scores among healthy older adults. Under this method, MCI is diagnosed if five or more out of ten CERAD subtests fall below the 16th percentile (<1 SD), because 90 % of healthy normative controls have up to four "deviant" CERAD scores (this is the normative "base rate" of impairment). As a result, the threshold of overall impairment across all CERAD subtests is close to the 10th percentile ($z = 1.28$) of the normative controls. This MCI definition avoids an artificial inflation of MCI "diagnoses" when considering a large number of subtests with a liberal (1 SD) deficit criterion. This base-rate adjusted MCI largely overlaps with other MCI definitions, it has been biologically and prospectively validated in memory clinic patients (Polcher et al., 2022) and is well applicable to the CERAD data.

2.3. Statistical analyses

All analyses were performed with SPSS version 27. Baseline characteristics (sex, age, education, GDS score, and raw CERAD total score) were compared between treatment groups (LLD-CBT, SUI) using *t*-tests or chi-squared tests.

To determine whether baseline cognitive performance differed from age-adjusted norms, we conducted one-sample *t*-tests (hypothesized population mean $\mu = 0$) using z-standardized scores for each CERAD variable, including the total score. We assessed the correlations between cognitive performance (standardized scores of 12 subtests, as well as standardized and raw CERAD total scores) and depression severity (GDS) at baseline using Pearson correlations. One-sample t-tests comparing cognitive performance (standardized CERAD scores) at baseline and follow-up were conducted to rule out cognitive change as a confounder. Nominal *p*-values are reported for all CERAD-plus scores. The significance threshold was set at $\alpha = 0.05$ (two-tailed), and Bonferroni correction was applied post hoc to control for multiple comparisons.

Primary outcome variables were change scores in GDS from baseline to end-of-treatment (T0–T2) and from baseline to follow-up (T0–T3), where more positive values indicate greater symptom reduction. These change scores were used as dependent variables in all subsequent analyses.

To examine the effect of baseline cognitive performance on treatment efficacy, we conducted two linear regression analyses using the change in GDS as the dependent variable (for T0–T2 and T0–T3). Raw CERAD total score and treatment group were used as independent variables, and age, education, and sex were included as covariates.

To explore the impact of specific cognitive domains, we repeated both regression analyses, this time including the raw scores of the 12 CERAD subtests and treatment group as independent variables. Again, age, education, and sex were included as covariates.

To analyze the influence of MCI status, we conducted two additional regression models, with MCI (MCI vs. non-MCI) and treatment group as independent variables, and age, sex, and education as covariates.

Additionally, we explored interaction effects between treatment group and baseline global cognitive performance by including an interaction term treatment group × cognition (using LLD-CBT as the reference) in the regression models for both time points. Independent variables included treatment group, raw CERAD total score, the interaction term, and covariates (age, sex, education). We also tested a second interaction model using age × treatment group instead of cognition × treatment group. All continuous predictors were mean-centered before inclusion in interaction models.

Lastly, to examine specific age effects on treatment outcome, participants were divided into commonly used categories "old" (<75 years) vs. "old-old" (≥75 years; Roose et al., 2004). Post hoc independent *t*-tests compared outcomes between these age groups at both the end of treatment and follow-up. Additional independent *t*-tests assessed differences between both age groups in treatment outcome at follow-up

within each treatment group. To check for potential biases, we tested whether age groups were equally distributed between treatment arms using a chi-square test, and we also compared baseline cognition (raw CERAD total score) and GDS scores to rule out confounding. We used a significance threshold of 0.05 (two-tailed).

3. Results

3.1. Baseline characteristics of the study sample

Participants (n = 212, T0) were between 60 and 92 years old (M = 70.2, SD = 7.2) and had completed, on average, 14.9 years of education (SD = 3.3). A total of 65.7 % of the sample were female. The mean baseline GDS score was 20.7 (SD = 4.2), indicating moderate to severe depression (see Table I in the Supplements). Among all variables (dependent, independent, and covariate), the only significant difference between treatment groups (LLD-CBT vs. SUI) was in sex distribution ($\chi^2(1) = 5.32$, $p < .05$; LLD-CBT: female = 77, male = 28; SUI: female = 63, male = 45). There were no significant differences in baseline GDS scores, age, or education. Similarly, no significant differences were found in the CERAD total scores (raw score and z-standardized score) between LLD-CBT and SUI at baseline (see Table I in the Supplements).

3.2. Cognitive performance at baseline

At baseline, LLD patients had only very mild cognitive deficits, averaging up to one standard deviation below the z-standardized norm in verbal fluency (animals), word list learning, word list delayed recall, and the CERAD total score (see Table 1). Performance in confrontation naming (BNT) and word list recognition (discriminability) was slightly better than predicted. These effects remained statistically significant after Bonferroni correction, except for discriminability.

No significant correlations were observed between the standardized CERAD subtest scores and the CERAD total score (standardized and raw score) and GDS score at baseline ($r = -0.12$ to 0.08). A total of 32 out of 212 participants (15 %) were classified as having MCI at baseline.

Comparison of cognitive performance between baseline and follow-up (in participants with follow-up data) showed a slight improvement in word list learning, word list recognition (discriminability), and the CERAD total score, though these changes were not statistically significant after Bonferroni correction (see Table II in the Supplements).

Table 1
Standardized cognitive performance of the study sample at baseline (CERAD-plus battery).

	N	M (SD)	t	p
Verbal fluency (animals)	212	−0.37 (1.24)	−4.33	.00
Verbal fluency (S-words)	212	0.08 (1.32)	0.92	.36
BNT	212	0.29 (1.00)	4.25	.00
Word list learning	211	−0.52 (1.21)	−6.26	.00
Word list delayed recall	211	−0.40 (1.05)	−5.54	.00
Savings	211	0.003 (3.53)	0.01	.99
Discriminability	212	0.15 (0.93)	2.29	.02
Constructive praxis	212	−0.15 (1.20)	−1.79	.07
Figural memory	212	−0.11 (1.29)	−1.25	.21
Figural savings	212	−0.03 (1.07)	−0.44	.66
TMT-A	210	−0.15 (1.34)	−1.56	.12
TMT-B	203	−0.07 (1.30)	−0.71	.48
CERAD total score	211	−0.44 (1.13)	−5.60	.00

BNT: Boston Naming Test; TMT-A/B: Trail Making Test A/B. All values are z-standardized against German CERAD-plus norms. Means and standard deviations of z-standardized subtest performances are presented. One-sample t-tests tested against a normative mean of 0 (by definition, the mean of the demographically adjusted scores of the CERAD-plus normative sample).

3.3. Effects of cognition and age on treatment efficacy

The multiple regression analysis model examining baseline global cognitive performance (raw CERAD total score) and age as predictors of treatment efficacy was marginally significant at the end of treatment ($F(5, 200) = 2.23$, $p = .05$, adj. $R^2 = 0.03$, p = .05), and significant at follow-up ($F(5, 190) = 4.19$, $p < .01$, adj. $R^2 = 0.08$, p < .01).

At end-of-treatment, only age significantly predicted treatment efficacy (B = −0.18, SE = 0.08, $p < .05$), while cognitive performance did not (B = 0.02, SE = 0.06, $p = .81$). Similarly, at follow-up, age remained a significant predictor (B = −0.25, SE = 0.08, p < .05), but cognitive performance did not (B = 0.06, SE = 0.07, $p = .33$). Thus, higher age was associated with a poorer psychotherapy response at both time points.

3.4. Effects of specific cognitive functions on treatment efficacy

To explore effects of specific cognitive tasks, we calculated two separate regression models for the two dependent variables: change in GDS score at the end of treatment and follow-up. The independent variables in both models were the raw scores of the 12 CERAD subtests, including executive tasks, which are not part of the CERAD total score. As in the previous regression models, we included age, sex, and education as covariates. The regression model for treatment efficacy at the end of treatment was not significant ($F(16, 126) = 1.02$, $p = .441$, $adj.\ R^2 = 0.002$, $p = .44$) and neither age nor any of the specific cognitive functions were significant predictors.

In contrast, the model for treatment efficacy at follow-up was significant ($F(16, 126) = 2.01$, $p < .05$; $adj.\ R^2 = 0.10$, $p < .05$). Within this model, age was the only significant predictor ($B = -0.29$, $SE = 0.11$, $p < .05$).

3.5. Effect of MCI status on treatment efficacy

The regression models on treatment efficacy at the end of treatment and at follow-up, including MCI status and treatment group as predictors and age, sex and education as covariates, were both significant (end of treatment: $F(5, 201) = 2.34$, $p < .05$, $adj.\ R^2 = 0.03$, $p < .05$; follow-up: $F(5, 191) = 4.08$, $p < .01$, $adj.\ R^2 = 0.07$, $p < .01$). However, in both models, age was the only significant predictor, while MCI status was not (end of treatment: age: $B = -0.18$, $SE = 0.07$, $p < .05$, MCI status: $B = -1.10$, $SE = 1.49$, $p = .46$; follow-up: age: $B = -0.28$, $SE = 0.08$, $p < .001$, MCI status: $B = -0.86$, $SE = 1.48$, $p = .56$).

3.6. Interaction of cognition and treatment type on treatment efficacy

In our subsequent exploratory analyses, we tested the interaction effect of treatment group with baseline global cognitive performance as predictor of treatment efficacy at the end of treatment and at follow-up. The overall regression model for treatment efficacy at the end of treatment did not reach statistical significance ($F(6, 199) = 2.04$, $p = .06$, $adj.\ R^2 = 0.03$, $p = .06$). Age was the only significant predictor in this model, while baseline cognition, treatment group, and their interaction were not (age: $B = -0.19$, $SE = 0.82$, $p < .05$; baseline cognition: $B = 0.07$, $SE = 0.08$, $p = .41$; treatment group: $B = 1.04$, $SE = 1.04$, $p = .32$; $\text{interaction}_{(\text{cognition x treatment})}$: $B = -0.12$, $SE = 0.11$, $p = .30$).

In contrast, the regression model for treatment efficacy at follow-up was significant, explaining 10 % of the total variance ($F(6, 189) = 4.44$, $p < .001$, $adj.\ R^2 = 0.10$, $p < .001$). Significant predictors in this model were age, baseline cognition, and the interaction of baseline cognition and treatment group (age: $B = -0.26$, $SE = 0.08$, $p < .01$; baseline cognition: $B = 0.18$, $SE = 0.08$, $p < .05$; treatment group: $B = 1.45$, $SE = 1.04$, $p = .16$; $\text{interaction}_{(\text{cognition x treatment})}$: $B = -0.26$, $SE = 0.11$, $p < .05$). The interaction effect was mainly driven by poorer treatment efficacy in participants with lower cognitive performance in the SUI group (see Fig. 2).

To validate this interpretation, we conducted a post-hoc analysis

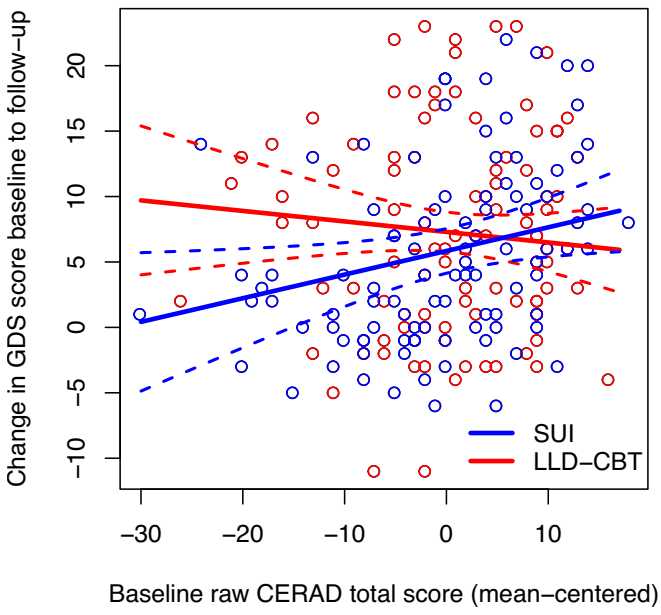

Fig. 2. Interaction: Association of baseline cognitive performance (mean-centered raw CERAD total score) with treatment efficacy at follow-up (T3, 6 months after randomization), stratified by treatment group (LLD-CBT vs. SUI), plotted with R version 4.3.2. Lower baseline global cognitive performance in the SUI group was associated with less improvement in depressive symptoms at follow-up (GDS change T0-T3).

with two separate regression models for the LLD-CBT and SUI groups, using treatment efficacy at follow-up as the dependent variable, and baseline cognitive performance as the independent variable. Age, education, and sex were included as covariates. Only the model for the SUI group was significant ($F(4, 94) = 5.82$, $p < .001$, *adj.* $R^2 = 0.16$, $p < .001$), with age and baseline cognition as significant predictors (age: $B = -0.27$, $SE = 0.11$, $p < .05$; baseline CERAD total score: $B = 0.19$, $SE = 0.08$, $p < .05$). The model for the LLD-CBT group was not significant ($F(4, 92) = 1.08$, $p = .37$, *adj.* $R^2 = 0.003$, $p = .37$), and baseline cognition was not a significant predictor ($B = -0.08$, $SE = 0.11$, $p = .45$), while age remained significant ($B = -0.26$, $SE = 0.13$, $p < .05$).

Taken together, these results indicate that lower baseline cognitive performance negatively affects treatment efficacy at follow-up only in the SUI group, while higher age reduces treatment efficacy at both time points in both treatment groups.

To rule out any major effects of specific cognitive functions in the SUI group at follow-up, we conducted another post hoc analysis to investigate the effects of the CERAD subtests on the treatment efficacy at follow-up within the SUI group only. The overall regression model, including all 12 baseline raw CERAD subtest scores and the covariates age, sex, and education was significant ($F(15, 61) = 2.35$, $p = .01$, adj. $R^2 = 0.21$, $p = .01$). However, none of the predictors were statistically significant.

As age emerged as an important predictor of treatment efficacy, we repeated the previous interaction analysis, replacing the cognition × treatment group interaction with an age × treatment group interaction. The regression model for treatment efficacy at the end of treatment was not significant ($F(6, 199) = 2.01$, $p = .07$, *adj.* $R^2 = 0.03$, $p = .07$), and the interaction term was also not significant ($B = 0.14$, $SE = 0.14$, $p = .34$). For treatment efficacy at follow-up, the regression model was significant ($F(6, 189) = 3.73$, $p < .01$, *adj.* $R^2 = 0.08$, $p < .01$), but the interaction of age and treatment group was again not significant ($B = 0.17$, $SE = 0.15$, $p = .25$).

The post hoc analysis of age effects showed that the old-old group (≥75 years) had a significantly poorer treatment outcome at follow-up compared to the old group (<75 years, $t(195) = 2.2$, $p < .05$, $d = 0.36$; ≥75: $M = 4.3$; $SD = 7.0$; <75: $M = 7.0$; $SD = 7.5$), but not at end-of-treatment ($t(206) = 1.4$, $p = .16$, $d = 0.22$; ≥75: $M = 5.9$; $SD = 6.8$; <75: $M = 7.5$; $SD = 7.5$). Stratified analysis revealed that, within the SUI group, old-old participants showed significantly poorer treatment outcomes at follow-up than old participants ($t(64) = 2.7$, $p < .01$, $d = 0.53$; ≥75: $M = 2.8$; $SD = 5.5$; <75: $M = 6.4$; $SD = 7.2$). This difference was not significant within the LLD-CBT group ($t(95) = 0.8$, $p = .42$, $d = 0.193$; ≥75: $M = 6.0$; $SD = 8.2$; <75: $M = 7.5$; $SD = 7.9$). Age groups were equally distributed across treatment groups ($X^2 = 0.89$ (1), $p = .35$, *Cramér's* $V = 0.07$). The old-old did not differ between treatment groups in baseline cognition (raw CERAD Total Score; $t(57) = -0.65$, $p = .52$, $d = -0.17$; ≥75: $M = 76.6$; $SD = 9.4$; <75: $M = 75.0$; $SD = 8.7$) or GDS scores ($t(57) = 0.52$, $p = .60$, $d = 0.18$; ≥75: $M = 20.0$; $SD = 4.5$; <75: $M = 20.6$; $SD = 4.1$).

4. Discussion

This study is one of the largest to date examining the role of cognition and age in the treatment outcome of cognitive behavioral therapy (LLD-CBT) and supportive therapy (SUI) for late-life depression (LLD). We found that baseline cognitive performance did not significantly influence the efficacy of psychotherapy - neither in continuous analyses nor when comparing extreme groups (MCI vs. non-MCI). However, two important associations with efficacy of psychotherapy emerged: (a) higher age was related to reduced treatment outcomes at both end-of-treatment and follow-up, regardless of baseline cognition and treatment group (b) lower baseline cognitive performance was associated with reduced long-term treatment outcomes only in the SUI group.

4.1. Cognitive performance and psychotherapy efficacy

In our study, neither the global cognitive performance nor specific cognitive functions at baseline predicted psychotherapy efficacy at end-of-treatment or follow-up. To our knowledge, no prior study in LLD patients has assessed global cognitive performance as a predictor of psychotherapy efficacy, which supports current international guidelines recommending psychotherapy for older adults regardless of cognitive performance.

Several previous studies have examined the role of specific cognitive domains - particularly verbal memory and executive functioning - but most involved younger adults (<60 years). For instance, two studies in younger depressive outpatients found a positive association between verbal memory/verbal fluency and response to CBT (Kundermann et al., 2015; Carter et al., 2018). Another study in middle-aged adults (Age: 18–65, M = 40.2, SD = 13.1) with bipolar disorder reported similar findings for both CBT and SUI (Deckersbach et al., 2018). Dong et al. (2017) also showed that CBT responders were able to recall more treatment content during the therapy phase, suggesting that memory functions play a role in treatment engagement.

These results suggest that verbal memory may influence psychotherapy outcomes in younger and middle-aged adults (≤65 years). For LLD (≥60), however, findings on cognitive predictors of psychotherapy efficacy are more mixed. One study in LLD found that better executive functioning predicted better CBT outcomes (Dobkin et al., 2012), whereas two others revealed that poorer executive functioning was associated with better outcomes in both CBT and SUI (Beaudreau et al., 2015; Goodkind et al., 2016). The latter may be explained by the correlation between more severe depression and executive dysfunction, with greater symptom improvement in more severely affected individuals (Beaudreau et al., 2015). Thus, the association of specific cognitive functions with psychotherapy efficacy requires a larger database for more substantial scientific conclusions.

In general, mild cognitive impairments may not affect psychotherapy efficacy because therapists naturally adapt their interventions to patients' needs, including cognitive limitations. Clinically, we observe that therapists often use more repetition and a greater focus on behavioral

techniques in patients with cognitive deficits as part of the individualized process of psychotherapy. A systematic evaluation of such adaptations would require a dedicated, process-focused study design.

Another reason for the lack of an effect of cognition in our study might be the relatively high cognitive functioning of our sample. Only 15 % of participants met MCI criteria - lower than the 40–60 % prevalence of clinically relevant cognitive deficits reported in other studies (Butters et al., 2004). Two large cohort studies investigated the prevalence of cognitive deficits in an elderly outpatient population diagnosed with major depression and found cognitive deficits mostly in processing speed and executive functions (Butters et al., 2004) as well as in memory (Butters et al., 2004; Heser et al., 2013). Our sample also had high educational attainment and participated in a demanding outpatient program (sessions twice a week) requiring high demands on self-organization. Therefore, a selection bias and a ceiling effect of cognitive function cannot be ruled out.

4.2. MCI and psychotherapy efficacy

Approximately 15 % of our participants met MCI criteria. Consistent with our global cognition findings, MCI status was not associated with psychotherapy efficacy. Although formal MCI definitions are not commonly used in LLD research, our results align with a case report showing that a 30-min, 8-week CBT intervention was effective for an older adult with MCI and depression (Kashimura et al., 2020). While we excluded participants with dementia and used an MMSE cutoff of <26, and our findings apply only to cognitively healthy to mildly impaired individuals, a meta-analysis has shown that CBT reduces depressive symptoms also in patients with MCI and dementia (Orgeta et al., 2022).

4.3. Interaction between cognition and treatment group

Although we did not find a main effect of baseline cognition on treatment outcome overall, we conducted an exploratory analysis on its interaction with treatment group. At end-of-treatment, no interaction effect was found. At follow-up, however, there was a significant interaction: lower baseline cognition predicted poorer outcomes in the SUI group only. This might indicate that psychotherapy - both LLD-CBT and SUI - is generally effective regardless of baseline cognition, but that maintaining the long-term effects of SUI may be more difficult for patients with lower cognitive performance. Further investigation is needed to explore mechanisms behind long-term psychotherapy efficacy in LLD.

4.4. Age and psychotherapy efficacy

Numerous meta-analyses and systematic reviews support the efficacy of psychotherapy, including CBT and supportive therapy, for treating depression in older adults (Cuijpers et al., 2006; Peng et al., 2009; Huang et al., 2015; Jayasekara et al., 2015). However, we found that older age was associated with reduced treatment efficacy, both at the end of treatment and at follow-up - independent of cognitive performance.

This aligns with other psychotherapy studies in LLD that found higher age predicts poorer treatment response in older depressed patients (Tunvirachaisakul et al., 2018) and suggests that age-related factors may moderate therapy outcomes. Reduced social support (Woods et al., 2021), higher comorbidity, and impaired subjective health (Lenze et al., 2001; Bosworth et al., 2002) might be important age-associated moderators. In recent exploratory analyses from CBTlate, we found that subjective physical health and childhood maltreatment history differentially influenced treatment response across therapy methods (Dafsari et al., 2023, 2024; Müller et al., 2024).

Additionally, the stratified post hoc analysis implicated that the old-old in the SUI treatment group benefited the least from psychotherapy at follow-up. However, studies with larger sample sizes of old-old are needed to investigate whether CBT may yield superior long-term outcomes compared to SUI in this age group.

4.5. Strengths and limitations

This study benefits from a large sample size, comprehensive cognitive assessments, and the comparison of two active psychotherapy conditions in a multicenter design -factors that enhance its robustness. A strength of our study is the detailed and standardized cognitive assessment at two time points. We used a validated, state-of-the-art test battery, thereby obtaining a detailed representation of cognitive performance both globally and across all relevant, specific cognitive functions. In addition, the randomized comparison of two active psychotherapeutic treatments (LLD-CBT vs. SUI) allowed us to explore whether baseline cognition and age might be differentially associated with treatment outcomes.

However, the low prevalence of MCI may have limited our ability to detect moderating effects of cognition. In addition, the exclusion of individuals with MMSE scores <26 means that our findings are applicable only to cognitively healthy or mildly impaired individuals. Whether more severe cognitive impairment influences the efficacy of psychotherapy remains an open question for future research. Another limitation of our study is a potential self-selection bias. Participants proactively enrolled in an outpatient psychotherapy study, suggesting a high level of self-organization and motivation. Our conclusions may therefore apply primarily to relatively healthy, mobile, and highly motivated individuals. Moreover, we did not examine psychotherapy process variables that may mediate or moderate treatment outcomes - such as the therapeutic alliance (Orlinsky and Howard, 1987), which could involve specific therapist adaptations to meet individual patient needs. For example, therapists may speak more loudly when working with patients who are hard of hearing or repeat information more frequently for those with cognitive impairments. These individualized adjustments could enhance patients' attention and motivation, thereby strengthen therapeutic engagement and ultimately contribute to more favorable treatment outcomes.

5. Conclusion

Mild levels of cognitive impairment do not reduce efficacy in psychotherapy for LLD. But higher age - independent of cognition and of therapy method - is associated with reduced psychotherapy efficacy. This does not imply that it is “too late” for psychotherapy as an effective antidepressant treatment after age 75. Rather, this suggests that the old-old may have distinct treatment needs compared to patients in their sixties or early seventies. Future research could explore non-cognitive age-related patient and process variables that might affect treatment efficacy of psychotherapy in very old adults more specifically.

CRediT authorship contribution statement

Bettina Bewernick: Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Julijana Buschmann:** Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Conceptualization. **Kathrin Heser:** Writing – review & editing, Investigation, Conceptualization. **Luca Kleineidam:** Writing – review & editing, Visualization, Methodology, Formal analysis. **Katharina Domschke:** Writing – review & editing, Investigation, Conceptualization. **Moritz Elsaesser:** Writing – review & editing, Investigation. **Nadine Zehender:** Writing – review & editing, Investigation. **Melanie Luppa:** Writing – review & editing, Supervision, Investigation, Funding acquisition, Conceptualization. **Martin Hellmich:** Writing – review & editing, Methodology, Formal analysis, Data curation. **Oliver Peters:** Writing – review & editing, Supervision, Investigation, Funding acquisition, Conceptualization. **Lutz Froelich:** Writing – review & editing, Supervision, Investigation, Funding acquisition, Conceptualization. **Steffi Riedel-Heller:** Writing – review & editing, Supervision, Investigation, Funding acquisition, Conceptualization. **Elisabeth Schramm:**

Writing – review & editing, Investigation, Funding acquisition, Conceptualization. **Martin Hautzinger:** Writing – review & editing, Supervision, Investigation, Funding acquisition, Conceptualization. **Frank Jessen:** Writing – review & editing, Supervision, Investigation, Funding acquisition, Conceptualization. **Forugh S. Dafsari:** Writing – review & editing, Supervision, Project administration, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Michael Wagner:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used OpenAi sources (ChatGBT) in order to improve readability and language of the work. After using this service, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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Declaration of competing interest

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Appendix A. Supplementary data

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