

Research Article

Cite this article: Haritos R, Küppers V, Samea F, Riemann D, Jessen F, Eickhoff SB, Dafsari FS, Tahmasian M (2025). The effect of psychotherapy on the multivariate association between insomnia and depressive symptoms in late-life depression. *European Psychiatry*, 68(1), e120, 1–11
<https://doi.org/10.1192/j.eurpsy.2025.10088>

Received: 01 April 2025

Revised: 29 July 2025

Accepted: 01 August 2025

Keywords:

canonical correlation analysis; insomnia; late-life depression; machine learning; psychotherapy





Corresponding author:

Masoud Tahmasian;

Email: m.tahmasian@fz-juelich.de

R.H. and V.K. these authors contributed equally.

The effect of psychotherapy on the multivariate association between insomnia and depressive symptoms in late-life depression

Rafailia Haritos^{1,2}, Vincent Küppers^{1,3,4} , Fateme Samea^{1,3,5}, Dieter Riemann⁶ , Frank Jessen⁷, Simon B. Eickhoff^{1,3}, Forugh S. Dafsari⁷ , and Masoud Tahmasian^{1,3,4} 

¹Institute of Neuroscience and Medicine, Brain and Behaviour (INM-7), Research Center Jülich, Jülich, Germany; ²Department of Psychology, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany; ³Institute of Systems Neuroscience, Medical Faculty, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany; ⁴Department of Nuclear Medicine, University Hospital and Medical Faculty, University of Cologne, Cologne, Germany; ⁵Clinic and Polyclinic for Child and Adolescent Psychiatry, Psychotherapy, and Psychosomatics, Medical Faculty, Leipzig University, Leipzig, Germany; ⁶Department of Psychiatry and Psychotherapy, Medical Centre, University of Freiburg, Faculty of Medicine, Freiburg, Germany and ⁷Department of Psychiatry and Psychotherapy, University of Cologne, Faculty of Medicine Cologne, Germany

Abstract

Background. Late-life depression (LLD) is prevalent in older adults and linked to increased disability, mortality, and suicide risk. Insomnia symptoms are considered common remaining symptoms of LLD following treatment. However, the multivariate relationship between insomnia and depressive symptoms and the impact of psychotherapy on their interrelationship is insufficiently assessed.

Methods. We conducted a secondary analysis of data from 185 patients with LLD, recruited from seven university hospitals in Germany as part of a larger original cohort study. Participants had undergone eight-week psychotherapy interventions (cognitive behavioral therapy or supportive unspecific intervention). Three regularized canonical correlation analyses (rCCA) assessed the multivariate association between insomnia and depressive symptoms at baseline, post-treatment, and six-month follow-up. rCCA was conducted within a machine learning framework with 100 repeated hold-out splits and permutation tests to ensure robust findings. Canonical loadings and cross-loading difference scores were calculated to examine symptom changes before/after psychotherapy (Holm-Bonferroni corrected p -value < 0.05).

Results. At baseline, a moderate association was observed between insomnia and depressive symptoms ($r = 0.24$). Interestingly, this association slightly increased after the eight-week treatment period ($r = 0.42$, $p_{\text{corrected}} = 0.064$) and remained significantly elevated at the follow-up session ($r = 0.48$, $p_{\text{corrected}} = 0.018$). At baseline, anxiety-related depressive symptoms were mainly associated with insomnia, while at post-treatment and follow-up sessions, somatic and negative affective symptoms showed the strongest correlation with insomnia symptoms. While the relative relationship of depressive symptoms with insomnia altered after psychotherapy, the pattern of insomnia symptoms remained stable.

Conclusions. The observed changes in the association between insomnia and depressive symptoms after psychotherapy highlight the necessity to consider targeting insomnia for effective LLD treatment.

Introduction

Late-life depression (LLD) refers to a major depressive disorder (MDD) in individuals aged 60 years or older [1]. It includes a first episode of depression in older adults or recurrent depressive episodes that began earlier in life but re-emerged at an advanced age. LLD is one of the most prevalent mental disorders among older adults, with a prevalence of approximately 14% [2]. With the rapid growth of the aging population and the high prevalence of LLD, the demand for geriatric mental health care is expected to rise substantially [3]. Beyond this burden, LLD is linked to higher relapse rates and severe health consequences, including accelerated somatic multimorbidity, cognitive decline, and increased mortality [4–8]. Additionally, depressive symptoms vary across the lifespan, posing challenges for interventions. Older adults are more likely to experience somatic and vegetative symptoms, such as insomnia symptoms, including difficulties in sleep initiation, early morning awakening, difficulty staying asleep, and daytime dysfunctions, compared to younger depressed patients [9, 10].

Existing evidence suggests that insomnia and depression exhibit a bidirectional relationship with shared underlying mechanisms, including shared genetic factors, hyperactivity of the

© The Author(s), 2025. Published by Cambridge University Press on behalf of European Psychiatric Association. This is an Open Access article, distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike licence (<http://creativecommons.org/licenses/by-nc-sa/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the same Creative Commons licence is used to distribute the re-used or adapted article and the original article is properly cited. The written permission of Cambridge University Press must be obtained prior to any commercial use.



EUROPEAN PSYCHIATRIC ASSOCIATION

arousal system, disruptions in synaptic plasticity, alterations in the biological timekeeping system, and shared macroscale neuroanatomical abnormalities [11–15]. Several meta-analyses and longitudinal studies demonstrated that insomnia symptoms and poor sleep are key risk factors for developing depression [16–18]. Conversely, the presence of depression may adversely affect sleep patterns and induce insomnia symptoms [19], which are one of the most prevalent residual symptoms following LLD treatment, with a prevalence of approximately 50% [20, 21]. These symptoms have been demonstrated to be associated with the onset, worsening, and recurrence of depressive symptoms, as well as suicidal ideations, particularly in older adults [22–25]. More severe insomnia symptoms are associated with higher rates of non-response to antidepressant treatment, failed remission, and relapse in LLD [26, 27]. To address the association between insomnia and depressive symptoms, multivariate approaches should be employed, as relying solely on the total scores of questionnaires may obscure changes at the individual symptom level of a very heterogeneous clinical condition such as LLD.

Current interventions for LLD include pharmacotherapy and psychotherapy (e.g., cognitive behavioral therapy (CBT)), although suboptimal response to antidepressants and an increased risk of adverse effects, such as hyponatremia, have been reported in older adults [28–30]. Thus, the present study aimed to explore the multivariate interrelationship between insomnia and depressive symptoms before and after psychotherapy using canonical correlation analysis (CCA) as conducted previously [31, 32]. This method allows us to assess bidirectional associations between two sets of variables to identify 1) how much insomnia and depressive symptoms are related to each other in patients with LLD at baseline, and 2) to determine whether and how psychotherapy treatment may modify their overall multivariate association, as well as each individual variables of both insomnia and depressive scales.

Methods

Participants

The current study analyzed a subset of data from a larger, multi-center, randomized controlled trial conducted at seven trial sites in Germany (Cognitive Behavioral Therapy for Late-Life Depression – CBTlate trial) [3]. From the original cohort of 251 participants with moderate to severe LLD, we included 185 participants with available scores for assessing insomnia and depressive symptoms at three time points (baseline, end-of-treatment, and follow-up sessions) (Figure 1a,b). Inclusion criteria were the following: 1) outpatients with age ≥ 60 years; 2) the Geriatric Depression Scale (GDS-30) score > 10 ; 3) the Quick Inventory of Depressive Symptomatology, Clinician Rating (QIDS-C) score > 10 ; 4) the Mini-Mental Status Test (MMST) score > 25 , to ensure not including patients with severe cognitive impairment; 5) not received or been stable on pharmacological treatment for at least six weeks before and during the eight weeks of treatment (Table 1). In view of conditions that could additionally alter sleep patterns, exclusion criteria were: 1) existing comorbidities, including bipolar depression or psychotic disorders; 2) regular use of hypnotics or benzodiazepine medications; 3) other chronic medical/somatic conditions. For ethical reasons, 38% of patients continued to take their current antidepressants without restrictions on medication type. Any change in dosage or medication led to exclusion from the study. More details on the in-/exclusion criteria and the interventions in the original trial are available elsewhere [3]. This clinical trial is registered at ClinicalTrials.gov (NCT03735576) and DRKS (DRKS0013769). The study was approved by the Institutional Review Board/Institutional Ethical Committee (IRB/IEC) of University Hospital Cologne (Nr. 18–129) and the participating sites prior to trial initiation. All participants provided written informed consent before all study procedures.

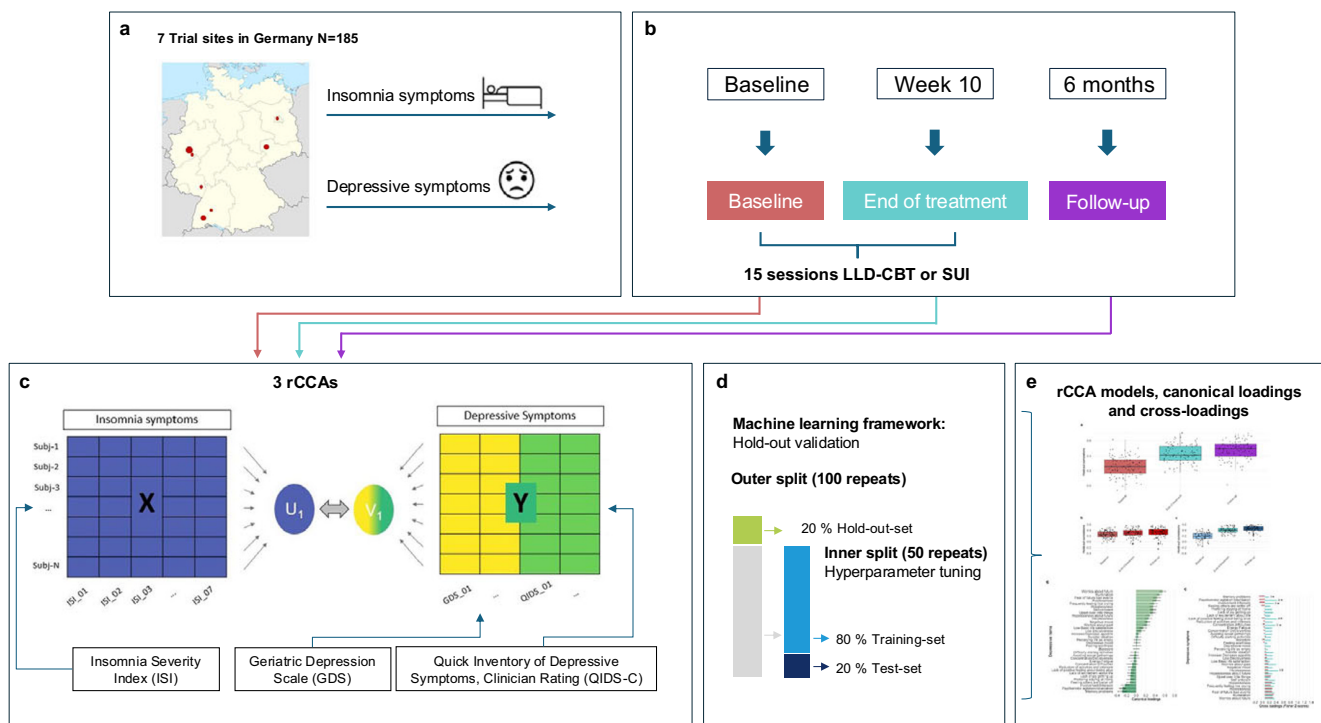


Figure 1. Overview of the study procedure: (a) Distribution of participants across seven trial sites and available data; (b) Assessment and intervention time points; (c) rCCA model representation of insomnia and depressive symptoms domains; (d) Machine learning framework (outer and inner split of data); (e) rCCA output: canonical correlation coefficients, canonical loadings and cross-loadings. LLD-CBT: Late-life depression cognitive behavioral therapy; SUI: Supportive unspecific intervention.

Table 1. Patient characteristics

Baseline characteristic	Full sample (N = 185)	
	n	%
Gender		
Female	123	66
Male	62	34
Marital status		
Living with partner	67	36
Married/partnered	24	13
Living separately from partner	9	5
Single	16	9
Divorced	45	24
Widowed	24	13
Have children ^a	150	81
Currently employed ^a	20	11
Previous psychological intervention ^a	9	5
Current psychotropic medication ^a	71	38
Psychotropic medication type of medicated patients*		
SSRI	60	64
SNRI	21	23
Heterocyclics/TCAs	6	6
MAO-Hemmer	3	3
Other antidepressants	2	2
Lithium	2	2
Treatment groups		
LLD-CBT	91	49
SUI	94	51
Trial site		
Cologne	54	29
Berlin	19	10
Bonn	12	7
Freiburg	39	21
Tübingen	10	5
Leipzig	31	17
Mannheim	20	11
GDS, mean (SD)		
Baseline	20.51 (4.12)	NA
End-of-treatment	13.26 (6.85)	
Follow-up	14.04 (6.82)	
QIDS-C, mean (SD)		
Baseline	11.89 (2.35)	NA
End-of-treatment	5.48 (4.22)	
Follow-up	5.99 (4.64)	
ISI, mean (SD)		
Baseline	13.9 (6.21)	NA
End-of-treatment	10.83 (6.65)	

Continued

Table 1. Continued

Baseline characteristic	Full sample (N = 185)	
	n	%
Follow-up	10.44	(6.55)

Note: Participants had an average of 69.7 years old ($SD = 7.1$). Abbreviations: LLD-CBT: Late-life-depression specific cognitive behavioral therapy, SUI: supportive unspecific intervention, GDS: Geriatric Depression Scale (possible score range 0–30), QIDS-C: Quick Inventory of Depressive Symptomatology-Clinician rating (possible score range 0–27), ISI: Insomnia Severity Index (possible score range 0–28), NA: not available.

^aReflects the number and percentage of participants answering “yes” to this question.

*These patients were among the 38% who received stable pharmacological treatment before and during the study, with some patients partially represented in multiple medication categories.

Assessments and interventions

Three different assessment time points were considered: baseline scores, at the end of the treatment period (week 10), and the six-month follow-up (Figure 1b).

Depressive and insomnia symptoms: The German versions of the Geriatric Depression Scale (GDS) questionnaire [33, 34] and the Quick Inventory of Depressive Symptomatology (QIDS) [35, 36] were used to measure depressive symptoms. Insomnia symptoms were assessed using the German version of the Insomnia Severity Index (ISI) [37, 38]. For more details, see [Supplementary Material](#).

Psychotherapeutic treatment: Scores on the GDS and ISI were considered at the baseline assessment before treatment and after receiving either the LLD-specific cognitive behavioral therapy (LLD-CBT) or the supportive unspecific intervention (SUI). Both groups underwent a structured manual-based treatment consisting of 15 sessions, conducted twice weekly over an eight-week period. Further details on the interventions have been published elsewhere [3, 39].

Multivariate and statistical analyses

Regularized canonical correlation analyses (rCCA): We applied CCA and conducted three separate analyses for the baseline, end-of-treatment, and follow-up individual scores of insomnia and depressive symptoms. CCA is a multivariate, data-driven statistical method integrating various symptoms into a single model to identify latent dimensions where specific items from both sets are maximally correlated [40]. A “canonical variate” represents the specific linear combination of variables within each set, and a pair of canonical variates constitutes a mode (Figure 1c). To interpret each mode, we computed the “canonical correlation,” which quantifies the overall strength of association between the paired canonical variates. In addition, we calculated “canonical loadings,” defined as the Pearson correlations between each original variable and its corresponding canonical variate. These loadings indicate how much each symptom contributes to shaping its domain in a way that maximizes its connection to the other domain. Symptoms with high canonical loadings play a central role in the shared relationship between the two domains, highlighting core features within each domain that are clinically relevant for understanding cross-domain interactions and informing targeted treatment strategies. We also computed “cross-loadings,” which are the correlations between each original variable and the canonical variate from the opposite set. Cross-loadings reflect how strongly a symptom from one domain (e.g., insomnia symptoms) is associated with the broader pattern of variance in another domain (e.g., depressive symptoms) (Figure 1c). Such cross-domain associations are particularly relevant in the context of

comorbid conditions such as insomnia and depression, as they can help identify bridging symptoms (i.e., symptoms that link two domains), may reflect shared underlying mechanisms, and could serve as important targets for transdiagnostic interventions.

One set of variables (domain X) represented the insomnia dimension, which consisted of scores from seven items of ISI. The other set of variables (domain Y) represented depressive symptoms, comprising scores from 26 GDS items and eight QIDS-C items (Figure 1c). Four items of the GDS (sadness, feeling downhearted, feeling without energy, not feeling clear-minded) were excluded, as they showed an extremely skewed distribution in our sample. Notably, the sleep disturbance criterion domain (which includes initial, middle, and late insomnia or hypersomnia) from the QIDS-C was excluded, as performed previously [41]. This decision was made to avoid including any sleep-related items within the depressive domain, as doing so could result in an inaccurately higher association between the two sets. Since both LLD-CBT and SUI significantly reduced depressive symptoms without evidence for the superiority of LLD-CBT in the initial trial [3, 39], all participants were pooled for the current analyses, regardless of the allocation to the treatment groups. The analyses were implemented by using the CCA/PLS Toolkit (v1.0.0, https://github.com/anaston/cca_pls_toolkit/) in MATLAB Runtime (v9.14 (R2023b)) [42]. Age, gender, and trial site were included as confounding variables in the analyses.

To address potential limitations of CCA (i.e., overfitting and multicollinearity among variables in each behavioral domain), a regularized version of CCA (rCCA) was implemented within a machine learning framework [31, 32]. A multiple hold-out framework was utilized by dividing the dataset into an 80% optimization set and a 20% hold-out set, using 100 random repetitions. This approach evaluates the model's generalizability by examining how well the associations identified in the training set can apply to an independent test set. In this process, the hold-out set was projected onto the optimal rCCA model obtained from the optimization set, aiming to estimate the canonical correlation of the hold-out set. The optimization set was further split into an 80% training set and a 20% test set through an inner split, repeated 50 times. During this inner split, optimal hyperparameters were estimated using L2 norm regularization (Figure 1d). This additional constraint forces the weights to be small but not zero. By mitigating multicollinearity, these hyperparameters help enhance the stability of the rCCA weights [43].

We further assessed the longitudinal stability and alteration of the associations across time points by testing whether pre-treatment associations persist post-treatment and whether new relationships emerge after treatment. Therefore, the end-of-treatment and follow-up data were projected onto the weights derived from the baseline rCCA model. Additionally, the baseline and follow-up data were projected onto the weights of the end-of-treatment model. The model was initially trained at the baseline, after which it was tested on the hold-out set from the baseline time point. Subsequently, the model was tested on the hold-out sets from the other two time points, and this process was repeated for the end-of-treatment model. This process was repeated for all 100 hold-out repetitions to ensure the robustness of rCCA correlation results.

Fisher's Z transformation and statistical comparisons: We used Fisher's Z transformation to compare the correlation coefficients from our rCCA analyses before and after treatment, assessing whether the treatment significantly altered the association between insomnia and depressive symptoms. First, we normalized canonical

correlation coefficients, loadings, and cross-loadings by computing their Fisher's Z scores. Using Fisher's Z-test, we then compared the canonical correlation coefficients from baseline to the end of treatment and follow-up, applying the Holm–Bonferroni correction for multiple comparisons. By comparing these coefficients, we assessed whether treatment alters the strength of the relationship between domains.

To further identify symptom-specific changes and detect treatment-sensitive or persistent symptoms, we examined shifts in canonical loadings and cross-loadings. Delta scores (Δ ; end of treatment – baseline Fisher's Z) were tested using Fisher's Z-test to detect significant changes, highlighting symptom-level interactions influenced by treatment. Changes in canonical loadings indicate which symptoms become more or less central to the part of a domain that is linked to the other. Changes in cross-loadings reveal how treatment affects the bridging symptoms. Together, these “symptom-level” changes provide clinical insight into how the structure and interaction of symptom networks evolve in response to treatment. This information could not be captured by “domain-level” canonical correlation coefficients alone.

Results

Descriptive statistics

The data set comprised 185 participants, with an average age of 69.7 years old (SD = 7.1) of whom 66% were female. Patients were recruited from seven university hospitals in Germany (Table 1).

Alteration of multivariate association between insomnia and depressive symptoms after psychotherapy

At baseline, a hold-out set correlation of $r = 0.24$ (SD = 0.13) was observed between insomnia symptoms and depressive symptoms. By the end of the treatment, this correlation slightly increased ($r = 0.42$, SD = 0.12) and remained consistently high at the six-month follow-up session ($r = 0.48$, SD = 0.12) (Figure 2a). Notably, the increase in the hold-out correlation from baseline to the end of treatment was not significant after applying the Holm–Bonferroni correction ($p_{\text{corrected}} = 0.064$). However, the increase from baseline to follow-up was significant ($p_{\text{corrected}} = 0.018$). Testing the baseline model on the post-treatment hold-out set shows a similar pattern, reflecting the stability of the identified associations (Figure 2b). Conversely, when testing the end of the treatment model on the baseline hold-out set, a decrease in the correlation can be observed, indicating new association patterns that were not present at baseline (Figure 2c).

At baseline, insomnia symptoms were positively associated with depressive symptoms, indicating that greater insomnia symptom severity was linked to more severe depressive symptoms. Higher canonical loadings were observed for general dissatisfaction with the sleep pattern ($r = 0.88$), the interference of sleep problems with daily functioning ($r = 0.82$), and difficulty staying asleep ($r = 0.81$) (Figure 3a). Higher canonical loadings were observed mainly for anxiety-related depressive symptoms, such as worrying about the future ($r = 0.52$), excessive rumination ($r = 0.46$), fear of the occurrence of future bad events ($r = 0.43$) or general feelings of restlessness ($r = 0.4$). In contrast, decreased involvement and interest in daily life ($r = -0.31$), increased hopelessness about the future ($r = -0.28$), negative mood ($r = -0.26$), psychomotor agitation or retardation ($r = -0.26$), and increased memory problems ($r = -0.22$) showed negative

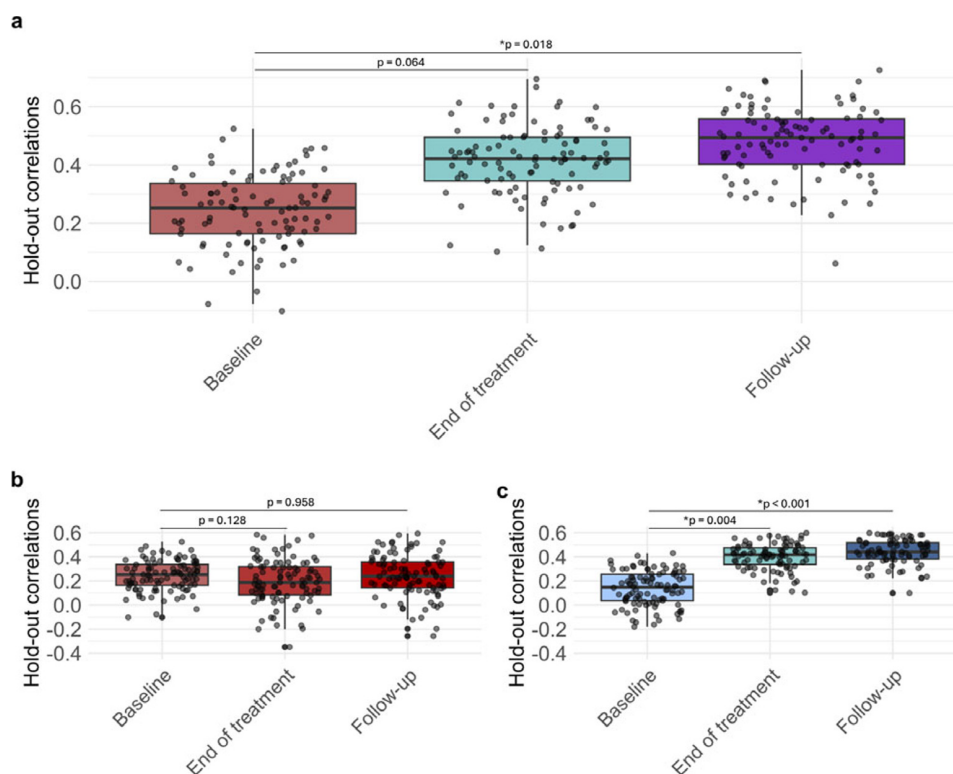


Figure 2. Hold-out correlations of each regularized canonical correlation analysis (rCCA) model: (a) rCCA model between insomnia and depressive symptoms for baseline, end-of-treatment and follow-up time points; (b) Testing the baseline rCCA model on each time point's hold-out set; (c) Testing the end-of-treatment model on each time point's hold-out set. Dots represent the hold-out correlations for each of the 100 repetitions. Black horizontal lines indicate the mean hold-out correlation coefficients. (*) Holm–Bonferroni corrected significant differences (p -value <0.05).

canonical loadings, indicating associations with less insomnia symptoms (Figure 3c).

At the end of treatment, the canonical loadings for all insomnia symptoms were positively associated with depressive symptoms. The strongest associations were observed for sleep problems being noticeable to others ($r = 0.89$), sleep problems interfering with daily functioning ($r = 0.82$), general dissatisfaction with sleep pattern ($r = 0.75$), and difficulty falling asleep ($r = 0.74$) (Figure 3b). All depressive symptoms following psychotherapy intervention showed a positive association with insomnia symptoms. The highest loadings were seen in negative affective symptoms, such as overall depressive mood ($r = 0.71$), restlessness ($r = 0.59$), perceiving life as empty ($r = 0.58$), feeling hopeless about the future ($r = 0.57$) and having a low basic life satisfaction ($r = 0.57$). Additionally, somatic symptoms, such as low energy and high fatigue, were also strongly and positively associated with insomnia symptoms ($r = 0.63$) (Figure 3d).

At follow-up, the loadings for insomnia symptoms remained consistent with the canonical loadings at the end of treatment. Similarly, all depressive symptoms at follow-up remained positively associated with insomnia symptoms (Supplementary Material).

Changes in canonical loadings and cross-loadings after psychotherapy

The canonical loadings of most depressive items changed significantly after psychotherapy compared to baseline (corrected p -values between 0.002 and 0.005) (Figure 4a). The calculated difference (delta) scores for the “canonical loadings” revealed the most significant changes in items related to reduced activities

(delta = 0.501, $p < 0.001$), interests, and involvement in daily life (delta = 0.546, $p < 0.001$), psychomotor agitation or retardation (delta = 0.54, $p < 0.001$), memory problems (delta = 0.543, $p < 0.001$), difficulty concentrating and decisiveness (delta = 0.504, $p < 0.001$) (see Figures 4a and 5 for all items). In contrast, the canonical loadings of insomnia symptoms showed no significant changes after treatment for any items (Figure 4b).

With regard to the cross-loadings of depressive symptoms (as the association with the insomnia canonical variate), significant changes after psychotherapy were observed for lower energy and higher fatigue (delta = 0.429, $p = 0.001$), decrease in involvement and interests (delta = 0.41, $p = 0.003$), increased negative mood (delta = 0.368, $p = 0.015$), increased depressive mood (delta = 0.363, $p = 0.018$), and avoiding social gatherings (delta = 0.334, $p = 0.049$) (Figure 4c). Conversely, the cross-loadings of insomnia symptoms (as the association with the depressive symptoms canonical variate) did not show any significant changes (Figure 4d), which emphasized that the insomnia symptoms pattern remained stable and independent from changes in depressive symptoms following CBT/SUI psychotherapy.

Discussion

In the present study, we found a moderate association between insomnia and depressive symptoms at baseline, providing further evidence of their bidirectional relationship in LLD. This association increased at the end of treatment and at the six-month follow-up. Interestingly, while we observed improvement in depressive symptoms, insomnia symptoms did not change after psychotherapy. We observed a trend of increasing multivariate associations between

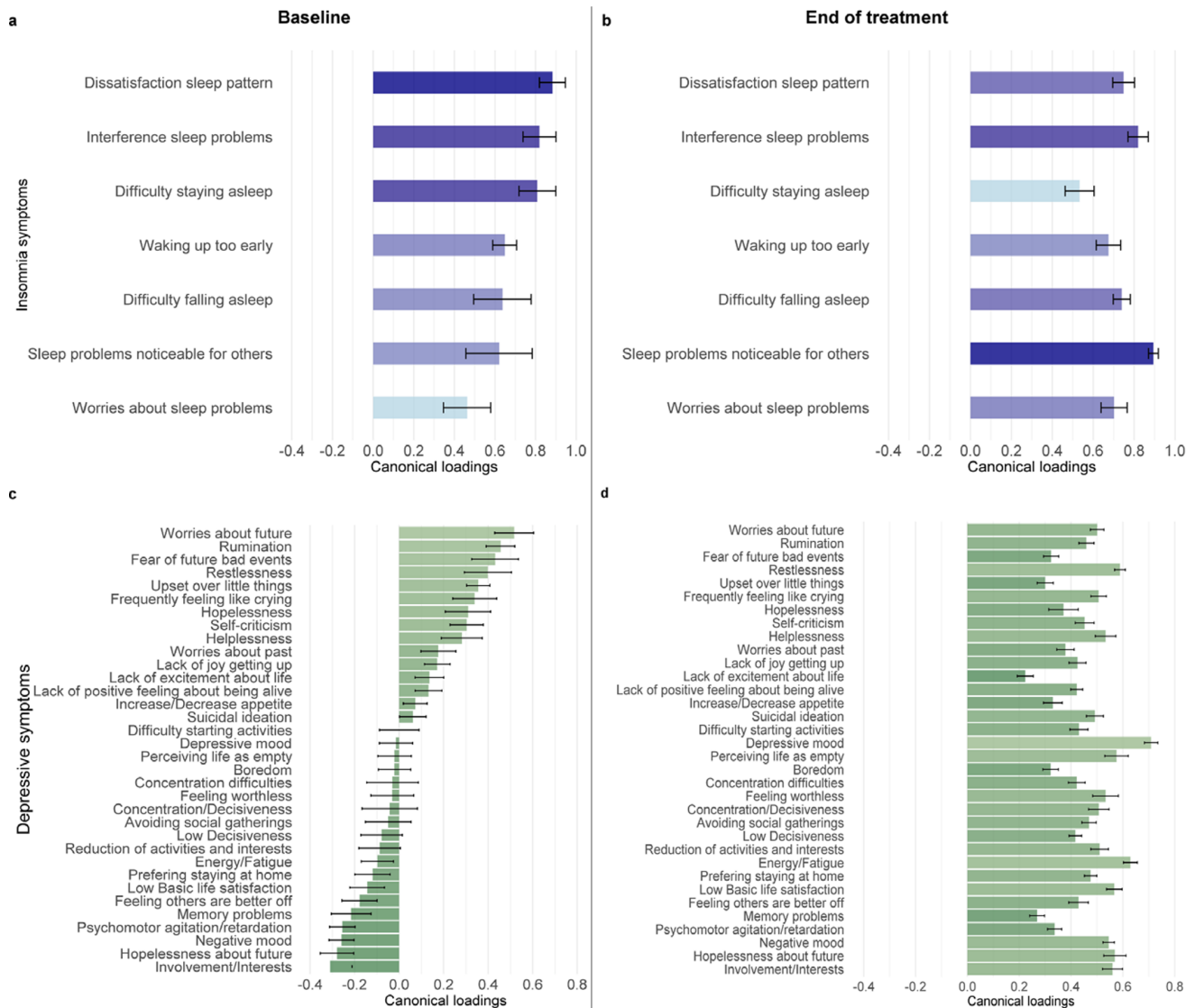


Figure 3. Canonical loadings before and after psychotherapeutic treatment: (a) Canonical loadings of insomnia symptoms at baseline; (b) Canonical loadings of insomnia symptoms at the end of treatment; (c) Canonical loadings of depressive symptoms at baseline; (d) Canonical loadings of depressive symptoms at the end of treatment. Canonical loadings correspond to Pearson correlations between the input variables and the canonical variates. Negative loadings of depressive symptoms indicate more insomnia symptoms, and less depressive symptoms, while positive loadings indicate more insomnia symptoms and more depressive symptoms. Black lines represent error bars (one standard deviation below or above the mean).

insomnia and depressive symptoms after psychotherapy. Additionally, by projecting the end of the treatment model onto the baseline test set, we observed a decrease in the observed correlation, highlighting the emergence of new or increased patterns of association after psychotherapy that could not be captured by the baseline model. Since the applied interventions primarily addressed depressive symptoms rather than insomnia, unresolved sleep problems could have exacerbated specific depressive symptoms, thereby strengthening their interrelationship. Of note, changes between the baseline and the end of the treatment model were not significant after correction for multiple comparisons, probably due to our small sample size and high data variability. However, changes between the baseline and the follow-up sessions were significant. Several existing studies performed CCA analyses to identify biotypes of depression using the brain's functional connectivity data in patients with MDD [44–46]. Some studies also applied CCA analysis between depression and anxiety symptoms among college

students [47] or between sleep quality, depressive symptoms, brain structure, and motor performance in the general population samples [31]. However, to the best of our knowledge, no existing study has assessed the role of psychotherapy intervention on the interplay between insomnia and depressive symptoms in LLD using such multivariate analysis.

It has been shown that pharmacotherapy treatment and commonly used psychotherapy interventions alleviate certain types of depressive symptoms but fail to fully resolve insomnia symptoms in depressed patients [48, 49]. For example, clusters of negative emotional and cognitive bias and neurovegetative symptoms remained after 6 weeks of antidepressant treatment in patients with MDD [48]. These residual insomnia symptoms increase vulnerability to depressive relapse (in the same episode) or recurrence (in the new episode) and a lower likelihood for patients to have full benefit from treatment [50, 51]. Residual insomnia symptoms are then often overlooked or treated with hypnotic medications or particular

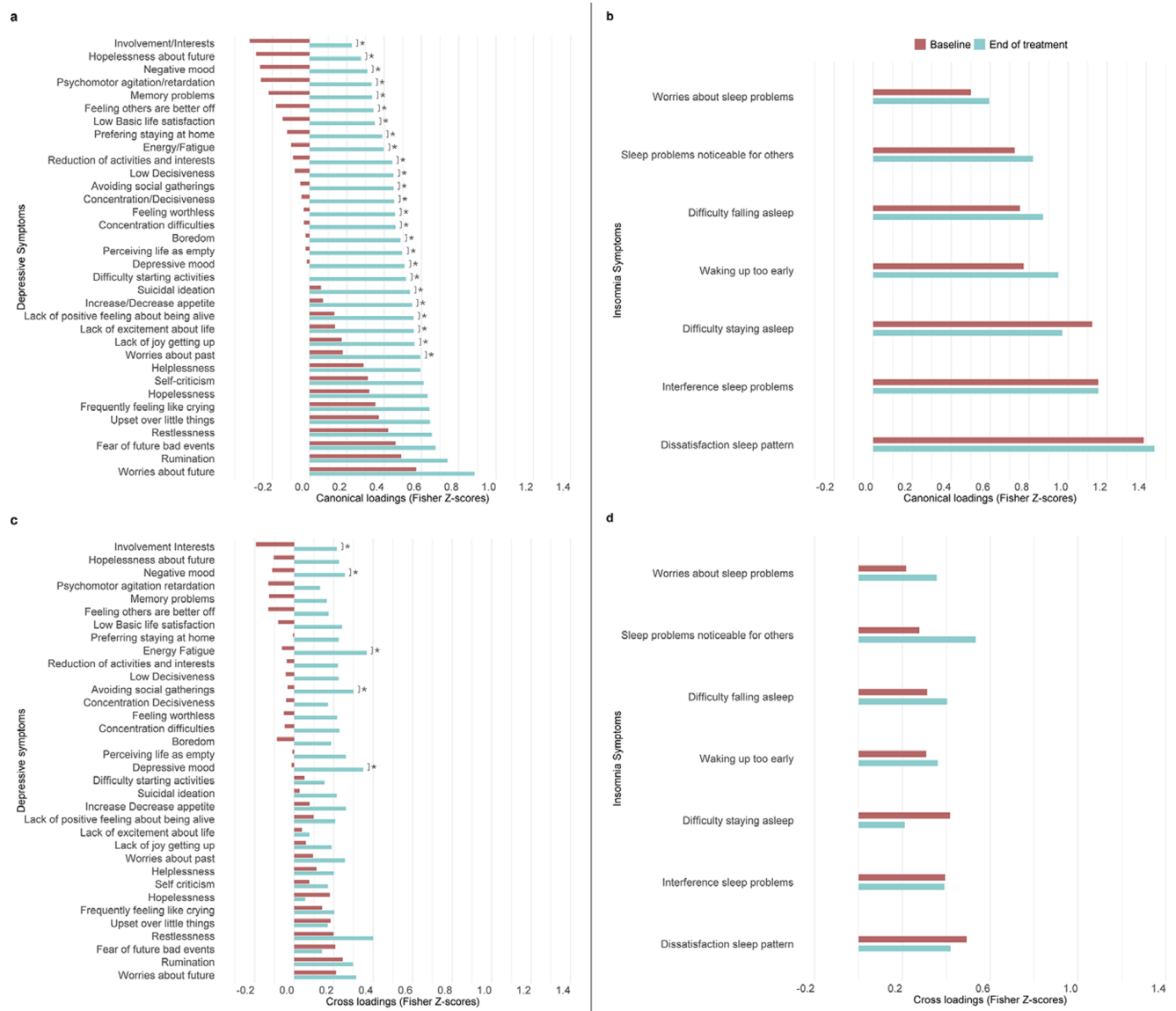


Figure 4. Changes in canonical loadings and cross-loadings before and after psychotherapeutic treatment: (a) Fisher z-scores of canonical loadings at baseline and after treatment for depressive symptoms; (b) Fisher z-scores of canonical loadings at baseline and after treatment for insomnia symptoms; (c) Fisher z-scores of cross-loadings at baseline and after treatment for depressive symptoms; (d) Fisher z-scores of cross-loadings at baseline and after treatment for insomnia symptoms. (*) Holm–Bonferroni corrected significant differences between time points (p -value <0.05).

antidepressants despite the risks of side effects (e.g., daytime impairment, amnesia, falling down, and dependency), particularly in older adults, who are nearly five times more likely to receive prescriptions of medications than younger individuals [52–54]. Given these concerns, a non-pharmacological approach, such as cognitive behavioral therapy for insomnia (CBT-I)—which includes cognitive therapy, stimulus control, sleep restriction, sleep hygiene, and relaxation techniques—may be an additional and effective first-line treatment and could be integrated into clinical practice for older adults with LLD to prevent residual insomnia [21, 55]. CBT-I is suggested as an early effective intervention not only for insomnia disorder but also in mood disorders [56]. The stable association observed between insomnia and depressive symptoms after a six-month follow-up in the present study suggests a persistent relationship and symptoms’ interaction pattern. Interestingly, a study based on the Growth Mixture Modeling in patients with MDD demonstrated that

characteristics of insomnia can predict long-term depression outcomes. In particular, patients with lower insomnia severity were the optimal responders to psychotherapy and exhibited more favorable treatment responses, even at a two-year follow-up, compared to patients with higher insomnia severity [57]. These findings support the need to consider careful management of insomnia symptoms during the treatment of clinical depression.

At baseline, our canonical loadings indicated a positive relationship between insomnia symptoms and anxiety-related depressive symptoms, particularly excessive worry, rumination, and feelings of restlessness (Figure 4a). Excessive uncontrollable worry, rumination, emotion dysregulation, and intrusive thoughts have been associated with increased insomnia symptoms in previous studies due to hyperarousal conditions [58–61], also for older patients [62]. In this study, after psychotherapy and at follow-up, this association shifted, with insomnia symptoms becoming more

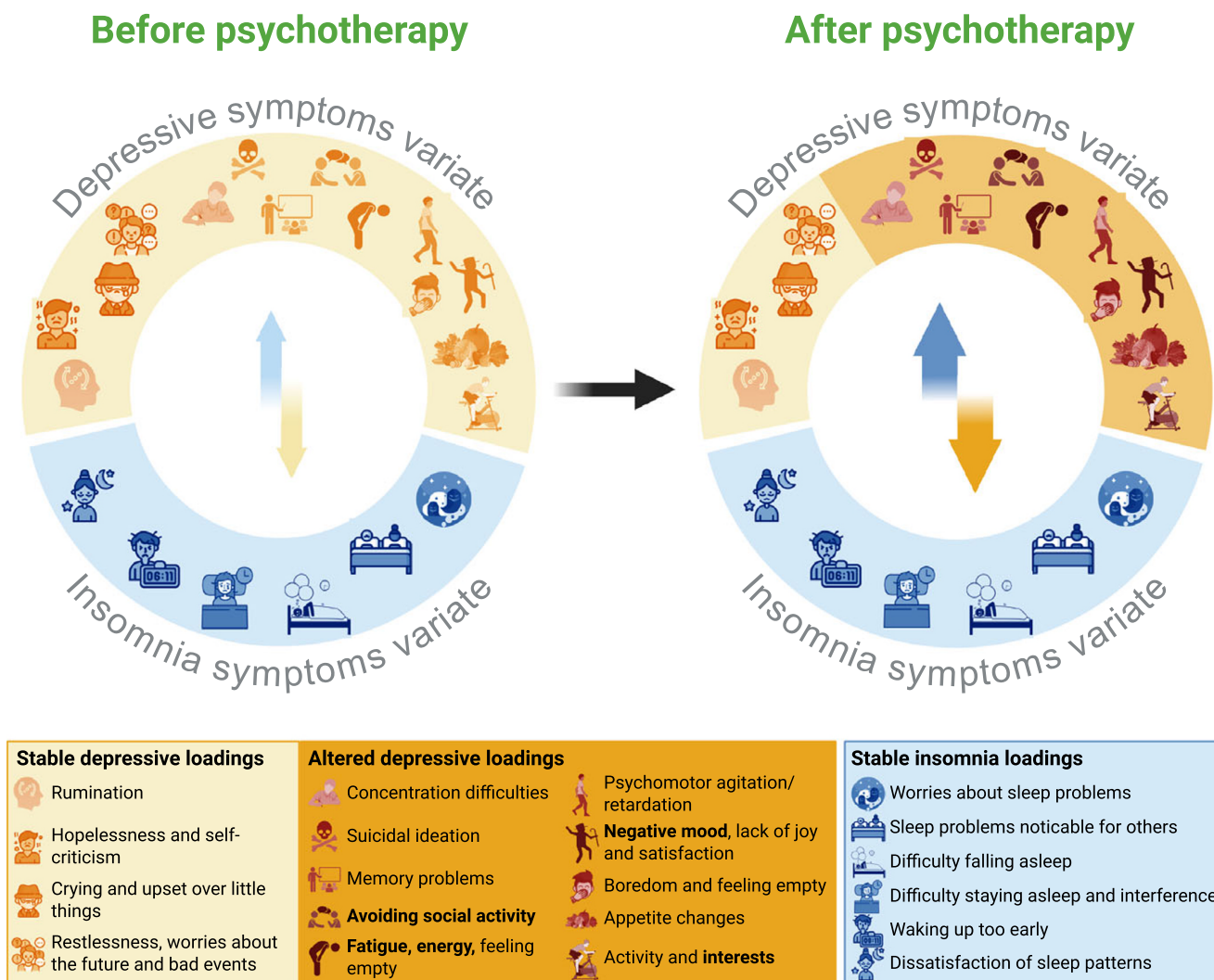


Figure 5. Schematic representation of canonical loadings and cross-loadings shifts in the multivariate association between depressive symptoms and insomnia symptoms following psychotherapeutic intervention: Some insomnia-related depressive symptom loadings altered after treatment (dark orange – canonical loadings; bold names in legend – canonical cross-loadings) based on Holm-Bonferroni corrected significant differences between time points (p -value <0.05), while the others remained stable (light orange). Interestingly, depressive-related insomnia items remained fully unchanged. The thickness of the two-sided arrow shows the multivariate association between insomnia and depressive symptoms before ($r = 0.24$) and after ($r = 0.42$) treatment. This figure was created with Biorender.com.

strongly linked to negative affective symptoms, such as low mood, negative outlook, and reduced life satisfaction, as well as somatic symptoms, including low energy and heightened fatigue (Figure 4). Figure 5 provides a schematic representation of significant shifts in the association of canonical loadings. This further suggests that while CBT/SUI treatment may have focused more on cognitive aspects, sleep-related and somatic symptoms remained unchanged, contributing to persistent negative mood. It has been shown that older MDD patients with insomnia, compared to those without sleep problems, were more likely to experience somatic symptoms such as low energy, which were, in turn, associated with persistent negative affect [63].

Individuals with the same severity of depression can exhibit substantial differences in how their symptoms interact [64]. A novel “person-specific symptom network” model suggests that examining individual symptom relationships could help identify maladaptive patterns, enabling personalized treatment approaches to weaken these persistent associations [65]. We observed that psychomotor

agitation or retardation, memory and concentration difficulties, and decreased engagement in daily activities were negatively associated with insomnia at baseline but became positively linked by the end of treatment and follow-up. Items such as decreased involvement and interests and somatic symptoms such as higher fatigue showed the highest cross-loading delta scores, reflecting significant shifts in their relationship with insomnia over time (Figure 4c-d). Psychomotor agitation has been linked to depression in older adults, often alongside increased insomnia symptoms [66]. Agitated depression may represent a distinct LLD subtype, where heightened agitation initially masks perceived sleep difficulties, explaining the negative correlation at baseline. After therapy, patients may have gained a greater awareness of their sleep disturbances, leading to the observed change in the association. Current models of insomnia emphasize its role in hyperarousal driven by central and peripheral activation of the stress system and its involvement in GABAergic transmission [67]. This dysregulation may contribute to symptoms such as psychomotor agitation or retardation.

Recognizing our limitations can guide future research to strengthen and expand our findings. For example, recall/response bias is common in self-report questionnaires. Moreover, psychotherapy may enhance introspection and self-awareness, enabling patients to better recognize the connection between sleep disturbances and depressive symptoms, making this relationship more apparent after the treatment [68]. In addition to psychotherapy, 38% of our patients were also receiving antidepressant medication. However, their pharmacological treatment was required to remain stable before and throughout the intervention. A supplementary analysis including the use of psychotropic medication as an additional confound showed no significant difference in the results (see [Supplementary Figure S2, S3](#)). Moreover, while individual depressive symptoms showed varying canonical loadings, all depressive symptoms exhibited high loadings post-treatment and at follow-up. Notably, individuals with mood disorders often report excessive sleep disturbances and poor sleep quality, though objective measures like polysomnography may show different results [69, 70]. This study relied solely on the ISI scale, which focuses on insomnia; incorporating additional subjective and objective sleep measures, such as sleep duration and efficiency, could provide a more comprehensive assessment on the sleep-depression relationship. Future research should also compare different treatment modalities, particularly LLD-CBT, versus insomnia-specific interventions (e.g., CBT-I). Neuroimaging data could further reveal underlying neurobiological substrates of interventions. Patients in this study received either LLD-CBT or SUI, but separate rCCA models for each group were not statistically valid due to sample size limitations. Larger datasets are needed to confirm these findings and perform clustering approaches based on the link between sleep and depression, as suggested recently [71, 72].

In conclusion, this study demonstrated increased multivariate association between insomnia and depressive symptoms in LLD patients following psychotherapy, alongside a shift in the pattern of depressive symptoms, while insomnia symptoms remained unchanged. These findings emphasize the need to consider their relationship when assessing treatment effects. Furthermore, the findings underscore the value of multivariate approaches in examining symptom interactions, ultimately aiming to enhance clinical treatment.

Supplementary material. The supplementary material for this article can be found at <http://doi.org/10.1192/j.eurpsy.2025.10088>.

Data availability statement. The data supporting this study's findings are not publicly available due to ethics restrictions but are available from Dr. Forugh Salimi Dafsari upon reasonable request with individual permission from the local institutions' ethics board. The preprint of this work is online in medRxiv (<https://doi.org/10.1101/2025.03.28.25324836>).

Acknowledgements. The authors would like to thank all participating patients, therapists, and outcome evaluators who participated in the study.

Author contribution. Conception and study design: R.H., V.K., F.D., and M.T.; Preprocessing and data analysis: R.H., V.K., F.S.; Interpretation F.S., F.D., D.R., S.B.E., F.J., and M.T. Paper writing and editing: all authors.

Financial support. The initial randomized controlled trial was funded by grant BMBF 01KG1716 from the German Federal Ministry of Education and Research (BMBF). V.K. is supported by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) - Project-ID 431549029 - SFB 1451. The current analyses received no specific grant from any funding agency, commercial or not-for-profit sectors.

Competing interests. The authors declare no conflict of interest.

References

- [1] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. 2013. <https://doi.org/10.1176/appi.books.9780890425596>.
- [2] Andreas S, Schulz H, Volkert J, Dehoust M, Sehner S, Suling A, et al. Prevalence of mental disorders in elderly people: the European MentDis_ICF65+ study. *Br J Psychiatry*. 2017;210(2):125–31. <https://doi.org/10.1192/bjp.bp.115.180463>
- [3] Dafsari FS, Bewernick B, Böhringer S, Domschke K, Elsaesser M, Löbner M, et al. Cognitive behavioral therapy for late-life depression (CBTlate): results of a multicenter, randomized, observer-blinded, controlled trial. *Psychother Psychosom*. 2023;92(3):180–92. <https://doi.org/10.1159/000529445>
- [4] Choi NG, Kim J, Marti CN, Chen GJ. Late-life depression and cardiovascular disease burden: Examination of reciprocal relationship. *Psychiatry*. 2014;22(12):1522–9. <https://doi.org/10.1016/j.jagp.2014.04.004>
- [5] Ding OJ, Kennedy GJ. Understanding vulnerability to late-life suicide. *Geriatr Disord*. 2021;23(9):58. <https://doi.org/10.1007/s11920-021-01268-2>.
- [6] Jamieson A, Goodwill AM, Termine M, Campbell S, Szoeko C. Depression-related cerebral pathology and its relationship with cognitive functioning: a systematic review. *J Affect Disord*. 2019;250:410–8. <https://doi.org/10.1016/j.jad.2019.03.042>
- [7] Koenig AM, Bhalla RK, Butters MA. Cognitive functioning and late-life depression. *J Int Neuropsychol Soc*. 2014;20(5):461–7. <https://doi.org/10.1017/S1355617714000198>
- [8] Van den Berg KS, Wiersema C, Hegeman JH, van den Brink RHS, Rhebergen D, Merijnissen RM, et al. Clinical characteristics of late-life depression predicting mortality. *Aging Ment Health*. 2016;25(3):476–83. <https://doi.org/10.1080/13607863.2019.1699900>
- [9] Schaakxs R, Comijs HC, Lamers F, Beekman ATF, Penninx BWJH. Age-related variability in the presentation of symptoms of major depressive disorder. *Psychol Med*. 2016;47(3):543–52. <https://doi.org/10.1017/S0033291716002579>
- [10] Schaakxs R, Comijs HC, Lamers F, Kok RM, Beekman ATF, Penninx BWJH. Associations between age and the course of major depressive disorder: a 2-year longitudinal cohort study. *Lancet Psychiatry*. 2018; 5(7):581–90. [https://doi.org/10.1016/s2215-0366\(18\)30166-4](https://doi.org/10.1016/s2215-0366(18)30166-4)
- [11] Bagherzadeh-Azbari S, Khazaie H, Zarei M, Spiegelhalter K, Walter M, Leerssen J, et al. Neuroimaging insights into the link between depression and insomnia: a systematic review. *J Affect Disord*. 2019;258:133–43. <https://doi.org/10.1016/j.jad.2019.07.089>
- [12] Huang L, Xi Y, Peng Y, Yang Y, Huang X, Fu Y, et al. A visual circuit related to habenula underlies the antidepressive effect of light therapy. *Neuron*. 2019;102:128–42. <https://doi.org/10.1016/j.neuron.2019.01.037>
- [13] Peng C, Wang K, Wang J, Wassing R, Eickhoff SB, Tahmasian M, et al. Neural correlates of insomnia with depression and anxiety from a neuroimaging perspective: a systematic review. *Sleep Med Rev*. 2025;e:102093. <https://doi.org/10.1016/j.smrv.2025.102093>.
- [14] Riemann D, Krone LB, Wulff K, Nissen C. Sleep, insomnia and depression. *Neuropsychopharmacology*. 2020;45(1):74–89. <https://doi.org/10.1038/s41386-019-0411-y>.
- [15] Wang Y, Tian Y, Long Z, Dong D, He Q, Qiu J, et al. Volume of the dentate gyrus/CA4 hippocampal subfield mediates the interplay between sleep quality and depressive symptoms. *Int J Clin Health Psychol*. 2024;24(1): 100432. <https://doi.org/10.1016/j.ijchp.2023.100432>.
- [16] Hertenstein E, Benz F, Schneider CL, Baglioni C. Insomnia—a risk factor for mental disorders. *J Sleep Res*. 2023;32(6):e13930 <https://doi.org/10.1111/jsr.13930>.
- [17] Li Y, Wu Y, Zhai L, Wang T, Sun Y, Zhang D. Longitudinal association of sleep duration with depressive symptoms among middle-aged and older Chinese. *Sci Rep*. 2017;7:11794. <https://doi.org/10.1038/s41598-017-12182-0>.
- [18] Yokoyama E, Kaneita Y, Saito Y, Uchiyama M, Matsuzaki Y, Tamaki T, et al. Association between depression and insomnia subtypes: a longitudinal study on the elderly in Japan. *Sleep*. 2010;33(12):1693–702. <https://doi.org/10.1093/sleep/33.12.1693>
- [19] Pandi-Perumal SN, Monti JM, Burman D, Karthikeyan R, BaHammam AS, Spence DW, et al. Clarifying the role of sleep in depression: a narrative review. *Psychiatry Res*. 2020;291:113239 <https://doi.org/10.1016/j.psychres.2020.113239>.

- [20] Patel DP, Steinberg J, Patel P. Insomnia in the elderly: Aareview. *J Clin Sleep Med*. 2018;14(6):1017–24. <https://doi.org/10.5664/jcsm.7172>
- [21] Irwin MR, Carrillo C, Sadeghi N, Bjurstrom MF, Breen EC, Olmstead R. Prevention of incident and recurrent major depression in older adults with insomnia: a randomized clinical trial. *JAMA Psychiatry*. 2021;79(1):33–41. <https://doi.org/10.1001/jamapsychiatry.2021.3422>.
- [22] Bao Y, Han Y, Ma J, Wang R, Shi L, Wang T, et al. Co-occurrence and bidirectional prediction of sleep disturbances and depression in older adults: meta-analysis and systematic review. *Neurosci Biobehav Rev*. 2017;75:257–73. <https://doi.org/10.1016/j.neubiorev.2017.01.032>
- [23] Inada K, Enomoto M, Yamato K, Marumoto T, Takeshima M, Mishima K. Effect of residual insomnia and use of hypnotics on relapse of depression: a retrospective cohort study using a health insurance claims database. *J Affect Disord*. 2021;281:539–46. <https://doi.org/10.1016/j.jad.2020.12.040>
- [24] McCall WN, Blocker JN, D'Agostino R, Kimball J, Boggs N, Lasater B, et al. Insomnia severity is an indicator of suicidal ideation during a depression clinical trial. *Sleep Med*. 2010;11(9):822–7. <https://doi.org/10.1016/j.sleep.2010.04.004>
- [25] Wang X, Cheng S, Xu H. Systematic review and meta-analysis of the relationship between sleep disorders and suicidal behaviour in patients with depression. *BMC Psychiatry*. 2019;19:303. <https://doi.org/10.1186/s12888-019-2302-5>.
- [26] Gebara MA, Kasckow J, Smagula SF, DiNapoli EA, Karp JF, Lenze EJ, et al. The role of late-life depressive symptoms on the trajectories of insomnia symptoms during antidepressant treatment. *J Psychiatr Res*. 2018;96:162–6. <https://doi.org/10.1016/j.jpsychires.2017.10.013>
- [27] Pigeon WR, Hegel M, Ünützer J, Fan MY, Sateia MJ, Lyness JM et al. Is insomnia a perpetuating factor for late-life depression in the IMPACT cohort? *Sleep*. 2008;31(4):481–8. <https://doi.org/10.1093/sleep/31.4.481>
- [28] Ji M, Sun Y, Zhou J, Li X, Wei H, Wang Z. Comparative effectiveness and acceptability of psychotherapies for late-life depression: a systematic review and network meta-analysis. *J Affect Disord*. 2023;323:409–16. <https://doi.org/10.1016/j.jad.2022.11.089>
- [29] Kok RM, Reynolds CF. Management of depression in older adults: a review. *JAMA*. 2017;317(20):2114–22. <https://doi.org/10.1001/jama.2017.5706>
- [30] Nelson CJ. Management of late-life depression. In: Macaluso M, Preskorn S, eds. *Antidepressants*. Handbook of experimental pharmacology. Vol. 250. Cham: Springer; 2018, pp. 39–47. https://doi.org/10.1007/164_2018_170.
- [31] Küppers V, Bi H, Nicolaisen-Sobesky E, Hoffstaedter F, Yeo BTT, Drzezga A, et al. Lower motor performance is linked with poor sleep quality, depressive symptoms, and grey matter volume alterations. [Preprint]. *BioRxiv*. 2024. <https://doi.org/10.1101/2024.06.07.597666>
- [32] Nicolaisen-Sobesky E, Mihalik A, Kharabian-Masouleh S, Ferreira FS, Hoffstaedter F, Schwender H, et al. A cross-cohort replicable and heritable latent dimension linking behaviour to multi-featured brain structure. *Commun Biol*. 2022;5(1):1297. <https://doi.org/10.1038/s42003-022-04244-5>.
- [33] Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey MB, et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res*. 1983;17:37–49. [https://doi.org/10.1016/0022-3956\(82\)90033-4](https://doi.org/10.1016/0022-3956(82)90033-4).
- [34] Gauggel S, Birkner B. Validität und Reliabilität einer deutschen Version der Geriatrischen Depressionsskala (GDS). *Klin Psychol Psychother*. 1999;28(1): <https://doi.org/10.1026//0084-5345.28.1.18>.
- [35] Rush AJ, Trivedi MH, Ibrahim HM, Carmody TJ, Arnow B, Klein DN, et al. The 16-item quick inventory of depressive symptomatology (QIDS), clinician rating (QIDS-C), and self-report (QIDS-SR): a psychometric evaluation in patients with chronic major depression. *Biol Psychiatry*. 2003;54(5):573–83. [https://doi.org/10.1016/s0006-3223\(02\)01866-8](https://doi.org/10.1016/s0006-3223(02)01866-8)
- [36] Roniger A, Spaeth C, Schweiger U, Klein JP. A psychometric evaluation of the German version of the quick inventory of depressive symptomatology (QIDS-SR16) in outpatients with depression. *Fortschr Neurol Psychiatr*. 2015;83(12):17–22. <https://doi.org/10.1055/s-0041-110203>.
- [37] Bastien CH, Vallieres A, Morin CM. Validation of the insomnia severity index as an outcome measure for insomnia research. *Sleep Med*. 2001;2: 297–307. [https://doi.org/10.1016/s1389-9457\(00\)00065-4](https://doi.org/10.1016/s1389-9457(00)00065-4).
- [38] Gerber M, Lang C, Lemola S, Colledge F, Kalak N, Holsboer-Trachsler E, et al. Validation of the German version of the insomnia severity index in adolescents, young adults and adult workers: results from three cross-sectional studies. *BMC Psychiatry*. 2016;16:174. <https://doi.org/10.1186/s12888-016-0876-8>.
- [39] Dafsari FS, Bewernick B, Biewer M, Christ H, Domschke K, Froelich L, et al. Cognitive behavioural therapy for the treatment of late-life depression: study protocol of a multicentre, randomized, observer-blinded, controlled trial (CBTlate). *BMC Psychiatry*. 2019;19(1):423. <https://doi.org/10.1186/s12888-019-2412-0>.
- [40] Hotelling H. Relations between two sets of variates. *Biometrika*. 1936; 28(3/4):321. <https://doi.org/10.2307/2333955>.
- [41] Olfati M, Samea F, Faghihroohi S, Balajoo SM, Küppers V, Genon S, et al. Prediction of depressive symptoms severity based on sleep quality, anxiety, and gray matter volume: a generalizable machine learning approach across three datasets. *EBioMedicine*. 2024;108:105313. <https://doi.org/10.1016/j.ebiom.2024.105313>.
- [42] The MathWorks Inc. MATLAB version: 9.14.0 (R2023a). Natick: The MathWorks Inc. <https://www.mathworks.com>.
- [43] Mihalik A, Chapman J, Adams RA, Winter NR, Ferreira FS, Shawe-Taylor J, et al. Canonical correlation analysis and partial least squares for identifying brain-behavior associations: a tutorial and a comparative study. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2022;7(11):1055–67. <https://doi.org/10.1016/j.bpsc.2022.07.012>
- [44] Drysdale A, Grosenick L, Downar J, et al. Resting-state connectivity biomarkers define neurophysiological subtypes of depression. *Nat Med*. 2017;23:28–38. <https://doi.org/10.1038/nm.4246>.
- [45] Mihalik A, Adams RA, Huys Q. Canonical correlation analysis for identifying biotypes of depression. *Bio Psych*. 2020;5(5):478–80. <https://doi.org/10.1016/j.bpsc.2020.02.002>
- [46] Dinga R, Schmaal L, Marquand AF. A closer look at depression biotypes: Correspondence relating to Grosenick (2019). *Bio Psych*. 2020;5(5):554–5. <https://doi.org/10.1016/j.bpsc.2019.09.011>
- [47] Li L, Wang P, Li S, et al. Canonical correlation analysis of depression and anxiety symptoms among college students and their relationship with physical activity. *Sci Rep*. 2023;13:e11516. <https://doi.org/10.1038/s41598-023-38682-w>.
- [48] Danon M, Poupon D, Courtet P, Gorwood P. Clustering and drivers of symptoms observed at week six after antidepressant treatment in depressed outpatients. *Eur Psychiatry*. 2025;67(1):e85 <https://doi.org/10.1192/j.eurpsy.2024.1801>.
- [49] Staner L. Comorbidity of insomnia and depression. *Sleep Med Rev*. 2010; 14(1):35–46. <https://doi.org/10.1016/j.smrv.2009.09.003>.
- [50] Kwasny A, Włodarczyk A, Dywel A, Szarmach J, Strandberg O, Cubala WJ. Residual insomnia in major depressive disorder: a systematic review. *Front Psych*. 2023;14. <https://doi.org/10.3389/fpsy.2023.1190415>.
- [51] Lustberg L, Reynolds CF. Depression and insomnia: questions of cause and effect. *Sleep Med Rev*. 2000;4(3):253–62. <https://doi.org/10.1053/smr.1999.0075>
- [52] Abad VC, Guilleminault C. Insomnia in elderly patients: recommendations for pharmacological management. *Drugs Aging*. 2018;35(9):791–817. <https://doi.org/10.1007/s40266-018-0569-8>.
- [53] Nguyen V, George T, Brewster GS. Insomnia in older adults. *Curr Geriatr Rep*. 2019;8:271–90. <https://doi.org/10.1007/s13670-019-00300-x>
- [54] Hauglund NL, Andersen M, Tokarska K, Radovanovic T, Kjaerby C, Sorensen FL, et al. Norepinephrine-mediated slow vasomotion drives glymphatic clearance during sleep. *Cell*. 2025;188(3):606–22.e17. <https://doi.org/10.1016/j.cell.2024.11.027>
- [55] Riemann D, Espie CA, Altena ES, Arnardottir ES, Baglioni C, Bassetti CLA, et al. The European insomnia guideline: an update on the diagnosis and treatment of insomnia. *J Sleep Res*. 2023;32(6):e14035. <https://doi.org/10.1111/jsr.14035>.
- [56] Palagini L, Aquino G, Alfi G, Massoni L, Gambini M, Miniati M, et al. CBT-I for prevention and early intervention in mental disturbances: a systematic review and meta-analysis. *Sleep Med*. 2024;124:650–8. <https://doi.org/10.1016/j.sleep.2024.10.033>
- [57] Bei B, Asarnow LD, Krystal A, Edinger JD, Buysse DJ, Manber R. Treating insomnia in depression: insomnia-related factors predict long-term depression trajectories. *J Consult Clin Psychol*. 2018;86(3):282–93. <https://doi.org/10.1037/ccp0000282>

- [58] Kirwan M, Pickett SM, Jarrett NL. Emotion regulation as a moderator between anxiety symptoms and insomnia symptom severity. *Psychiatry Res.* 2017;254:40–7. <https://doi.org/10.1016/j.psychres.2017.04.028>.
- [59] Meneo D, Samea F, Tahmasian M, Baglioni C. The emotional component of insomnia disorder: a focus on emotion regulation and affect dynamics in relation to sleep quality and insomnia. *J Sleep Res.* 2023;32(6):e13983 <https://doi.org/10.1111/jsr.13983>.
- [60] Ong JC, Ulmer CS, Manber R. Improving sleep with mindfulness and acceptance: a metacognitive model of insomnia. *Behav Res Ther.* 2012; 50(11):651–60. <https://doi.org/10.1016/j.brat.2012.08.001>.
- [61] Samea F, Mortazavi N, Reimann GM, Ebneabbasi A, Zarei M, Khazaie H, et al. Insomnia and emotion dysregulation: a meta-analytical perspective integrating regulatory strategies and dispositional difficulties. *Sleep Med Rev.* 2025;e:102111. <https://doi.org/10.1016/j.smrv.2025.102111>.
- [62] Zhou Z, Birditt KS, Leger KA, Fingerhann KL. Daily worry, rumination, and sleep in late life. *J Psychosom Res.* 2024;179:111622. <https://doi.org/10.1016/j.jpsychores.2024.111622>.
- [63] Zhao J, Liu H, Wu Z, Wang Y, Cao T, Lyu D, et al. Clinical features of the patients with major depressive disorder co-occurring insomnia and hypersomnia symptoms: a report of NSSD study. *Sleep Med.* 2021;81:375–81. <https://doi.org/10.1016/j.sleep.2021.03.005>.
- [64] Ebrahimi OV, Borsboom D, Hoekstra RHA, Epskamp S, Ostinelli EG, Bastiaansen JA, et al. Towards precision in the diagnostic profiling of patients: leveraging symptom dynamics as a clinical characterisation dimension in the assessment of major depressive disorder. *Br J Psychiatry.* 2024; 224(5):157–63. <https://doi.org/10.1192/bjp.2024.19>.
- [65] Schumacher L, Klein JP, Hautzinger M, Härter M, Schramm E, Kriston L. Predicting the outcome of psychotherapy for chronic depression by person-specific symptom networks. *World Psychiatry.* 2024;23(3):411–20. <https://doi.org/10.1002/wps.21241>.
- [66] Olgiati P, Serretti A, Colombo C. Retrospective analysis of psychomotor agitation, hypomanic symptoms, and suicidal ideation in unipolar depression. *Depress Anxiety.* 2006;23(7):389–97. <https://doi.org/10.1002/da.20191>.
- [67] Palagini L, Bianchini C. Pharmacotherapeutic management of insomnia and effects on sleep processes, neural plasticity, and brain systems modulating stress: a narrative review. *Front Neurosci.* 2022;16:893015. <https://doi.org/10.3389/fnins.2022.893015>.
- [68] Wampold BE. How important are the common factors in psychotherapy? An update. *World Psychiatry.* 2015;14(3):270–7. <https://doi.org/10.1002/wps.20238>.
- [69] Rumble ME, White KH, Benca RM. Sleep disturbances in mood disorders. *Psychiatr Clin.* 2015;38(4):743–59. <https://doi.org/10.1016/j.psc.2015.07.006>.
- [70] Scarlett S, Nolan HN, Kenny RA, O'Connell MDL. Discrepancies in self-reported and actigraphy-based sleep duration are associated with self-reported insomnia symptoms in community-dwelling older adults. *Sleep Health.* 2021;7(1):83–92. <https://doi.org/10.1016/j.sleh.2020.06.003>.
- [71] Solomonov N, Lee J, Banerjee S, Chen SZ, Sirey JA, Gunning FM, et al. MD1 course of subtypes of late-life depression identified by bipartite network analysis during psychosocial interventions. *JAMA Psychiatry.* 2023;80(6):621–9. <https://doi.org/10.1001/jamapsychiatry.2023.0815>.
- [72] Tozzi L, Zhang X, Pines A, Olmsted AM, Zhai ES, Anene ET, et al. Personalized brain circuit scores identify clinically distinct biotypes in depression and anxiety. *Nat Med.* 2024;30:2076–87. <https://doi.org/10.1038/s41591-024-03057-9>.