BMC Neurology

SYSTEMATIC REVIEW Open Access

Cognitive behavioral therapy approaches to the improvement of mental health in Parkinson's disease patients: a systematic review and meta-analysis

Xiaoke Wu[1†], Mengmeng Shi[2†], Yajun Lian[1*] and Haifeng Zhang[1*]

Abstract

Background Non-motor symptoms (NMS) such as impaired cognition, anxiety, and depression can have a strong adverse effect on the quality of life (QoL) of Parkinson's disease (PD) patients. The clinical application of cognitive behavioral therapy (CBT) offers an opportunity to improve cognitive function, mental health, and overall QoL for these patients.

Objective CBT is frequently applied as a treatment option aimed at benefiting the mental health of PD patients, but the relative utility of CBT in this patient population has yet to be rigorously assessed. The present review was thus conducted with the goal of examining the relative safety and efficacy of CBT as a treatment option for PD patients suffering from cognitive impairment, anxiety, and depression, with a particular focus on the impact of CBT on PD patient QoL.

Methods The PubMed, Embase, Medline, and Cochrane Library databases were searched for all studies published from their inception to present using keywords including "cognitive behavioral therapy" and "Parkinson's disease". Two reviewers independently screened these published studies and extracted relevant data from studies that met with defined inclusion/exclusion criteria, in addition to assessing the risk of bias. Those randomized controlled trials (RCTs) assessing the impact of CBT on older PD patients were eligible for study inclusion. In total, 22 articles incorporating 1,053 patients were included in this meta-analysis. Study quality was examined as per the Cochrane risk of bias framework. Heterogeneity and associated outcomes were assessed based on mean difference (MD), I^2, and 95% confidence interval (95%CI) values.

Results In total, 22 RCTs were ultimately found to be eligible for inclusion in the present meta-analysis. The results of this meta-analysis indicated that CBT significantly impacted cognition as compared to other treatment options (including placebo treatment, clinical monitoring, clinic-based treatment, psychoeducation, physical activity training,

†Xiaoke Wu and Mengmeng Shi contributed equally to this work.

*Correspondence:
Yajun Lian
lianyajun840317@163.com
Haifeng Zhang
zhf840317@163.com

Full list of author information is available at the end of the article

health enhancement) (I^2 = 49%, MD = 0.23, 95%CI: 0.03–0.44, *P* = 0.03). CBT was also associated with significant improvements in PD patient QoL (I^2 = 0%, MD = 3.45, 95%CI: 1.13–5.57, *P* = 0.04), anxiety symptoms (I^2 = 57%, MD = -2.01, 95%CI: -4.01–0.01, *P* = 0.05), and depression symptoms (I^2 = 74%, MD = -3.94, 95%CI: -6.47 to -1.42, *P* = 0.04).

Conclusions These results reveal that CBT can have beneficial effects on PD patient cognitive status and QoL. Notably, CBT represents an effective option for treating NMS such as anxiety and depression in PD patients. These results offer strong evidence in favor of applying CBT as a means of enhancing the mental health, cognition, and QoL of individuals with PD. However, additional high-quality large-scale studies will be essential to confirm and expand upon these results.

Keywords Cognitive behavioral therapy, Psychological health, Parkinson's disease, Systematic review, Meta-analysis

Introduction

Parkinson's disease (PD) is a clinically important neurodegenerative disease that results in characteristic symptoms such as bradykinesia, postural instability, rigidity, resting tremor, and non-motor symptoms (NMS) including cognitive impairment, anxiety, and depression [1–3]. As PD progresses, patients experience worsening deterioration of their motor function and quality of life (QoL) together with increasingly severe cognitive outcomes and poorer mental health in many instances [4]. An estimated 0.1–0.2% of people throughout the globe are affected by PD, including over 1% of adults over the age of 60 [5, 6]. Patients with PD are five to six times more likely to develop dementia compared with healthy aging populations, and the presence of mild cognitive impairment is believed to be one of the best indicators for the early detection of dementia in patients with PD, as about 25% of PD patients with intact cognitive function converted to PD-associated mild cognitive impairment and 2% to dementia [7, 8]. The average prevalence of anxiety disorders in patients with PD has been found to be 31%, with non-episodic anxiety being more prevalent than episodic anxiety [9, 10]. The frequency of depressive disorders was estimated at 30.7%, with major depressive disorder apparent in 14.0% of PD patients [11, 12].

As research focused on the pathogenesis of PD continues to advance, a number of treatment options have emerged. First-line treatment generally consists of pharmacotherapy [13]. But long-term drug treatment can result in serious side effects that can hamper this interventional approach due to neurological or gastrointestinal symptoms [14]. A cross-sectional study observed the presence of NMS in the early to middle PD stages in patients from East and Southeast Asian regions [15]. The patients of PD with mild cognitive impairment were found have social dysfunction through the Mini-mental state examination (MMSE) and optimal cut-off score of the Parkinson's disease social functioning scale (PDSFS) [16]. As NMS play mediating roles in the pathways between psychological distress and health-related quality of life, PD interventions should address the spiritual resilience of patients in addition to providing psychological care and relief of physical symptoms [17]. Compared with conventional stretching exercises, yoga was found to reduce anxiety and depression in patients with PD, indicating its positive effects on health-related quality of life [18]. Psychiatric treatment is often offered to patients for NMS treatment, with cognitive-behavioral therapy (CBT) and mind-body exercise regimens both being common in this setting [19–22]. These mental health-focused interventions can significantly alleviate depression, anxiety, and cognitive impairment, thereby improving PD patient QoL.

CBT is a non-pharmacological approach to improving mental health through individualized interventions including thought monitoring and restructuring, worry control, relaxation training, adjustments to sleep hygiene, and other strategies capable of altering the cognition and behavior of patients [23]. Secker et al. demonstrated the preliminary value of CBT as a means of managing psychological morbidity in PD patients in a randomized controlled trial (RCT) of 30 individuals in 2005, while Dobkin et al. expanded on these findings in a pilot controlled study of 15 individuals in 2007, highlighting the feasibility and efficacy of CBT as a treatment for depression in individuals with PD [24, 25]. Recent pilot studies and RCTs have found that CBT is effective for relieving symptoms in people with dementia accompanied by anxiety or depression [26, 27], as well as patients with multiple sclerosis with insomnia, depression, or anxiety [28–30]. The brief psychotherapy (which includes both CBT and psychodynamic therapy) is probable effective in the management of depression in PD patients from a systematic review and meta-analysis [31]. CBT has also been confirmed to improve anxiety symptoms in patients with PD (including situational and social anxiety, as well as avoidance behavior), with recent RCTs showing functional changes in reversing the imbalance between PD-related anxiety circuits and reinforcing cognitive control of emotional processing [20, 32]. Abundant clinical evidence thus suggests that CBT can improve PD patient NMS. The number of RCTs assessing the efficacy of CBT for treating NMS, such as anxiety and depression in patients with PD, are increasing, and the results may

show some differences in the treatment effects. The accuracy of these results can be adversely affected by inappropriate study design and small sample size. Although a previous meta-analysis revealed that CBT was effective in relieving depression and anxiety in patients with PD, the analysis included only 7 studies with 191 patients [33]. The results of another meta-analysis of 14 studies including 507 patients were consistent with those of the above study, showing no significant impact of CBT on fatigue or QoL [34]. Although many RCTs and several reviews have been conducted to compare the effectiveness of CBT, each of these compared only two or a few NMS. There is thus a lack of integrated and systematic evidence on the relative efficacy of CBT for treating NMS in PD. Therefore, a meta-analysis of suitable studies is needed to provide better guidance for the clinical application of CBT for treating and improving the lives of patients with PD.

This study was developed with the goal of quantitatively assessing the results from published RCTs exploring the relative efficacy of CBT as a treatment for NMS including anxiety, depression, and cognitive impairment in PD patients while assessing associated effects on patient QoL. The resultant data indicated that CBT offers varying levels of value as a means of alleviating these NMS and improving the QoL of PD patients, suggesting that this therapeutic option should be considered as a key facet of efforts aimed at improving these symptoms in individuals suffering from PD.

Methods

Search strategy

The PubMed, Embase, Medline, and Cochrane Library databases were searched for all English language RCTs assessing the effects of CBT in PD patients published from their inception to present. The MeSH/Emtree and title/abstract keyword combination search terms included "cognitive behavioral therapy" and "Parkinson's disease". For details regarding this search strategy and the results thereof, see Supplemental Table 1 This review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [35].

Inclusion and exclusion criteria

Studies eligible for meta-analysis inclusion were: (1) Studies on NMS (anxiety, depression, cognitive impairment) and QoL in PD patients; (2) Studies that specifically evaluated the effects of CBT or other treatments on NMS and QoL in PD patients; (3) Studies on evaluating improvements in NMS and QoL scores in PD patients; (4) Studies that were RCTs and were published in English.

Studies were excluded if: (1) They were focused on the motor symptoms of PD patients; (2) They analyzed PD cases that were not treated with CBT; (3) The full text was unavailable. Investigators worked together to screen for relevant studies, initially performing title/abstract review before subjecting potentially relevant articles to full-text review.

Data extraction

Two investigators (XW, MS) independently screened all studies to determine their eligibility for inclusion, with any discrepancies being resolved through discussion with a third investigator (HZ). Data were then extracted from eligible studies, including the title, authors, country, study type, study duration, mean patient age, sample size, CBT frequency, anxiety, depression, cognitive function, and QoL metrics and any other relevant information relating to the utilized scales employed for NMS evaluation.

Statistical analysis

Data in this meta-analysis were analyzed based on I^2, mean difference (MD), and 95% confidence interval (95% CI) values. Specifically, the I^2 values were utilized for quantitative analyses of heterogeneity among studies, with a value above 50% being indicative of a high degree of heterogeneity. Heterogeneity was assessed using a random effects model and the stability of the results was verified with sensitivity analysis. The Cochrane Collaboration assessment tool was independently used by two investigators to assess the risk of bias for all included studies, which were determined to exhibit a low, high, or unclear risk of bias for each of the following items: random sequence generation, allocation concealment, outcome assessor blinding, participant/personnel blinding, incomplete outcome data, selective outcome reporting, and other forms of bias. All analyses were performed using the software of Review Manager 5.4 (Cochrane Library).

Results

Study selection and study characteristics

An initial search of the selected databases identified 1,149 studies of potential relevance, with 302 remaining following the removal of duplicate records. Additionally, 636 studies were excluded following preliminary title and abstract review, while the remaining 213 articles were subjected to full-text review. In total, 22 RCTs were ultimately found to be eligible for inclusion in the present meta-analysis (Fig. 1).

Patients in 20 of the included RCTs other than two conducted in 2019 were older than 60 years of age. NMS in these patients were analyzed with appropriate clinical scales of varying levels of demonstrated reliability and validity. Cognition was then evaluated with the Montreal Cognitive Assessment (MoCA) Scale or the World Health Organization Quality of Life -Brief (WOQOL) Scale. Depression was analyzed with scales including

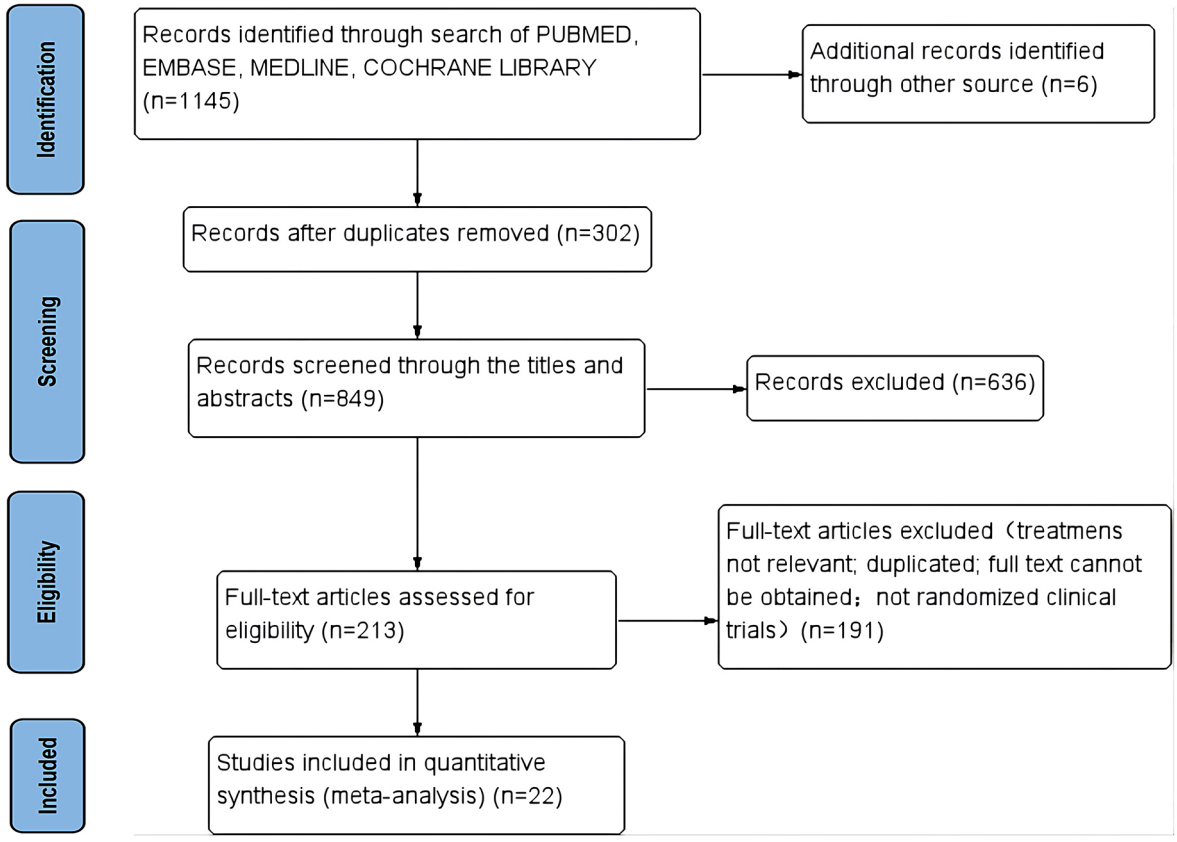

Fig. 1 Flow chart of the literature search strategy in this meta-analysis

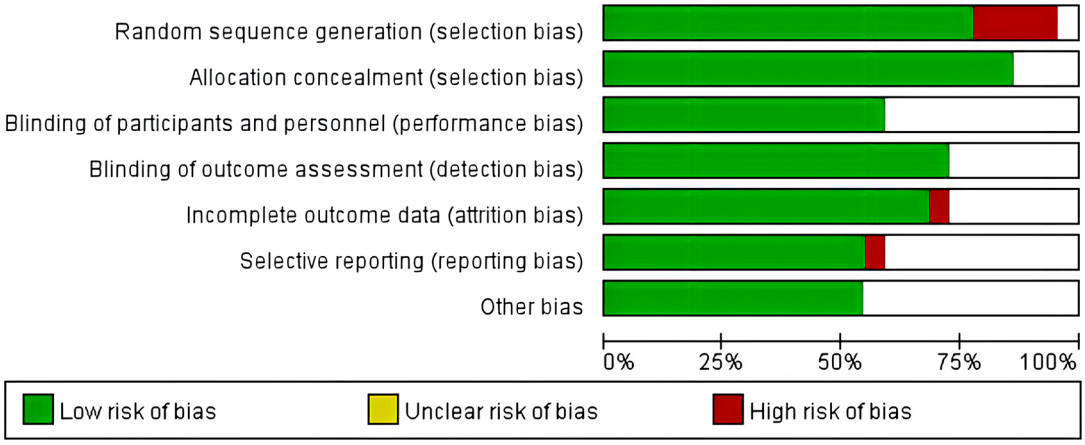

Fig. 2 Risk of bias graph. Reviewing authors' judgements about each risk of bias item presented as percentages across all included studies

the Hamilton Depression Rating (HAM-D) Scale, the Beck Depression Inventory (BDI), the Geriatric Depression Scale-15 (GDS-15), and the Patient Health Questionnaire-9 (PHQ-9). Anxiety was assessed with scales including the Hamilton Anxiety Rating (HAM-A) Scale and the Beck Anxiety Inventory (BAI).

Some of the included studies were conducted in the USA (n=6 [21, 36–40]), Italy (n=4 [41–44]), Australia (n=3 [45–47]), the Netherlands (n=3 [20, 48, 49]), Germany (n=2 [50, 51]), Britain (n=1 [52]), Switzerland (n=1 [53]), and Canada (n=1 [54]). Included PD patients underwent CBT for 3–12 weeks. Detailed information on the characteristics of the included studies is provided in Supplemental Table 2.

Assessment of risk of bias

The Cochrane Collaboration risk of bias tool was used to assess the potential biases of each of these studies (Fig. 2).

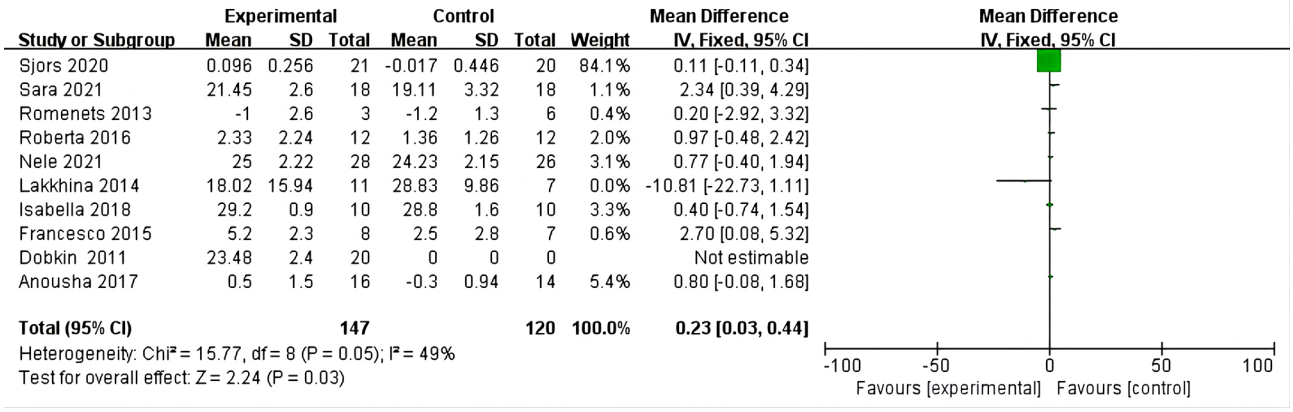

Fig. 3 Meta-analysis of overall pooled MDs with 95% CIs across studies for cognition. Forest plot showing that CBT significantly improved the cognition of PD from older adults. *Abbreviations* MD, mean difference; CI, confidence interval; CBT, cognitive behavioral therapy; PD, Parkinson's disease

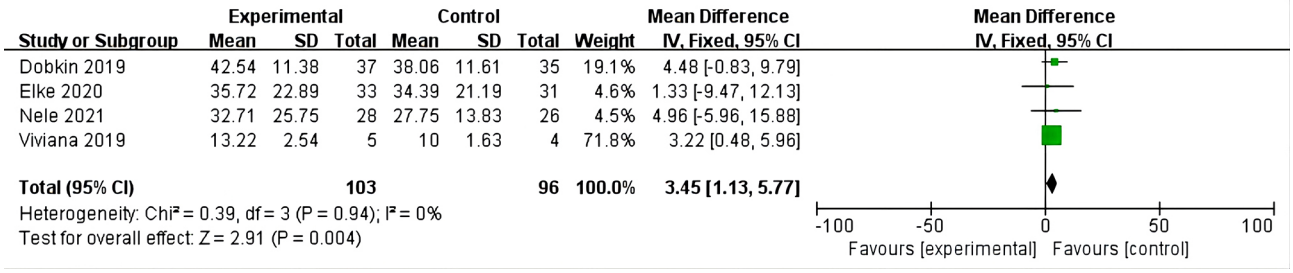

Fig. 4 Meta-analysis of overall pooled MDs with 95% CIs across studies for QoL. Forest plot showing that CBT significantly improved the QoL of PD from older adults. *Abbreviations* MD, mean difference; CI, confidence interval; QoL, quality of life; PD, Parkinson's disease

In total, 4 studies exhibited a high risk of selection bias, while some had a high risk of reporting or attrition bias. Additionally, missing outcome data from 9 studies were considered consistent with an unclear risk of bias.

Effects of CBT on PD

This meta-analysis included 22 studies of 1,053 PD patients. The patients had no amentia. NMS in these patients was evaluated after treatment. The 10 studies that reported on cognition exhibited an I^2=49% and P=0.05, consistent with low heterogeneity such that results were analyzed with a fixed-effects model (compared with placebo treatment, clinical monitoring, clinic-based treatment, psychoeducation, physical activity training, health enhancement). Pooled results exhibited significant improvements in cognition following CBT treatment in PD patients (MD=0.23, 95%CI: 0.03–0.44, P=0.03) (Fig. 3). CBT also had a significant impact on the QoL of PD patients (I^2=0%, MD=3.45, 95%CI: 1.13–5.57, P=0.04) in 12 studies (Fig. 4), and on anxiety in 9 studies (I^2=57%, MD = -2.01, 95%CI: -4.01 to 0.01, P=0.05) (Fig. 5). Moreover, CBT significantly impacted depression in these PD patients (I^2=74%, MD = -3.94, 95%CI: -6.47 to -1.42, P=0.04) (Fig. 5). Overall, these findings and corresponding forest plots indicated that CBT was able to significantly improve PD patient cognition, QoL, and mental health.

The meta-analysis of depression and anxiety in PD patients treated with CBT showed a high degree of statistical heterogeneity among the results of the studies. The reasons for this heterogeneity may have been as follows: (1) Differences in disease severity and duration that led to differences in the treatment effect; (2) Potential subjectivity of the anxiety and depression scores, with differences in patient perception of the degree of anxiety and depression; (3) Patients from different countries and regions, as well as differences in research design; (4) Differences in the therapeutic and subjective roles of therapists involved in CBT. Sensitivity analyses were performed using a fixed-effects model, and the meta-analysis showed that the results of CBT efficacy for depression (I2=74%, MD = -3.30, 95%CI: -4.49 to -2.11, P<0.01) and anxiety (I2=57%, MD = -2.55, 95%CI: -3.66 to -1.45, P<0.01) in PD patients remained statistically significant (Fig. 6), which is consistent with the results of the random effects model and can thus be considered a more stable result.

In summary, based on the results of forest plots of the effects of CBT on PD, we concluded that CBT improve the cognition, mental health and the quality of life for PD patients.

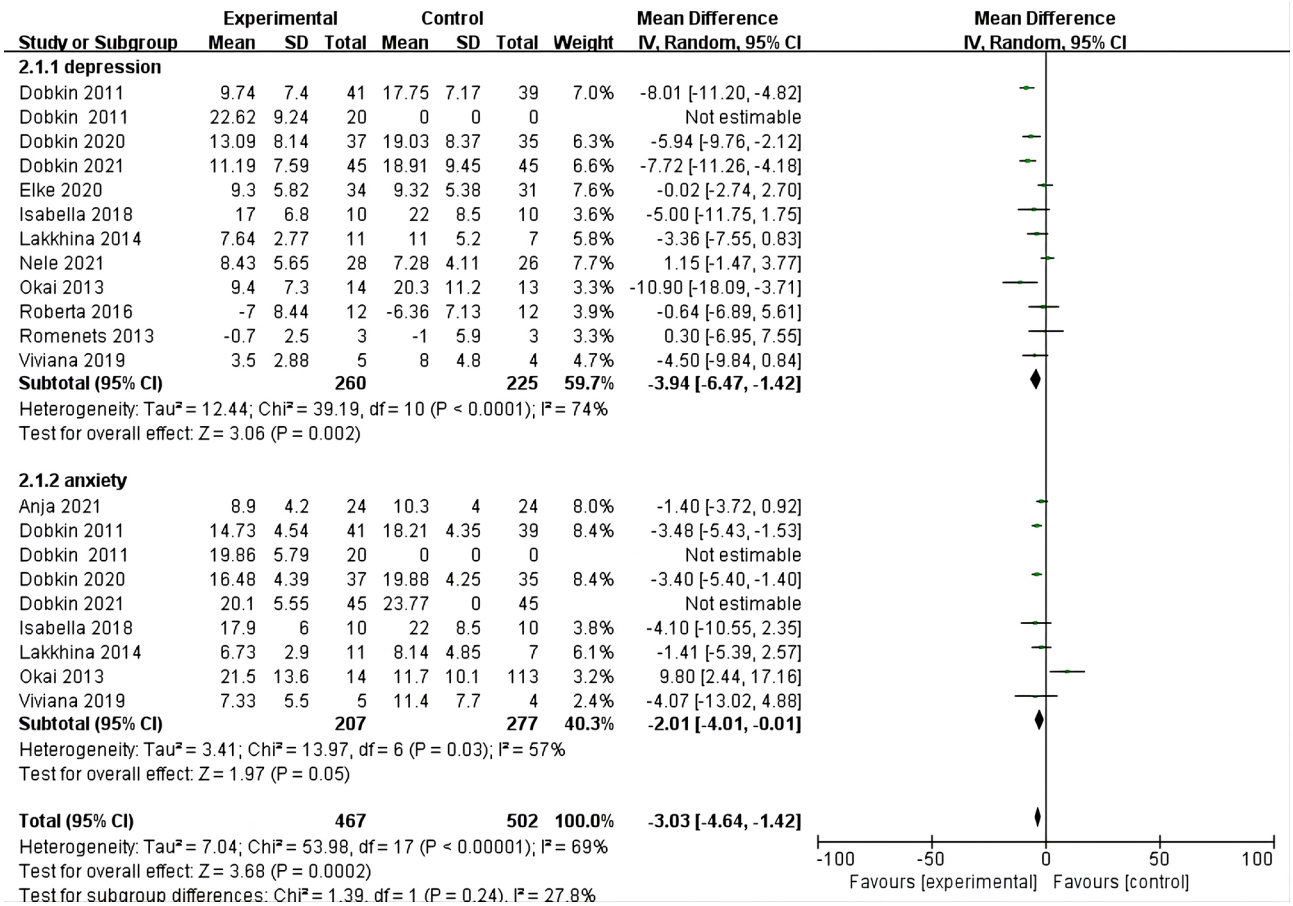

Fig. 5 Meta-analysis of overall pooled MDs with 95% CIs across studies for depression and anxiety. Forest plot showing that CBT significantly improved the depression and anxiety of PD from older adults. *Abbreviations* MD, mean difference; CI, confidence interval; CBT, cognitive behavioral therapy; PD, Parkinson's disease

Discussion

In this meta-analysis, 22 studies incorporating 1,053 PD patients treated with CBT were evaluated, revealing improved cognition, QoL, anxiety, and depression following such treatment. As such, CBT may hold therapeutic value as a tool for addressing NMS in PD patients. Significant heterogeneity was detected with respect to the results of depression and anxiety. Such heterogeneity can stem from a range of factors including potential bias in study selection, limited study numbers, differences in CBT frequency or modality, or different evaluation approaches. Further clinical research will thus be vital to fully clarify the benefits of CBT as a treatment for PD patient NMS.

PD is among the most common forms of serious neurodegenerative disease in the world, and it presents with a complex array of physiological and psychiatric symptoms [55]. Mechanistically, patients experience classical motor symptoms resulting from dopaminergic neuron loss in the substantia nigra and Lewy bodies, while NMS can also contribute to disease progression and adverse health outcomes in affected patients [56]. A comparison of the effects of a modified mindfulness meditation program versus stretching and resistance training exercises in patients with mild-to-moderate PD in an RCT showed that the former was effective for relieving depression and maintaining emotional stability, with comparable benefits on cognitive performance [57]. Besides, the mindfulness yoga program was found to be as effective in improving motor dysfunction and mobility, with the additional benefits of reducing anxiety and depressive symptoms and increasing spiritual well-being and health-related quality of life, as shown by another RCT [58]. CBT has been increasingly applied as a treatment tool for PD patients in recent years [20, 36, 45]. Meta-analyses provide an opportunity to comprehensively summarize and analyze the results of a variety of studies focused on a particular topic, translating results from RCTs in a systematic and objective fashion to clarify the relative advantages and limitations of particular therapeutic regimens.

There are multiple strengths to this meta-analysis. For one, all included studies were RCTs and they were identified through a thorough search of the literature. These analyses thus provide a comprehensive overview of the

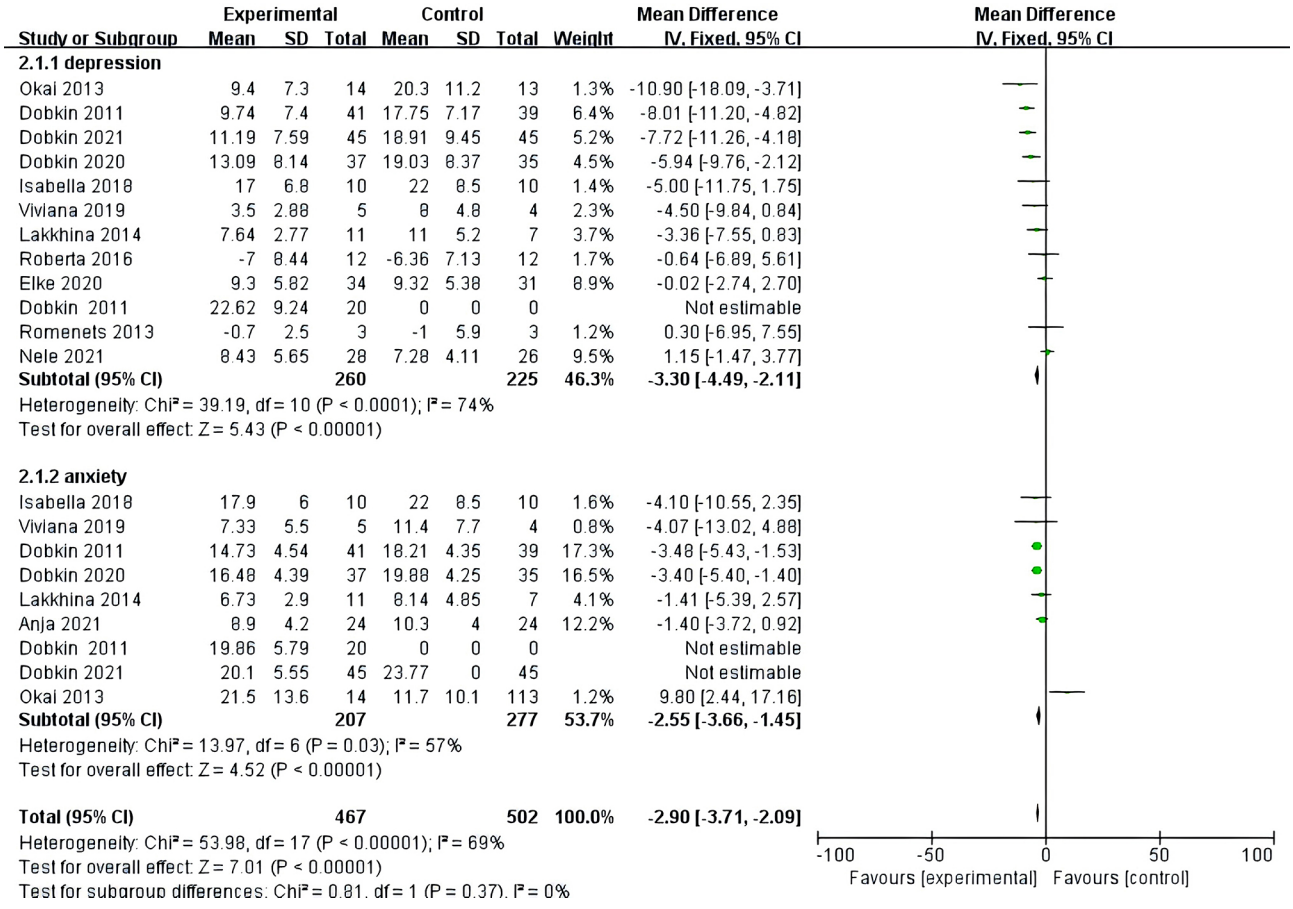

Fig. 6 Sensitive analysisof overall pooled MDs with 95% CIs across studies for depression and anxiety. Forest plot showing that CBT significantly improved the depression and anxiety of PD from older adults. *Abbreviations* MD, mean difference; CI, confidence interval; CBT, cognitive behavioral therapy; PD, Parkinson's disease

impact of CBT on NMS in PD patients. The study considers that CBT can alleviate psychological problems in patients with PD, which is in line with the findings of previously published investigations [59, 60]. CBT could thus be used as a complementary therapy for treating the psychological and non-motor symptoms of PD and could be integrated into current treatment protocols for PD.

Even so, these findings are subject to some limitations. First, despite a thorough searching of the literature, relevant studies may have been missed as only studies published in English were included. The included studies may also have bias due to screening criteria and investigators. Besides, some reports included in this analysis exhibited significant clinical or methodological heterogeneity, and a random-effects model was thus utilized to minimize any discrepancies between these scales to maximize the reliability of these findings. Moreover, the studies we included whether suitable for the evaluate the efficacy of CBT for PD patients. In addition, all the included RCTs enrolled patients with PD in terms of the previous criteria for PD definition; however, it is not known whether there were differences in the accuracy of the relevant scales used to assess patient psychology. As such, the certainty of these results is limited by the imprecision inherent in the included studies. We did not prospectively register the protocol on International prospective register of systematic reviews (PROSPERO) which is also considered a major limitation. In the future, we will continue to investigate in depth the impact of CBT on mental health in patients with PD through pre-registration the protocol on PROSPERO.

Conclusion

In summary, the present systematic review and meta-analysis offers insight into the relative efficacy of CBT as a therapeutic option for PD patients. These findings indicated that CBT was an effective means of improving QoL and NMS such as depression and cognitive function, in addition to trending towards a significant impact on anxiety symptoms. As such, CBT should be considered as a standard clinical option for PD patients suffering from NMS, and the most efficacious forms of this psychotherapy strategy should be studied in further detail. Overall, these findings emphasize the potential value of CBT

as a means of improving QoL, cognition, anxiety, and depression among individuals with PD, and to provide a theoretical basis for the future CBT clinical trial design. In addition, large, randomized, prospective clinical trials are needed to determine the effectiveness and efficiency of CBT in treating PD patients with psychological problems, thus greatly improving the current treatment options. Further investigations with longer follow-up periods and low risk of bias are needed to examine the long-term effects of CBT on patients with PD. The effectiveness of CBT in different PD stages, together with evaluating its outcomes when combined with other therapeutic modalities, and the potential effects and interactions of factors that might influence these outcomes should be addressed.

Abbreviations

NMS	Non-motor symptoms
PD	Parkinson's disease
MMSE	Mini-mental state examination
PDSFS	Parkinson's disease social functioning scale
QoL	Quality of life
CBT	Cognitive behavioral therapy
RCT	Randomized controlled trial
MD	Mean difference
CI	Confidence interval
MoCA	Montreal Cognitive Assessment
WOQOL	World Health Organization Quality of Life-Brief
HAM-D	Hamilton Depression Rating
BDI	Beck Depression Inventory
GDS-15	Geriatric Depression Scale-15
PHQ-9	Patient Health Questionnaire-9
HAM	A-Hamilton Anxiety Rating
BAI	Beck Anxiety Inventory
PROSPERO	International prospective register of systematic reviews

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12883-024-03859-x.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Acknowledgements
The authors would like to thank all the reviewers who participated in the review and MJEditor (www.mjeditor.com) for its linguistic assistance during the preparation of this manuscript.

Author contributions
XW and MS contributed equally to this work. HZ, XW conceived the idea of this study and contributed to the data extraction. MS computed and evaluated the pooled outcomes. XW, HZ contributed to the study protocol and wrote the article. YL revised the article. All authors contributed to the article and approved the final manuscript.

Funding
This work was supported by grants from the National Natural Science Foundation of China (No. 81701271) and the China Association against Epilepsy Foundation (No.UCB-2023-056).

Data availability
Data is provided within the manuscript or supplementary information files.

Declarations

Consent to participate
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Neurology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan 450052, China
[2]Department of Ophthalmology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan 450052, China

Received: 25 February 2024 / Accepted: 10 September 2024
Published online: 19 September 2024

References

1. Samii A, Nutt JG, Ransom BR. Parkinson's Disease Lancet. 2004;363(9423):1783–93.
2. Kalia LV, Lang AE. Parkinson's Disease Lancet. 2015;386(9996):896–912.
3. Tolosa E, Wenning G, Poewe W. The diagnosis of Parkinson's disease. Lancet Neurol. 2006;5(1):75–86.
4. Weintraub D, et al. The neuropsychiatry of Parkinson's disease: advances and challenges. Lancet Neurol. 2022;21(1):89–102.
5. Dorsey ER, et al. The emerging evidence of the Parkinson pandemic. J Parkinsons Dis. 2018;8(s1):S3–8.
6. Tysnes OB, Storstein A. Epidemiology of Parkinson's disease. J Neural Transm (Vienna). 2017;124(8):901–5.
7. Yu RL, Wu RM. Mild cognitive impairment in patients with Parkinson's disease: an updated mini-review and future outlook. Front Aging Neurosci. 2022;14:943438.
8. Saredakis D, et al. Conversion to MCI and dementia in Parkinson's disease: a systematic review and meta-analysis. Parkinsonism Relat Disord. 2019;65:20–31.
9. Broen MP, et al. Prevalence of anxiety in Parkinson's disease: a systematic review and meta-analysis. Mov Disord. 2016;31(8):1125–33.
10. Dissanayaka NN, et al. Phenomenology of atypical anxiety disorders in Parkinson's Disease: a systematic review. Am J Geriatr Psychiatry. 2022;30(9):1026–50.
11. Chendo I, et al. Frequency of depressive disorders in Parkinson's Disease: a systematic review and Meta-analysis. J Parkinsons Dis. 2022;12(5):1409–18.
12. Cong S, et al. Prevalence and clinical aspects of depression in Parkinson's disease: a systematic review and meta–analysis of 129 studies. Neurosci Biobehav Rev. 2022;141:104749.
13. Lees AJ, Hardy J, Revesz T. Parkinson's Disease Lancet. 2009;373(9680):2055–66.
14. Chen JJ, Swope DM. Pharmacotherapy for Parkinson's disease. Pharmacotherapy. 2007;27(12 Pt 2):s161–73.
15. Kwok JYY, et al. Symptom Burden and Unmet Support needs of patients with Parkinson's Disease: a cross-sectional study in Asia-Pacific regions. J Am Med Dir Assoc. 2021;22(6):1255–64.
16. Chen YR, et al. Investigating the interaction between neuropsychiatry features and daily activities on social function in patients with Parkinson's disease with mild cognitive impairment. BJPsych Open. 2022;8(6):e205.
17. Kwok JYY, et al. Effects of spiritual resilience on psychological distress and health-related quality of life in Chinese people with Parkinson's disease. Qual Life Res. 2020;29(11):3065–73.
18. Kwok JYY, et al. Effects of Mindfulness yoga Versus Conventional Physical exercises on Symptom experiences and Health-related quality of life in people with Parkinson's Disease: the potential mediating roles of anxiety and depression. Ann Behav Med. 2022;56(10):1068–81.
19. Li Z, et al. Study protocol for a single-blind randomised controlled trial to evaluate the clinical effects of an Integrated Qigong exercise intervention on freezing of gait in Parkinson's disease. BMJ Open. 2019;9(9):e028869.
20. Moonen AJH, et al. Cognitive behavioral therapy for anxiety in Parkinson's Disease: a Randomized Controlled Trial. Mov Disord. 2021;36(11):2539–48.
21. Dobkin RD, et al. Telephone-based cognitive behavioral therapy for depression in Parkinson disease: a randomized controlled trial. Neurology. 2020;94(16):e1764–73.

22. Uitti RJ. Treatment of Parkinson's disease: focus on quality of life issues. Parkinsonism Relat Disord. 2012;18(Suppl 1):S34–6.
23. Otte C. Cognitive behavioral therapy in anxiety disorders: current state of the evidence. Dialogues Clin Neurosci. 2011;13(4):413–21.
24. Secker DL, Brown RG. Cognitive behavioural therapy (CBT) for carers of patients with Parkinson's disease: a preliminary randomised controlled trial. J Neurol Neurosurg Psychiatry. 2005;76(4):491–7.
25. Dobkin RD, Allen LA, Menza M. Cognitive-behavioral therapy for depression in Parkinson's disease: a pilot study. Mov Disord. 2007;22(7):946–52.
26. Forstmeier S, et al. Cognitive behavioural treatment for mild Alzheimer's patients and their caregivers (CBTAC): study protocol for a randomized controlled trial. Trials. 2015;16:526.
27. García-Alberca JM. Cognitive-behavioral treatment for depressed patients with Alzheimer's disease. An open trial. Arch Gerontol Geriatr. 2017;71:1–8.
28. Siengsukon CF, et al. Feasibility and treatment effect of cognitive behavioral therapy for insomnia in individuals with multiple sclerosis: a pilot randomized controlled trial. Mult Scler Relat Disord. 2020;40:101958.
29. Gold SM, et al. Internet-delivered cognitive behavioural therapy programme to reduce depressive symptoms in patients with multiple sclerosis: a multicentre, randomised, controlled, phase 3 trial. Lancet Digit Health. 2023;5(10):e668–78.
30. Pouyanfard S, et al. Effectiveness of mindfulness-integrated cognitive behavior therapy on anxiety, depression and hope in multiple sclerosis patients: a randomized clinical trial. Trends Psychiatry Psychother. 2020;42(1):55–63.
31. Xie CL, et al. A systematic review and meta-analysis of cognitive behavioral and psychodynamic therapy for depression in Parkinson's disease patients. Neurol Sci. 2015;36(6):833–43.
32. Carey G, et al. Cognitive behavioral therapy for anxiety in Parkinson's Disease induces functional brain changes. J Parkinsons Dis. 2023;13(1):93–103.
33. Zhang Q, et al. Cognitive behavioral therapy for depression and anxiety of Parkinson's disease: a systematic review and meta-analysis. Complement Ther Clin Pract. 2020;39:101111.
34. Luo F, et al. Efficacy of cognitive behavioral therapy on Mood disorders, sleep, fatigue, and quality of life in Parkinson's Disease: a systematic review and Meta-analysis. Front Psychiatry. 2021;12:793804.
35. Page MJ, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
36. Dobkin RD, et al. Cognitive-behavioral therapy for depression in Parkinson's disease: a randomized, controlled trial. Am J Psychiatry. 2011;168(10):1066–74.
37. Dobkin RD, et al. Cognitive behavioral therapy improves diverse profiles of depressive symptoms in Parkinson's disease. Int J Geriatr Psychiatry. 2019;34(5):722–9.
38. Dobkin RD, et al. Innovating Parkinson's care: a Randomized Controlled Trial of Telemedicine Depression Treatment. Mov Disord. 2021;36(11):2549–58.
39. Dobkin RD, et al. Telephone-based cognitive-behavioral therapy for depression in Parkinson disease. J Geriatr Psychiatry Neurol. 2011;24(4):206–14.
40. París AP, et al. Blind randomized controlled study of the efficacy of cognitive training in Parkinson's disease. Mov Disord. 2011;26(7):1251–8.
41. Angelucci F, et al. A pilot study on the effect of cognitive training on BDNF serum levels in individuals with Parkinson's disease. Front Hum Neurosci. 2015;9:130.
42. Berardelli I, et al. Cognitive behavioral group therapy versus psychoeducational intervention in Parkinson's disease. Neuropsychiatr Dis Treat. 2018;14:399–405.
43. Bernini S, et al. A double-blind randomized controlled trial of the efficacy of cognitive training delivered using two different methods in mild cognitive impairment in Parkinson's disease: preliminary report of benefits associated with the use of a computerized tool. Aging Clin Exp Res. 2021;33(6):1567–75.
44. Biundo R, et al. Double-blind Randomized Trial of tDCS Versus Sham in Parkinson patients with mild cognitive impairment receiving cognitive training. Brain Stimul. 2015;8(6):1223–5.
45. Wuthrich VM, Rapee RM. Telephone-delivered cognitive behavioural therapy for treating symptoms of anxiety and depression in Parkinson's Disease: a pilot trial. Clin Gerontol. 2019;42(4):444–53.
46. Troeung L, Egan SJ, Gasson N. A waitlist-controlled trial of group cognitive behavioural therapy for depression and anxiety in Parkinson's disease. BMC Psychiatry. 2014;14:19.
47. Lawrence BJ, et al. Cognitive training and Transcranial Direct current stimulation for mild cognitive impairment in Parkinson's Disease: a Randomized Controlled Trial. Parkinsons Dis. 2018;2018:p4318475.
48. van de Weijer SCF, et al. Feasibility of a cognitive training game in Parkinson's Disease: the randomized parkin'play study. Eur Neurol. 2020;83(4):426–32.
49. van Balkom TD, et al. COGTIPS: a double-blind randomized active controlled trial protocol to study the effect of home-based, online cognitive training on cognition and brain networks in Parkinson's disease. BMC Neurol. 2019;19(1):179.
50. Schmidt N, et al. Memory enhancement by multidomain group cognitive training in patients with Parkinson's disease and mild cognitive impairment: long-term effects of a multicenter randomized controlled trial. J Neurol. 2021;268(12):4655–66.
51. Kalbe E, et al. Enhancement of executive functions but not memory by Multidomain Group Cognitive Training in patients with Parkinson's disease and mild cognitive impairment: a Multicenter Randomized Controlled Trial. Parkinsons Dis. 2020;2020:p4068706.
52. Okai D, et al. Trial of CBT for impulse control behaviors affecting Parkinson patients and their caregivers. Neurology. 2013;80(9):792–9.
53. Hadinia A, et al. Cognitive behavioral Group Therapy reduces stress and improves the quality of life in patients with Parkinson's Disease. Front Psychol. 2016;7:1975.
54. Rios Romenets S, et al. Doxepin and cognitive behavioural therapy for insomnia in patients with Parkinson's disease -- a randomized study. Parkinsonism Relat Disord. 2013;19(7):670–5.
55. Lee A, Gilbert RM. Epidemiology of Parkinson Disease. Neurol Clin. 2016;34(4):955–65.
56. Wakabayashi K, et al. The Lewy body in Parkinson's disease and related neurodegenerative disorders. Mol Neurobiol. 2013;47(2):495–508.
57. Kwok JYY, et al. A randomized clinical trial of mindfulness meditation versus exercise in Parkinson's disease during social unrest. NPJ Parkinsons Dis. 2023;9(1):7.
58. Kwok JYY, et al. Effects of Mindfulness yoga vs stretching and resistance training exercises on anxiety and depression for people with Parkinson Disease: a Randomized Clinical Trial. JAMA Neurol. 2019;76(7):755–63.
59. Apostol AE, et al. CBT for generalized anxiety disorder in Parkinson's Disease: a Case Study. Clin Gerontol. 2024;47(2):352–61.
60. Lebrun C, et al. Efficacy of cognitive behavioral therapy for insomnia comorbid to Parkinson's disease: a focus on psychological and daytime functioning with a single-case design with multiple baselines. J Clin Psychol. 2020;76(3):356–76.

Publisher's note