

Alternative Therapies for Non-Motor Symptoms in Parkinson's Disease: A Mini Review

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Abstract: Parkinson's disease (PD) is primarily recognized for its motor symptoms, yet non-motor symptoms (NMS) such as neuropsychiatric disturbances, sleep disorders, autonomic dysfunction, and sensory abnormalities significantly contribute to the disease's overall burden. While traditional pharmacological and surgical treatments have primarily targeted motor symptoms, alternative therapies such as acupuncture, cognitive therapy, and Traditional Chinese Medicine (TCM) are gaining attention for managing NMS. This review provides a comprehensive analysis of alternative therapies for NMS in PD, drawing on evidence from international guidelines and TCM. The review highlights the current gaps in research, emphasizing the need for high-quality randomized controlled trials (RCTs) and standardized protocols, particularly in the evaluation of TCM therapies. Additionally, it underscores the potential of integrated treatment approaches that combine traditional and modern medicine, offering a personalized strategy for managing NMS in PD. By addressing these challenges, this review aims to enhance the understanding and application of alternative therapies, ultimately improving the quality of life for PD patients. These therapies, particularly those emphasizing holistic and individualized approaches, such as cognitive therapy and TCM, offer potential solutions to the unmet needs in PD management without causing side effects associated with medications or fluctuations in drug plasma levels.

Keywords: Parkinson's disease, non-motor symptoms, alternative therapies, traditional Chinese medicine

Introduction

Parkinson's disease (PD) is widely recognized for its hallmark motor symptoms, such as tremors, rigidity, and bradykinesia. However, non-motor symptoms (NMS)- including neuropsychiatric disturbances, sleep disorders, autonomic dysfunction, and sensory abnormalities- are increasingly acknowledged as significant contributors to the disease's overall burden. Studies indicate that the prevalence of NMS in PD patients ranges from 70% to 88%, with approximately 11% of patients experiencing five or more different NMS.^{1,2} The prevalence of neuropsychiatric symptoms in patients with PD is between 20% and 58%.^{3,4} Among these, sleep disturbances occur in 82%, depression in 45–76%, anxiety in 68%, apathy in 62%, and mild cognitive impairment (MCI) in 20–57%.^{4,5} Additionally, the cumulative prevalence of PD dementia is reported to be 75–90%.³ These symptoms often manifest years before the onset of motor symptoms and persist throughout the disease course, profoundly impacting patients' quality of life.⁶ Additionally, they can fluctuate alongside motor fluctuations (non-motor fluctuations), complicating the management of PD due to this interplay. While traditional pharmacological⁷ and surgical treatments primarily target motor symptoms, there is growing interest in alternative therapies that may provide relief for NMS, either as standalone interventions or in conjunction with conventional therapies.

Materials and Methods

This brief review offers an overview of alternative therapies for NMS in PD, as outlined in the guidelines from the American Academy of Neurology (AAN), the European Federation of Neurological Societies and the Movement Disorder Society-European Section (EFNS/MDS-ES), the National Institute for Health and Care Excellence (NICE),

the Canadian Medical Association(CMA), the evidence-based reviews of NMS treatment and clinical experiences from China. In this review, alternative therapies do not include cutting-edge biotechnological approaches such as cell therapy.⁸ This review focuses on the aforementioned materials to conduct a narrative analysis.

Results

Alternative Therapies for Neuropsychiatric Symptoms

A lot of international guidelines suggest that pharmacological treatment for neuropsychiatric symptoms in PD may be unnecessary when symptoms are tolerable. The AAN and EFNS/MDS-ES guidelines indicate that the efficacy of repetitive transcranial magnetic stimulation(rTMS), electroconvulsive therapy(ECT), and psychotherapy in treating NMS remains uncertain.^{1,9} The Chinese PD Blue Book offers an overview of current research on the use of gaming and virtual reality (VR) technology for the rehabilitating memory and attention.¹⁰ While acupuncture, manual therapy, and the Alexander Technique(AT) are mentioned in various international guidelines as potential treatments, the evidence supporting their efficacy is currently insufficient. Recent studies have indicated an association between particulate matter 2.5 (PM2.5) exposure and anxiety. However, whether air purification could serve as an alternative therapy for anxiety in PD patients remains unknown.¹¹

The evidence-based review of NMS treatment suggests that rTMS and cognitive behavioral therapy (CBT) may be beneficial for Parkinson's-related depression, with CBT also potentially useful in managing impulse control disorders. The role of acupuncture in alleviating PD-related fatigue requires further investigation.¹² The authoritative review on PD-related cognitive impairment^{13,14} and the Chinese guideline¹⁵ acknowledge the benefits of cognitive training, physical exercise, and non-invasive brain stimulation in improving cognitive deficits, with short-term benefits being well established. Although the benefits of Cognitive Stimulation Therapy (CST) for patients with PD dementia remain unclear, it has significantly improved the quality of life and relationship quality of care partners.¹⁶ Additionally, studies indicate that Vitamin D3 and Vitamin B1 may support cognitive function in PD.¹⁷ Studies have shown that the pathophysiological mechanisms and clinical subtypes of cognitive impairment in PD exhibit significant heterogeneity.^{18,19} Future research should not only aim to identify potential therapeutic targets but also focus on providing individualized alternative therapies tailored to specific subtypes of cognitive impairment.

For the treatment of depression in PD, TCM recommended herbs such as Bupleurum (Chai Hu), Cyperus (Xiang Fu), and Rose Flower (Mei Gui Hua).²⁰

Previous research has shown that subthalamic nucleus deep brain stimulation (STN-DBS) may adversely affect executive function and verbal fluency in PD patients. However, as DBS is not classified as an alternative therapy, it will not be discussed further in this review.²¹ Patients with primary progressive freezing of gait, similar to those with PD, also experience NMS such as fatigue.²² However, research on alternative therapies for neuropsychiatric symptoms in this rare population is scarce, and no recommendations are currently available. With the rapid advancements in artificial intelligence(AI) technology, some researchers have begun exploring the potential benefits of AI-based chatbots for addressing neuropsychiatric symptoms in PD patients.²³ However, such studies remain scarce, the efficacy is yet unknown, and this alternative therapy is not currently included in clinical guidelines or consensus recommendations.

Alternative Therapies for Sleep Disorders

Sleep disturbances are prevalent among PD patients, with studies indicating that 77.5% experience such issues, and 49.9% suffer from multiple types of sleep disorders.²⁴ The EFNS/MDS-ES guidelines recommend evaluating patients with daytime sleepiness and sudden-onset sleep for potential nighttime sleep disorders.⁹ TCM offers extensive experience in managing sleep disorders, and a consensus has been published on managing sleep disturbances in PD.²⁵ The consensus emphasizes the importance of good sleep hygiene, including establishing a regular sleep schedule, consistent bedtimes and wake times, and aligning sleep patterns with seasonal changes. For instance, in spring and summer, it is advised to “stay up later and rise earlier”, while in autumn, “go to bed early and wake up early”, and in winter, “go to bed early and rise later”. For patients with insomnia and excessive daytime sleepiness (EDS), moderate daytime exercise, particularly with increased sunlight exposure, is recommended. Practices such as Tai Chi, Baduanjin and table tennis

(Ping-Pong)^{26,27} are beneficial for both PD symptoms and sleep disturbances. The consensus also advises dietary considerations: for patients with insomnia and rapid eye movement sleep behavior disorder (RBD), a light balanced diet is recommended, avoiding stimulants like coffee and tea, as well as “yang”-enhancing foods like lamb and leeks. Conversely, for those with EDS, these foods may be consumed in moderation. It is also crucial to consider the impact of medications on sleep disturbances in PD. Light therapy and CBT are potential treatment options. The TCM consensus recommends specific formulas for different types of sleep disorders. For insomnia, suggested formulas include “Zhen Gan Xi Feng Tang” combined with “Huang Lian E Jiao Tang”, “Gui Pi Tang”, “Huang Lian Wen Dan Tang” combined with “Xue Fu Zhu Yu Tang”, and “You Gui Wan” combined with “An Shen Ding Zhi Wan”. Additionally, TCM suggests adding Ziziphi Spinosae Semen (Suan Zao Ren), Dragon Bone (Long Chi), and Poria with Hostwood (Fu Shen) to the basic formula.²⁰ For RBD, recommended formulas are “Zi Shui Qing Gan Yin” combined with “Bai He Di Huang Tang”, “Gui Pi Tang” combined with “Chai Hu Jia Long Gu Mu Li Tang”, and “Wen Dan Tang” combined with “An Shen Ding Zhi Wan”. For restless legs syndrome (RLS), recommended formulas include “Zhen Gan Xi Feng Tang” combined with “Shao Yao Gan Cao Tang”, “Gui Pi Tang” combined with “Huang Qi Gui Zhi Wu Wu Tang”, “Shen Tong Zhu Yu Tang”, and “You Gui Wan” combined with “Dang Gui Si Ni Tang”. For EDS, suggested formulas include “Gui Pi Tang” combined with “Gui Zhi Gan Cao Long Gu Mu Li Tang”, “Xue Fu Zhu Yu Tang” combined with “Chang Pu Yu Jin Tang”, and “Zuo Gui Wan” combined with “Xin Jia Fu Zi Tang”. Detailed content of these TCM formulas is provided in [Appendix 1](#).

Alternative Therapies for Autonomic Dysfunction

Constipation

The EFNS/MDS-ES and CMA guidelines recommend increasing fluid and fiber intake, along with enhancing physical activity.^{9,28} The TCM consensus suggests incorporating laxatives, such as wine-processed rhubarb (Jiu Da Huang) and immature bitter orange (Zhi Shi), into the basic syndrome-based treatment. For patients with abdominal distension, Magnolia bark (Hou Po) is advised, while those with hard or dry stools may benefit from hemp seed (Huo Ma Ren) or mirabilite (Mang Xiao) powder dissolved in water. Recommended proprietary Chinese medicines include Ma Ren Soft Capsules, Tongfu Xingshen Capsules, and Ma Ren Zhi Pi Wan.²⁰

The recommended TCM formulas include “Xing Lou Cheng Qi Tang”, “Zeng Ye Cheng Qi Tang” combined with “Zuo Gui Wan”, and “Ji Chuan Jian”,² as detailed in [Appendix 1](#).

Dysphagia

The EFNS/MDS-ES guidelines recommend speech therapy for the assessment of swallowing, provision of swallowing strategies, and performing instrumental examinations when necessary. Rehabilitation therapy and dietary modifications may also be effective for some patients.⁹

Sialorrhea

The EFNS/MDS-ES guidelines prioritize speech therapy over medication for treating sialorrhea.⁹ Multidisciplinary therapy, including occupational therapists, physiotherapists, dietitians, and speech and language therapists, can reduce or prevent sialorrhea.²⁹ The TCM expert consensus also supports the effectiveness of rehabilitation therapies such as chewing gum, behavioral correction, swallowing training, and vocal training.² Additionally, the latest review suggests that sucking on hard candies may be beneficial.¹² Recommended TCM formulas include “Li Zhong Tang”, “Gui Shao Di Huang Tang” and “Shen Qi Wan” combined with “Suo Quan Wan”,² as detailed in [Appendix 1](#).

Orthostatic Hypotension (OH)

The EFNS/MDS-ES and CMA guidelines recommend avoiding factors that aggravate OH, such as large meals, alcohol, warm environments, and fluid deficiency.^{9,28} Suggested interventions include increasing salt intake, raising the head of the bed by 30–40 degrees at night, wearing high-waisted elastic stockings and/or an abdominal binder, engaging in tolerated exercise, and using counter-maneuvers like leg crossing, toe raising, and thigh contraction.⁹ Increasing water (up to 2.5 l/day) and salt (6–10 g/day) intake represents a key non-pharmacological measure to combat OH.³⁰ Drinking

a 500 mL bolus of water can significantly raise blood pressure within 30 to 90 minutes, and patients may time their water intake according to planned activities to benefit from this pressor effect.³⁰

The TCM expert consensus also recommends raising the head of the bed by 10–15 cm, ensuring adequate limb movement when transitioning from a lying or sitting position to standing, reducing or avoiding caffeine and sugary drinks, and eating smaller, more frequent meals.²

Recommended TCM formulas include “Da Ding Feng Zhu”, “Shen Mai Yin” combined with “Bu Zhong Yi Qi Tang”, “Di Huang Yin Zi”, and “Jin Kui Shen Qi Wan” combined with “Bao Yuan Tang”,² as detailed in [Appendix 1](#). Astragalus (Huang Qi), Ginseng (Ren Shen), and Prepared Aconite (Pao Tian Xiong) may be added to the basic formula.²⁰

Urinary Issues

Most patients with PD experience urinary problems, such as urgency, frequency, and nocturia, with detrusor overactivity being the most common issue. Severe urinary incontinence is often associated with advanced stages of the disease. The EFNS/MDS-ES guidelines recommend reducing fluid intake after 6 PM and elevating the head of the bed during sleep to manage nocturia. Referral to a urologist is advised for severe incontinence or ineffective treatment.⁹

The TCM expert consensus suggests that bladder training, pelvic floor muscle exercises, and biofeedback can help alleviate urinary incontinence in PD patients.² The CMA guideline recommends regular bathroom visits to prevent urgency and restricting water and caffeinated drinks after dinner to reduce nocturia.²⁸ TCM treatment options include “Da Ding Feng Zhu”, “Sheng Mai Yin”, “He Bu Zhong Yi Qi Tang”, “Di Huang Yin Zi”, “Jin Gui Shen Qi Wan”, and “He Bao Yuan Tang”,² as detailed in [Appendix 1](#).

Alternative Therapies for Sensory Disturbances

International guidelines generally do not address alternative therapies for sensory disturbances in PD. However, the TCM consensus recommends adding Corydalis (Yan Hu Suo), Clematis (Wei Ling Xian), and Processed Aconite Root (Zhi Chuan Wu) to the basic symptomatic treatment. For lower body or limb pain, “Danggui Sini Tang” or “Duhuo Jisheng Tang” is advised, while “Ge Gen Tang” or Cinnamon Twig (Gui Zhi) is recommended for upper body or limb pain. In severe cases, “Wutou Tang” or “Wutou Guizhi Tang” may be considered.²⁰

Although Neurotrophin, developed in Japan, has been shown to effectively alleviate PD-related pain, it is beyond the scope of alternative treatments discussed in this review. Additionally, the authoritative review have indicated that therapies such as aerobic exercise, dual-task training, and care management have strong evidence supporting their effectiveness in improving PD outcomes. Virtual reality-enhanced gait and balance training, combined approaches, occupational therapy, mindfulness and yoga, and palliative care have moderate-level evidence for their benefits.³¹

Discussion

Despite the potential of alternative therapies in managing NMS in PD, current research still faces several limitations that need to be addressed in future studies.

Firstly, while therapies such as acupuncture, manual therapy, and AT are mentioned in various international guidelines, there is a lack of high-quality evidence supporting their efficacy. Many studies suffer from small sample sizes,³² a lack of randomized controlled trials (RCTs), and reliance on subjective outcomes without objective clinical measures. Future research should focus on large-scale, multicenter RCTs to provide robust evidence for the role of these therapies in managing NMS.

Secondly, TCM therapies, including acupuncture and herbal medicine, are challenging to evaluate within the framework of evidence-based medicine due to their individualized treatment approaches. TCM emphasizes syndrome differentiation, where treatment plans are tailored to the specific symptoms and constitution of each patient. While this approach is effective in clinical practice, it poses significant challenges in research design. Future studies should consider developing standardized TCM treatment protocols and validating their efficacy through RCTs, while also exploring integrated approaches that combine traditional and modern medicine. Recently, a large, randomized, placebo-controlled, double-blind clinical trial demonstrated no significant effect of the traditional Chinese medicine herbal compound FYTF-

919 (Zhongfeng Xingnao oral prescription) on functional recovery, survival, or health-related quality of life in patients with moderate to severe intracerebral hemorrhage.³³ This study serves as a model for further investigation into the efficacy of traditional Chinese medicine in treating NMS of PD. The Nobel laureate Professor Tu Youyou's extraction and discovery of the effective anti-malarial component artemisinin from traditional Chinese medicine serves as another paradigm for further research into the treatment of NMS with Chinese medicine.

Additionally, the efficacy of certain alternative therapies, such as rTMS and ECT, remains uncertain in treating PD-related depression. Although these therapies have shown potential in treating neuropsychiatric disorders, their application in PD patients requires further investigation. Future research should clarify the long-term safety and efficacy of these therapies, particularly when combination with pharmacotherapy.

Moreover, while rehabilitation therapies such as Tai Chi and Baduanjin have shown promise in improving sleep disorders and motor symptoms in PD patients, their long-term effects and sustainability require further study. Research should explore long-term adherence and effectiveness, considering differences in efficacy across various patient populations, such as early- versus late-stage PD patients.

Future research directions for managing NMS in PD should include:

Objective Efficacy Assessment

Develop and validate objective assessment tools to better quantify the effects of alternative therapies on NMS.

Currently, there is a limited understanding of the mechanisms underlying these alternative therapies. Consequently, general findings often rely on subjective measurements of clinical improvement, which may introduce bias in the interpretation of results. A number of studies exploring the anti-Parkinsonian mechanisms of herbal components in animal models of PD provide clinical insights, utilizing objective indicators such as: the ethanolic extract of *Mucuna pruriens* (Mp) protects dopaminergic neurons in the substantia nigra from nitric oxide (NO)-induced damage in a paraquat (PQ)-induced PD mouse model;³⁴ Ursolic Acid (UA: 3 β -hydroxy-urs-12-en-28-oic acid) restored dopamine levels in MPTP-intoxicated mice;³⁵ and the ethanolic root extract of *Withania somnifera* (Ws) offers nigrostriatal dopaminergic neuroprotection against MB-PQ-induced Parkinsonism by modulating oxidative stress and apoptotic mechanisms,³⁶ among others. Certainly, many objective indicators observed in animal models are not readily accessible in clinical settings; thus, exploring biochemical markers from other tissue sites and relevant imaging indicators in corresponding regions could enhance the objectivity of the results.

Integrated Treatment Approaches

Explore integrated approaches that combine traditional and modern medicine to optimize overall management for PD patients.

The majority of existing studies tend to focus on specific therapies without exploring integrative approaches that may yield better outcomes for patients. For instance, combining cognitive behavioral therapy with pharmacological treatments or incorporating physical exercise alongside dietary modifications may enhance the overall effectiveness of the interventions. The feasibility of integrated treatment approaches varies across healthcare settings. In China, most comprehensive hospitals are equipped with specialists in Western medicine, TCM, acupuncture, and rehabilitation, facilitating multidisciplinary collaboration in the treatment of PD. By contrast, countries in Europe and North America possess some of the most advanced technologies and cutting-edge methodologies for clinical research and therapeutic development. However, their healthcare systems often face a shortage of experts in TCM and acupuncture, which are essential for exploring the full potential of integrated treatment approaches. This limitation makes it more challenging to implement and study these therapies in clinical practice, thereby affecting the feasibility of internationally applicable studies. Despite these constraints, international collaboration remains crucial to advancing integrative treatment strategies for global healthcare improvement.

Personalized Treatment

Investigate how to tailor alternative therapies based on individual symptoms, disease progression, and lifestyle to enhance efficacy and adherence.

The heterogeneity of NMS among PD patients complicates the assessment of treatment efficacy. NMS can vary significantly in type, severity, and duration, making it challenging to design studies that can generalize findings across the diverse patient population. The interplay between motor and non-motor symptoms further complicates the evaluation of alternative therapies, as improvements in one domain may not translate to the other. By tailoring treatments to individual symptoms, incorporating patient preferences, and monitoring outcomes through validated tools, clinicians can enhance the clinical relevance and applicability of alternative therapies.

Long-Term Follow-Up Studies

Conduct long-term studies to evaluate the durability and safety of alternative therapies, particularly those showing short-term benefits.

More robust funding and collaboration between researchers, healthcare providers, and patients are necessary to advance the field. Encouraging participation in clinical trials and promoting patient-centered research could provide valuable insights into the long-term effects and safety of alternative therapies for NMS.

Conclusion

In conclusion, alternative therapies for NMS in PD are emerging as viable options that circumvent the limitations of traditional pharmacological interventions. The accumulating evidence for their efficacy suggests a promising future for these treatments. The integration of early and personalized alternative therapies could significantly meet the unmet clinical demands in PD management. Despite their potential, research gaps remain, necessitating future studies to adopt stringent methodologies, expand sample sizes, and embrace integrative approaches. These efforts are crucial for deepening our understanding of alternative therapies and for enhancing the quality of life for individuals with PD.

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Disclosure

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