



RESEARCH ARTICLE

RECENT ADVANCEMENTS IN REHABILITATION OF PARKINSON DISORDER IN GERIATRIC POPULATION

1*Prakhar Garg, 1*Pinky Singh, 1*Soumya Srivastav and 2*Dr. Shivpriya Sharma

1*BPT, Sharda University

2*Assistant Professor, Shardauniversity

ARTICLE INFO

Article History:

Received 18th May, 2023
Received in revised form
10th June, 2023
Accepted 26th July, 2023
Published online 15th August, 2023

Key Words:

Good Corporate Governance,
Organizational Flexibility, Strategic
Change Management, Knowledge
Management, Organizational Performance.

ABSTRACT

Objective: To investigate the recent advancements in availability of a number of interventions/treatment strategies and their efficacy in treatment of Parkinson disorder. **Data Sources:** Searches were made until April 2020 from the electronic databases such as MEDLINE, PUBMED, PUBMED CENTRAL, PEDRO, COCHRANE, CINAHL. **Study Selection:** RCT's, Systematic Reviews, Meta Analysis, Clinical Trials were studied and compared with standard care, Parkinson disorder patients were included, majorly focussed on adult and older adult population, articles had to be available in English. **Data extraction:** Reviewers had independently studied the article without any biases and studied the complete full text, abstract, conclusion for eligibility. Data extraction included title of study, methodology, result, conclusion. **Conclusion:** The aim of study was to study the was to study all the latest advancements in management of Parkinson disorder under which we had studied various kind of intervention but we had founded that the musical therapy which was working on the principle of rhythmic auditory stimulation was directly or indirectly affecting the prognosis and the musical therapy was also showing the promising results in management of Parkinson disorder.

INTRODUCTION

Parkinson disease is a neurodegenerative ailment that typically manifests in later life with at least one of the other symptoms of resting tremor or rigidity and slowness of movements (bradykinesia). Loss of smell, sleeping disorder, mood disorders, excessive salivation, constipation, and excessive periodic limb movements while sleeping (REM behavior disorder) are additional symptoms Mild motor symptoms, RBD, hyposmia/anosmia (a frequent and extremely specific illness), comparatively general characteristic), neuropsychiatric manifestations (such as the presence of autonomic symptoms (such as sadness and anxiety), dizziness and fatigue, pain, and urinary and sexual dysfunction are currently the best-established prodromal features.^{[1][2]}The vagal nerve has a role in the transfer of pathology from relation between the CNS and the Enteric NS, as well as other well-known hereditary or environmental risk factors, such as type 2 diabetes or gastric pathology. Our understanding of how the illness progresses has been greatly expanded by the identification of these risk factors, early extrastriatal brain disease that appeared years before PD diagnosis, Lewy body pathology in peripheral organs, and prodromal symptoms of PD.^[2] Cardinal motor symptoms of PD include tremor, bradykinesia, rigidity, and postural instability.

Non-motor symptoms include rapid eye movement sleep disorder, anosmia, constipation, depression, cognitive decline, and dysautonomia. The enteric and ANS also function improperly, leading to symptoms like hyperhidrosis, dysuria, and orthostatic hypotension^[3] According to estimates, there will be 13 million instances of Parkinson's disease (PD) worldwide by 2040. 1 Males are typically affected by PD more commonly than females in observational studies, although the causes are unknown. A male prevalence of PD is less obvious in various regions of the globe (such Bolivia, Japan, and South Korea).Case identification (access to specialists), socioeconomic factors (health perspectives).^[4]insurance), or risk elements (such as a person's genetic makeup, their surroundings or interplay) may all be used to explain variations in prevalence. According to a research by Pringsheim *et al.* 3, the male/female prevalence ratio increased with age and dropped in Asian nations diagnosis: Reduced numbers of DA Brain cells in the substantia nigra pars compacta and characteristic intraneuronal A pathologically verified diagnosis of PD requires the presence of inclusions known as Lewy bodies (LBs) in regions of predilection. (SNc).^[5] pathogenetic theory says that, gastrointestinal system is where pathogenic alterations in PD first appear. Dysbiosis can affect the first stage of the subsequent cascade of neurodegeneration in PD by destroying integrity in intestinal epithelial barrier. Markers of intestinal barrier permeability such as fecal zonulin and -1-antitrypsin have been reported to be elevated in PD clients.

*Corresponding author: Dr. Shivpriya Sharma
Assistant Professor, Sharda University.

Additionally, it was discovered that stimulated intestinal mobility is associated with PD patients' decreased expression of tight junction proteins (TJs). Nevertheless, elevated fecal markers were not associated with other clinical PD features, indicating that a subset of PD patients should be considered when enlisting PD cohorts. Increased intestinal permeability in older, -synuclein transgenic mice led to the accumulation of -synuclein in dopaminergic neurons of the substantia nigra and enteric neurons, which ultimately resulted in neuronal degeneration.

In addition, LPS administration sped up the development of motor symptoms in ASO mice and impaired the integrity of the intestinal barrier.^[3] Electrophysiological recordings conducted in parkinsonian animals, such as monkeys treated with MPTP, show that the mean firing rate of neurons in the pallidal and cerebellar portions of the thalamus increases during tremor.

Single unit analyses and invasive recordings in Parkinson's disease (PD) show tremor-related activity in the thalamus and basal ganglia, which is consistent with prior studies.^[6] Physical therapy and exercise can help PD symptoms including gait impairment and freezing, postural instability, falls, and non-motor symptoms like depression, constipation, apathy, and exhaustion that are typically not helped by DRT. It is recommended that all individuals with a recent PD diagnosis engage in physical activity. On the other hand, those with advanced PD are more likely to suffer an accident when exercising and require a tailored strategy. Physical treatment at his point should concentrate on preventing falls and enhancing transfers, posture, balance and gait^[7].

MATERIALS AND METHODS

This study's goal was to evaluate each publication over the previous five years in regards to rehabilitation of Parkinson disorder various databases like Google scholar, pubmed were searched using keywords Parkinson disorder. Total 36 articles have been collected out of which 5 articles were excluded on the basis of exclusion criteria.

Systematic review is a almost gold standard type of study which re surfaces the useful and advanced evidence on the top for a particular topic to improvise the clinical decision making and to develop effective treatment strategies in regards to formulate the best treatment protocol for the improvement of patients as well as in clinical practices, In contrary to the actual research study the systematic review provides the wider group of discussions in order to go towards specificity in treatment. All the parameters and recommendations are been recorded in the form inclusion and exclusion criteria. Out of 36 articles 31 articles were included in the study and the 5 were excluded on the basis of deviation from the rehabilitation\

ELIGIBILITY CRITERIA AND RISK OF BIAS

CONDITIONS FOR INCLUSION

All the peer reviewed articles. Randomized controlled trials and systematic reviews and meta analysis published under pubmed databases. The studies done in recent 5 years. The studies which had worked on rehabilitation of parkinson disorder using physical rehabilitation. The articles which were having free excess were used

CONDITIONS FOR EXCLUSION

Studies other than systematic review, meta analysis and randomized control trials, clinical trials, Study focusing on the treatment of disorder using techniques other than physical rehabilitation and assistive rehabilitation, Articles published older than 5 years and The articles with paid access were excluded

INFORMATION SOURCES AND SEARCH COMBINATIONS

PUBMED AND MeSH databases, using keyword parkinson disorder, articles published under 5 years, the gold standard studies that is RCT and Systematic reviews, free full text articles. The search of articles had started with the keywords that is parkinson disorder, recent 5 years articles, on late adult population, all RCT and systematic reviews were included. Selection of the studies was done on the basis of the recent advancements in the rehabilitation/interventions used in the last 5 years for treatment in parkinson disorder and its associated symptoms. Data was extracted on the basis of the keywords and on the basis of the adherence to the topic i.e recent advancements in rehabilitation of parkinson disorder, and it's been listed in the tabular form below.

OUTCOME MEASURES USED IN THESE STUDIES

HOEHN AND YAHR SCALE: Grade- 0 to 5. Validity and reliability - scale has been used as a successful indicator of PD progression in clinical trial studies. Stage 1 = 2, Stage 2 = 11, Stage 2.5 = 6, Stage 3 = 3, and Stage 4 = 2. Specificity - 98% stage 3 Sensitivity - 21% stage 3.

UPDRS III: Total score ranged from 4 to 73 points. Validity and reliability - Inter-rater reliability was found to be adequate for the total UPDRS as well as the ADL. Sensitivity - 85% Specificity - 77%.

BERG BALANCE SCALE: 14 items scored, ranging with a maximum total score of 56, the scale ranges from 0 to 4 (0 denotes the lowest level and 4 the greatest level). Validity and reliability - minimal detectable change with 95% confidence varying between 2.8/56 and 6.6/56. Sensitivity - 82% Specificity - 67%.

TIME UP AND GO TEST: Grade -1 to 5 (1 indicates normal function and 5 indicates severely abnormal function). Validity and Reliability - The test is a valid and reliable method for measuring functional mobility that may be used to track changes in a patient's condition over time. Sensitivity - 80% Specificity - 56%.

PDQ39 SCORE QUESTIONNAIRE: Score - 39 items. This questionnaire used for Parkinson disease patients.

FGA TEST: Total score - 30. Validity and reliability - reliable and valid outcomes measure for assessing gait and balance deficits, reliability - 0.80

MINI BEST TEST: A 14-item exam with an emphasis on dynamic balance includes questions on anticipatory transitions, postural reactions, sensory orientation, and dynamic walking.

INTERVENTION	METHODOLOGY	RESULTS	CONCLUSION
MUSICAL THERAPY ^{[8], [9], [10], [11]}	1. Petra Pohl et al. conducted a randomized controlled experiment on 46 patients who were split into an intervention group and a control group to examine the effects of group-based music therapy on Parkinson's disease. 2. A group of people with Parkinson's disease were researched by Hyunjung Lee et al. to determine the benefits of music intervention, specifically on both motor and non-motor symptoms. while other related conditions such as Alzheimer's disease were excluded, under systematic review and meta analysis. 3. Manuel Joaquin Machado Sotomayor et al. conducted a comprehensive evaluation with 598 participants to examine the effects of music therapy in Parkinson's disease. 4. Mauro Murgia et al. conducted a randomized controlled experiment to examine the utility of footstep sound as rhythmic auditory stimulation for gait rehabilitation in Parkinson's disease. Their study was on 32 participant which were divided into two groups, groups are artificial RAS and Ecological RAS with outcome measure of Hoehn and yarn scale for 5 weeks.	1. Their research revealed a notable improvement in the importance of mood, alertness, and quality of life. 2. Their study had been done on 13 articles and had reported that musical therapy or interventions based on it can show the significant improvements in PD subjects, improvement was characterized in context of stride length, cadence, velocity, mobility, cognitive flexibility, inhibition, quality of life, sensitivity analysis. 3. According to their research, music therapy help individuals with Parkinson's disease live better. Additionally, they discovered the advantages of singing treatment programmes for Parkinson's disease patients, both individually as well as in groups, on communication, swallowing, breathing, and the emotional aspects. 4. In their study they had reported the both group interventions are improved by the biomechanical and clinical measures but ecological RAS showed more promising results on Spatio temporal parameters.	1. Their research proved valuable for improving quality of life and emotional alertness, but not for dual tasking or cognitive balance. 2. According to their research, the musically based intervention significantly reduces both the motor and non-motor symptoms experienced by PD patients. 3. Additionally, certain research focusing on the motor component, which may be addressed through listening, body rhythm, and rhythmic stimulation, were shown to be highly successful in enhancing the quality of daily life. 4. Their study's stance was that while both therapies were beneficial, the ecological RAS group was significantly superior based on data from exploratory analysis.
TRANSCRANIAL MAGNETIC STIMULATION ^[22]	1. Transcranial magnetic stimulation (rTMS) was used in a randomized, double-blind, placebo-controlled experiment with 51 volunteers who had Parkinson's disease. The subjects received 12 sessions of rTMS (25Hz, 1Hz, or Sham) before engaging in treadmill activity.	1. In their study they found that rTMS priming with 1hz and 25 hz can enhance the advantages of treadmill training and provide long-term effects of motor improvement for 3 months after intervention.	1. The main findings of their study was that treadmill training could enhance the long-term effects of motor development.
ACUPUNCTURE ^[23]	1. Jing - qi Fan et al. had studied the effect of Acupuncture for anxiety intervention under randomized controlled trial study on 64 parkinson disease patients which were divided into 2 groups: Real acupuncture group and Sam acupuncture group for 8 weeks.	1. In their study they had reported significant improvement in subjects of both groups but improvement was more prominent in the real acupuncture group quantified on the basis of HAM-A, UPDRS and PDQ-39 score.	1. They found in study that both of the interventions were useful for parkinson disease & anxiety but the subjects who had received Real acupuncture had responded better than the Sam acupuncture.
DIET ^[27]	1. Matthew CL Phillips et al had studied the effect of low-fat versus ketogenic diet under randomized controlled trial study on 47 patients which were divided into 2 groups: low -fat group and ketogenic group for 8 weeks.	1. In their study they had reported significant improvement in the subjects of both groups. But the ketogenic group showed better improvement in non - motor symptoms.	1. The findings of their study was that both groups have good intervention but the ketogenic group is more prominent than the low fat group.
TAI CHI ^[29]	1. In a study by Gen Li et al., 95 early-stage Parkinson's patients were separated into 3 groups: Tai Chi (32 patients), brisk walking (31 patients), and no exercise groups (32 patients), and the effects of long-term Tai Chi training on motor symptoms were examined.	1. In their research, they found that the Tai Chi group outperformed the control group on the step width, timed up and go, unified PD rating scale, and Berg Balance Scale assessments. Because of this, Tai Chi was more effective in improving BBS and Step Width than brisk walking.	1. They discovered that regular Tai Chi practice improves the balance and gait of persons with Parkinson's disease.
TREADMILL + MUSIC ^[30]	1. Rocco Salvatore Calabrò et al had studied the effect of Treadmill plus Music in which 50 patients with parkinson disease are chosen randomly and divided into GaitTrainer3 with and without RAS for at least 8 weeks of training.	1. Their study had reported that treadmill+music (Rhythmic auditory stimulation) had shown improvement in various gait parameters in the patient's with parkinson disorder.	1. They found that the rhythmic auditory stimulation can stimulate various cerebral centers which are responsible for gait abnormality in PD patients.
TELE-REHABILITATION ^[31]	1. Through database searches in PubMed, Medline, the Cochrane Library, Scopus, and PEDro, Chaira Vellata et al. conducted a systematic review to examine the benefits of telerehabilitation systems in treating both motor and non-motor symptoms, which included 421 Parkinson disease patients.	1. In their study they found that the telerehabilitation is found to be reasonable and effective in maintaining or improving the both clinical and non-clinical symptoms such as balance and gait, speech and voice, quality of life, etc in patients with PD.	1. They found that the telerehabilitation system is quite useful and found to be very effective in managing both clinical and other non-clinical effects.
SPORTS TRAINING ^[32]	1. Agnes Langer and colleagues have investigated the feasibility and efficacy of sport climbing at a single center using randomized controlled trials. semi-blind trial which includes 48 Parkinson disease patients who do not have any experience in climbing so they were divided into two groups: (for 12 weeks) sports climbing course (SC) and an unsupervised physical training group (UT).	1. In their study they found that the individuals who had received sports training had shown a very high degree of improvement in all motor as well as cognitive aspects of clients of PD.	1. Their study's main finding was that sport climbing is highly helpful and practicable for Parkinson patients who have mild to moderate symptoms.
SELFCARE REHABILITATION ^{[33], [34]}	1. JuHee Lee et al had studied the effects of use of mobile apps for self care in older age parkinson disorder patients under systematic review of literature on 17 studies. 2. Lorna Kenny et al had done studied about the needs and views of people with parkinson disorder in respect of wearable sensors and devices in order to get the best results with the use of technological rehabilitation.	1. In their study they had found that the use of mobile apps in self care rehabilitation is majorly focussing on the motor symptoms of PD which was measured with the help of sensors. 2. They had done 32 surveys by the parkinson disease patients and they had found that the patients with parkinson disease take these wearable sensors very positively and the patient majorly treat these devices as the instrument which is used to send data to their health care professional.	1. They had found that the strategies for self management are very insufficient for PD. There are no mobile apps present for PD patients but there is a need for more research in the domain of self management for various neurological conditions. 2. They had found that the wearable devices should be made according to the comfort of the patient, and the approach should be widened while thinking about the comfort factor of the devices.
SENSORY EXERCISE ^[35]	1. Eric N. Beck et al. conducted a non-randomized control study with 35 individuals who were split into two groups: PD-SAFEx and SHAM, in order to investigate if sensory focused exercise reduces anxiety.	1. In their study they have found some changes in the total score of Parkinson Anxiety Scale (PAS) questionnaire pre and post intervention of the sensory focused exercises. They have noticed the significant reduction in the SAFEx group whereas SHAM group did not Show such effects.	1. In their study they have reported that the SAFEx group shows a significant reduction in episodic anxiety scores but SHAM did not.
ELECTRICAL STIMULATION ^[36]	1. After meeting the inclusion criteria, Lorenzo Brognara et al. included 11 papers in their study of the impact of mechanical plantar foot stimulation in Parkinson's disease under both clinical and randomized control trials.	1. According to their research, raising BDNF levels and lowering cortisol levels in the blood can both enhance patient's quality of life and their mental health. Additionally, it has positive effects on orthostatic hypotension, which may significantly reduce the patient's risk of falling and increase the improvement in gait metrics and sensory foot sense.	1. It has been shown that mechanical foot sensory stimulation is a valid neuro-rehabilitative therapy for Parkinson's disease (PD) symptoms associated with gait impairment; however, long term studies are required to demonstrate the efficacy of these therapies in avoiding falls in PD patients.

For the mini-best test, reliability was greater (ICC:0.96). Sensitivity - 85%. Specificity -75%.

MMSESCORE: Totalscore-30,25-30=normal,21-24=mild,10-20=moderate,9or lower = severe dementia. Validity - [0.76(0.67,0.85)]. Reliability - moderate high levels of reliability. Sensitivity - 0.87%. Specificity -0.82%

DISCUSSION

Our research purpose was to look at the recent advancement in rehabilitation of parkinson disorder in 5 years articles in which we had studied the various kind of new interventions in rehabilitation of parkinson disorder such as music therapy, dance therapy, sensory exercise, treadmill+music and acupuncture however we had studied various interventions too but these had shown very significant improvement not only in motor aspect but on the holistic health which is the need of the hour in present scenario in respect of the complete well being of the patient, the studies had also taken fall assessment into the consideration which is a very relevant and most important key factor in multiple neurological conditions these interventions are not merely only related to parkinson disorder but can also be used in symptomatic management of various disorders.

Music Therapy: The music-based intervention shows a noticeable improvement in multitasking tasks that require participants to quickly switch attention between motor and cognitive tasks while interpreting visual symbols, synchronizing arms and legs in complex coordinated movements, and simultaneously pronouncing a specific word to the beat of music. For individuals with PD, music-based treatment was proposed as complementary management alternatives. For instance, it has been demonstrated that dancing enhances cognitive multitasking, results linked to gait, and general cognitive abilities. Clients with PD frequently experience difficulties in motor-cognition related dual tasking, which can be alleviated with focused therapies. Studies have concentrated on the motor aspect, which may be improved through listening, body rhythm, and rhythmic auditory stimulation. In order to enhance the quality of life of patients with Parkinson's disease, programmes that emphasize singing, either individually or in groups, have been shown to have positive impacts on communication, swallowing, breathing, and the emotional side.

Dance Therapy: Dance therapy is a very efficient method for Parkinson's disease patients to recover. This method can help Parkinson's disease patients with their posture, core strength, and coordination. Dance therapy is also very beneficial for improving gait training and enhancing motor function through dance steps.

Sensory exercise: Anxiety is a non-motor symptom that first manifests in Parkinson's disease (PD) patients early in the illness progression, usually before motor symptoms, and has been linked to sensory symptoms and sensory abnormalities that affect balance and motor coordination. A study found that anxiety had less of an impact on walking when sensory feedback in virtual reality that simulated stepping on a plank was provided. These results provide credence to the hypothesis that anxiety may have a lessened effect on mobility by emphasizing sensory uncertainty reduction approaches.

Overall, sensory feedback, attention, and anxiety may all play a role in the movement abnormalities associated with Parkinson's disease. Attentional focused exercise to reduce sensory ambiguity may be a beneficial rehabilitative therapy for PD patients to help them feel less anxious. Electrical Stimulation: Different stimulation procedures have been assessed with regard to the instrument and pressure employed. The majority of research applied mechanical stimulation to the plantar foot, stimulating the head of the big toe and the base of the first metatarsal bone. Mechanical plantar foot stimulation has been shown to affect spatiotemporal gait parameters differently in several studies. Plantar stimulation of the foot improved sensory awareness at the foot level. Improvements in other organs and tissues, such as muscle activity, autonomic regulation of heart rate and blood pressure, and blood levels of the neurotrophins brain derived neurotrophic factor (BDNF) and cortisol, were seen along with the beneficial effects of mechanical plantar foot stimulation on gait. The improvement in BDNF levels after plantar stimulation as well as the improvements to TUG performance, stride length, and gait speed. One of BDNF's roles is to maintain the survival and growth of dopaminergic neurons by stopping the apoptosis-mediated cell death and degeneration that would otherwise occur. According to the study, increasing BDNF levels and lowering cortisol levels in the blood has a positive impact on patient's mental health and improves their quality of life. By reducing their risk of falling, these individuals may gain significantly from the orthostatic hypotension-beneficial effects of plantar foot stimulation.

CONCLUSION

The study's objective was to review the present literature of last 5 years from various databases such as pubmed, pubmed central, google scholar, pedro for the management of parkinson disorder which had majorly focused upon the alternative therapies and its effects such as musical therapy, dance therapy, combination therapy (such as treadmill + music), and we have found that the effects of musical therapy which had worked on the principle of rhythmic auditory stimulation and had shown the best promising results in not merely the motor symptoms but also had shown improvement in cognition, confidence etc. the similar study in which musical therapy was connected with the treadmill training, even in dance therapy too musical therapy was used. So in this study we conclude that combining conventional therapeutic approaches with musical therapy will show promising results in clinical practices.

Conflict Of Interest: The author had reported that there is no conflict of interest.

GLOSSARY OF ABBREVIATIONS

PD = Parkinson Disorder
Hoehn And Yarn Scale
BBS = Besrg Balance Scale
REM = Rapid Eye Movement

REFERENCES

1. Zafar, S. and Yaddanapudi, S.S., 2022. Parkinson disease. In *StatPearls [Internet]*. StatPearls Publishing.
2. Schrag, A., Bohlken, J., Dammertz, L., Teipel, S., Hermann, W., Akmatov, M.K., Bätzing, J. and Holstiege,

- J., 2023. Widening the Spectrum of Risk Factors, Comorbidities, and Prodromal Features of Parkinson Disease. *JAMA neurology*, 80(2), pp.161-171.
3. Zhu, M., Liu, X., Ye, Y., Yan, X., Cheng, Y., Zhao, L., Chen, F. and Ling, Z., 2022. Gut Microbiota: A novel therapeutic target for Parkinson's disease. *Frontiers in Immunology*, p.3123.
 4. Zirra, A., Rao, S.C., Bestwick, J., Rajalingam, R., Marras, C., Blauwendraat, C., Mata, I.F. and Noyce, A.J., 2023. Gender Differences in the Prevalence of Parkinson's disease. *Movement Disorders Clinical Practice*, 10(1), pp.86-93.
 5. Alexander, G.E., 2022. Biology of Parkinson's disease: pathogenesis and pathophysiology of a multisystem neurodegenerative disorder. *Dialogues in clinical neuroscience*.
 6. Dirkx, M.F. and Bologna, M., 2022. The pathophysiology of Parkinson's disease tremor. *Journal of the Neurological Sciences*, p.120196.
 7. Barbosa, E.R., Limongi, J.C.P., Chien, H.F., Barbosa, P.M. and Torres, M.R.C., 2022. How I treat Parkinson's disease. *Arquivos de Neuro-Psiquiatria*, 80, pp.94-104.
 8. Pohl, P., Wressle, E., Lundin, F., Enthoven, P. and Dizdar, N., 2020. Group-based music intervention in Parkinson's disease—findings from a mixed-methods study. *Clinical rehabilitation*, 34(4), pp.533-544.
 9. Lee, H. and Ko, B., 2023. Effects of Music-Based Interventions on Motor and Non-Motor Symptoms in Patients with Parkinson's Disease: A Systematic Review and Meta-Analysis. *International Journal of Environmental Research and Public Health*, 20(2), p.1046.
 10. Machado Sotomayor, M.J., Arufe-Giráldez, V., Ruíz-Rico, G. and Navarro-Patón, R., 2021. Music therapy and Parkinson's disease: a systematic review from 2015–2020. *International journal of environmental research and public health*, 18(21), p.11618.
 11. Murgia, M., Pili, R., Corona, F., Sors, F., Agostini, T.A., Bernardis, P., Casula, C., Cossu, G., Guicciardi, M. and Pau, M., 2018. The use of footstep sounds as rhythmic auditory stimulation for gait rehabilitation in Parkinson's disease: a randomized controlled trial. *Frontiers in neurology*, 9, p.348.
 12. Feng, H., Li, C., Liu, J., Wang, L., Ma, J., Li, G., Gan, L., Shang, X. and Wu, Z., 2019. Virtual reality rehabilitation versus conventional physical therapy for improving balance and gait in Parkinson's disease patients: a randomized controlled trial. *Medical science monitor: international medical journal of experimental and clinical research*, 25, p.4186.
 13. Kashif, M., Ahmad, A., Bandpei, M.A.M., Gilani, S.A., Hanif, A. and Iram, H., 2022. Combined effects of virtual reality techniques and motor imagery on balance, motor function and activities of daily living in patients with Parkinson's disease: a randomized controlled trial. *BMC geriatrics*, 22(1), pp.1-14.
 14. Ashburn, A., Pickering, R., McIntosh, E., Hulbert, S., Rochester, L., Roberts, H.C., Nieuwboer, A., Kunkel, D., Goodwin, V.A., Lamb, S.E. and Ballinger, C., 2019. Exercise-and strategy-based physiotherapy-delivered intervention for preventing repeat falls in people with Parkinson's: the PDSAFE RCT. *Health Technology Assessment (Winchester, England)*, 23(36), p.1.
 15. Ferreira, R.M., Alves, W.M.G.D.C., Lima, T.A.D., Alves, T.G.G., Alves Filho, P.A.M., Pimentel, C.P., Sousa, E.C. and Cortinhas-Alves, E.A., 2018. O efeito do treinamento resistido sobre sintomas de ansiedade e qualidade de vida em idosos com doença de Parkinson's: ensaio randomizado controlado. *Arquivos de Neuro-Psiquiatria*, 76(8), pp.499-506.
 16. Sangarapillai, K., Norman, B.M. and Almeida, Q.J., 2021. Boxing vs sensory exercise for Parkinson's disease: A double-blinded randomized controlled trial. *Neurorehabilitation and Neural Repair*, 35(9), pp.769-777.
 17. Bhidayasiri, R., Phuenpathom, W., Tan, A.H., Leta, V., Phumphid, S., Chaudhuri, K.R. and Pal, P.K., 2022. Management of dysphagia and gastroparesis in Parkinson's disease in real-world clinical practice—Balancing pharmacological and non-pharmacological approaches. *Frontiers in Aging Neuroscience*, 14.
 18. Ramig, L., Halpern, A., Spielman, J., Fox, C. and Freeman, K., 2018. Speech treatment in Parkinson's disease: Randomized controlled trial (RCT). *Movement Disorders*, 33(11), pp.1777-1791.
 19. Hasan, S.M., Alshafie, S., Hasabo, E.A., Saleh, M.M., Elnaiem, W., Qasem, A., Alzu'bi, Y.O., Khaled, A., Zaaouee, M.S., Ragab, K.M. and Nourelden, A.Z., 2022. Efficacy of dance for Parkinson's disease: a pooled analysis of 372 patients. *Journal of Neurology*, 269(3), pp.1195-1208.
 20. Kwok, J.Y.Y., Kwan, J.C.Y., Auyeung, M., Mok, V.C.T., Lau, C.K.Y., Choi, K.C. and Chan, H.Y., L.(2019). *Effects of mindfulness Yoga vs stretching and resistance training exercises on anxiety and depression for people with Parkinson disease: A randomized clinical trial. JAMA Neurology*, 76(7), pp.755-763.
 21. Johansson, M.E., Cameron, I.G., Van der Kolk, N.M., de Vries, N.M., Klimars, E., Toni, I., Bloem, B.R. and Helmich, R.C., 2022. Aerobic exercise alters brain function and structure in Parkinson's disease: a randomized controlled trial. *Annals of Neurology*, 91(2), pp.203-216.
 22. Chung, C.L.H., Mak, M.K.Y. and Hallett, M., 2020. Transcranial magnetic stimulation promotes gait training in Parkinson disease. *Annals of neurology*, 88(5), pp.933-945.
 23. Fan, J.Q., Lu, W.J., Tan, W.Q., Liu, X., Wang, Y.T., Wang, N.B. and Zhuang, L.X., 2022. Effectiveness of acupuncture for anxiety among patients with Parkinson disease: a randomized clinical trial. *JAMA Network Open*, 5(9), pp.e2232133-e2232133.
 24. Gilat, M., Coeytaux Jackson, A., Marshall, N.S., Hammond, D., Mullins, A.E., Hall, J.M., Fang, B.A., Yee, B.J., Wong, K.K., Grunstein, R.R. and Lewis, S.J., 2020. Melatonin for rapid eye movement sleep behavior disorder in Parkinson's disease: a randomised controlled trial. *Movement Disorders*, 35(2), pp.344-349.
 25. Brakedal, B., Dölle, C., Riemer, F., Ma, Y., Nido, G.S., Skeie, G.O., Craven, A.R., Schwarzlmüller, T., Brekke, N., Diab, J. and Sverkeli, L., 2022. The NADPARK study: A randomized phase I trial of nicotinamide riboside supplementation in Parkinson's disease. *Cell metabolism*, 34(3), pp.396-407.
 26. Picillo, M., Phokaewvarangkul, O., Poon, Y.Y., McIntyre, C.C., Beylertgil, S.B., Munhoz, R.P., Kalia, S.K., Hodaie, M., Lozano, A.M. and Fasano, A., 2021. Levodopa versus dopamine agonist after subthalamic stimulation in Parkinson's disease. *Movement Disorders*, 36(3), pp.672-680.

27. Phillips, M.C., Murtagh, D.K., Gilbertson, L.J., Asztely, F.J. and Lynch, C.D., 2018. Low-fat versus ketogenic diet in Parkinson's disease: a pilot randomized controlled trial. *Movement Disorders*, 33(8), pp.1306-1314.
28. Capecci, M., Pournajaf, S., Galafate, D., Sale, P., Le Pera, D., Goffredo, M., De Pandis, M.F., Andrenelli, E., Pennacchioni, M., Ceravolo, M.G. and Franceschini, M., 2019. Clinical effects of robot-assisted gait training and treadmill training for Parkinson's disease. A randomized controlled trial. *Annals of physical and rehabilitation medicine*, 62(5), pp.303-312.
29. Zhang, L., Jiang, W.F. and Sun, C.H., 2017. Progress in Tai Chi Quan for treatment of motor and non-motor symptoms of Parkinson's disease. *Journal of Neurology and Neurorehabilitation*, 13, pp.138-41.
30. Calabrò, R.S., Naro, A., Filoni, S., Pullia, M., Billeri, L., Tomasello, P., Portaro, S., Di Lorenzo, G., Tomaino, C. and Bramanti, P., 2019. Walking to your right music: a randomized controlled trial on the novel use of treadmill plus music in Parkinson's disease. *Journal of neuroengineering and rehabilitation*, 16(1), pp.1-14.
31. Vellata, C., Belli, S., Balsamo, F., Giordano, A., Colombo, R. and Maggioni, G., 2021. Effectiveness of telerehabilitation on motor impairments, non-motor symptoms and compliance in patients with Parkinson's disease: A systematic review. *Frontiers in Neurology*, 12, p.627999.
32. Langer, A., Hasenauer, S., Gassner, L., Pokan, R., Dabnichki, P., Wizany, L., Gruber, J., Roth, D., Zimmel, S., Treven, M. and Schmoeger, M., 2021. A randomised controlled trial on effectiveness and feasibility of sport climbing in Parkinson's disease. *npj Parkinson's Disease*, 7(1), p.49.
33. Lee, J., Yeom, I., Chung, M.L., Kim, Y., Yoo, S. and Kim, E., 2022. Use of mobile apps for self-care in people with Parkinson disease: systematic review. *JMIR mHealth and uHealth*, 10(1), p.e33944.
34. Kenny, L., Moore, K., O'Riordan, C., Fox, S., Barton, J., Tedesco, S., Sica, M., Crowe, C., Alamäki, A., Condell, J. and Nordström, A., 2022. The Views and Needs of People With Parkinson Disease Regarding Wearable Devices for Disease Monitoring: Mixed Methods Exploration. *JMIR Formative Research*, 6(1), p.e27418.
35. Beck, E.N., Wang, M.T., Intzandt, B.N., Almeida, Q.J. and Ehgoetz Martens, K.A., 2020. Sensory focused exercise improves anxiety in Parkinson's disease: A randomized controlled trial. *Plos one*, 15(4), p.e0230803.
36. Brognara, L. and Cauli, O., 2020. Mechanical Plantar Foot Stimulation in Parkinson's Disease: A Scoping Review. *Diseases*, 8(2), p.12.
