Efficacy of osteopathic manipulative treatment in patients with Parkinson’s disease: a narrative review

Raymond Li*, OMS IV, Ann Jose, OMS IV, Jessica Poon, OMS IV, Cindy Zou, OMS IV, Maria Istafanos, OMS IV and Sheldon C. Yao, DO

https://doi.org/10.1515/jom-2021-0081
Received March 9, 2021; accepted July 7, 2021; published online September 22, 2021

Abstract

Context: Parkinson’s disease (PD) is a neurodegenerative disease that leads to impaired motor and non-motor function in patients. PD is non-curative and gradually reduces quality of life, leading patients to seek treatment for symptom management. Osteopathic manipulative treatment (OMT) applies the biomechanical, neurologic, circulatory, metabolic, and psychosocial models in approaching and treating the major symptomatology of PD patients.

Objectives: This article evaluates the literature published in the past 10 years analyzing evidence on OMT and its functional application on gait, balance, motor function, bradykinesia, and autonomic dysfunctions, and to identify promising avenues for further investigation.

Methods: The authors obtained studies from the research databases MEDLINE/PubMed, ScienceDaily, and EBSCO, as well as the Journal of American Osteopathic Association’s published archives. Searches were conducted in December 2020 utilizing the search phrases “OMM” (osteopathic manipulative medicine), “OMT,” “osteopathic,” “Parkinson Disease,” “manual therapy,” “physical therapy,” “training,” “autonomics,” “gait,” and “balance.” Articles published between 2010 and 2021 including subjects with Parkinson’s disease and the use of OMT or any other form of manual therapy were included. Five authors independently performed literature searches and methodically resolved any disagreements over article selection together.

Results: There were a total of 10,064 hits, from which 53 articles were considered, and five articles were selected based on the criteria.

Conclusions: The progressive nature of PD places symptom management on the forefront of maintaining patients’ quality of life. OMT has demonstrated the greatest efficacy on managing motor-related and neurologic symptoms and assists in treating the greater prevalence of somatic dysfunctions that arise from the disease. Research in this field remains limited and should be the target of future research.

Keywords: OMM; OMT; osteopathic manipulative treatment; Parkinson disease; therapy.

Parkinson’s disease (PD) is one of the most common neurodegenerative diseases, with patients developing classic motor and non-motor symptoms as the disease progresses [1]. Motor symptoms include bradykinesia, stiffness, resting tremor, and postural instability, while non-motor symptoms include cognitive and autonomic impairment and depression [1, 2]. Because PD remains non-curative, treatments focus on managing symptoms and slowing disease progression [1, 3]. Conventional treatments are primarily pharmacologic; more invasive treatments, such as deep brain stimulation, are reserved for use in advanced disease [1]. Specialty care with physiotherapists, occupational therapists, speech and language therapists, and dietitians is considered if applicable to symptomatology [4].

Extensive research has been conducted on physical therapy and other forms of exercise therapies and their benefits on the PD population [5–7]. Improvements have been found in handgrip strength, aerobic endurance, gait speed, flexibility, and balance when exercise therapies were utilized in conjunction with pharmacological treatment [7]. Benefits extend into mental well-being, with another study finding a decrease in PD symptoms and depression with aerobic training [8]. The function of other
complementary considerations in treating the various symptomatology of PD have varying degrees of support: the evidence for yoga is high, whereas evidence for other activities like tai chi, acupuncture, manipulative practices, and meditation have moderate to low evidence for helping symptoms [4]. Even so, patients and researchers alike continue to search for alternative treatments to alleviate the debilitating symptoms of PD.

In osteopathic medicine, somatic dysfunction describes the impaired or altered function of various body components including the somatic, skeletal, myofascial, vascular, lymphatic, and neural systems [9]. Osteopathic manipulative treatment (OMT) aims to promote homeostasis by targeting and treating these somatic dysfunctions to improve biomechanical, neurological, circulatory, metabolic, and behavioral functions [9]. Given the prominence of both motor and non-motor symptoms in PD, as well as the use of specialist care in treatment plans, OMT has presented itself as a treatment modality to reduce symptoms and improve quality of life. Ever since the landmark study in 1999 by Wells [10] demonstrated statistically significant improvements in gait patterns such as stride length and cadence after OMT treatment, the effectiveness of OMT as a resource for PD patients has been explored with growing interest and intriguing results.

OMT can improve the biomechanical functions of joints and muscles, leading researchers to consider OMT as a possibility to manage musculoskeletal symptoms of PD by promoting more fluid motion in the extremities and trunk [10]. While a previous retrospective cohort study of 490 patients [11] found PD patients to have a higher incidence of musculoskeletal pain compared to control with a hazard ratio of 1.31, direct studies on the effect of OMT on musculoskeletal pain specifically in PD patients have not been conducted. However, a study of 16 PD patients [12] determined postural deformities of PD patients as a major contributor to worse back function and pain. An abstract retrospectively examining the charts of 80 PD patients [13] found a greater prevalence of cranial and cervical dysfunctions in PD patients compared to the control group, with dysfunctions found in significantly more body regions. OMT utilizes a variety of techniques to treat dysfunctions, including spinal manipulation, which according to one literature review of 14 articles determined that spinal manipulation has a positive outcome on PD patients’ symptomatology [14].

Neurologic symptoms in PD patients are most apparent through bradykinesia (generalized slow movement), shuffling, freezing (abrupt cessation of movement during walking), and other gait impairments [15]. While interest in utilizing OMT to treat neurologic symptoms of PD remains high, a systematic review in 2016 of 10 articles [16] evaluating OMT’s efficacy in patients with neurologic diseases revealed the scarcity and heterogeneity of literature on this topic. One study of 27 subjects [17] utilized standard-of-care soft-tissue articulatory and muscle energy OMT techniques on PD patients to increase mobility and range of motion. Although quantitative pre-post scores did not show statistically significant results between treatment and sham (control) groups, clinically significant trends toward improvement were revealed and patients commented on benefits post-treatment that carried over to other activities of daily living [17]. Another study [18] comparing 30 PD patients with 20 controls observed a greater frequency of cranial strain patterns in PD patients than the controls, with the frequency decreasing over subsequent visits and treatments.

Autonomic instability is a major component of PD that affects all organ systems of the body yet is often under-diagnosed [1]. OMT influences the autonomic nervous system (ANS) by increasing parasympathetic and decreasing sympathetic activity via a vagal response, leading to autonomic improvements [19, 20]. Unfortunately, while there are extensive treatment options for controlling symptoms such as dysphagia, gastroparesis, constipation, bladder incontinence, and sexual dysfunction [21], studies researching the efficacy of OMT on autonemics in PD patients remain very limited.

The purpose of this study is to conduct a narrative review that provides current information from the past 10 years regarding the use and success of OMT as a treatment option for musculoskeletal, neurologic, and autonomic symptoms of PD.

Methods

Studies were obtained from the research databases MEDLINE/PubMed, ScienceDaily, and EBSCO, as well as the Journal of American Osteopathic Association’s published archives. Searches were done once on August 11, 2019, and again on February 28, 2021. The key words utilized during the search were “OMM” (osteopathic manipulative medicine), “OMT,” “osteopathic,” “Parkinson Disease,” “manual therapy,” “physical therapy,” “training,” “autonemics,” “gait,” and “balance.”

Studies were selected through the following inclusion criteria: article published between 2010 and 2021; subjects included Parkinson’s disease patients; and techniques included OMT or other forms of manual therapy utilizing similar techniques. Exclusions included case studies, conference abstracts, and articles not in English.

Five authors (R.L., A.J., P.P., C.M., M.I.) independently performed literature searches on PubMed, ScienceDaily, EBSCO, and the Journal of American Osteopathic Association’s published archives. The selected articles were collectively reviewed by all authors to apply the selection criteria and to settle any disagreements. Articles that did not perform OMT or other manual therapies on PD patients were excluded. For manual therapies to be included, the utilized
technique was evaluated for similarity in execution and theory to an existing OMT technique. After selection, data were extracted from the articles detailing study size, study design, treatments given, and outcomes reported. Finally, the selected articles were examined for limitations and deficiencies that may inform direction for future research.

Abstracts and posters that examined the use of OMT in PD patients were excluded in the Results but will be discussed in the Discussion as they identify promising areas for further investigation. The methods are summarized in the PRISMA diagram in Figure 1.

Results

There were a total of 10,064 hits, from which 53 articles were considered and five articles [22–26] were selected based on the criteria. While many published articles discussed either the efficacy of OMT or treatments for PD, few analyzed the use of OMT specifically for the treatment or symptom management of PD. Details on the articles are summarized in Table 1.
Table 1: The methods and findings of the articles found based on the inclusion and exclusion criteria of this study.

| Study                      | No. of subjects | Methods                                                                 | Findings                                                                                                                                 |
|----------------------------|-----------------|-------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| DiFrancisco-Donoghue et al. [22] | 11 PD subjects (6 received counseling followed by OMM, 5 received OMM first followed by counseling) | 5 subjects were placed in a control group, which received counseling for 6 weeks followed by OMM for 6 weeks. 6 subjects were placed in an OMM group, which received OMM for 6 weeks followed by counseling for 6 weeks. OMM was administered twice a week for 30 min each session, performing the same techniques each time. Counseling, which was once weekly for 60 min, consisted of mental health, diet, exercise, wellness techniques, etc. Subjects completed the SOT, Mini-BESTest, MDS-UPDRS during day 1 and week 6. Note: During the study, two subjects dropped out, making the total 9 subjects. | The MDS-UPDRS showed statistically significant changes after OMM in both the control and experimental group (OMM improved −1.7 ± 12.3 vs. control 3.2 ± 10.7), p=0.021. The Mini-BESTest showed no significant change (OMM 2.1 ± 2.4 vs. control 2.7 ± 2.7), p=0.21. SOT showed no statistically significant improvement (OMM 4.8 ± 5.1 vs. control 1.8 ± 6.0), p=0.39. |
| Donoyama et al. [23]       | 21 PD subjects   | The 21 PD patients received one 40 min whole-body Anma massage session (excluding the face, head, and abdomen). Six patients went on to do continuous weekly Anma massages for 7 weeks. VAS scores, which show how patients would rank the severity of symptoms along a 100 mm length of paper, were done after each session to determine any improvements. | After one Anma massage session: Muscle stiffness decreased (22.3 [mean] ± 18.3 [SD] vs. 52.0 ± 26.3, p=0.001). Movement difficulties improved (18.2 ± 13.2 vs. 48.6 ± 19.8; p=0.0019). Pain improved (27.2 ± 20.4 vs. 55.7 ± 19.5; p=0.048). Fatigue decreased (26.9 ± 26.8 vs. 48.9 ± 29.3; p=0.0047). Upper limb function improved on timed pegboard test (36.8 ± 14.5 s vs. 39.9 ± 14.6 s; p=0.002). Gait speed was shorter (19.4 ± 3.8 s vs. 20.4 ± 4.5 s, p=0.0017). Stride length was longer (60.4 ± 7.4 cm, vs. 57.7 ± 7.6 cm, p=0.0011). Cadence showed little change (120.4 ± 12.7 m vs. 119.0 ± 14.5 m, p=0.3336). Shoulder increased ROM (flexion, 147 ± 13.6 vs. 136.5 ± 17.8 before, p=0.0040) (abduction, 147 ± 14.0 vs. 130.5 ± 18.0; abduction, p=0.0039). Results from the group that received one treatment and the continuous group were very similar. |
| Zhao et al. [24]           | 36 PD subjects (22 in CMT group, 14 in control group) | The treatment group received CMT consisting of dry-land swimming for 30 min/day and paraspinal muscle relaxation for 3 min followed by stretching exercises for 3 min. Clinical characteristics such as motor, balance, and cardiac function were measured at baseline, 6 months, and 12 months using UPDRS, BBS, and TUG scores along with LVEF. Biochemical tests were also done at 0 and 12 months upon the completion of the study. | In the CMT group: BBS improved from 42.36 (±10.04) to 46.09 (±9.4) over 1 year (p=0.005) UPDRS dropped from 67.97 (±5.63) to 43.57 (±24.88) in CMT group (p=0.001) In the control group: BBS worsened from 43.36 (±5.84) to 39.36 (±6.62) over 1 year (p=0.008). UPDRS increased from 57.18 (±21.56) to 69.82 (±23.56) in control group (p=0.001) |
| Muller and Pietsch [25]    | 18 PD subjects   | The PD patients received 2 days of treatment, with one gait training session and one OCF session each day. A 10 m walking test was conducted directly before and after each treatment session to assess the interval and frequency of steps. | Gait training reduced the number of steps (p<0.05) by 0.75 steps/10 m (SD ± 1.0) but not the interval. OCF reduced the interval (p<0.01) by 0.5 s/10 m (SD ± 0.7) but not step quantity. There were significant correlations between UPDRS gait score and the computed differences in the number of steps (R=0.68) and intervals (R=−0.63). |
**Table 1**: (continued)

| Study | No. of subjects | Methods | Findings |
|-------|-----------------|---------|----------|
| Mancini et al. [26] | 6 PD subjects | The PD patients were followed for 10 weeks (4 weeks control, 4 weeks with weekly OMM treatment, and 2 weeks no intervention), with stool samples collected at weeks 3, 5, 7, 9, and 10. Treatment sessions targeted the ANS, ENS, thoracic excursion, and pelvic floor. Microbial changes from pre- to post-OMM were analyzed using two-tailed, repeated-measures ANOVA. Constipation and quality of life were measured by PAC-SYM and PAC-QOL surveys. | Mean constipation severity significantly decreased (p=0.010, d=1.508) | Mean quality of life significantly improved (p=0.041, d=1.072) There were changes to different normalized phyla (Actinobacteria p=0.040, d=0.845; Verrucomicrobia p=0.024, d=0.675; Roseburia p=0.033, d=1.109; Interinstimonas p=0.035, d=0.627; Anaerotruncus p=0.004) |

ANOVA, analysis of variance; ANS, autonomic nervous system; ENS, enteric nervous system; LVEF, left ventricular ejection fraction; MDS, Movement Disorder Society; OCF, osteopathy in the cranial field; OMM, osteopathic manipulative medicine; PAC-QOL, Patient Assessment of Constipation-Quality of Life; PAC-SYM, Patient Assessment of Constipation-Symptoms; PD, Parkinson’s disease; ROM, range of motion; SD, standard deviation; SOT, sensory organization test; TUG, timed up and go; UPDRS, Unified Parkinson’s Disease Rating Scale; VAS, Visual Analog Scale.

**Discussion**

**Effectiveness of OMT/manual therapy on motor function**

Gait, balance, and motor function are compromised in PD, impairing patients’ ability to perform activities of daily living and maintain independence [3]. These issues are caused in part by rigidity, muscle tension, and poor postural reflexes [22]. In an attempt to tackle this, one study of 11 PD patients [22] explored the effects of OMT on motor function, balance, and gait stability by treating the spine and extremities with myofascial, muscle energy, articulatory, and compression of the fourth ventricle (CV4) techniques. Patients were divided into two groups; one group received weekly counseling for 6 weeks followed by OMT twice a week for 6 weeks, while the other group received OMT before counseling. This design was chosen to control for order effect. After OMT, on average, a statistically significant improvement was found in motor function (4.3%) but not in balance [22]. Overall, a clinical significance was observed; gait, balance, and motor function all improved in both the experimental group receiving OMT and the control group. While there was no overall statistical significance, this study is limited by its small sample size. Nonetheless, this article introduces a set OMT protocols that has the potential to improve the quality of life for PD patients.

A before-and-after study with 21 PD patients [23] found significant improvement in movement restriction through the use of Anma massage in reducing muscle stiffness by 57.1%, movement difficulties by 62.6%, pain by 48.8%, and fatigue by 51.2%; in addition, gait speed was 5.0% faster, stride length 4.7% longer, and shoulder mobility improved 7.7% in flexion and 12.6% in abduction. Anma massage utilizes techniques such as kneading, stroking, and pressing in rhythmic motions to target muscles and joints, traditionally along meridians [23]. Reported findings were similar whether the patient had a single Anma massage or weekly massages for 7 weeks [23]. While not identical, Anma massage finds some similarities to OMT myofascial release, which is a soft tissue technique that engages the tissue barrier to relieve tension [27]. These results suggest a possible use of myofascial release to reduce movement restrictions in PD patients and should be a point of further research.

**Effectiveness of OMT/manual therapy on neurologic function**

A study with 36 PD patients [24] examined how coordination and manipulation therapy (CMT), a combination of exercise therapy and paraspinal muscle stretching, could improve the motor skills, balance, and cardiac functions in PD patients. Patients in the CMT group performed dry-land swimming and paraspinal manipulation therapy for 30 min every weekday compared to the control group. Over 1 year, findings revealed that patients who underwent CMT had improved their Berg Balance Scale scores by 8.8%, and
their Unified Parkinson’s Disease Rating Scale (UPDRS) scores dropped by 35.9%, while the opposite was found to be true for the control group (BBS worsened 9.2% and UPDRS increased by 22.1%) [24]. This suggests that PD patients who undergo regular training have improved motor skills and balance compared to those who do not. Paraspinal manipulation aimed at relaxing the multifidus muscle for the CMT group is thought to slow the degradation of the muscle and thus improve spinal stability and limb coordination, although the exact effects of manipulation were not measured [24]. Paraspinal muscle stretching is among one of the techniques also utilized in OMT, and physicians can utilize this overlap to provide symptomatic and clinical benefits to improve the quality of life of patients and to delay the progression of PD. Because the myofascial technique was utilized in conjunction with exercise therapy, the use of this technique should be combined with exercise therapy until future studies explore the clinical benefits of manipulation alone.

One study [25] of 18 PD patients sought to address gait asymmetry, stride length changes, shuffling, and postural stooping with osteopathic cranial manipulative medicine (OCMM), which is utilized in practice for pain, gross motor function, and ANS function [28]. Each patient underwent one gait training and one OCMM session over 2 days, doing a 10 m walking test before and after each training and session. Nine patients were evaluated for gait training before OCMM, while the other nine patients were evaluated for OCMM before gait training. The study found that gait training reduced the number of steps by 0.75 steps/10 m but did not significantly affect the interval; meanwhile, OCMM reduced the interval by 0.5 s/10 m but not the number of steps [25]. Both interventions can be considered based on the needs of the patient, although only the immediate symptomatic benefit of OCMM treatment was assessed in this study, thus the long-term benefits remain unexplored.

Effectiveness of OMT/manual therapy on autonomic imbalance

Autonomic imbalance in PD can manifest in different ways such as dysphagia, gastroparesis, constipation, bladder incontinence, and sexual dysfunction [1]. One study with six PD patients [26] was conducted to analyze the effects of OMT on the gut microbiome and constipation. Patients were followed for 10 weeks, during which 4 weeks were control, 4 weeks had OMT, and 2 weeks had no intervention. The OMT sessions targeted the ANS, enteric nervous system (ENS), thoracic excursion, and pelvic floor. Results from this study revealed that mean constipation severity significantly decreased by 40.0%, mean quality of life significantly improved by 29.0%, and significant changes to different normalized phyla in the gut, such as *Actinobacteria, Verrucomicrobia, Roseburia, Interstimonas,* and *Anaerotruncus,* were observed. These results point to a potential use of OMT to help improve constipation for PD patients, although the sample size was very small and further research will have to be conducted to determine the validity of these outcomes.

Limitations and future research considerations

Although the use of OMT-like treatments to improve PD outcomes is promising, research on OMT and PD remains sparse. Most studies focused on the biomechanical and neurologic components of PD, utilizing techniques such as myofascial, articulation, and muscle energy to improve mobility and range of motion. Current research on autonomic treatments remains limited, making it an avenue of exploration for future research. The psychosocial and behavioral effects of OMT on PD should also be a focus of future research.

The studies available are not without limitations: the number of subjects remained low (<50 in all of the studies), and not all of the results were statistically significant. The reported clinical significance of the results should not be discounted, however; as PD treatment focuses on symptomatic management, improving patients’ quality of life with the use of OMT may satisfy their goals for receiving treatment. The low number of subjects in part reflects the difficulty in conducting OMT research across the board; hands-on treatment requires significant time and effort from doctors, researchers, and subjects and remains a barrier in hosting large-scale studies. Funding and support will be instrumental for progress in the field and PD. Our analysis reveals several key points for future research: exploration of OMT to treat autonomic symptoms of PD, greater use of OMT techniques, and an increase in population size to identify more concrete trends.

While future research is required, abstracts and posters found during our literature search show promise in the future direction of PD and OMT research. PD research is currently being conducted at the New York Institute of Technology College of Osteopathic Medicine (NYITCOM). A pilot study was conducted that suggests possible significance of OMT in reducing tremor in PD patients [29]. The effects of OMT on PD subjects with severe bradykinesia and dyskinesia is also being explored, along with the use of a newly FDA-approved watch that can detect PD.
biometrics [30]. Biomarkers in PD subjects are also being examined to determine if OMT has beneficial effects on oxidative stress markers [31]. The University of California, San Diego has published an abstract [32] examining the use of OMT to improve non-motor symptoms of PD in 16 individuals, reporting findings that cognition (p=0.015) and perceived stress (p=0.02) improved, anxiety (p=0.064) and sleep quality (p=0.08) trended toward improvement, and motor symptoms were unchanged (p=0.56). A full study based on this study is in preparation. Additional studies investigating the potential benefits of OMT on PD subjects utilizing new technology and methodologies are needed.

Conclusions

PD is a progressive disease that has a variety of presentations in patients. OMT has been shown to be most beneficial in addressing motor-related and neurologic symptoms, and therapies such as Asma massage, similar to OMT’s myofascial release, are found to be beneficial. Research in this field remains extremely limited, and future studies are imperative to further our understanding.

Research funding: None reported.
Author contributions: All authors provided substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; all authors drafted the article or revised it critically for important intellectual content; all authors gave final approval of the version of the article to be published; and all authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
Competing interests: None reported.

References

1. Kalia LV, Lang AE. Parkinson’s disease. Lancet 2015;386:896–912.
2. Schneider RB, lourinets J, Richard IH. Parkinson’s disease psychosis: presentation, diagnosis, and management. Neurodegener Dis Manag 2017;7. https://doi.org/10.2217/nmd-2017-0028.
3. Rogers G, Davies D, Pink J, Cooper P. Parkinson’s disease: summary of updated NICE guidance. BMJ 2017;358:j1951.
4. Moon S, Sarmento CVM, Colgrove Y, Liu W. Complementary health approaches for people with Parkinson disease. Arch Phys Med Rehabil 2020;101:1475–7.
5. Earhart GM, Falvo MJ. Parkinson disease and exercise. Comp Physiol 2013;3:833–48.
6. Radder DLM, Sturkenboom IH, van Nimwegen M, Keus SH, Bloem BR, de Vries NM. Physical therapy and occupational therapy in Parkinson’s disease. Int J Neurosci 2017;127:930–43.
7. Leal LC, Abrahim O, Rodrigues RP, Silva MC, Araújo AP, Sousa EC, et al. Low-volume resistance training improves the functional capacity of older individuals with Parkinson’s disease. Geriatr Gerontol Int 2019;19:635–40.
8. Wu PL, Lee M, Huang TT. Effectiveness of physical activity on patients with depression and Parkinson disease: a systematic review. PLoS One 2017;12:e0181515.
9. Seffinger M. Glossary of osteopathic terminology. In: Seffinger M, editor. Foundations of osteopathic medicine, 4th ed Philadelphia: Lippincott Williams & Wilkins; 2018:1563–94 pp.
10. Wells MR, Giantinoto S, D’agata D, Areman RD, Fazzini EA, Dowling D, et al. Standard osteopathic manipulative treatment acutely improves gait performance in patients with Parkinson’s disease. J Am Osteopath Assoc 1999;99:92–8.
11. Lien WH, Lien WC, Kuan TS, Wu ST, Chen YT, Chiu CJ. Parkinson disease and musculoskeletal pain: an 8 year population-based cohort study. Pain 2017;158:1234–40.
12. Alwardat M, Schirinzzi T, Di Lazzaro G, Franco D, Sinibaldi Salimei P, Mercuri NB, et al. The effect of postural deformities on back function and pain in patients with Parkinson’s disease. NeuroRehabilitation 2019;44:419–24.
13. Catanzaro MP, Vazzana KM, Chen A, Mancini JD, Yao SC. Is there a place for osteopathy in Parkinson disease management? A retrospective case control study. Am Acad Osteopathy J 2014;24:26.
14. Norkus S, Ryan S. The effect of spinal manipulation as complementary therapy for Parkinson’s disease symptomatology: a literature review. J Contemp Chiropr 2020;3:7–13.
15. McKinley JE, Perkins A. Neurologic conditions: Parkinson disease. FP Essent 2019;477:16–21.
16. Cerritelli R, Ruffini N, Lacorte E, Vanacore N. Osteopathic manipulative treatment in neurological diseases: systematic review of the literature. J Neurol Sci 2016;369:333–41.
17. Snider T, La Croix C, Jones L, Nunney T, Colwell S, Wilde B, et al. Effectiveness of osteopathic manipulative treatment for Parkinson disease. J Ariz Nev Acad Sci 2007;39:48–50.
18. Rivera-Martinez S, Wells MR, Capobianco JD. A retrospective study of cranial strain patterns in patients with idiopathic Parkinson’s disease. J Am Osteopath Assoc 2002;102:417–22.
19. Henley CE, Ivins D, Mills M, Wen FK, Benjamin BA. Osteopathic manipulative treatment and its relationship to autonomic nervous system activity as demonstrated by heart rate variability: a repeated measures study. Osteopath Med Prim Care 2008;2. https://doi.org/10.1186/1750-4732-2-7.
20. Ruffini N, D’Alessandro G, Mariani N, Pollastrelli A, Cardinali L, Cerritelli F. Variations of high frequency parameter of heart rate variability following osteopathic manipulative treatment in healthy subjects compared to control group and sham therapy: randomized controlled trial. Front Neurosci 2015;9. https://doi.org/10.3389/fnins.2015.00272.
21. Palma JA, Kaufmann H. Treatment of autonomic dysfunction in Parkinson disease and other synucleinopathies. Mov Disord: Off J Mov Disord Soc 2018;33:372–90.
22. DiFrancisco-Donoghue J, Aposhian T, de Vries K, Jung MK, Mancini J, Yao S. Osteopathic manipulation as a complementary...
approach to Parkinson’s disease: a controlled pilot study. NeuroRehabilitation 2017;40:145–51.

23. Donoyama N, Suoh S, Ohkoshi N. Effectiveness of Anma massage therapy in alleviating physical symptoms in outpatients with Parkinson’s disease: a before-after study. Compl Ther Clin Pract 2014;20:251–61.

24. Zhao M, Hu C, Wu Z, Chen Y, Li Z, Zhang M. Effects of coordination and manipulation therapy for patients with Parkinson disease. Int J Neurosci 2017;127:762–9.

25. Muller T, Pietsch A. Comparison of gait training versus cranial osteopathy in patients with Parkinson’s disease: a pilot study. NeuroRehabilitation 2013;32:135–40.

26. Mancini JD, Yao S, Martinez LR, Shakil H, Li TS. Gut microbiome changes with osteopathic treatment of constipation in Parkinson’s disease: a pilot study. EC Neurology 2021;13:19–33.

27. Barnes MF. The basic science of myofascial release: morphologic change in connective tissue. J Bodyw Mov Ther 1997;1:231–8.

28. Jäkel A, von Hauenschild P. Therapeutic effects of cranial osteopathic manipulative medicine: a systematic review. J Am Osteopath Assoc 2011;111:685–93.

29. Li R, Docherty JEB, Koo SL, Shinners J, Terzella MJ, Yao S. Managing tremor in Parkinson’s disease using osteopathic manipulative medicine. J Am Osteopath Assoc 2018;118:e166–7.

30. Poon J, Docherty JEB, Mancini JD, DiFrancisco-Donoghue J, Cherian G, Leder A, et al. Using wearable technology to measure the effectiveness of osteopathic manipulative treatment on Parkinson’s disease motor symptoms. J Am Osteopath Assoc 2018;118:e150–1.

31. Docherty JEB, Chu K, Orshon D, Kulason LA, Cherian G, DiFrancisco-Donoghue J, et al. The effect of osteopathic manipulative treatment on reactive oxygen species in Parkinson’s disease. J Am Osteopath Assoc 2018;118:e173–4.

32. Whiteley N, King H, Cabrera Tuazon A, Pluim C, Nakhla M, Mills P. Osteopathic manipulative treatment improves non-motor symptoms in Parkinson’s disease: a preliminary study. Arch Clin Neuropsychol 2019;34:971.