

REVIEW PAPER

Non-pharmacological therapies for sleep disturbances in people with Parkinson's disease: A systematic review

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Abstract

Aim: To determine the effectiveness of non-pharmacological therapies for sleep disturbances in people with Parkinson's disease (PD).

Background: Sleep disturbances, which are common in people with PD, may diminish their quality of life. Non-pharmacological therapies are preferred over pharmacological therapies for improving sleep quality, owing to fewer adverse effects.

Design: Systematic literature review.

Data sources: A systematic search of eight databases and hand searching was conducted for papers published between 1 January 2000 – 1 January 2016.

Review methods: The Cochrane methods were followed. Risk of bias was assessed using the Cochrane Collaboration Risk of Bias Tool.

Results: Eight studies were identified for data extraction. Therapeutic domains included physical exercise, cognitive behavioural and complementary interventions. Therapies in four of the eight studies significantly improved sleep quality and the unified PD rating scale score. Other studies showed no clear effects on sleep ($N = 1$), limited effects on sleep ($N = 1$) or effects in both the intervention and control groups, indicating that the intervention had no distinctive effects ($N = 2$).

Conclusions: The non-pharmacological intervention types and sleep-related measured outcomes were heterogeneous. Most therapies had inconsistent effects on sleep. The insufficient evidence for non-pharmacological treatments seems related to the unique motor-associated clinical features of PD, which restrict the use of physical exercise therapy, or to individual "wearing-off" periods, which limit group therapy. Further studies on non-pharmacological therapies are required to identify the best interventions for improving sleep quality in people with PD.

KEYWORDS

non-pharmacological, Parkinson's disease, sleep, systematic review

1 | INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disorder that is accompanied by psychiatric, cognitive, sensory and autonomic

symptoms, as well as a decline in motor function (LeDoux, 2014). PD requires long-term management of these symptoms; the role of the nurse is important for continuum of care. About 95% of people with PD experience non-motor complaints, such as

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depression, fatigue, urinary dysfunction and sleep disorders. These complaints have quite significant effects on the daily experiences and quality of life (QOL) of people with PD and their caregivers (Adler, 2005; Chaudhuri et al., 2010; Leroi, Baker, Kehoe, Daniel, & Byrne, 2010). Despite their negative effects on QOL, non-motor features are likely to be underrecognized and undertreated, as more attention is paid to motor symptoms, which are often treated with medications (Modugno et al., 2010). Indeed, pharmacological management is a common approach to managing motor symptoms in PD. Since the 1960s, treatments for PD have focused on replacing or supplementing dopamine to address the dopamine deficiency (Li, Dong, Cheng, & Le, 2016). Currently, dopaminergic agents are regarded as the most effective pharmacological medications for treating PD (e.g., levodopa and ropinirole) (Poewe, 2009). However, long-term use of levodopa causes motor complications such as levodopa-induced dyskinesia and painful dystonia (Zesiewicz & Evatt, 2009). Given the limitations of pharmacological treatments (Siebern, Suh, & Nowakowski, 2012), the focus is now turning to non-pharmacological therapies, as they may offer symptomatic relief and aid in disease modification by addressing both the psychological and clinical symptoms of PD (Lee, Choi, & Yoo, 2016; Li et al., 2016).

1.1 | Background

Sleep is a dynamic physiological process that is necessary for proper function. Unfortunately, sleep disturbances are common in people with PD. In fact, in a large survey on non-motor symptoms in PD, 64.1% of people complained of sleep disorders (Barone et al., 2009). Moreover, compared with healthy older adults, people with PD report 20% more sleep difficulties. The PD-specific sleep-related symptoms include sleep fragmentation, sleep initiation difficulties, excessive daytime sleepiness (EDS), restless leg syndrome and rapid eye movement behaviour disorder (Crabb, 2001). Of these, the most common and disabling sleep symptom is sleep fragmentation, which is defined as the interruption of the sleep stages resulting in either a stage of lighter sleep or awakening that affects the normal sleep structure (Claassen & Kutscher, 2011). Collectively, these sleep-related problems cause fatigue, morning headaches, and cognitive and mood disturbances including depression, which may lead to a loss of productivity, work-related accidents and withdrawal from social activities (Buttaro, Trybulski, Polgar-Bailey, & Sandberg-Cook, 2012). Clearly, sleep complaints and sleep-related problems interfere with daily activities and motor skills and ultimately negatively affect a person's QOL (Frazzitta et al., 2015; Happe & Berger, 2001; Silvestri, 2012).

According to the International Classification of Sleep Disorders (2014), several PD-specific features contribute to these sleep disturbances. Neurochemical and structural changes in the sleep-wake generating neurons of people with PD affect sleep-wake regulation and these changes generally worsen as the disease progresses (Kumar, Bhatia, & Behari, 2002; Silvestri, 2012). Circadian rhythms may interfere with the disease process itself, which then leads to

Why is this review needed?

- Non-pharmacological treatments for sleep disturbances in people with Parkinson's disease are increasingly being required, as they are safer and more effective in the long-term than pharmacological treatments.
- Clinical trial studies on the use of non-pharmacological treatments for sleep disturbances in people with Parkinson's disease are limited in quantity and quality.

What are the key findings?

- Non-pharmacological therapies for sleep disturbances in people with Parkinson's disease vary in type, duration, dosage, measurement of sleep complaints and effectiveness.
- The quality of the included studies was acceptable, but there was a paucity of Parkinson's disease-specific interventions.
- Evidence for the effectiveness of non-pharmacological treatments for sleep disturbances in people with Parkinson's disease is still lacking.

How should the findings be used to influence policy, practice, research, or education?

- When planning interventions, nurses should consider each therapy's limitations and provide non-pharmacological treatments that take into account the characteristics (e.g., motor, non-motor and secondary psychological symptoms) of Parkinson's disease.
- Further studies are required to examine the underlying mechanisms of non-pharmacological interventions for sleep disturbances in Parkinson's disease and the factors influencing their effects.

nighttime insomnia and EDS. Bradykinesia and rigidity lead to feelings of discomfort and increase the frequency of awakenings. Dopamine agonists and anticholinergic medications are the most common predisposing factors for the development of sleep disruption (American Academy of Sleep Medicine, 2014). Other incidental factors are immobilization, anxiety and depression (Crabb, 2001; Gregory, Morgan, & Lynall, 2012; Leroi et al., 2010; Suzuki, Miyamoto, Miyamoto, & Hirata, 2015; Wells, Sawatzky, & McMillan, 2009).

Treatments for sleep complaints are mostly pharmacological (Morin, Mimeault, & Gagne, 1999; Siebern et al., 2012). Sleep medications are used widely, but may cause adverse effects in people with PD, such as nocturia, depression, hallucination and dependency (Braak et al., 2003). The use of sleep medications may also produce or worsen nocturnal confusion in people with PD (Silvestri, 2012). As mentioned above, sleep disturbances can be exacerbated by medication use and the associated toxicity (American Academy of Sleep

Medicine, 2014). Therefore, non-pharmacological therapies have garnered increasing attention and are recommended as first-line therapies before initiating pharmacologic treatments (Tamrat, Huynh-Le, & Goyal, 2014; Young, Bourgeois, Hilty, & Hardin, 2009). However, recent non-pharmacological trials on the sleep disturbances in people with PD have been limited in quantity and quality (Videnovic, 2017). In addition, inconsistencies in the effects of these interventions have been reported. This systematic review is, thus, required to examine the non-pharmacological approaches that have been used to treat the sleep disturbances in people with PD to suggest applicable nursing care.

2 | THE REVIEW

2.1 | Aim

This systematic review aimed to determine the effectiveness of non-pharmacological treatments for sleep disturbances in people with PD.

2.2 | Design

This review followed the Cochrane Handbook for Systematic Reviews of Interventions (Higgins & Green, 2011). The results are reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines (Liberati et al., 2009).

2.3 | Search methods

Eight databases (PubMed, Embase, CINAHL, Cochrane library, MEDLINE, KoreaMed, Research Information Sharing Service and Korean Studies Information Service System) were systematically searched. Searches were supplemented by hand searching. The searches were performed for articles published between 1 January 2000 – 1 January 2016. The following search terms were used: *parkinson* AND sleep* (nonpharmacolog* OR physical OR cognitive OR behavioral OR complementary)*. The primary outcome of interest was a change in overall sleep pattern, as measured using (a) subjective/objective improvements in frequency, duration, intensity of daytime sleepiness episodes, or sleep problems associated with PD; and (b) changes in sleep quality assessments.

The inclusion criteria were as follows: assessments of sleep disturbances performed using instruments previously shown to be valid, people with PD who were 18 years of age or older, randomized controlled trial (RCT) or quasi-experimental design and published in the English or Korean language. The exclusion criteria were as follows: non-primary research, grey literature, interventions not independently implemented by Registered Nurses and reviews or other types of commentary.

2.4 | Search outcomes

Thirty-nine articles were found through database searching and 10 articles were found through hand searching. After removing

duplicates, 40 articles remained. Based on screening of the title and abstract of each study, 28 articles were removed because they described pharmacological studies ($N = 3$), did not describe clinical trials ($N = 11$), were not relevant to PD ($N = 8$), or were not RCTs or did not use a quasi-experimental design ($N = 6$). The 12 remaining articles were assessed in full-text; however, four studies were excluded because their interventions were not independently implemented by Registered Nurses. These interventions included Qigong, continuous positive airway pressure use and repetitive transcranial magnetic stimulation. Finally, eight studies were included in our review and were evaluated for quality. Figure 1 outlines the selection process.

2.5 | Quality of appraisal

The Cochrane Collaboration's tool for assessing the risk of bias was used (Higgins & Green, 2011). Eight studies were examined to determine the adequacy of randomization sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other sources of bias. All criteria were evaluated as high, low or unclear risk. Consensus was reached through discussion for all disagreements or misunderstandings. Three independent authors conducted a quality assessment of all included publications and consensus was reached. No studies were discarded.

Figure 2 shows a risk-of-bias graph for the eight studies. Random sequence generation was judged as "low risk of bias" in six studies. The studies used random numbers tables or computer programs to generate a random number so that comparability between the experimental and control groups was warranted. Only one study assigned participants according to their general characteristics. The risk of bias for allocation concealment was evaluated as low in six of the eight studies. Blinding of participants and personnel was unclear in three studies, owing to insufficient information. This is problematic, as a lack of blinding of personnel may lead to researchers obtaining favourable results. Blinding of outcome assessment was judged as unclear risk in six studies. Three studies were assessed as high risk because they had incomplete outcome data. One study was evaluated as having high reporting bias because they did not report data for all of the pre-specified outcomes. More than half of the studies had high or unclear risk for other biases, including differences in baseline characteristics (Higgins & Green, 2011). Figure 3 shows a summary of the risk of bias for these studies.

2.6 | Data abstraction

Data abstracted from each article comprised the first author; country where the study was performed; year of publication; participants' characteristics, including mean ages and mean disease duration; and sample sizes of both the intervention group and the control group, including the number of men. The characteristics of the interventions

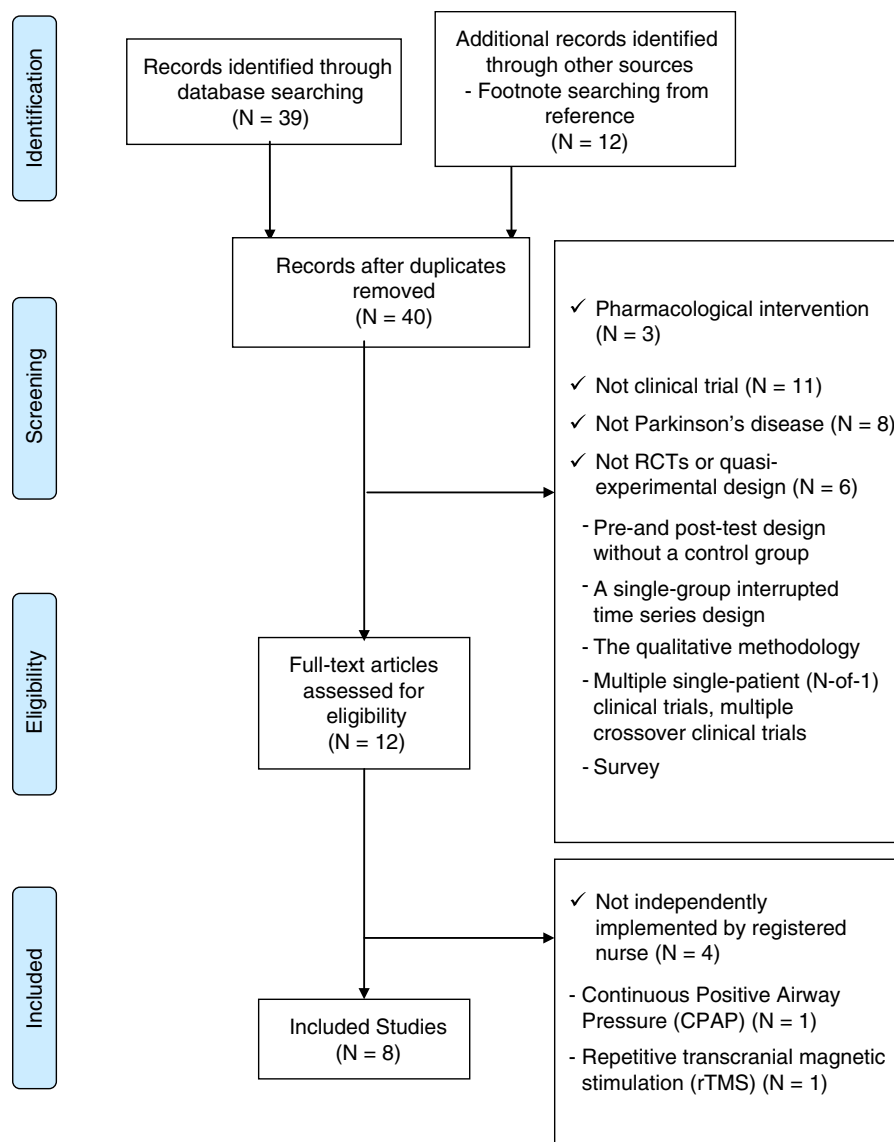


FIGURE 1 Flow diagram of study selection (PRISMA) [Colour figure can be viewed at wileyonlinelibrary.com]

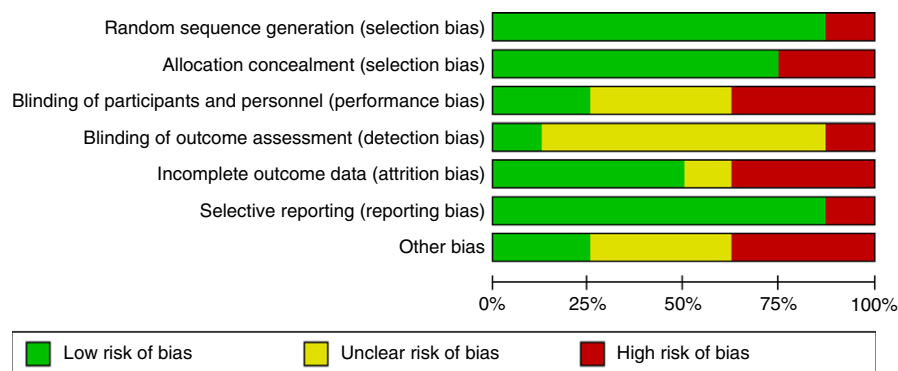


FIGURE 2 Risk-of-bias graph for included studies [Colour figure can be viewed at wileyonlinelibrary.com]

that were abstracted were the frequency, duration, dosage, method and outcomes. The extracted data used for quality appraisal were entered into the Review Manager program (version 5.3), which is used for preparing and maintaining Cochrane Reviews (Collaboration, 2014). Three independent authors reviewed and crosschecked both data files.

2.7 | Synthesis

All included studies were summarized and analysed to ensure a thorough understanding of each therapy. We used a systematic review approach for this process because of the significant heterogeneity in the studies. A meta-analysis was not possible because the included

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Leroi 2010	+	+	-	-	+	+	-
Modugno 2010	+	+	-	?	-	-	-
Nascimento 2014	-	+	-	?	-	+	?
Pan 2013	+	+	+	?	?	+	+
Paus 2007	+	-	+	+	-	+	-
Postuma 2012	+	+	?	?	+	+	?
Romenets 2013	+	-	?	?	+	+	?
Skogar 2013	+	+	?	?	+	+	+

FIGURE 3 Risk-of-bias summary for included studies [Colour figure can be viewed at wileyonlinelibrary.com]

studies did not test similar outcome measures, and thus, narrative summaries are reported. Furthermore, the Grades of Recommendation Assessment, Development and Evaluation approach was not undertaken for the following reasons: (a) sleep quality was not the sole outcome measure in many studies; (b) sleep was assessed using different measurement tools; (c) the studies had small sample sizes or were pilot studies; and (d) many studies were determined to have an “unclear risk of bias.” Therefore, it was not possible to draw comprehensive conclusions for making recommendations based on the current evidence.

3 | RESULTS

3.1 | Characteristics of the included studies

The key characteristics of the included studies are summarized in Table 1. All included studies were RCTs published between 2000 – 2015. The number of study participants ranged from 15–138, and the total number of participants was 465. Except for one study (Skogar et al., 2013) where only the age range was specified, the mean age of the participants was 66.58 years. With the exception of one

study (Skogar et al., 2013) that did not include information on the disease duration, the mean disease duration of the participants was 6.60 years. The studies were conducted in several countries, including United Kingdom ($N = 1$), Italy ($n = 1$), China ($N = 1$), Germany ($N = 1$), Sweden ($N = 1$), Canada and Brazil ($N = 3$). All studies were published in English.

3.2 | Effectiveness of therapies

Overall, theatre training, multimodal exercise, Yans-Xue-Qing-Nao Granules (YXQN), bright light therapy (BLT) and cognitive behavioural therapy (CBT) with BLT showed statistically significant results and clinically important changes. Table 1 presents a summary of findings.

3.3 | Types of therapies

Various non-pharmacological treatments for sleep disturbances exist, and there is evidence to support the short-term efficacy of these therapies in individuals without PD (National Institutes of Health, 2005). However, few RCTs have investigated the utility of non-pharmacological therapies for sleep disturbances in people with PD. Therefore, it is essential that the non-pharmacological therapies that have been performed to date be fully evaluated. Several different types of non-pharmacological therapy were identified through this review. The therapies were classified as physical exercise, cognitive behavioural and complementary.

3.3.1 | Physical exercise therapy

One study we identified employed physical exercise therapy (Nascimento et al., 2014). In that study, the physical exercise therapy included warm-up, muscle stretching/resistance, callisthenic, balance training and aerobic fitness exercises that aimed to stimulate aerobic metabolism. A heart rate monitor was used to modulate the intensity of the training. The control groups did not perform exercise, only maintaining medical routine care.

3.3.2 | Cognitive behavioural therapy

Cognitive behavioural therapy for insomnia generally aims to alter patient's dysfunctional beliefs about sleep (Bootzin & Stevens, 2005). Two of the studies we evaluated, combined with multi-component sleep therapy (MST) (Leroi et al., 2010) and BLT (Rios Romenets et al., 2013). MST was conducted together with CBT, stimulus control therapy and sleep hygiene education (Leroi et al., 2010). The American Association of Sleep Medicine suggested that MST, which combines psychological and behavioural (e.g., stimulus control, progressive muscle relaxation) aspects, including sleep hygiene education, is the most effective (Morgenthaler et al., 2006). In Leroi et al.'s (2010), the intervention comprised both behavioural and educational components. The main activity performed during CBT is an active discussion regarding sleep problems and a review of medication use. CBT was performed in a group setting (Leroi et al., 2010).

TABLE 1 Characteristics of included studies

Author (year), country	Study design	Mean age (SD)	Mean disease duration	Intervention group (n = sample size)	Control group (n = sample size)	Frequency	Duration	Main outcomes measure	Results
Leroi et al. (2010), UK	RCT	I: 72.5 (10.2) C: 71.9 (9.3)	I: 75 (15.4) C: 63.4 (29.2)	Multi-component sleep therapy (N = 8)	Sleep hygiene education (N = 7)	Every 2 weeks	6 weeks	ESS	Both the MST group ($p = 0.07$, two-tailed) and sleep hygiene education group ($p = 0.08$) improved significantly in the ESS
Modugno et al. (2010), Italy	RCT	I: 62 (1.58) C: 63.2 (1.13)	I: 10 (1.8) C: 9.4 (1.1)	Theatre training (N = 10)	Physiotherapy (N = 10)	Once or twice per month	3 years	ESS	They showed a very quick improvement in the sleep quality ($p < 0.001$)
Nascimento et al. (2014), Brazil	Quasi	I: 67.8 (6.8) C: 66.3 (8.1)	I: 5.1 (3.9) C: 4.6 (3.7)	Multimodal exercise (N = 17)	Standard medical care routine (N = 17)	Three times per week	6 months	MSQ	Physical exercise intervention for 6 months presented positive effects on the PD patients ($F_{1,32} = 14.6$; $p = 0.001$)
Pan et al. (2013), China	RCT	I: 68.6 (9.2) C: 67.1 (10.2)	I: 5.9 (4.7) C: 6.1 (4.9)	YXQN (N = 31)	Placebo granules (N = 30)	Three times per day	12 weeks	PDSS, DFA, actigraphy	Significant improvements in EA ($p < 0.04$), DA ($p < 0.05$) and PDSS scores ($p < 0.04$) were observed in the YXQN group
Paus et al. (2007), Germany	RCT	I: 63.6 (9.8) C: 63.4 (9.7)	I: 7.4 (4.3) C: 7.9 (4.7)	BLT (N = 18)	Placebo BLT (N = 18)	Everyday	15 days	ESS	ESS score was reduced in both BLT group ($p < 0.05$) and placebo group ($p < 0.05$)
Postuma et al. (2012), Canada and Brazil	RCT	I: 65.2 (8.3) C: 67.8 (11.2)	I: 7.8 (3.5) C: 8.0 (4.8)	Caffeine (N = 30)	Placebo caffeine (N = 31)	Every 3 weeks	6 weeks	ESS, PSQI	Caffeine resulted in a no significant reduction in Epworth Sleepiness Scale score (-1.71 points; 95% CI $-3.57, 0.13$) and PSQI (-0.29 ; $-1.42, 0.84$)
Rios Romenets et al. (2013), Canada	RCT	I: 64.5 (16.3) Doxepin: 65.3 (10.5) Placebo: 69.5 (10.5)	I: 5.2 (1.8) Doxepin: 4.8 (3.6) Placebo: 5.2 (4.4)	CBT with BLT (N = 6)	(1) Doxepin (N = 6) (2) Placebo (N = 6)	Every week	6 weeks	SCOPA, PDSS, insomnia Severity Index, Daily Sleep Diary, PSQI, Actigraphy, SHI, DBAS-16, ESS	Insomnia Severity Index significantly improved in CBT compared with placebo ($p = 0.03$), and the examiner-reported CGI-change improved significantly ($p = 0.006$)
Skogar et al. (2013), Sweden	RCT	–	–	Tactile Touch (N = 29)	Rest to Music (N = 15)	10 times per 8 weeks	8 weeks	PDSS	Differences between groups were not significant ($p = 0.056$)

Note. The studies are listed as alphabetical order of author's last name. Mean age was reported in years of mean and standard deviation (SD) except for Skogar et al. (2013) who reported age by range. Mean disease duration was reported in years of mean and SD except for Leroi et al. (2010) who reported it in months of mean and SD and Skogar et al. (2013) who did not report it. RCT: randomized controlled trial; I: intervention group; C: control group; ESS: Epworth Sleepiness Scale; MSQ: Mini-Sleep Questionnaire; PDSS: the Unified Parkinson's Disease Sleep Scale; DFA: Difficulty Falling Asleep; CGI-C: Clinical Global Impression of Change; PSQI: Pittsburgh Sleep Quality Index; SCOPA: Parkinson's Disease Sleep Scale; SHI: Sleep Hygiene Index; DBAS-16: Dysfunctional Beliefs and Attitudes about Sleep; CI: confidence interval.

The control group received sleep hygiene education but did not undergo any active behavioural changes (Leroi et al., 2010).

In a trial of CBT combined with BLT (Rios Romenets et al., 2013), six participants were involved in the intervention group. In that trial, the BLT consisted of exposure to a light with 10.00 lux of intensity at a head-to-light distance of 20 cm. The control group received 10 mg of doxepin daily at bedtime, while the placebo group underwent an inactive intervention consisting of 30 min of light therapy using red light (Rios Romenets et al., 2013).

3.3.3 | Complementary therapies

Several of the identified studies used complementary therapies that incorporated tactile touch (Skogar et al., 2013), BLT alone (Paus et al., 2007), caffeine (Postuma et al., 2012), Chinese herbal compounds (Pan, Kwak, Li, Chen, & Cai, 2013) and theatre training (Modugno et al., 2010). In tactile touch therapy, the participant's skin was stroked using a steady flow and soft pressure and was intended to make the participant feel comfortable. In the study by Skogar et al. (2013), one group received this therapy while the control group rested and listened to music. The study that employed BLT alone (Paus et al., 2007) was conducted 1 hr after awakening, as the release of melatonin is inhibited by retinal exposure to light. A light box was used at a head-to-light distance of 20 cm. The light intensity used was 7.500 lux. The control group received placebo BLT at a head-to-light distance of 100 cm with a 950-lux light source (Paus et al., 2007). In the study investigating caffeine (Postuma et al., 2012), the intervention group was treated with 100 mg of caffeine twice daily, while the control group received placebo tablets. Caffeine and placebo tablets were identically encapsulated for blinding (Postuma et al., 2012). Pan et al. (2013) used the Chinese herbal compound Yans-Xue-Qing-Nao (YXQN), which is composed of 11 herbs. The YXQN and placebo granules were identical in shape and colour to ensure they were indistinguishable. Placebo granules were administered on the same time schedule as that used for the intervention group (Pan et al., 2013). Finally, the study that used theatre training (Modugno et al., 2010) consisted of three parts. In the first part, the participants exercised basic skills based on a vocal warm-up. The second part focused on expressing oneself and communicating with others through rehearsing. In the third part, which was performed after training, the participants with PD performed for an audience with the help of the director. The control group underwent physiotherapy (Modugno et al., 2010).

3.4 | Frequency, duration and dosage of therapies

The frequencies of the therapies varied widely from three times per day (Pan et al., 2013) to once per month (Modugno et al., 2010). The duration of each therapy ranged from 15 days (Paus et al., 2007) to 3 years (Modugno et al., 2010). The therapies in four of the eight studies were conducted for 6 weeks (Leroi et al., 2010; Nascimento et al., 2014; Postuma et al., 2012; Rios Romenets et al., 2013). The dosages of the therapies also varied from 30 min (Paus et al., 2007) to 6 hr (Modugno et al., 2010), with the therapies in

three of the eight studies being performed for 1 hr (Leroi et al., 2010; Nascimento et al., 2014; Skogar et al., 2013).

3.5 | Sleep measurement

The assessment tools used to investigate sleep disturbances in all of the included studies can be classified into three groups. The one kinds of tools obtained quantitative measurements mechanically, for example, by using actigraphy, which objectively measures the total time in bed, total sleep duration, sleep efficiency and waking-up time after sleep using a machine. The other kinds of tools involved the use of self-reports to quantitatively assess sleep in people with PD. These reports included the Unified Parkinson's Disease Sleep Scale and the Epworth Sleepiness Scale (ESS). Another group included qualitative assessments, such as daily sleep diaries, which were used to evaluate sleep onset, sleep duration, daytime naps and nighttime awakening.

The instruments used in the eight studies assessing sleep disturbances in PD were the Parkinson's Disease Sleep Scale, ESS, Mini-Sleep Questionnaire, subscale of the Clinical Global Impression of Change, Pittsburgh Sleep Quality Index, subscale of the Scales for Outcomes in Parkinson's disease, Insomnia Severity Index, Sleep Hygiene Index, Dysfunctional Beliefs and Attitudes about Sleep, actigraphy and daily sleep diary. More than half of the included studies used ESS to assess EDS (Leroi et al., 2010; Modugno et al., 2010; Paus et al., 2007; Postuma et al., 2012; Rios Romenets et al., 2013) (Table 1).

3.6 | Effectiveness of therapies on sleep disturbances

Four of the eight studies reported statistically significant effects on sleep disturbances when compared with the control group (Table 1). These studies used theatre training ($p < 0.001$) (Modugno et al., 2010), YXQN granules ($p = 0.034$, 0.028 and 0.029) (Pan et al., 2013), tactile touch ($p = 0.035$) (Skogar et al., 2013) and a multi-modal exercise programme ($p = 0.001$) (Nascimento et al., 2014). The effects of these treatments lasted throughout the follow-up period, even after the intervention was completed.

While significant effects were apparent following treatment with MST ($p = 0.07$, two-tailed) (Leroi et al., 2010) and BLT ($p < 0.05$) (Paus et al., 2007), the control groups in these studies also exhibited improvements in sleep disturbances. This indicates that MST and BLT had no distinctive effects. CBT combined with BLT (Rios Romenets et al., 2013) had no clear effect on sleep. Similarly, caffeine (Postuma et al., 2012) led to indefinite improvements in EDS (-1.71 points; 95% confidence interval: -3.57 , 0.13). Only two of the nine sleep measurements used demonstrated significant differences in sleep, while the other seven measurements did not.

4 | DISCUSSION

This systematic review of eight studies examined the effects of various nurse-implemented non-pharmacological therapies on sleep

disturbances in people with PD. This suggests that research on the utility of non-pharmacological therapies for sleep disturbances in people with PD is limited in quantity. All included articles in our study were evaluated as having acceptable quality. Half of the studies found statistically significant effects on sleep complaints (Modugno et al., 2010; Nascimento et al., 2014; Pan et al., 2013; Skogar et al., 2013).

In this review, we found that mild to moderate multimodal exercise programmes lasting for over 6 months attenuated insomnia and EDS (Nascimento et al., 2014). Consistent with these findings, one retrospective study reported a positive effect of physical exercise on sleep quality and daytime somnolence in people with PD (Frazzitta et al., 2015). However, few clinical trials on the effects of physical activity for sleep disturbances have been performed in people with PD. Therefore, more research on exercise and physical activity are required for the clinical benefits although the motor impairments may limit their ability to perform physical exercise in people with PD (Frazzitta et al., 2015; Korczyn, 2006).

None of the studies we reviewed that employed CBT demonstrated distinct effects on sleep. CBT is a broad category of therapies that includes sleep education, sleep hygiene, stimulus control, relaxation and cognitive therapy (Williams, Roth, Vathauer, & McCrae, 2013). Although MST significantly improved sleep disturbances, no distinct effects were identified in the intervention group versus the control group (Leroi et al., 2010). This may be because the control group underwent only sleep hygiene education (Leroi et al., 2010). Conversely, MST achieved significant improvements in sleep and helped participants discontinue the use of sedative medication in several other studies (Bei et al., 2013; Bootzin & Stevens, 2005). The study we reviewed that used CBT combined with BLT found reductions in the examiner-reported clinical global impression of change and Insomnia Severity Index, although no significant effects were identified when using other sleep instruments (Rios Romenets et al., 2013). The limited effects of these two studies on sleep disturbances should be viewed with caution, as they were both exploratory studies. In addition, there is some discrepancy in the literature regarding the effects of CBT on sleep in other elderly groups. For instance, Montgomery and Dennis (2003) reported limited effects of CBT on sleep, while other studies have shown strong effects of CBT on sleep (Williams et al., 2013). Therefore, continued research is required to explore the influence of CBT on sleep in people with PD. In particular, CBT may be a valuable treatment prior to pharmacologic therapy in people with PD due to its effectiveness, safety and high durability (Vitiello, 2017).

A wide range of complementary therapies exists for people with PD (Lokk & Nilsson, 2010). Of the studies, we reviewed that used complementary interventions, tactile touch had a significant effect on nighttime restlessness and early awakening (Skogar et al., 2013). Harris, Richards, and Grando (2012) indicated that slow-stroke back massage is effective for sleep promotion in people with dementia. While the elderly are likely to perceive massage therapy as very pleasant, the role of touch and its effects on sleep currently remain

unknown (Schiff, 2006), and thus, additional studies into its effects are needed.

It is known that BLT inhibits the release of melatonin. Melatonin, which is known as the "hormone of darkness," suppresses dopamine release in the central nervous system (Zisapel, 2001). As such, BLT has been used as a treatment for sleep disorders because it is a natural therapy and does not cause residual effects and tolerance, which are often associated with pharmacological therapy (van Maanen, Meijer, van der Heijden, & Oort, 2016). Unfortunately, there are conflicting results on the effects of BLT in the literature. In a case series study of people with PD, BLT significantly improved sleep complaints (Willis & Turner, 2007), whereas the RCTs included in our study showed no distinctive effects of BLT on sleep in people with PD (Paus et al., 2007). In another study of BLT in people with PD, melatonin administration improved sleep time modestly; hence, the clinical significance of BLT's effects is limited (Dowling et al., 2005). A review of 53 studies on the effects of BLT reported that this therapy was effective in several populations including people with Alzheimer's disease or dementia (van Maanen et al., 2016). However, most of the effect sizes in that review were small to medium (van Maanen et al., 2016). Thus, continued research on the efficacy of BLT for the treatment of sleep disturbances in people with PD is warranted.

According to the study we reviewed, caffeine had no significant effect on excessive somnolence (Postuma et al., 2012). It is generally accepted that caffeine promotes wakefulness by antagonizing adenosine receptors (Nehlig, Daval, & Debry, 1992). Nevertheless, in a multiple crossover clinical trial that compared the effects of espresso coffee and decaffeinated coffee in people with PD, half of the PD people benefitted from caffeine on EDS, while no clear effects were observed in the other half (Ferreira et al., 2016). Since caffeine commonly increases daytime alertness in the general population, the mechanisms underlying its varied effects on sleep should be explored further in future studies.

In the study by Pan et al. (2013), YXQN granules, which are composed of 11 herbs, improved sleep dysfunction, as assessed with actigraphy. Approved as a treatment in China in 1996, the YXQN granules contain antioxidants aid in the treatment of headache and dizziness that are associated with cerebrovascular diseases (Xu et al., 2009). However, little research has been conducted on the utility of these granules on sleep. In addition, the exact mechanisms underlying the effects of YXQN on sleep disturbances remain to be determined (Pan et al., 2013). Therefore, further studies of various herbal medicines, including YXQN, are required, as the current evidence is insufficient to evaluate their efficacy and safety in people with PD (Chung et al., 2006).

In the study we reviewed, theatre training was administered in combination with listening to music, physical movement, sensory stimulation and expression of emotions (Modugno et al., 2010). This combination significantly improved the activities of daily living, QOL, depression and EDS in people with PD. However, due to the complexity of this therapy, it can only be applied in the mild to moderate stages of PD. Furthermore, people with PD have different degree of

aphasia and motor symptoms individually, making it difficult to involve group setting such as theatre training. Regardless, repeated studies of this treatment are warranted due to its potential benefits. Indeed, another study found that sound, music and movement improved psychological well-being measures, such as happiness and QOL, in people with PD (Pacchetti et al., 2000). Collectively, such findings support that treatments employing auditory stimulation, motor control and dance with music may have therapeutic potential for PD (Bienkiewicz & Craig, 2016).

Several limitations of this review should be noted. The first is the small number of included studies. Currently, literature on sleep disturbances in people with PD is scarce, likely because of the specific characteristics of this disease, such as the wearing-off period and cognitive complaints. Furthermore, there is a relative paucity of nurse-led intervention studies primarily focused on sleep disturbances in people with PD. However, this limitation was acceptable, as the rigorous selection process only allowed for the inclusion of RCTs and studies with quasi-experimental designs. Second, a meta-analysis was not possible due to the significant heterogeneity of the sleep-related measured outcomes among the included studies, and thus, narrative summaries were reported.

Despite these limitations, we think that our review examining the evidence for the effectiveness of non-pharmacological treatments for sleep disturbances in people with PD is important. To date, sleep management strategies consisting of pharmacological, non-pharmacological and surgical interventions have been reviewed (Videnovic, 2017). Critically, one systematic meta-analysis and review demonstrated that nurse-led care for sleep complaints is not inferior to physician-led care (Gong et al., 2017). Here, we focused on non-pharmacological therapies, more specifically, those that can be performed by Registered Nurses independently. Therefore, clinical nurses may use our results practically.

5 | CONCLUSION

Our review established that the types and effectiveness of non-pharmacological therapies for sleep disturbances in people with PD were heterogeneous. Further, the inconsistent effects of the therapies on sleep limited their utility. The insufficient evidence for non-pharmacological treatments may be due to the unique clinical features of PD, such as the progressive functional decline and severity of motor symptoms, which restricts the use of various types of physical exercise therapy; or to the individual fluctuation of motor symptoms from "wearing-off" periods, which limit group therapy. Given the small sample of studies, we evaluated the heterogeneous nature of the therapies. Therefore, precise conclusions cannot be drawn regarding what non-pharmacological therapies were the most effective or appropriate for sleep disturbances in PD. Additional RCTs examining the effects of non-pharmacological therapies are required to determine whether they can be used in nursing practice to improve the sleep quality in people with PD.

AUTHOR CONTRIBUTIONS

All authors have agreed on the final version and meet at least one of the following criteria (recommended by the ICMJE [<http://www.icmje.org/recommendations/>]):

1. substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data;
2. drafting the article or revising it critically for important intellectual content.

DECLARATION OF CONFLICT OF INTEREST

No conflict of interest has been declared by the authors.

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