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Effects of Meditation and Yoga on Anxiety, Depression and Chronic Inflammation in Patients with Parkinson's Disease: A Randomized Clinical Trial

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Keywords
Mindfulness · Meditation · Yoga · Parkinson's disease · Psychological distress

Abstract

Introduction: Clinical guidelines recommend a holistic approach to Parkinson's disease (PD) care, yet randomized trials examining mindfulness-based interventions in this context are scarce. This study investigated the effects of two mindfulness practices – meditation and yoga – on biopsychosocial outcomes in PD patients, including anxiety symptoms, depressive symptoms, motor/nonmotor symptoms, health-related quality-of-life (HRQOL), mindfulness, and stress and inflammation biomarkers, compared to usual care. ***Methods:*** 159 participants with a clinical diagnosis of idiopathic PD and a Hoehn and Yahr stage of 1, 2, and 3, were randomized into meditation (n = 53), yoga (n = 52), and control (n = 54). Meditation and yoga were

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delivered in 90-min groups for 8 weeks. Primary outcomes included anxiety symptoms and depressive symptoms. Secondary outcomes included motor and nonmotor symptoms, HRQOL, mindfulness, and serum levels of interleukin-6, cortisol and TNF-alpha. Assessments were done at baseline (T0), 2 months (T1), and 6 months (T2). Linear mixed models were conducted following intention-to-treat principle. ***Results:*** Compared to control, both meditation, and yoga groups had significant improvements in anxiety symptoms (meditation: mean difference [MD] = −1.36, 95% CI: −2.46 to−0.26; yoga: MD = −1.61, CI: −2.70 to −0.52), motor symptoms (meditation: MD = −5.35, CI: −8.61 to−2.09; yoga: MD = −6.59, CI: −9.82 to−3.36), HRQOL (meditation: MD = −2.01, CI: −3.41 to−0.62; yoga: MD = −1.45, CI: −2.83 to−0.08), and describing skills (meditation: MD = 0.97, CI: 0.04–1.89; yoga: MD = 0.92, CI: 0.01–1.84) at T1, and significant reductions in serum interleukin-6 levels (meditation: MD = −1.14, CI: −2.18 to−0.10; yoga: MD = −1.11, CI: −2.09 to−0.13) at T2. Only meditation significantly reduced depression (MD = −1.44, CI: −2.57 to−0.30) at T1 and sustained the motor and HRQOL improvements at T2. ***Conclusion:*** Meditation and yoga significantly improved anxiety symptoms, chronic inflammation, motor symptoms, mindfulness-describing facet, and HRQOL in PD patients. Meditation provided additional benefits in reducing depressive symptoms and sustaining motor and HRQOL improvements.

Introduction

As the second most common neurodegenerative disease, Parkinson's disease (PD) is a chronic condition that results in not only motor disorders, but also a spectrum of non-motor, neuropsychiatric symptoms such as anxiety, major depressive disorder, and apathy [1–4]. Psychological distress, including anxiety and depression, affects 40%–50% of patients with PD, and is associated with fast progression, poor treatment compliance, increased comorbid conditions and mortality, high healthcare utilization and high caregiver distress [5]. While pharmacotherapy, including dopaminergic medications like levodopa, improves motor symptoms in the early stages of PD, it often leads to response fluctuations and complications such as dyskinesias and psychosis as the disease progresses [6–8]. The "on-off" phenomenon, particularly associated with levodopa treatment, delineates the unpredictable oscillations in motor function, where patients experience periods of improved mobility ("on" periods) followed by episodes of reduced mobility or increased symptoms ("off" periods) [9]. Clinical guidelines recommend non-pharmacological, lifestyle approaches, such as physical activity and stress management, to address the psychosocial needs of PD patients throughout the course of the illness [10]. However, maintaining a healthy, active lifestyle could be particularly challenging for PD patients due to the physical, psychosocial, and cognitive limitations posed by the disease [11].

Emerging empirical evidence suggests that mindfulness-based interventions, encompassing both mentally focused meditation and movement-guided yoga practices, can facilitate psychological coping and regulate physiological stress responses [12, 13]. Recent meta-analyses reported that mindfulness reduces physiological stress markers, rebalance the HPA axis with decreased cortisol levels and improve inflammatory responses with reduced levels of pro-inflammatory cytokines interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) in general populations [14]. Meanwhile, emerging neurobiological evidence suggests that psychological distress plays a role in PD pathogenesis by modulating the disease course [15, 16]. Hence, understanding the effects of mindfulness-based interventions on psychological distress, symptom manifestations, and underlying neurobiological mechanisms in PD is crucial.

While recent systematic reviews and meta-analyses [17, 18] have highlighted the potential benefits of mindfulness and meditation interventions for PD patients, most existing trials have been constrained by relatively small sample sizes and considerable heterogeneity. Previous randomized clinical trials (RCTs) have yielded inconclusive findings regarding the psychosocial effects of these interventions and have not examined the neurobiological markers of stress and inflammation [19–23]. Therefore, this study aimed to fill this gap by investigating the effects of mentally focused meditation and physically guided yoga – in comparison to usual care on anxiety, depression, motor and non-motor symptoms, health-related quality-of-life (HRQOL), mindfulness attributes, and biomarkers of stress and inflammation (plasma cortisol, IL-6, and TNF-α) in PD patients over a 6-month study period. It is the first study to validate and expand upon previous mindfulness research by examining two distinct mindfulness practices and exploring their neurobiological mechanisms related to stress and inflammation.

For PD patients who experience motor impairments and on-off symptom fluctuations, the investigation of distinct mindfulness approaches is crucial to inform clinical recommendations and their choices in lifestyle management strategies. If clinically meaningful effects are demonstrated, offering mindfulness interventions tailored to PD patients could serve as an effective lifestyle strategy to combat the global burden of psychiatric comorbidities through prevention.

Methods

Study Design

This assessor-blinded, multicentered, three-arm randomized controlled trial compared mindfulness meditation and mindfulness yoga to usual care as waitlist control. The trial protocol was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (HKU/HA HKW IRB, reference number: UW 19-446). Assessments were conducted at the University of Hong Kong. The interventions were delivered at four local community centers with similar settings, covering four major districts in Hong Kong (Central and Western, Eastern, Southern and Sha Tin). The full protocol, including detailed descriptions of the intervention and statistical analysis plan, has been published previously [24]. The trial protocol is available in Supplement 1 (for all online suppl. material, see https://doi.org/10.1159/000543457). All tests employed in this research were validated.

Participants

Participants were eligible for inclusion if they met the following criteria: a clinical diagnosis of idiopathic, mild-to-moderate PD as indicated by Hoehn and Yahr Scale's stages 1, 2, or 3, aged ≥18 years and able to provide written consent. Patients were excluded if they regularly participated in instructor-led mind-body interventions once a week or more during the past 6 months, were currently participating in any other behavioral (e.g., cognitive-behavioral therapy, physical exercise programs, mindfulness-based interventions, or other psychosocial interventions, etc.) or pharmacological (e.g., antidepressants, anxiolytics, or other pharmacological agent, etc.) trials, had significant cognitive impairment (Abbreviated Mental Test <6) [25] or had other contraindications or severe comorbidities that could limit full participation (e.g., severe hearing or vision impairment).

Participants were recruited through neurology outpatient clinics at three regional hospitals (Queen Mary Hospital, Tung Wah Hospital, and Pamela Youde Nethersole Eastern Hospital), and 3 patient support groups, including the Hong Kong PD Foundation, the Hong Kong PD Association and the Community Rehabilitation Network (with six community rehabilitation centers, the largest community rehabilitation organization for people with disabilities in Hong Kong). These sites covered three major regions of Hong Kong to enhance sample accessibility and representativeness. A combination of recruitment strategies was used, including electronic mailing and disseminating newsletters amongst patient support groups. All promotional materials and registration were made accessible online. Eligibility screening was conducted via telephone or in neurology clinics. Eligible participants were invited to undergo baseline assessments at the University of Hong Kong. All patients provided written informed consent before the start of baseline assessments. All participants received routine outpatient services (medication follow-up with potential medication adjustments if needed, as well as minimal health education on disease management and physical activity advice).

Randomization and Masking

After baseline assessment, participants were randomly assigned (in a 1:1:1 ratio) to one of the following groups by using permuted block with random block sizes of 3, 6, and 9: meditation, yoga, or waitlist control. The randomization sequence was computer-generated by an independent researcher who was not involved in patient recruitment, assessment or data analysis. The allocation sequences remained concealed in opaque envelopes from other researchers and participants until the time of assignment. Independent personnel who were not involved in assessment informed the participants of their assigned group. Blinding was not possible for the participants due to the nature of the trial interventions. The information sheet stated that the study aimed to evaluate the effects and experiences of mindfulness on symptom management by comparing two mindfulness programs to a waitlist control group, without specifying the program components and details. Researchers who assessed the outcomes or conducted data analyses were masked to group allocation. The participants were instructed not to discuss the content of their mindfulness programs during post-intervention visits, and that they could contact an independent research assistant if they encountered any problems during trial participation.

Procedures

Mindfulness Meditation Group

The mindfulness meditation group received a weekly in-person 90 min session for 8 weeks at local community centers, with 12 contact hours in total. The average group size was 12 participants. The mindfulness meditation program focused on cultivating mindfulness through a series of relatively nonphysical exerting meditation techniques. The program was adapted from the structured 8-week Mindfulness-Based Stress Reduction (MBSR) program conceptualized by Jon Kabat-Zin [13], modified based on the authors' previous pilot study of

meditation amongst local patients with PD [26], and delivered in neutral terminology free from any religious affiliation by an instructor who is certified as a teacher in MBSR, Mindfulness-Based Cognitive Therapy (MBCT), and Mindfulness-Based Cognitive Therapy for Life (MBCT-L). The outline of the mindfulness meditation program is shown in online supplementary sTable 1 in Supplement 2. The weekly session consisted of standardized core elements of mindfulness meditation practices, including mindful breathing, body scan, mindful movement, and mindful walking. The mindful movements incorporated in the program were gentle in nature, and they involved minimal physical exertion. The participants were provided with paper handouts, guided videos, and audios to facilitate their skill mastery and invited to perform at least 20 min home-based self-practice twice a week.

Mindfulness Yoga Group

The mindfulness yoga group received a weekly in-person 90 min session for 8 weeks at local community centers, with 12 contact hours in total. The mindfulness yoga program followed the same format, group size, and theme as the mindfulness meditation program. The program was delivered by an instructor who is certified as a teacher in mindful yoga, MBSR, MBCT, and MBCT-L. The program was adapted and modified based on the authors' previously tested mindfulness yoga protocol for PD, with the goal of cultivating mindfulness through physically exerting Raja yoga practices [19]. The weekly session consisted of standardized core elements of yoga practices, including controlled breathing; mindfulness practice of yoga sequences (12 modified postures of sun salutations) and guided meditation techniques, including body scan, visualization, mantra meditation, and love-kindness meditation. The outline of the mindfulness yoga program is shown in online supplementary sTable 1 in Supplement 2. The participants were provided with paper handouts, guided videos and audios to facilitate their skill mastery and invited to perform 20 min home-based self-practice twice a week.

Waitlist Control, Usual Care Group

The waitlist control group received routine outpatient services (medication follow-up with potential medication adjustment if needed, as well as minimal health education on disease management and physical activity advice). The participants received either one of the mindfulness programs upon completion of the 6-month study period.

Data Sources and Assessments

Data Collection

Study data were collected using Qualtrics platform. Outcomes were assessed at three timepoints: baseline (prior to randomization, T0), 2 months (post-intervention, T1), and 6 months (4 months post-intervention, T2). Information regarding psychiatric diagnoses was obtained through self-reports during the baseline assessment. Additionally, participants were requested to bring their medication packages to record medication use at each follow-up assessment. All assessments were conducted during the "on" state of levodopa treatment to minimize motor fluctuations amongst participants, if indicated. Outcome assessors were trained and masked to group allocation. Two trained and certified assessors performed motor examinations for a single patient in real time. All motor assessments were video-recorded and sent to a blinded assessor for validation. Blood samples were collected by a registered nurse.

Outcomes

The primary outcomes, which are the between-group differences in anxiety and depressive symptoms at 2 months, were measured using the validated Hospital Anxiety and Depression Scale (HADS, Chinese-Cantonese) [27]. HADS is a self-report questionnaire with anxiety and depression subscales, each consisting of seven items rated on a four-point scale. Higher scores represent higher level of anxiety/depressive symptoms. HADS has demonstrated good internal consistency (anxiety $\alpha = 0.86$, depression $\alpha = 0.78$) and construct validity, as no somatic symptom assessment is included because such symptoms may be confused with Parkinsonian manifestations [28].

Secondary outcomes included the following: (i) PD-related motor and non-motor symptoms, as measured by the validated Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS, Chinese) parts I–III [29], which assesses non-motor experiences of daily living, motor experiences of daily living and motor symptoms, respectively; (ii) perceived mindfulness as measured by the Chinese short-form Five-Facet Mindfulness Questionnaire (FFMQ) [30]; (3) HRQOL, as measured by the validated eight-item Parkinson's Disease Questionnaire (Chinese version) [31]; (iv) plasma levels of cortisol, IL-6 and TNF-α, with all blood samples collected at 14:00–16:00 to control for variations of cortisol levels over the circadian rhythm because the cortisol level in this sub-period is relatively stable and highly correlated with mean 24 h cortisol level [32] (the detailed methodology of plasma preparation and

biomarker measurements is shown in online suppl. Supplement 3); (v) respondent's expectation on treatment credibility in terms of the reasonableness of treatment effect, opinion toward the instructor, expectation for improvement, willingness to apply mindfulness skills in daily life and likelihood to recommend the treatment to others, on a 10-point scale [33]. Details and validation of the outcome instruments are available in online supplementary 1.

Sample-Size Calculation

The power calculation is detailed elsewhere [24]. The sample-size calculation was based on the primary comparison of psychological distress between the intervention and waitlist control groups. With psychological distress as a primary outcome, a previous systematic review reported an effect size of 0.4 for meditation compared to cognitive-behavioral therapy control [34], while our previous clinical trial reported an effect size of 0.6 for yoga compared to exercise control [19]. Adopting a conservative approach, a moderate effect size of 0.6 was anticipated for the primary outcome despite the comparison being made to usual care. Using power analysis software Gpower 3.1, assuming an attrition rate of 20%, a sample size of 168 participants with 56 per arm was required to provide a three-arm trial with a power of 80% to detect an effect size of at least 0.6 at 5% level of significance.

Statistical Analysis

Data analysis was performed in SPSS Statistics 28.0.1 software (IBM) via the intention-to-treat approach. Linear mixed-effect models (LMEMs) were used to assess the intervention effects on the primary and secondary outcomes, with time (as a continuous variable), group and group-by-time interaction included as independent variables. Linear contrasts were used to obtain between-group differences. Multiplicity due to multiple comparisons amongst the three groups at the two follow-up timepoints was accounted for using the Bonferroni approach. The normality of the residuals and random effects was assessed using normal probability plots. Missing values were not replaced because mixed-effect models can accommodate participants with at least one outcome measurement [35]. A 5% level of significance was assumed, and all significance tests were two-sided. The initial statistical analysis plan can be found in the trial protocol in online Supplementary 1, and it was modified: the current analysis adopted LMEM instead of generalized estimating equations on the basis of recent literature indicating that LMEM is preferred due to its closer coverage probability to the 95% confidence interval and its ability to maintain the correct type-I error rate [36]. Sensitivity analyses included adjusting for demographics and clinical characteristics (age, gender, educational level, marital status, Hoehn and Yahr stage, and levodopa equivalent dose), as well as subgroup analyses for participants at risk of psychological distress, those with high session attendance (attended≥ 6 out of 8 sessions), and non-dropouts. The optimal balance cut-off scores of the HADS (HADS total score ≥13, HADS-anxiety ≥7, and HADS-depression ≥5) identified in previous research were adopted for early identification of individuals at risk of psychological distress [37].

Patient Involvement

In this study, PD patients were involved from the initial development and feasibility stages of the research process. In-depth semi-structured interviews with PD patients helped identify unmet care needs and outcomes, such as anxiety, depression, and HRQOL, which informed the research questions, study design, and choices of outcome measures. They provided feedback on the intervention's burden and the time commitment required, ensuring that the study was feasible and respectful of participants' needs. Patients were also engaged in the recruitment process, promoting the study within their communities and assisting in outreach efforts. Additionally, plans for disseminating results were shaped through discussions with patient representatives from Hong Kong PD Foundation and Hong Kong PD Association, ensuring that findings would be shared with the wider community in accessible formats.

Role of the Funding Source

The General Research Fund of Research Grants Council funded the study but played no role in study design, data collection, data analysis, data interpretation, or writing of the manuscript.

Results

Between March 30, 2021, and June 25, 2022, 196 potential participants were screened. Fourteen (7.1%) did not meet the eligibility criteria, and 23 (11.7%) declined to participate (enrolment rate: 81.1%, Fig. 1). A total of 159 participants were randomized into meditation group (n = 53), yoga group (n = 52), and control group (n = 54). The mean (SD) attendance rates were 6.8 (1.6) and 7.4 (0.8) sessions for the

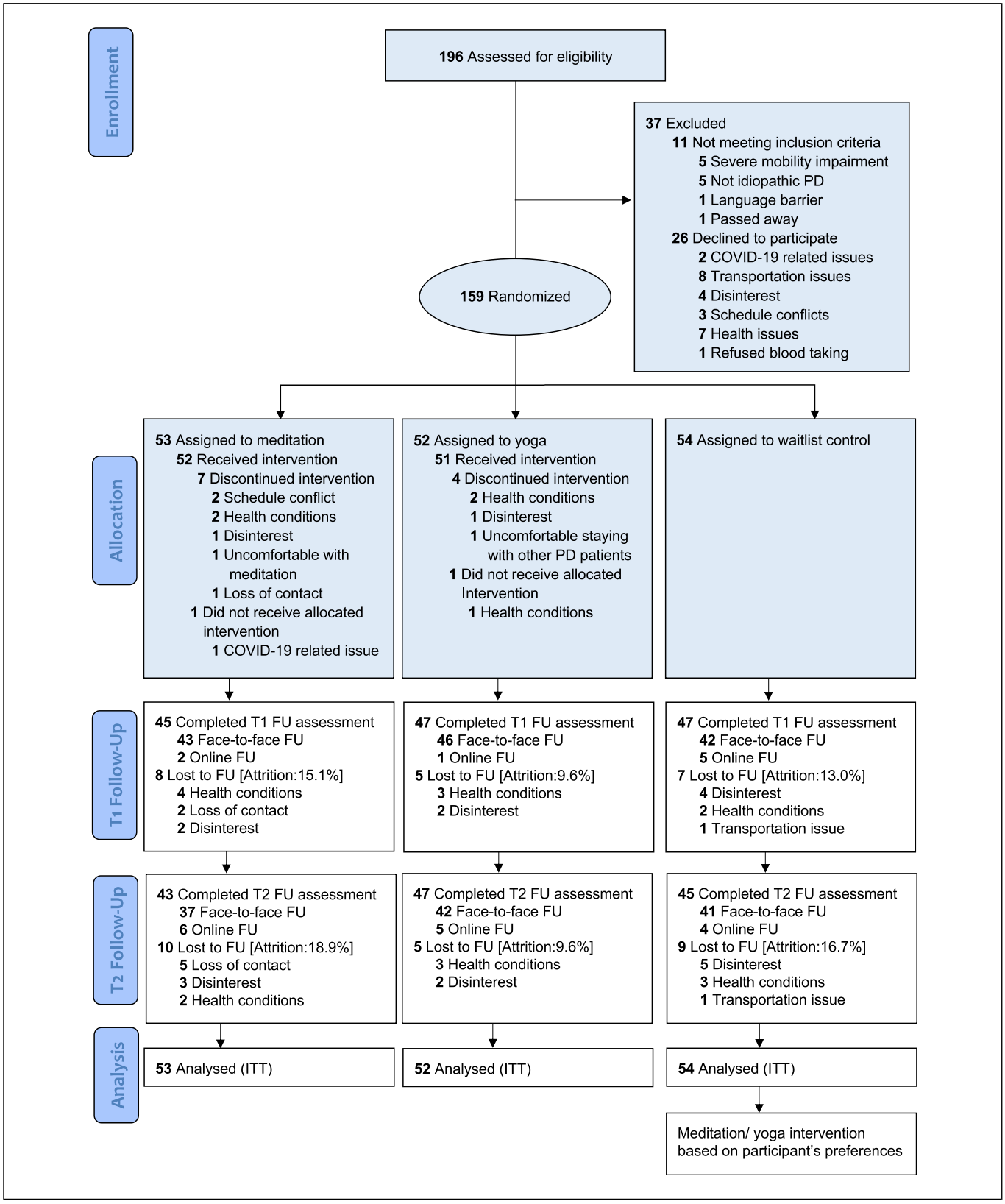

Fig. 1. CONSORT flow diagram.

Table 1. Baseline sociodemographic and clinical data

Characteristics	Participants, *N* (%)			
	total (*n* = 159)	yoga (*n* = 52)	meditation (*n* = 53)	control (*n* = 54)
Age, mean (SD), years	64.8 (7.9)	66.9 (7.9)	64.3 (8.0)	63.3 (7.5)
Sex				
Male	76 (47.8)	28 (53.8)	28 (52.8)	20 (37.0)
Female	83 (52.2)	24 (46.2)	25 (47.2)	34 (63.0)
Marital status				
Single, separated, divorced, or widowed	47 (29.6)	15 (28.8)	16 (30.2)	16 (29.6)
Married	112 (70.4)	37 (71.2)	37 (69.8)	38 (70.4)
Education level				
Illiterate or primary	19 (11.9)	7 (13.5)	9 (17.0)	3 (5.6)
Secondary	94 (59.1)	33 (63.4)	30 (56.6)	31 (57.4)
Tertiary	46 (28.9)	12 (23.1)	14 (26.4)	20 (37.0)
Religion				
Christianity	25 (15.7)	4 (7.7)	11 (20.8)	10 (18.5)
Catholicity	14 (8.8)	7 (13.5)	3 (5.7)	4 (7.4)
Buddhism	14 (8.8)	3 (5.8)	5 (9.4)	6 (11.1)
Chinese folks beliefs	2 (1.3)	1 (1.9)	1 (1.9)	0 (0)
Muslim	1 (0.6)	0 (0)	0 (0)	1 (1.9)
No religion	103 (64.8)	37 (71.2)	33 (62.3)	33 (61.1)
Living status				
Alone	23 (14.5)	8 (15.4)	9 (17.0)	6 (11.1)
With spouse, family, domestic helper, or colleagues	136 (85.5)	44 (84.6)	44 (83.0)	48 (88.9)
Social security allowance	99 (62.3)	33 (63.5)	35 (66.1)	31 (57.4)
Working situation				
Paid work	23 (14.5)	4 (7.7)	11 (20.7)	8 (14.9)
Retired	117 (73.6)	43 (82.7)	35 (66.0)	39 (72.2)
Unemployed due to medical reasons	3 (1.9)	1 (1.9)	1 (1.9)	1 (1.9)
Housewives/househusbands	16 (10.11)	4 (7.7)	6 (11.3)	6 (11.1)
Hoehn and Yahr stage[a]				
I	1 (0.6)	0 (0)	1 (1.9)	0 (0)
II	51 (32.1)	18 (34.6)	15 (28.3)	18 (33.3)
III	107 (67.3)	34 (65.4)	37 (69.8)	36 (66.7)
Levodopa equivalent dose (mg), mean (SD)	520.5 (323.5)	537.6 (327.1)	500.1 (303.8)	523.7 (343.2)
Use of antidepressants	13 (8.2)	2 (3.9)	5 (9.4)	6 (11.1)
Use of benzodiazepines	34 (21.4)	8 (15.4)	14 (26.4)	12 (22.2)
Clinical diagnosis of depression	15 (9.4)	3 (5.8)	5 (9.4)	7 (13.0)
Clinical diagnosis of anxiety	5 (3.1)	0 (0)	2 (3.8)	3 (5.6)

[a]Disease staging measured by Hoehn and Yahr scale (stage I: unilateral involvement; stage II: early bilateral involvement, independent activities of daily living and no postural instability; stage III: postural instability; stage IV: assistance for activities of daily living/ambulation activities; stage V: dependent for activities of daily living).

meditation and yoga groups, respectively. Thirty-seven of 53 (69.8%) participants attended at least six sessions of meditation, and 45 of 52 (95.7%) participants attended at least six sessions of yoga. The overall dropout rates were 20 of 159 (12.6%) at T1 (meditation: 15.1%; yoga: 9.6%; control: 13.0%) and 15.1% at T2 (meditation: 18.9%; yoga: 16.7%; control: 16.7%). Details on completion of baseline and follow-up assessments are provided in online Supplementary 4: sTable 2.

Baseline Characteristics of Participants

The 159 participants had a mean (SD) age of 64.8 (7.9) years, and 52.2% were female. Most (107; 67.3%) had moderate PD (Hoehn and Yahr scale, stage 3). Baseline characteristics were well-balanced across groups (Table 1). Their mean (SD) MDS-UPDRS score was 37.7 (10.1). At baseline, 54 of 159 (34.0%) participants were at risk of anxiety and 96 (60.4%) were at risk of depression, with mean (SD) HADS scores of 11.3 (6.8). Treatment credibility was similar at baseline but the yoga group showed higher satisfaction than the meditation group at 2 and 6 months (online suppl. 5: sTable 3). Specifically, both meditation (7.41 ± 2.12 out of 10) and yoga (7.50 ± 1.76 out of 10) participants showed a higher willingness to apply the learned mindfulness skills post-intervention.

Coprimary Outcomes

For anxiety symptoms, a statistically significant greater reduction was found in the meditation and yoga groups than in the control group at T1 (meditation: between-group mean difference [MD] = −1.36, 95% CI: −2.46 to −0.26, Cohen's d = 0.57; yoga: between-group MD = −1.61, CI: −2.70 to −0.52, Cohen's d = 0.69; Table 2; online suppl. 6: sFigure 1). The findings were consistent in subgroup analyses for participants at risk of psychological distress, at risk of depression, high session attendance, and non-dropouts (see details in online suppl. 7, 9–11).

For depressive symptoms, a statistically significant greater reduction was observed in the meditation group than in the control group at T1 (meditation: between-group MD = −1.44, CI: −2.57 to −0.30, Cohen's d = 0.59). No significant improvement was noted in anxiety and depressive symptoms at T2. However, in subgroup analyses of participants at risk of psychological distress, anxiety, and depression, those with high attendance, the meditation group showed significant greater reductions in depressive symptoms compared to the control group (online suppl. 7–10). Such improvements were sustained at T2 among those at-risk of psychological distress, anxiety, and depression.

Secondary Outcomes

At T1, both the meditation and yoga groups showed significantly greater improvements in motor symptoms (meditation: between-group MD = −5.35, CI: −8.61 to −2.09, Cohen's d = 0.76; yoga: between-group MD = −6.59, CI: −9.82 to −3.36, Cohen's d = 0.96), HRQOL (meditation: between-group MD = −2.01, CI: −3.41 to −0.62, Cohen's d = 0.67; yoga: between-group MD = 1.45, CI: −2.83 to −0.08, Cohen's d = 0.49) and describing trait of mindfulness (meditation: between-group MD = 0.97, CI: 0.04–1.89, Cohen's d = 0.49; yoga: between-group MD = 0.92, CI: 0.01–1.84, Cohen's d = 0.47) than the control group (Table 3; online suppl. 6: sFig. 1).

At T2, both meditation and yoga groups showed a statistically significant greater reductions in IL-6 levels compared to the control (meditation: between-group MD = −1.14, CI: −2.18 to −0.10, Cohen's d = 0.51; yoga: between-group MD = −1.11, CI: −2.09 to −0.13, Cohen's d = 0.53). However, only the meditation group demonstrated sustained improvements in motor symptoms (between-group MD = −4.01, CI: −7.43 to −0.59, Cohen's d = 0.55) and HRQOL (between-group MD = −1.96, CI: −3.40 to −0.52, Cohen's d = 0.64) versus the control. The meditation group also significantly improved motor experiences of daily living compared to yoga at T2 (between-group MD = −2.19, CI: −4.03 to −0.35) (Table 3). Online supplementary 12 shows the individual items of motor symptoms. Compared to control, both meditation and yoga significantly improved motor performance like toe tapping, arising from chair and rest tremor at T1, as well as hand movements at T2. However, only yoga significantly improved motor functions related to rigidity, finger tapping, kinetic tremor of hands at T1, and body bradykinesia at T2, compared to the control group.

In subgroup analyses of participants at risk of psychological distress, anxiety, and depression, meditation significantly improved overall mindfulness traits compared to yoga and control at T1 and T2 (online suppl. 7–9). At T2, the yoga group showed statistically significant reductions in mindfulness traits of acting with awareness and non-judgment compared to the control group. For participants at-risks of depression, both meditation and yoga significantly improved HRQOL compared to the control at T1, but sustained improvement was only reported in the meditation group (online suppl. 9: sTable 6). The adjusted analyses results showed largely consistent results as the crude analyses, except that the describing trait of mindfulness did not show a statistically significant greater improvement in yoga group compared to the control group at T1 (online suppl. 13).

Adverse Events

A total of 14 participants in the meditation group and eight participants in the yoga group encountered adverse events. Although most events were unrelated to the interventions, a potential relationship amongst three participants (5.7%) in the meditation group and

Table 2. Comparison of primary outcome between intervention groups (Intention-to-treat analysis)[a]

Measures	Estimates across all follow-ups, mean (95% CI)			Meditation versus usual care		Yoga versus usual care		Meditation versus yoga		*p* value for overall between-group difference
	meditation (*n* = 53)	yoga (*n* = 52)	usual care (*n* = 54)	MD (95% CI)	group × time interaction effect, *p* value	MD (95% CI)	group × time interaction effect, *p* value	MD (95% CI)	group × time interaction effect, *p* value	
HADS-anxiety[b]										
T0	5.33 (4.74–5.93)	5.16 (4.56–5.76)	5.24 (4.65–5.83)	NA	NA	NA	NA	NA	NA	NA
T1	4.79 (4.15–5.44)	4.54 (3.91–5.17)	6.15 (5.52–6.78)	−1.36 (−2.46 to −0.26)	0.01	−1.61 (−2.70 to −0.52)	<0.001	0.26 (−0.85 to 1.36)	1.00	<0.001
T2	5.22 (4.55–5.89)	5.61 (4.98–6.23)	5.90 (5.26–6.54)	−0.68 (−1.81 to 0.45)	0.45	−0.30 (−1.39 to 0.80)	1.00	−0.39 (−1.50 to 0.73)	1.00	0.35
HADS-depression[b]										
T0	6.05 (5.43–6.66)	5.96 (5.34–6.58)	5.90 (5.29–6.51)	NA	NA	NA	NA	NA	NA	NA
T1	4.37 (3.70–5.03)	5.26 (4.61–5.91)	5.80 (5.15–6.45)	−1.44 (−2.57 to −0.30)	0.01	−0.54 (−1.66 to 0.58)	0.75	−0.89 (−2.03 to 0.24)	0.18	0.01
T2	5.42 (4.73–6.10)	5.51 (4.86–6.15)	6.05 (5.38–6.72)	−0.64 (−1.81 to 0.54)	0.58	−0.54 (−1.68 to 0.59)	0.75	−0.09 (−1.24 to 1.06)	1.00	0.36

HADS, Hospital Anxiety and Depression Scale; NA, not applicable; T0, baseline; T1, immediate post-intervention (2 months); T2, 4 months post-intervention (6 months). [a]All participants analyzed according to allocation (*N* = 159); adjusted for baseline values and repeated measurements within participants. [b]Each HADS subscale for anxiety or depression is scored on a range of 0–21. Higher scores indicate greater levels of anxiety or depression.

three participants (5.8%) in the yoga group could not be excluded. In the meditation group, one participant experienced a gentle fall whilst transitioning from lying to sitting, without any physical injury; another two participants had nightmares associated with preexisting conditions, but no medical attention was required. In the yoga group, one participant reported worsening of back pain related to a preexisting condition, and another participant reported temporary wrist pain during yoga sequences, which resolved with pose modifications and rest. Additionally, one participant in the yoga group discontinued the intervention after the first session due to emotional burden from witnessing patients with more advanced disease during the group practice. No serious adverse events were reported.

Discussion

Principal Findings

This three-arm RCT demonstrated that both meditation and yoga significantly improved anxiety symptoms, motor symptoms, describing facet of mindfulness, and HRQOL compared to usual care at the 2-month follow-up. The self-reported psychosocial improvements were corroborated by significant reductions in the pro-inflammatory cytokine IL-6 at 6 months in both meditation and yoga groups versus control. The meditation group showed added benefits than yoga versus control, including greater reduction in depressive symptoms at 2 months and sustained improvements in motor symptoms and HRQOL at the 6-month follow-up. Importantly, for PD patients

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Table 3. Comparison of secondary outcomes between intervention groups (intention-to-treat analysis)[a]

Measures	Estimates across all follow-ups, mean (95% CI)			Meditation versus usual care		Yoga versus usual care		Meditation versus yoga		*p* value for overall between-group difference
	meditation (*n* = 53)	yoga (*n* = 52)	usual care (*n* = 54)	MD (95% CI)	group × time interaction effect, *p* value	MD (95% CI)	group × time interaction effect, *p* value	MD (95% CI)	group × time interaction effect, *p* value	
MDS-UPDRS[b]-I										
T0	10.15 (8.56 to 11.75)	10.03 (8.42 to 11.64)	10.64 (9.03 to 12.25)	NA	NA	NA	NA	NA	NA	NA
T1	8.31 (6.63 to 9.98)	9.26 (7.59 to 10.92)	9.37 (7.67 to 11.08)	−1.06 (−3.99 to 1.86)	1.00	−0.12 (−3.04 to 2.80)	1.00	−0.95 (−3.80 to 1.90)	1.00	0.62
T2	9.92 (8.14 to 11.69)	10.33 (8.65 to 12.01)	9.78 (8.04 to 11.51)	0.14 (−2.90 to 3.18)	1.00	0.55 (−2.41 to 3.51)	1.00	−0.41 (−3.36 to 2.54)	1.00	0.90
MDS-UPDRS[b]-II										
T0	12.80 (11.81 to 13.78)	12.88 (11.89 to 13.87)	12.90 (11.93 to 13.88)	NA	NA	NA	NA	NA	NA	NA
T1	12.60 (11.54 to 13.65)	14.21 (13.18 to 15.25)	13.01 (11.98 to 14.05)	−0.42 (−2.23 to 1.39)	1.00	1.20 (−0.59 to 2.99)	0.33	−1.62 (−3.42 to 0.19)	0.09	0.08
T2	12.87 (11.77 to 13.97)	15.07 (14.03 to 16.10)	13.46 (12.39 to 14.52)	−0.58 (−2.46 to 1.29)	1.00	1.61 (−0.20 to 3.42)	0.10	−2.19 (−4.03 to −0.35)	0.01	0.01
MDS-UPDRS[b]-III										
T0	37.15 (35.47 to 38.83)	37.40 (35.69 to 39.11)	36.91 (35.22 to 38.59)	NA	NA	NA	NA	NA	NA	NA
T1	30.63 (28.77 to 32.49)	29.39 (27.58 to 31.20)	35.98 (34.07 to 37.89)	−5.35 (−8.61 to −2.09)	<0.001	−6.59 (−9.82 to −3.36)	<0.001	1.24 (−1.93 to −4.42)	1.00	<0.001
T2	33.53 (31.51 to 35.55)	34.77 (32.91 to 36.62)	37.54 (35.61 to 39.47)	−4.01 (−7.43 to −0.59)	0.02	−2.77 (−6.06 to 0.51)	0.13	−1.24 (−4.59 to 2.11)	1.00	0.02
PDQ-8 summary index[c]										
T0	9.62 (8.86 to 10.37)	9.70 (8.93 to 10.46)	9.33 (8.58 to 10.08)	NA	NA	NA	NA	NA	NA	NA
T1	8.29 (7.48 to 9.10)	8.85 (8.06 to 9.65)	10.30 (9.50 to 11.10)	−2.01 (−3.41 to −0.62)	<0.001	−1.45 (−2.83 to −0.08)	0.03	−0.56 (−1.95 to 0.83)	0.99	<0.01
T2	8.62 (7.77 to 9.46)	9.88 (9.09 to 10.67)	10.58 (9.76 to 11.39)	−1.96 (−3.40 to −0.52)	<0.001	−0.70 (−2.09 to 0.69)	0.69	−1.27 (−2.68 to 0.14)	0.09	<0.01
FFMQ-total										
T0	64.84 (63.60 to 66.08)	65.10 (63.85 to 66.35)	64.98 (63.76 to 66.21)	NA	NA	NA	NA	NA	NA	NA
T1	66.64 (65.31 to 67.98)	65.26 (63.95 to 66.57)	64.64 (63.33 to 65.95)	2.00 (−0.28 to 4.28)	0.11	0.62 (−1.64 to 2.88)	1.00	1.38 (−0.90 to 3.67)	0.44	0.10

Table 3 (continued)

Measures	Estimates across all follow-ups, mean (95% CI)			Meditation versus usual care		Yoga versus usual care		Meditation versus yoga		*p* value for overall between-group difference
	meditation (*n* = 53)	yoga (*n* = 52)	usual care (*n* = 54)	MD (95% CI)	group × time interaction effect, *p* value	MD (95% CI)	group × time interaction effect, *p* value	MD (95% CI)	group × time interaction effect, *p* value	
T2	65.35 (63.96 to 66.73)	64.08 (62.78 to 65.38)	65.26 (63.92 to 66.60)	0.08 (−2.27 to 2.44)	1.00	−1.18 (−3.46 to 1.10)	0.64	1.27 (−1.06 to 3.59)	0.57	0.33
FFMQ[d]-observing										
T0	13.06 (12.50 to 13.62)	13.19 (12.63 to 13.75)	13.23 (12.68 to 13.79)	NA	NA	NA	NA	NA	NA	NA
T1	13.85 (13.25 to 14.45)	13.63 (13.04 to 14.22)	13.08 (12.49 to 13.67)	0.77 (−0.27 to 1.80)	0.22	0.55 (−0.47 to 1.57)	0.58	0.21 (−0.82 to 1.24)	1.00	0.18
T2	13.63 (13.01 to 14.26)	13.38 (12.79 to 13.96)	13.31 (12.70 to 13.91)	0.33 (−0.74 to 1.39)	1.00	0.07 (−0.95 to 1.10)	1.00	0.25 (−0.79 to 1.30)	1.00	0.74
FFMQ[d]-describing										
T0	13.15 (12.65 to 13.65)	13.11 (12.60 to 13.61)	13.22 (12.72 to 13.71)	NA	NA	NA	NA	NA	NA	NA
T1	13.75 (13.21 to 14.29)	13.70 (13.17 to 14.23)	12.78 (12.25 to 13.31)	0.97 (0.04 to 1.89)	0.04	0.92 (0.01 to 1.84)	0.05	0.05 (−0.88 to 0.97)	1.00	0.02
T2	13.42 (12.85 to 13.97)	13.07 (12.54 to 13.59)	13.26 (12.72 to 13.80)	0.15 (−0.80 to 1.11)	1.00	−0.19 (−1.12 to 0.73)	1.00	0.35 (−0.59 to 1.28)	1.00	0.67
FFMQ[d]-act with awareness										
T0	13.62 (13.17 to 14.07)	13.68 (13.22 to 14.14)	13.54 (13.09 to 13.98)	NA	NA	NA	NA	NA	NA	NA
T1	13.52 (13.03 to 14.00)	13.32 (12.84 to 13.80)	13.53 (13.05 to 14.01)	−0.01 (−0.85 to 0.83)	1.00	−0.21 (−1.04 to 0.62)	1.00	0.20 (−0.64 to 1.03)	1.00	0.79
T2	12.94 (12.43 to 13.44)	13.31 (12.83 to 13.78)	13.65 (13.15 to 14.14)	−0.71 (−1.57 to 0.15)	0.15	−0.34 (−1.18 to 0.50)	0.98	−0.37 (−1.22 to 0.48)	0.89	0.14
FFMQ[d]-non-judging										
T0	11.90 (11.35 to 12.44)	12.21 (11.66 to 12.76)	11.92 (11.38 to 12.46)	NA	NA	NA	NA	NA	NA	NA
T1	11.70 (11.11 to 12.28)	11.70 (11.12 to 12.28)	12.14 (11.56 to 12.72)	−0.44 (−1.45 to 0.56)	0.87	−0.44 (−1.44 to 0.56)	0.88	0.00 (−1.01 to 1.01)	1.00	0.47
T2	11.68 (11.07 to 12.29)	11.26 (10.68 to 11.83)	11.92 (11.33 to 12.51)	−0.24 (−1.28 to 0.79)	1.00	−0.67 (−1.67 to 0.34)	0.34	0.42 (−0.60 to 1.45)	0.97	0.27
FFMQ[d]-non-reacting										
T0	13.04 (12.58 to 13.51)	12.97 (12.50 to 13.45)	13.06 (12.59 to 13.52)	NA	NA	NA	NA	NA	NA	NA
T1	13.76 (13.25 to 14.27)	13.01 (12.51 to 13.51)	13.08 (12.58 to 13.57)	0.68 (−0.18 to 1.55)	0.18	−0.07 (−0.93 to 0.79)	1.00	0.75 (−0.12 to 1.62)	0.11	0.07

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Table 3 (continued)

Measures	Estimates across all follow-ups, mean (95% CI)			Meditation versus usual care		Yoga versus usual care		Meditation versus yoga		*p* value for overall between-group difference
	meditation (*n* = 53)	yoga (*n* = 52)	usual care (*n* = 54)	MD (95% CI)	group × time interaction effect, *p* value	MD (95% CI)	group × time interaction effect, *p* value	MD (95% CI)	group × time interaction effect, *p* value	
T2	13.59 (13.07 to 14.12)	13.17 (12.68 to 13.66)	13.11 (12.60 to 13.61)	0.49 (−0.41 to 1.38)	0.58	0.06 (−0.80 to 0.92)	1.00	0.43 (−0.45 to 1.30)	0.73	0.36
IL-6[e]										
T0	3.21 (2.70 to 3.72)	3.38 (2.86 to 3.89)	3.28 (2.78 to 3.77)	NA	NA	NA	NA	NA	NA	NA
T1	3.46 (2.89 to 4.03)	3.65 (3.11 to 4.19)	3.38 (2.80 to 3.96)	0.08 (−0.91 to 1.07)	1.00	0.27 (−0.70 to 1.24)	1.00	−0.19 (−1.14 to 0.77)	1.00	0.79
T2	2.90 (2.27 to 3.53)	2.93 (2.37 to 3.49)	4.04 (3.47 to 4.61)	−1.14 (−2.18 to −0.10)	0.03	−1.11 (−2.09 to −0.13)	0.02	−0.03 (−1.06 to 1.00)	1.00	0.01
Cortisol[f]										
T0	245.25 (223.23 to 267.27)	249.98 (225.76 to 270.19)	253.64 (232.04 to 275.24)	NA	NA	NA	NA	NA	NA	NA
T1	265.14 (240.69 to 289.60)	276.90 (253.53 to 300.26)	264.24 (239.22 to 289.26)	0.90 (−41.90 to 43.70)	1.00	12.64 (−29.22 to 54.52)	1.00	−11.75 (−53.10 to 29.59)	1.00	0.71
T2	234.72 (207.55 to 261.89)	240.42 (216.24 to 264.59)	270.69 (245.90 to 295.48)	−35.97 (−80.98 to 9.04)	0.17	−30.28 (−72.59 to 12.04)	0.26	−5.69 (−50.17 to 38.79)	1.00	0.11
TNF-alpha[g]										
T0	0.68 (0.53 to 0.82)	0.71 (0.56 to 0.86)	0.68 (0.53 to 0.82)	NA	NA	NA	NA	NA	NA	NA
T1	1.29 (1.13 to 1.46)	1.12 (0.97 to 1.28)	1.11 (0.95 to 1.28)	0.18 (−0.10 to 0.46)	0.36	0.01 (−0.27 to 0.29)	1.00	0.17 (−0.10 to 0.44)	1.00	0.21
T2	0.99 (0.81 to 1.16)	0.92 (0.76 to 1.08)	0.93 (0.77 to 1.09)	0.05 (−0.24 to 0.35)	1.00	−0.01 (−0.29 to 0.27)	1.00	0.07 (−0.23 to 0.36)	1.00	0.85

FFMQ-SF, Five-Facet Mindfulness Questionnaire – Short Form; IL-6, plasma interleukin-6; MDS-UPDRS, Movement Disorder Society – Unified Parkinson's Disease Rating Scale; NA, not applicable. PDQ-8, 8-item Parkinson's Disease Questionnaire; TNF-alpha, plasma tumor necrosis factor-alpha; T0, baseline; T1, immediate post-intervention (2 months); T2, 4 months post-intervention (6 months). [a]All participants analyzed according to allocation ($N = 159$); adjusted for baseline values and repeated measurements within participants. [b]MDS-UPDRS, part I (non-motor experiences of daily living, with a range of 0–52); part II (motor experiences of daily living, with a range of 0–52); and part III (motor examination: with a range of 0–132); higher scores indicate more severe disease signs. [c]Higher scores in PDQ-8 summary index indicate worse disease-specific quality-of-life. [d]FFMQ-SF assesses five subscales of perceived mindfulness domains: observing, describing, acting with awareness, non-judgement of inner experiences, and non-reaction to inner experience. Higher scores indicate higher levels of mindfulness. [e]Higher levels of IL-6 are associated with higher levels of chronic inflammation in the body. [f]Cortisol: plasma cortisol; higher levels are associated with higher levels of stress. [g]Higher levels of TNF-alpha are associated with chronic inflammation and tissue damage in the body.

at risk of depression, meditation appears to be more effective than yoga in managing anxiety symptoms, depressive symptoms, mindfulness traits (describing, non-judging, and non-reacting facets), and HRQOL.

Comparison with Other Studies

Previous meta-analyses have shown that non-pharmacological interventions like physical therapy and mind-body exercises can improve motor function, gait, and balance in patients with PD [12, 38]. However, the effects of these interventions on anxiety, depression, non-motor symptoms, and HRQOL remain inconclusive. These discrepancies may be attributed to variations in treatment modalities and dosages, as well as methodological limitations including small sample sizes (ranging from 12 to 138), lack of masking, and absence of an intention-to-treat analysis. Additionally, long-term effects of mindfulness practices have been scarcely investigated in previous trials. Our study expands on this existing research by exploring two distinct mindfulness practices (mentally focused meditation versus movement-guided yoga) and incorporating both subjective and objective outcomes, including biomarkers of stress and inflammation. Results showed that both meditation and yoga had significant positive effects on anxiety symptoms, motor symptoms, mindfulness-describing skills, and HRQOL at 2 months in patients with PD. The reductions in anxiety symptoms were found to be moderately large compared to usual care (Cohen's *d*: meditation = 0.57, yoga = 0.69), similar to evidence-based behavioral treatments for psychiatric conditions in PD [39]. Notably, meditation also demonstrated a moderate effect (Cohen's $d = 0.59$) in reducing depressive symptoms. These significant between-group differences in anxiety and depressive symptoms reached minimal clinically important differences (MCID) [40], suggesting that both mindfulness interventions could serve as effective lifestyle strategies to mitigate psychiatric comorbidities in individuals with PD.

The study also confirmed the self-reported psychological improvements through a significant reduction in IL-6 levels at 6 months. The delayed response is likely due to the long-term response of mindfulness practice, as the study participants reported a high willingness to apply these techniques in their daily lives. The literature suggests that the effect of physical activity, such as exercise, can cause a temporary increase in IL-6 levels, but the long-term response to regular exercise can lead to a decrease in basal IL-6 levels [41]. Similarly, a previous study by McClintock et al. [42] found a significant association between increased time of mindfulness practice and reduced IL-6 levels in individuals with alcohol use disorder. Substantial evidence indicates peripheral inflammation plays a role in PD pathogenesis and prognosis [43]. Specifically, pro-inflammatory cytokines like IL-6, TNFα, and IL-1β can modulate signaling pathways, induce oxidative stress, disrupt neuronal function, and contribute to neurodegeneration. Conversely, anti-inflammatory cytokines like IL-10, IL-4, and IL-1RA exhibit protective effects [44]. Higher pro-inflammatory or lower anti-inflammatory serum markers have been shown to predict a more rapid progression of motor symptoms [16]. Considering that mood disorders are not solely a reaction to the diagnosis and living with PD but also a part of the neuropathological process involved, mindfulness practices that regulate emotions and suppress pro-inflammatory cytokines like IL-6 may serve as a potential therapeutic target in the absence of disease-modifying agents. Future endeavors should prioritize translating center-based supervised formal mindfulness practices in home-based setting, as well as developing strategies to support on-going and informal mindfulness practices during and after formal training to promote the long-term benefits [45].

Nevertheless, the current evidence on the relationship between mindfulness and stress biomarkers is still in its early stages for neurogenerative conditions. Previous systematic review and meta-analyses have found no significant effects of mindfulness on serum IL-6 and TNF-alpha across diverse populations, including healthy adults, caregivers and those with disease conditions like chronic pain, cancer, heart disease [14, 46, 47]. In contrast, trials of mindfulness for anxiety and depressive disorders showed significant reductions in IL-6 and TNF-alpha compared to attention control up to 3 months post-intervention [48, 49]. However, this study did not find significant changes in cortisol and TNF-alpha. The conflicting findings may be attributed to several factors, including the "black box" of mindfulness interventions, where the specific components, intensity, and fidelity are not well-quantified; small sample sizes; and the single blood sampling at each timepoint, which might not be sensitive enough to capture the complexity of neurobiological effects in mediating health conditions [50]. Future longitudinal studies should further explore the temporal dynamic effects of mindfulness on PD progression, specially by examining both peripheral and central neuroinflammatory mechanisms, including the diurnal cortisol slopes and gut-brain responses [51]; while also controlling for confounding factors like physical activity, sleep, and diet.

Beyond psychological symptoms, it is noteworthy that meditation was more effective than yoga in managing perceived motor experiences in daily living at 6 months. Moreover, meditation exerted comparable yet more sustained effects compared to yoga in reducing assessor-rated severity of motor symptoms and improving HRQOL. The between-group differences in MDS-UPDRS motor scores were 5.35 and 6.59 points in favor of meditation and yoga practices, which exceed MCID and are comparable to physical exercise [52]. This is crucial, as improved mood is associated with optimized medication response and motor performance in PD [53]. Given the high comorbidity and interference of mood and motor symptoms, it is important to prioritize effective stress management in PD care. These findings expand the non-pharmacological treatment options and underscore the promise of mindfulness practices, particularly meditation, as a non-physically demanding option for individuals with physical impairments. Further research is needed to investigate whether patients in more advanced stages of the disease could equally benefit from the tested meditation practice.

The study also found that only meditation, but not yoga, significantly reduced depressive symptoms at 2 months compared to the control group. Subgroup analyses revealed that, for participants at risk of depression, meditation appear to be more effective than yoga in managing anxiety symptoms, depressive symptoms, mindfulness traits (particularly in describing, non-judging, and non-reacting facets), and HRQOL. Particularly, the yoga participants at risk of psychological distress showed reduced mindfulness traits related to acting with awareness and non-judging. This suggests meditation may be more beneficial for distressed PD patients than yoga [54]. Corroborating previous literature, meditation, and yoga may regulate emotional disturbances via different pathways [55]. The mentally focused meditation approach targeting metacognitive awareness may be particularly helpful for addressing past-oriented rumination and depressive symptoms. In addition, the relatively non-physically exerting nature of meditation practice may provide more opportunities for distressed PD patients to reflect on their internal experiences and cultivate a heightened state of mindfulness [56]. In contrast, during yoga practice, participants were invited to be aware of their in-present experiences alongside body movement, which sometimes may induce negative or difficult feelings. Distressed participants may find it more difficult to remain fully present and non-judgmental, thus making it more difficult to sustain and translate state mindfulness to trait mindfulness.

Nevertheless, the findings on self-reported trait mindfulness should be interpreted cautiously. Literature suggests individuals vary in their rates of change in state mindfulness during practice, leading to differing effects on trait mindfulness [57]. While participants may have experienced heightened state mindfulness contributing to reduced distress, changes in their general, dispositional trait mindfulness may not have been fully captured within the study timeframe [58]. Additionally, FFMQ has been critiqued as having face validity issues and biases that may hinder its ability to accurately capture daily mindful awareness [59, 60]. Future study should further explore the mechanisms and mediating factors to better understand the complex relationship between mindfulness interventions and trait-level changes, especially for psychologically vulnerable populations.

Strengths and Limitations of the Study

The study's strengths included an assessor-blind, powered randomized clinical design, multiple follow-up timepoints, and comprehensive measurement of physio-psychosocial outcomes with objective stress biomarkers. However, the limitations of this study must be acknowledged. First, this study was implemented during the COVID-19 pandemic, which posed challenges for participant enrolment and adherence. The final sample (n = 159) was slightly smaller (5%) than initially proposed (n = 168), but the attrition rates (T1:12.6%; T2:15.1%) were within expectation (i.e., 20%) during power calculation. The pandemic may have influenced participants engagement with mindfulness interventions. Still, the intervention adherence was satisfactory and comparable to a previous mindfulness trial [19]. Beyond improved anxiety symptoms, motor symptoms, mindfulness-describing facet, and HRQOL, mediation group demonstrated additional benefits in reducing depressive symptoms. Nonetheless, the yoga group reported slightly higher treatment credibility and satisfaction compared to the meditation group. This underscores the importance of exploring individual preferences regarding mindfulness practices and satisfaction when evaluating treatment effectiveness. Second, while the HADS is validated for Chinese PD populations and is widely utilized in similar research, it does present inherent challenges. The mix of positively and negatively worded items limits its capacity to provide a unidimensional measure of either anxiety or depression [61]. For future studies, it may be beneficial to consider more sensitive patient-reported measures such as the revised Hopkins Symptom Checklist (SCL-90-R) to gain a more comprehensive understanding of mood disorders in this population [62]. Nevertheless, since the

current study primarily focused on symptom-related outcomes, future research should incorporate a combination of symptom-related scales, measures of psychospiritual wellbeing measures, and coping strategies. This approach would enable a more holistic evaluation of the safety and efficacy of clinical interventions for PD population. Third, psychiatric diagnoses were obtained through self-reports without a formal DSM-5 TR diagnostic assessment, and medication data were not cross-verified with hospital records. This reliance on self-reported data may affect the accuracy of diagnoses and medication use. However, the absence of changes in psychiatric medication dosages throughout the study suggests that the intervention effects were unlikely influenced by medication adjustments. Additionally, the use of a waitlist control may induce expectation bias. Future studies could further examine mindfulness treatment effects by using active controls such as progressive relaxation exercises. This study may have been subject to selection bias, as participants were enrolled through convenience sampling. The participants who volunteered for this study might be more active in seeking community resources and more willing to practice mindfulness compared with those who declined to participate or withdrew from the study. Finally, people who had severe motor limitations, uncontrolled/active psychiatric disorders or significant cognitive impairment were excluded. Thus, the PD population was only partially represented. All these factors may have limited the generalizability of the study findings to the entire PD population.

Conclusions and Policy Implications

Mindfulness-based meditation and yoga practices demonstrated significant short-term improvements in anxiety symptoms, motor symptoms, and HRQOL, as well as delayed reduction in pro-inflammatory cytokine (IL-6) in patients with mild-to-moderate PD. Specifically, meditation appeared more effective than yoga for managing mood symptoms and improving mindfulness traits, especially in participants at risk of depression. This finding suggests the importance of incorporating mindfulness-based interventions into routine care to address the biopsychosocial challenges faced by individuals with PD. Future research should further examine and validate the potential neuroprotective mechanisms of mindfulness, as well as explore strategies to optimize its integration into sustainable clinical care for neurodegenerative conditions. This would ultimately enhance whole-person care for individuals with PD and similar disorders.

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Statement of Ethics

The trial protocol was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (HKU/HA HKW IRB, reference No. UW 19-446). The study was registered at the WHO Primary Registry – Chinese Clinical Trials Registry: ChiCTR2100045939. All participants provided written informed consent at enrolment.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Dr. Kwok had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study conceptualization and design: Jojo Kwok (lead), Daniel Fong (supporting), and Rainbow Ho (supporting). Acquisition, analysis, or interpretation of data: Jojo Kwok (lead), Lily Chan (supporting), Charis Lai (supporting), Philip HO (supporting), Zoe Choi (supporting), Edmond Choi (supporting), Man Auyeung (supporting), Shirley Pang (supporting), and Daniel

Fong (supporting). Drafting of the manuscript: Jojo Kwok (lead), Lily Chan (supporting), Charis Lai (supporting), and Zoe Choi (supporting). Critical revision of the manuscript for important intellectual content: Jojo Kwok (lead), Lily Chan (lead), Philip Ho (supporting), Edmond Choi (supporting), Man Auyeung (supporting), Shirley Pang (supporting), Daniel Fong (supporting), Doris Yu (supporting), CC Lin (supporting), Samuel Wong (supporting), Richard Walker (supporting), and Rainbow Ho (supporting). Statistical analysis: Jojo Kwok (lead), Lily Chan (supporting), and Daniel Fong (supporting). Obtained funding: Jojo Kwok (lead), Man Auyeung (supporting), Shirley Pang (supporting), Philip Ho (supporting), Doris Yu (supporting), Daniel Fong (supporting), CC Lin (supporting), Samuel Wong (supporting), Richard WALKER (supporting), and Rainbow Ho (supporting). Administrative, technical, or material support: Jojo Kwok (lead), Lily Chan (supporting), Charis Lai (supporting), Philip Ho (supporting), Zoe Choi (supporting), Edmond Choi (supporting), Man Auyeung (supporting), Shirley Pang (supporting), CC Lin (supporting), Rainbow Ho (supporting). Study supervision: Jojo Kwok (lead), and Man Auyeung (supporting).

Data Availability Statement

The data supporting the findings of this study are not publicly available due to their containing information that could compromise the privacy of study participants. Reasonable requests for patient level data should be made to the corresponding author and will be considered by the trial management group. Consent for data sharing was not obtained but the presented data are anonymized and risk of identification is low.

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