Multiple Case Studies on the Effects of Aroma Massage for Pain Relief and Quality of Life in Parkinson's Disease Patients

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Objective: This study investigated the effects of Aromatherapy Massage on chronic pain and quality of life (QOL) in four patients with Parkinson's disease (PD) whose pain was unresponsive to medication.
Methods: A three-arm crossover trial was conducted, consisting of Inhalation (I), Massage (M), and Aromatherapy Massage (AM), each over three weeks. Pain was assessed using the Visual Analog Scale (VAS) and King's PD Pain Scale (KPPS). Plasma dopamine and β-endorphin levels and electroencephalography (EEG) were used as objective indicators. QOL was measured using the PDQ-39. Data were analyzed with linear mixed models ($p < 0.05$).
Results: Only AM significantly increased plasma dopamine. Both M and AM elevated β-endorphin levels and reduced VAS scores during and after intervention. KPPS scores improved following AM. EEG showed the highest peak alpha frequency during AM. PDQ-39 scores improved by 3.75 points after AM.
Conclusion: Aromatherapy massage may offer effective multisensory stimulation for alleviating chronic pain and enhancing QOL in PD patients. It may serve as a useful complementary strategy in pain management.

Key words: Parkinson's disease, chronic pain, aromatherapy, massage, quality of life

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor symptoms such as tremors, rigidity, and bradykinesia, as well as non-motor symptoms including cognitive decline and chronic pain. It has been reported that approximately 65–85% of individuals with PD experience chronic pain [1], which can significantly impair vitality and mental well-being. This often leads to anxiety, disuse syndrome, and depression, resulting in a substantial decline in activities of daily living (ADL) and quality of life (QOL) [2].

Although pharmacological treatment remains the primary strategy for managing pain in PD, it often fails to address the complex interplay of physical, psychological, and social factors associated with chronic pain. This underscores the importance of adopting a more comprehensive and integrative approach to care. In recent years, complementary and alternative medicine (CAM) has garnered increasing attention, with approximately 40% of PD patients in the United States reportedly using CAM modalities for symptom relief. Among these, aromatherapy and massage are particularly popular in both the United Kingdom and the United States [3].

Aromatherapy is believed to enhance olfactory input to the limbic system, stimulating brainstem pathways that regulate neurotransmitters such as serotonin and norepinephrine. These effects are thought to activate the descending pain modulation system and inhibit excessive pain transmission. Essential oils used in aromatherapy have been shown to directly influence serotonin and norepinephrine levels [4]. Given that PD patients often exhibit reduced levels of dopamine, serotonin, and norepinephrine, it is hypothesized that aromatherapy may help alleviate pain by addressing these neurochemical deficiencies.

In addition to olfactory stimulation, aroma massage provides tactile input that activates the serotonin system through stimulation of C-fiber receptors in the skin. This dual mechanism — combining essential oil inhalation and transdermal absorption with physical touch — suggests that aroma massage may be particularly effective in reducing pain symptoms.

Despite growing international interest, research on the use of aromatherapy massage for chronic pain management in PD patients remains limited in Japan. A recent systematic review found that existing studies often lack objective assessments of chronic pain, and few have investigated the long-term effects of such interventions. Moreover, subjective pain evaluations alone are insufficient. It is essential to use pain assessment tools that are tailored to the specific types of pain experienced in PD, and to evaluate how pain symptoms affect daily functioning.

Additionally, before initiating interventions like aromatherapy massage, clinicians must consider individual patient factors such as disease severity, olfactory dysfunction, and cognitive impairment, all of which may influence treatment effectiveness. Therefore, to rigorously evaluate the potential benefits of aroma-

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therapy massage for chronic pain relief in PD, both subjective and objective methods should be employed.

This study aims to contribute to improving chronic pain management in PD patients by examining the effectiveness of aromatherapy massage from multiple perspectives.

RESEARCH OBJECTIVE

This study aims to explore the effects of Aroma massage on pain relief and QOL improvement in individuals with PD who experience chronic pain.

RESEARCH METHODS

1) Research Design

This study was designed as a single-arm crossover trial involving four patients with Parkinson's disease (PD). Each participant underwent three different treatment modalities — Inhalation (I), Massage (M), and Aroma Massage (AM) — each administered for 20 minutes. Given the small sample size, statistical analyses were conducted as exploratory assessments to identify potential trends and patterns across individual cases. The results should be interpreted with caution, emphasizing observed tendencies rather than definitive conclusions.

2) Measurement Tools

(1) Patient Attributes

Age, Sex, and Medical History

Hoehn & Yahr Stage: This scale evaluates the severity of PD, with stages ranging from I to V, where higher values correspond to more severe disease [5].

Disability Level: A scale categorizing the degree of disability in PD patients, ranging from I to III [6].

Unified Parkinson's Disease Rating Scale (UPDRS): A comprehensive tool used to assess the severity of PD across multiple domains, including mental status, activities of daily living (ADLs), motor ability, and complications. Higher scores indicate greater impairment [7].

Mini-Mental State Examination (MMSE): This cognitive assessment tool measures overall cognitive function, with scores below 24 suggesting possible cognitive impairment [8].

The Odor Stick Identification Test for the Japanese (OSIT-J): A test used to assess olfactory dysfunction, with a score of 8 or more correct answers out of 13 indicating normal olfactory function [9].

(2) Evaluation Criteria

Objective Chronic Pain

Blood Tests

Data for blood tests were gathered from electronic medical records by the attending physician during outpatient visits. The following biomarkers were measured: plasma dopamine and plasma β-endorphin levels. Blood samples were collected just prior to medication intake to minimize the influence of drugs on the blood concentrations. Samples were taken at the trough level (approximately 30 minutes before the next scheduled dose).

Electroencephalography (EEG) Measurement

EEG recordings were performed using the wireless biosignal device "Polymate Pocket® MP208" (Miyuki Giken, Japan). The reference points for recording were located at the mid-occipital region and the earlobe. Data were collected using MP208 Monitor Program Version 2.01 (Miyuki Giken, Japan) and analyzed via frequency analysis [10].

Conditioned Pain Modulation (CPM)

CPM refers to the process where pain perception is influenced by a conditioned stimulus. A diminished CPM response is indicative of impaired descending pain inhibition. CPM measurements were performed on the deltoid and anterior tibialis muscles both before and after each treatment modality.

Subjective Chronic Pain

Visual Analogue Scale (VAS)

Pain intensity was measured using a 10 cm scale. A score of 0 indicated no pain, 1–3 represented mild pain, 4–6 indicated moderate pain, and 7–10 indicated severe pain [12].

King's Parkinson's Disease Pain Scale (KPPS)

This scale is a quantitative tool designed specifically for assessing pain in PD patients. It categorizes pain into seven domains, based on both the type of pain and its variability throughout the day [13].

(3) Quality of Life (QOL)

Parkinson's Disease Questionnaire-39 (PDQ39)

This 39-item questionnaire assesses the quality of life in PD patients across eight domains: Activity, ADL, Emotional Health, Embarrassment, Social Support, Cognition, Communication, and Bodily Discomfort. Higher scores in these domains correspond to a decline in QOL. The total score ranges from 0 to 156, with higher scores indicating worse QOL [14].

RESEARCH IMPLEMENTATION PROCEDURE

The study was conducted weekly during outpatient visits. The researcher, an experienced aromatherapist and nurse, administered the following treatments over a period of three weeks. Additionally, participants were instructed to continue the treatments independently between outpatient visits (Table 1).

- **Inhalation (20 minutes)**: Lemongrass essential oil (I)
- **Pain Area Massage (20 minutes)**: 10 ml of jojoba oil (M)
- **Aroma Massage for Pain Area (20 minutes)**: 10 ml of jojoba oil with 3% lemongrass essential oil (AM)

Based on prior studies indicating that aroma massage (AM) may alleviate chronic pain after two weeks of treatment, a three-week duration was selected for this study. A one-week interval between treatments was included to minimize patient burden and account for the metabolic effects of essential oils. However, this washout period may be insufficient to eliminate carryover effects. Therefore, the possibility of carryover effects should be considered when interpreting the results.AM was chosen due to its high content of Citral, a compound in lemongrass believed to aid in pain alleviation [15]. A patch test was conducted before the start of the treatments to check for allergic reactions.

Table 1 Treatment Schedule

		Inhalation (I)			Massage (M)			Aroma Massage (AM)		
Time period		Week 1	Week 2	Week 3	Week 1	Week 2	Week 3	Week 1	Week 2	Week 3
Frequency (6 times at home, 1 time in the outpatient clinic)		7 times	7 times	7 times	7 times	7 times	7 times	7 times	7 times	7 times
Evaluation Measurement	EEG, CPM, VAS	●	●	●	●	●	●	●	●	●
	KPPS, PDQ39, Blood Test	●		●	●		●	●		●

Table 2 Linear Mixed-Model Analysis Conditions for Blood Samples

Dependent Variable	Blood test data values
Fixed Effects	Implementation week (week 0, week 3), pattern (I, M, AM), and their interaction term (implementation week * pattern)
Random Factor	Subject
Covariance Structure	Compound Symmetry Selected

Table 3 Conditions and Calculation Procedures for VAS Linear Mixed-Model Analysis

Dependent Variable	VAS value
Fixed Effects	Measurement time points (before implementation, during implementation, immediately after implementation, 1 hour after implementation), implementation week (week 1, week 2, week 3), pattern (I, M, AM), and their interaction terms (measurement time point * implementation week, measurement time point * pattern, implementation week * pattern, measurement time point * implementation week * pattern)
Random Factor	Subject
Covariance Structure	Compound Symmetry Selected

1. Calculate the least squares estimates for each measurement time point of each pattern in each week and for the 3-week integration.
2. Calculate the least squares estimates for each measurement time point of each pattern in each week and for the 3-week integration.
3. Calculate the least squares estimates for the changes from before implementation to each implementation time point and perform pre-post comparison tests.
4. Calculate the least squares estimates for the changes from immediately after implementation to 1 hour after implementation and perform pre-post comparison tests.

A consistent light stroking technique was employed by both the researcher and the patients for the M and AM treatments.

ANALYTICAL METHODS

The data on pain and QOL were analyzed using basic statistical methods, followed by linear mixed-model analysis. This approach was deemed appropriate due to the small sample size of four participants and the repeated measures design of the study.

Linear mixed models are particularly suited for small sample sizes as they allow for the modeling of both fixed effects — such as treatment effects — and random effects — such as individual variability — simultaneously. This capability enables the extraction of reliable estimates even with limited data.

Furthermore, linear mixed models can handle unbalanced data more effectively than traditional methods, reducing potential biases and increasing the robustness of the findings.Statistical analysis was performed using SPSS version 25, with a significance threshold set at $p < 0.05$.

(1) Objective Chronic Pain Assessment

Blood Tests

Changes in blood test results before and after each treatment were analyzed using linear mixed-model analysis, following the conditions specified in Table 2. The least-squares estimates for each treatment modality and week were calculated, and pre- and post-treatment comparisons were performed, with pairwise comparisons between treatment patterns. Additionally, the change rate at the three-week mark was compared to the baseline value at week zero, using the same analysis model. Neurochemical substances, such as catecholamines, were analyzed for changes pre- and post-treatment due to individual variability.

Electroencephalogram (EEG) Measurement

Peak Alpha Frequency (PAF) is a recognized marker of brain wave activity related to pain relief. The relationship between subjective pain intensity, mood states, and PAF was analyzed to evaluate the effects of pain relief. PAF decreases during pain episodes. EEG was recorded for two minutes with the patient's eyes closed, and PAF was assessed by comparing resting baseline levels with post-treatment levels [16]. EEG measurements were recorded from the occipital (Oz) and auricular (A1) regions, which are known to exhibit alpha rhythms (8–13 Hz) during wakefulness.

Conditioned Pain Modulation (CPM)

CPM was assessed before and after each treatment, following the same methodology used for the Visual Analogue Scale (VAS). The measurements were taken at two time points: pre-treatment and post-treatment.

(2) Subjective Pain Assessment

Visual Analogue Scale (VAS)

VAS was measured during outpatient visits on a weekly basis before, during, immediately after, and one hour after each treatment. Linear mixed-model analysis was used to evaluate pre- and post-treatment differences for each treatment modality (Table 3). If the interaction term for the week (measurement point * week * treatment modality) was significant, the data were analyzed separately for each week. If no significant inter-

Table 4 Linear Mixed-Model Analysis Conditions for KPPS

Dependent Variable	KPPS value
Fixed Effects	Implementation week (before implementation, week 1, week 2, week 3), pattern (I, M, AM), and their interaction term (implementation week * pattern)
Random Factor	Subject
Covariance Structure	Compound Symmetry Selected

Table 5 Linear Mixed-Model Analysis Conditions for PDQ-39

Dependent Variable	Total PDQ39 score
Fixed Effects	Measurement time points (before implementation, after I, after M, after AM)
Random Factor	Subject
Covariance Structure	Compound Symmetry Selected

1. Calculate the least squares estimates for each measurement time point.
2. Conduct comparison tests between before implementation and each measurement time point.
3. Perform pairwise comparison tests between each pattern after implementation.

Table 6 Participant Characteristics (n = 4)

Item \ Subject	A	B	C	D
Age	Early 60s	Late 50s	Late 70s	Early 60s
Gender	Male	FeMale	Male	Male
Medical history (years)	12	1	3	8
Hoehn & Yahr severity, level of disability	Ⅲ/2	Ⅱ/1	Ⅲ/2	Ⅲ/2
MMSE (out of 30 points)	29	29	28	29
UPDRS (out of 176 points)	20	21	20	20
OSIT-J (Olfactory Dysfunction)	None	Mild	None	Mild

Table 7 Plasma Dopamine and β-Endorphin Levels in the I, M, and AM Groups (Individual Data)

A

Parameter / Pre-Post (N)		Plasma Dopamine (ng/ml)	Rate of Change	β-Endorphin (pg/ml)	Rate of Change(%)
Aroma Massage	Pre	529.2	13.6	5.5	74.5
	3 Weeks Later	601.5		9.6	
Massage	Pre	467.7	7.1	5.5	63.6
	3 Weeks Later	500.9		9.0	
Inhalation	Pre	439.4	6.4	4.8	14.5
	3 Weeks Later	467.7		5.5	

B

Parameter / Pre-Post (N)		Plasma Dopamine (ng/ml)	Rate of Change	β-Endorphin (pg/ml)	Rate of Change (%)
Aroma Massage	Pre	141.1	73.6	5.1	100.0
	3 Weeks Later	245.6		10.2	
Massage	Pre	145.8	50.0	3.5	48.5
	3 Weeks Later	218.8		5.2	
Inhalation	Pre	150.6	38.5	2.8	35.7
	3 Weeks Later	208.7		3.8	

C

Parameter / Pre-Post (N)		Plasma Dopamine (ng/ml)	Rate of Change	β-Endorphin (pg/ml)	Rate of Change (%)
Aroma Massage	Pre	200.4	10.7	5.0	112.0
	3 Weeks Later	221.8		10.6	
Massage	Pre	203.7	0.7	3.4	67.6
	3 Weeks Later	205.1		5.7	
Inhalation	Pre	209.6	3.7	2.2	63.6
	3 Weeks Later	217.3		3.6	

D

Parameter / Pre-Post (N)		Plasma Dopamine (ng/ml)	Rate of Change	β-Endorphin (pg/ml)	Rate of Change (%)
Aroma Massage	Pre	124.3	17.3	5.1	68.6
	3 Weeks Later	145.9		8.6	
Massage	Pre	142.5	9.1	5.5	50.9
	3 Weeks Later	155.4		8.3	
Inhalation	Pre	146.2	1.8	4.0	5.0
	3 Weeks Later	148.9		4.2	

action was found, data from all three weeks were integrated for analysis.

King's Parkinson's Disease Pain Scale (KPPS)

Differences in KPPS scores across treatment modalities were analyzed using linear mixed-model analysis, as shown in Table 4. Least-squares estimates for each treatment modality and week were calculated, followed by pre- and post-treatment comparisons and pairwise comparisons between modalities.

(3) QOL Assessment

Changes in the total PDQ-39 scores between treatment patterns were analyzed using linear mixed-model analysis, based on the conditions and procedures outlined in Table 5.

ETHICAL CONSIDERATIONS

This study was conducted in full accordance with the ethical principles outlined in the Declaration of Helsinki (World Medical Association). Prior to participation, all individuals were provided with comprehensive information — both verbally and in writing — regarding the objectives, research methodology, potential benefits and risks, procedures for managing health-related issues, compensation mechanisms, and plans for the dissemination of study results. Informed consent was obtained from all participants based on their voluntary agreement to participate.

Participation was entirely voluntary, and all participants were informed that they could withdraw from the study at any point without incurring any disadvantage or penalty. To ensure privacy and confidentiality, all collected data were anonymized and securely stored under strict data management protocols. No conflicts of interest were reported by the investigators.

This study received ethical approval from the Research Ethics Committee of Tokai University (Approval No. 21A-095).

RESULTS

1) Participant Characteristics

A total of four patients met the inclusion criteria and completed the 3-week treatment protocol. All participants provided written informed consent prior to enrollment. The mean age was 64.5 years (range: 57–75 years), comprising three males and one female (Table 6).

Only participants with sufficient cognitive function to complete the evaluation tasks were included in the analysis. All individuals scored 24 or higher on the Mini-Mental State Examination (MMSE), indicating no cognitive impairment. According to the Hoehn and Yahr staging system for Parkinson's disease severity, one participant was classified as Stage II and three as Stage III. Functional disability levels were rated as Stage 2 in three participants and Stage 1 in one participant.

All participants reported pain as their primary source of discomfort. None had a history of allergies. In the olfactory assessment using the Odor Stick Identification Test for Japanese (OSIT-J), two participants showed mild olfactory impairment. However, all participants responded appropriately to the essential oil scents used in the study.

Table 8 Plasma Dopamine and β-Endorphin Levels in the I, M, and AM Groups (Linear Mixed Model Analysis)

		Inhalation (I)				Massage (M)				Aroma Massage (AM)				P-value		
		LS mean	95%CI		P-value	LS mean	95%CI		P-value	LS mean	95%CI		P-value	I vs. M	I vs. AM	M vs. AM
dopamine (ng/ml)	Before implementation	236.45	0.00	491.12	–	239.92	0.00	494.59	–	248.75	0.00	503.42	–	–	–	–
	3 weeks later	260.65	5.98	515.32	–	270.05	15.38	524.72	–	303.70	49.03	558.37	–	–	–	–
	Amount of change from before implementation															
	3 weeks later	24.20	−24.17	72.57	0.303	30.12	−18.25	78.50	0.204	54.95	6.58	103.32	0.029	0.685	0.077	0.159
	Rate of change from before implementation															
	After 3 weeks (%)	12.63	−23.33	48.58		16.75	−19.20	52.70		28.98	−6.98	64.93		0.430	0.015	0.046
β endorphins (pg/ml)	Before implementation	3.45	2.20	4.70	–	4.48	3.23	5.72	–	5.18	3.93	6.42	–	–	–	–
	3 weeks later	4.28	3.03	5.52	–	7.05	5.80	8.30	–	9.75	8.50	11.00	–	–	–	–
	Amount of change from before implementation															
	3 weeks later	0.82	−0.59	2.24	0.234	2.58	1.16	3.99	0.002	4.58	3.16	5.99	< 0.001	0.001	< 0.001	0.001
	Rate of change from before implementation															
	After 3 weeks (%)	29.73	4.57	54.88		57.68	32.52	82.83		88.78	63.62	113.93		0.021	0.001	0.013

LS mean: least square mean; 95%CI: 95% confidence interval

Analysis: Linear Mixed Model [Fixed effects: Implementation time point (before implementation, 3 weeks after implementation), Group (Aromatherapy, Massage, Aromatherapy Massage)]

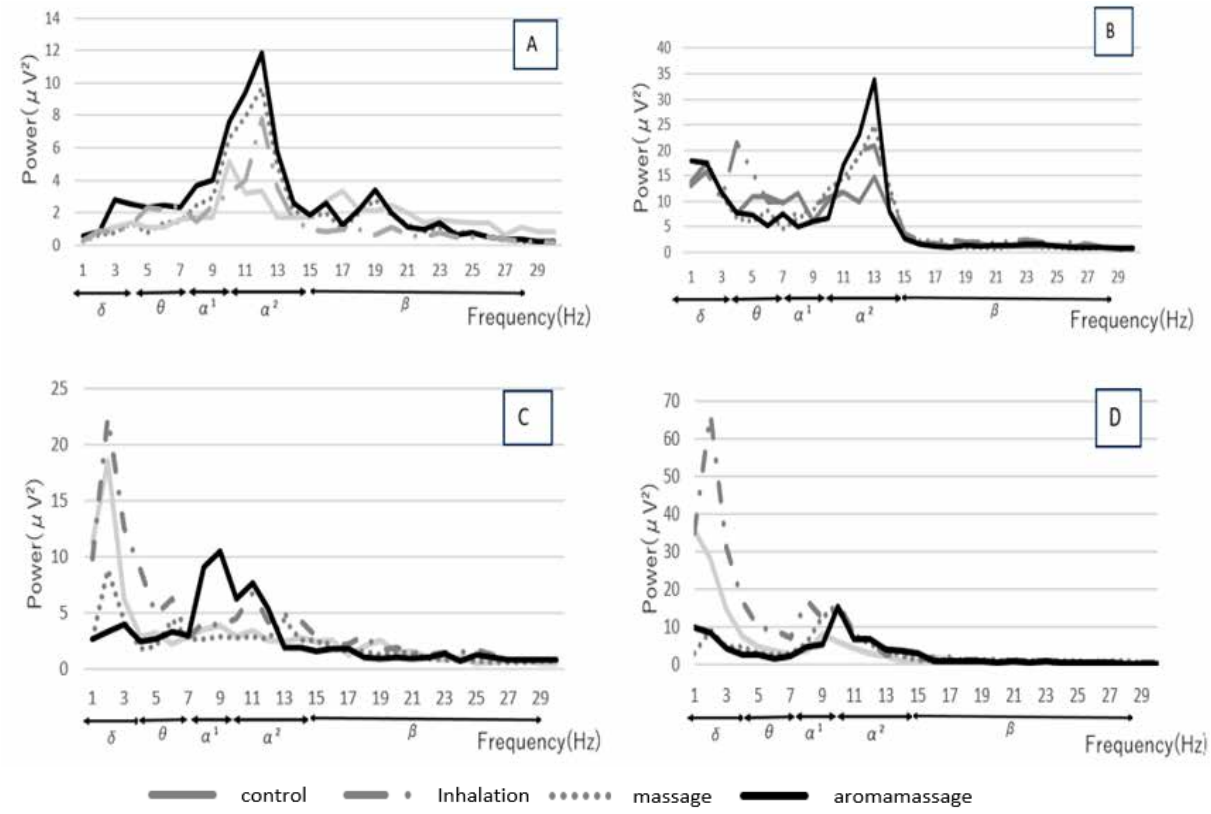

Figure Changes in EEG Power Spectrum (PAF) for I, M, and AM
The EEG power spectrum shows a rightward shift in alpha wave peaks after all treatments — Inhalation (I), Massage (M), and Aromatherapy Massage (AM) — indicating increased Peak Alpha Frequency (PAF) linked to pain relief. AM produced the greatest PAF increase, from 8.79 Hz to 11.72 Hz, significantly higher than I and M.

2) Objective Assessment of Chronic Pain

(1) Blood Biomarkers

Plasma Dopamine

After the 3-week intervention, plasma dopamine levels exhibited an increasing trend exclusively in the AM group (I: + 24.2 ng/mL, + 12.6%; M: + 30.1 ng/mL, + 16.8%; AM: + 54.95 ng/mL, + 28.9%). No significant differences in absolute changes were observed among the groups (I vs. M: $p = 0.685$; AM vs. I: $p = 0.077$; M vs. AM: $p = 0.159$).

However, the percentage increase in dopamine levels was significantly higher in the AM group compared to both the I and M groups (I vs. AM: $p = 0.015$; M vs. AM: $p = 0.046$), as shown in Table 7. No significant difference was found between the I and M groups ($p = 0.430$).

Plasma β-Endorphins

Plasma β-endorphin levels showed an increasing trend in both the M and AM groups after the intervention (I: + 0.82 pg/ml, + 29.73%; M: + 2.58 pg/ml, + 57.68%; AM: + 4.58 pg/ml, + 88.78%). Comparisons among the three groups revealed significant differences in both absolute and percentage changes (absolute change: $p < 0.001$; percentage change: I vs. M: $p = 0.021$; I vs. AM: $p < 0.001$; M vs. AM: $p < 0.013$), as detailed in Table 7. Further analysis using a linear mixed model, presented in Table 8, confirmed these significant differences among the groups.

(2) Electroencephalogram (EEG) Analysis

Figure presents the EEG power spectrum data, highlighting peak alpha frequency (PAF) values. Compared to the resting baseline, all treatment groups showed a rightward shift in peak frequency, indicative of increased PAF, which is associated with pain modulation. Among the three groups, the AM group demonstrated the greatest increase, from 8.79 Hz to 11.72 Hz, which was significantly higher than both the I and M groups.

(3) Conditioned Pain Modulation (CPM)

Pressure pain threshold (PPT) measurements were taken pre- and post-intervention for both the deltoid and tibialis anterior muscles. Initial PPT values ranged from 19.0 N to 36.0 N for the deltoid, and from 20.0 N to 46.0 N for the tibialis anterior.

Post-intervention analyses revealed an increasing trend in PPT values in the AM group for both muscle sites ($p < 0.0001$). No significant interaction effects with treatment week were observed, indicating the consistency of AM's effect over time.

When comparing mean changes across groups, both M and AM groups showed greater increases than the I group (Deltoid: I: + 0.83 N, $p = 0.335$; M: + 11.67 N, $p < 0.001$; AM: + 10.67 N, $p < 0.001$. Tibialis anterior: I: + 0.17 N, $p = 0.872$; M: + 9.33 N, $p < 0.0001$; AM: + 8.00 N, $p < 0.001$). However, no significant differences were observed between the M and AM groups in the magnitude of increase (Deltoid: $p = 0.44$; Tibialis anterior: $p = 0.298$).

As shown in Table 9, individual data on CPM responses indicated that the AM group exhibited a more pronounced inhibitory effect compared to the I and M groups. Table 10's linear mixed model analysis further confirmed significant differences among the groups,

Table 9 CPM in the I, M, and AM Groups (Individual Data)

A

	Inhalation						Massage						Aroma Massage					
Pre/post (N) \ Priod	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD
Pre																		
TA	36.0	38.0	40.0	38.0	38.0	1.6	36.0	41.0	34.0	36.0	37.0	2.9	37.0	37.0	36.0	37.0	36.7	0.5
Del	43.0	45.0	41.0	43.0	43.0	1.6	42.0	43.0	41.0	42.0	42.0	0.8	45.0	50.0	42.0	45.0	45.7	3.3
Post																		
TA	38.0	40.0	41.0	40.0	39.7	1.2	45.0	50.0	47.0	47.0	47.3	2.1	47.0	48.0	49.0	48.0	48.0	0.8
Del	42.0	46.0	40.0	42.0	42.7	2.5	50.0	55.0	44.0	50.0	49.7	4.5	46.0	48.0	50.0	48.0	48.0	1.6
TA: Increase	2.0	2.0	1.0	2.0	1.7	0.5	9.0	9.0	13.0	11.0	10.3	1.9	10.0	11.0	13.0	11.0	11.3	1.2
Del: Increase	0.0	1.0	0.0	0.0	0.3	0.5	8.0	12.0	2.0	8.0	7.3	4.1	1.0		8.0	3.0	4.5	3.5

B

CPM (N)	Inhalation						Massage						Aroma Massage					
Pre/post (N) \ Priod	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD
Pre																		
TA	19.0	20.0	22.0	20.0	20.3	1.2	20.0	21.0	22.0	21.0	21.0	0.8	20.0	22.0	23.0	22.0	21.7	1.2
Del	20.0	20.0	22.0	20.0	20.7	0.9	20.0	21.0	22.0	21.0	21.0	0.8	20.0	22.0	23.0	22.0	21.7	1.2
Post																		
TA	19.0	20.0	22.0	20.0	20.3	1.2	28.0	30.0	32.0	30.0	30.0	1.6	30.0	31.0	32.0	31.0	31.0	0.8
Del	20.0	20.0	22.0	20.0	20.7	0.9	28.0	30.0	32.0	30.0	30.0	1.6	30.0	31.0	32.0	31.0	31.0	0.8
TA: Increase	0.0	0.0	0.0	0.0	0.0	0.0	8.0	9.0	10.0	11.0	9.0	0.8	10.0	9.0	9.0	9.0	9.3	0.5
Del: Increase	0.0	0.0	0.0	0.0	0.0	0.0	8.0	9.0	0.0	8.0	5.7	4.0	10.0	9.0	9.0	9.0	9.3	0.5

C

	Inhalation						Massage						Aroma Massage					
Pre/post (N) \ Priod	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD
Pre																		
TA	36.0	38.0	40.0	38.0	38.0	1.6	36.0	41.0	34.0	36.0	37.0	2.9	37.0	37.0	36.0	37.0	36.7	0.5
Del	43.0	45.0	45.0	45.0	44.3	0.9	42.0	43.0	41.0	42.0	42.0	0.8	45.0	43.0	42.0	45.0	43.3	1.2
Post																		
TA	38.0	40.0	41.0	40.0	39.7	1.2	45.0	50.0	47.0	47.0	47.3	2.1	47.0	48.0	49.0	48.0	48.0	0.8
Del	44.0	46.0	45.0	45.0	45.0	0.8	52.0	55.0	56.0	55.0	54.3	1.7	56.0	56.0	54.0	56.0	55.3	0.9
TA: Increase	2.0	2.0	1.0	2.0	1.7	0.5	9.0	9.0	13.0	11.0	10.3	1.9	10.0	11.0	13.0	11.0	11.3	1.2
Del: Increase	1.0	1.0	0.0	0.0	0.7	0.5	10.0	12.0	15.0	12.0	12.3	2.1	11.0	13.0	12.0	12.0	12.0	0.8

D

	Inhalation						Massage						Aroma Massage					
Pre/post (N) \ Priod	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD
Pre																		
TA	26.0	30.0	28.0	28.0	28.0	1.6	22.0	26.0	27.0	26.0	25.0	2.2	24.0	28.0	27.0	27.0	26.3	1.7
Del	46.0	45.0	41.0	45.0	44.0	2.2	44.0	42.0	40.0	42.0	42.0	1.6	46.0	48.0	44.0	45.0	46.0	1.6
Post																		
TA	26.0	30.0	28.0	28.0	28.0	1.6	40.0	38.0	48.0	40.0	42.0	4.3	32.0	39.0	40.0	39.0	37.0	3.6
Del	46.0	45.0	42.0	45.0	44.3	1.7	50.0	55.0	46.0	50.0	50.3	3.7	55.0	58.0	50.0	55.0	54.3	3.3
TA: Increase	0.0	0.0	0.0	0.0	0.0	0.0	18.0	12.0	21.0	11.0	17.0	3.7	8.0	11.0	13.0	11.0	10.7	2.1
Del: Increase	0.0	0.0	1.0	0.0	0.3	0.5	6.0	13.0	6.0	6.0	8.3	3.3	9.0	10.0	6.0	10.0	8.3	1.7

highlighting the robust modulatory effect of AM.

3) Subjective Chronic Pain Evaluation

(1) Visual Analogue Scale (VAS)

VAS measurements were obtained at four time points: pre-treatment, during treatment, immediately post-treatment, and one hour post-treatment. Given the lack of a significant interaction between treatment week and treatment group, the average values across all three weeks were utilized for analysis.

In the I group, no significant reduction in pain was observed at any time point compared to pre-treatment (Pre-treatment: 6.25 cm; During treatment: 5.46 cm; Immediately post-treatment: 5.46 cm; One hour post-treatment: 5.75 cm; $p = 0.077$).

Conversely, both M and AM groups exhibited consistent reductions in pain at all time points (M: Pre-treatment: 6.75 cm; During treatment: 0.25 cm; Immediately post-treatment: 0.25 cm; One hour post-treatment: 3.17 cm; $p < 0.001$; AM: Pre-treatment: 6.42 cm; During treatment: 0.25 cm; Immediately post-treatment: 0.25 cm; $p < 0.001$). Notably, the AM group demonstrated the most substantial reduction in pain, with a consistent decrease of −4.33 cm at one hour post-treatment($p < 0.001$).

While pain levels increased after treatment in both M and AM groups, the increase was more gradual in the AM group (M: + 2.92 cm; AM: + 1.83 cm; $p < 0.001$).

At all time points, M and AM groups showed greater pain reductions compared to the I group, with no significant difference between M and AM ($p = 0.999$). However, at one hour post-treatment, the AM group exhibited a greater reduction in pain compared to the M group ($p = 0.016$).

As shown in Table 11, individual data on VAS scores indicated that both M and AM groups exhibited consistent reductions in pain at all time points. In contrast, the I group did not show significant changes compared to pre-treatment levels. Table 12's linear mixed model analysis further explored these trends,

Table 10 CPM in the I, M, and AM Groups (Linear Mixed Model Analysis)

			Inhalation				Massage				Aroma Massage				P-value		
			LS mean	95%CI		P-value	LS mean	95%CI		P-value	LS mean	95%CI		P-value	I vs. M	I vs. AM	M vs. AM
TA	Weekly Integration	implementation	31.08	17.97	44.20	–	30.00	16.88	43.12	–	30.33	17.22	43.45	–	–	–	–
		After implementation	31.92	18.80	45.03	–	41.67	28.55	54.78	–	41.00	27.88	54.12	–	–	–	–
		Change from before implementation															
		After implementation	0.83	−0.89	2.55	0.335	11.67	9.95	13.39	< 0.001	10.67	8.95	12.39	< 0.001	< 0.001	< 0.001	0.440
	Week 1	Before implementation	29.25	16.41	42.09		28.50	15.66	41.34		29.50	16.66	42.34				
		After implementation	30.25	17.41	43.09		39.50	26.66	52.34		39.00	26.16	51.84				
	Week 2	Before implementation	31.50	18.66	44.34		32.25	19.41	45.09		31.00	18.16	43.84				
		After implementation	32.50	19.66	45.34		42.00	29.16	54.84		41.50	28.66	54.34				
	Week 3	Before implementation	32.50	19.66	45.34		29.25	16.41	42.09		30.50	17.66	43.34				
		After implementation	33.00	20.16	45.84		43.50	30.66	56.34		42.50	29.66	55.34				
Del	Weekly Integration	implementation	38.00	20.35	55.65	–	36.75	19.10	54.40	–	39.17	21.52	56.82	–	–	–	–
		After implementation	38.17	20.52	55.82	–	46.08	28.43	63.73	–	47.17	29.52	64.82	–	–	–	–
		Change from before implementation															
		After implementation	0.17	−1.90	2.23	0.872	9.33	7.27	11.40	< 0.001	8.00	5.93	10.07	< 0.001	< 0.001	< 0.001	0.298
	Week 1	Before implementation	38.00	20.66	55.34		37.00	19.66	54.34		39.00	21.66	56.34				
		After implementation	38.00	20.66	55.34		45.00	27.66	62.34		46.75	29.41	64.09				
	Week 2	Before implementation	38.75	21.41	56.09		37.25	19.91	54.59		40.75	23.41	58.09				
		After implementation	39.25	21.91	56.59		48.75	31.41	66.09		48.25	30.91	65.59				
	Week 3	Before implementation	37.25	19.91	54.59		36.00	18.66	53.34		37.75	20.41	55.09				
		After implementation	37.25	19.91	54.59		44.50	27.16	61.84		46.50	29.16	63.84				

LS mean: least square mean; 95%CI: 95% confidence interval

Analysis: Linear Mixed Model [Fixed effects: Measurement time point (before implementation, after implementation), Implementation week (week 1, week 2, week 3), Group (Inhalation, Massage, Aromatherapy Massage)]

Testing of interaction terms:

Measurement time point * Implementation week * Group: P = 0.486 (TA); P = 0.765 (Del)

Measurement time point * Implementation week: P = 0.242 (TA); P = 0.690 (Del)

Implementation week * Group: P = 0.856 (TA); P = 0.980 (Del)

Measurement time point * Group: P < 0.001 (TA); P < 0.001 (Del)

Table 11 VAS for I, M, and AM (Individual Data)

A

Implementation Period \ Group	Inhalation						Massage						Aroma Massage					
Week	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD
Before implementation	8.0	7.0	8.0	8.0	7.7	0.4	8.0	8.0	8.0	8.0	8.0	0.0	8.0	8.0	7.0	8.0	7.7	0.4
During implementation	7.0	6.0	7.0	7.0	6.7	0.4	1.0	0.0	0.0	0.0	0.3	0.4	0.0	1.0	0.0	0.0	0.3	0.4
Immediately after implementation	7.0	6.0	7.0	7.0	6.7	0.4	1.0	0.0	0.0	0.0	0.3	0.4	0.0	1.0	0.0	0.0	0.3	0.4
1 hour after implementation	8.0	7.0	7.0	7.0	7.3	0.4	5.0	5.0	4.0	5.0	4.7	0.4	3.0	3.0	2.0	3.0	2.7	0.4

B

Implementation Period \ Group	Inhalation						Massage						Aroma Massage					
Week	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD
Before implementation	4.0	2.0	3.0	3.0	3.0	0.6	3.0	3.0	3.0	3.0	3.0	0.0	3.0	3.0	2.0	3.0	2.7	0.4
During implementation	3.5	1.5	2.5	2.5	2.5	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Immediately after implementation	3.5	1.5	2.5	2.5	2.5	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1 hour after implementation	4.0	2.0	3.0	3.0	3.0	0.6	2.0	2.0	2.0	2.0	2.0	0.0	2.0	2.0	1.0	2.0	1.7	0.4

C

Implementation Period \ Group	Inhalation						Massage						Aroma Massage					
Week	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD
Before implementation	8.0	8.0	8.0	8.0	8.0	0.0	8.0	8.0	8.0	8.0	8.0	0.0	9.0	8.0	6.0	8.0	7.7	1.0
During implementation	7.0	6.0	6.0	6.0	6.3	0.4	1.0	0.0	0.0	0.0	0.3	0.4	0.0	1.0	0.0	0.0	0.3	0.4
Immediately after implementation	7.0	6.0	6.0	6.0	6.3	0.4	1.0	0.0	0.0	0.0	0.3	0.4	0.0	1.0	0.0	0.0	0.3	0.4
1 hour after implementation	7.0	6.0	6.0	6.0	6.3	0.4	3.0	2.0	3.0	3.0	2.7	0.4	2.0	1.0	1.0	1.0	1.3	0.4

D

Implementation Period \ Group	Inhalation						Massage						Aroma Massage					
Week	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD	Week1	Week2	Week3	Median	Mean	SD
Before implementation	7.0	6.0	6.0	6.0	6.3	0.4	8.0	8.0	8.0	8.0	8.0	0.0	8.0	8.0	7.0	8.0	7.7	0.4
During implementation	7.0	6.0	6.0	6.0	6.3	0.4	1.0	0.0	0.0	0.0	0.3	0.4	0.0	1.0	0.0	0.0	0.3	0.4
Immediately after implementation	7.0	6.0	6.0	6.0	6.3	0.4	1.0	0.0	0.0	0.0	0.3	0.4	0.0	1.0	0.0	0.0	0.3	0.4
1 hour after implementation	7.0	6.0	6.0	6.0	6.3	0.4	3.0	3.0	4.0	3.0	3.3	0.4	3.0	3.0	2.0	3.0	2.7	0.4

revealing significant differences among the groups.

(2) King's Parkinson's Disease Pain Scale (KPPS)

Analysis of KPPS scores indicated a trend toward reductions in both the severity and frequency of pain in the "Off-state body pain" and "Deep body pain" domains. No significant changes were observed in the I group across all weeks (Week 1: 37.0; $p = 0.720$; Week 2: 36.0; $p = 0.720$; Week 3: 34.75; $p = 0.249$). The M group showed consistent reductions at Weeks 2 and 3 (Week 1: 34.5; $p = 0.215$; Week 2: 28.00; $p = 0.001$; Week 3: 27.25; $p < 0.001$). The AM group exhibited consistent reductions in all weeks (Week 1: 32.00; $p = 0.038$; Week 2: 25.00; $p < 0.001$; Week 3: 23.25; $p < 0.001$), with the most pronounced reduction among the three groups. While no significant difference was found between AM and I in Week 1 (AM: 32 points; $p = 0.373$), the AM group showed greater reductions compared to the I group in Weeks 2 and 3 (Week 2: I vs M $p = 0.007$; I vs AM $p < 0.001$; Week 3: I vs M $p = 0.011$; I vs AM $p < 0.001$). No significant difference was observed between M and AM groups ($p = 0.158$). As shown in Table 13, individual data on KPPS scores indicated that the AM group exhibited a more pronounced reduction in pain compared to the I and M groups. Linear mixed model analysis in Table 14 revealed significant differences among the groups; however, due to the small sample size, these results should be interpreted as exploratory analyses.

4) Quality of Life (QOL)

(1) PDQ-39

PDQ-39 Comparison of pre- and post-treatment scores across the three groups indicated that only the AM group showed a consistent decrease of 3.75 points after 3 weeks (Post-I: Estimated Mean = 29.5; Post-M: Estimated Mean = 27.5; Post-AM: Estimated Mean = 25.75; $p = 0.005$). No significant difference was found between the I and M groups ($p = 0.121$), but the AM group demonstrated a greater decrease compared to the I group ($p = 0.005$). Although the AM group showed a greater reduction compared to the M group, the difference was not statistically significant ($p = 0.082$)

As shown in Table 15, individual data on PDQ-39 scores indicated that the AM group consistently demonstrated improvement compared to the other groups. Linear mixed model analysis (Table 16) revealed that the AM group showed significant improvement compared to the I group ($p = 0.005$). However, no significant difference was observed between the AM and M groups ($p = 0.082$).

These analyses are exploratory in nature and should be interpreted with caution. The p-values reported are descriptive and do not provide conclusive evidence of treatment effects.

DISCUSSION

1) Pain Relief Through Aroma Massage

Among the three treatment patterns (I, M, and AM), the AM group demonstrated the most significant pain relief, with a slower return of pain compared to the other groups. Based on the physiological mechanisms of action, the following discussion focuses on the effects of AM.

(1) Activation of the Midbrain Limbic Dopamine System

As shown in Figure 1, the AM group exhibited a significant increase in PAF compared to both the I and M groups. Additionally, plasma dopamine levels were significantly higher by the third week (Table 7). Significant differences in β-endorphin levels and VAS scores were observed between the I group and both the M and AM groups. The observed increases in plasma dopamine and β-endorphin levels in the M and AM groups (Table 12) can be attributed to the activation of the midbrain-limbic dopamine system, as suggested by Meijer [17].

According to Meijer, when comfort outweighs pain, the dopamine release activates the endogenous pain suppression system. This mechanism may be involved in the effects observed in this study.

Furthermore, the increase in PAF and the reduction in VAS observed in AM are consistent with previous research, which demonstrated a correlation between pain intensity reduction and increased PAF. Increased α-wave activity, which is associated with relaxation and comfort, was observed during these periods [18]. Additionally, a study on electrical acupuncture in PD patients with chronic pain reported a decrease of 2.14 cm in VAS [19]. The significant reduction in pain (greater than 6 cm) observed during and immediately after the intervention in this study indicates substantial pain relief.

However, this study employed a crossover design with a one-week washout period between treatments. This washout period may be insufficient to eliminate carryover effects. Therefore, the possibility of carryover effects should be considered when interpreting the results.

(2) Activation of the Descending Pain Inhibition System

As shown in Table 9, both M and AM groups exhibited significant increases in the estimated average values for the deltoid and tibialis anterior muscles compared to the I group, suggesting improvements in the CPM response and an elevated pain threshold.

However, there were no significant differences between M and AM in CPM, VAS, and KPPS scores. This suggests that simply smelling the scent may not be sufficient for pain relief and that the tactile stimulation from the massage played a significant role.

Previous studies have shown that the diminished CPM response in PD patients reflects a weakened descending pain inhibition function [20]. Furthermore, the average PPT values for healthy Japanese individuals are 34.0 N for the deltoid and 44.7 N for the tibialis anterior [21]. In comparison, the participants in this study exhibited lower values, indicating heightened pain sensitivity. The observed reduction in pain severity and frequency in the KPPS suggests

Table 12 VAS for I, M, and AM (Linear Mixed Model Analysis)

		Inhalation				Massage			Aroma Massage			P-value		
		LS mean	95%CI		P-value	LS mean	95%CI		P-value	LS mean	95%CI		P-value	I vs. M	I vs. AM	M vs. AM
Weekly Integration	Before implementation	6.25	4.44	8.07	–	6.75	4.94	8.57	–	6.42	4.60	8.23	–	–	–	–
	During implementation	5.46	3.64	7.27	–	0.25	−1.57	2.07	–	0.25	−1.57	2.07	–	–	–	–
	Immediately after implementation	5.46	3.64	7.27	–	0.25	−1.57	2.07	–	0.25	−1.57	2.07	–	–	–	–
	1 hour after implementation	5.75	3.94	7.57	–	3.17	1.35	4.98	–	2.08	0.27	3.90	–	–	–	–
	Change from before implementation															
	During implementation	−0.79	−1.67	0.09	0.077	−6.50	−7.38	−5.62	< 0.001*	−6.17	−7.05	−5.29	< 0.001*	< 0.001*	< 0.001*	0.999
	Immediately after implementation	−0.79	−1.67	0.09	0.077	−6.50	−7.38	−5.62	< 0.001*	−6.17	−7.05	−5.29	< 0.001*	< 0.001*	< 0.001*	0.999
	1 hour after implementation	−0.50	−1.38	0.38	0.262	−3.58	−4.46	−2.70	< 0.001*	−4.33	−5.21	−3.45	< 0.001*	< 0.001*	< 0.001*	0.016*
	Change from immediately after implementation															
	1 hour after implementation	0.292	−0.59	1.2	0.512	2.92	2.04	3.80	< 0.001*	1.83	0.95	2.71	< 0.001*	–	–	–

LS mean: least square mean; 95%CI: 95% confidence interval

Analysis: Linear Mixed Effects Model [Fixed Effects: Measurement time points (before implementation, during implementation, immediately after implementation, 1 hour after implementation), implementation week. (Week 1, Week 2, Week 3), Group (Inhalation, Massage, Aroma Massage)]

Testing of interaction terms:

Measurement time point * Implementation week * Group: P = 0.971

Measurement time point * Implementation week: P = 0.999

Implementation week * Group: P = 0.065

Measurement time point * Group: P < 0.001

*P < 0.05

Table 13 KPPS for I, M, and AM (Individual Data)

A

		Inhalation							Massage							Aroma Massage						
Week		Pre	Week1	Week2	Week3	Median	Mean	SD	Pre	Week1	Week2	Week3	Median	Mean	SD	Pre	Week1	Week2	Week3	Median	Mean	SD
Total Score		38	36	36	36	36	36	0	38	34	32	32	32	32.7	1	38	34	32	30	32	32	2
Domains		Severity × Frequency							Severity × Frequency							Severity × Frequency						
1. Musculoskeletal Pain		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2. Chronic Pain	2. Chronic Pain	8	8	8	8	8	8	0	8	8	8	8	8	8	0	8	6	6	6	6	6	0
3. Pain Related to Symptom Fluctuation	6. Generalised "off" period pain (pain in whole body or areas distant to dystonia)	8	6	6	6	6	6	0	8	6	6	6	6	6	0	8	6	6	4	6	5.3	1
4. Night Pain	7. Pain related to jerking leg movements during the night (PLM) or an unpleasant burning sensation in the legs which improves with movement (RLS)	8	8	8	8	8	8	0	8	8	8	8	8	8	0	8	8	8	8	8	8	0
	8. Nocturnal Pain	6	6	6	6	6	6	0	6	6	4	4	4	4.67	1	6	6	6	6	6	6	0
5. Orofacial Pain		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6. Discoloration;Edema/ Swelling		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7. Radicular Pain	14. Radicular Pain	8	8	8	8	8	8	0	8	6	6	6	6	6	0	8	6	6	6	6	6	0

B

		Inhalation							Massage							Aroma Massage						
Week		Pre	Week1	Week2	Week3	Median	Mean	SD	Pre	Week1	Week2	Week3	Median	Mean	SD	Pre	Week1	Week2	Week3	Median	Mean	SD
Total Score		28	28	28	26	28	27	1	28	28	16	16	16	20	7	28	28	13	11	13	17	9
Domains		Severity × Frequency							Severity × Frequency							Severity × Frequency						
1. Musculoskeletal Pain	1. Musculoskeletal Pain	4	4	4	2	4	3.3	1	4	4	2	2	2	2.67	1	4	4	1	1	1	2	2
2. Chronic Pain	2. Deep Pain (Persistent, Dull, Aching Pain - Central Pain)	8	8	8	8	8	8	0	8	8	4	4	4	5.33	2	8	8	4	4	4	5.3	2
3. Pain Related to Symptom Fluctuation		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4. Night Pain	8. Nocturnal Pain	8	8	8	8	8	8	0	8	8	6	6	6	6.67	1	8	8	4	2	4	4.7	3
5. Orofacial Pain		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6. Discoloration;Edema/ Swelling		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7. Radicular Pain	14. Radicular Pain	8	8	8	8	8	8	0	8	8	4	4	4	5.33	2	8	8	4	4	4	5.3	2

C

		Inhalation							Massage							Aroma Massage						
Week		Pre	Week1	Week2	Week3	Median	Mean	SD	Pre	Week1	Week2	Week3	Median	Mean	SD	Pre	Week1	Week2	Week3	Median	Mean	SD
Total Score		52	50	46	43	46	46	4	52	46	36	33	36	38.3	7	52	36	27	24	27	29	6
Domains		Severity × Frequency							Severity × Frequency							Severity × Frequency						
1. Musculoskeletal Pain	1. Musculoskeletal Pain	12	12	12	9	12	11	2	12	12	9	9	9	10	2	12	9	6	6	6	7	2
2. Chronic Pain	2. Deep Pain (Persistent, Dull, Aching Pain - Central Pain)	8	8	6	6	6	6.7	1	8	4	3	3	3	3.33	1	8	3	3	3	3	3	0
	3. Visceral Pain	8	8	6	6	6	6.7	1	8	6	6	3	6	5	2	8	6	3	3	3	4	2
3. Pain Related to Symptom Fluctuation	4. Pain Related to Dyskinesia	8	8	8	8	8	8	0	8	8	8	8	8	8	0	8	8	8	8	8	8	0
4. Night Pain	8. Nocturnal Pain	8	8	8	8	8	8	0	8	8	6	6	6	6.67	1	8	6	4	2	4	4	2
5. Orofacial Pain		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6. Discoloration; Edema/ Swelling		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7. Radicular Pain	14. Radicular Pain	8	6	6	6	6	6	0	8	8	4	4	4	5.33	2	8	4	3	2	3	3	1

D

		Inhalation							Massage							Aroma Massage						
Week		Pre	Week1	Week2	Week3	Median	Mean	SD	Pre	Week1	Week2	Week3	Median	Mean	SD	Pre	Week1	Week2	Week3	Median	Mean	SD
Total Score		34	34	34	34	34	34	0	34	30	28	28	28	28.7	1	34	30	28	28	28	29	1
Domains		Severity × Frequency							Severity × Frequency							Severity × Frequency						
1. Musculoskeletal Pain	1. Musculoskeletal Pain	4	4	4	4	4	4	0	4	4	2	2	2	2.67	1	4	4	2	2	2	2.7	1
2. Chronic Pain	2. Deep Pain (Persistent, Dull, Aching Pain - Central Pain)	6	6	6	6	6	6	0	6	4	4	4	4	4	0	6	4	4	4	4	4	0
3. Pain Related to Symptom Fluctuation	6. Generalised "off" period pain (pain in whole body or areas distant to dystonia)	6	6	6	6	6	6	0	6	6	6	6	6	6	0	6	6	6	6	6	6	0
4. Night Pain	7. Pain related to jerking leg movements during the night (PLM) or an unpleasant burning sensation in the legs which improves with movement (RLS)	8	8	8	8	8	8	0	8	8	8	8	8	8	0	8	8	8	8	8	8	0
	8. Nocturnal Pain	6	6	6	6	6	6	0	6	6	6	6	6	6	0	6	6	6	6	6	6	0
5. Orofacial Pain		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6. Discoloration;Edema/ Swelling		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7. Radicular Pain	14. Radicular Pain	4	4	4	4	4	4	0	4	2	2	2	2	2	0	4	2	2	2	2	2	0

Table 14 KPPS for I, M, and AM (Linear Mixed Model Analysis)

	Inhalation				Massage				Aroma Massage				P-value		
	LS mean	95%CI		P-value	LS mean	95%CI		P-value	LS mean	95%CI		P-value	I vs. M	I vs. AM	M vs. AM
KPPS total score															
pre	38.00	26.85	49.15	–	38.00	26.85	49.15	–	38.00	26.85	49.15	–	–	–	–
1week	37.00	25.85	48.15	0.720	34.50	23.35	45.65	0.215	32.00	20.85	43.15	0.038	0.373	0.080	0.373
2week	36.00	24.85	47.15	0.475	28.00	16.85	39.15	0.001	25.00	13.85	36.15	< 0.001	0.007	< 0.001	0.287
3week	34.75	23.60	45.90	0.249	27.25	16.10	38.40	< 0.001	23.25	12.10	34.40	< 0.001	0.011	< 0.001	0.158

LS mean: least square mean; 95%CI: 95% confidence interval

Analysis: Linear Mixed Effects Model [Fixed effects: Time point (Pre-treatment, Week 1, Week 2, Week 3), Group (Inhalation, Massage, Aroma Massage)]

Test of interaction terms:

Implementation week * Group: P = 0.083

that AM may have been more effective in pain relief compared to M (Table 13).

However, in all three patterns, pain gradually returned one hour after the intervention. The return of pain was slower in the AM group compared to M, suggesting that the scent may have influenced the differences observed between M and AM.

As shown in Table 14, both M and AM groups exhibited significant pain relief during weeks 2 and 3 on the KPPS, suggesting that continued intervention may lead to long-term reductions in pain severity and frequency.

Based on these findings, it is suggested that AM may be an appropriate care method for PD patients, who often experience unpredictable pain fluctuations with the "on-off" phenomenon. AM appears to be a suitable approach for the four participants in this study, providing relief from fluctuating pain.

Prior research has highlighted massage therapy as a non-pharmacological strategy for pain management in PD [22]. For instance, RCT involving PD patients with chronic pain demonstrated that the massage group experienced improvements in both pain and sleep quality [23]. Conversely, a non-randomized trial comparing acupuncture to no intervention showed pain relief on the KPPS, but no significant changes in other measures such as the VAS, depression, sleep, or quality of life indicators [24]. In contrast, our study found that combining aromatherapy with massage resulted in greater reductions in pain compared to massage alone. Additionally, this combined approach showed trends toward improvement in KPPS, VAS, and the PDQ-39, which assesses quality of life, including aspects of depression and sleep. These findings suggest that integrating aromatherapy with massage may offer more comprehensive benefits for PD patients.

These results support the efficacy of non-pharmacological therapies in managing pain in PD patients and suggest that combining aromatherapy with massage could be a valuable addition to clinical practice. However, further research with larger sample sizes and rigorous methodologies is needed to confirm these findings and establish standardized treatment protocols.

2) Improvement in QOL through Aroma Massage

(1) Expectations for Alleviating Negative Psychological States

Among the three treatment patterns (I, M, and AM), only the AM group showed a significant reduction in the total PDQ-39 score (Table 15). This reduction was associated with improvements in the subscales of "mobility," "ADL," "social support," "cognition," "communication," and "physical discomfort." These results suggest that AM may help alleviate negative psychological states.

Previous studies have reported that the intervention of PD medications, such as safinamide, resulted in a 4.07-point reduction in the PDQ-39 score and improved QOL in physical function domains (Table 16) [25]. In contrast, our study found that AM not only improved physical function but also enhanced social and emotional health aspects, which are effects not typically seen with medication treatments ($p = 0.005$). However, no significant difference was observed in PDQ-39 score reduction between M and AM, highlighting the need to further clarify the differences between these two interventions.

The pathophysiology of PD is characterized by a weakened descending pain inhibition system and reduced dopamine release, which contributes to decreased motivation and increased anxiety [26]. Moreover, PD patients experience stress from invisible pain symptoms that are often misunderstood by those around them, further suppressing dopamine secretion [26]. Given these findings, the significant improvement in multiple PDQ-39 items following AM suggests that it was an appropriate care method for the four PD patients in this study.

(2) Expectations for Behavioral Changes toward Increased Physical Activity

The pain relief achieved through AM led to reductions in scores related to "joint and body pain" in the "physical discomfort" subscale of PDQ-39, as well as "difficulty with desired leisure activities" and "difficulty walking 100 meters" in the "mobility" subscale. These improvements suggest that AM expanded the participants' ability to engage in daily activities.

One of the key approaches in chronic pain management is to change the perception of pain, which has been shown to be effective [27]. A study of back massage reported significant differences in dopamine levels and motivation scores compared to daily activities [28]. This suggests that pleasurable stimuli, such as a massage, may increase dopamine and enhance motivation and expectations, thereby promoting behavioral changes [29]. Therefore, AM could potentially encourage voluntary physical activity, reducing excessive rest and fostering a behavioral shift toward more active movement.

Table 15 PDQ-39 Scores for I, M, andAM (Individual Data)

		A				B				C				D			
	項目	Pre	I	M	AM	Pre	I	M	AM	Pre	I	M	AM	Pre	I	M	AM
Mobility	1. Had difficulty doing leisure activities	0	0	0	0	3	3	3	2	3	3	3	3	0	0	0	0
	2. Had difficulty looking after your home	2	2	2	2	2	2	1	1	2	2	2	2	0	0	0	0
	3. Had difficulty carrying bags of shopping	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0
	4. Had problems walking half a mile	2	2	2	2	3	3	3	3	3	3	2	2	0	0	0	0
	5. Had problems walking 100 yards	1	1	1	1	2	2	1	1	2	2	1	1	0	0	0	0
	6. Had problems getting around the house	0	0	0	0	1	1	1	1	1	1	1	1	0	0	0	0
	7. Had problems getting around in public places	0	0	0	0	3	3	3	3	3	3	3	3	0	0	0	0
	8. Needed to be accompanied when out	0	0	0	0	0	0	0	0	4	4	4	4	0	0	0	0
	9. Frightened or worried about falling in public	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
	10. Been confined to the house more than you would like	1	1	1	1	1	1	0	0	1	1	1	0	0	0	0	0
ADL	11. Had difficulty washing yourself	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0
	12. Had difficulty dressing yourself	0	0	0	0	1	1	1	1	1	1	1	1	0	0	0	0
	13. Had problems doing up buttons or shoelaces	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0
	14. Had problems writing clearly	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1
	15. Had difficulty cutting up your food	0	0	0	0	1	1	1	1	1	1	1	1	0	0	0	0
	17. Felt depressed	0	0	0	0	1	1	1	0	1	1	1	1	0	0	0	0
Emotional Well-being	20. Felt angry or bitter	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
	21. Felt anxious	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0
	22. Felt worried about your future	1	1	1	1	2	2	2	2	2	2	2	2	0	0	0	0
Stigma	24. Avoided situations which involved eating or drinking in public	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
	25. Felt embarrassed in public due to having Parkinson's disease	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
	26. Felt worried by other people's reaction to you	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
Social Support	28. Felt you didn't get the support you needed from your spouse or partner	0	0	0	0	0	0	0	0	1	1	1	1	4	4	4	4
	29. Felt you didn't get the support you needed from your family or close friends	0	0	0	0	0	0	0	0	1	1	1	1	4	4	4	2
Cognition	30. Unexpectedly fell asleep during the day	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0
	31Had problems concentrating when watching TV or reading	2	2	2	2	2	2	2	2	2	2	2	2	0	0	0	0
	32. Felt your memory was poor	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1
	33. Had distressing dreams or hallucinations	0	0	0	0	0	0	0	0	2	2	2	0	0	0	0	0
Communication	34. Had difficulty with your speech	2	2	2	2	2	2	2	2	2	2	2	2	0	0	0	0
	35. Felt unable to communicate properly	2	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0
Bodily Discomfort	38. Had painful muscle cramps or joints	3	3	3	3	4	4	4	4	4	4	3	2	2	2	1	1
	39. Felt unpleasantly hot or cold	2	2	2	2	2	2	2	2	2	2	2	2	0	0	0	0
	Total score	30	30	30	30	34	34	31	29	44	44	41	37	12	12	11	9

Table 16 PDQ-39 Scores for I, M, andAM (Linear Mixed Model)

						P-value (vs. Pre)			P-value (Comparison group)		
		Pre-treatment	After inhalation	After Massage	After Aroma Massage	I	M	AM	I vs. M	I vs. AM	M vs. AM
PDQ-39Total score	LS mean	29.50	29.50	27.75	25.75	1.000	0.121	0.005	0.121	0.005	0.082
	95%CI	9.34 - 49.66	9.34 - 49.658	7.59 - 47.91	5.59 - 45.91						

LS mean: least square mean; 95%CI: 95% confidence interval
Analysis: Linear Mixed Model [Fixed Effects: Groups (Pre-treatment, Inhalation, Massage, Aromatherapy Massage)]

LIMITATIONS AND CHALLENGES OF THIS STUDY

This study had a limited sample size, comprising only four participants. Consequently, while a reduction in evaluation scores was observed, no statistically significant differences were found between the M and AM groups for many of the measures. To validate the findings and explore the differences between M and AM more conclusively, future research should include a larger sample size. Additionally, while chronic pain in PD patients is multifactorial, the analysis in this study predominantly focused on total scores. A more detailed analysis of individual items in the KPPS and PDQ-39 would be valuable to further assess the effects of pain relief and improvements in QOL.

Furthermore, this study did not implement blinding for participants, therapists, or evaluators. Given that subjective outcome measures such as pain intensity and quality of life are susceptible to observer bias, the lack of blinding introduces a potential risk of bias. This limitation should be considered when interpreting the results.

Moreover, while blood samples were collected prior to medication intake, the possibility of residual drug effects or timing-related variability cannot be entirely excluded. Such factors may influence the accuracy of biochemical measurements and introduce variability in the results. This potential confounding factor should be considered when interpreting the findings.

CONCLUSION

This study compared the effects of AM, M, and I on pain relief and QOL improvement in Parkinson's disease patients with chronic pain.

Objective Pain Evaluation: AM demonstrated a significant increase in plasma dopamine levels, and both M and AM significantly elevated plasma β-endorphin levels. EEG measurements revealed the most significant increase in PAF in the AM group compared to other treatments. CPM measurements showed significant increases in both M and AM.

Subjective Pain Evaluation: Both M and AM significantly reduced the estimated average VAS score during and immediately following the interventions, indicating immediate pain relief. In the KPPS, AM significantly reduced pain severity relative to baseline in all weeks.

QOL Evaluation: The total PDQ-39 score showed a significant reduction of 3.75 points in the AM group, indicating an improvement in QOL.

Overall, AM contributed the most to chronic pain relief and potential improvements in QOL compared to I and M. These results suggest that sensory stimulation provided by AM, which includes both olfactory and tactile components, combined with caregiver involvement, may alleviate chronic pain in PD patients. Future studies should focus on increasing the sample size to enhance the reliability and generalizability of these findings.

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