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Short Communication

Can therapeutic Thai massage improve upper limb muscle strength in Parkinson's disease? An objective randomized-controlled trial



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ABSTRACT

Muscle weakness is a frequent complaint amongst Parkinson's disease (PD) patients. However, evidencebased therapeutic options for this symptom are limited. We objectively measure the efficacy of therapeutic Thai massage (TTM) on upper limb muscle strength, using an isokinetic dynamometer. A total of 60 PD patients with muscle weakness that is not related to their 'off' periods or other neurological causes were equally randomized to TTM intervention (n = 30), consisting of six TTM sessions over a 3-week period, or standard medical care (no intervention, n = 30). Primary outcomes included peak extension and flexion torques. Scale-based outcomes, including Unified Parkinson's Disease Rating Scale (UPDRS) and visual analogue scale for pain (VAS) were also performed. From baseline to end of treatment, patients in the intervention group showed significant improvement on primary objective outcomes, including peak flexion torque (F = 30.613, p < .001) and peak extension torque (F = 35.569, p < .001) and time to maximal flexion speed (F = 14.216, p = .001). Scale-based assessments mirrored improvements in the objective outcomes with a significant improvement from baseline to end of treatment of the UPDRSbradykinesia of a more affected upper limb (F = 9.239, p = .005), and VAS (F = 69.864, p < .001) following the TTM intervention, compared to the control group. No patients reported adverse events in association with TTM. Our findings provide objective evidence that TTM used in combination with standard medical therapies is effective in improving upper limb muscle strength in patients with PD. Further studies are needed to determine the efficacy of TTM on other motor and non-motor symptoms in PD.

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1. Introduction

By the time a diagnosis of Parkinson's disease (PD) is made, upper limb motor symptoms are usually evident. Besides the cardinal features (bradykinesia, rigidity, and rest tremor) in the upper limb, reduced muscle strength or weakness is one of the most

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frequent complaints amongst early PD patients with difficulties in manipulating objects or undertaking daily tasks reported. ^{1,2} While weakness in PD is usually relative, not apparent on standard neurological examination and may be attributed to fatigue, a number of well-designed studies have established a relationship between reduced muscle power and bradykinesia. ^{3,4} This combination of weakness and bradykinesia can contribute to reduced muscle strength, when patients fail to energize their muscles fully, for a number of reasons, including a lack of full volitional effort, insufficient recruitment of muscle force, and inability to maintain constant force. ⁵

Although levodopa is an effective treatment of bradykinesia in PD, from a patient's perspectives, the benefit of levodopa is less

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impressive. In a recent study, there was only moderate patientclinician agreement for the effect of levodopa on bradykinesia and rigidity when better concordance was demonstrated for tremor.⁶ Moreover, weakness, as manifested by impaired dexterity of the upper limb, was found to be minimally responsive to levodopa. Consequently, PD patients often seek complementary and alternative therapies (CAT) to try and improve weaknesses and/or bradykinesia. Early evidence of benefits of massage has been demonstrated for a range of PD symptoms, including reduction of tremors, enhancing shoulder range-of-motion, and improvements on gait, activities of daily livings (ADLs) and quality of life (QoL).^{8–10} Therapeutic Thai massage (TTM, also known as 'Nuad Thai' in Thai) has been part of Thai traditional medicine for centuries and is a popular choice amongst Thai PD patients. TTM involves slow rhythmical stroking and kneading of the skin using different levels of strength on acupressure points and stretching along 10 major and 72000 minor energy lines, called 'SEN lines'. 11 The underlying mechanisms of TTM are likely to be complex involving stimulation of the parasympathetic nervous system or tissues underneath the skin resulting alleviating spasms, increasing circulation, reducing adhesions, and ultimately producing relaxation.¹²

While the beneficial effects of massage have been demonstrated as an improvement in a number of clinical rating scales, very few studies have evaluated the muscle strength of upper limbs in PD patients and objective measurements are seldom be included as primary outcomes in randomized controlled trial involving CAT in PD patients. Our initial pilot study demonstrated a positive effect of TTM on hand functions in PD patients as demonstrated by isometric hand grip score. Herefore, we further evaluate the efficacy of TTM as an add-on intervention to conventional therapies in a randomized-controlled trial on upper limbs muscle strength in PD patients who complain of muscle weakness that are not related to their 'off' symptoms using the isokinetic dynamometer method that allows objective measurement of muscular forces in dynamic conditions, reflecting muscle strength.

2. Patients and methods

2.1. Patients

Patients with a diagnosis of PD according to the United Kingdom Parkinson's Disease Society Brain Bank criteria, were screen by two movement disorder neurologists (OJ and RB). Inclusion criteria were: 1) Hoehn and Yahr stage 1-3, 2) stable pharmacological treatment during the past three months, 3) mini-mental state examination score (MMSE) > 25, and 4) complaints of muscle weakness in the upper limbs that were not related to their 'off' symptoms as identified during clinical interviews, and confirmed by PD diaries. Patients were excluded if muscle weakness was due to other neurological causes rather than PD (such as stroke, radiculopathies, myopathies, etc.), or they had other neck, shoulder, or elbow dysfunctions that could interfere with the performance. Wheelchair and bed-bound patients were not enrolled due to their difficulty attaining correct positioning during isokinetic tests. Of the 60 PD patients who were enrolled into this study, 30 were randomized to TTM intervention whereas the rest received no intervention, designated as a control group. Ethical approval was given by the Human Ethics Committee of the Faculty of Medicine, Chulalongkorn University (IRB No. 083/58, COA No. 388/2015) and the study was executed in accordance with the declaration of Helsinki. All patients provided written informed consent before randomization.

2.2. Study design

This was a randomized, single-blinded, controlled study conducted in a single center (Chulalongkorn Center of Excellence for Parkinson's Disease & Related Disorders, www.chulapd.org) between July 2015 and June 2016. Screening took place up to 4 weeks before baseline evaluation on Day 1 when patients were randomized (1:1) to treatment with TTM or control (standard medical care. no TTM). Interventions were performed during patients' 'on' period. Patients in the intervention group received six TTM sessions over a 3-week period, conducted by the investigator (YM) who is a certified TTM practitioner (under the Ministry of Education, Thailand) and over 10 years of experience (Fig. 1a). The TTM protocol used in this study was the standard TTM protocol, listed in the benchmark training curriculum for 'Nuad Thai' of the World Health Organization and approved by Thai Ministry of Education. 11 Each 30-minute TTM session consisted of kneading and pressing with moderate intensity, within patient's range of comfort, along six designated 'SEN' lines of the upper limbs (Fig. 1b-c). Detailed descriptions of the TTM protocol were included in the supplementary data 1. The control group received no intervention. During the 3week study period, all participants were instructed not to undergo additional TTM or similar interventions and activity diaries were checked to ensure that all patients complied to the study protocol.

2.3. Isokinetic muscle strength

Elbow flexor and extensor muscle strength was assessed with an isokinetic dynamometer (CON-TREX®, Physiomed Elctromedizin AG, Germany). Patients were seated with fully pronated forearm, positioned horizontally and flexed 90°, with respect to their upper arm (Supplementary data 2). The forearm was attached at the wrist to a stiff bar by Velcro straps. Muscle strength was measured in both upper limbs using a previously published protocol, 60°/second with a five-second interval isometric holding and a 30-second rest period between each test. 16,17 Three submaximal cycles and one maximal cycle were completed as practice runs before the collection of three maximal repetitions at 60°/second. The best value (peak torque) was retained for further statistical analysis. The same investigator (NA) conducted the tests for all subjects.

2.4. Scale-based assessments

Scale-based assessments were performed at baseline and study end by the same investigator (JS) who was blinded to all subjects. Rating scales included Unified Parkinson's Disease Rating Scale (UPDRS) total scores, UPDRS-III (motor) sub-score, the Visual Analogue Scale for Pain (VAS), and the scoring index of the eightitem Parkinson's Disease Questionnaire (PDQ-8 SI).

2.5. Statistical analysis

Baseline characteristics were summarized using either means, standard deviation, frequencies or percentages as appropriate. Comparisons for categorical and continuous variables were carried out by the Chi-square test and independent *t*-test respectively. Maximal torque and clinical scale endpoints were mean change from baseline to end of treatment period, using observed data. To determine intervention effects between intervention and control groups from baseline to end-of-treatment, we utilized two-way mixed ANOVA with one within-subjects factor and one betweengroups factor. Category refers to the between-subjects factor, whereas sequence refers to the within-subjects factor. Pearson's correlation was performed to determine correlation coefficients

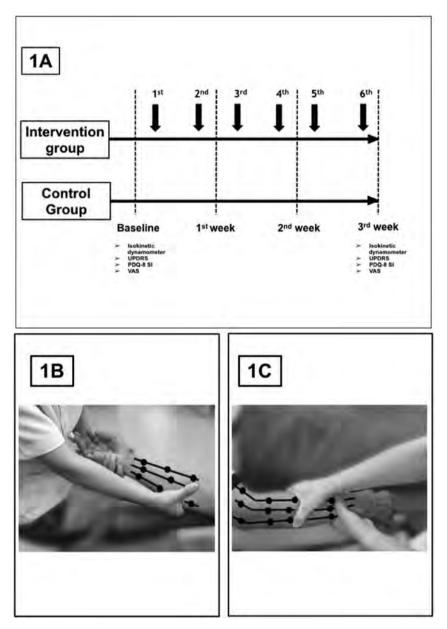


Fig. 1. 1A: Study design; 1B and 1C: Therapeutic Thai massage of the upper limb uses different levels of strength on acupressure points (black circles) along the 'SEN' energy lines (black lines) of the inner (1B) and outer (1C) arm. UPDRS: Unified Parkinson's Disease Rating Scale; PDQ-8 SI: Scoring index of the eight-item Parkinson's Disease Questionnaire; VAS: Visual Analogue Scale for Pain.

between mean change of maximal torque and mean change of clinical scales. A *p* value less than 0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 22.0 software (SPSS Inc., Chicago IL).

3. Results

Of the 60 patients enrolled in this study, 30 were randomized to the TTM intervention while 30 received no intervention, and none dropped-out. Both groups demographic and clinical parameters were balanced (Table 1). Significant interaction effect was demonstrated between category and sequence from baseline to end-of-treatment (Table 2). For peak flexion torque, the main effect of sequence was significant with an F ratio of F(1,29) = 20.764 (p < .001). When impact of sequence was controlled, the category effect was also significant with an F ratio of F(1,29) = 11.522

(p=.002), with the intervention group demonstrating significant higher peak flexion torque than control group. Significant interaction between effect was seen with an F ratio of F(1,29)=30.613 (p<.001). Similar significant results were also observed with peak extension torque when the main effect of sequence was significant with an F ratio of F(1,29)=26.851 (p<.001). When impact of sequence was controlled, the category effect was significant with an F ratio of F(1,29)=10.186 (p=.003), with the intervention group demonstrating significant higher peak extension torque than control group. The interaction between effect was also significant with an F ratio of F(1,29)=35.569 (p<.001).

Significant results were also obtained with time to maximal flexion. The main effect of sequence was significant with an F ratio of F(1,29) = 14.958 (p = .001). When impact of sequence was controlled, the category effect was insignificant with an F ratio of F(1,29) = 1.072 (p = .309), indicating no significant different in time

 Table 1

 Clinical demographics between Parkinson's disease patients in the intervention and control groups.

Variables	Intervention group (n = 30)	Control group (n = 30)	<i>p</i> -value
Age (year)	66.37 ± 7.32	64.10 ± 10.83	.350 ^χ
Male gender	19 (63.3)	14 (46.7)	$.440^{\beta}$
Duration of PD (year)	8.53 ± 4.73	9.17 ± 7.76	$.700^{\chi}$
H&Y	2.10 ± 0.31	2.27 ± 0.45	$.100^{\chi}$
LED (mg)	833.06 ± 369.42	816.26 ± 461.35	$.900^{\chi}$
Weight (kg)	56.26 ± 7.88	55.60 ± 4.92	$.696^{\chi}$
BMI	22.02 ± 1.90	22.18 ± 2.23	.166 ^{χ}

^{*:} Statistical significance at p < .05; β : Chi-square test; γ : Unpaired t-test; Values in parenthesis indicate percentage. H&Y: Hoehn &Yahr stage; LED: Levodopa equivalent dosage; BMI: Body mass index.

to maximal flexion between intervention and control groups. However, the interaction between effect was significant with an F ratio of F(1,29) = 14.216 (p = .001).

For the UPDRS-bradykinesia of a more affected upper limb, the main effect of sequence was significant with an F ratio of F(1,29) = 7.745 (p = .009). When impact of sequence was controlled, the category effect was insignificant with an F ratio of F(1,29) = 0.144 (p = .707), indicating no significant difference in the UPDRS-bradykinesia of a more affected upper limb between intervention and control groups. However, the interaction between effect was significant with an F ratio of F(1,29) = 9.239 (p = .005).

Regarding the VAS, the main effect of sequence was significant

with an F ratio of F(1,29) = 79.238 (p < .001). When impact of sequence was controlled, the category effect was significant with an F ratio of F(1,29) = 9.087 (p = .005), with the intervention group demonstrating less VAS score than the control group. The interaction between effect was also significant with an F ratio of F(1,29) = 69.864 (p < .001).

Correlations were performed between mean change from baseline to end-of-treatment of the primary objective outcomes and clinical rating scales (Supplementary data 3). Significant moderate correlations were observed between mean improvement of UPDRS-bradykinesia of more affected limb and both peak torque extension (r = -0.367, p = .046), and peak torque flexion

 Table 2

 Outcomes and rating scales comparison between intervention and control groups.

Objective and clinical measurement	Intervention group $(n=30)$		Control group (n = 30)		<i>p</i> -value
	Baseline	End of treatment	Baseline	3 rd week follow-up	
Peak flexion torque	23.80 ± 9.10	38.71 ± 14.35	22.95 ± 11.98	23.25 ± 10.93	$P_{c} = 0.002^{a\delta}$ $P_{s} < 0.001^{a\delta}$ $P_{cs} < 0.001^{a\delta}$
Peak extension torque	24.32 ± 9.53	38.40 ± 14.00	23.97 ± 11.75	23.68 ± 10.82	$P_{c} = 0.003^{a\delta}$ $P_{s} < 0.001^{a\delta}$ $P_{cs} < 0.001^{a\delta}$
Time to maximal flexion speed	0.88 ± 0.42	0.58 ± 0.23	0.82 ± 0.31	0.79 ± 0.35	$P_{\rm c} = 0.309$ $P_{\rm s} = 0.001^{\rm a\delta}$ $P_{\rm cs} = 0.001^{\rm a}$
Time to maximal extension speed	1.08 ± 0.72	0.61 ± 0.24	1.09 ± 0.51	0.91 ± 0.45	$P_{c} = 0.113^{\delta}$ $P_{s} = 0.003^{a\delta}$ $P_{cs} = 0.113^{\delta}$
UPDRS total score	40.03 ± 15.41	34.83 ± 16.79	36.00 ± 16.79	37.67 ± 17.97	$P_{c} = 0.892^{\delta}$ $P_{s} = 0.208^{\delta}$ $P_{cs} = 0.020^{a}$
UPDRS-Bradykinesia of more affected upper limb	3.73 ± 1.86	2.67 ± 1.90	2.97 ± 1.88	3.07 ± 1.98	$P_{cs} = 0.020$ $P_{c} = 0.707^{\delta}$ $P_{s} = 0.009^{a\delta}$ $P_{cs} = 0.005^{a}$
UPDRS-Bradykinesia of less affected upper limb	2.93 ± 1.48	2.10 ± 1.52	2.47 ± 2.30	2.83 ± 2.34	$P_{cs} = 0.003$ $P_{c} = 0.792^{\delta}$ $P_{s} = 0.174^{\delta}$ $P_{cs} = 0.003^{a}$
JPDRS-II	11.67 ± 5.84	10.10 ± 5.47	9.17 ± 5.05	8.87 ± 4.81	$P_{cs} = 0.303$ $P_{c} = 0.173^{\delta}$ $P_{s} = 0.044^{a\delta}$ $P_{cs} = 0.245^{\delta}$
JPDRS-III	22.07 ± 9.85	19.07 ± 10.18	21.00 ± 12.35	21.53 ± 13.44	$P_{cs} = 0.213$ $P_{c} = 0.880^{\delta}$ $P_{s} = 0.214^{\delta}$ $P_{cs} = 0.073^{\delta}$
VAS	6.43 ± 1.46	2.70 ± 1.12	5.63 ± 1.79	5.43 ± 1.70	$P_{\rm c} = 0.005^{\rm a\delta}$ $P_{\rm s} < 0.001^{\rm a\delta}$ $P_{\rm cs} < 0.001^{\rm a\delta}$
PDQ-8 SI	25.73 ± 17.34	19.90 ± 14.15	31.98 ± 14.86	29.79 ± 14.35	$P_{c} = 0.041^{a\delta}$ $P_{s} = 0.015^{a\delta}$ $P_{cs} = 0.258^{\delta}$

UPDRS: The Unified Parkinson's Disease Rating Scale; UPDRS-II: Activities of daily living section of the UPDRS; UPDRS-III: Motor section of the UPDRS; VAS: Visual analogue scale for pain; PDQ-8 SI: Scoring index of the eight-item of Parkinson's Disease Questionnaire.

C represents category: The category is between-subjects factor that can be divided into intervention group and control group.

S represents sequence: The sequence is within-subjects factor that can be divided into baseline and end of treatment/3rd week follow-up.

CS represents category X sequence: The category X sequence indicates the interaction between category and sequence.

^a Statistical significance at *p*-value of <0.05; δ : Two-Way mixed AVOVA.

(r=-0.385, p=.036). None of the intervention group reported any adverse events and 80% of subjects in this group expressed their satisfaction with the TTM, associated with a subjective feeling of improved upper limb muscle weakness at a 1-month follow-up visit.

4. Discussion

Our study highlights the benefit of TTM on upper limb muscle strength in PD patients, demonstrating significant increases in peak torque for both elbow flexion and extension, paralleled by an improvement in clinical rating scales, particularly total UPDRS and UPDRS-bradykinesia scores of both upper limbs. The correlations between UPDRS-bradykinesia score and muscle strength, as reflected by peak torques, further confirms the previously reported relationship between muscle weakness and bradykinesia.^{3,4} However, the mechanisms behind TTM's ability to enhance muscle power are probably complex and multifactorial. Kneading, pressing, and stroking are likely to provide a direct biomechanical effect alleviating muscle spasms and promoting relaxation. Other indirect mechanisms that promote muscle flexibility, circulation, adhesions lysis, stimulation of parasympathetic activities, reduction of neuromuscular excitability and psychological stressors (e.g. anxiety) may also contribute.12

Our study addresses two important symptoms (muscle weakness and pain) that are under-recognized and probably undertreated in PD. Muscle weakness in PD can be very difficult to detect clinically, with manifestations ranging from impaired dexterity, difficulty to rise from a chair to flexed posture.^{3,18} Treatment of muscle weakness can be challenging as levodopa, although clinically proved to be effective, is perceived by patients as minimally effective.^{3,7} Exercise, in a form of resistance training, can provide additional benefits on muscle strength when combined with dopaminergic medications. 19,20 Pain in PD usually occurs on the side where motor symptoms first appear or are more severe.²¹ While pain associated with PD has different etiologies, musculoskeletal pain is the most common, frequently associated with bradykinesia and rigidity as well as postural abnormalities.²² Patient's pain thresholds are low during 'off' periods, but return to normal after levodopa administration; however, pain reduction with levodopa may be inconsistent, and many patients use CAT to relieve this symptom. Anma massage is shown to reduce pain and improved shoulder range of motion in PD patients.¹⁰ Here, we objectively demonstrate improvement in upper limb muscle strength in PD patients following TTM intervention with evidence of reduced upper limb pain via the patients' subjective rating scales. TTM was also found to be safe and efficacious as long as the procedure is administered by certified professionals, therefore, TTM could be considered, in conjunction with standard treatment for patients with muscle weakness and pain, particularly in the upper extremities.

Objective outcomes are increasingly utilized in clinical trials in PD; however, previous studies of CAT in PD have rarely included objective assessments. Our study uniquely combines both objective and clinical assessments in the evaluation of the efficacy of CAT as a controlled trial. Despite positive findings, our study has limitations. All TTM sessions and measurements were only conducted during 'on' periods and a lack of objective evaluation of clinical outcomes and pain during follow-up visits limits understanding of a duration of effect of TTM. Further evaluations of TTM during both 'off' and 'on' states are needed to determine the effectiveness of TTM in the management of other motor and non-motor symptoms in PD, with specific protocols developed for certain symptom domains in PD, for example, pain, gait and postural instability, anxiety, and sleep dysfunction.

The objective benefits of TTM on upper limb muscle strength supports the use of TTM as a safe and evidence-based CAT for PD. This cost-effective complementary therapy is a viable option for certain PD symptoms that are partially or completely unresponsive to conventional therapies, and unlikely to add financial strain to patients, families, and healthcare systems.

Conflicts of interest

The authors have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jtcme.2018.01.004.

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