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Effects of Tai Chi on Beta Endorphin and Inflammatory Markers in Older Adults with Chronic Pain: An Exploratory Study

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Abstract

The purpose of this exploratory study was to examine the effects of Tai Chi on blood levels of beta endorphin (β-endorphin) and inflammatory markers in older adults with chronic pain. Forty community-dwelling older adults with chronic pain were randomized to Tai Chi or light physical exercise, each offered twice weekly for 12 weeks. Following the 12-week intervention, neither Tai Chi nor light physical exercise changed levels of β-endorphin and inflammatory markers. However, in older adults who completed 70% or more classes, Tai Chi significantly lowered levels of β-endorphin ($p<0.05$), whereas light physical exercise did not change levels of β-endorphin. The results suggest that Tai Chi may reduce levels of β-endorphin in older adults with chronic pain. Future studies are needed to better understand the role of the opioid analgesic system and

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Conflicts of Interest
The authors declare no conflicts of interest.

Compliance with Ethical Standards
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Ethical Approval
The study protocols and consent procedures were approved by the University of Massachusetts Boston Institutional Review Board.

Informed Consent
Informed consent was obtained from all individual participants included in the study.

immune system in regulating pain with aging and the long-term effects of Tai Chi on pain-related biomarkers.

Keywords

Tai Chi; Chronic Pain; Older Adults; Beta Endorphin; Inflammation

Background

Chronic musculoskeletal pain is associated with dysfunction of the opioid analgesic system and the immune system [1]. Elevated circulating levels of beta-endorphin (β-endorphin), an endogenous opioid hormone, are a potential biomarker for endogenous opioid analgesic capacity and are often related to chronic pain [2]. Chronic, low-grade inflammation is an independent risk factor for several age-related diseases and conditions, and is directly related to joint pain and poor physical function in older adults [3].

Pain-relieving agents include analgesics and anti-inflammatory drugs; however, guidelines recommend cautious use of these drugs in the elderly due to their increased sensitivity to drug side effects, drug-drug interactions and associated co-morbidities [4]. Among nonpharmacologic approaches, both physical exercise and meditation have analgesic-like and anti-inflammatory effects, likely through distinct biological pathways [5–7], suggesting that mind-body exercise such as Tai Chi, that combines light physical exercise with mindfulness meditation, may have advantages over light physical exercise alone for chronic pain and pain-related outcomes. Despite the substantial growing interests in examining the effect of mind-body therapies (e.g. Tai Chi, Yoga, Qigong, and meditation) on chronic systematic inflammation, the current evidence on Tai Chi shows mixed results [8]. Furthermore, the effect of Tai Chi, compared to light physical exercise, on pain-related biomarkers, such as analgesic and inflammatory markers, in individuals with chronic musculoskeletal pain is still unknown.

The aim of this study was to explore the effects of Tai Chi on blood levels of β-endorphin and inflammatory markers, including C-reactive protein (CRP), interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-α), in older adults with chronic musculoskeletal pain. We hypothesized that Tai Chi, comparing to light physical exercise, would lower plasma levels of β-endorphin and inflammatory markers in older adults with chronic multisite pain.

Methods

This exploratory study focused on the secondary outcomes of the Helping Elders Living with Pain (HELP) Study, an NIH-supported randomized controlled trial designed to examine the feasibility and acceptability of Tai Chi in older adults with chronic multisite musculoskeletal pain [9]. The HELP Study's protocols and consent procedures were approved by the University of Massachusetts Boston Institutional Review Board.

Participants, recruited from Boston and surrounding areas, were older adults (aged ≥ 65 years) with chronic multisite musculoskeletal (≥ 2 sites) pain who reported falling in the past year or current use of a cane or walker. After initial screening, participants were invited for a baseline assessment visit, which included informed consent, a fasting blood draw, and a health assessment and interview. Older adults with cognitive impairment (Mini-Mental State Examination (MMSE) score < 18) were further excluded. Sociodemographic characteristics including age, gender, race, and education were collected. Body mass index (BMI) was assessed and pain characteristics including pain severity and pain interference were measured by the Brief Pain Inventory (BPI) scale [10]. For the BPI severity subscale, individuals were asked to rate their pain according to four conditions: 1) worst pain, 2) least pain, 3) average pain, and 4) pain now, referring to an 11-point (0–10) rating scale. The pain severity score is the average of the 4-item ratings. Pain interference was assessed by asking participants to rate how pain has interfered with: 1) general activity, 2) mood, 3) walking ability, 4) normal work, 5) relations with other people, 6) sleep, and 7) enjoyment of life, referring to an 11-point (0–10) rating scale. The BPI pain interference score is the average of the 7-item ratings for each individual.

After the baseline assessment, participants were randomly assigned to either the Tai Chi group (n=28) or light physical exercise group (n=26). Individuals in the Tai Chi group practiced the 8-Form Yang Style for 1 hour each class twice per week, for 12 weeks, led by a certified Tai Chi instructor. Individuals in the light physical exercise group participated in walking, light resistance exercise, stretching, and health education discussions for 1 hour each class twice per week, for 12 weeks, led by a certified exercise physiologist. Participants in both groups were encouraged to practice the exercises at home at least once per week. Participants underwent post-intervention testing, including a blood draw, health assessment and interview, on a day at least 48 hours after the last exercise class. The majority of the participants completed their post assessment between 2–14 days after their scheduled exercise session. Further details on the study methods and participant recruitment were published previously [9].

Blood samples were collected after 12-hr fasting via venipuncture in the early morning. Samples were collected in EDTA-treated vacutainers and plasma were separated after centrifugation. Aliquots of plasma were stored at −80°C for the purpose of measuring circulating biomarkers. Plasma levels of β-endorphin and inflammatory markers (CRP, IL-6, and TNF-α) were measured using multiplexed magnetic bead immunoassays assays (Millipore Sigma Corp., Billerica, MA) that were miniaturized with the DropArray plate and washer system (Curiox Biosystems, Inc., San Carolos, CA). Quantitation of all biomarker assays were performed on a Luminex Magpix (Luminex Corp., Austin, TX) instrument equipped with xPONENT 4.2 software. Quality control for the assays were accomplished by adding dual quality controls (QC1 and QC2) provided by the manufacturer (Millipore Sigma Corp., Billerica, MA) onto each plate. This ensures both reliability and repeatability of the assay across multiple plates.

All data analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). Normality of distribution for each variable was examined, and significant outliers (>3 standard deviations away from the mean, inlduing 1 observation for β-endorphin, 1 observation for IL-6, and 3 observations for CRP) were excluded. The variables that were not normally distributed were log transformed. Paired t-tests were used to compare levels of biomarkers before and after the 12-week interventions within each group. Independent t-tests were used to compare the pre-post changes between the two groups. Comparisons between the treatment groups were performed using both intention-to-treat analyses and "per protocol" analyses in which only participants who adhered to the protocol (defined as attending 70% or more classes) were included. Effect size (Cohen's *d*) was also calculated by taking the mean difference and dividing by the pooled standard deviation for the per protocol analysis.

Results

Among the 40 participants who completed the study, 19 participants in the Tai Chi group and 21 participants in the light physical exercise group provided blood samples. The average age of the 40 participants was 74 years (range 65–87 years); 42.5% were women and 95% were white. At baseline, there were no differences in age, gender, race, education, BMI, MMSE score, pain severity and pain interference between the two groups (Table 1). There were no differences in sociodemographic characteristics between the two exercise groups for those who had an attendance rate of 70% or higher.

There were no significant group differences in changes of β-endorphin and inflammatory markers over the 12-week intervention (Tables 2, 3). Across all 40 participants, neither Tai Chi nor light physical exercise altered levels of plasma β-endorphin and inflammatory markers (CRP, IL-6 and TNF-α) over the 12-week intervention (Table 2). However, in older adults who attended 70% or more classes, Tai Chi significantly lowered β-endorphin levels ($p<0.05$) from baseline to post-intervention whereas light physical exercise did not change β-endorphin levels (Table 3).

Discussion

In this exploratory study, although we did not see a significant effect of group differences between Tai Chi and light physical exercise in altering plasma β-endorphin levels, we did observe a trend of Tai Chi lowering β-endorphin levels, especially in those participants who attended at least 70% of exercise classes. Although we observed a medium effect size on β-endorphin levels, the overall results were not surprising to us, as this was a pilot study and had limited power to detect a significant difference in our secondary outcomes.

In a previous study, individuals with pain and stress may have increased basal β-endorphin levels, and physical exercise training reduced the elevated β-endorphin levels, indicating that physical exercise could possibly increase endogenous opioid capacity in these individuals [11]. An earlier review suggested that meditation and mind-body exercise may decrease β-endorphin levels [12]. The effect of Tai Chi on β-endorphin levels has not been investigated in older adults with chronic pain. However, a 16-week Tai Chi program did not change β-endorphin levels in postsurgical non-small cell lung cancer survivors [13]. It is possible that the potential Tai Chi effect in lowering β-endorphin levels could be due to an independent effect of the cognitive component of Tai Chi in regulating the endogenous opioid analgesic system. The definite effect of Tai Chi on β-endorphin levels in this special group of older adults and its underlying mechanism need to be further investigated.

In this study, we did not see a significant effect of Tai Chi or light physical exercise on inflammatory markers in older adults with chronic pain. Current evidence based on limited number of randomized controlled studies does not support a strong anti-inflammatory effect of Tai Chi in cancer survivors, older adults with various diseases/conditions and other populations, possibly; however, Tai Chi may influence cytokine production by circulating mononuclear cells, another important source of elevated inflammation [8]. In the current study, the lack of hypothesized changes in inflammatory markers could be due to the small sample size.

Conclusions

Compared to light physical exercise, Tai Chi tended to lower plasma β-endorphin levels, especially in those with a class attendance of 70% or higher. Considering the small sample size of the current study, a future full-size study is needed to observe the definitive effects of Tai Chi on endogenous opioids and inflammatory markers in older adults with chronic multisite pain.

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Table 1.

Baseline sociodemographic and pain characteristics in 40 study participants

Characteristics	Tai Chi Group (n=19)	Light Physical Exercise Group (n=21)
Age (years)	72.74±6.60	74.90±7.31
Gender		
Male	5(26.32)	4(19.05)
Female	14(73.68)	17(80.95)
Race		
White	17(89.47)	21(100)
Asian	1(5.26)	0(0)
Other	1(5.26)	0(0)
Education		
≤High School Graduate	11(57.89)	6(28.57)
College Graduate	8(42.11)	15(71.43)
BMI (kg/m^2)	31.94±7.42	29.41±5.43
MMSE	27.74±1.88	28.14±1.46
BPI Pain Severity	4.58±1.70	3.81±1.79
BPI Pain Interference	4.41±2.53	4.30±2.20

All in Mean±SD or n(%). BMI: Body Mass Index. MMSE: Mini–Mental State Examination. BPI: Brief Pain Inventory.

Table 2.

Plasma levels of β-endorphin and inflammatory markers in the light physical exercise and Tai Chi groups before and after the 12-week intervention

For all subjects (intention to treat analysis):							
	Tai Chi Group (n=19)			**Light Physical Exercise Group (n=21)**			**Difference in Change**
	Pre	**Post**	**Change**	**Pre**	**Post**	**Change**	
β-Endorp hin (pg/ml)	164.04±55.48	149.40±43.72	−14.64±48.51	165.69±52.42	172.12±53.17	6.43±66.28	−21.06±18.88
CRP (ug/ml)	12.64±15.54	10.96±7.33	−1.68±16.51	19.27±22.67	14.86±15.42	4.41±17.69	2.72±5.71
IL-6 (pg/ml)	19.39±38.53	21.29±42.56	1.90±6.24	11.47±8.50	12.04±8.29	0.56±6.46	1.34±2.01
TNF-α (pg/ml)	14.82±7.09	15.32±9.10	0.50±6.23	13.24±7.41	13.28±6.57	0.04±4.36	0.46±1.69

For β-endorphin, 1) *p<0.05 compared to baseline; 2) group difference: Cohen's *d* = 0.53

All in mean±SD. β-endorphin: beta endorphin. CRP: C-reactive protein. IL-6: interleukin 6. TNF-α: tumor necrosis factor alpha.

Table 3.

Plasma levels of β-endorphin and inflammatory markers in the light physical exercise and Tai Chi groups before and after the 12-week intervention

For participants with an attendance rate of 70% or higher (per protocol analysis):							
	Tai Chi Group (n=11)			**Light Physical Exercise Group (n=19)**			**Difference in Change**
	Pre	**Post**	**Change**	**Pre**	**Post**	**Change**	
β-Endorphin (pg/ml)	164.23±57.42	138.12±45.74 *	−26.11±37.10	163.74±48.41	166.62±49.93	2.88±68.37	−28.99±22.40
CRP(ug/ml)	10.90±6.31	11.11±8.22	0.22±12.12	17.90±20.93	15.82±15.93	−2.08±13.75	2.30±5.17
IL-6(pg/ml)	10.00±6.79	11.56±10.05	1.56±6.60	10.93±8.44	11.68±8.20	0.75±6.77	0.81±2.54
TNF-α(pg/ml)	14.93±6.54	14.04±7.61	−0.89±5.91	13.45±7.64	13.71±6.51	0.27±4.52	−1.16±1.92

For β-endorphin, 1) *p<0.05 compared to baseline; 2) group difference: Cohen’s $d = 0.53$

All in mean±SD. β-endorphin: beta endorphin. CRP: C-reactive protein. IL-6: interleukin 6. TNF-α: tumor necrosis factor alpha.