Tai Chi Improves Brain Metabolism and Muscle Energetics in Older Adults

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ABSTRACT

BACKGROUND AND PURPOSE: Tai Chi is a mind-body exercise that has been shown to improve both mental and physical health. As a result, recent literature suggests the use of Tai Chi to treat both physical and psychological disorders. However, the underlying physiological changes have not been characterized. The aim of this pilot study is to assess the changes in brain metabolites and muscle energetics after Tai Chi training in an aging population using a combined brain-muscle magnetic resonance spectroscopy (MRS) examination.

METHODS: Six healthy older adults were prospectively recruited and enrolled into a 12-week Tai Chi program. A brain ^{1}H MRS and a muscle ^{31}P MRS were scanned before and after the training, and postprocessed to measure N-acetylaspartate to creatine (NAA/Cr) ratios and phosphocreatine (PCr) recovery time. Wilcoxon-signed rank tests were utilized to assess the differences between pre- and post-Tai Chi training.

RESULTS: A significant within-subject increase in both the NAA/Cr ratios ($P = .046$) and the PCr recovery time ($P = .046$) was observed between the baseline and the posttraining scans. The median percentage changes were 5.38% and 16.51% for NAA/Cr and PCr recovery time, respectively.

CONCLUSIONS: Our pilot study demonstrates significant increase of NAA/Cr ratios in posterior cingulate gyrus and significantly improved PCr recovery time in leg muscles in older adults following short-term Tai Chi training, and thus provides insight into the beneficial mechanisms.

Keywords: Tai Chi, magnetic resonance spectroscopy, N-acetylaspartate, phosphocreatine recovery time.

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Introduction

Tai Chi is a mind-body exercise that utilizes continuous, curved, and spiral body movements.[1] It is a moderate-intensity aerobic exercise that utilizes 50–58% of heart rate reserve during Tai Chi practice, and requires strong concentration with breathing control when performed properly.[1–3] This combination results in physical benefits, such as improvements in aerobic capacity, muscle strength, balance, and motor control, as well as psychological benefits of improved attentiveness, reduced stress and anxiety, and cardiovascular improvements.[1,4] Numerous studies have shown that Tai Chi results in the strengthening of muscles in the lower limb particularly in knee flexor and extensor muscle groups such as the quadriceps.[5–7] Multiple studies have shown the benefits of Tai Chi with improved cognition.[8] Furthermore, a growing body of evidence consisting of morphological magnetic resonance imaging (MRI) and functional MRI data suggests that Tai Chi can induce beneficial neuroplasticity.[9–11] As a result, recent literature suggests the use of Tai Chi to treat both physical and psychological disorders, including stroke, Parkinson's disease, traumatic brain injury, and depression.[1,12–14] However, the beneficial mechanisms of Tai Chi are not well understood. Noninvasive and objective measures are required to better understand the physiological changes that the brain and body undergo during Tai Chi training.

Magnetic resonance spectroscopy (MRS) can noninvasively measure the endogenous chemicals of body tissues. In the brain, ^{1}H MRS has long been used to measure concentrations of different metabolites to study the biochemical processes. Previous studies in aerobic exercise have shown that N-acetylaspartate (NAA) is a neuronal marker that can assess neuronal health.[15–17] In the leg muscles, ^{31}P MRS can quantify mitochondrial function by measuring the rate of recovery of phosphocreatine (PCr) following exercise.[18] Together, these measures can be used to track changes in the brain and muscle due to mind-body interventions such as Tai Chi and yoga.

The goal of this pilot study is to assess the changes that occur in brain metabolites and muscle energetics after Tai Chi training in the aging population using a combined brain-muscle MRS examination. To the best of our knowledge, this is the first study to investigate the responses of brain and leg muscles to Tai Chi exercise by noninvasive MRS.

Methods

Participants

This pilot study was approved by the Brigham and Women's Hospital Institutional Review Board, and all subjects provided written informed consent. Healthy older adults from the local community center were prospectively recruited based on the following inclusion and exclusion criteria.

The inclusion criteria were: (1) age 55 or older, (2) no Tai Chi training in the past 12 months, and (3) willing to participate in a 12-week Tai Chi class.

The exclusion criteria included: (1) signs or symptoms of upper motor neuron syndrome; (2) any major systemic illness or unstable condition, which could interfere with protocol compliance, including the diagnosis of major depression; (3) active psychiatric disease that would interfere with participation; (4) psychiatric diagnoses; (5) agitation, or behavioral problems within the last 3 months; (6) history of alcohol/substance abuse or dependence within the past 2 years; (7) any neurological diseases; (8) participation in other clinical studies involving neuropsychological measures collected more than one time per year; and (9) unable to undergo MRI for any reason such as claustrophobia or presence of magnetic resonance (MR) incompatible implants.

Tai Chi Training

After enrollment, all participants received a 12-week Tai Chi training under the instruction of a certified teacher at Greater Boston Golden Age Center (Boston, MA, USA). All subjects underwent at least two practices per week, each practice of 60 minutes.

The ^{1}H brain and ^{31}P muscle MRS scans were conducted in a single session before and after Tai Chi training.

^{1}H Brain MRS Acquisition

^{1}H brain MRS was performed on a clinical 3.0 Tesla MR scanner (Siemens TIM Skyra, VD13) with a 32-channel head coil. Axial 3-dimensional magnetization prepared rapid-acquisition gradient echo (3D-MPRAGE, Repetition time (TR)/Echo time (TE) = 1,760 ms/3.43 ms, Field of View (FOV) = 268 × 209 mm^{2}, matrix = 268 × 209) images were acquired prior to spectroscopy, and reconstructed in the sagittal and coronal planes with 2 mm slice resolution for accurate localization of the voxel.

The ^{1}H brain MRS utilized a single voxel point-resolved spectroscopy (PRESS) sequence. The acquisition parameters included: TR/TE = 2,000 ms/30 ms, voxel size = 30 × 30 × 30 mm^{3}, 64 averages, 833 ms dwell time, 1,024 points, and total scan time = 3 minutes. The voxel was positioned in the posterior cingulate gyrus (PCG, Fig 1) to include as much of the gray matter as possible while avoiding the scalp tissue. The PCG was chosen due to its sensitivity to a broad range of diseases and because it is one of the most homogenous parts of the brain, thus providing excellent quality spectra.[19,20] Each voxel underwent automated optimization including 3-dimensional shimming, transmit gain, frequency adjustment, and water suppression. When the full width at half maximum (FWHM) of the water signal was ≥14 Hz, manual shimming was performed to optimize the magnetic field homogeneity of the selected spectroscopy volume of interest to a line width of <14 Hz FWHM of the water signal.

A screenshot of the pretraining ^{1}H MRS voxel position was saved, and care was taken to place the excitation volume to anatomically match the initial MRS scan in the posttraining follow-up.

^{1}H Brain MRS Data Analysis

LCModel software (Version 6.2, LCMODEL Inc., Oakville, Canada) was used for the ^{1}H brain single voxel spectroscopy spectral fitting, using simulated spectra of 20 metabolites as a customized basis set. All spectra were quality controlled by examining the FWHM of the unsuppressed water spectrum and signal-to-noise ratio (SNR). Total NAA to total creatine (Cr) ratios were calculated in the LCModel output, and included in the further analysis.

^{31}P MRS Acquisition

^{31}P data acquisition was performed in the same scanner as the ^{1}H brain MRS. A single channel ^{31}P tuned transmit/receive surface coil was strapped to the right thigh at the vastus medialis muscle of the quadriceps. First, the transmitter gain of a 500-μs hard excitation pulse was adjusted to determine the value giving the highest PCr peak. A simple pulse-acquire sequence (TR = 2,000 ms, bandwidth = 3,000 Hz) was then performed continuously during 10-minute scan consisting of: 2 minutes of rest, 3 minutes of leg-lifting exercise, and 5 minutes of recovery rest. During the protocol, 300 free induction decays (FIDs), with 2,048 complex data points per FID, were acquired continuously.

Exercise During ^{31}P MRS Acquisition

The ^{31}P MRS scan leg-lifting exercise was done inside the MR scanner. Subjects performed this exercise in a supine position with a custom-built dynamic knee extension apparatus. This apparatus has a bar that rests across the subjects' shins and attaches to weights in the back of the MR scanner by means of a pulley. The subjects extended their knees, pushing up the bar to lift the weights. Subjects were familiarized with the leg-lifting exercise and asked to perform constant-load leg lifting at a steady rate (every 2 seconds) until exhaustion, limited by symptoms, or 3 minutes duration. The constant-load was set to 30% of the maximum work capacity at the time of familiarization, which was determined by a 3-second knee extension test using different weights.

^{31}P MRS Data Analysis

The ^{31}P MRS data was postprocessed offline, with the spectral improvement by Fourier thresholding (SIFT) method described elsewhere.[21] Briefly, the SIFT was applied to improve SNR and smooth temporal trajectories of the 300 spectra. The spectra were then fit using a simulated basis set to obtain the ^{31}P metabolite areas.[21] The postexercise PCr amplitudes were fit to a monoexponential recovery function $A + B^{\exp(-\frac{t}{\tau})}$ to determine the recovery time constant τ.

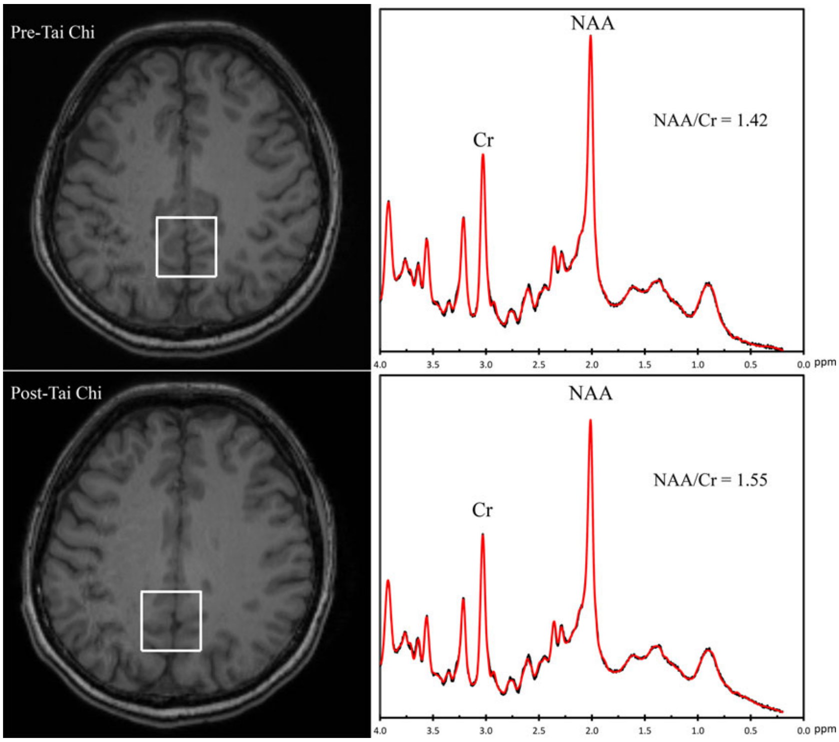

Fig 1. Representative ^{1}H MRI images (left) from subject 5 and the voxel placed in the posterior cingulate gyrus area from which the localized ^{1}H MRS spectra (right) were obtained. N-acetylaspartate to creatine(NAA/Cr) ratios increased from 1.42 before to 1.55 after 12 weeks of Tai Chi training.

Statistical Analysis

Related-samples Wilcoxon-signed rank tests were used to assess the differences in NAA/Cr ratios and PCr recovery time between pre- and post-Tai Chi training. A *P*-value of <.05 was considered significant. Statistical analyses were performed using SPSS (Version 21, IBM Corporation, NY, USA).

Results

Participants

Seven subjects were enrolled in this study. One subject withdrew due to conflicts with the Tai Chi class schedule, so six subjects completed the 12-week Tai Chi program. All six subjects were Tai Chi-naive at their first scan. The changes of the NAA/Cr ratios and the PCr recovery time between pre- and post-Tai Chi training, as well as the subject demographic characteristics, are summarized in Table 1. Representative ^{1}H brain MRS and ^{31}P muscle MRS are shown in Figures 1 and 2.

Changes of NAA/Cr Ratios

A significant within-subject increase in NAA/Cr ratios was observed between the baseline and the posttraining scans ($P = .046$). Five of six subjects showed an increase in NAA/Cr ratios after 12 weeks of Tai Chi training (Fig 3). The median percentage change was 5.38%, and the mean NAA/Cr ratio difference was .08 ± .07 (mean ± standard deviation) between baseline and posttraining scans.

PCr Recovery

There was a significant within-subject decrease in PCr recovery time between the pre- and the post-Tai Chi scans ($P = .046$). Improved PCr recovery rates were observed in five of six

Table 1. Subject Demographics and Changes of N-Acetylaspartate/Creatine Ratios and Phosphocreatine Recovery Time

Subjects	Gender*	Age (Year)	BMI† (kg/m^2)	Δ NAA/Cr Ratios (Percentage Change)‡	Δ PCr Recovery Time, Seconds (Percentage Change)§
1	F	69	20.34	.17 (12.85%)	−3.97 (−16.82%)
2	F	69	26.22	−.04 (−2.38%)	−26.04 (−53.66%)
3	M	70	26.56	.05 (3.78%)	−15.65 (−42.61%)
4	F	72	23.24	.08 (5.48%)	−3.54 (−11.33%)
5	F	51	22.72	.13 (9.08%)	−4.35 (−16.20%)
6	F	51	23.62	.08 (5.27%)	1.66 (9.56%)

*F = female; M = male.
†BMI = body mass index.
‡NAA = N-acetylaspartate; Cr = creatine; Δ NAA/Cr Ratios = $NAA/Cr_{post\text{-}Tai\ Chi} - NAA/Cr_{pre\text{-}Tai\ Chi}$; Percentage Change = (Δ NAA/Cr Ratios)/($NAA/Cr_{pre\text{-}Tai\ Chi}$).
§PCr = phosphocreatine; Δ PCr Recovery Time = PCr Recovery $Time_{post\text{-}Tai\ Chi}$ − PCr Recovery $Time_{pre\text{-}Tai\ Chi}$; Percentage Change = (Δ PCr Recovery Time)/(PCr Recovery $Time_{pre\text{-}Tai\ Chi}$).

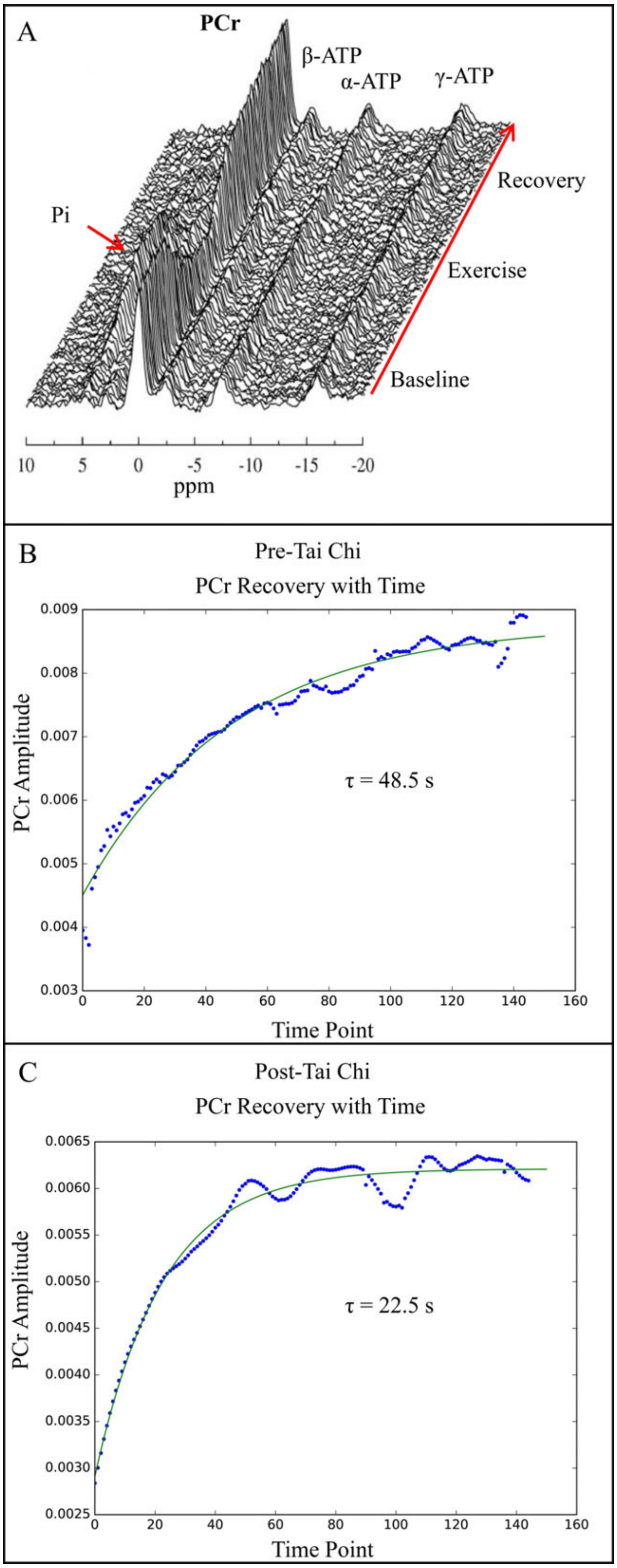

Fig 2. Panel A: A stacked plot of 300 ^{31}P spectra after spectral improvement by Fourier thresholding processing. Panels B and C: Temporal plots of phosphocreatine (PCr) areas during the recovery of subject 2 from lifting exercise and the result of a monoexponential fit (green line), which yields the PCr recovery rate. PCr recovery time decreased from 48.5 to 22.5 seconds after 12 weeks of Tai Chi training. α, β, γ-ATP = adenosine triphosphate resonances (alpha, beta, and gamma); Pi = inorganic phosphate; ppm = parts per million; τ = recovery time constant.

participants following 12 weeks of Tai Chi training as shown in Figure 3. The PCr recovery time decreased 16.51% (median), or 8.65 ± 10.24 (mean ± standard deviation) from baseline scan, after Tai Chi training.

Discussion

In our study, we found significantly increased NAA/Cr ratios in posterior cingulate gyrus and significantly improved PCr recovery time in leg muscles in older adults with 12 weeks of Tai Chi training. Our results suggest that Tai Chi, as a mind-body exercise, may effectively promote neuroplasticity and increase lower extremity muscle oxidative capacity in older adults.

NAA is a metabolite found almost exclusively within cell bodies of neurons, and directly reflecting neuron cell number.[22] A decrease of NAA level is an indication of neuronal loss, as is typically observed in healthy aging, Alzheimer's disease, stroke, multiple sclerosis, schizophrenia, epilepsy, and bipolar disorder.[17,23–25] A growing body of research indicates that aerobic fitness promotes neuronal integrity and viability. A study of 137 healthy older adults demonstrated that higher aerobic fitness level correlated with increased NAA levels in the frontal cortex.[15] Another study compared neurochemical concentrations between sedentary and endurance-trained middle-aged adults, and found that endurance-trained adults had significantly higher NAA/Cr in the frontal gray matter.[16] Our results demonstrated significantly increased NAA/Cr in healthy older adults after 12 weeks of Tai Chi training, suggesting either increased neuroplasticity, or potentially, a protective effect of Tai Chi on neurons. Of note, different from the prior studies, we acquired the MRS data in posterior cingulate gyrus, which has been shown to be more sensitive to global changes in the brain.[19] Furthermore, the PCG plays an important role in cognitive processes such as attention,[26] which has been shown to be enhanced by Tai Chi.[8] Finally, the PCG was also selected because it is highly reproducible with a covariance of 2-2.5% for NAA.[27]

Our results also showed significant increase in the PCr recovery of the thigh muscles in our subjects after 12 weeks of Tai Chi training. PCr recovery time, measured by ^{31}P MRS, is a reliable indicator of skeletal muscle mitochondrial metabolism.[18,28] It is very reproducible with a covariance of 8%.[29] It reflects the mitochondrial ATP synthesis during recovery from exercise, which is driven by oxidative metabolism.[30,31] Our findings of decreased PCr recovery time indicate that Tai Chi training accelerates ATP synthesis and improves muscle mitochondrial function of older adults. Choi et al accessed the muscle bioenergetics by postexercise PCr recovery rate in a study with 126 participants and showed that muscle bioenergetics were highly correlated with walking speed.[32] Furthermore, a study by Zane et al with 326 participants demonstrated that impaired muscle mitochondrial energetics accessed by PCr resynthesis rate affected muscle strength, and through this mechanism, had a negative effect on walking performance.[33] Thus, our results provide an insight into the physiological mechanisms of the increased lower extremity muscular strength and improved motor control following Tai Chi exercise. Our pilot study is, however, limited by a small sample size, and these encouraging findings need to be confirmed in a larger study.

Higher NAA level in prefrontal cortex has also been observed in subjects with higher aerobic fitness level in prior

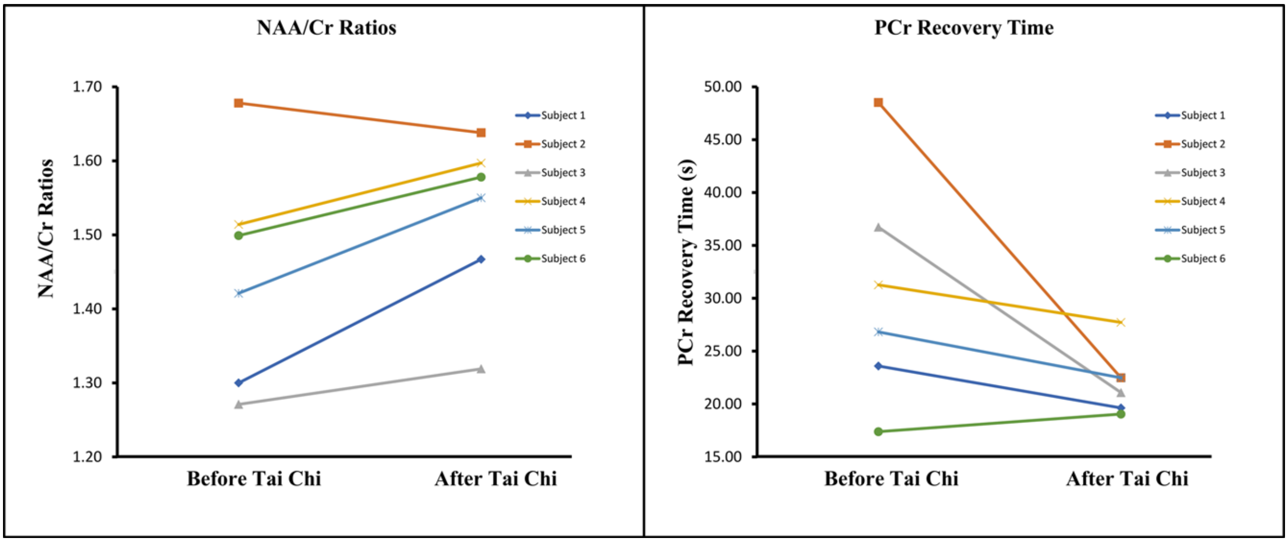

Fig 3. The changes of N-acetylaspartate to creatine(NAA/Cr) ratios (left panel) and phosphocreatine (PCr) recovery rates (right panel). There were significant within-subject increase of NAA/Cr ratios ($P = .046$) and decrease of PCr recovery time ($P = .046$) after 12 weeks of Tai Chi training.

studies.[15,16] Thus, multivoxel MRS sequence could be added in the protocol to explore the global effect that Tai Chi training has on the brain. Moreover, multiple covariates especially aerobic fitness level before enrollment could be analyzed to help explain the variation of changes of NAA and PCr recovery time discovered in our pilot study.[15] Finally, different control groups including regular aerobic exercise or yoga could be designed to better understand the effect of Tai Chi training. In conclusion, our pilot study demonstrates significant increase of NAA/Cr ratios in posterior cingulate gyrus and significantly improved PCr recovery time in the leg muscles of older adults following short-term Tai Chi training. Our results support the recent findings of the physical and psychological benefits of Tai Chi exercise, and provide an insight into the beneficial mechanisms. Further well-designed and larger studies are needed to validate our findings.

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