ORIGINAL ARTICLE

# Impact of Short- and Long-term Tai Chi Mind-Body Exercise Training on Cognitive Function in Healthy Adults: Results From a Hybrid Observational Study and Randomized Trial

## 短期和长期太极身心训练对健康成人认知功能的影响：从混合观察性研究与随机试验中得出的结果

## Impacto del entrenamiento con ejercicios mente-cuerpo de taichí a corto y largo plazo en la función cognitiva en adultos sanos: Resultados de un estudio observacional híbrido y ensayo aleatorizado

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Aging, tai chi, cognitive function, dementia

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## ABSTRACT

**Background:** Cognitive decline amongst older adults is a significant public health concern. There is growing interest in behavioral interventions, including exercise, for improving cognition. Studies to date suggest tai chi (TC) may be a safe and potentially effective exercise for preserving cognitive function with aging; however, its short-term and potential long-term impact on physically active, healthy adults is unclear.

**Objective:** To compare differences in cognitive function among long-term TC expert practitioners and age-matched and gender-matched TC-naïve adults and to determine the effects of short-term TC training on measures of cognitive function in healthy, nonsedentary adults.

**Design:** A hybrid design including an observational comparison and a 2-arm randomized clinical trial (RCT)

**Participants:** Healthy, nonsedentary, TC-naive adults (50 y-79 y) and age-matched and gender-matched long-term TC experts

**Methods:** A cross-sectional comparison of cognitive function in healthy TC-naïve (n=60) and TC expert (24.5 y ± 12 y experience; n=27) adults: TC-naïve adults then completed a 6-month, 2-arm, wait-list randomized clinical trial of TC training. Six measures of cognitive function were assessed for both cross-sectional and longitudinal comparisons.

**Results:** TC experts exhibited trends towards better scores on all cognitive measures, significantly so for category fluency (*P*=.01), as well as a composite *z* score summarizing all 6 cognitive assessments (*P*=.03). In contrast, random assignment to 6 months of TC training in TC-naïve adults did not significantly improve any measures of cognitive function.

**Conclusions:** In healthy nonsedentary adults, long-term TC training may help preserve cognitive function; however, the effect of short-term TC training in healthy adults remains unclear.

**Trial Registration:** ClinicalTrials.gov NCT01340365

## 摘要

背景：老年人认知功能衰退是一个重要的公共健康问题。通过行为干预（包括锻炼）来改善认知功能日益受到关注。现有研究表明，太极拳可能是防止认知功能随年龄衰退的安全有效锻炼方式，但它对经常运动的健康成人的短期和长期作用尚不明确。

目的：比较长期打太极拳的高手与未打过太极拳的同等年龄和性别的成人在认知功能方面的差异，并确定短期太极拳运动对健康非久坐成人的认知功能的影响。

设计：采用混合设计，既包括观察性比较，也包括一项两分组随机临床试验（RCT）

参与者：未打过太极拳的健康非久坐成人（50–79 岁）与年龄及性别相仿的长期打太极拳高手

方法：对未打过太极拳的健康成人（n=60）和太极拳高手（拥有 24.5 ± 12 年的经验；n=27）的认知功能进行比较：未打过太极拳的成人随后按侯选表，完成了一项为期 6 个月、两分组太极训练随机临床试验。不管是剖面代表性比较，还是纵向比较，均评估了 6 项认知功能指标。

结果：太极拳高手在所有认知功能指标上均表现出更高得分倾向，在流利度项目上尤其显著 (P=0.01)，在 6 个指标的综合评分 z 值上亦如此 (P=0.03)。相对之下，未打过太极拳的成人经随机分配接受 6 个月的太极拳训练后，其认知功能指标未出现显著改善。

结论：健康非久坐成人接受长期太极拳训练可能有助于保存认知功能，但短期太极拳训练对健康成人的效果仍不明确。

试验注册编号：ClinicalTrials.gov NCT01340365

## SINOPSIS

**Antecedentes:** El deterioro cognitivo entre los adultos más mayores es un importante problema de salud pública. Existe un creciente interés en las intervenciones conductuales, incluido el ejercicio, para mejorar la cognición. Los estudios realizados hasta la fecha sugieren que el taichí (TC) podría ser un ejercicio seguro y posiblemente eficaz para preservar la función cognitiva con el envejecimiento; sin embargo, su impacto a corto plazo y su posible impacto a largo plazo en adultos sanos y físicamente activos no está claro.

**Objetivo:** Comparar las diferencias en la función cognitiva entre las personas expertas que practican TC a largo plazo y adultos que no habían practicado TC anteriormente de la misma edad y sexo y determinar los efectos del entrenamiento con TC a corto plazo en las medidas de la función cognitiva en adultos no sedentarios sanos.

**Diseño:** Diseño híbrido que incluía una comparación observacional y un ensayo clínico aleatorizado (ECA) de 2 grupos

**Participantes:** Adultos no sedentarios sanos que no habían practicado TC anteriormente (50 años y 79 años) y expertos en TC a largo plazo de la misma edad y sexo

**Métodos:** Comparación transversal de la función cognitiva en adultos santos que no habían practicado TC anteriormente (n = 60) y expertos en TC (24,5 ﬄ 12 años de experiencia; n = 27) adultos: adultos santos que no habían practicado TC anteriormente completaron un ensayo clínico aleatorizado de lista de espera de entrenamiento con TC de 2 grupos y 6 meses de duración. Se evaluaron seis medidas de la función cognitiva para realizar comparaciones tanto transversales como longitudinales.

**Resultados:** Los expertos en TC mostraron tendencias hacia mejores puntuaciones en todas las medidas cognitivas, que fueron significativas en la categoría de fluidez (P = 0,01), así como en la puntuación z compuesta que resumía las 6 evaluaciones cognitivas (P = 0,03). Por el contrario, la asignación aleatoria a los 6 meses de entrenamiento con TC en adultos que no habían practicado TC anteriormente no mejoró significativamente ninguna de las medidas de la función cognitiva.

**Conclusiones:** En los adultos sanos no sedentarios, el entrenamiento con TC a largo plazo podría ayudar a preservar la función cognitiva; sin embargo, el efecto del entrenamiento con TC a corto plazo en adultos sanos sigue sin estar claro.

Registro del ensayo: ClinicalTrials.gov NCT01340365

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## INTRODUCTION

Cognitive decline amongst older adults is a significant and growing public health concern. In the United States, the prevalence of mild cognitive impairment (MCI) in adults over 70 years of age was estimated to be 5.4 million in 2010 with an additional 3.4 million older adults suffering from dementia.[1] Worldwide costs for treating age-related cognitive impairment in 2010 were estimated at $150 billion.[2] Both prevalence and costs of dementia are expected to grow in many countries as demographics shift to greater proportions of older adults.[3] These concerns, as well growing evidence that cognitive decline may be evident even in adult midlife, have led to an interest in interventions that aim to prevent cognitive decline across a broad range of the adult age span.[4,5]

Effective treatment options for arresting cognitive decline associated with aging have not been well developed. Behavioral interventions, including exercise, are increasingly being considered for enhancing cognition in older adults. Both long-term cohort studies as well as short-term clinical trials support the idea that exercise and physical activity may be associated with preservation and restoration of cognitive function with aging[6]; however, optimal exercise programs have yet to be defined. Some evidence suggests that multimodal training that integrates a variety of physical, cognitive, and social activities may be more effective than any one intervention alone.[7]

Tai chi (TC) is an increasingly popular multimodal mind-body exercise that incorporates physical, cognitive, social, and meditative components within the same activity.[8] Previous studies support the potential of TC to attenuate age-related declines in cardiovascular disease,[9] balance,[10] and emotional well-being.[8,11] These studies also suggest that TC is safe for older adults[12] and an enjoyable activity with the potential for long-term adherence and exercise maintenance. Recent meta-analyses support the potential for TC to improve executive function in healthy older adults and global cognitive function in adults with existing cognitive impairments.[13] Novel imaging studies are beginning to support plausible neural mechanisms underlying TC's observed effects on cognitive function.[14-16]

While studies to date suggest TC may be a safe and potentially effective exercise for preserving and/or restoring cognitive function within aging populations, multiple gaps in knowledge persist that are relevant to informing clinical recommendations. Importantly, studies that have included cognitive outcomes have typically evaluated sedentary older adults who are frail,[17] transitioning to frailty,[18] or afflicted with existing chronic medical conditions.[19,20] Relatively little is known of the impact of TC on cognitive function in already active, healthy adults who are interested in exercise to preserve cognitive function. Additionally, no studies have employed common screening and outcome measures to study cognitive function in expert TC practitioners (operationally defined here as a minimum of 5 y training experience) as compared to age-matched, TC-naïve individuals before and after a short-term TC training intervention. To address these knowledge gaps, we employed a hybrid study design to answer the following questions.

1. Do TC experts (aged 50 y-79 y) exhibit greater cognitive function as compared to age-matched and gender-matched, nonsedentary, TC-naive adults?
2. Does the addition of a 6-month TC training program to background physical activity and usual care improve cognitive function in TC-naïve adults compared to background physical activity and usual care alone?

## METHODS

### Study Design

We employed a hybrid study design that included a 2-arm randomized clinical trial (RCT) along with an additional observational comparison group. Long-term TC training effects on cognitive outcomes were assessed through comparisons of TC-naïve healthy adults vs an age-matched sample of expert TC practitioners. Short-term effects of TC training were assessed by randomly assigning the TC-naïve healthy adults to either 6 months of TC plus usual care or to usual care alone. The Institutional Review Board at Brigham and Women's Hospital, Boston, Massachusetts, approved this study, and all work was carried out with the ethical standards set forth in the World Medical Association's 2008 Declaration of Helsinki. The RCT component of this study was registered at clinicaltrials.gov (NCT01340365). Cognitive function outcomes reported herein were secondary outcomes in our study. Primary outcomes related to balance, gait, and heart rate dynamics will be reported elsewhere.[21,22]

#### *Randomized Trial Design*

A total of 60 healthy adults, aged 50 year to 79 years, were randomized to receive 6 months of TC training or to usual healthcare alone. Randomization was stratified by age (50 y-59 y, 60 y-69 y, or 70 y -79 y) using a permuted-blocks randomization scheme with randomly-varying block sizes. All outcomes were assessed at baseline and 6 months. Further details related to RCT design are reported elsewhere.[23]

#### *Recruitment for Randomized Trial Targeting Community-dwelling Healthy Adults*

Inclusion criteria were (1) age of 50 years to 79 years and (2) willingness to adhere to a 6-month TC protocol. Exclusion criteria were (1) chronic medical condition including cardiovascular disease, stroke, active cancer, neurological conditions, or significant musculoskeletal conditions requiring chronic use of pain medication; (2) acute condition requiring hospitalization within the past 6 months; (3) self-reported inability to walk continuously for 15 minutes; (4) regular TC practice within past 5 years; (5) regular participation in physical exercise on average 4 or more times per week; and (6) Mini Mental State Examination (MMSE) score less than 24.[23] Interested individuals underwent both an initial phone screening and an in-person screening at our clinical research center. Eligible individuals provided written informed consent and underwent baseline testing prior to randomization.

All TC interventions were administered pragmatically at 1 of 5 prescreened TC schools within the Boston area that met specific guidelines described elsewhere.[23,24] In brief, schools were chosen to ensure that they provided valid, stable TC programs led by experienced teachers. Eligibility criteria included long-standing community-based programs, curricula taught in English language that emphasized core TC principles, and curricula based on Yang, Wu, Chen, or Sun TC styles. Ancillary exercises, such as qigong warm-ups or 2-person push hands were allowed, but TC training integrating weapons or contact sparring was not allowed. Because interventions were designed to be pragmatic with high levels of generalizability, instructors were asked to teach using the same approach and protocols used for non-study community participants.

Study participants were asked to attend 2 classes per week on average over the 6-month intervention. They were also asked to practice a minimum of 30 minutes on 2 additional days per week. Attendance at TC classes was recorded by instructors, and home practice was tracked by participants using a weekly practice log. Participants attending a minimum of 70% of all classes and completing 70% or more of prescribed home practice were considered compliant or "per protocol."

#### *Adverse Events*

Adverse events were systematically monitored using a detailed protocol described elsewhere.[21] A total of 4 nonserious adverse events were reported throughout study. All events were reported by participants randomized to the TC group. Only 2 of the 4 events were determined to be related to the TC intervention (both minor musculoskeletal injuries [one wrist, one ankle]); neither event was associated with cognitive or emotional distress.

#### *Nonrandomized Comparison Group: Tai Chi Experts*

Twenty-seven healthy adults (aged 50 y-79 y) currently engaged in an active TC training regimen, each with over 5 years of TC practice, were recruited for a single observational visit. No limitation was set on TC style. Eligibility and screening procedures for TC experts were identical to those for healthy adults enrolled in the RCT.

### Measurements

A battery of validated tests including the Trail Making Test (TMT) A and B[25]; the Controlled Oral

Word Association Test (COWAT) reported here separately as category fluency (animals and supermarket items total) and letter fluency[26]; and the Digit Span (DS) tests[26] were used to evaluate visuomotor processing speed, visual attention, rapid set-shifting,[27] verbal attention, verbal working memory,[28] and activation retrieval[29] respectively. Physical activity level was self-reported using the Physical Activity Status Scale (PASS), and physical and mental quality of life was assessed with the Medical Outcomes Survey Form (SF-36) health status survey.

### *Cognitive Tests*

Cognitive function was assessed with validated measures of executive function, working memory, and short-term memory. TMT is a widely used instrument that is administered in 2 parts, A and B.[25] TMT-A is a visual-scanning task; the time required to draw lines sequentially connecting numbered circles from 1 to 25 is recorded. TMT-B assesses time required to connect the same number of circles in an alternating sequence of numbers and letters. TMT-B is considered to evaluate executive control and is correlated with other executive function measures.[30] TMT is a sensitive indicator of overall neurological impairment[25] and has good reliability.[31] COWAT examines working memory span and verbal fluency.[26] COWAT combines 2 tests, letter fluency and category fluency: one requires the participant to produce as many words as possible that begin with a given letter of the alphabet (F, A, S) and the other requires the participant to name as many items as possible in a given category (animal naming, supermarket items). There is 1 minute allowed for each of the 3 letters and 1 minute allowed per category. The score of letter fluency is the sum of all acceptable words produced in the 3 trials; similarly, the sum of all acceptable words produced in the 2 category trials determines the category fluency score. COWAT has good reliability and validity.[26,32,33] DS is a widely used measure of short-term memory: ie, the number of digits a person can absorb and recall in correct serial order both forward (DSF) and backward (DSB). The number sequences start out easy, with just 2 numbers, and get progressively more difficult, the last being 9 digits for DSF and 8 digits for DSB. Both DSF and DSB are administered until the participant consecutively fails 2 trials of the same digit span length. Scores for DSF and DSB are based on the number of digits of the longest correct span. DS has good reliability and validity.[26] All 3 measures have been employed in studies evaluating the impact of exercise on cognitive function in elders.[34,35]

### *Outcomes Used to Screen and Characterize Population*

Global cognition was screened at baseline using the MMSE. Potential participants were excluded for having a MMSE score less than 24. Physical activity level was assessed using PASS.[36] Participants were asked to estimate their general physical activity during the previous week using an 11-point scale (ie, 0-10). The scale quantifies physical activity duration by a combination of the minutes of exercise per week and the intensity of this exercise (heavy, modest, or none). The concurrent validity of the scale has been documented in both men and women, and scores correlate with maximal oxygen consumption in younger and older adults.[37] Health-related quality of life was assessed using the SF-36. The SF-36 has been validated in a variety of populations including older healthy individuals and has good test-retest reliability.[38,39]

### Statistical Analyses

Cross-sectional measures of cognitive function in TC experts and TC naïfs were compared in a linear model controlling for age, body mass index (BMI), gender, physical activity, and education. Trajectories of cognitive function over the 6-month intervention were compared between groups using a random-slopes model with shared baseline. All longitudinal analyses were conducted according to the intention-to-treat paradigm. The model included fixed effect of time, time x treatment, age, BMI, gender, physical activity, education, and interactions between time and age. The model included random participant-specific intercepts and slopes with unstructured covariance. The shared baseline assumption, enforced by omitting a treatment main-effect term, properly reflects the true state of the population sampled prior to randomization and has the advantage of adjusting for any chance differences at baseline in a manner similar to analysis of covariance (ANCOVA).[40] Treatment-group differences and adjusted means for mean age, BMI, physical activity, and education were estimated as well as their 95% confidence intervals. All inferential tests were 2-tailed at alpha =0.05. We chose to report comparison-wise *P*-values without adjustment for multiple comparisons to avoid inflating type II errors, recognizing that the nominal *P*-values underestimate the overall experiment-wise type I error rate. Our results are intended as hypothesis generating, not definitive tests of efficacy for TC on any specific measure of cognition. All analyses were performed in SAS (version 9.3, SAS Institute, Cary, North Carolina).

As a secondary analysis, we calculated a composite $z$ score to assess performance across all cognitive measures in our observational comparison. For each cognitive measure, a $z$ score was determined by calculating the overall mean and pooled standard deviation among TC expert and TC-naïve groups combined. The overall mean was subtracted from each individual's score for a given cognitive measure and then divided by the pooled standard deviation. Conservatively, missing values were assigned a $z$ score of 0. The sign was reversed for $z$ scores of measures for which higher values indicates worse performance (TMT A and TMT B). The composite $z$ score was calculated as the sum of the individual $z$ scores across all 6 cognitive measures.

### *Sample Size Considerations*

For cross-sectional comparisons, we estimated that a sample size of 27 TC expert and 60 TC-naïve participants would provide power to detect an effect size of 0.63. For the randomized trial, we estimated that the sample of 60 participants, randomized 1 to 1, would give us 80% power to detect a main effect of treatment if the true effect size was at least 0.74 based on a 2-tailed test at $P<.05$.

## RESULTS

### Baseline Characteristics and Study Flow

Sociodemographic characteristics of the TC experts were well-matched with the TC-naïve group with respect to average age, global cognitive status, and both physical and mental quality of life. Compared with naïve controls, TC experts had lower BMI and higher levels of physical activity and education (Table 1). TC experts reported an average of 24.6±12 years of TC training (median 20 y, range 10 y-50 y). Approximately equal numbers reported Yang (n=12) and Wu (n=15) style TC as their primary styles; however, all reported having training experience in other styles of TC, related martial arts, and/or mind-body practices (eg, yoga, meditation). TC-naïve adults randomized to TC plus usual care vs usual care alone were comparable at baseline (Table 1).

### Participant Flow Through the Study

Participants reported to the Beth Israel Deaconess Medical Center (BIDMC) Clinical Research Center, Boston, Massachusetts, where they underwent final in-person screening procedures: MMSE and an electrocardiogram (ECG). The MMSE was graded by trained

**Table 1** Baseline Characteristics

| | Randomized Groups | | Observational Group |
|---|---|---|---|
| | Usual Care (n=29) | TC (n=31) | Long-term TC (n=27) |
| **Age, y** AVG ± SD | 64.45±7.42 | 63.94±8.02 | 62.78±7.57 |
| **Gender** n (%) | | | |
| Male | 11 (37.9%) | 9 (29%) | 13 (48.1%) |
| Female | 18 (62.1%) | 22 (71%) | 14 (51.9%) |
| **Race** n (%) | | | |
| White | 26 (89.7%) | 29 (93.5%) | 22 (81.5%) |
| African American | 3 (10.3%) | 0 (0%) | 1 (3.7%) |
| Asian | 0 (0%) | 2 (6.5%) | 4 (14.8%) |
| **Ethnicity** n (%) | | | |
| Non-Hispanic/Non-Latino | 29 (100%) | 30 (96.8%) | 26 (96.3%) |
| Hispanic/Latino | 0 (0%) | 1 (3.2%) | 1 (3.7%) |
| **Education, y** AVG ± SD | 16.19±3.03 | 17.13±3.41 | 18.44±3.34 |
| **MMSE** AVG ± SD | 29.21±0.82 | 29.03±1.17 | 29.07±1.11 |
| **BMI ($kg/m^2$)** AVG ± SD | 26.54±5.83 | 26.38±5.19 | 23.54±2.35[b] |
| **Medication subset** n (%) | | | |
| Self-reported hypertension | 5 (17.2%) | 7 (22.6%) | 1 (3.7%) |
| On hypertensive medication | 5 (17.2%) | 8 (25.8%) | 1 (3.7%) |
| Hypertensive at baseline assessment | 17 (58.6%) | 15 (48.4%) | 13 (48.1%) |
| **Physical activity level[a]** AVG ± SD | 4.0±2.0 | 4.0±2.0 | 6.0±2.0[b] |
| **Quality of life: mental component summary** | 54.8±4.8 | 53.8±8.3 | 54.3±5.8 |
| **Quality of life: physical component summary** | 54.5±3.3 | 51.9±6.2 | 54.4±4.3 |

[a]4=run about 1 mi/wk OR walk about 1.3 mi/wk OR spend about 30 min/wk in comparable physical activity; 6=run about 6-10 mi/wk OR walk about 7-13 mi/wk OR spend about 1-3 h/wk in comparable physical activity.
[b]Comparisons between TC experts and TC naïve at baseline; *P*<.05
Abbreviations: AVG, average; BMI, body mass index; MMSE, Mini-Mental State Examination; SD, standard deviation; TC, tai chi.

study staff, and the ECG was interpreted by a study doctor. Participants with an MMSE greater than 24 and no abnormal findings on their ECG were eligible to participate in the study. All outcome measurements were assessed at the Syncope and Falls in the Elderly (SAFE) laboratory at BIDMC. Outcomes related to cognitive function reported here were part of a larger battery of tests that lasted an average of 3.5 hours (including balance, cardiovascular, and gait outcomes to be reported elsewhere).

A CONSORT flowchart detailing study recruitment, randomization, and retention for the RCT component of the study can be found in Figure 1. Sixty healthy adults were successfully screened and enrolled, and 97% (28/29) and 87% (27/31) of individuals in the usual care and TC group completed the primary 6-month follow-up assessment, respectively.

Adherence to the TC protocol was variable. Two participants in the TC group formally withdrew participation due to time commitment and an unrelated injury. Of the remaining 29 participants in the TC group, 21 (72%) were defined as per protocol attending 70% of classes and completing 70% of required home practice over the entire course of the trial. This compliant subgroup had a mean exposure to TC training of 89.3 hours; in comparison, the intention-to-treat group had a mean exposure of 60.9 hours.

### Cognitive Function in Tai Chi Experts vs Tai Chi–naïve Adults

Comparison between TC experts and TC-naïve adults based on a single observation indicated trends towards greater cognitive performance in TC experts for all outcome measures (Table 2, Figure 2). Linear models indicated statistically significant differences for category fluency ($P$=.012) and weaker evidence for differences in TMT-A ($P$=.066). Composite $z$ scores summarizing net improvement or decline over all 6 cognitive assessments suggested significantly higher cognitive function among TC experts ($P$=.028). Overall age-related trends were only observed for TMT-A ($P$=<.001), with evidence of an age-associated decline for this outcome; however, there were no age x group (experts vs naïve) interactions observed for any cognitive outcome.

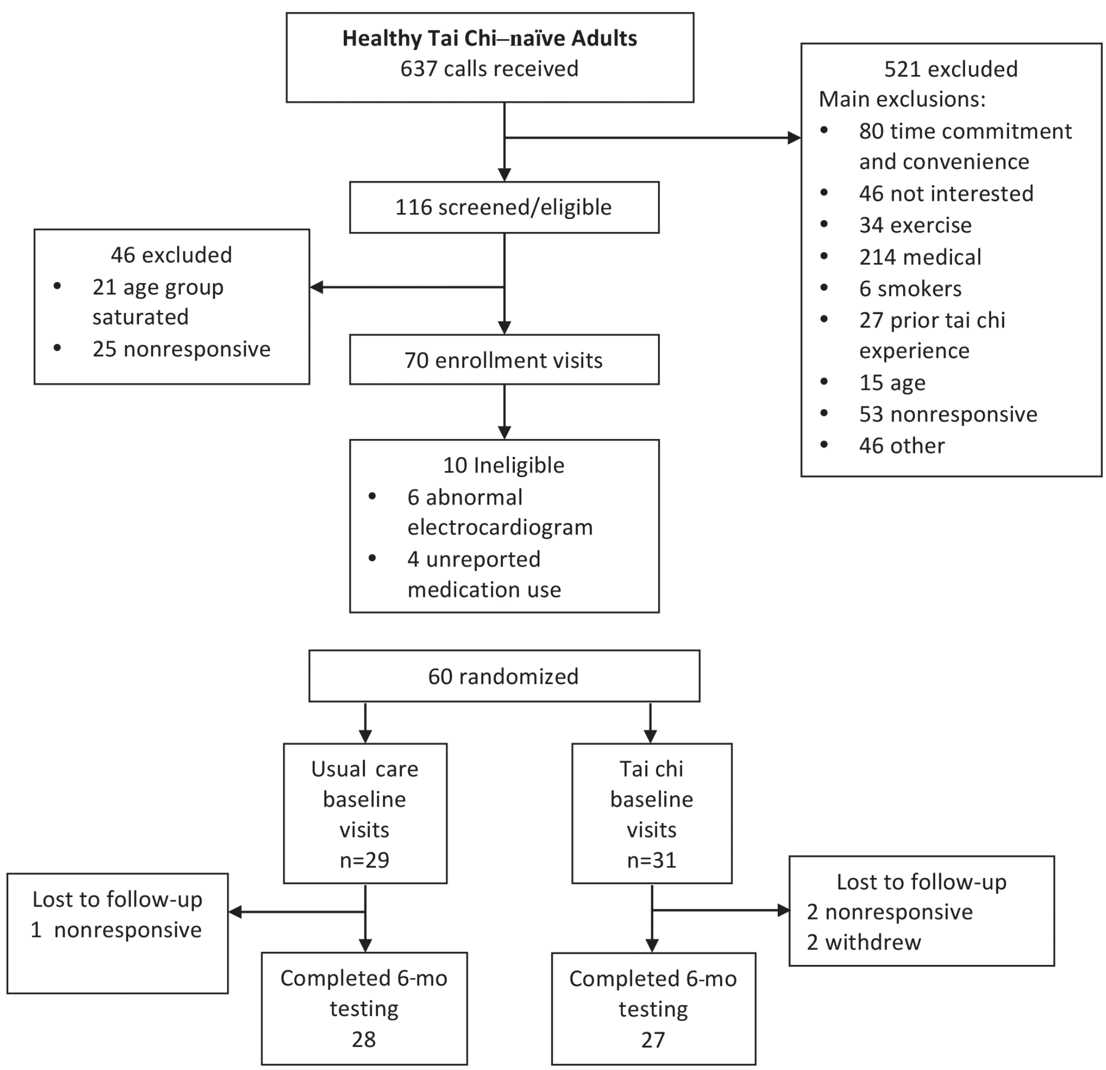


**Figure 1** CONSORT Flow.

**Table 2** Comparisons of Cognitive Performance Between TC Expert and TC Naïve Adults[a]

| Outcome Measure | TC Expert (n=27) Mean (95% CI) | TC Naïve (n=60) Mean (95% CI) | Between-group Estimate (95% CI) | Between-group Difference *P* value |
|---|---|---|---|---|
| TMT-A | 26.13 (23.2, 29.0) | 29.56 (27.6, 31.5) | -3.43 (-7.1, 0.23) | 0.066 |
| TMT-B | 53.53 (44.6, 62.5) | 60.11 (54.1, 66.2) | -6.58 (-17.9, 4.7) | 0.249 |
| DS LONGESTFWD | 7.96 (7.4, 8.5) | 7.7 (7.3, 8.1) | 0.27 (-0.43, 0.97) | 0.445 |
| DS LONGESTBKWD | 5.84 (5.3, 6.4) | 5.77 (5.4, 6.2) | 0.07 (-0.66, 0.80) | 0.850 |
| Letter fluency | 44.99 (40.8, 49.2) | 41.51 (38.7, 44.3) | 3.48 (-1.8, 8.8) | 0.196 |
| Category fluency | 46.48 (44.0, 49.0) | 42.47 (40.8, 44.1) | 4.01 (0.90, 7.1) | 0.012 |
| Z score | 1.30 (-0.06, 2.7) | -0.63 (-1.5, 0.28) | 1.93 (0.22, 3.6) | 0.028 |

[a]Estimates, means, confidence intervals, and between-group comparisons based on linear models controlling for age, gender, body mass index, physical activity level, and education. The between-group estimate shows the difference of experts minus naive.

Abbreviations: CI, 95% confidence interval; DS LONGESTBKWD, digit span longest backward span; DS LONGESTFWD, digit span longest forward span; TC, tai chi; TMT-A, Trail Making Test Part A; TMT-B, Trail Making Test Part B.

### Effect of Short-term Tai Chi Training on Cognitive Outcomes

Changes in all outcomes from baseline to 6-month follow-up in the RCT were generally small for both the TC and control group with no significant group effect for any cognitive outcomes (Table 3). Overall age effects were also modest, indicating trends towards lower cognitive function with increasing age only for TMT-A and TMT-B ($P$=.003 and $P$=.006, respectively); treatment x age interactions for all outcomes were not statistically significant. Post hoc per-protocol analyses (ie, limited to participants who were TC compliant) did not change within-group and between-group observed patterns and trends.

## DISCUSSION

To our knowledge, this study is the first to compare the potential long-term and short-term effects of TC on cognitive function in healthy active adults using common screening and outcome assessment protocols. We found in our cross-sectional analysis that experienced TC practitioners displayed a higher level of cognitive function compared to age-matched and gender-matched TC-naïve adults. The TC experts outperformed the TC-naïve group in nearly all measures of cognitive function with statistically significant differences in one measures as well as an overall composite *z* score, indicating that TC could have the potential to preserve cognitive function with aging. In contrast, a 6-month community-based TC program did not impact any cognitive outcomes in our sample of healthy adults.

Our findings in the TC expert group are supported by other observational studies. Studies based in Hong Kong have reported that individuals engaged in long-term TC practice perform better on multiple cognitive tests, most notably in tests of verbal fluency, memory and attention[41,42]; furthermore, long-term TC practitioners show increased memory preservation (including learning, retention, and retrieval) across ages.[43] However, these larger scale epidemiological studies likely included older adults with multiple comorbidities and a broader range of cognitive function, including MCI and dementia, thus direct comparison with results from our relatively healthy adults may be limited. Other experimental studies have found that compared to age-matched controls, experienced TC practitioners perform better on the auditory Stroop task when it is administered alone and in combination with a dual stepping task.[44]

Published reports of the impact of short-term TC training on cognitive function are varied.[13] Multiple RCTs have reported positive effects of 2.5 months to 12 months of TC training on executive function, global cognition, language, learning, and memory domains,[7,15,19,45-49] and other trials have found no effects of short-term TC training.[17,50,51] One likely explanation for lack of any observed effect in our shorter-term RCT is the high level of baseline cognitive function among our healthy adults. Comparison of our population with normative data for all cognitive outcomes suggests that the majority of our participants performed at or slightly above average[52-55] for this age group, so they possessed limited room for improvement. It is also possible that the cognitive tests we employed were not sensitive enough to delineate the impact of short-term TC training. Future studies of healthy active adults may need to employ more challenging tests to discern change in cognition. Finally, it is possible that 6 months of TC was simply not sufficient to effect changes and a longer exposure, as in some RCTs, may reveal a larger effect of TC on cognitive outcomes.

There are a number of potentially therapeutic elements inherent in TC that may underlie the positive effect on cognition observed in this and other studies.[8,13] First, TC is moderately aerobic which has been shown by both human and animal studies to positively impact cognition and neurophysiological changes such as brain-derived neurotropic factor levels.[56-60] Second, TC improves agility and mobility, which some evidence suggests affects cognitive function through neurophysiological pathways different from those associated with aerobic exercise.[61] Third, TC involves learning and memorization of new movement patterns; studies of other skill-based learning activities (eg,

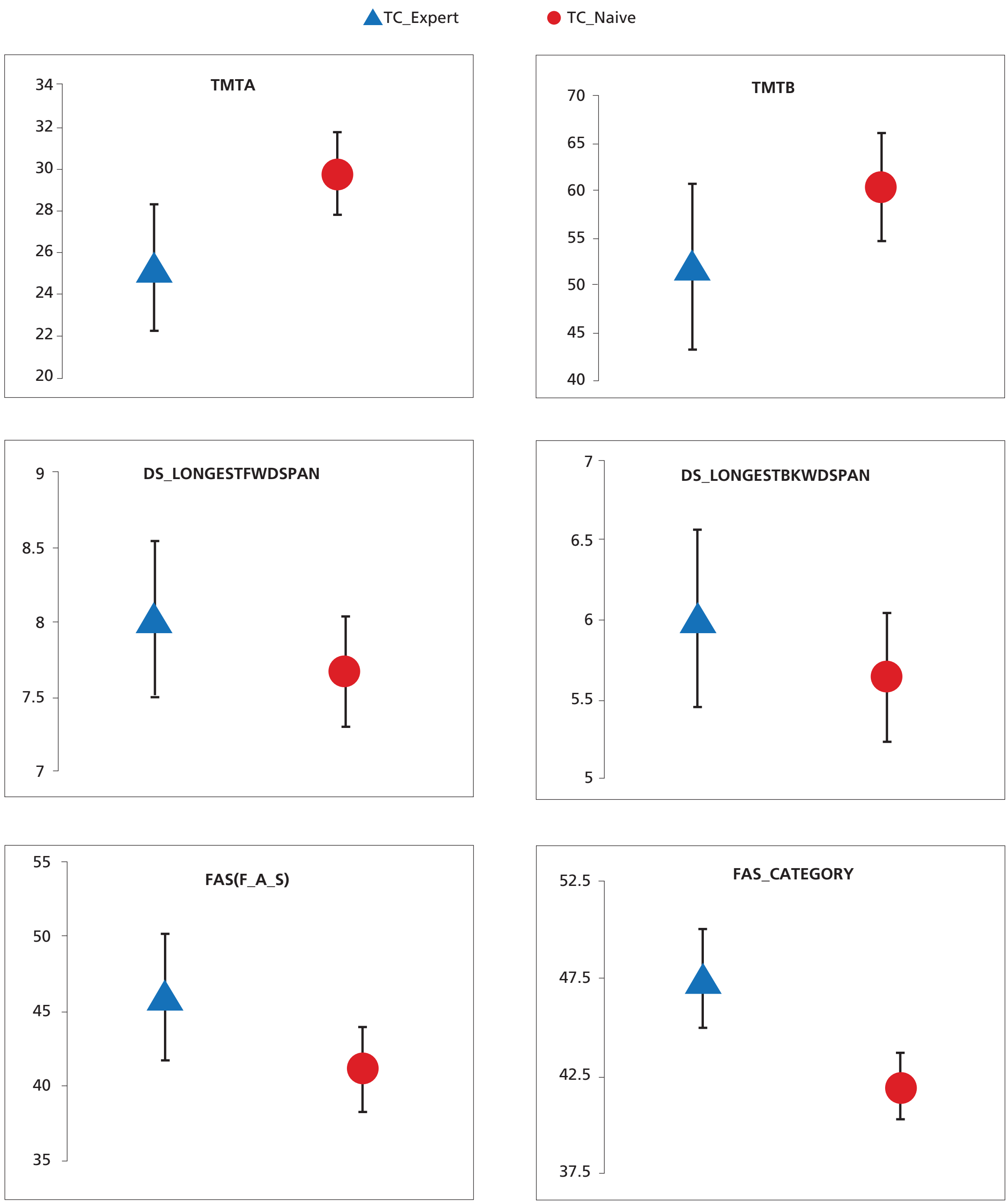


**Figure 2** Comparisons of cognitive performance between tai chi (TC) expert and TC-naïve adults. Symbols represent group means along with standard errors. Means were estimated using linear models controlling for education, age, gender, body mass index, and physical activity level (**P*<.01). TC experts had significantly higher net cognitive function based on a composite *z* score calculated as the sum of *z* scores from all 6 cognitive outcomes (*P*=.028; see Table 2).

**Abbreviations:** DS LONGESTBKWD, Digit Span longest backward span; DS LONGESTFWD, Digit Span longest forward Span; TC, tai chi; TMTA, Trail Making Test Part A; TMTB, Trail Making Test Part B. "FAS" represents letter fluency; "FAS_CATEGORY" represents category fluency.

dance, juggling) have shown improvements in cognition and underlying neural mechanisms.[62-65] Fourth, TC includes training in sustained attentional focus, shifting, and multitasking, which could help train working memory, divided attention, and overall executive function.[66] Fifth, the meditative elements of TC have been shown to reduce anxiety and depression,[11] which may affect stress-related pathways of cognitive decline.[67] Finally, a number of qualitative studies have highlighted that participants in TC programs experience significant social support related to the rich relationships that they develop both with instructors and classmates, the latter often extending beyond the classroom to additional leisurely activities.[68,69] Greater time

**Table 3** Cognitive Performance at Baseline and 6 Months for Adults Randomly Assigned to 6 Months of TC Training or Usual Care[a]

| Outcome Measure | TC (n=31) Baseline Mean (CI) | TC (n=31) 6 Mo. Mean (CI) | TC (n=31) Within-group *P* value | Usual Care (n=29) Baseline Mean (CI) | Usual Care (n=29) 6 Mo. Mean (CI) | Usual Care (n=29) Within-group *P* value | Between-group Difference *P* value |
|---|---|---|---|---|---|---|---|
| TMT-A | 29.90 (27.4, 32.4) | 27.18 (24.2, 30.2) | 0.064 | 29.90 (27.4, 32.4) | 25.04 (21.9, 28.2) | 0.002 | 0.227 |
| TMT-B | 58.86 (51.6, 66.1) | 54.48 (47.4, 61.5) | 0.256 | 58.86 (51.6, 66.1) | 49.40 (42.0, 56.8) | 0.019 | 0.229 |
| DS LONGESTFWD | 7.66 (7.2, 8.2) | 7.28 (6.7, 7.8) | 0.177 | 7.66 (7.2, 8.2) | 7.60 (7.0, 8.2) | 0.836 | 0.292 |
| DS LONGESTBKWD | 5.61 (5.1, 6.1) | 6.11 (5.6, 6.7) | 0.050 | 5.61 (5.1, 6.1) | 6.00 (5.4, 6.6) | 0.171 | 0.728 |
| Letter fluency | 42.85 (39.4, 46.3) | 46.57 (42.6, 50.5) | 0.012 | 42.85 (39.4, 46.3) | 48.08 (44.0, 52.1) | 0.001 | 0.415 |
| Category fluency | 43.25 (41.2, 45.3) | 46.68 (44.4, 49.0) | 0.002 | 43.25 (41.2, 45.3) | 47.28 (44.9, 49.7) | 0.002 | 0.661 |

[a]Estimates, means, confidence intervals, and between-group comparisons are based on models controlling for age, gender, body mass index, physical activity level and education. The between-group estimate shows the difference of TC minus usual care.

Abbreviations: CI, 95% confidence interval; DS LONGESTBKWD, Digit Span longest backward span; DS LONGESTFWD, Digit Span longest forward Span; TC, tai chi; TMT-A, Trail Making Test Part A; TMT-B, Trail Making Test Part B.

engaged in social activities has been associated with preserved cognitive function.[70,71]

### Limitations

Our study has important limitations. Samples for both the cross-sectional comparison and RCT were small and could have resulted in type II errors. Additionally, as with any cross-sectional study, comparisons between TC experts and TC naïfs may be confounded by differences between groups other than TC exposure. While linear models that included multiple potential confounders suggested an association with TC even after these factors were taken into account, other factors, including training in other martial arts and lifestyle, could not be fully accounted for.

In the current study, we did not observe much significant age or any treatment x age effects on cognition. As age effects on cognition are widely reported in the literature,[1-3] our observed lack of an association may reflect a bias in our study sampling design. Because our eligibility criteria for TC-naive adults were quite narrow with respect to acceptable comorbidities and use of medications, our sample reflects a very healthy adult population. As the number of individuals that met our eligibility criteria decreased with age, those in the oldest stratified age group (70 y-79 y) were more likely to represent extremely healthy individuals, whereas those on our younger group (50 y-59 y) who met our eligibility criteria were more likely to be of average health. This interpretation is supported by our physical function data reported elsewhere.[21] Average Timed-Up-and-Go (TUG) scores for our group aged 60 to 69 years and for our group aged 70 to 79 years group were 6.1 and 6.2 seconds; in comparison, normative data for ambulatory adults in these 2 age groups is 8 and 9 seconds. Due to this bias, our ability to evaluate the direct effects of age on cognition, as well as how age may impact cognitive response to TC is partially limited.

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## CONCLUSIONS

For healthy and active adults, long-term TC shows potential for maintaining high-level cognitive functioning; however, these results must be interpreted carefully due to the observational nature of these data. Six months of community-based TC training displayed no apparent effects on cognition in our healthy population. Longer-term TC exposure and/or use of more discriminating cognitive tests may better inform the potential of TC in healthy adults. Further studies are required to inform the potential benefits of TC for improving and preserving cognitive function with age.

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#### REFERENCES

1. Plassman BL, Langa KM, Fisher GG, et al. Prevalence of dementia in the United States: the aging, demographics, and memory study. Neuroepidemiology. 2007;29(1-2):125-32.

2. Wimo A, Winblad B, Jönsson L. The worldwide societal costs of dementia: Estimates for 2009. Alzheimers Dement. 2010;6(2):98-103.
3. Hurd MD, Martorell P, Delavande A, Mullen KJ, Langa KM. Monetary costs of dementia in the United States. N Engl J Med. 2013;368(14):1326-34.
4. Belsky DW, Caspi A, Israel S, Blumenthal JA, Poulton R, Moffitt TE. Cardiorespiratory fitness and cognitive function in midlife: neuroprotection or neuroselection? Ann Neurol. 2015;77(4):607-17.
5. Lee PL. Cognitive function in midlife and beyond: physical and cognitive activity related to episodic memory and executive functions. Int J Aging Hum Dev. 2015;79(4):263-78.
6. Kelly ME, Loughrey D, Lawlor BA, Robertson IH, Walsh C, Brennan S. The impact of exercise on the cognitive functioning of healthy older adults: a systematic review and meta-analysis. Ageing Res Rev. 2014 Jul;16:12-31.
7. Burgener SC, Yang Y, Gilbert R, Marsh-Yant S. The effects of a multimodal intervention on outcomes of persons with early-stage dementia. Am J Alzheimers Dis Other Demen. 2008;23(4):382-94.
8. Wayne PM, Fuerst ML. The Harvard Medical School guide to tai chi. Boston: Shambhala Publications, Inc; 2013.
9. Yeh GY, Wang C, Wayne PM, Phillips R. Tai chi exercise for patients with cardiovascular conditions and risk factors: A systematic review. J Cardiopulm Rehabil Prev. 2009;29(3):1521-60.
10. Logghe IH, Verhagen AP, Rademaker AC, et al. The effects of Tai Chi on fall prevention, fear of falling and balance in older people: A meta-analysis. Prev Med. 2010;51(3/4):222-7.
11. Wang C, Bannuru R, Ramel J, et al Kupelnick B, Scott T, Schmid CH. Tai Chi on psychological well-being: systematic review and meta-analysis. BMC Complement Altern Med. 2010 May 21;10:23.
12. Wayne PM, Berkowitz DL, Litrownik DE, Buring JE, Yeh GY. What do we really know about the safety of tai chi?: A systematic review of adverse event reports in randomized trials. Arch Phys Med Rehabil. 2014;95(12):2470-83.
13. Wayne PM, Walsh JN, Taylor-Piliae RE, et al. Effect of tai chi on cognitive performance in older adults: systematic review and meta-analysis. J Am Geriatr Soc. 2014;62(1):25-39.
14. Li R, Zhu X, Yin S, et al. Multimodal intervention in older adults improves resting-state functional connectivity between the medial prefrontal cortex and medial temporal lobe. Front Aging Neurosci. 2014 Mar 10;6:39.
15. Mortimer JA, Ding D, Borenstein AR, et al. Changes in brain volume and cognition in a randomized trial of exercise and social interaction in a community-based sample of non-demented Chinese elders. J Alzheimers Dis. 2012;30(4):757-66.
16. Wei GX, Xu T, Fan FM, et al. Can Taichi reshape the brain? A brain morphometry study. PloS One. 2013;8(4):e61038.
17. Deschamps A, Onifade C, Decamps A, Bourdel-Marchasson I. Health-related quality of life in frail institutionalized elderly: effects of a cognition-action intervention and Tai Chi. J Aging Phys Act. 2009;17(2):236-48.
18. Lam LC, Chau RC, Wong BM, et al. Interim follow-up of a randomized controlled trial comparing Chinese style mind body (Tai Chi) and stretching exercises on cognitive function in subjects at risk of progressive cognitive decline. Int J Geriatr Psychiatry. 2011;26(7):733-40.
19. Lavretsky H, Alstein LL, Olmstead RE, et al. Complementary use of tai chi chih augments escitalopram treatment of geriatric depression: a randomized controlled trial. Am J Geriatr Psychiatry. 2011;19(10):839-50.
20. Reid-Arndt SA, Matsuda S, Cox CR. Tai Chi effects on neuropsychological, emotional, and physical functioning following cancer treatment: a pilot study. Complement Ther Clin Pract. 2012;18(1):26-30.
21. Wayne PM, Gow BJ, Costa MD, et al. Complexity-based measures inform effects of tai chi training on standing postural control: cross-sectional and randomized trial studies. PLoS One. 2014;9(12):e114731.
22. Wayne PM, Hausdorff JM, Lough M, et al. Tai Chi training reduces dual task gait variability, a potential mediator of fall risk, in healthy older adults: cross-sectional and randomized trial studies. Front Hum Neurosci. Neuroscience 2015; In press.
23. Wayne PM, Manor B, Novak V, et al. A systems biology approach to studying Tai Chi, physiological complexity and healthy aging: design and rationale of a pragmatic randomized controlled trial. Contemp Clin Trials. 2013;34(1):21-34.
24. Fischer M, Fugate-Woods N, Wayne PM. Use of pragmatic community-based interventions to enhance recruitment and adherence in a randomized trial of Tai Chi for women with osteopenia: insights from a qualitative substudy. Menopause. 2014;21(11):1181-9.
25. Bowie CR, Harvey PD. Administration and interpretation of the Trail Making Test. Nat Protoc. 2006;1(5):2277-81.
26. Strauss E, Sherman E, Spreen O. A compendium of neuropsychological tests. 3rd ed. New York: Oxford University Press, Inc.; 2006.
27. Reitan R. Validity of the Trail Making Test as an indicator of organic brain damage. In: Goldstein G, Beers SR, editors. Comprehensive handbook of psychological assessment, intellectual and neuropsychological assessment: John Wiley &Sons, Ltd; 1958: 271-6.
28. Blankenship AB. Memory span: a review of the literature. Psychol Bull. 1938;35(1):1-25
29. Benton AL, Sivam AB, Hamsher Kd, Varney N, Spreen O. Contributions to neuropsychological assessment: a clinical mannual. New York: Oxford University Press; 1983.
30. Arbuthnott K, Frank J. Trail making test, part B as a measure of executive control: validation using a set-switching paradigm. J Clin Exp Neuropsychol. 2000;22(4):518-28.
31. Franzen M. Cross-validation of the alternative forms of reliability of the Trailmaking Test. Arch Clin Neuropsychol. 1996;11(5):390-1.
32. Ross TP, Calhoun E, Cox T, Wenner C, Kono W, Pleasant M. The reliability and validity of qualitative scores for the Controlled Oral Word Association Test. Arch Clin Neuropsychol. 2007;22(4):475-88.
33. Ross TP, Furr AE, Carter SE, Weinberg M. The psychometric equivalence of two alternate forms of the Controlled Oral Word Association Test. Clin Neuropsychol. 2006;20(3):414-31.
34. Angevaren M, Aufdemkampe G, Verhaar HJ, Aleman A, Vanhees L. Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment. Cochrane Database Syst Rev. 2008 Jul 16(3):CD005381.
35. Brown AK, Liu-Ambrose T, Tate R, Lord SR. The effect of group-based exercise on cognitive performance and mood in seniors residing in intermediate care and self-care retirement facilities: a randomised controlled trial. Br J Sports Med. 2009;43(8):608-14.
36. Baumgartner T, Jackson A, Mahar M, Rowe D. (2006) Measurement for evaluation in physical education and exercise science. New York: McGraw-Hill; 2006.
37. Heil DP, Freedson PS, Ahlquist LE, Price J, Rippe JM. Nonexercise regression models to estimate peak oxygen consumption. Med Sci Sports Exer. 1995;27(4):599-606.
38. Ware JE, Kosinski M. Interpreting SF-36 summary health measures: a response. Qual Life Res. 2001;10(5):405-13; discussion 415-20.
39. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. Med Care. 1992;30:473-83.
40. Liang KY, Zeger SL. Longitudinal data analysis of continuous and discrete responses for pre-post designs. Indian J Stat (Series B). 2000;62(1):134-48.
41. Man DW, Tsang WW, Hui-Chan CW. Do older t'ai chi practitioners have better attention and memory function? J Altern Complement Med. 2010;16(12):1259-64.
42. Lam LC, Tam CW, Lui VW, et al. Modality of physical exercise and cognitive function in Hong Kong older Chinese community. Int J Geriatr Psychiatry. 2009;24(1):48-53.
43. Chan AS, Ho YC, Cheung MC, Albert MS, Chiu HF, Lam LC. Association between mind-body and cardiovascular exercises and memory in older adults. J Am Geriatr Soc. 2005;53(10):1754-60.
44. Lu X, Siu KC, Fu SN, Hui-Chan CW, Tsang WW. Tai Chi practitioners have better postural control and selective attention in stepping down with and without a concurrent auditory response task. Eur J Appl Physiol. 2013;113(8):1939-45.
45. Cheng ST, Chow PK, Song YQ, et al. Mental and physical activities delay cognitive decline in older persons with dementia. Am J Geriatr Psychiatry. 2014;22(1):63-74.
46. Lam LC, Chau RC, Wong BM, et al. A 1-year randomized controlled trial comparing mind body exercise (Tai Chi) with stretching and toning exercise on cognitive function in older Chinese adults at risk of cognitive decline. J Am Med Dir Assoc. 2012;13(6):568.
47. Nguyen MH, Kruse A. A randomized controlled trial of Tai chi for balance, sleep quality and cognitive performance in elderly Vietnamese. Clin Interv Aging. 2012;7:185-90.
48. Taylor-Piliae RE, Newell KA, Cherin R, Lee MJ, King AC, Haskell WL. Effects of Tai Chi and Western exercise on physical and cognitive functioning in healthy community-dwelling older adults. J Aging Phys Act. 2010;18(3):261-79.
49. Tsai PF, Chang JY, Beck C, Kuo YF, Keefe FJ. A pilot cluster-randomized trial of a 20-week Tai Chi program in elders with cognitive impairment and osteoarthritic knee: effects on pain and other health outcomes. J Pain Symptom Manage. 2012;45(4):660-9.
50. Dechamps A, Diolez P, Thiaudière E, et al. Effects of exercise programs to prevent decline in health-related quality of life in highly deconditioned institutionalized elderly persons: a randomized controlled trial. Arch Intern Med. 2010;170(2):162-9.
51. Wang W, Sawada M, Noriyama Y, et al. Tai Chi exercise versus rehabilitation for the elderly with cerebral vascular disorder: a single-blinded randomized controlled trial. Psychogeriatrics. 2010;10(3):160-6.
52. Crum RM, Anthony JC, Bassett SS, Folstein MF. Population-based norms for the Mini-Mental State Examination by age and educational level. JAMA. 1993;269(18):2386-91.
53. Hester RL, Kinsella GJ, Ong B. Effect of age on forward and backward span tasks. J Int Neuropsychol Soc. 2004;10(4):475-81.
54. Tombaugh TN. Trail Making Test A and B: normative data stratified by age

and education. Arch Clin Neuropsychol. 2004;19(2):203-14.
55. Tombaugh TN, Kozak J, Rees L. Normative data stratified by age and education for two measures of verbal fluency: FAS and animal naming. Arch Clin Neuropsychol. 1999;14(2):167-77.
56. Fang ZH, Lee CH, Seo MK et al. Effect of treadmill exercise on the BDNF-mediated pathway in the hippocampus of stressed rats. Neurosci Res. 2013;76(4):187-94.
57. Erickson KI, Voss MW, Prakash RS, et al. Exercise training increases size of hippocampus and improves memory. Proc Natl Acad Sci U S A. 2011;108(7):3017-22.
58. Colcombe SJ, Erickson KI, Scalf PE, et al. Aerobic exercise training increases brain volume in aging humans. J Gerontol A Biol Sci Med Sci. 2006;61(11):1166-70.
59. Pereira AC, Huddleston DE, Brickman AM, et al. An in vivo correlate of exercise-induced neurogenesis in the adult dentate gyrus. Proc Natl Acad Sci U S A. 2007;104(13):5638-43.
60. Voss MW, Prakash RS, Erickson KI, et al. Plasticity of brain networks in a randomized intervention trial of exercise training in older adults. Front Aging Neurosci. 2010 Aug 26;2.
61. Voelcker-Rehage C, Godde B, Staudinger UM. Cardiovascular and coordination training differentially improve cognitive performance and neural processing in older adults. Front Hum Neurosci. 2011 Mar 17;5:26.
62. Driemeyer J, Boyke J, Gaser C, Büchel C, May A. Changes in gray matter induced by learning—revisited. PloS One. 2008;3(7):e2669.
63. Herdener M, Esposito F, di Salle F, et al. Musical training induces functional plasticity in human hippocampus. J Neurosci. 2010;30(4):1377-84.
64. Hufner K, Binetti C, Hamilton DA, et al. Structural and functional plasticity of the hippocampal formation in professional dancers and slackliners. Hippocampus. 2011;21(8):855-65.
65. Kattenstroth JC, Kolankowska I, Kalisch T, Dinse HR. Superior sensory, motor, and cognitive performance in elderly individuals with multi-year dancing activities. Front Aging Neurosci. 2010 Jul 21;2:31.
66. Tsang WW, Kwok JC, Hui-Chan CW. Effects of aging and tai chi on a finger-pointing task with a choice paradigm. Evid Based Complementary Alternat Med. 2013;2013:653437.
67. Lupien SJ, de Leon M, de Santi S, et al. Cortisol levels during human aging predict hippocampal atrophy and memory deficits. Nature Neurosci. 1998;1(1):69-73.
68. Fischer M, Fugate-Woods N, Wayne PM. Use of pragmatic community-based interventions to enhance recruitment and adherence in a randomized trial of Tai Chi for women with osteopenia: insights from a qualitative substudy. Menopause. 2014;21(11):1181-9.
69. Yang Y, Decelle S, Reed M, Rosengren K, Schlagal R, Greene J. Subjective experiences of older adults practicing taiji and qigong. J Aging Res. 2011;2011:650210.
70. Verghese J, Lipton RB, Katz MJ, et al. Leisure activities and the risk of dementia in the elderly. N Engl J Med. 2003;348(25):2508-16.
71. Fratiglioni L, Wang H-X, Ericsson K, Maytan M, Winblad B. Influence of social network on occurrence of dementia: a community-based longitudinal study. Lancet. 2000;355(9212):1315-19.