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ORIGINAL ARTICLE

Distinct effects of long-term Tai Chi Chuan and aerobic exercise interventions on motor and neurocognitive performance in early-stage Parkinson's disease: a randomized controlled trial

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ABSTRACT

BACKGROUND: Parkinson's disease (PD) is a neurodegenerative condition characterized by movement disorders and probable cognitive impairment. Exercise plays an important role in PD management, and recent studies have reported improvement in motor symptoms and cognitive function following aerobic and Tai Chi Chuan exercise.

AIM: To explore the different effects of Tai Chi Chuan and aerobic exercise on the clinical motor status and neurocognitive performance of patients with early-stage PD.

DESIGN: A randomized controlled trial.

SETTING: Parkinson's Disease Center at Kaohsiung Chang Gung Memorial Hospital and National Cheng Kung University Hospital.

POPULATION: Patients with idiopathic PD.

METHODS: Fifty-six patients with PD were recruited and divided into three groups: aerobic exercise (AE, N.=14), Tai Chi Chuan exercise (TE, N.=16), and control (CG, N.=13). Before and after a 12-week intervention period, we used unified Parkinson's disease rating scale Part III (UPDRS-III) scores and neuropsychological (*e.g.*, accuracy rates [ARs] and reaction times [RTs]) and neurophysiological (*e.g.*, event-related potential [ERP] N2 and P3 latencies and amplitudes) parameters to respectively assess the patients' clinical motor symptoms and neurocognitive performance when performing a working memory (WM) task.

RESULTS: Compared to baseline, UPDRS-III scores were significantly lower in the AE and TE groups after the intervention period, whereas those for the CG group were higher. In terms of the neurocognitive parameters, when performing the WM task after the intervention period, the AE group exhibited significantly faster RTs and larger ERP P3 amplitudes, the TE group exhibited an improvement only in ERP P3 amplitude, and the CG group exhibited a significantly reduced ERP P3 amplitude. However, neither the TE nor the AE group exhibited improved ARs and ERP N2 performance.

CONCLUSIONS: The present study supported the distinct effectiveness of Tai Chi Chuan and aerobic exercise for improving motor symptoms and providing neurocognitive benefits in PD patients.
CLINICAL REHABILITATION IMPACT: These results have important implications regarding the use of these exercise interventions for managing PD, particularly in the early stages.

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KEY WORDS: Parkinson's disease; Exercise; Rehabilitation; Cognition; Electroencephalography; Randomized controlled trial.

Parkinson's disease (PD) is a progressive neurodegenerative disease characterized by dysfunction of the dopamine system in the basal ganglia and deficiency of the dopaminergic neurons in the substantia nigra, leading to movement disorders such as bradykinesia, resting tremors, postural instability, and gait disturbance.[1] In addition, recent studies have increasingly highlighted the occurrence of nonmotor symptoms, particularly cognitive impairment, in patients with PD. The movement disorder society (MDS) and the MDS Task Force published clinical criteria in 2007 and 2012, respectively, clarifying that decline in cognitive function is a common feature of PD and can lead to mild cognitive impairment (MCI) or even PD dementia.[2, 3]

Working memory (WM) is a component of executive function and plays an important role in daily life. Its functioning involves giving attention to, encoding, maintaining, and retrieving information, which requires the cooperation of the frontoparietal network.[4] Impairment of the WM features prominently in cognitive degeneration due to PD,[5] and may be caused by reduced activity in the frontal striatal neuron, reduced binding of dopamine transporter in the caudate, depletion of dopamine in the nigrostriatal pathway, and disruption of the putamen-frontal circuits.[6-8]

Neurocognitive function can be assessed using both neuropsychological (*e.g.*, accuracy rate [AR] and reaction time [RT]) and neurophysiological (*e.g.*, event-related potentials [ERPs] from electroencephalography [EEG]) measurements. Recent studies have adopted the approach of identifying the characteristics of neural activity that may differ between patients with PD and healthy controls.[9, 10] For example, PD patients tend to exhibit a reduced amplitude and prolonged latency in their ERP N2 and P3 components when performing cognitive tasks (*e.g.*, S1-S2 task), reflecting deficits in information processing that may be due to declining inhibition control and attentional resource allocation.[7] In cognitive tasks involving the WM, the ERP N2 component is thought to be a reliable index of executive function that reflects abilities related to stimulus detection, selective attention to the task-relevant target, and suppression of response. The ERP P3 component represents the amount of attention allocated to specific stimuli and is interpreted as neural processing in the retrieving phase of the WM.[11, 12] Despite the noted neurophysiological deficits in patients with PD mentioned above,[7, 9, 10] none of the previous studies have attempted to explore the effects of interventional approaches on ERP components in this population.

Exercise is often considered an effective nonpharmacological intervention for managing motor and nonmotor impairments in early-stage PD.[13-15] For example, Fisher *et al.*[16] suggested that treadmill training enhances corticomotor excitability and improves motor function in patients with early PD. Additionally, mind-body exercises have been shown to have potential as rehabilitation methods for improving motor and nonmotor function in PD.[17, 18]

It is well established that regular aerobic exercise has beneficial effects on neurocognitive performance in late middle-aged and older adults[19-21] and patients with neurodegenerative diseases.[22, 23] For instance, six months of aerobic exercise in older adults led to improved neurocognitive performance (*e.g.*, higher ARs and larger P3 amplitudes) in both low- and high-load WM tasks.[20] In PD specifically, exercise regimes aimed at enhancing cardiorespiratory fitness with a duration of 12 weeks have been found to improve cognitive function, physical fitness, and quality of life, and have a symptomatic effect on motor function.[22, 24, 25] Although van der Kolk *et al.*[26] reported no significant improvement in Mini-Mental State Examination (MMSE) score after an aerobic exercise intervention in PD patients, aerobic exercise has been shown to be beneficial for their neurocognitive performance. In addition, aerobic exercise, compared to stretching exercise, provides greater benefits in neuropsychological aspects (*e.g.*, faster RTs in the Stroop test)[22] and neurophysiological performance (*e.g.*, a larger functional connectivity within the frontoparietal network, as observed through resting-state functional magnetic resonance imaging (fMRI), and a lower atrophy rate in global percentage-based volume)[23] in PD patients. Recently, Tsai and Lin[13] found that a single bout of aerobic exercise including both moderate- and high-intensity exercise could improve RTs and ERP P3 amplitudes in PD patients when performing a WM task. However, because the effects of acute exercise on neurocognition are transient,[27] further research is needed to better understand the long-term effect of aerobic exercise on neurocognitive function in PD.

Cognitive status plays a pivotal role in determining the success of rehabilitation outcomes in PD. Unlike aerobic exercise which primarily focuses on cardiovascular functions and endurance capacity, interventions targeting sensory and cognitive elements or incorporating attentional demand with dual-task characteristic may be more effective for improving cognitive impairment in PD patients.[28, 29] Tai Chi Chuan, a traditional Chinese mind-body exercise, embodies these characteristics and is increasingly popular among elderly adults. Due to its low-impact, low injury risk nature, and positive effects on motor and non-motor symptoms, neuromuscular control ability, fall prevention, and quality of life, Tai Chi Chuan is recommended as an intervention for managing early-stage PD patients.[30-33] Indeed, studies have demonstrated that this type of exercise can also effectively improve WM in older adults. For example, Taylor-Piliae *et al.*[34] revealed a significant pre- and post-Tai Chi Chuan effect on the digit span backwards task in healthy older adults, with participants retaining and manipulating more numbers in their mind. However, there is a lack of research focusing on the neurocognitive effects of Tai Chi Chuan in individuals with PD. A systematic review by Lim *et al.*[35] suggested that a minimum of two Tai Chi Chuan training sessions per week, each lasting 30 minutes, for a period of 12 weeks, could improve WM in individuals with neurodegenerative diseases. Another review reported that relative to multicomponent exercise, mind-body exercise produces a larger effect size on WM in older adults.[36] Based on these findings and concepts, Tai Chi Chuan could offer a feasible and practical approach to improving motor function and the neurocognitive functioning of the WM.

In summary, the aim of this longitudinal study was to comprehensively investigate and compare the effects of Tai Chi Chuan and aerobic exercise interventions on motor and neurocognitive functioning in PD patients, while conducting neurophysiological measurements (*i.e.*, ERPs) to provide a deeper understanding of the mechanisms underlying exercise-induced neuropsychological changes. The exercise prescription regarding duration and total intervention period was designed based on previous research demonstrating the potential positive effects of both exercise modalities on cognitive performance in PD patients.[22, 25, 30, 37] Since the two types of exercise involve distinct characteristics in terms of physiological demand (cardiorespiratory *vs.* muscular fitness) and cognitive load (single *versus* dual tasks) during training, it was hypothesized that 12-week interventions of Tai Chi Chuan and aerobic exercise would improve motor and neurocognitive functioning in PD patients, with varying degrees of benefits.

Materials and methods

Participants

The minimum required sample size was subjected to an *a-priori* power analysis using the G*Power software. Since no previous studies had simultaneously examined the longitudinal effects of Tai Chi Chuan and aerobic exercise on both motor and neurocognitive function in PD patients, we referred to Tsai and Pai's study[38] to calculate the applicable effect-size value. That study examined the long-term effect of exercise on neurocognitive indices in people with neurodegenerative diseases, using two exercise groups and a control group. The type of statistical test was set to "ANOVA: Repeated Measures, Within-between Interaction," and the test family was set to "*F*-tests." Three intervention modes with two repetitions (for the three groups [aerobic exercise, Tai Chi Chuan, and control] × two time periods [pre-intervention *vs.* post-intervention]) were selected. The power level was set to at least 0.95, and the type I error probability was set at 0.05. The effect size was set to 0.20. The total sample size required was estimated as 21, meaning that a minimum of 21 people were needed to achieve a power level of 0.9717.

Through referrals from neurologists, we recruited 56 patients (26 male, 30 female) with idiopathic PD from the Parkinson's Disease Center at Kaohsiung Chang Gung Memorial Hospital and National Cheng Kung University Hospital. After the participants' baseline assessments had been performed as described below, they were randomly assigned to the aerobic exercise group (AE, N.=18), the Tai Chi Chuan exercise group (TE, N.=20), or the control group (CG, N.=18). The clinical inclusion criteria were as follows: 1) a confirmed diagnosis of PD by neurologists at the Neurology Department of one of the above hospitals, and a medically stable status; 2) a modified Hoehn and Yahr Score between 1 and 2, indicating early-stage PD; 3) the absence of any major comorbidities, such as dementia or depression; 4) no brain abnormalities (*e.g.*, stroke or malignant brain tumor) on structural MRI scans; 5) age between 50 and 80 years; 6) confirmed ability to complete exercise training, as determined using the Physical Activity Readiness Questionnaire (PAR-Q) and by their treating neurologist; and 7) willingness to be randomly assigned to one of the exercise intervention groups or the control group. Exclusion criteria were as follows: 1) a history of any neurological disease other than PD; 2) a diagnosis of dementia based on a Montreal Cognitive Assessment (MoCA) score of <24;[39] 3) moderate or significant depression, as assessed based on a score of >16 for the Beck Depression Inventory-II (BDI-II); 4) use of medication that interferes with cognition, alertness, or attention; or 5) previous or current participation in an exercise training program. Written informed consent, as approved by the institutional review board of Kaohsiung Chang Gung Memorial Hospital and the Human Research Ethics Center of National Cheng Kung University, was obtained from all the participants.

The cognitive task

Li *et al.*[7] and Wang *et al.*[40] reported that PD patients exhibited deficits in their performance of the delayed matching S1-S2 paradigm. In addition, a previous study has demonstrated that neurocognitive performance during cognitive tasks can be altered in PD patients by a single bout of exercise.[13] Hence, we used a modified version of the delayed matching S1-S2 paradigm to elicit ERPs (Figure 1). For this task, the visual stimuli were displayed on a computer screen that was 43 cm wide, with a black background. First, a signal stimulus consisting of a white fixation cross was shown for 500 ms. The first stimulus (S1) was then shown for 100 ms, followed by a 1600 ms pause, and then the second stimulus (S2), also for 100 ms. The next trial began 2600 ms after S2 was presented. The participants were instructed to accurately and rapidly compare S1 and S2. They had to use their right index finger to push the "M" key on the computer keyboard when S2 and S1 were the same (a congruent condition) and their left index finger to push the "N" key when S2 and S1 were not the same (an incongruent condition). All participants were instructed to complete 270 trials (135 trials × 2 blocks) consisting of 180 incongruent (2/3) and 90 congruent conditions (1/3). A 3-minute rest period was implemented between the two blocks to mitigate mental fatigue. Before the formal test, a practice session was conducted until the participants had achieved the standard ARs (an error rate of 5% or less). Neuropsychological performance (ARs and RTs) and neurophysiological parameters (ERP N2 and P3 components) were recorded throughout the task.

ERP recording and data processing

The EEG activity was recorded using an electrode cap with 32 scalp sites (Quik-Cap, Compumedics Neuroscan, El Paso, TX, USA) designed for the International 10-20 System with an A/D rate of 500 Hz/channel. Before recording, all interelectrode impedance was maintained at <5 kΩ. All scalp locations were referenced to the linked mastoid electrode, with the ground electrode placed on the mid-forehead. Adhesive electrodes were placed on the superolateral right canthus and below and lateral to the left eye to capture vertical and horizontal electrooculographic activity and possible artifacts induced by eye movements. The raw EEG signal was acquired and stored on a hard

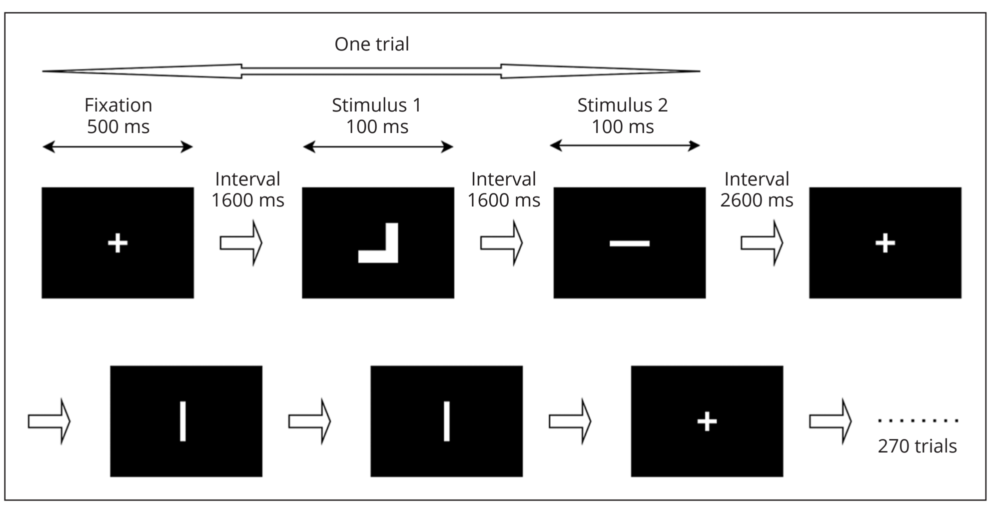

Figure 1.—Delayed matching S1–S2 paradigm.

disk using a SynAmps amplifier equipped with a 60 Hz notch filter. The EEG data were analyzed offline using SCAN4.5 analysis software from Compumedics Neuroscan (El Paso, TX, USA). Before the analysis was done, the raw EEG signal was filtered using a bandpass filter, with the cutoff frequencies set as 0.1 and 50 Hz.

The neuropsychological measurements (ARs and RTs) were processed using SCAN4.5. To avoid skewing the group mean and standard deviation, trials with errors, missed responses, anticipatory errors (RTs faster than 200 ms), or delay errors (RTs slower than two standard deviations) were excluded from the analysis.

In the analysis of the neurophysiological parameters (ERP N2 and P3 latencies and amplitudes), the EEG data were divided into epochs, with each epoch covering the time interval from −100 ms to 1000 ms relative to stimulus onset. To eliminate artifacts related to eye movements, an ocular-artifact-reduction transformation was applied. Additionally, any sweep with an interference amplitude below -100 μV or above +100 μV was rejected. The latencies and amplitudes of the ERP N2 and P3 components for both congruent and incongruent conditions were then examined at the Fz, Cz, and Pz electrodes, using the time windows 180-350 ms and 300-800 ms, respectively.

Experimental procedure

In order to alleviate the mental and physical fatigue induced by the experiment, all participants were asked to visit the laboratory twice within a 7-day period for clinical and neurocognitive assessments prior to commencing the formal exercise intervention. To minimize any bias related to medication cycle or circadian influence, all measurements were performed during the "on" medication state and between 09:00 and 12:00. In addition, the participants had to avoid any activities that would affect their neurocognitive function for 24 h prior to the assessments, such as strenuous exercise. Ingesting stimulant substances (*e.g.*, coffee, alcohol, and smoke) was also prohibited. During the initial visit, the participants were given detailed information about the experimental procedure and asked to provide written informed consent. Additionally, they underwent a comprehensive set of assessments, including a basic information form for demographic data, a medical history questionnaire, cognitive function assessments (MoCA), the BDI-II, a social participation questionnaire, the PAR-Q, and a seven-day physical-activity recall questionnaire (7-day PAR).[41] These measures were implemented to minimize the impact of potential confounding factors on neurocognitive performance. After completing the questionnaires, the unified Parkinson's disease rating scale Part III (UPDRS-III) was administered to evaluate the severity of both motor and nonmotor symptoms. Further, a certified physical therapist measured the participants' body composition, including height, weight, and body mass index (BMI), as well as their cardiopulmonary fitness using the six-minute step test. The load of the assessment for each participant was calculated using equation 1, and the estimated VO_{2max} of the male and female participants was then calculated using equations 2 and 3, respectively:[42] Load = (step rate · step height · Wt + 5)+(step rate · step height · Wt + 5)/3 (1); man: $VO_{2max} = 1.29 \cdot \sqrt{(load/(peak\ HR - 60)*e(-0.0088*age)}$ (2); woman: $VO_{2max} = 1.18 \cdot \sqrt{load/(peak\ HR - 60)*e} - 0.0090*age$ (3).

On a separate day during the same week, the participants were instructed to visit our acoustically shielded EEG laboratory, which was maintained under controlled lighting and at a temperature of 23-25 °C. Upon arrival, each participant was seated comfortably in front of a computer screen and an EEG cap and electro-oculographic electrodes were applied to their head using reference landmarks. A cognitive task was then administered while EEG data were recorded to analyze their ERPs.

At the end of the 12-week parallel-design intervention period, the participants were asked to return to the laboratory twice in the following week for the post-intervention assessment. The procedures were identical to those conducted during the pre-intervention phase. To minimize tester or rater bias, the same research assistant conducted all assessments both before and after the intervention. The assistant was blinded to group assignments to ensure accuracy and objectivity in the assessment process.

Interventions

Aerobic exercise group

The 12-week aerobic exercise program consisted of a 30 min training session performed three times weekly on a recumbent stationary bicycle. Before every training session, each participant's resting heart rate was measured to calculate their heart rate reserve (HRR). The aerobic exercise protocol included a 4 min warm-up phase, followed by 24 min of moderate-to-high-intensity interval aerobic training (eight cycles of 1 min with 70-75% HRR followed by a 2 min active recovery period [target Rating of Perceived Exertion (RPE): 9-11]), and finally a 2 min cool-down period. The target HR was monitored using a Polar HR monitor (RS800CX, Polar Electro Oy, Kempele, Finland). The participants were verbally encouraged to achieve the appropriate intensity for each phase, and they exercised under the medical supervision of a physical therapist.

Tai Chi Chuan group

The 12-week Tai Chi Chuan program comprised two 60 min sessions per week, and each session was led by a Tai Chi Chuan master with over 20 years of experience. The session consisted of a warm-up and the main exercise, and all movements were adapted from the Yang-style short form.[34, 43] The warm-up session included the bear swing, the Tai Chi walk, and a range of motion exercises. It focused on kinesthetic awareness, mind-body preparation, and stretching, and incorporated high-amplitude and diagonal movements. The main exercise phase encompassed all 24 postures in the Yang-style short form, since this Tai Chi Chung form has proven effective for cognitive function in individuals with or without PD.[34, 43] Movements such as roll back, ward off, push, press, single whip, and others emphasized weight-shifting skills, bilateral coordination, and postural control. The Tai Chi master first demonstrated a movement, then deconstructed it and taught it step by step. To ensure accuracy, the master corrected each participant's movements. One to two new movements were taught in each session, and the entire sequence of learned postures was practiced together to reinforce the connection between the mental tracking and the physical aspect. In addition to the postures, the participants were taught other essential elements of Tai Chi Chuan, such as body orientation, breathing, and relaxation.[34, 44, 45]

Control group

The participants assigned to the control group maintained their normal daily physical activity patterns during the 12-week period. Furthermore, they were instructed to refrain from engaging in any organized exercise classes or structured physical activities throughout the intervention period. In order to mitigate potential bias stemming from lifestyle alterations, participants were tasked with keeping an activity log, which was subsequently reviewed by the investigators.

Data processing and statistical analysis

One-way analyses of variance (ANOVAs) were used to assess group differences in pre- and post-intervention demographic characteristics and clinical assessment scores:

- 3 (groups: AE, TE, and CG) ×2 (time: pre- and post-intervention) ×2 (condition: congruent and incongruent);
- 3 (groups: AE, TE, and CG)×2 (time: pre- and post-intervention) ×3 (electrode sites: Fz, Cz, and Pz) ×2 (condition: congruent and incongruent).

The sexual variable was conducted using Pearson's Chi-squared Test. The neuropsychological indices (ARs and RTs) were subjected to a mixed-model repeated measures ANOVA (RM-ANOVA). A mixed-model RM-ANOVA was applied to the neurophysiological indices (ERP N2 and P3 latencies and amplitudes). When a significant main effect was found, we performed Bonferroni *post-hoc* tests to determine the specific difference. The Greenhouse-Geisser correction was applied when the sphericity assumption was not fulfilled. The Kolmogorov-Smirnov and Levene's tests were used to test the data for normality and homogeneity, respectively. To complement the significance testing, we calculated the partial eta-squared (η^2_p) to estimate the effect size of the group differences. A significance level of α=0.05 was used; in other words, P values of <0.05 were considered statistically significant.

Results

The Consolidated Standards of Reporting Trials (CONSORT) chart illustrating the flow of participants from initial contact to post-intervention assessment is presented in Figure 2. The adherence rate for both exercise interventions exceeded 85%, indicating a high level of participant

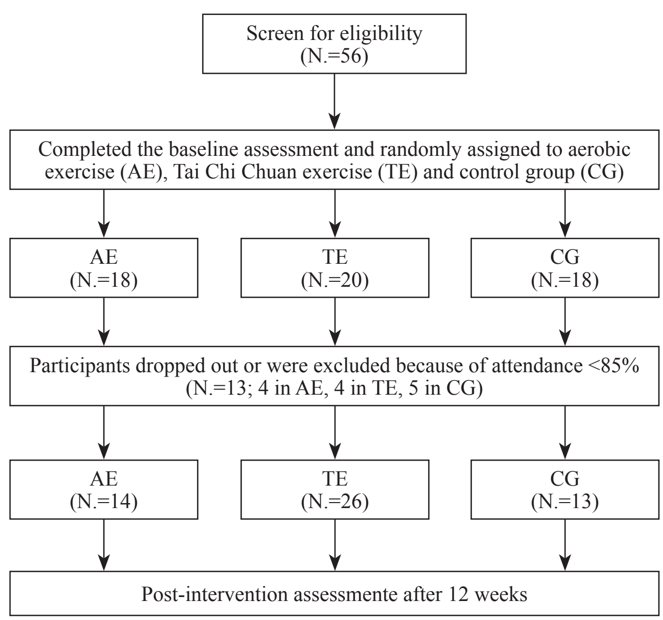

Figure 2.—The Consolidated Standards of Reporting Trials (CONSORT) chart illustrating the flow of participants from initial contact to post-intervention assessment.

Table I.—*Demographic characteristics (mean±SD) of the participants.*

Characteristics	Control (N.=13)	Aerobic exercise (N.=14)	Tai Chi Chuan (N.=16)	P value
Gender (M/F)	6/7	5/9	7/9	0.637
Age (years)	63.15±7.95	64.43±7.37	66.31±6.54	0.503
Illness duration	6.77±6.84	6.57±7.92	6.75±5.49	0.996
BMI (kg/m^2)	23.92±2.82	23.15±4.27	24.16±3.60	0.738
Pre-intervention				
MoCA	26.92±2.75	27.36±3.07	26.75±3.53	0.867
BDI-II	6.31±7.21	7.79±6.98	6.31±6.23	0.801
Social participation	8.15±2.04	9.21±2.39	9.06±1.39	0.324
7-day PAR (Kcal/day)	1312.59±810.26	1126.00±844.24	1507.79±1136.46	0.555
VO_{2max} (mL/kg/min)	29.40±9.39	30.79±9.11	27.98±8.28	0.672
UPDRS-total	18.15±8.95	15.50±10.65	15.19±9.19	0.677
UPDRS-III	6.92±4.39	6.43±5.02	8.00±5.27	0.673
Post-intervention				
MoCA	24.77±3.29	26.57±4.64	26.81±3.56	0.330
BDI-II	8.31±9.60	4.43±5.38	4.75±4.78	0.265
Social participation	8.23±1.54	8.50±1.16	9.56±2.16	0.091
VO_{2max} (mL/kg/min)	27.81±8.59	38.73±11.66	27.62±5.93	0.002
UPDRS-total	22.00±10.32	10.50±7.33	11.50±7.38	0.001
UPDRS-III	9.77±4.64	3.79±2.15	4.69±2.92	<0.001

MoCA: Montreal Cognitive Assessment; BDI-II: Beck Depression Inventory—Second Edition; 7-day PAR: seven-day physical activity recall questionnaire; UPDRS: unified Parkinson's disease rating scale; UPDRS-III: unified Parkinson's disease rating scale-motor subscale.

compliance with the prescribed exercise programs. Importantly, no falls or adverse events related to the exercise program were reported during the intervention period, indicating that the interventions were safe and well tolerated. Thirteen participants withdrew during the four-year experimental period because of COVID-19 restrictions, personal time limitations, or transportation issues. Additionally, two participants were excluded from the analysis because of insufficient attendance.

At baseline, there were no significant differences in any characteristics or potential confounding factors (age, illness duration, BMI, MoCA, BDI-II scores, social participation, VO_{2max}, 7-day PAR, and UPDRS total and UPDRS-III scores) that may have affected neurocognitive performance (Table I). After the 12-week intervention, there was a significant between-group difference in VO_{2max}, with the value in the AE group being significantly higher than that in the TE and CG groups. In addition, VO_{2max} values were significantly enhanced after the intervention in the AE group relative to before the intervention (P=0.015), but not in the other two groups.

Unified Parkinson's disease rating scale scores

In the RM-ANOVA, a significant *group* × *time* interaction effect (F[2,40]=7.59, P=0.002, η^2_P=0.28) was observed for the UPDRS-total scores. *Post-hoc* analyses revealed that, in both the AE (pre- *vs.* post-intervention: 15.50±10.65 *vs.* 10.50±7.33; P=0.005) and TE (pre- *vs.* post-intervention: 15.19±9.19 *vs.* 4.69±2.92; P=0.026) groups, the UPDRS-total scores were lower post-intervention than pre-intervention. In contrast, in the CG group, the post-intervention clinical score was significantly higher than the pre-intervention score (pre- *vs.* post-intervention: 18.15±8.95 *vs.* 22.00±10.32; P=0.035).

In the RM-ANOVA, a significant *group* × *time* interaction effect (F[2,40] = 11.47, P<0.001, η^2_P=0.36) was observed for the UPDRS-III motor subscale scores. *Post hoc* analyses revealed that the UPDRS-III motor subscale scores were lower post-intervention than pre-intervention in the AE (pre- *vs.* post-intervention: 6.43±5.02 *vs.* 3.79±2.15; P=0.011) and TE (pre- *vs.* post-intervention: 8.00±5.27 *vs.* 4.69±2.92; P=0.001) groups. In contrast, in the CG group, the post-intervention clinical score was significantly higher than the baseline clinical score (pre- *vs.* post-intervention: 6.92±4.39 *vs.* 9.77±4.64; P=0.008) (Table I).

Neuropsychological indices

Reaction times

As illustrated in Figure 3, the RM-ANOVA for the RTs revealed a significant main effect of *condition* (F[1,40]=6.44, P=0.015, η^2_P=0.15), with faster RTs in the congruent condition than the incongruent condition (congruent *vs.* incongruent: 552.89±21.37 *vs.* 588.85±24.23 ms; P=0.015). Additionally, there was a significant *group* × *time* interaction

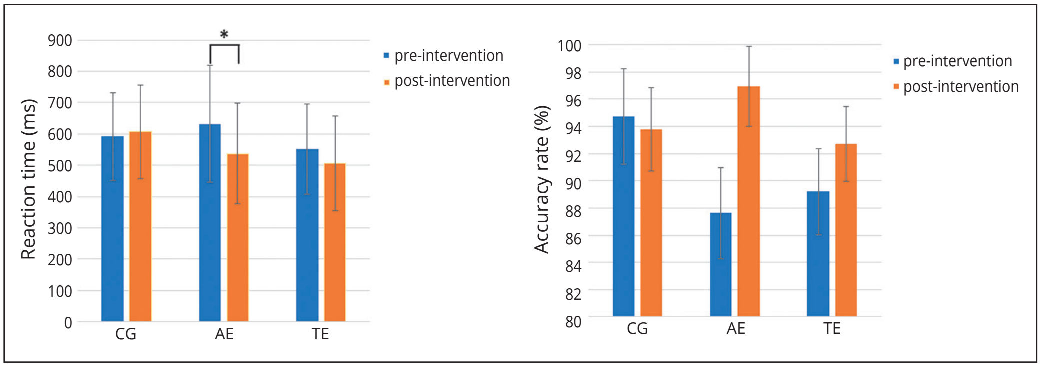

Figure 3.—Reaction times and accuracy rates (mean±SD) during the delayed matching S1–S2 paradigm for the three groups (aerobic exercise group [AE]; Tai Chi Chuan group [TE]; control group [CG]) before and after the 12-week intervention period.

effect (F[2,40]=4.86, P=0.013, η^2_P=0.19). *Post-hoc* analyses revealed that the post-intervention RTs were faster than the pre-intervention RTs (pre- *vs.* post-intervention: 632.41±40.56 *vs.* 537.54±39.15; P<0.001) in the AE group only. No significant main effects of *group* or *time* or any other interactions between factors were observed.

Accuracy rates

The RM-ANOVA for the ARs revealed a significant main effect of *condition* (F[1,40]=12.5, P=0.001, η^2_P=0.23), with higher ARs in the incongruent condition than the congruent condition (congruent *vs.* incongruent: 91.32±1.58% *vs.* 93.68±1.50%; P=0.001). No significant main effects of *group* or *time* or any other interactions between factors were observed.

Neurophysiological indices

N2 latency

As shown in Figure 4, the RM-ANOVA for the ERP N2 latency revealed a significant main effect of *condition* (F[1,40]=6.26, P=0.017, η^2_P=0.13), with significantly shorter N2 latency for the incongruent condition than the congruent condition (congruent *vs.* incongruent, 226.70±4.36 *vs.* 215.10±4.15 ms; P=0.017). No significant main effects of *group*, *time*, or *electrode* or any other interactions between factors were observed.

N2 amplitude

The RM-ANOVA for ERP N2 amplitude revealed no significant main effects of *group*, *time*, *condition*, or *electrode* or any significant interactions between the four factors.

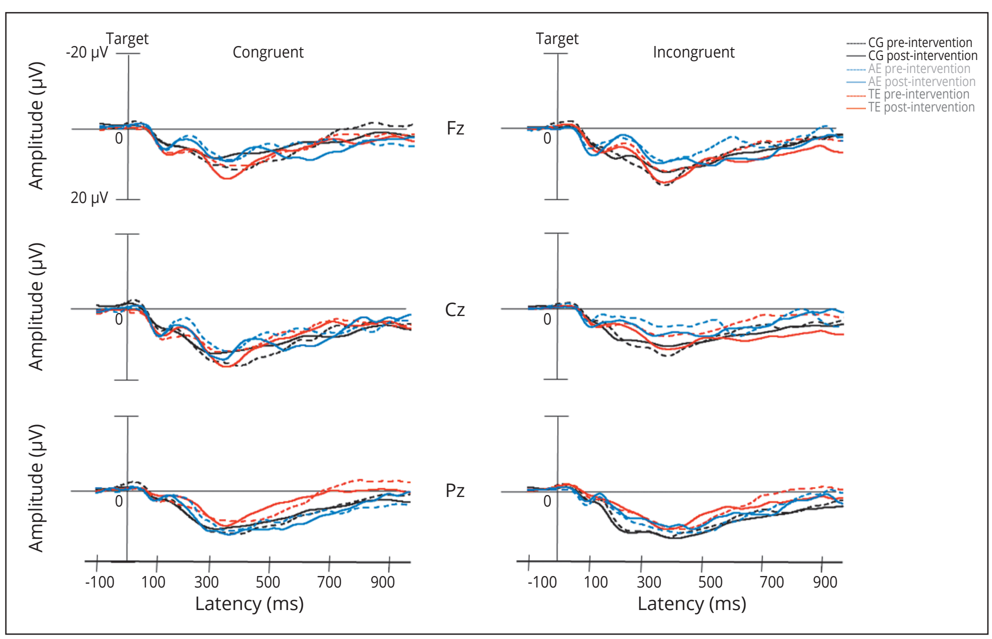

Figure 4.—The grand average ERP waveforms for the congruent and incongruent conditions during the delayed matching S1-S2 paradigm for the three groups (aerobic exercise group [AE]; Tai Chi Chuan group [TE]; control group [CG]) before and after the 12-week intervention period.

P3 latency

The RM-ANOVA for ERP P3 latency revealed no significant main effects of *group*, *time*, *condition*, or *electrode* or any significant interactions between the four factors.

P3 amplitude

The RM-ANOVA for ERP P3 amplitude revealed a significant interaction effect of *group* × *time* (F[2,40] = 7.68, P=0.001, n^2_p=0.27). *Post hoc* analyses revealed a significant increase in P3 amplitude post-intervention relative to pre-intervention in the AE (pre- *vs.* post-intervention: 9.92±1.66 µV *vs.* 11.67±1.37 µV; P=0.028) and TE (pre- *vs.* post-intervention: 11.86±1.55 µV *vs.* 13.40±1.29 µV; P=0.038) groups across the two conditions and three electrode sites. In contrast, P3 amplitude in the CG group decreased significantly during the intervention period (pre- *vs.* post-intervention: 13.78±1.72 µV *vs.* 11.56±1.43 µV; P=0.008).

Discussion

Main findings

The present study investigated and compared the effects of 12-week Tai Chi Chuan and aerobic exercise interventions on neurocognitive performance in patients with early-stage PD. Although the participants' post-intervention UPDRS motor subscale scores and ERP P3 amplitude were significantly improved compared to their pre-intervention scores in both exercise groups, only the AE group showed improved RT performance, as assessed using the WM task. However, neither intervention improved ARs or the ERP N2 performance measured during the cognitive task. In contrast, the control group exhibited a significant increase in UPDRS-III motor scores and a decrease in P3 amplitude over the 12-week period, suggesting that maintaining their usual daily physical activity patterns and refraining from participating in organized exercise classes resulted in further motor and neurophysiological decline.

Neuropsychological indices

Relative to the pre-intervention assessments, only the AE group exhibited significantly faster RTs in the S1-S2 task after the intervention period. It is worth mentioning that the potential learning and practice effects from repeated cognitive tests may have been minimized, since the interval between pre- and post-intervention assessments exceeded one month[46] and a control group was incorporated[47, 48] into the current RCT study. Consequently, participants undergoing 12 weeks of aerobic exercise showed reduced RTs post-intervention compared to pre-intervention, indicating that this type of exercise could effectively improve the information-processing speed (*i.e.*, initial activation, maintenance of information, and suppression of irrelevant information) of the WM in PD patients.[13] Since within-group analysis of pre- and post-intervention ARs revealed significant improvements across both the congruent and incongruent conditions in the AE group after the intervention, this indicates that the speed-accuracy trade-off did not occur in the present study. Also, Bo *et al.*[49] suggested that faster RTs represent a better WM capacity. Accordingly, the significantly faster RTs observed in the AE group after the intervention imply that WM capacity and processing speed could be improved through exercise aimed at enhancing cardiorespiratory fitness. This supports the existence of a positive correlation between cardiopulmonary fitness and WM performance.[27, 50] Indeed, the AE group exhibited a significant improvement in VO_{2max} after the intervention. These aerobic-exercise-induced neuropsychological benefits for cognitive functioning could be attributable to increased functional connectivity in the dorsolateral prefrontal cortex and to deceleration of brain atrophy in PD.[23] In addition, increased concentrations of the brain-derived neurotrophic factor (BDNF), preservation of dopamine neurons, and strengthening of synaptic transmission are other potential benefits of aerobic exercise in PD. All of these benefits are neuroprotective, underlie neuroplasticity, and lead to better cognitive performance.[29]

However, the TE group exhibited no significant improvements in neuropsychological parameters (RTs and ARs) when performing the WM task, although there was a trend toward improving RTs (pre- *vs.* post-intervention: 551.13±37.94 *vs.* 505.74±36.62 ms). These findings align with those of previous studies, which indicate that mind-body exercises such as Tai Chi Chuan may not yield a robust effect on neuropsychological performance in patients with neurodegenerative diseases.[18, 31, 43] Our finding may be attributable to the low intensity of the Tai Chi Chuan exercise used in our intervention,[37] which may not have been able to enhance patients' BDNF levels as much as the moderate-to-high-intensity aerobic exercise,[51] because this molecular biomarker plays an important role in WM. Other plausible mechanisms underlying the neuropsychological findings in the TE group could be that in the current study Tai Chi Chuan intervention did not promote cardiorespiratory fitness, which is strongly correlated with WM function. Based on the evidence discussed above, we propose that engaging in moderate-to-high-intensity exercise, particularly activities that can enhance VO_{2max}, is likely to promote processing speed in WM tasks in PD patients. Along these lines, it would be informative in the future to investigate the neuropsychological effects on WM by studying alternative forms of Tai Chi Chuan that can enhance the cardiorespiratory fitness in individuals with PD. This conjecture is somewhat speculative, but provides a basis for further investigation.

Neurophysiological indices

Neither the aerobic exercise nor Tai Chi Chuan affected the ERP N2 component in PD patients in the present study, indicating that neither exercise intervention improved the neural processing phase associated with inhibitory control during stimulus discrimination, detection, and cognitive control.[11, 12] However, Duchesne *et al.*[22] observed a significant improvement in inhibitory control functioning among PD patients following a three-month aerobic training intervention, as assessed using the Stroop test. Similarly, some studies have reported the benefits of Tai Chi Chuan, including a simplified 24-form Tai Chi Chuan incorporating styles like Ye Ma Feng Zong, Shou Hui Pi Ba, and Dao Juan Hong, on inhibitory control in both young and older adults through cognitive tasks such as go/no-go, Stroop, and Flanker tasks.[52-54] These findings suggest that the cognitive task employed in the present study, such as the delayed matching S1-S2 paradigm, may impose less cognitive load on inhibition control, potentially explaining the disparate findings. Another possible explanation is that the ERP N2 deficits of WM observed in PD patients in a previous study[7] could not be ameliorated through 12 weeks of Yang-style short-form Tai Chi Chuan adopted in the current study. However, the specific neurophysiological effects of Tai Chi Chuan and aerobic exercise modes on the ERP P2 component in PD patients remain to be elucidated, particularly through the use of cognitive tasks imposing greater demands on inhibitory control or by exploring different Tai Chi Chuan and aerobic exercise modalities.

The P3 amplitudes in the TE and AE groups were significantly increased post-intervention, suggesting that in patients with PD, attention resource allocation and cognitive processing of WM can be enhanced by both Tai Chi Chuan and aerobic exercise. Yang-style Tai Chi Chuan involves slow, rhythmic movements and requires focused attention and mental effort to remember the sequences for each form. During the practice process, there is potentially increased activity in the middle and dorsolateral prefrontal cortex, as well as the frontoparietal network, leading to improvement in memory function.[55] Additionally, engaging in mindfulness meditation, focusing on body orientation and breathing, could enhance WM capacity.[44, 45] Because of the unique combination of physical and mental activity, the dual-task nature of the Tai Chi Chuan exercise may positively affect attention performance in PD patients when they perform the WM task.[34]

Similarly, the AE group exhibited a significant increase in ERP P3 amplitude, which was in line with the results of previous studies.[19, 20] These findings suggest that 12 weeks of aerobic exercise can also enhance neural processing efficiency and attentional resource allocation in PD patients. However, relative to the TE group, the AE group engaged in moderate-to-high-intensity exercise, to the extent that it was sufficient to enhance their cardiorespiratory fitness levels. In addition, they exhibited significant improvements not only in RTs but also in P3 amplitude. Aerobic fitness has been reported as a crucial factor for improving WM in older adults.[56] Previous studies have shown that moderate-to-high intensity aerobic exercise not only enhances cardiorespiratory capacity but also improves neuropsychological and neurophysiological performance.[50, 57] Therefore, the improvements observed in RT and P3 amplitude in the AE group may be attributed to significant enhancements in VO_{2max} through moderate to high-intensity aerobic exercise intervention. From the perspectives of neuroanatomy and neurophysiology, Rodriguez-Oroz *et al.*[58] found that P3 amplitude was correlated to subcortical gray matter volume or deterioration of the nigrostriatal dopaminergic system. The present findings thus provide insight into the potential of Tai Chi Chuan and aerobic exercise for reversing deterioration, enhancing neuroplasticity, and improving neurocognitive function in PD.

Importantly, the control group in the current study exhibited significantly smaller P3 amplitudes post- than pre-intervention. This indicates that the progression of neurophysiological decline can appear in patients with early-stage PD if they maintain a sedentary lifestyle. Indeed, because PD is a neurodegenerative condition, patients without a regular exercise habit can exhibit a significant decrease in dopamine release in the putamen, which may contribute to the progression of cognitive function impairments in PD.[59]

Nevertheless, no significant changes in P3 latency were observed post-intervention in either of the exercise groups. This implies that neither Tai Chi Chuan nor aerobic exercise improved the speed of neural processing, specifically during the pairing of the second stimulus with first one while it was retained in the participant's mind. The present finding aligns with previous studies wherein the P3 amplitude significantly increased while P3 latency remained unchanged in healthy older adults undertaking long-term aerobic exercise and Tai Chi Chuan interventions, as observed during a WM task (*e.g.*, n-back).[20, 60] Additionally, Fong *et al.*[61] reported consistent P3 latency in older adults with regular Tai Chi Chuan and endurance exercise habits. Therefore, the current finding extends the existing knowledge from healthy elderly individuals to those with PD. Notably, previous studies have suggested that P3 latency is correlated with task load[62] and illness duration.[40] Therefore, the null effect of our exercise interventions on P3 latency may be attributable to the facts that the WM task involved a lower memory load and that our study participants had only early-stage PD. Further research is warranted in this area.

Parkinsonism motor symptoms

The participants' UPDRS-III scores decreased significantly following both 12-week exercise interventions. This decline reflects an improvement in motor problems such as tremor, finger-tapping difficulties, balance impairment, and gait disturbances. These findings support previous meta-analysis results reporting the positive effects of regular Tai Chi Chuan and aerobic exercise on the motor status of patients with PD.[15, 31]

It is worth noting that we found no significant difference in the extent of improvement in UPDRS-III motor scores between the AE and TE groups, indicating that the two exercise modes can have similar positive effects on motor ability in PD patients. The aerobic exercise intervention used in this study was designed to improve cardiopulmonary fitness *via* lower-extremity cycling, while the Tai Chi Chuan intervention emphasized bilateral coordination and balance. These specific exercise characteristics seem to be crucial for improving the motor status of patients with early-stage PD.

Importantly, our results also revealed that the motor symptoms of the participants in the control group, even though their PD was early stage, declined significantly in the 12 weeks during which they maintained usual daily physical activity patterns and refrained from participating in organized exercise classes. These study findings thus suggest that there are significant negative correlations between maintaining an active lifestyle and motor impairment in PD.

Limitations of the study

This study extended existing knowledge regarding the benefits of two types of long-term exercise for PD patients. However, some limitations should be considered when interpreting the present findings. First, this study focused only on the medication "on" state, during which PD patients experience somewhat improved motor symptoms because of their medication. This limits the generalizability of our findings to the "off" state and restricts further exploration of the potential interaction between exercise and medication effects.[24] Future studies should consider conducting assessments during both "on" and "off" periods to provide a more comprehensive understanding of the long-term effects of exercise interventions on PD symptoms.

Secondly, due to the diverse styles encompassed within Tai Chi Chuan, it's challenging to dismiss the neurocognitive benefits (*e.g.*, RT and ERP N2 component) of such an exercise modality in PD. For instance, Zou *et al.*[63] found that the modified Chen-style (18-form), which emphasizes balance and cognitive aspects with additional skipping movements, exhibited a stronger cognitive effect than the Yang-style (24-form) in late middle-aged and older adults. Moreover, Cui *et al.*[64] reported that the neuroplasticity effect of Bafa Wubu Tai Chi was significantly superior to moderate-intensity aerobic exercise. It is noteworthy that open-skill exercises seem to be more effective in cognitive processing involving inhibitory control compared to closed-skill exercises.[20, 65] Hence, further research in this area is warranted, potentially exploring the neurocognitive effects through different Tai Chi Chuan styles and open-skill exercises in PD.

Thirdly, in order to gain a more comprehensive understanding of the molecular mechanisms underlying the beneficial effects of long-term exercise on neurocognitive performance, future studies should incorporate the measurement of cognition-related biochemical markers (*e.g.*, dopamine and BDNF) in PD.[66-68]

Conclusions

This is the first study to investigate and compare the neurocognitive effects of 12-week Tai Chi Chuan and aerobic exercise in patients with early-stage PD. The study supported the effectiveness of the two exercise modes for improving motor symptoms, as observed *via* UPDRS part-III scores. The neurocognitive indices assessed revealed that 12 weeks of Tai Chi Chuan and aerobic exercise provided different levels of benefits to PD patients. Some neuropsychological (*e.g.*, RTs) and neurophysiological (*e.g.*, ERP P3 amplitude) indices involved in the WM task were improved as a result of the aerobic exercise, whereas the Tai Chi Chuan enhanced only the neurophysiological biomarker. The results have important implications for developing effective exercise interventions to manage PD-related WM decline, particularly in the early stages of the disease.

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Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Authors' contributions

Cheng-Liang Chang, Chia-Liang Tsai, and Tsu-Kung Lin made substantial contributions to the conception or design of the manuscript. Chien-Yu Pan, Tsai-Chiao Wang, and Yu-Ting Tseng contributed to the acquisition, analysis, and interpretation of the data. All authors participated in drafting the manuscript and critically revised it. All authors read and approved the final version of the manuscript.

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