

Research Article

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Tai Chi Exercise to Improve Non-Motor Symptoms of Parkinson's Disease

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Abstract

Background: A substantial number of individuals with Parkinson's disease exhibit debilitating non-motor symptoms that decrease quality of life. To date, few treatment options exist for the non-motor symptomatology related to Parkinson's disease. The goal of this pilot investigation was to determine the effects of Tai Chi exercise on the non-motor symptomology in Parkinson's disease.

Methods: Twenty-one individuals with Parkinson's disease were enrolled in a Tai Chi intervention (n=15) or a noncontact control group (n=6). Participants assigned to Tai Chi participated in 60-minute Tai Chi sessions three times per week, for 16 weeks.

Pre and post measures included indices of cognitive-executive function including visuomotor tracking and attention, selective attention, working memory, inhibition, processing speed and task switching. Additionally, all participants were evaluated on the Parkinson's disease Questionnaire-39 and Tinetti's Falls Efficacy Scale.

Results: Results indicated that the Tai Chi training group had significantly better scores following the intervention than the control group on the Parkinson's disease Questionnaire-39 total score as well as the emotional well-being sub score. Trends for improvement were noted for the Tai Chi group on Digits Backwards, Tinetti's Falls Efficacy Scale, and the activities of daily living and communication sub scores of the Parkinson's disease Questionnaire-39.

Conclusions: This research provides initial data that supports future studies to definitively establish efficacy of Tai Chi to improve non-motor features of Parkinson's disease.

Keywords: Neurodegenerative disease; Exercise; Cognition

Abbreviations: PD: Parkinson's Disease; H&Y: Hoehn and Yahr; QOL: Quality of Life; PDQ-39: Parkinson Disease Questionnaire 39; MMSE: Mini Mental Status Examination; DV: Dependent Variable

Introduction

A substantial number of individuals with Parkinson's disease (PD) exhibit debilitating non-motor symptoms including sleep disturbance, cognitive decline and depression. Non-motor symptoms such as progressive cognitive decline also contribute to the worsening of physical function commonly demonstrated in PD [1,2]. Importantly, in healthy older adults and PD patients alike, physical exercise has been demonstrated to beneficially improve cognitive function and delay cognitive decay [3,4]. Possible mechanisms for the positive effect include improved brain blood flow and oxygen profusion as well as exercise-induced production of growth factors which enhance neurogenesis [5,6]. Importantly, the greatest neuroplastic effects seem to be localized to the frontal and prefrontal areas of the cortex, which support cognitive-executive functions [3,7]. These localized effects are meaningful because frontally mediated cognitive functions exhibit the highest suitability to PD related cognitive decline [8]. Additional benefits of physical exercise involve increased sense of wellbeing, improved mood as well as reduced anxiety and depression [9].

Although the positive influence that exercise exerts on cognition and well-being outcomes are increasingly apparent, the ideal modality has yet to be identified. Identifying candidate modalities in PD is complicated by commonly demonstrated decreases in physical function which may limit some potential exercise treatment options. Previous work on Tai Chi exercise has demonstrated its efficacy for improving motor function in PD [10-12] while others have not [13]. Because Tai Chi is a form of physical activity that demands high cognitive involvement, it may serve as an effective modality for non-motor symptoms of the PD beyond the proven physical outcomes. Interestingly, Lam et al. [14] demonstrated one year of Tai Chi training significantly improved not only balance function but also visual attention in older adults at risks of progressive cognitive decline. They hypothesized that 'apart from being a form of physical activity, Tai Chi demands memory training for the complex motor sequences, as well as coordinated pathway between attention, voluntary motor action, postural control, verbal, and visual imagery which provides increased cognitive stimulation'. Additionally, Tai Chi appears to lower feelings of stress and increase vigor in patient's population [15].

In this context, the current pilot study was undertaken to determine whether the potential effect of Tai Chi on non-motor symptoms of PD is worthwhile. Specifically the purpose of this study was to address, (1) there is a positive effect of Tai Chi on cognition in specific indices of executive function. And (2) is quality of life (QOL) as measured by the Parkinson Disease Questionnaire 39 (PDQ-39) and balance confidence positively impacted following Tai Chi in persons with PD? We hypothesized that because Tai Chi is a form of physical activity that requires a high degree of cognitive involvement, cognitive

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Received May 13, 2013; Accepted August 19, 2013; Published August 22, 2013

Citation: Nocera JR, Amano S, Vallabhajosula S, Hass CJ (2013) Tai Chi Exercise to Improve Non-Motor Symptoms of Parkinson's Disease. J Yoga Phys Ther 3: 137. doi:10.4172/2157-7595.1000137

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improvements would be demonstrated in executive functions while concurrently benefiting QOL outcomes and balance confidence.

Materials and Methods

A convenience sample of community dwelling participants with idiopathic PD was recruited for this study. The study protocol was approved by the institutional ethical review board and written informed consent was obtained from all subjects.

The diagnosis of idiopathic PD was made by a neurologist with fellowship training in Movement Disorders using standard diagnostic criteria (UK Brain Bank Criteria for PD). Participants were included if they: (1) had a disease rating of stage I to III on the Hoehn and Yahr (H&Y) scale, (2) were between the age of 60-80 years old, (3) had stable medication usage, (4) were "non-fluctuators" meaning their motor symptoms did not change appreciably during the waking medication cycle, and (5) were willing to be assigned to the intervention or control group. Participants were excluded if they had: (1) any history or evidence of neurological deficit other than PD, (2) dementia [determined by a Mini Mental Status Examination (MMSE) less than 26], (3) moderate or significant depression as measured by $a \ge 17$ on the Beck Depression Inventory, (4) an inability to walk independently, (5) were on medications affecting balance or alertness/attention (6) previous training in the any forms of Tai Chi or current participation of any exercise programs, or (7) an inability to understand the protocol.

Data collection

All participants visited the Applied Neuromechanics laboratory within one week prior to initiating the Tai Chi training (or control) and within one week of completing the intervention (or control). Evaluations included executive function tasks including visuomotor tracking and attention, selective attention, working memory, inhibition, processing speed and task switching. Additional outcomes included the PDQ-39 as well as Tinetti's Falls Efficacy Scale. All participants were tested in the medicated state at the same time of day for pre-and postmeasurements. All measurements were conducted with a standardized script with specific instruction for each task to ensure consistency. Alternative version of the tasks were given when available and equated for sensitivity and difficulty. The evaluator was blind to treatment arm.

Outcomes

Digit Span Backward Subtest from Wechsler Memory Scale– Third Edition [16] - requires selective attention and working memory. (Dependent Variable (DV)=total backward score).

Letter Verbal Fluency [17] - a verbal fluency test that requires processing speed, selective attention, inhibitory functions, and the ability to rapidly shift mental set. (DV=total word output in 60 seconds per letter for 3 letters).

Category Verbal Fluency [17] - is a verbal fluency test associated with processing speed but also semantic knowledge integrity. (DV=total number of different words generated).

Stroop Color Word Test [18] - requires selective attention and cognitive control by requiring participants to suppress the automatic tendency to read aloud words rather than the color ink words appear on the page in (DV=Color-word score, total read in 45 seconds).

Trails A and B [19] - two version 'connect-the-dots' task which requires visual attention and task switching (DV= time to complete).

Parkinson Disease Questionnaire 39 (PDQ-39) [20] - is a widely

used patient health questionnaire specifically for PD. Patients are instructed to respond, "never", "occasionally", "sometimes", "often" or "always or cannot do at all". (DV=total score, mobility, activities of daily living score, emotional well-being, stigma, social interaction, cognition, and communication and body discomfort scores).

Tinetti's Falls Efficacy Scale [21] - a commonly index utilized to measure confidence in multiple, progressively more difficult activities of daily living. Each item is answered on a scale of one (i.e., very confident) to ten (i.e., not confident at all). (DV=total score (maximum=100) (DV=total score).

Statistical analyses

The change score from pre-testing to post-testing for all outcome measures were calculated and used for further statistical analyses using SPSS 20 (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp). An independent *t*-test was conducted to compare the change scores between the groups. Cohen's *d* was used to calculate the effect (ES) for the dependent variables that satisfied the normality assumption (>.2 small, >.5 medium, >.8 large). Pearson's correlation coefficient was used to calculate the effect size when the normality assumption was violated (Mann-Whittney U test >.1 small, >.3 medium, >.5 large). The level of significance was set as p=0.05.

Randomization and intervention

Participants were randomized in a 2:1 intervention to control design to either a Tai Chi intervention or a noncontact control group, respectively. The patients assigned to the Tai Chi group participated in the 60-minute Tai Chi session three times per week. The Tai Chi intervention was conducted for 16 weeks in small groups with an instructor to participant ratio of 1 to \leq 5. Each 60 minute session was led by a single Tai Chi master with over 20 years of experience in Tai Chi instruction to older adults 75-90 years old and patients with PD disease. All form movements, sequences, and exercises were adapted from the Yang style short form. In addition, standing meditation and visualization techniques were introduced to encourage creative understanding of the Tai Chi movements and to bring variety to the course.

Each Tai Chisession began with a typical warm-up focused on kinesthetic awareness of the body in space, relaxed breathing and mental relaxation. These warm-up movements were designed to prepare the body for more complex Tai Chi form movements by promoting correct postural alignment while at rest (still) and during movement. Warmup movements included: Swing bear, Bear gathers chi, and T-stance stretch.

Following warm-up during the first four weeks of the intervention developmental movements were initiated. Developmental movements were extracted from the Yang style short form and represented building blocks for the form practice itself. These movements were referred to throughout the course of the study to re-enforce specific aspects of Tai Chi movement. The developmental movements included: Big roll-back and Six-count walking.

Lastly, traditional movements were incorporated using the first eight motions of the Yang style short form. These movements represented actions that are common to most forms of Tai Chi thus embodying the essence of Tai Chi movement principles. Traditional movements included: Wuji posture, Commence Tai Chi, Ward-off left, Ward-off right, Roll-back, Press, Push, and Single whip.

The participants assigned to control group did not participate

in any interventions. The amount of voluntary, "at-home" physical activity performed by the control group was estimated and monitored throughout the 16-week control period using the Godin Leisure-time exercise questionnaire [22] and the Yale physical activity questionnaire [23]. All participants in both experiments maintained a stable regimen of medication throughout the intervention/control period.

Results

Thirty PD patients were screened for the study, 23 initiated the study and 21 completed both pre and post assessments. Two participants withdrew from the Tai Chi group as a result f transportation/scheduling conflicts. As such, the final completed groups consisted of 15 Tai Chi participants and six controls. No adverse events were reported during the study. The demographic data and the baseline statistics are shown in Table 1. No significant differences were reported between the groups in any of the demographic and baseline variables (*p*>0.05).

Pre and post means of all outcomes are depicted in Table 2. Tai Chi training produced a significant improvement in the PDQ-39 total score [ES=1.03, p=0.04]. Large, but non-statistically significant, effect sizes were also found for the Digits Backward Test (ES=0.89, p=0.08) and the Activities of Daily Living sub score of the PDQ-39 (ES=0.90, p=0.07). Medium effect sizes were demonstrated in multiple PDQ-39 sub-scores including, emotional well-being (ES=0.46, p=0.04), and communication (ES=0.42, p=.06). Lastly, medium non-significant effect size was also noted on the Tinetti's Fall Efficacy Scale (ES=-0.39, p=0.07) (Table 3). Small, non-significant effect sizes were found for Trails A (ES=-0.26, p=0.24) and B (ES=0.52, p=0.32), the Letter Verbal Fluency (ES=0.43, p=0.39), the Category Verbal Fluency (ES=-0.10, p=0.64), and the Stroop Color Word Test (ES=-0.07, p=0.75).

Discussions

The goal of this study was to explore the ability of Tai Chi to positively affect non-motor symptoms of PD. The results of this pilot investigation suggest Tai Chi was successful at limiting disease related decline of important aspect of QOL as measured by the in PDQ-39 total score as well as the emotional well being sub score of the PDQ-39. We believe the large and medium, non-significant, effects sizes demonstrated in the Digits Backward, as well as multiple sub scores of the PDQ-39 (activities of daily living and communication) and the Fall Efficacy Scale provide initial support for the efficacy of Tai Chi to potentially improve or at least decelerate the decline of non-motor symptoms of PD. Therefore, we believe the findings justify the rationale for a larger, controlled trial investigating the non-motor symptoms of

Group	Tai Chi	Control		
N	15	6		
Age (y/o)	66 (11)	65 (7)		
Gender (M/F)	7/8	4/2		
Height (cm)	166.7 (10.5)	167.6 (9.9)		
Mass (kg)	76.2 (14.3)	71.3 (7.3)		
Disease Duration (months)	97 (65)	82 (22)		
Age at Onset (years)	58 (10)	59 (7)		
H&Y scale	2-3	2-3		
UPDRS Total	34.7 (7.4)	35.4 (13.4)		
Years of education (years)	16 (3)	15 (2)		
MMSE	27.5 (2.2)	28.2 (2.3)		
BDI	6.2 (3.1)	6.0 (5.4)		

H&Y=Hoehn and Yahr; UPDRS=Unified Parkinson's Disease Rating Scale; MMSE=Mini Mental State Exam; BDI=Beck Depression Inventory

Table 1: Mean (SD) for baseline characteristics of participating patients.

	Tai Chi (n=15)				Control (n=6)					
	Pre		Post		Pre		Post			
Executive Function Measures										
Trails-A (sec)	52.3	(37.8)	40.8	(13.3)	38.5	(7.9)	38.3	(10.6)		
Trails-B (sec)	123.5	(46.8)	108.1	(49.0)	91.8	(23.1)	84.0	(19.1)		
Letter Verbal Fluency	31.5	(15.3)	33.9	(11.2)	36.2	(9.6)	34.8	(9.5)		
Category Verbal Fluency	16.3	(6.5)	18.1	(7.1)	15.8	(4.6)	15.3	(6.1)		
Stroop Color Word	31.3	(9.5)	35.1	(12.8)	34.3	(3.8)	35.2	(5.2)		
Digits Backwards	5	(2)	6	(3)	7	(2)	7	(2)		
Parkinson's Disea	se Ques	stionnai	re 39							
Total	31.4	(20.4)	32.5	(19.4)	29.0	(28.4)	38.0	(30.6)		
Sub score										
Mobility	18.8	(19.3)	21.0	(20.4)	19.6	(26.8)	22.9	(29.6)		
Activities of Daily Living	27.2	(23.1)	22.2	(18.9)	20.8	(24.2)	24.3	(28.3)		
Emotional Wellbeing	15.8	(15.7)	13.9	(16.0)	16.7	(15.8)	27.8	(25.6)		
Stigma	17.1	(20.7)	17.1	(21.7)	8.3	(9.4)	9.4	(8.6)		
Social interaction	5.6	(10.3)	10.6	(12.8)	12.5	(20.9)	12.5	(20.9)		
Cognition	20.8	(14.3)	27.1	(17.9)	22.9	(12.9)	32.3	(17.9)		
Communication	25.0	(19.9)	23.3	(21.6)	18.1	(19.3)	29.2	(14.7)		
Bodily discomfort	31.7	(19.0)	35.6	(19.8)	29.2	(22.2)	38.9	(25.6)		
Scale	29.7	(21.7)	23.9	(17.9)	21.7	(22.3)	26.5	(26.7)		

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 Table 2: Pre and post intervention comparison of dependent variables in respective groups.

Tai Chi in patients with PD.

The non-motor symptomologyobserved in PD is highly impactful on QOL. In fact, the incidence of cognitive decline has been reported to be as high as 85% of patients with 15 years of disease duration [24]. To date, most studies have investigated motor outcomes following Tai Chi exercise in various populations and many have demonstrated improvements [10,11]. However, most have failed to investigate the potential additional benefits to non-motorsymptoms of this alternative type of intervention. This is surprising consideringthe high level of attention and memory required to learn and complete Tai Chi sequences.

In this study we measured specific areas of cognitive executive function following a Tai Chi exercise intervention based on 1) these are precise areas of cognitive function area most notably impaired in PD patients [8], 2) executive functions have been demonstrated to improve as a result of physical exercise [3,4] and lastly 3) based on the specific requirements of Tai Chi overlapping with the measures of interest (e.g. attention and working memory). At first glance, our findings indicate that Tai Chi may not be an ideal mode to improve cognitive executive function in patients with PD. However, our results may be indicative of the limited sample size in this pilot investigation. For example, the Tai Chi group did demonstrate improvements over that of the control group in our measures of attention and working memory. More specifically, the Tai Chi group improved better than control on Trails A by 27.8%, Trails B by 4.9%, Stroop by 8.4%, and Digits Backward by 19.2%. Importantly, these tests each require selective and/or visual attention [16,18,19]. While these increases failed to reach statistical significance when compared to control, they are consistent with the findings from Lam et al. [14] in which patients at risk for progressive cognitive decline improved in attention span following a Tai Chi intervention.

Perhaps the most intriguing findings from this pilot investigation are the findings related to health related QOL in the Tai Chi group. QOL

	Tai (n=	Chi :15)	Coi (n	ntrol =6)	Statistics	р	Eff	ect size	
Executive Function Measures									
Trails-A (sec)§	-11.5	(28.5)	-0.2	(5.3)	-1.17	0.24		NS	
Trail-B (sec)	-15.4	(24.2)	-7.8	(22.9)	-0.66	0.52		NS	
Letter Verbal Fluency	2.4	(9.8)	-1.3	(4.1)	0.89	0.39		NS	
Category Verbal Fluency §	1.9	(8.1)	-0.5	(4.8)	-0.47	0.64		NS	
Stroop Color Word	3.8	(8.6)	0.8	(5.2)	-0.31	0.75		NS	
Digits Backwards	0.5	(1.2)	-0.7	(1.8)	1.83	0.08		NS	
Parkinson's Dis	ease Q	uestior	nnaire	39					
Total	1.1	(7.5)	9.0	(8.5)	-2.11	0.05*	1.03	(Large)	
Sub score									
Mobility	2.2	(10.4)	3.3	(12.6)	-0.22	0.83	0.11	NS	
Activities of Daily Living	-5.0	(10.4)	3.5	(6.1)	-1.86	0.08	0.90	NS	
Emotional Wellbeing §	-1.9	(6.5)	11.1	(12.3)	-2.10	0.04*	0.46	(Medium)	
Stigma §	0.0	(9.7)	1.0	(10.0)	-0.04	0.97	0.01	NS	
Social Interaction [§]	5.0	(9.3)	0.0	(0.0)	-1.17	0.24	0.26	NS	
Cognition	6.3	(11.8)	9.4	(8.6)	-0.59	0.57	0.29	NS	
Communication §	-1.7	(14.5)	11.1	(10.1)	-1.92	0.06	0.42	NS	
Bodily discomfort	3.9	(20.9)	9.7	(22.0)	-0.57	0.58	0.28	NS	
Scales	-5.8	(15.7)	4.8	(8.8)	-1.80	0.07	0.39	NS	

 s Indicates the data was not normally distributed. Mann-Whitney U test was performed to compare across the groups. Pearson's correlation coefficient (*r*) was used to evaluate the effect size.

NS=Not significant; ⁺ indicates statistically significant (p<0.05)

Table 3: Change scores and statistics of dependent variables.

is a critical component of a patients' wellbeing and is defined as "the perception and evaluation by patients themselves of the impact caused on their life by the disease and its consequences [25]". In the present study, Tai Chi was effective at limiting the decline of the patients' perceptions of their disease related QOL as reflected PDQ-39 total score. Whereas the control group experienced a nine point increase (worsening) in their perception of disease related disease related QOL perception. This finding is noteworthy as the PDQ-39 has been shown to correlate with clinical measures, is internally consistent, reproducible, and is the most widely used PD specific QOL scale in the literature [20]. Further, Tai chi group experienced significant improvement in the emotional well being subscore relative to the 11 point increase (worsening) demonstrated by the control group. Considering psychological wellbeing incorporates, and highly correlates with, personal characteristic factors such as selfesteem, coping styles and sense of personal control this finding may be substantial. Research has demonstrated that patients with PD indeed have difficulty with these outcomes which in turn reduces QOL above and beyond the impact of the physical features [26].

An important element to implementing any life style intervention is to ensure adherence and track attrition. Previous studies examining the use of Tai Chi in various populations have reported success with participants adhering to the program [10]. Similarly, discounting the two participants who dropped out due to schedule/transportation issues this study demonstrated a 92% attendance rate. Of equal importance, the Tai Group was limited to 12% attrition. Previous studies examining high intensity tango have demonstrated a similar attrition rate of Page 4 of 5

14%, while other studies of high intensity balance training showed an attrition rate of greater than 30% [27,28]. However, as previous studies have been unable to determine ideal dosage and length of Tai Chi intervention in PD [13], future research is needed to address how Tai Chi implementation can be maximized for optimal effectiveness in the general PD population.

As a pilot study this research provided initial data that supports future studies to definitively establish efficacy of Tai chi to improve cognitive and QOL among patients with PD. However, there are limitations of this study which can be easily corrected in larger scale trials; most notably include the use of a non-contact control. The use of a non-contact control served to disproportionately increase contact time with those in the Tai Chi group. This increased contact time with interventionist and study staff could potentially biased the findings. However, we suspect that increased interaction time would not selectively benefit non-motor aspects of PD. Further, an obvious limitation in sample size is noted in the current study as well as an increased risk of false positive due to the large battery of outcomes selected for this pilot study that would need to be adjusted for in larger clinical trials.

Conclusions

We believe the results of this pilot study justify the potential for a larger, randomized controlled trial to better understand the implications on cognitive functioning and psychological wellbeing of patients with PD following Tai Chi exercise. Considering the substantial impact of the non-motor symptoms of PD there is a great need to identify treatments that will have an impact from a physical, cognitive and psychological perspective.

Acknowledgements

This work was supported by National Institute Health NIH 5R03HD054594-02 and the Department of Veterans Affairs RR&D E6860M.

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