

ORIGINAL REPORT

EFFECT OF 12-WEEK TAI CHI CHUAN EXERCISE ON PERIPHERAL NERVE MODULATION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Objective: To examine the effect of tai chi chuan exercise on peripheral nerve modulation in patients with type 2 diabetes mellitus.

Design: Parallel group comparative study with a pre- and post- design.

Subjects: Twenty-eight participants with diabetes mellitus and 32 healthy adult controls from communities in Kaohsiung, Taiwan.

Methods: Cheng's tai chi chuan, 3 times a week for 12 weeks. Fasting blood glucose levels, insulin resistance index and nerve conduction studies were measured.

Results: A 12-week tai chi chuan programme significantly improved fasting blood glucose ($p=0.035$) and increased nerve conduction velocities in all nerves tested ($p=0.046$, right; $p=0.041$, left) in diabetic patients. Tai chi chuan exercise did not advance the nerve conduction velocities of normal adults; however, it significantly improved the motor nerve conduction velocities of bilateral median and tibial nerves, and distal sensory latencies of bilateral ulnar nerves in diabetic patients. Tai chi chuan exercise had no significant effect on amplitudes of all nerves tested in diabetic patients.

Conclusions: Results from this study suggest that fasting blood glucose and peripheral nerve conduction velocities in diabetic patients can be improved by 12 weeks tai chi chuan exercise. A further larger randomized controlled clinical trial with longer follow-up time is needed.

Key words: tai chi chuan, peripheral nerve modulation, diabetes mellitus.

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INTRODUCTION

Diabetic neuropathy is a long-term complication in patients with diabetes, which develops early in the course of the disease and tends to worsen over time (1); the prevalence ranges from 5% to 80% (2). Diabetic neuropathy is frequently associated with pain,

infection and sensory loss in affected patients (1, 3, 4). Moreover, diabetic neuropathy can cause a variety of complications. Postural instability is a common finding in diabetic sensory neuropathy that can lead to unperceived minor foot trauma resulting in an increased risk of ulcers (3) and lower extremity amputation (5). It has been estimated that 50–70% of all non-traumatic amputations in the UK and the USA are diabetic patients with neuropathy (5). The serious complications that can come with a long period of asymptomatic progression of neuropathy make the early prevention of diabetic neuropathy important.

Tai chi chuan (TCC) is a traditional Chinese martial art that has been practised for many centuries. It combines deep diaphragmatic breathing and relaxation with movement involving many fundamental postural stances that flow imperceptibly and smoothly from one to the other through slow and gentle movements (6). Some studies have provided positive evidence that TCC can reduce the risks of falls in elderly people (7). TCC practitioners have better balance (8) muscle strength (9) and improved proprioception (10) than those without TCC practice. This evidence leads to the suggestion that TCC might be beneficial to patients with diabetic neuropathy who have poor muscle strength and balance control associated with a higher risk of falling (11, 12). Very few studies on prevention of diabetic neuropathy through exercise have been reported, and no study utilizing TCC exercise for the prevention of neuropathy or improvement of the nerve conduction studies in patients with diabetes mellitus (DM) has been reported in the literature. We therefore initiated this study to examine the effect of TCC on peripheral nerve modulation in patients with DM.

METHODS

Research design and participants

We pursued a comparative study with pre-/post-design to measure the effect of TCC on peripheral nerve modulation in patients with DM and normal controls before and after 12 weeks of intervention. Participants with DM were recruited from Kaohsiung County, Taiwan. Age-matched non-diabetic adult volunteers from the same county were recruited in parallel as controls. All patients had type 2 DM and were on a daily regimen of oral hypoglycemic agents (OHA), receiving metformin, sulfonylurea, or both. Their medical histories were reviewed to ensure that there were no contraindications to moderate exercise and no history of cardiovascular,

pulmonary or neurologic disorders other than DM; none of them had previously practised TCC. The study was approved by the Hospital's Institutional Review Board; and all participants signed an informed consent form.

A total of 65 participants were recruited prior to the TCC exercise study, but 3 patients with DM and 2 healthy controls did not complete the study due to moving away from the area, changing work schedule, or family obligations. A total of 28 patients with DM and 32 healthy controls completed this study. There were slightly more men in the control group (50% vs 44%) but the difference was not statistically significant ($p=0.628$). The patients with DM had a disease duration of 0.5–7 years (mean = 3.1 years). The average age of the DM group was (mean (standard deviation (SD)) 58.1 (13.4) years, which was not significantly different from that of the controls 56.6 (SD 13.3) ($p=0.663$). Pre-testing results indicated that all healthy controls had normal nerve conduction studies, while 5 patients with DM had abnormal nerve conduction (using Dyck's neuropathy scoring criteria) (13), and one patient with DM had symptomatic peripheral neuropathy.

Tai chi chuan

After pre-test recording all participants, together as a single group, practised Cheng's TCC, for 3 sessions a week, 60 min a session. Each session included a 10-min warm-up (including stretching and balancing exercises), 40 min TCC exercise, and a 10-min cool-down, from 8.30 am to 9.30 am. A TCC teacher was always present and led the regular TCC practice. Each set of Cheng's TCC is made up of 37 movements (14). During the second week of TCC exercise, each patient's heart rate was monitored twice after 10 min of TCC practice and patients were asked by a research nurse to rate perceived exertion (RPE) (15) to determine the exercise intensity of TCC.

Outcome measures

Fasting blood glucose. Fasting blood glucose level was measured by enzymatic ultraviolet test for the quantitative determination of glucose in human serum on Olympus analysers (Olympus Diagnostica GmbH, Hamburg, Germany) (16). Senior technicians recalibrated the assay every 30 days, based on the Olympus System Calibrator Cat No. 66300, which is traceable to the National Institute of Standard and Technology (NIST) Standard Reference Material (SRM) 965.

Insulin resistance index. Insulin resistance was estimated by determining fasting plasma glucose and insulin, using the homeostasis model assessment (17). Fasting insulin level was analysed by Gamma Radiation Counter Cobra II (Packard Co., Connecticut, USA) (18). To ensure precision, the Gamma Radiation Counter Cobra II was calibrated and normalized following standard protocol.

Nerve conduction studies. Nerve conduction studies (NCS) were performed using a Nicolet Viking IV Electorecorder (Nicolet Biomedical Inc, Ohio, USA) (19) in an air-conditioned room with a constant room temperature of 23°C. At this temperature, the average skin temperatures of hand and leg of the participants were kept between 33.4°C and 33.5°C. Bilateral median, ulnar, peroneal, and tibial nerves were studied. In general, supra-maximal stimulation was applied. The distal stimulation sites were 6 cm from the recording electrode for motor NCS and 14 cm for sensory NCS. Median motor NCS was recorded at the abductor pollicis brevis muscle, stimulated at middle of wrist and antecubital fossa. Ulnar motor NCS was recorded at the abductor digiti minimi muscle, stimulated at medial wrist and above medial epicondyle. Peroneal motor NCS was recorded at the extensor digitorum brevis muscle, stimulated at anterior ankle and lateral popliteal fossa. Tibial motor NCS was recorded at the abductor hallucis muscle, stimulated at medial ankle and mid-popliteal fossa. Sensory nerve conducting studies were assessed antidromically. Median sensory NCS was recorded at digit 2 (index finger), ulnar sensory NCS was recorded at digit 5.

The measurements included the distal latency, amplitude of the motor/sensory response and the motor/sensory nerve conduction velocity. Distal latency was the time from stimulus to initial deflection from baseline. Amplitudes of the compound muscle action potential (CMAP) were determined from peak to peak, sensory nerve action

potential (SNAP) from baseline to negative peak. The conducting velocities were calculated with action potentials onset latencies between the distal and the proximal stimulation. All of the nerve conduction studies were carried out by the same technician who was blinded as to the group of participants being studied.

Statistical analysis

Whether the changes in all outcome measures, when tested simultaneously, were significant was tested using a multivariate repeated measures analysis of variance (ANOVA). Another multivariate repeated measures ANOVA was carried out to examine whether the change from pre- to post-intervention was the same between the 2 groups. In the former repeated measures ANOVA, time (2 levels: pre- and post-) was treated as a within-subject factor, but there was no between-subject factor; in the latter repeated measures ANOVA, group (2 levels: DM vs control) was fitted into the model as a between-subject factor. Before carrying out any of the above analyses, missing data (less than 1%) were replaced using the expectation-maximization algorithm (20). The Statistical Package for Social Sciences (SPSS Inc., Chicago, USA) version 13.0 for Windows was used for all data analysis.

RESULTS

Tai chi chuan exercise intensity

Participants perceived that the TCC exercise was a light to moderate exercise by rating using the Borg RPE 6–20 scales during the second week of TCC exercise (mean 11.6, range 11–13). The mean peak heart rate of the participants was at the level of 55.3% (range 41–77%) of their own maximum heart rate. This demonstrated that the relative intensity of TCC was light to moderate (21).

Changes in diabetic indices

Before the exercise programme the patients with DM had a mean fasting blood sugar level of 160.6 (SD 53.8) mg/dl, and a mean insulin resistance index of 8.2 (SD 7.9). After 12 weeks of TCC, these levels decreased by 11%, and 23% to 142.6 (SD 44.0) and 6.3 (SD 6.2), respectively (Table I). In contrast, the reduction in these levels in the control group was substantially less (–0.6% and 11% for the 2 outcome variables, respectively). Statistical significance was reached when comparing the change in fasting blood sugar levels ($p=0.035$) between the 2 groups; while the pre- and post-TCC difference in patients with DM was nearly significant for insulin resistance index ($p=0.079$).

Table I. Comparisons of fasting blood glucose, insulin resistance index before and after tai chi chuan exercise between patients with diabetes mellitus (DM) and control groups

Variables	Group		<i>p</i> -value*
	DM (<i>n</i> =28)	Control (<i>n</i> =32)	
	Mean (SD)	Mean (SD)	
Fasting blood glucose (mg/dl)			
Pre-	160.6 (53.8)	93.3 (7.6)	0.035
Post-	142.6 (44.0)	93.9 (8.6)	
Insulin resistance index			
Pre-	8.2 (7.9)	3.8 (2.5)	0.079
Post-	6.3 (6.2)	3.4 (1.7)	

**p*-values for testing interaction; used to compare whether the changes from pre- to post-intervention between the 2 groups were significantly different.

SD: standard deviation.

Changes in nerve conducting velocities

Experiments were performed to test whether the changes between DM and control participants, within patients with DM, and within controls in nerve conduction velocity (NCV) values were significantly different from a vector of zeroes (Table II). As seen from the *p*-values in parentheses, normal adults had better NCV studies in all 6 nerves at pre- and post-TCC tests. Patients with DM improved significantly, both in right NCVs (*p*=0.046) and left NCVs (*p*=0.041); while no significant improvements were detected in the control group. On analysis of the changes in the 2 groups for each individual NCV, we found that the improvements in the DM group were attributable mainly to bilateral me-

Table II. Comparisons of nerve conduction velocity (NCV) before and after tai chi chuan between diabetes mellitus (DM) and control groups

NCV, m/sec	DM (n=28)		<i>p</i> -value
	Mean (SD)	Mean (SD)	
<i>Right</i>	<i>p</i> =0.046‡		0.195†
Motor, median			
Pre-	51.3 (5.0)	57.3 (3.6)	0.037*
Post-	52.5 (5.4)	56.8 (3.2)	
Motor, ulnar			
Pre-	51.1 (3.7)	54.6 (3.7)	
Post-	51.2 (3.9)	54.7 (3.6)	
Motor, peroneal			
Pre-	45.8 (4.4)	48.4 (3.9)	
Post-	45.6 (3.3)	48.8 (4.1)	
Motor, tibial			0.027*
Pre-	43.4 (5.2)	47.8 (4.4)	
Post-	45.5 (4.4)	47.9 (4.0)	
Sensory, median			
Pre-	58.7 (4.1)	61.8 (5.0)	
Post-	59.4 (4.3)	62.1 (5.1)	
Sensory, ulnar			
Pre-	56.5 (3.9)	59.8 (4.5)	
Post-	56.5 (5.2)	60.3 (4.6)	
<i>Left</i>	<i>p</i> =0.041‡		0.249†
Motor, median			
Pre-	53.0 (4.6)	57.7 (3.1)	0.043*
Post-	54.1 (4.5)	57.8 (3.1)	
Motor, ulnar			
Pre-	51.6 (4.3)	54.9 (3.7)	
Post-	51.8 (4.8)	54.8 (3.4)	
Motor, peroneal			
Pre-	45.9 (4.9)	48.4 (3.3)	
Post-	45.6 (3.2)	48.4 (4.1)	
Motor, tibial			0.036*
Pre-	44.1 (4.9)	47.5 (4.4)	
Post-	45.3 (4.3)	47.4 (4.5)	
Sensory, median			
Pre-	59.6 (4.6)	62.7 (4.7)	
Post-	59.8 (4.8)	63.6 (4.5)	
Sensory, ulnar			
Pre-	56.2 (4.9)	60.1 (4.9)	
Post-	56.7 (5.2)	59.9 (5.1)	

Interpretation of the various *p*-values presented:

‡Multivariate analysis comparing pre- and post- measurements within a group;

†Comparison of the 2 groups on the change from pre- to post- for the 6 NCV measures simultaneously;

*Comparison of the 2 groups on the change from pre- to post- for individual outcome measures.

dian (right: *p*=0.037; left: *p*=0.043) and tibial (right: *p*=0.027; left: *p*=0.036) motor NCVs. Patients with DM revealed higher NCV values after TCC exercise in almost all NCVs studied, but only bilateral medial and tibial NCVs reached a significant improvement after TCC exercise. The controls revealed no further advancement of the NCVs tested after TCC exercise when tested using a multivariate repeated measures ANOVA.

Changes in distal latency

Comparisons of distal latency before and after TCC are shown in Table III. The overall changes from pre- to post-intervention were not significant in either of the 2 groups. To compare the

Table III. Comparisons of distal latency before and after tai chi chuan (TCC) between diabetes mellitus (DM) and control groups

Distal latency, msec	DM (n=28)		<i>p</i> -value
	Mean (SD)	Mean (SD)	
<i>Right</i>	<i>p</i> =0.728‡		0.736†
Motor, median			
Pre-	4.16 (0.99)	3.20 (0.47)	
Post-	4.14 (0.97)	3.19 (0.41)	
Motor, ulnar			
Pre-	2.51 (0.27)	2.30 (0.25)	
Post-	2.47 (0.29)	2.28 (0.27)	
Motor, peroneal			
Pre-	3.62 (0.74)	3.38 (0.56)	
Post-	3.62 (0.70)	3.43 (0.46)	
Motor, tibial			
Pre-	3.89 (0.77)	3.63 (0.53)	
Post-	3.89 (1.0)	3.59 (0.60)	
Sensory, median			
Pre-	2.74 (0.60)	2.27 (0.30)	
Post-	2.71 (0.60)	2.27 (0.28)	
Sensory, ulnar			0.044*
Pre-	1.98 (0.25)	1.98 (0.26)	
Post-	1.87 (0.23)	1.97 (0.31)	
<i>Left</i>	<i>p</i> =0.382‡		0.813†
Motor, median			
Pre-	3.75 (0.82)	3.08 (0.41)	
Post-	3.71 (0.83)	3.08 (0.35)	
Motor, ulnar			
Pre-	2.45 (0.30)	2.33 (0.32)	
Post-	2.42 (0.31)	2.29 (0.34)	
Motor, peroneal			
Pre-	3.45 (0.50)	3.48 (0.51)	
Post-	3.45 (0.53)	3.44 (0.47)	
Motor, tibial			
Pre-	4.08 (0.86)	3.73 (0.58)	
Post-	3.86 (0.83)	3.68 (0.52)	
Sensory, median			
Pre-	2.76 (0.69)	2.22 (0.37)	
Post-	2.75 (0.68)	2.18 (0.29)	
Sensory, ulnar			0.047*
Pre-	2.02 (0.25)	1.89 (0.27)	
Post-	1.92 (0.23)	1.88 (0.28)	

Interpretation of the various *p*-values presented:

‡Multivariate analysis comparing pre and post measurements within a group;

†Comparison of the 2 groups on the change from pre- to post- for the 6 NCV measures simultaneously;

*Comparison of the 2 groups on the change from pre- to post- for individual outcome measures.

pre- and post-TCC distal latency in individual nerves, it was found that distal sensory latency of bilateral ulnar nerves (right: $p=0.044$; left: $p=0.047$) revealed a significant shortening after TCC exercise in patients with DM.

Changes in proximal and distal amplitudes

Changes in proximal segments' amplitudes before and after TCC exercise are shown in Table IV. Patients with DM tended to have worse proximal amplitudes of sensory nerves than normal adults compared with those of motor nerves. After TCC exercise, the proximal amplitudes increased in the DM group, but did not reach a significant increase (right: $p=0.077$; left: $p=0.085$). In studies of distal amplitudes, again, we found that

patients with DM had worse sensory distal amplitudes than age-matched normal adults. After 12 weeks of TCC exercise, the distal amplitude of 6 nerves in the DM group did not significantly change (right: $p=0.833$; left: $p=0.617$).

DISCUSSION

This study is the first to show that a 12-week programme of TCC exercise significantly improves the motor conduction velocities of tibial and median nerve and distal sensory latency of ulnar nerves in patients with DM, compared with non-diabetic normal control group. A previous cohort study (22), showed that the NCV in patients with DM decreased by ~ 0.5 m/sec annually. Our results indicated that a 12-week programme of TCC exercise may provide an even better improvement in diabetic neuropathies. By contrast, there were no significant improvements in NCVs detected in the normal control group. The result parallels the differences seen post-TCC in fasting blood glucose concentration between non-diabetic and diabetic persons. Moderate intensity exercise in non-diabetic persons had little effect on blood glucose concentrations; whereas it is usually associated with a decrease in blood glucose in patients with type 2 diabetes (23).

Technically, the comparison between pre- and post- values requires computing the mean and SD of the difference (defined as pre- minus post-) for each individual. If the SD associated with the within-group difference is small (i.e. every participant in the group consistently has slight improvement), then the result could still be statistically significant. This, in fact, was the case for the DM group, but not for the control group. In the control group, some participants improved, but the performance for others was worse after intervention, so that the SD associated with the mean change in the control group was large (a larger SD will make it more difficult for the overall result to be significant). As a result, significant changes were detected only in the DM group, but not in the control group, when within-group comparison (from pre- to post-) was analysed.

There have been very few studies addressing improvement in NCV through exercise in patients with DM. A study by Tesfaye et al. (24) investigating sensory conduction velocity of sural nerves (SSCV) showed that SSCV increased significantly after less than 10 min of strenuous exercise in normal participants and participants with non-neuropathic diabetes, but not in participants with neuropathic diabetes. Balducci et al. (25) reported that patients with DM who participate in long-term aerobic exercise had less progression of diabetic neuropathy. Richerson & Rosendale (26) showed that elderly patients who had plantar sensory loss due to diabetic peripheral neuropathy and other diseases attained significant improvement in sensory ability after 6 months of TCC training. We showed that motor NCV of bilateral tibial and median nerves and distal sensory latency of bilateral ulnar nerves significantly improved after 12 weeks of TCC exercise in patients with DM. The progression of diabetic neuropathy is related to diabetic duration and severity (27, 28). Balducci et al. (25) recruited only diabetic patients

Table IV. Comparisons of proximal amplitudes before and after tai chi chuan (TCC) between diabetes mellitus (DM) and control groups

Proximal Amplitude	DM (n=28)		p-value
	Mean (SD)	Mean (SD)	
<i>Right</i>	$p=0.077\ddagger$	$p=0.059\ddagger$	0.636†
Motor, median (mV)			
Pre-	10.5 (3.85)	12.9 (3.46)	
Post-	11.5 (3.84)	12.9 (3.50)	
Motor, ulnar (mV)			
Pre-	13.0 (2.30)	13.5 (3.30)	
Post-	13.7 (2.54)	13.9 (3.21)	
Motor, peroneal (mV)			
Pre-	6.04 (2.25)	7.74 (3.30)	
Post-	6.18 (2.34)	8.29 (3.95)	
Motor, tibial (mV)			
Pre-	11.5 (6.41)	16.3 (5.16)	
Post-	11.7 (7.13)	16.8 (4.79)	
Sensory, median (uV)			
Pre-	13.3 (6.01)	17.1 (7.56)	
Post-	14.2 (7.39)	18.2 (8.90)	
Sensory, ulnar (uV)			
Pre-	13.5 (7.13)	16.3 (9.05)	
Post-	13.7 (7.26)	17.0 (9.68)	
<i>Left</i>	$p=0.085\ddagger$	$p=0.274\ddagger$	0.856†
Motor, median (mV)			
Pre-	12.3 (2.90)	12.2 (2.28)	
Post-	12.9 (3.42)	12.7 (2.42)	
Motor, ulnar (mV)			
Pre-	11.7 (2.09)	12.8 (2.42)	
Post-	12.3 (3.06)	12.9 (2.55)	
Motor, peroneal (mV)			
Pre-	5.96 (2.54)	7.54 (3.32)	
Post-	6.30 (2.53)	8.01 (3.89)	
Motor, tibial (mV)			
Pre-	10.3 (6.37)	17.0 (5.78)	
Post-	10.7 (6.52)	17.3 (5.29)	
Sensory, median (uV)			
Pre-	16.1 (8.76)	24.1 (9.17)	
Post-	17.4 (9.13)	24.0 (9.49)	
Sensory, ulnar (uV)			
Pre-	14.6 (8.46)	19.7 (9.81)	
Post-	15.0 (9.15)	20.0 (8.98)	

Interpretation of the various p -values presented:

‡Multivariate analysis comparing pre and post measurements within a group;

†Comparison of the 2 groups on the change from pre- to post- for the 6 NCV measures simultaneously.

without signs or symptoms of distal peripheral neuropathy. Although all diabetic participants in the study by Richerson & Rosendale (26) had had type 2 diabetes for more than 5 years, their blood sugar was under control (mean HbA1c less than 7). As our diabetic patients had short duration of DM history (mean = 3.1 years), their blood sugar was adequately controlled (HbA1c levels were 7.33% (1.21%)) and nearly all cases had no symptomatic neuropathy, they were relatively vulnerable to reversal of the NCVs. Based on the above findings, we postulated that early TCC exercise intervention may be able to prevent or rescue patients with DM from progression of diabetic neuropathy.

The changes in nerve conduction associated with 12 weeks of TCC in patients with diabetic neuropathy were characterized by an increase in the speed of nerve conduction, but no obvious effects in the amplitude of CMAP or SNAP. Balducci et al. (25) also reported no significant difference in both peroneal and sural nerve action potential amplitude between the exercise group and control group. This is presumably because exercise does not affect the number of conducting fibres in diabetic patients.

Accumulated evidence suggests that the pathogenesis of diabetic neuropathy is multifactorial; however, hyperglycemia is probably the primary factor (27, 29). Glucose could damage nerve cells via increased glucose flux through the polyol pathway, non-enzymatic glycosylation of proteins, and oxidative stress. The UK Prospective Diabetes study (UKPDS) has provided evidence that improved glycaemic control can reduce some indices of peripheral nerve dysfunction in type 2 diabetes (30). Kikkawa et al. (31) found that glycaemic control quickly alters the speed of nerve conduction. We found that TCC plus conventional hypoglycaemic treatment improved certain motor and sensory conduction velocities, and found a statistically significant decrease in participants' fasting blood glucose, associated with the trend of decreasing insulin resistance index after TCC. Taken together, these results suggest that the improvement in NCV after TCC may be related to better blood sugar control and less insulin resistance. Further studies to validate the mechanism are needed.

The role of microangiopathy in diabetic neuropathy has long been emphasized (27, 29, 32). Tasfaye et al. (24) also found that subcutaneous temperature rose significantly in normal participants and non-neuropathic diabetic participants, but not in neuropathic participants after strenuous exercise. They concluded that the impairment of exercise conduction increment in diabetic neuropathy suggests impaired blood supply of nerves in diabetic neuropathy. Kilo et al. (32) suggest that nitric oxide (NO) interaction with the endothelium may play an important role in the development of diabetic neuropathy. Wang et al. (33) reported that 10 elderly men who practised TCC for 11.2 years had higher cutaneous microcirculatory function during exercise than 10 age-matched sedentary men, and this change may be partially through enhancement of NO release. Wang et al. (34) also found regular TCC practice was associated with enhanced endothelium-dependent dilation in skin vasculature of the elderly. Further study is needed to explore whether TCC can improve the microvascular insufficiency in

diabetic neuropathy via increasing NO production and enhancing endothelium-dependent endoneurial vascular dilation.

DM has recently been regarded as a chronic inflammatory illness. Our previous studies have shown that regular TCC exercise can increase regulatory T cells (35, 36), and enhance type 1 T helper (Th1) immune reaction. It is therefore not excluded that TCC exercise could improve immunity (37), resulting in less peripheral neuritis and enhancement of NCV.

Since diabetic patients with peripheral neuropathy have an increased risk of soft tissue and joint injuries, certain types of exercise such as running, jogging, or similar activities that may cause injury are contraindicated (38). TCC, a Chinese martial art, consists of slow and gentle movements (6). It is a low-velocity and low-impact activity, the kind of activity that comes with a reduced number of cardiovascular and orthopaedic complications (39). Similar to the report from Li et al. (40), who showed that TCC can be classified as a moderate exercise, as its intensity does not cause excess of 55% of maximum oxygen intake or 60% of the individual maximum heart rate, we found that TCC caused 55.3% increase in the individual maximum heart rate. Previous study has not only found TCC to be safer than other forms of exercise, but also has substantiated its health benefits (40). Our data have further indicated that the benefits of TCC for balance and flexibility can be extended to improvement of NCV in patients with DM. Richerson & Rosendale (26) also found that 6 months of TCC training could improve the sensory ability of diabetic peripheral neuropathy patients. Of note, the practice of TCC requires little in the way of equipment and can be implemented in the community at low cost. All of these factors make it suitable for patients with DM with neuropathy.

In conclusion, we have demonstrated that regular practice of TCC for 12 weeks improves NCVs in patients with DM. This study highlights the potential of TCC, a non-pharmacological intervention, in modifying the natural history of diabetic neuropathy. A large-scale randomized clinical trial with a longer duration of TCC training is needed to substantiate the use of TCC as an effective non-invasive treatment of diabetic neuropathy.

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REFERENCES

1. Pirart J. Diabète et complications dégénératives présentation d'une étude prospective portant sur 4400 cas observés entre 1947 et 1973. 3rd and last part. *Diabet Metab* 1977; 3: 97-107.
2. Dyck PJ, Kratz KM, Karnes JL, Litchy WJ, Klein R, Pach JM, et al. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester Diabetic Neuropathy Study. *Neurology* 1993; 43: 817-824.

3. Katoulis EC, Ebdon-Parry M, Hollis S, Harrison AJ, Vileikyte L, Kulkarni J, et al. Postural instability in diabetic neuropathic patients at risk of foot ulceration. *Diabet Med* 1997; 14: 296–300.
4. Thomas PK, Eliasson SG. Diabetic neuropathy. In: Dyck PJ, Thomas PK, Lambert EH, Bunge R, editors. *Peripheral neuropathy*. 2nd ed. Philadelphia, PA: WB Saunders; 1984, p. 1773–1810.
5. Comi G, Fedele D, Coscelli C, Cucinotta D, Feldman EL, Ghirlanda G, et al. The Italian multicentre study on the prevalence of distal symmetric polyneuropathy: correlation between clinical variables and nerve conduction parameters. *Italian Diabetic Neuropathy Committee. Electroencephalogr Clin Neurophysiol Suppl* 1999; 50: 546–552.
6. Chinese Sport. Simplified “Taijiquan” 2nd ed. Beijing, PRC: China Publications Center; 1983, p. 1–5.
7. Wolf SL, Barnhart HX, Kutner NG, McNeely E, Coogler C, Xu T. Reducing frailty and falls in older persons: an investigation of Tai Chi and computerized balance training. Atlanta FICSIT Group. Frailty and Injuries: Cooperative Studies of Intervention Techniques. *J Am Geriatr Soc* 1996; 44: 489–497.
8. Tsang WW, Wong VS, Fu SN, Hui-chan CW. Tai Chi improves standing balance control under reduced or conflicting sensory conditions. *Arch Phys Med Rehabil* 2004; 85: 129–137.
9. Wu G, Zhao F, Zhou X, Wei L. Improvement of isokinetic knee extensor strength and reduction of postural sway in the elderly from long-term Tai Chi exercise. *Arch Phys Med Rehabil* 2002; 83: 1364–1369.
10. Xu D, Hong Y, Li J, Chan K. Effect of Tai Chi exercise on proprioception of ankle and knee joints in old people. *Br J Sports Med* 2004; 38: 50–54.
11. Kao MY, Chuang LM, Hu MH, Hsieh ST, Wu YT. Exercise capability and balance performance in patients with diabetic neuropathy. *Formosan J Med* 2004; 8: 323–331.
12. Gutierrez EM, Helber MD, Dealva D, Ashton-Miller JA, Richardson JK. Mild diabetic neuropathy affects ankle motor function. *Clin Biomech (Bristol, Avon)* 2001; 16: 522–528.
13. Dyck PJ. Detection, characterization, and staging of polyneuropathy: assessed in diabetics. *Muscle Nerve* 1988; 11: 21–32.
14. Cheng MC. *Tai Chi Chuan: a simplified method of calisthenics for health and self defense*. Berkeley, CA: North Atlantic Book; 1981, p. 32–111.
15. Borg G. Perceived exertion as an indicator of somatic stress. *Scand J Rehabil Med* 1970; 2: 92–98.
16. Olympus Diagnostica GmbH. Operator’s manual of Olympus analysers. Hamburg, Germany: Author; 2004.
17. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985; 28: 412–419.
18. Packard Instrument Co. Reference manual volume I: Cobra series, Auto-Gamma counting systems. Meriden, CT; 1992.
19. Nicolet Biomedical Inc. User manual of Nicolet Viking IV. Madison, WI; 1998.
20. Dempster AP, Laird NM, Rubin DB. Maximum likelihood from incomplete data via the EM algorithm. *J Royal Statistical Soc, Series B*, 1977; 39: 1–38.
21. American College of Sports Medicine Position Stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Med Sci Sports Exerc* 1998; 30: 975–991.
22. Arezzo JC. The use of electrophysiology for assessment of diabetic neuropathy. *Neurosci Res Commun* 1997; 21: 13–23.
23. Schneider SH, Amorosa LF, Khachadurian AK, Ruderman NB. Studies on the mechanism of improved glucose control during regular exercise in type 2 (non-insulin-dependent) diabetes. *Diabetologia* 1984; 26: 355–360.
24. Tesfaye S, Harris ND, Wilson RM, Ward JD. Exercise-induced conduction velocity increment: a marker of impaired peripheral nerve blood flow in diabetic neuropathy. *Diabetologia* 1992; 35: 155–159.
25. Balducci S, Iacobellis G, Parisi L, Di Biase N, Calandriello E, Leonetti F, et al. Exercise training can modify the natural history of diabetic peripheral neuropathy. *J Diabetes Complications* 2006; 20: 216–223.
26. Richerson S, Rosendale K. Does tai chi improve plantar sensory ability? A pilot study. *Diabetes Technol Ther* 2007; 9: 276–286.
27. Tomlinson DR. Pathogenesis of diabetic neuropathies. In: Pickup JC, Williams G, editors. *Textbook of diabetes vol. 2*. Oxford, UK: Blackwell Science; 2003, p. 50.3–50.9.
28. Tesfaye S, Chaturvedi N, Eaton SE, Ward JD, Manes C, Ionescu-Tirgoviste C, et al. Vascular risk factors and diabetic neuropathy. *N Engl J Med* 2005; 352: 341–350.
29. Chiasera JM, Ward-Cook KM, McCune SA, Wardlaw GM. Effect of aerobic training on diabetic nephropathy in a rat model of type 2 diabetes mellitus. *Ann Clin Lab Sci* 2000; 30: 346–353.
30. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ* 1998; 317: 703–713.
31. Kikkawa Y, Kuwabara S, Misawa S, Tamura N, Kitano Y, Ogawara K, et al. The acute effects of glycemic control on nerve conduction in human diabetics. *Clin Neurophysiol* 2005; 116: 270–274.
32. Kilo S, Berghoff M, Hilz M, Freeman R. Neural and endothelial control of the microcirculation in diabetic peripheral neuropathy. *Neurology* 2000; 54: 1246–1252.
33. Wang JS, Lan C, Wong MK. Tai chi chuan training to enhance microcirculatory function in healthy elderly men. *Arch Phys Med Rehabil* 2001; 82: 1176–1180.
34. Wang JS, Lan C, Chen SY, Wong MK. Tai chi chuan training is associated with enhanced endothelium-dependent dilation in skin vasculature of healthy older men. *J Am Geriatr Soc* 2002; 50: 1024–1030.
35. Yeh SH, Chuang H, Lin LW, Hsiao CY, Eng HL. Regular tai chi chuan exercise enhances functional mobility and CD4CD25 regulatory T cells. *Br J Sports Med* 2006; 40: 239–243.
36. Yeh SH, Chuang H, Lin LW, Hsiao CY, Wang PW, Yang KD. Tai chi chuan exercise decreases A1C levels along with increase of regulatory T-cells and decrease of cytotoxic T-cell population in type 2 diabetic patients. *Diabetes Care* 2007; 30: 716–718.
37. Yeh SH, Chuang H, Lin LW, Hsiao CY, Wang PW, Liu RT, et al. Regular tai chi chuan exercise improves T cell helper function of type 2 DM patients with an increase in T-bet transcription factor and IL-12 production. *Br J Sports Med* 2008 Apr 2 [Epub ahead of print].
38. Hamdy O, Goodyear LJ, Horton ES. Diet and exercise in type 2 diabetes mellitus. *Endocrinol Metab Clin North Am* 2001; 30: 883–907.
39. American College of Sports Medicine. *Guidelines for graded exercise testing and exercise prescription*. 4th ed. Philadelphia, PA: Lea & Febiger; 1991, p. 5–9.
40. Li JX, Hong Y, Chan KM. Tai chi: physiological characteristics and beneficial effects on health. *Br J Sports Med* 2001; 35: 148–156.