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Revealing the Neural Mechanisms Underlying the Beneficial Effects of Tai Chi: A Neuroimaging Perspective

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Abstract: Tai Chi Chuan (TCC), a traditional Chinese martial art, is well-documented to result in beneficial consequences in physical and mental health. TCC is regarded as a mind-body exercise that is comprised of physical exercise and meditation. Favorable effects of TCC on body balance, gait, bone mineral density, metabolic parameters, anxiety, depression, cognitive function, and sleep have been previously reported. However, the underlying mechanisms explaining the effects of TCC remain largely unclear. Recently, advances in

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neuroimaging technology have offered new investigative opportunities to reveal the effects of TCC on anatomical morphologies and neurological activities in different regions of the brain. These neuroimaging findings have provided new clues for revealing the mechanisms behind the observed effects of TCC. In this review paper, we discussed the possible effects of TCC-induced modulation of brain morphology, functional homogeneity and connectivity, regional activity and macro-scale network activity on health. Moreover, we identified possible links between the alterations in brain and beneficial effects of TCC, such as improved motor functions, pain perception, metabolic profile, cognitive functions, mental health and sleep quality. This paper aimed to stimulate further mechanistic neuroimaging studies in TCC and its effects on brain morphology, functional homogeneity and connectivity, regional activity and macro-scale network activity, which ultimately lead to a better understanding of the mechanisms responsible for the beneficial effects of TCC on human health.

Keywords: Traditional Chinese Exercise; Cognitive Function; Mood; Pain; Review.

Introduction

Tai Chi Chuan (TCC) is a traditional Chinese martial art that has been practiced in China for centuries. Deep diaphragmatic breathing, relaxation and the imperceptibly smooth flow of body postures are signature features of TCC (Wolf *et al.*, 1997). Indeed, TCC has been considered to be a tenant of traditional wisdom and a powerful martial art in China, which was only taught to a limited population before the 1950s. This traditional martial art was then gradually simplified and made into a common sport in 1950s, aimed at promoting a healthy lifestyle among the general public of Mainland China. TCC has evolved into different styles during its development with Yang being one of the most popular. As a mind-body exercise, TCC requires practicing individuals to not only build their physical strength, but also to treat their body and mind as a whole in order to improve the mind-body control (Wolf *et al.*, 1997). The health values of TCC have been highly recognized in recent researches. Although a number of the beneficial effects of TCC on human health have been identified, the underlying mechanisms mediating those effects remain largely unknown. In the current review, we summarized the beneficial effects of TCC on different populations and recent advances in neuroimaging findings on TCC-induced changes in brain morphology, functional homogeneity and connectivity, regional activity and macro-scale network activity.

Beneficial Effects of Tai Chi

TCC consists of training in both physical and mental components. A number of research studies have revealed the beneficial effects of TCC on both physical and psychiatric health in different populations. Previous systematic reviews have provided evidence that TCC is beneficial to a number of specific medical conditions, such as falls, Parkinson's disease, depression, cognitive impairment and dementia, rehabilitations of stroke, cardiac disease and chronic obstructive pulmonary disease, by improving balance, muscle strength, aerobic capacity and general well-being (Del-Pino-Casado *et al.*, 2016; Huston and McFarlane, 2016). The current review focuses on the potential mechanisms that mediate the effects of TCC through the modulation of brain morphology, functional homogeneity, activity and connectivity. The beneficial effects of TCC in different populations, together with the major outcomes and interventions employed, are briefly summarized in Table 1.

Neuroimaging Findings on the Effects of Tai Chi Chuan on Brain Structure, Functional Homogeneity and Connectivity, Regional Activity and Macro-scale Network Activity

Numerous studies have reported the beneficial effects of TCC on physical and mental health; however, the underlying mechanisms mediating those beneficial effects remain largely unknown. Fortunately, advances in neuroimaging technologies have provided some clues for understanding the neurological adaptation to TCC. A keyword search on the PubMed database was performed to access all the articles that were related to TCC-associated changes in brain, using the following terms: (1) “Tai Chi” or “Tai Chi Chih” or “Tai Chi Chuan” or “Tai Chi Quan” or “Taiji” or “Tai ji Quan” and (2) “magnetic resonance imaging” or “MRI” or “functional magnetic resonance imaging” or “fMRI” or “brain structure” or “neuroimaging”. Manual assessment was performed to filter out articles that were not related to TCC-induced alterations in brain. Until November 2017, there were a total of eight original studies that demonstrated changes in brain associated with TCC training or included intervention mechanisms that consisted of TCC. These eight articles were all included in this review. The changes in brain that associated with TCC are summarized in Table 2 and are briefly described as below.

TCC intervention has been found to bring several positive changes in brain function and structure. A study reported in 2012 has compared the normalized brain volume before and after the participants received TCC training (Mortimer *et al.*, 2012). The intracranial volume of brains of the participants was increased by 47% after 40 weeks of TCC training (Mortimer *et al.*, 2012), whereas significant change in brain volume was not observed in participants after receiving walking exercise intervention and in sedentary control subjects (Mortimer *et al.*, 2012). Indeed, our previous study has also revealed that the cortical thickness of several parts of the brain, including right precentral gyrus, right middle frontal sulcus, right inferior segment of the circular sulcus of insula, left medial occipitotemporal sulcus, left lingual sulcus, and left superior temporal gyrus were larger in TCC practicers compared with people who did not practice TCC (Wei *et al.*, 2013). The changes in cortical thickness of those brain regions were correlated with the practicing hours of TCC training, while the increase in cortical thickness of superior temporal gyrus of Tai Chi practicers was correlated with their shorter reaction time in an Attention Network Test (Wei *et al.*, 2013).

Apart from the alterations of the brain morphology, TCC intervention has been demonstrated to modulate the functional homogeneity (i.e., temporal synchronizations of brain functional activity within a small region) in several sections of the brain. By using the technique of functional magnetic resonance imaging (fMRI), increased functional homogeneity of right postcentral gyrus, together with decreased functional homogeneity of anterior cingulate cortex and superior frontal cortex, were observed in participants with long-term TCC training (Wei *et al.*, 2014). Notably, the changes in functional

Table 1. Summary of the Beneficial Effects of Tai Chi

Beneficial Effect	Studied Population	Outcome Indicator	Intervention/Experience	Reference
Flexibility	Fall-pone older adults	• Sit and reach test	60 min per section, 3 sections per week, 12 weeks	Choi *et al.* (2005)
	College students	• Sit and reach test	60 min per section, 3 sections per week, 12 weeks	Zheng *et al.* (2015a)
Balance and Gait	Fall-pone older adults	• Single leg stand test	35 min per section, 3 sections per week, 12 weeks	Choi *et al.* (2005)
	Older adults with mobility disability	• CoP mediolateral displacement and velocity in locomotion phase • CoP mediolateral excursions and resultant CoP center of mass distance in medial and forward conditions	60 min per section, 3 sections per week, 16 weeks	Vallabhajosula *et al.* (2014)
	College students	• Open eye perimeter and close eye perimeter in Pro-Kin system	60 min per section, 3 sections per week, 12 weeks	Zheng *et al.* (2015a)
	Elderly women	• Comprehensive shake index • Front and back shake index	40 min per section, 6 sections per week, 12 months	Song *et al.* (2014)
	Female older adults with knee osteoarthritis	• Single leg stand test with eyes closed	20 min per section, 3 sections per week, 12 weeks, 12 forms of Sun style	Song *et al.* (2003)
	Patients with stroke	• Berg balance score	Meta-analysis summary: A total of 8 studies on 704 subjects Mean difference (95%CI) = 11.85 [5.41, 18.3], $P < 0.00001$	Chen *et al.* (2015)
	Patients with Parkinson's disease	• Berg balance score • Timed up and go test	Meta-analysis summary: A total of 8 studies Berg balance score mean difference (95%CI) = 1.22 [0.8,1.65], $P < 0.00001$ Timed up and go test mean difference (95% CI) = 1.06 [0.68,1.44], $P < 0.0001$	Yang *et al.* (2014)

Table 1. (*Continued*)

Beneficial Effect	Studied Population	Outcome Indicator	Intervention/Experience	Reference
	Patients with MS	• Multiple balance and coordination tests includes single leg stand test and walk test in different situations	90 min per section, 2 sections per week, 6 months	Burschka *et al.* (2014)
	Patients with fibromyalgia	• Single leg stand test • Maximum reach test	90 min per section, 2 sections per week, 12 weeks, 8 forms of Yang style	Jones *et al.* (2012)
	Irradiated nasopharyngeal cancer survivors	• Single leg stand test with eye closed	Trained with 18 forms of Tai Chi Qigong for more than 6 months	Fong *et al.* (2014b)
	Female cancer survivors	• Single leg stand test • Multidirectional reach test • Habitual gait speed	60 min per section, 2 sections per week, 10 weeks	Reid-Arndt *et al.* (2012)
	Elderly	• Single leg stand test	60 min per section, 3 sections per week, 24 weeks	Li *et al.* (2004)
Motor Function and Exercise Capacity	Patients with COPD	• 6-min walk test	40 min per section, 3 sections per week, 6 months	Niu *et al.* (2014)
	Patients with COPD	• 6-min walk test	Meta-analysis summary: A total of 11 studies on 824 subjects Mean difference (95%CI) = 35.99 [15.63-56.35], $P < 0.0005$	Wu *et al.* (2014)
	Patients with chronic systolic heart failure	• Cardiac exercise self-efficacy instrument	60 min per section, 2 sections per week, 12 weeks	Yeh *et al.* (2011)
	Patients with chronic systolic heart failure	• 6-min walk test	50 min per section, 4 sections per week, 12 weeks, 10 forms of Yang style	Caminiti *et al.* (2011)
	Patients with MS	• FSMC	90 min per section, 2 sections per week, 6 months	Burschka *et al.* (2014)
	Patients with fibromyalgia	• 6-min walk test	60 min per section, 2 sections per week, 12 weeks, 10 forms of Yang style	Wang *et al.* (2010a)
	Patients with fibromyalgia	• Timed up and go test	90 min per section, 2 sections per week, 12 weeks, 8 forms of Yang style	Jones *et al.* (2012)

Table 1. (*Continued*)

Beneficial Effect	Studied Population	Outcome Indicator	Intervention/Experience	Reference
	Patients with peripheral neuropathy	• Timed up and go test • 6-min walk test	60 min per section, 3 sections per week, 24 weeks, 8 forms of Yang style	Li and Manor (2010)
	Female postmenopausal breast cancer survivors	• Fatigue symptom inventory	Two 60 min section and five 30 min sections per week for first 2 weeks, followed by one 60 min section and five 30 min sections per week for 10 weeks	Larkey *et al.* (2015)
	Nasopharyngeal cancer survivors	• 6-minute walk test	90 min per section, 1 sections per week, 6 months, 18 forms Tai Chi Qigong	Fong *et al.* (2014c)
	Female cancer survivors	• Timed up and go test • Five times sit to stand test	60 min per section, 2 sections per week, 10 weeks	Reid-Arndt *et al.* (2012)
	Elderly	• Timed chair rise test • 50-foot speed walk	60 min per section, 3 sections per week, 24 weeks	Li *et al.* (2004)
Lung Function	Patients with COPD	• Forced expiratory volume • Twitch oesophageal pressure • Twitch gastric pressure • Twitch transdiaphragmatic pressure	40 min per section, 3 sections per week, 6 months	Niu *et al.* (2014)
	Patients with COPD	• Dyspnea • Forced expiratory volume in 1s • Forced vital capacity	Meta-analysis summary: A total of 8 studies on 544 subjects Dyspnea mean difference (95%CI) = −0.86 [−1.44, −0.28], $P = 0.004$ FEV1 mean difference (95%CI) = 0.07 [0.02,0.13], $P = 0.01$ FVC mean difference (95%CI) = 0.12 [0.00, 0.23], $P = 0.04$	Yan *et al.* (2013)

Table 1. (*Continued*)

Beneficial Effect	Studied Population	Outcome Indicator	Intervention/Experience	Reference
Muscle Strength	Elderly women	• Extension strength of hip and knee	40 min per section, 6 sections per week, 12 months	Song *et al.* (2014)
	Female older adults with knee osteoarthritis	• Abdominal strength by number of sit-ups performed in 30 s	20 min per section, 3 sections per week, 12 weeks, 12 forms of Sun style	Song *et al.* (2003)
	Patients with chronic systolic heart failure	• Peak torque of the quadriceps muscles	50 min per section, 4 sections per week, 12 weeks, 10 forms of Yang style	Caminiti *et al.* (2011)
	Patients with peripheral neuropathy	• Knee extensor and flexor peak torque	60 min per section, 3 sections per week, 24 weeks, 8 forms of Yang style	Li and Manor (2010)
	Central obese adults with depression	• Number of stands in 30s	60–90 min per section, 3 sections per week, 12 weeks, Kaimai style	Liu *et al.* (2015)
Pain Relieve	Elderly with knee osteoarthritis	• Verbal descriptor Scale • Pain behaviors	20–40 min per section, 3 sections per week, 20 weeks, Sun style	Tsai *et al.* (2015)
	Female older adults with knee osteoarthritis	• K-WOMAC	20 min per section, 3 sections per week, 12 weeks, 12 forms of Sun style	Song *et al.* (2003)
	Patients with fibromyalgia	• Visual-analogue scale • Chronic plain self-efficacy scale	60 min per section, 2 sections per week, 12 weeks, 10 forms of Yang style	Wang *et al.* (2010a)
	Patients with fibromyalgia	• FIQ pain • Brief pain inventory • ASEQ for pain	90 min per section, 2 sections per week, 12 weeks, 8 forms of Yang style	Jones *et al.* (2012)
Metabolic Abnormality	Inactive adults	• Waist circumference • Fasting blood glucose	30 min per section, 5 sections per week, 12 weeks, 32 forms of Sun style	Hui *et al.* (2015)

Table 1. (*Continued*)

Beneficial Effect	**Studied Population**	**Outcome Indicator**	**Intervention/Experience**	**Reference**
	Adults with borderline hypertension	• Systolic blood pressure • Diastolic blood pressure • Blood HDL	50 min per section, 3 sections per week, 12 weeks, 108 forms of Yang style	Tsai *et al.* (2003)
	Patients with chronic systolic heart failure	• Systolic blood pressure	50 min per section, 4 sections per week, 12 weeks, 10 forms of Yang style	Caminiti *et al.* (2011)
Microcirculatory Function	Inactive elderly men	• Skin blood flow • Cutaneous vascular conductance • Skin temperature • VO_2 Max	54 min per section, 5.1 ± 1.8 sections per week, 11.2 ± 3.4 years, Yang style	Wang *et al.* (2001)
Cognitive Function	Female cancer survivors	• MASQ • Rey Auditory Verbal Learning Test • Trail Making Test A • Trail Making Test B • Stroop Test • Controlled Oral Word Association Test	60 min per section, 2 sections per week, 10 weeks	Reid-Arndt *et al.* (2012)
	Elderly with cognitive impairments	• MMSE • Digit Symbol-Coding Scores	20–40 min per section, 2 sections per week, 15 weeks, 12 forms of Sun style	Chang *et al.* (2011)
	Older adults	• Reaction time of task switching • P3 amplitude in brain	78.8 ± 15 min per section, 6.1 ± 1.2 sections per week, 13.6 ± 8.6 years, Yang style	Fong *et al.* (2014a)
	Elderly	• Trail Making Test A • Trail Making Test B	60 min per section, 2 sections per week, 6 months, 24 forms of Yang style	Nguyen and Kruse (2012)

Table 1. (*Continued*)

Beneficial Effect	Studied Population	Outcome Indicator	Intervention/Experience	Reference
Quality of Life	Patients with COPD	• SGRQ • CRQ	Meta-analysis summary: A total of 11 studies on 824 subjects SGRQ mean difference (95%CI) $= -10.02$ $[-17.59, -2.45]$, $P = 0.009$ CRQ mean difference (95%CI) $= 0.95$ $[0.22,1.67]$, $P = 0.01$	Wu *et al.* (2014)
	Patients with chronic systolic heart failure	• MLHFQ	60 min per section, 2 sections per week, 12 weeks	Yeh *et al.* (2011)
	Patients with MS	• Questionnaire of life satisfaction	90 min per section, 2 sections per week, 6 months	Burschka *et al.* (2014)
	Patients with fibromyalgia	• SF-36	60 min per section, 2 sections per week, 12 weeks, 10 forms of Yang style	Wang *et al.* (2010a)
	Elderly with MDD under escitalopram treatment	• SF-36	120 min per section, 1 sections per week, 10 weeks	Lavretsky *et al.* (2011)
	Patients with stable symptomatic chronic heart failure	• MLHFQ	55 min per section, 2 sections per week, 16 weeks	Barrow *et al.* (2007)
	Adults with functional class I or II rheumatoid arthritis	• Vitality subscale of SF-36	60 min per section, 2 sections per week, 12 weeks, Yang style	Wang (2008)
	Elderly	• SF-12 physical score	60 min per section, 3 sections per week, 24 weeks	Li *et al.* (2004)
Anxiety	Adults with borderline hypertension	• State-trait anxiety inventory	50 min per section, 3 sections per week, 12 weeks, 108 forms of Yang style	Tsai *et al.* (2003)
	Central obese adults with depression	• DASS anxiety score	60–90 min per section, 3 sections per week, 12 weeks, Kaimai style	Liu *et al.* (2015)

Table 1. (*Continued*)

Beneficial Effect	Studied Population	Outcome Indicator	Intervention/Experience	Reference
	Patients with stable symptomatic chronic heart failure	• SCL-90-R anxiety	55 min per section, 2 sections per week, 16 weeks	Barrow *et al.* (2007)
	Older adults with cerebral vascular disorder	• GHQ anxiety/insomnia	50 min per section, 1 sections per week, 12 weeks, Yang style	Wang *et al.* (2010b)
Depression	Patients with MS	• CES-D	90 min per section, 2 sections per week, 6 months	Burschka *et al.* (2014)
	Patients with fibromyalgia	• CES-D	60 min per section, 2 sections per week, 12 weeks, 10 forms of Yang style	Wang *et al.* (2010a)
	Female cancer survivors	• Impact of event scale-revised	60 min per section, 2 sections per week, 10 weeks	Reid-Arndt *et al.* (2012)
	Central obese adults with depression	• DASS depression score • CES-D	60–90 min per section, 3 sections per week, 12 weeks, Kaimai style	Liu *et al.* (2015)
	Elderly with MDD under escitalopram treatment	• Hamilton depression rating score	120 min per section, 1 sections per week, 10 weeks	Lavretsky *et al.* (2011)
	Patients with stable symptomatic chronic heart failure	• SCL-90-R depression	55 min per section, 2 sections per week, 16 weeks	Barrow *et al.* (2007)
	Adults with functional class I or II rheumatoid arthritis	• CES-D	60 min per section, 2 sections per week, 12 weeks, Yang style	Wang (2008)
	Older adults with cerebral vascular disorder	• severe depression	50 min per section, 1 sections per week, 12 weeks, Yang style	Wang *et al.* (2010b)
Insomnia	Patients with fibromyalgia	• PSQI	60 min per section, 2 sections per week, 12 weeks, 10 forms of Yang style	Wang *et al.* (2010a)

Table 1. (*Continued*)

Beneficial Effect	Studied Population	Outcome Indicator	Intervention/Experience	Reference
	Patients with fibromyalgia	• PSQI	90 min per section, 2 sections per week, 12 weeks, 8 forms of Yang style	Jones *et al.* (2012)
	Older adults with cerebral vascular disorder	• PSQI • GHQ anxiety/insomnia	50 min per section, 1 sections per week, 12 weeks, Yang style	Wang *et al.* (2010b)
	Elderly	• PSQI • ESS	60 min per section, 3 sections per week, 24 weeks	Li *et al.* (2004)
	Elderly	• PSQI	40 min per section, 3 sections per week, 16 weeks	Irwin *et al.* (2008)
	Elderly	• PSQI	60 min per section, 2 sections per week, 6 months, 24 forms of Yang style	Nguyen and Kruse (2012)
	Elderly	• PSQI	5 min per section in the first week, 5 min were added to each section per week until the fourth week, 25 min per section, 3 sections per week for the rest 8 weeks, 10 forms of Yang style	Hosseini *et al.* (2011)

Notes: COPD = chronic obstructive pulmonary disease; MS = multiple sclerosis; K-WOMAC = Korean version of the Western Ontario-McMaster Universities OA index; FSMC = Fatigue Scale of Motor and Cognitive Functions; CES-D = Center for Epidemiological Studies Depression Scale; DASS = Depression Anxiety Stress Scale 21; HDL = high-density lipoprotein cholesterol; SGRQ = St. George's Respiratory Questionnaire; CRQ = Chronic Respiratory Disease Questionnaire; MASQ = Multiple Abilities Self-Report Questionnaire; MLHFQ = Minnesota with Heart Failure Questionnaire; FIQ = Fibromyalgia Impact Questionnaire; ASEQ = Arthritis Self-Efficacy Questionnaire; SF-36 = Medical Outcome Study 36-item Short Form Health Survey; SF-12 = 12-item Short Form Health Survey MMSE = Mini Mental State Exam; MDD = unipolar major depressive disorder; SCL-90-R = Symptom CheckList-90-Revised; GHQ = General Health Questionnaire; PSQI = Pittsburgh Sleep Quality Index; ESS = Epworth Sleepiness Scale.

Table 2. Summary of Brain Regions Affected by Tai Chi and the Possible Beneficial Effects

Brain Region and Network	Function of this Region	Changes Induced by Tai Chi Intervention	Tai Chi Intervention/ Experience	Possible Related Beneficial Effects	Neuroimaging Technology	References
Total brain volume	General brain function	↑Intracranial volume of brain (∼47%)	50 min per section, 3 sections per week, 40 weeks	Cognitive functions	MRI	Mortimer *et al.* (2012)
Right precentral gyrus	Coordinate and plan for the voluntary movements	↑CT	14 ± 8 years of Tai Chi experience, 11 ± 3 hours per week, with styles included Yang, Wu, Sun and modified Chan	Gait and balance	MRI	Wei *et al.* (2013)
Right middle frontal sulcus	Short-term memory, theory of mind, evaluatierecency, plan, override automatics responses, calculation, analyze auditory information, infer intention and emotions of others, deducting information from spatial imagery	↑CT		Cognitive functions		
Left medial occipito-temporal sulcus	Process color and word information, face and body recognition	↑CT		Cognitive functions		
Left lingual sulcus	Visual memory, maintain visuo-limbo connection	↑CT		Cognitive functions		
Right inferior segment of the circular sulcus of insula	Sensory of emotions, sensory of inner body, generate appropriate body response to maintain homeostasis, pain sensation	↑CT		Pain management, moods, cognitive functions		

Table 2. (*Continued*)

Brain Region and Network	Function of this Region	Changes Induced by Tai Chi Intervention	Tai Chi Intervention/ Experience	Possible Related Beneficial Effects	Neuroimaging Technology	References
Left superior temporal gyrus	Social cognition, analyze face and auditory information, percept verbal and non-verbal information from others	↑CT	14 ± 8 years of Tai-Chi experience, 11 ± 3 hours per week, with styles included Yang, Wa, Sun and modified Chan	Cognitive functions	MRI	Wei *et al.* (2013)
		↑HGBOLD (∼16%)	Multiple interventions consist of 18 sections of 1 hour cognitive training, 18 sections of 1 hour Yang style 24-form Tai Chi training, 6 sections of 90 min group counseling		fMRI	Zheng *et al.* (2015)
Right postcentral gyrus	General body sensation	↑FH (Improved functional integration)	14.6 ± 8.6 years of Tai Chi experience, 11.9 ± 5.1 hours per week,	Gait and balance	fMRI	Wei *et al.* (2014)
Left anterior cingulate cortex	Cognitive regulation, pain management, emotional processing	↓FH (Improved functional specialization)		Cognitive functions, moods, pain management		

Table 2. (*Continued*)

Brain Region and Network	Function of this Region	Changes Induced by Tai Chi Intervention	Tai Chi Intervention/ Experience	Possible Related Beneficial Effects	Neuroimaging Technology	References
Right superior frontal cortex	Self-awareness, working memory, executive function,	↓FH (Improved functional specialization)		Cognitive functions		
Medial prefrontal cortex	Self-knowledge, familiar other-knowledge, social information processing, emotional processing, sadness suppression, morality	↑Resting state-FC with bilateral hippocampus	60 min per section, 5 sections per week, 12 weeks	Moods, cognitive functions	fMRI	Tao *et al.* (2017)
		↑Resting state-FC with medial temporal lobe	Multiple interventions consist of 18 sections of 60 min cognitive training, 18 sections of 1 hour Yang style 24-form Tai Chi training, 6 sections of 90 min group counseling		fMRI	Li *et al.* (2014)
Bilateral hippocampus	Learning, regulation of emotion, stress and memory	↑Resting state-FC with medial prefrontal cortex	60 min per section, 5 sections per week, 12 weeks	Moods, cognitive functions	fMRI	Tao *et al.* (2017)
Medial temporal lobe	Information processing, emotion processing, recollection and familiarity, recognition memory	↑Resting state-FC with medial prefrontal cortex		Cognitive functions		Li *et al.* (2014)

Table 2. (*Continued*)

Brain Region and Network	**Function of this Region**	**Changes Induced by Tai Chi Intervention**	**Tai Chi Intervention/ Experience**	**Possible Related Beneficial Effects**	**Neuroimaging Technology**	**References**
Middle temporal gyri	Face recognition, word processing	↓HGBOLD (∼7% for left side ∼10% for right side)	Multiple interventions consist of 18 sections of 1 hour cognitive training, 18 sections of 1 hour Yang style 24-form Tai Chi training, 6 sections of 90 min group counseling	Cognitive functions	fMRI	Zheng *et al.* (2015b)
Posterior cerebellum lobe	Coordination, precision and timing of motor functions	↑HGBOLD (∼10%)		Gait and balance		
Middle frontal gyrus	Executive function, Short-term memory, theory of mind, evaluate recency, plan, override automatics responses, calculation, analyze auditory information, infer intention and emotions of others, deducting information from spatial imagery	↑Resting state ALFF (∼13%)	Multiple interventions consist of 18 sections of 1 hour cognitive training, 18 sections of 1 hour Yang style 24-form Tai Chi training, 6 sections of 90 min group counseling	Cognitive functions	fMRI	Yin *et al.* (2014)

Table 2. (*Continued*)

Brain Region and Network	Function of this Region	Changes Induced by Tai Chi Intervention	Tai Chi Intervention/ Experience	Possible Related Beneficial Effects	Neuroimaging Technology	References
Superior frontal gyrus	Self-awareness, working memory, executive function	↑ Resting state ALFF (∼21%)		Cognitive functions		
Anterior cerebellum lobe	Coordination, precision and timing of motor function	↑Resting state ALFF (∼13%)		Gait and balance		
Default mode network	Self-generated cognition, social cognition, metalizing, memory retrieval.	↓Resting state fALFF (∼10%)	14.6 ± 8.6 years of Tai Chi experience, 11.9 ± 5.1 hours per week,	Cognitive functions, moods	fMRI	Wei *et al.* (2017)
Right lateralized frontoparietal network	Visual attention, visual capacity, attention control via the selection between spatial and non-spatial information, integration and control of cognitive representation	↓Resting state fALFF (∼10%)		Cognitive functions		
Left lateralized frontoparietal network	Visual attention, visual capacity, attention control via the selection between spatial and non-spatial information, integration and control of cognitive representation	↓Resting state fALFF (∼12%)		Cognitive functions		

Notes: CT = Cortex thickness; FH = functional homogeneity; FC = functional connectivity; HGBOLD = regional homogeneity of spontaneous fluctuations in the blood oxygen level-dependent signals; ALFF = amplitude of low frequency fluctuations; fALFF = fractional amplitude of low frequency fluctuations; ↑indicates increased; ↓indicates decreased.

homogeneities of postcentral gyrus and anterior cingulate cortex were correlated with the practical hours of Tai Chi training (Wei *et al.*, 2014). The decrease in the functional homogeneity of anterior cingulate cortex was negatively correlated with the log-transformed accuracy in the Attention Network Test. Other studies have also demonstrated that psychological-physical intervention, which consisted of TCC training, cognitive training and group counseling, altered the neurological activities in several brain regions (Li *et al.*, 2014; Yin *et al.*, 2014, Zheng *et al.*, 2015b). It has been demonstrated that the regional homogeneity of spontaneous fluctuations in the blood oxygen level-dependent signals (HGBOLD) in particular parts of the brain regions including left superior temporal gyri (increased by 16%), middle temporal gyri (decreased by 7% for left side and 10% for right side), and the posterior lobe of the cerebellum (increased by 10%) were altered after the psychological-physical intervention (Zheng *et al.*, 2015b). Furthermore, the psychological-physical intervention has been demonstrated to increase the resting state amplitude of the low frequency fluctuations (ALFF) in middle frontal gyrus (increased by 13%), superior frontal gyrus (increased by 21%) and anterior cerebellum lobe (increased by 13%) in elderly subjects (Yin *et al.*, 2014). These data suggested that TCC training might contribute to the increases in resting neurological activities in these brain regions and, hence, aid in improving the cognitive functioning and well-being of elders (Yin *et al.*, 2014). The functional connectivity between the medial prefrontal cortex and the parahippocampal cortex of the medial temporal lobe has been demonstrated to improved from -0.036 to 0.201 in healthy elders after receiving TCC-consisted psychological-physical intervention (Li *et al.*, 2014). Another recent study has demonstrated that 12 weeks of TCC training increased the resting state functional connectivity of bilateral hippocampus and medial prefrontal cortex (Tao *et al.*, 2017). The observations on the increased functional connectivities among these brain regions were associated with individual improvements in cognitive performance (Li *et al.*, 2014; Tao *et al.*, 2017).

Although it is well known that each brain region has its specified functions, it has been demonstrated that multiple brain regions, rather than a particular region, work coherently to perform a task (Wei *et al.*, 2017). Those brain regions that work coherently for task performance are regarded as a macro-scale brain network. Recent advancement in neuroimaging technology allows researchers to investigate macro-scale networks of the brain. Multiple networks in the human brain and their functions have been identified. A recent study has demonstrated that TCC training altered the resting state fractional amplitude of the low frequency fluctuations (fALFF) of the default mode network and the bilateralized frontoparietal network (Wei *et al.*, 2017). The resting state, fALFF, in the default mode network was shown to be 10% lower in people with long-term TCC training, compared with those who have never received TCC training (Wei *et al.*, 2017). The fALFF of left lateralized frontoparietal network and right lateralized frontoparietal network in experienced TCC practicers were observed to be 12% and 10% lower, respectively, compared with the people who had not practiced TCC (Wei *et al.*, 2017). Intriguingly, the TCC-induced change in fALFF of left lateralized frontoparietal network has been shown to be correlated with the performance of cognitive function (Wei *et al.*, 2017).

Potential Mechanisms Responsible for the Effects of Tai Chi Chuan through the Modulation of Brain Morphology, Functional Homogeneity and Connectivity, Regional Activity and Macro-scale Network Activity

Alterations of brain morphology, functional homogeneity and connectivity, regional activity and macro-scale network activity caused by TCC training might contribute to the underlying mechanisms of the observed beneficial effects of TCC on health consequences. In this section, we attempted to identify the possible links between the alterations in brain and beneficial effects of TCC.

Balance and Gait Performance

A systematic review has concluded that TCC intervention significantly improves flexibility and balance function in older adults (Huang and Liu, 2015). Increased cortical thickness of right precentral gyrus (Wei *et al.*, 2013) and elevated homogeneity of postcentral gyrus have been observed in long time TCC practicers (Wei *et al.*, 2014). Right precentral gyrus is the primary motor cortex that is responsible for coordinating and planning for voluntary movements of skeletal muscle, whereas the postcentral gyrus is the main sensory receptive brain area for the sense of touch. The coordination of timing and the amplitude of muscle responses to postural perturbations and the abilities of re-organizing sensory inputs and subsequently modify postural responses are two important aspects of balance control (Woollacott *et al.*, 1986). Improvement of the sensation of touch can thus provide more concise information to the brain in how to react and how to coordinate the muscles for better balance control. The TCC-associated increase in the cortical thickness of the right precentral gyrus (Wei *et al.*, 2013) and functional homogeneity of postcentral gyrus (Wei *et al.*, 2014) might be a possible mechanism to strengthen the coordination and planning of voluntary movement of brain. The cerebellum might be another brain region that is involved in the mechanism behind TCC-induced improvement in balance and gait. The cerebellum is known to be responsible for coordination, precision, and timing of motor functions. The increases in the basal activities of anterior cerebellum lobe (Yin *et al.*, 2014) and posterior cerebellum lobe (Zheng *et al.*, 2015b) after TCC-consisted psychological-physical intervention might lead to better functioning of cerebellum, and thus contribute to the better performance of balance and gait in TCC practicers. Further research is needed to confirm the involvement of these alterations in the brain in terms of the beneficial effects of TCC on balance and gait.

Metabolic Parameters

Metabolic syndrome refers to a sub-healthy condition consisting of a cluster of metabolic abnormalities including high blood pressure, central obesity, reduced blood high-density lipoprotein (HDL) cholesterol, elevated fasting blood glucose, and high blood triglyceride (Alberti and Zimmet, 1998). People with metabolic syndrome are more susceptible to the development of cardiovascular diseases, diabetes mellitus, and some cancers (Alberti and

Zimmet, 1998). TCC could be a possible intervention to prevent metabolic syndrome as it could elicit cardiorespiratory responses and energy expenditure to the level of moderate-intensity activity, which is associated with a reduced risk of developing metabolic syndrome. Previous studies have demonstrated that TCC intervention decreased systolic and diastolic blood pressure, blood triglyceride, low-density lipoprotein (LDL) cholesterol, postprandial blood glucose, fasting blood glucose, and increased HDL cholesterol (Hui *et al.*, 2015; Tsai *et al.*, 2003). However, it is known that TCC is an exercise with slow movement and moderate intensity, which might not be sufficient to dramatically alter metabolic rate. Thus, it is speculated that TCC might improve the metabolic parameters by an alternative mechanism. It has been demonstrated that the cortex of the inferior segment of the circular sulcus of insula is thickened in people with long-term TCC training (Wei *et al.*, 2013). The insular lobe is related to the sensory function of inner body (de Araujo *et al.*, 2012). It integrates information related to bodily states and instructs the body to generate appropriate responses such as food intake, blood pressure changes, and autonomic function, to maintain the homeostasis of the body (de Araujo *et al.*, 2012). Alteration in the thickness of inferior segment of the circular sulcus of insula might be a part of behind mechanism of TCC to improve the metabolic parameters. The thickening of the inferior segment of the circular sulcus of insula induced by TCC might result in improvement of the recognition of inner body status, and serves as a possible mechanism of how TCC adjusts metabolic parameters. Nonetheless, additional research studies are needed to confirm the link between TCC and metabolic adaptation via the modulation of circular sulcus of insula.

Pain Relief

Knee arthritis and low back pain can be caused by prolonged inappropriate posture and exertion habits. TCC has been reported to relieve pain in patients with knee osteoarthritis and chronic low back pain (Song *et al.*, 2003; Tsai *et al.*, 2015). Apart from the fact that TCC training corrects the exertion posture and strengthens the muscles of practicers in order to relieve pain, it is possible that the pain-relieving effect of TCC is attributed to the alteration of the brain activity induced by TCC training. Anterior cingulate cortex is a multi-functional brain region with registration on physical pain as one of the functions (Gu *et al.*, 2015). Moreover, the insular cortex has been demonstrated to be involved in the sensory processing of pain information, and is involved in modulating cognitive-evaluative, affective and sensory discriminative dimensions of pain by utilizing the cognitive information provided by other brain regions (Starr *et al.*, 2009). Increase in cortical thickness of the inferior segment of the circular sulcus of insula (Wei *et al.*, 2013), together with a decrease in functional homogeneity of the left anterior cingulate cortex has been observed in people under long-term TCC training (Wei *et al.*, 2014). The alterations of these brain regions might be involved in the mechanism behind TCC-mediated pain management. A previous study has suggested that inhibition of anterior cingulate cortex might help to relieve chronic pain (Gu *et al.*, 2015). It is possible that the improved functional specialization of anterior cingulate cortex after TCC training might contribute to better pain management and thus accounts for the pain-relieving effects of TCC. The insular cortex has been reported to be involved in pain perception, modulation and chronification (Lu *et al.*, 2016). The increase in cortical thickness of insula observed in long-term TCC practicers might also aid in improving pain management and reliving pain via a better processing of pain-related cognitive information. Further research on the direct correlation between perceived pain and the TCC-mediated changes on these brain regions is needed to unmask the mechanism behind the TCC-mediated pain alleviation.

Insomnia

Sleep complaints including difficulties in falling asleep, waking up during the sleeping period, awaking too early, and chronic insomnia are common sleep problems found in older adults (Foley *et al.*, 1995). It is estimated that sleep complaints exist in more than 50% of elders around the world (Foley *et al.*, 1995). About 20–40% of the elders worldwide have been diagnosed with chronic insomnia (Schubert *et al.*, 2002). The high morbidity of sleep impairments is an alarming public health issue since sleep disorder has been shown to be associated with impaired cognitive function and memory, reduction of attention span, increase in response time, anxiety, depression, risks of falls, hypertension, and heart diseases (Schubert *et al.*, 2002). TCC has been demonstrated to be beneficial in alleviating sleep complaints (Irwin *et al.*, 2008). Research studies have been conducted to reveal the differences in the brain structures of healthy controls and insomniac patients. The volume of the hippocampus (Riemann *et al.*, 2007) and the grey matter concentration in orbital frontal cortex have been shown to be decreased in patients with chronic insomnia when compared to non-insomniac people (Joo *et al.*, 2013). In contrast, the volume of rostral anterior cingulate cortex has been shown to be increased in patients with chronic insomnia (Winkelman *et a.*, 2013). There is currently no direct measurement reporting that TCC improves sleep, or alleviates sleep complaints and insomnia by altering the structure of the brain, however the brain regions that are involved in mindfulness meditation-induced improvement in insomnia have been reported. As meditation is regarded as an essential part of TCC training, those brain regions that are altered by meditation might provide clues to unmask the mechanisms behind the effects of TCC on improving sleep. It has been reported that mindfulness meditation increased the volume of hippocampus (Holzel *et al.*, 2011) and the grey matter concentration in orbital frontal cortex (Luders *et al.*, 2009). It is possible that TCC might improve insomnia by inducing similar changes in the brain. Indeed, several studies have reported that alterations of brain regions related to insomnia have been observed in people received TCC training. The decrease in the homogeneity of anterior cingulate cortex has been observed in long-term TCC practicers (Wei *et al.*, 2014). A recent study has demonstrated that the resting functional connectivity between bilateral hippocampus and prefrontal cortex was significantly increased after TCC training (Tao *et al.*, 2017). Although the alterations caused by TCC on those brain regions were not directly opposing the changes in brain observed in insomniac patients, alteration of those insomnia-related brain regions induced by TCC might be the possible mechanism that contributes to the sleep improvement.

Apart from the changes in morphology and activity, an altered pattern of functional connectivity in sub-regions of default mode network has been observed in insomniac patients' brains (Nie *et al.*, 2015). The functional connectivity between prefrontal cortex and right medial temporal lobe, and between left medial temporal lobe and left inferior parietal cortices have been demonstrated to be decreased in insomniac patients (Nie *et al.*, 2015). A previous study has shown that TCC-consisted psychological-physical intervention significantly increased the functional connectivity between medial prefrontal cortex and medial temporal lobe (Li *et al.*, 2014). The opposing change in the functional connectivity between prefrontal cortex and medial temporal lobe observed in insomniac patients and people trained with TCC-consisted psychological-physical intervention might imply that the modulation of functional connectivity between these two brain regions could be parts of the possible mechanisms for TCC to improve sleep. Of note, different diseases — Alzheimer's disease, depression, and schizophrenia — are related to decreased or disrupted functional connectivity. TCC might be a possible intervention for normalizing the resting functional connectivity in these diseases, as well as, insomnia. However, further research is needed to identify the involvement of brain alteration induced by TCC in alleviating sleep complaints.

Cognitive Function

Cognitive function includes a range of functionalities such as memory, information processing, learning ability, speech, and reading. Cognitive impairment is a common problem that affects the self-care ability and quality of life of elderly population (Leroi *et al.*, 2012). Elders with cognitive impairment might have impaired memory, unreasonable action, and fluctuated emotion, which generate a lot of stress to their caregivers (Leroi *et al.*, 2012). TCC has been demonstrated to prevent the decline in cognitive function as reflected by the findings that TCC practicers have a higher score in Mini Mental State Exam and Digit Symbol-Coding Score (Chang *et al.*, 2011), a shorter task-switching reaction time (Fong *et al.*, 2014a), and better immediate memory, attention and verbal fluency (Reid-Arndt *et al.*, 2012).

In fact, a number of the brain regions that are related to cognitive functions have been demonstrated to be responsive to TCC training. Increases in cortical thickness in several brain regions that contribute to cognitive function, including middle frontal sulcus, inferior segment of the circular sulcus of insula, superior temporal gyrus, middle frontal sulcus, occipitotemporal sulcus and lingual gyrus, have been observed in long-term TCC practicers (Wei *et al.*, 2013). Middle frontal sulcus is responsible for internal thought processing including short-term memory, recognition, theory of mind, evaluating recency, planning, overriding automatics responses, and calculation. It is also involved in the analysis of auditory information by controlling and sustaining auditory verbal attention for auditory stimuli. Insula cortex is involved in generating emotional senses (Starr *et al.*, 2009). Besides insula and middle frontal sulcus, superior temporal gyrus is another region of the brain that processes information of emotion from facial stimuli and analyzes the changeable characteristics in face and auditory stimuli to percept both verbal and non-verbal information from other individuals. Right middle frontal sulcus infers the intention and emotions of others, and deducts information from spatial imagery. The occipitotemporal sulcus processes color and word information and is also involved in face and body recognition. Lingual gyrus is involved in processing vision information for face and word recognition. Previous study has demonstrated that damage in lingual gyrus can lead to visual memory dysfunction and visuo-limbo disconnection, resulting in the impairment of motivation, memory, learning ability, and emotional control. The reported thickening of these aforementioned cortices in the brain regions induced by TCC might possibly strengthen the functionality of those regions and resulted in the observed improvements in memory, calculation, emotion sensory, theory of mind, auditory processing, recognition, and social cognition.

Apart from causing morphological changes in the brain, the functional connectivity between prefrontal cortex and medial temporal lobe has been observed to be increased after TCC-consisted psychological-physical intervention (Li *et al.*, 2014), while the functional connectivity between prefrontal cortex and bilaterial hippocampus was increased after 12 weeks of TCC training (Tao *et al.*, 2017). Importantly, the increases in functional connectivity of these regions are associated with the improvement of cognitive function. Prefrontal cortex is involved in cognitive control processes including decision-making, memory, performance monitoring and response inhibition while medial temporal lobe is associated with information processing, emotion processing, storage and retrieval of long term memories (Simons and Spiers, 2003). It has been suggested that the prefrontal cortex and temporal lobe work together in the remembering process (Simons and Spiers, 2003). Therefore, increase in functional connectivity between prefrontal cortex and medial temporal lobe might possibly imply a better performance in memory. The major role in conducting cognitive processes, including spatial information processing, temporal sequencing, formulation of the relationships between objects in the environment, learning, regulation of memory, emotion and stress, has made hippocampus an important brain region for cognitive function. The increase in the functional connectivity between prefrontal cortex and bilateral hippocampus might improve cognitive function by facilitating the logic processing and decision-making. Taken together, the modulation of the functional connectivity between these brain regions might be a possible mechanism of TCC that strengthens the cognitive function of the practicers. Apart from considering specific regions with specialized function, it has been demonstrated that the interplay between different brain regions might also contribute to the improved functional performance of the brain (Wei *et al.*, 2017). A recent study has demonstrated that fALFF in default mode network and bilateral frontoparietal network of experienced Tai Chi practicers are significantly lower compared with people without experience in mind-body exercise (Weible *et al.*, 2017). The default mode network consists of brain regions that relate to self-generated cognition, social cognition, mentalizing (Andrews-Hanna *et al.*, 2014), while the bilateral frontoparietal network consists of regions for visual attention and attention control (Scolari *et al.*, 2015). Notably, association between cognitive control function and alteration of fALFF of left frontoparietal network has been demonstrated (Weible *et al.*, 2017). In light of the alterations in activities of the macro-scale network that related to cognitive functions, it is speculated that TCC-induced modulation of the activity of macro-scale brain networks might be a part of behind mechanism of improving cognitive function.

Mood

As a traditional martial art, TCC requires practicers to relax their body in order to achieve fast reaction and quick movement for combating. It is mentioned in the traditional TCC literature that mental relaxation is a critical step for achieving the relaxation status of the body. Current researches have reviewed that mental relaxation and improvement in anxiety and depression can be achieved by mindfulness meditation intervention (Hofmann *et al.*, 2010). Thus, meditation, as an essential component of TCC, is believed to be a major contributor to the TCC favorable effects on alleviating anxiety, depression and mood disorder in different populations (Huston and McFarlane, 2016). The insula, thalamus, striatum, anterior cingulate cortex and amygdala are the brain regions that relate to anxiety (Gold *et al.*, 2015). The ventral hippocampus is also reported to be involved in emotional memory and anxiety due to its connection to the amygdala, hypothalamus and prefrontal cortex (Leuner and Gould, 2010). A previous study has demonstrated the role of insular cortex, anterior cingulate cortex and medial prefrontal cortex in emotional processing (Critchley *et al.*, 2004; Etkin *et al.*, 2011). Insula generates emotionally relevant contexts, such as emotional pain, happiness and sadness (Critchley *et al.*, 2004). The medial prefrontal cortex plays a role in increasing the attention of positive emotions and suppressing sadness, while both anterior cingulate cortex and medial prefrontal cortex have been suggested to be involved in emotional processing, especially in fear and anxiety (Etkin *et al.*, 2011). Both anterior cingulate cortex and medial prefrontal cortex work together to process fear memory and emotional conflict (Etkin *et al.*, 2011). Meditation has been previously reported to alleviate depression and anxiety via the modulation of functional connectivity between dorsal anterior cingulate cortex and insular cortex (Yang *et al.*, 2016). A recent study has employed an optogenetic technique to mimic meditation intervention on animals and has demonstrated that alleviation of anxiety can be achieved by modulating the activity of anterior cingulate cortex (Weible *et al.*, 2017). It is possible that TCC might share a similar mechanism (i.e., alteration of brain structure, activity and homogeneity) to achieve the reported favorable effects on mood. Indeed, previous studies have shown that TCC intervention altered the cortex thickness and function connectivity of some aforementioned emotion-related brain regions. Increased thickness of the right inferior segment of the circular sulcus of insula (Wei *et al.*, 2013) and improved functional specialization in anterior cingulate cortex are observed in experienced TCC practicers (Wei *et al.*, 2014). The thickening of the cortex of inferior segment of the circular sulcus of insula and improved functional specialization in anterior cingulate cortex might associate with a better emotional processing, recognition and adjustment and thus alleviate the mood disorders. However, further research is needed to confirm the association of the alleviation of mood disorders and the TCC-induced alterations in brain. In addition, the resting-state functional connectivity between medial prefrontal cortex and bilateral hippocampus has been shown to be increased after TCC training (Tao *et al.*, 2017). As mentioned in the above section, prefrontal cortex is involved in the regulation of memory (Simons and Spiers, 2003), while hippocampus is involved in regulation of both memory and emotion. The increase in the functional connectivity among these brain regions might improve the emotion processing by linking up the current emotion with previous events. These alterations in the brain caused by TCC might improve the ability of the practicers in dealing with negative emotion, and thus alleviate the moods disorders. Further investigation is needed to confirm whether these TCC-mediated alterations on brain are associated with the alleviation of mood disorders.

Limitation, Future Perspectives and Conclusion

TCC is a traditional Chinese martial art that is comprised of meditation and physical conditioning. The health favoring effects of TCC have been widely recognized. The exercise intensity of TCC is moderate and this makes it very accessible to different populations especially elderly individuals. There are numbers of studies demonstrating the beneficial effects of TCC exercise on various health aspects in a wide range of different populations. Altering brain morphologies and neural activities probably contribute to the underlying mechanisms of the beneficial effects of TCC on health. With the advanced technology of neuroimaging, the effects of TCC on the brain have been preliminarily investigated and revealed. In this review, we attempted to explore the possible mechanisms underlying the beneficial effects of TCC by matching the effects of TCC with the neurological changes in the brain as revealed by neuroimaging technology. However, it should be noticed that there are several limitations in this review. Firstly, although the number of TCC studies related to changes in brain morphology and neural activity has been increasing, the relatively small amount of studies may limit our discussion. Secondly, all of the available studies demonstrating the effects of TCC on brain are conducted in a relatively small scale (i.e., $\sim$20 participants in each intervention group). Large-scale randomized control trials are warranted to confirm the effects of TCC on the brain morphology, connectivity and activity of particular regions and macro-networks, and the association between the TCC-induced changes in brain and the beneficial effects. It should also be noted that three of the eight available studies demonstrating the effects of TCC on brain were using a TCC-consisted psychological-physical intervention protocol rather than TCC-alone intervention. It is possible that the non-TCC element (i.e., cognitive training or group counseling) in TCC-consisted psychological-physical intervention protocol may have contributed to the discussed morphological changes of the brain.

In the future, the effects of TCC on the prevention of neurodegeneration and the promotion of neuroprotection and the cellular activities in different parts of the brain involved in these effects should be comprehensively investigated. Data collected from multiple levels by using different techniques including functional neuroimaging, molecular biology techniques, neuropsychological tests and physiological measurements should be a promising strategy to fully uncover the mechanisms and the effects of TCC on the human brain and health.

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