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Review Article

Effects of Tai Chi Practice on Brain as Assessed with Neuroimaging Techniques – A Scoping Review

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Abstract

Introduction: Tai Chi (TC) has been often prescribed by geriatric clinicians to patients with a variety of neurological disorders. In the last 10 years, there has been an increase in the number of studies examining the effects of TC on brain morphology as assessed by neuroimaging including near infrared spectroscopy (NIRS) and structure and functional magnetic resonating imaging (sMRI & fMRI). Thus, the purpose of this scoping review is to evaluate how TC practice may affect the brain morphologically as assessed by neuroimaging techniques.

Methods: A comprehensive literature search was conducted using a variety of key words with different search engines to search from the last 10 years until May 2022. Studies were included if they investigated topographic brain responses after TC practice. A total of 24 original studies met the criteria and were included for the review process.

Results: The results showed increased oxygenation and volume of cortical grey matter, improved neural activity, and altered neural connectivity and homogeneity within and/or between different neural regions. These regions include the frontal, parietal, temporal, occipital lobes, cerebellum, basal ganglia, and/or limbic system. Such neural findings after TC practice are often associated with neurobehavioral improvements in cognition, memory, emotion, and functional integration and/or specialization.

Conclusions: TC is a promising exercise that is able to improve morphological capability and neurofunctional activity in the brain in both healthy people and patients with different medical diagnoses.

Keywords: *TC exercise, Brain, Neuroimaging, Rehabilitation*

Introduction

Clinically, mind-body exercises are frequently recommended by clinicians and mental health counselors among which Tai Chi (TC) is one of the most commonly used one [1]. As an ancient Chinese Martial art, TC integrates breathing, meditation, and body movement to achieve a great sense of inner peace and well-being in a calm, relaxed, and meditative way. During TC practice, the practitioner shifts their body weight or makes steps from one leg to the other through its coordinated and controlled slow, gentle, and graceful movements that emphasize smooth rotation of the trunk and arms as well as coordination between breathing and body part movements [2-4]. Its intensity is moderate and approximately equivalent to a walking speed of 6 kilometers or 3.7 miles per hour [5], but the intensity can vary depending on the training style, performance posture, and exercise parameters [6].

Currently, TC is recognized as an effective intervention for improving health, increasing physical performance and social participation, preventing falls, and enhancing posture for both the general population and for patients with neurological dysfunctions [1,2,5]. For example, TC has played a significant role in the recovery of patients who suffered from stroke, Parkinson disease, traumatic brain injury, and multiple sclerosis [6,7]. Because of its beneficial effects on health promotion and improvement of human dysfunctions including neurological disorders, TC has been considered as one of the most promising exercise programs that people with neurological diagnoses can practice to improve their physical and mental conditions [1,6]. Extensive research studies have demonstrated the beneficial effects of TC programs on different aspects, including flexibility, range of motion, muscle tone, strength, posture, balance, walking, psychological well-being, stress reduction, and quality of life [1,6].

In the last decade, an increasing number of studies have been conducted to investigate whether and how the human brain might respond to TC practice, assessed by using a variety of neuroimaging techniques which include the following. Functional near-infrared spectroscopy (FNIRS) is a cost-effective, wearable neuro-imaging technology that can safely assess the real-time brain activity during physical performance by monitor the hemodynamic response in the brain cortex using near-infrared light sources and detectors placed over the scalp of an individual [8]. Structural magnetic resonance imaging (sMRI) is a non-invasive imaging technique that can examine the morphological characterization of the brain in normal or pathological conditions [9]. Functional Magnetic Resonance Imaging (fMRI) is an imaging technique often used to assess two or more different states in an experimental functional condition in comparison to a control condition [10]. Magnetic resonance spectroscopy (MRS) is a companion MRI technique that is often used to non-invasively measure and evaluate the concentrations of different chemical components of the scanned tissue, and consequently provides metabolic and biochemical information within the tissues [11]. Also in fMRI, the voxel-mirrored homotopic connectivity (VMHC) is a method of resting state fMRI that is designed to directly compare the interhemispheric resting-state functional connectivity of two brain hemispheres and can be used to enquire and analyze functional homotopic (geometrically corresponding) connectivity and functional integration (↑VMHC) or specialization (↓VMHC) in each hemisphere or between two hemispheres [12]. Regional homogeneity (ReHo) and fractional amplitude of low-frequency fluctuations (fALFF), two different resting state fMRI parameter maps, have been introduced as well to study the brain. fMRI (ReHo) can be used to assess functional homogeneity between neural regions; increased homogeneity indicates improved functional integration, while decreased homogeneity indicates increased functional specialization between neural structures [10,12]. Further, fMRI (fALFF) can be used to assess local spontaneous neural activity of the brain [10,12].

Therefore, the purpose of this literature article was to review and examine if TC exercise might affect the brain as assessed through these neuroimaging techniques, and consequently to help healthcare professionals understand the possible implication of TC's effect on morphology and neural activity of the human brain.

Methods

Search Strategy

TC-related literature that investigated TC's effects on morphological responses of the brain was searched. The following sources were included in the literature search process: Pubmed, Scopus, Medline (US National Library of Medicine), the Physiotherapy Evidence Database (PEDro), the Cochrane Controlled Trials Register (Cochrane Library), Cumulative Index of Nursing and Allied Health Literature (CINAHL), and the oversea English version of China National Knowledge Infrastructure (CNKI), up to May 2022. The search strategy used the following keywords and variations: Tai Ji, TC, TCh, TC Quan, Tai Ji Quan, Tai Ji Chuan, Chinese martial arts, Chinese fitness exercise, neuroimaging, functional near-infrared spectroscopy (FNIRS), magnetic resonance spectroscopy (MRS), magnetic resonance imaging (MRI), voxel-mirrored homotopic connectivity (VMHC), fMRI Regional homogeneity (ReHo), and fractional amplitude of low-frequency fluctuations (fALFF). Published reviews and all relevant studies and their reference lists were also reviewed manually in search for other pertinent publications.

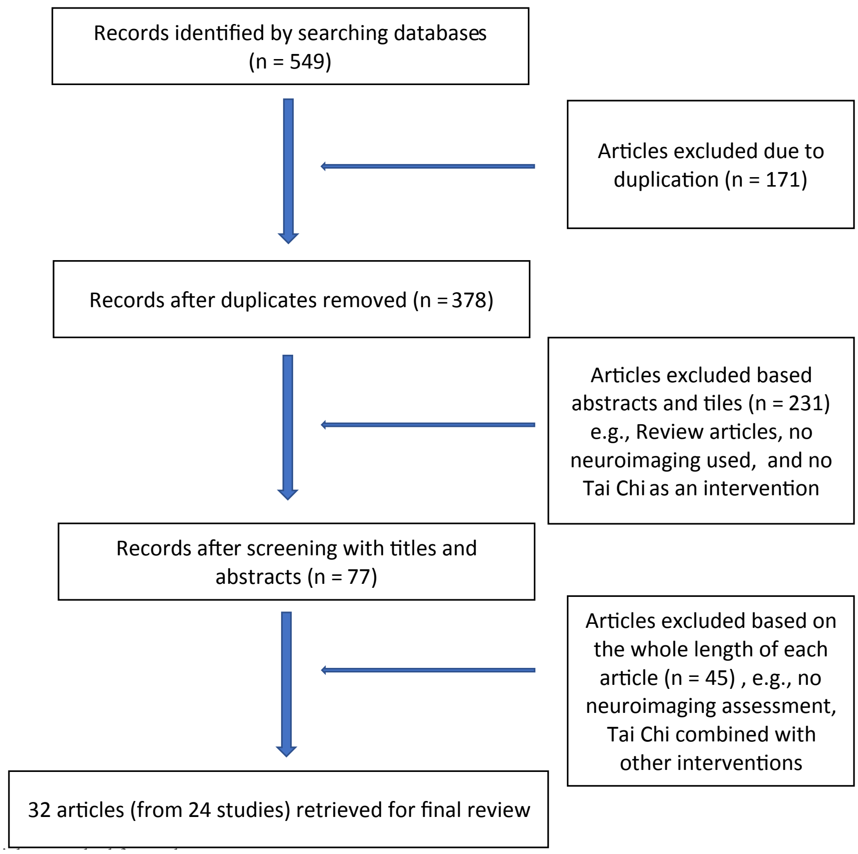

Figure 1: Flow chart of articles searched for analyses.

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Study Selection

Studies identified in the search were screened for inclusion. Articles that met the following criteria were selected: (1) studies investigating the effects of TC on brain response; (2) studies assessing the responses with FNIRS, sMRI, fMRI, MRS, and/or VHMC as the primary results; (3) participants were adults (age ≥18 years or older); (4) randomized control trials, single-group pre- and post- comparison, and cross-sectional studies comparing TC practitioners and non-practitioners; and (5) studies published in peer-reviewed English or Chinese journals from last 10 years until May 2022.

Data Extraction

Initially, all identified articles were assessed independently by two reviewers by scanning the titles and abstracts to determine whether it met the predetermined eligibility criteria. When there was uncertainty or disagreement between the two reviewers, the lead author was involved in the discussion until a consensus decision was reached. Data extracted from each of these studies included study design, participant characteristics, exercise program characteristics, neuroimaging techniques, and morphological changes identified by these techniques.

Quality Assessment

The quality of all studies in this scoping review were assessed based on the type of study. Physiotherapy Evidence Database (PEDro) scale was used for randomized controlled trials [13]. Newcastle–Ottawa Scale (NOS) was conducted for cohort or cross-sectional studies [14].

Data Analysis

Study designs, participants' characteristics, TC interventional parameters, neuroimaging, neurobehavior, and other functional assessments were all shown in Table 1. As the purpose of this review was to discuss TC's effects on brain morphology changes in humans, neuroimaging data and their associations with neuroimaging changes in these included studies were extracted, summarized, and synthesized in Tables 2-4.

Table 1: Tai Chi Studies Assessed with Neuroimaging Techniques.

Authors	Research Design	Subjects	Interventional Parameters	Assessment instruments	Quality Assessment
Shen, Watkins, Kahathuduwa, et al (2022)[15]	Single group Pre-and post-comparison	12 postmenopausal females with osteoarthritis, 40-50 yrs old	Yang style 24 forms, 60 mins, 3/wk for 8 wks	rs-fMRI, Pain Visual analog scale, WOMAC, plasma metabolites	6/10
Cui, Tao, Yin et al (2021)[16]	RCT	36 young healthy adults (18-25 y.o): 12 in each of 3 groups: TC, brisk walking, and usual care (as control	TC: Bafa Wubu,, 50-60 mins, 3/wk for 8 wks	rs-fMRI, Pain Visual analog scale, WOMAC, plasma metabolites	8/11
Kong, Huang, Liu et al, (2021) [17]	RCT	IG – 24 with fibromyalgia CG – 24 health subjects All subjects> 21 years old	TC; Yang style, 10 forms 60 mins each, 2/wk for 12 wks	fMRI More-odd shifting task for cognitive flexibility	6/11
Shen, Yin, Cui, et al, (2021)[18]	RCT	IG – n=12, TC (Yang style, 24 forms) CG – n=12, brisk walking Young health adults (<25 y.o)	50-60 mins, 3/wk for 8 wks	fMRI and modified Flanker Test	7/11
Xu, Zimmerman, Lazae et al (2020) [19]	Single group Pre-and post-comparison	16 adult patients with major depression	60 min each, 2/wk for 10 wks	fMRI Beck Depression Inventory SF-36	5/10
Adcock, Fankhauser et al (2020) [20]	RCT	IG – n =15 (77±6.4 y.o.) • CG – n=16 (70.9±5.0 y.o.) • All healthy elderly individuals	IG – TC + dancing +step-based cognitive games at home; 3/wk, 30-40 min each for 16 wks • CG – normal daily living	sMRI Victoria Stroop test for cognition • Trail Making test for psychomotor speed and executive function; • Wechsler Memory Scale for memory	7/11**
Yue, Zou, Mei et al (2020) [21] Yue, Yu, Zhang et al (2020) [22]	Cross-sectional	42 healthy elderly females • IG – TC, n=20 (62.9±2.38 y.o.) • CG – walking. n=22, (63.27±3.58 y.o.) • 90 min/each, 5/week, over 6 yrs	NA	fMRI (VHMC)	7/10*
Chen et al (2020) [23]	Cross-sectional	TC – 22 (aged: 52.4 ±6.8; TC experience 14.6±8.6 y.o.; Control – 18 (aged: 54.8 ±6.8) All healthy adults	NA	fMRI Attention network test (ANT)	8/10*
Yang, Chen, Shao et al (2020) [24]	RCT	13 TC vs 13 Control All healthy elderly individuals	TC: 45 min/each, 3/wk, for 8 wks Yang style, 24-form Control: routine and general daily activity	fNIRS Flanker task test	8/11**
Cui, Yin, Lyu et al (2019) [25]	RCT with 3 groups	36 young healthy college students (18-25 y.o.): TC: 12 Brisk walking: 12 Control: 12	IG1 - TC: 8 hand movement techniques and 5 TC foot-works based on Yang-style TC. IG2 – brisk walking Both TC and brisk walking groups: 60 min/each, 3/wk for 8 wks CG - routine daily activities	sMRI and fMRI	9/11**

Tsang et al (2019) [26]	Cross-sectional	8 practitioners (over 7 years of experience) and 8 non-practitioners All: 60-75 y.o.	NA	fNIRS	6/10*
Liu, Chen, Chen et al, (2019) [27] Liu, Chen, Tu et al (2019) [28]	RCT	IG1 - TC – n = 28 IG2 - BDJ – n = 29 IG3 - Stationary bike – n=27 CG - Health ed – n = 24 All (n = 108) 40-70 y.o.	60 min each, 5/wk for 12 wks	sMRI and fMRI Knee injury and osteoarthritis outcome score (KOOS)	7/11**
Xie, et al (2019) [29]	Cross-sectional	32 ordinary vs 25 long-term (>5 years) Chen-style TC practitioners (all 60-70 y.o.)	NA	fNIRS	7/10*
Liu, Li, Liu, Sun et al (2020) [30] Liu Li, Liu, Guo et al (2019) [31]	Cross-sectional	52 community-dwelling older adults (60-70 y.o.) IG - TC – 26 (10 years or more TC experience) VG - 26 (non-TC practitioners, but matched in physical activity level)	Both groups were asked to accomplish a sequential risk-taking task	sMRI and fMRI Beck Depression inventory NEO five-factor inventory Five facets mindfulness questionnaire, Mindful Attention Awareness Scale Barratt Impulsiveness Scale	9/10*
Kong et al (2019) [32]	RCT	21 patients with fibromyalgia (± 21 y.o.) 20 healthy matched participants	TC – 60 min/each, 2/wk, 12 wks, Yang style CG – no TC experience	fMRI Fibromyalgia Impact questionnaire (FIQR)	6/11**
Wu, Tang, Goh et al (2018) [33]	RCT	Community living older adults (60-69 y.o.) IG – n = 16 CG – n = 10	TC: 60 min each, 3/wk, 12 wks; Yang (10 min warm-up and 10 min cool down) CG – telephone consultation biweekly without changing lifestyle	fMRI	7/11**
Port, Santaella et al (2018) [34]	Cross-sectional	8 TC practitioners (>60 y.o.) 8 water aerobics practitioners (> 60 y.o.)	NA	fMRI during attention time • Stroop Word Color Task – SWCT • Working memory with N-back task	7/10*
Zhou, Liao, Sreepada et al (2018) [35]	Single group pre-and post-comparison	6 healthy elderly individuals (> 55 y.o.)	TC: 60 min each, ≥ 2/wk, 12 wks	MRS NAA: N-acetylaspartate; Cr: creatine PCr: phosphocreatine	5/10*
Liu, Wu, Li, Guo (2018) [36]	Cross-sectional	IG – TC, n = 26 (10.44±5.48 yrs TC experience) (65.19±2.30 y.o.) CG – matched group (63.92±2.87 y.o.) (no TC experience)	NA	fMRI	8/10*
Wei et al (2017) [37] Wei, Dong, Yang et al (2014) [38] Wei, Xu, Fan et al (2013) [39]	Cross-sectional	IG – TC, n = 22 (aged: 52.4 ±6.8; TC experience 14.6±8.6 years; CG – n = 18 (aged: 54.8 ±6.8)	NA	sMRI and fMRI Attention network test (ANT)	7/10*
Tao, Liu, Liu et al (2017) [40] Tao, Chen, Liu et al (2017) [41] Tao, Liu, Egorova et al (2016) [42]	RCT	TC-21 (62.38±4.55 y.o.) BDJ-15 (62.33±3.88 y.o.) CG - 25 (59.76±4.83 y.o.)	IG1 - TC: 60min, 5/wk, 12 wks; Yang-style, 24-form IG2 - BDJ: 60min, 5/wk, 12 wks; CG - health education	sMRI and fMRI (fALFF) Wechsler Memory Scale (WMS)	9/11**
Zheng et al (2015) [43]	RCT	Community dwellers IG – n = 17 (68.59 y.o.) CG – n = 17 (71.65 y.o.)	IG – combined interventions: 3/week for 6 wks 1. cognitive training – 18 hrs 2. TC 18 hrs, Yang-24 3. Group counseling (6 90-min sessions) CG – two 120-min health-related lectures	fMRI Paired associative learning test (PALT) (to examine episodic memory) Category Fluency test (CFT) (to examine speech production)	8/11**
Yin et al (2014) [44] Li, Zhu, Yin, Niu et al (2014) [45]	RCT	45 older community-dwellers IG - Multimodal intervention (TC + cognitive training + counseling – 26 CG - 19	Multimodal intervention include IG 1 - TC (Yang style, 24 form, 60 min each, 3/wk for 6wks) + IG 2 - Cognitive training: (60 min each, 3/wk, for 6wks) + counseling (90,im each, 1/wk for 6 wks) CG - daily routine, 2 120-min healthcare education	MRI MoCA Associative Learning Test (ALT) Digital Span forward and Backward Tasks Category Fluency Test Train Making Test Social Support Rating Scale Satisfaction with Life Scale	8/11**
Mortimer et al (2012) [46]	RCT	120 community-living older adults (primary females) – 30 in each group • IG1 - TC: 67.3±5.3 y.o., 19/30 females • IG2 - Walking: 67.8±5.0 y.o., 19/30 females • IG3 - Social: 67.9±6.5 y.o., 21/30 females • CG - No interventions: 68.2±6.5, 21/30 females	3/week for 40 wks IG1: TC: 50 mins - 20min warm-up, 20 min TC and 10 min cool-down), 3 IG2: Walking: 50 mins - 10 warm-up, 30 min brisk walking, and 10 min cool-down in a 400-meter track IG3: Social interaction: 60 min for any topics CG: No interventions	sMRI and fMRI	9/11**

Table 2: Effects of Tai Chi on Brain Assessed with Neuroimaging Techniques.

	Volume of Grey Matter (Cortical thickness) & HbO2 through sMRI, fNIRS, or MRS	**Functional Homogeneity – (assessed with ReHo); Spontaneous Neural Activity (assessed with fALFF) and Synchrony (assessed with VHMC)**	**Local Functional Connectivity (resting state functional connectivity)**
Frontal Lobe	• ↑ grey matter in: medial orbitofrontal cortex [27], precentral gyrus [39], dorsolateral prefrontal cortex (DLPFC) [39] • ↓ grey matter in: Frontal lobe [20] • ↑ HbO2 in: prefrontal cortical area* [24,26,29]	• neural activity in: left superior frontal gyrus [18,33,44], right middle frontal gyrus (MFG) [44], and DLPFC [41]. • ↓ synchronized pattern in: MFG and precentral gyrus [23].	• ↑ in frontal gyrus, right operculum and precentral gyrus [32]
Parietal Lobe	• ↑ grey matter in: right postcentral gyrus [39]	• functional homogeneity in: right postcentral gyrus [38]. • ↓ spontaneous neural activity in: bilateral tempo-parietal network and angular gyrus-dorsal prefrontal cortex-anterior cingulate cortex network [37]. • ↓ synchronized pattern in: bilateral precuneus, [23].	• in precuneus, angular and supramarginal gyri [32]
Temporal Lobe	• ↑ grey matter in: left superior temporal gyrus [25,39], left inferior temporal gyrus [22], right middle temporal gyrus, medial temporal region [22,40], hippocampus [22,31,40].	• ↑ spontaneous neural activity in: left superior and middle temporal gyri [43].	• ↑ in left temporal lobe [32] and medial temporal lobe [46].- • ↑ Extent of interconnectivity in bilateral olfactory cortex [16]
Occipital Lobe	• ↑ grey matter in: middle occipital gyrus [25], lingual sulcus and medial ocipito-temporal sulcus [39]- • ↑ HbO2 in: occipital cortex [29]	• neural activity in: right intra-calcarine cortex, lateral occipital cortex, and occipital pole during cognitive functioning (e.g., attention) time [34].	• ↑ in occipital gyrus [32]
Insula	• ↑ grey matter in: insula [40] and insular sulcus [39]	NA	NA
Limbic System	• ↑ grey matter in: hippocampus [22,31,40], left thalamus [31], positively associated decreased tendency of risk-taking behaviors assessed by a series of risk-taking tsk[31] • ↓ grey matter in: hippocampus [20] • ↑ NAA/Cr ratio in: posterior cingulate gyrus [35]	• ↑ functional homogeneity (indicating ↑functional integration) in: hippocampus and fusiform gyrus, and para-hippocampus [22]. • ↓functional homogeneity (indicating ↑functional specialization) in: left anterior cingulate cortex, [38] • ↓ spontaneous neural activity in: anterior cingulate cortex-dorsolateral prefrontal cortex-angular gyrus network [37].	• ↑ Extent of interconnectivity in left thalamus [16]
Basal Ganglia	• ↑ grey matter in: putamen [40]	NA	NA
Cerebellum	NA	• ↑ spontaneous neural activity in: posterior lobe of cerebellum [43] and left anterior lobe of cerebellum [44].	• in cerebellum [32]
Brainstem	NA	NA	• ↓ in brainstem [32]

fALFF: fractional amplitude of low-frequency fluctuations; HbO2: oxyhemoglobin; NA: not available; NAA/Cr: N-acetylaspartate/creatine; NIRS: near infrared spectroscopy; ReHo: regional homogeneity; VHMC: voxel-mirrored homologous connection; ↑: increased/increase; ↓: decreased/decrease. MRS: Magnetic resonance spectroscopy.

- fNIRS – to assess brain tissue oxygenation
- sMRI – to assess morphological change like grey matter volume (cortical thickness)
- MRS - to non-invasively measure and evaluate the concentrations of different chemical components of the scanned tissue.
- fMRI (VHMC) – to assess resting state functional connectivity and functional integration (↑VMHC); or specialization (↓VMHC) between left and right or within brain structures
- fMRI (Reho) for assessing neural activity and functional homogeneity between neural regions (↑homogeneity indicates improved functional integration, while ↓homogeneity indicates increased specialization between neural structures).
- fMRI (fALFF) - to assess local spontaneous neural activity of the brain

Results

Thirty-two articles from 24 studies were qualified for analysis (Table 1) [15-46]. There were 13 randomized control trials with 17 articles [16-18,20,24,25,27,28,32, 33,40-46], 8 cross-sectional studies with 12 articles [21-23,26,29-31,34,36-39], and 3 single group pre- and post-comparisons with 3 articles [15,19,35]. Among these 24 studies, 17 of them with 21 articles had elderly subjects who were 60 years and older [20-24,26,29-31,33-36,40-46], 4/24 studies with 8 articles had mixed age groups with subjects 21-70 years old [17,19,27,28,32,37-39], and 3 studies had healthy young subjects [16,18,25]. The majority of these studies used healthy subjects [15,16,18,20-31,33-46], but only four had subjects with a medical diagnosis of osteoarthritis [15], depression [19] or fibromyalgia [17,32]. Among 13 RCTs (17 articles), activities for the control groups or other intervention groups included normal daily activities [17,20,24,32], brisk walking [16,18,25,46], Baduanjin exercise [27,29,40-42], stationary biking [27, 29], health education [27,29,40-45] and social gathering interactions [46]. In 8 cross-sectional studies (12 articles), practitioners with 5 or more years of experiences in TC were compared with comparable subjects who walked every day [21, 22] or just non-TC practitioners [23,26,31,33,36-39].

With respect to quality assessment, 13 randomized controlled trials ranged from 6-9/11 in PEDro scale, indicating good to excellent studies [13]. Newcastle-Ottawa scale [14] showed 6-9 stars/10 in 8 cross-sectional studies (suggesting good to very good), and 5/10 in two sing-group cohort studies (indicating satisfactory), respectively.

Table 3: Tai Chi Effects on Inter-Regional Resting-State Functional Connectivity.

Increased Connectivity between	**Decreased Connectivity between**
• Left superior frontal gyrus --- posterior insula [19] • Left superior frontal gyrus --- ventral striatum [30] • Left middle frontal gyrus --- left superior parietal lobule [25] • Dorsolateral prefrontal cortex --- anterior cingulate cortex [27,32,37] • Dorsolateral prefrontal cortex --- medial prefrontal cortex [32] • Dorsolateral prefrontal cortex --- angular gyrus [37] • Bilateral prefrontal cortex ----- bilateral hippocampus [43] • Medial prefrontal cortex (mPFC) --- anterior cingulate cortex [32] • Medial prefrontal cortex --- medial temporal lobe [45] • Left superior parietal lobule --- right posterior insula & left superior temporal gyrus – right posterior insula [22] • Superior temporal gyrus --- right anterior cingulate cortex [22] • Right anterior insula --- superior temporal gyrus [22] • Bilateral amygdala --- medial prefrontal cortex (mPFC) [15] • Medial hypothalamus --- thalamus and amygdala in fibromyalgia [17]	• Medial orbito-frontal cortex --- periaqueduct grey (PAG) and ventral tegmental area [27] • Dorsolateral prefrontal cortex --- supplementary motor area and anterior cingulate cortex (ACC) [28] • Dorsolateral prefrontal cortex --- left thalamus and ventral striatum and right middle frontal gyrus [36] • Bilateral angular gyrus --- dorsal prefrontal cortex --- anterior cingulate cortex network [37] • Hippocampus/PAG --- ACC/mPFC [32]

Table 4: Function Improvements in Association with Neuroimaging Results after Tai Chi (TC) Practice.

Functional Improvements	**Assessment Tools**	**Neuroimaging Results**
↑ Cognitive Performance [16,23,45]	• Category fluency test [45] • Attention network test; and Number Cancellation Test [23] • More-odd shifting task [16]	• Associated with ↑ functional connectivity between medial prefrontal cortex and medial temporal lobe/cortex [45]. • Positively correlated with Tai Chi practice experience [23]. • Associated with ↓ VHMC (synchrony) in precentral gyrus and precuneus [23]. • Associated with ↑ functional specialization in left thalamus [16]
↑ Attention and inhibitory control [18,34,38]	• Stroop Word Color Task [34] • Attention Network Test (AKA: Flanker type test) [18,38]	• Need less neural activation of right intra-calcarine cortex, lateral occipital cortex, and occipital lobe (compared with aerobic exercise) [34]. • Associated with improving neural functional integration in postcentral gyrus and specialization in anterior cingulate cortex (ACC) and dorsolateral prefrontal cortex (DLPFC) [38]. • Associated with ↑ neural activity in left medial superior frontal gyrus [18]
↓ Tendency of Risk-Taking [31]	• A sequential risk-taking task	Associated with ↑ volume of left thalamus and left hippocampus.
↓ Errors in Switch & Non-switch task [33]	• Task-switching performances assessed by Intra/Extra-Dimensional Set Shift (IED) test	Associated with ↑ neural activation in left superior frontal gyrus.
↑ Memory function [40,41]	• Wechsler Memory Scale	• Associated with ↑spontaneous neuronal activities in right DLPFC [41]. • Associated with ↑volume of putamen and hippocampus [40].
↑ Working Memory [34]	• N Back Task	• Need less neural activation in right SFG and right frontal pole.
↑ Episodic (long-term) memory [22,43]	• Delayed recall of Montreal Cognitive Assessment Scale [22] Paired-associate learning test [43]	• Associated with ↑ volume of left hippocampus [22]. Correlated with ↓ spontaneous neural activity of right middle temporal gyrus assessed [43].
↑ Mindfulness [36]	Five Facets Mindfulness Questionnaire	Associated negatively with functional connectivity between DLPFC and middle frontal gyrus.
↑ Emotional regulation ability, stability, and judgement of inner experience [30,31,36]	• A sequential risk-taking task [30] • Five Facets Mindfulness Questionnaire [31,36] • Mindful Attention Awareness Scale [31] • Barratt Impulsiveness Scale [31]	• Associated with ↑ functional connectivity between frontal lobe (particularly the superior frontal gyrus - SFG) to ventral striatum [30]. • Associated with ↓functional connectivity between the DLPFC and middle frontal gyrus (MFG) [36].
↑ Speech production [43]	• Category fluency test	• Associated with improved superior temporal gyrus (STG) neural activity
↑ Vitality (Energy & fatigue) [19]	• SF-36	• Correlated with increased functional connectivity between posterior insula and left superior temporal gyrus and left superior parietal gyrus.
↑ Fibromyalgia improvement [17]	• Fibromyalgia Impact Questionaire -	• Associated with ↑functional connectivity between medial hypothalamus and right thalamus
↓ Knee Pain [15,27,28]	• Knee Injury and Osteoarthritis Outcome Score [27,28]; pain visual analogue scale and Brief Pain Index [15]	• Associated with ↑ grey matter volume in medial orbital prefrontal cortex [27] and supplementary motor area [28]. • Associated with ↑ connectivity between DLPFC and ACC [28]. • Associated with ↓ functional connectivity between medial orbital prefrontal cortex and periaqueduct grey and ventral tegmental area [27]. • Associated with ↑ connectivity between amygdala and medial prefrontal cortex (mPFC) bilaterally [15]
↓ Depression [19]	• Beck Depression Inventory	Correlated with increased functional connectivity between anterior insula and STG/caudate nucleus.

Exercise Parameters Related to TC Effects on Neuroimaging Assessments

Based on 16 prospective studies (20 articles) in this review, including 13 randomized control trials (17 articles) and 3 pre-and post-intervention comparison studies (3 articles), the TC exercise parameters varied from study to study, but some of the parameters were commonly prescribed by many TC providers. The length of each TC practice session ranged from 30-40 minutes [20], 45 minutes [24], 50-60 minutes [15-19,27,28,32,33,35,40-46] with the most commonly used one being 50-60 minutes. The exercise frequencies were 2/week [17,19,32], 2-3/week [35], 3/week [15,16,18,20,24,25,33,43-46] and 5/week [27,28,40-42] with the most common one being 3 times a week. The duration for these studies varied from 6 weeks [43-45], 8 weeks [15,16,18,24,25], 10 weeks [19], 12 weeks [17,27,28,32,33,35,40-42], 16 weeks [20] to 40 weeks [46] with 12 weeks as the most commonly used. Put together, 60 minutes per session, 3 times a week for 12 weeks are the most commonly used TC parameters by TC researchers to investigate TC effects on the human brain. However, none of these 16 prospective studies did a follow-up after their TC interventions were completed, but the effects from a longer duration of TC practice are available from 8 cross-sectional studies (12 articles), in which subjects had been practicing TC for a minimum of 5 years and showed greater changes than the control groups [21-23,26,29-31,34,36-39].

TC Effects on Different Regions of Brain

As shown in Tables 1 and 2, TC practice is able to affect the whole brain by increasing total brain volume [46], the oxygenated hemoglobin (HbO2) in the motor cortex [29], and the white matter network connectivity locally and globally in the brain [21]. In each individual brain region, TC can affect many brain areas including the frontal, parietal, temporal, and occipital lobes, insula, basal ganglia, and cerebellum, among which the frontal lobe is the area that has been studied more than others (Table 2) [15-46].

Frontal Lobe

TC practice is able to affect many regions of the frontal lobe (Table 2) by increasing 1) grey volume in the medial orbital prefrontal cortex [27], precentral gyrus [38], and dorsolateral prefrontal cortex (DLPFC) [39]; 2) oxyhemoglobin (HbO2) in the prefrontal cortical area [24,26,29]; and 3) neural activity in the left superior frontal gyrus [18,33;44]; right middle frontal gyrus (MFG) [44], and DLPFC [41]. The increased neural activity in the left superior frontal gyrus [33] and the dorsolateral prefrontal cortex [41] have been found to be associated positively and respectively with decreased error-making rates in switch/non-switch tasks [33], or with improved memory [41] in older community dwellers.

Further, increased connectivity was also reported locally in the frontal gyrus, right operculum, and precentral gyrus [32]. Decreased synchronized pattern in MFG and precentral gyrus as assessed by the VHMC technique was also found [23].

Parietal Lobe

The right postcentral gyrus shows increased cortical thickness and improved neural integration as indicated by increased functional homogeneity, which are positively associated with practitioners' time length of TC experience and improvement of cognitive attention [39]. Increased functional connectivities were identified locally in precuneus, angular, and supramarginal gyri [32], and the middle frontal gyrus [25]. Decreased synchrony, as indicated by decreased VMHC, was seen in the precuneus, which is correlated with years of TC practice experience [23]

Temporal Lobe

Increased thickness of the cortex was identified in the left superior temporal gyrus [25,39], left inferior temporal gyrus [22], right middle temporal gyrus, and medial temporal region [22,40]. More spontaneous neural activities through fALFF assessment were detected in the left superior and middle temporal gyri [43]. The rsFC fMRI technique exerted greater functional connectivity locally in the left temporal lobe [32], medial temporal lobe [45], and bilateral primary olfactory cortex (in the lower temporal lobe) [16].

Occipital Lobe

Randomized controlled trials showed that 8-week TC practice can enhance the volume of grey matter in the middle occipital gyrus [25] and a 12-week TC program can increase resting state functional connectivity in the occipital gyrus [32]. Moreover, cross-sectional studies revealed that TC practitioners with a minimum of 5-year experience demonstrated 1) more volume of grey matter in the lingual sulcus and medial occipito-temporal sulcus [39], 2) increased HbO2 in occipital cortex [29], and 3) less activation of the right intra-calcarine cortex, lateral occipital cortex, and occipital pole during cognitive functioning (e.g., attention) time [34].

Insula and Limbic System

Grey matter can become thicker in the insula [39,40], hippocampus [20,31,40] and left thalamus [31]. Increase of the NAA/Cr (N-acetyl aspartate/creatine) ratio, a biomarker of brain functionality, was found in posterior cingulate gyrus [35]. Functional homogeneity was increased in the hippocampus, fusiform gyrus, and para-hippocampus [22], but decreased in the left ACC which is associated with years of TC experience [38]. Also increased extent of interconnectivity was identified within the left thalamus [16].

Basal Ganglia, Thalamus, Cerebellum, and Brainstem

After TC practice, neuroimaging techniques showed more grey matter in the putamen [40], and more spontaneous neural activity in the anterior and posterior lobes of the cerebellum [43,44], but decreased neural activity in brainstem [32].

Inter-regional Connectivity

As shown in Table 3, changes of inter-regional functional connectivity after TC practice were identified between different brain regions, among which the frontal lobe [15,19,25,27,30,32,37,42,45] has many more structures to make such inter-regional connections than any other neural lobes or brain areas, followed by the temporal lobe [19,42,45], limbic system [17,19,27,32,37], parietal lobe

[19,25,37], insula [19], basal ganglia [30], and brainstem [32]. In the frontal lobe, the following structures, including superior, middle, and inferior frontal gyri, dorsolateral prefrontal cortex, medial prefrontal cortex, medial orbito-frontal cortex, and supplementary motor cortex, have either increased or decreased inter-regional connectivity with structures outside the frontal lobe (Table 3). In the temporal lobe and limbic system, the superior temporal gyrus, medial temporal lobe, hippocampus, cingulate gyrus, amygdala, and hypothalamus are involved in the TC-caused inter-regional connectivity. Further, the superior parietal lobule and angular gyrus in the parietal lobe, the ventral striatum in basal ganglia, the insula, and the ventral tegmentum and periaqueduct grey in the brainstem are involved as well (Table 3). Many of these connectivities are increased after TC exercise as seen in the left column of Table 3, while some of these connectivities are decreased in the right column of the table.

Neuropsychological Functional Assessments

Neuropsychological functions were assessed in some studies and their associations with TC-caused neuroimaging changes in the brain were presented in Table 4. These studies used a variety of instruments to assess neuropsychological functions and to see how they may associate with neuroimaging changes after the TC intervention. As seen in Table 4, changes of inter-regional neural connectivity and cortical thickness (grey matter volume) were found to be associated with neuropsychological improvements such as cognition [16,18, 22, 23, 30, 31, 33, 34, 36, 38,40,41,43,45], vitality [19], depression [19], pain [15,27,28], and even the overall aspects of the fibromyalgia [17]. The cognition-related improvements may include general cognitive performance [16,23,45], attention and increased inhibitory control during attention [18,34,38], decreased errors in switch and non-switch task [33] and decreased tendency of risk-taking [31], different memory performance [22,34,40,41,43], mindfulness [36], emotional stability and judgement of inner experience [30,31.36], and speech production [43]. For examples, emotion regulation ability [30], cognitive performance [45], depression [19] and vitality [19] improvements are positively and respectively correlated with increased connectivities between the left superior frontal cortex and ventral striatum [30], between the medial prefrontal cortex and medial temporal lobe [45], between the right ACC and superior temporal gyrus [19], or between the right posterior insula and both the left superior temporal gyrus and left superior parietal gyrus [19]. Other the other hand, decreased tendency of risk-taking behavior [31] seems to parallel with increased cortical thickness in the hippocampus and thalamus [31]. In patients with knee arthritis, decreased knee pain was positively associated 1) with increased volume of grey matter in the medial orbitofrontal cortex [24] and supplementary motor cortex [28], 2) with increased connectivity between the dorsolateral prefrontal cortex (DLPFC) and anterior cingulate cortex (ACC) [27,28], but 3) with decreased connectivity in the medial orbito-frontal cortex and both periaqueduct grey and ventral tegmental area [27,28]. In addition, patients with fibromyalgia have significant improvement in functional, overall, and symptoms aspects as assessed with the Fibromyalgia Impact Questionnaire after 12-week TC practice. The improvement is positively correlated with the increased connectivity between the medial hypothalamus and the right thalamus [17].

Discussion

Local Neural Responses in Different Brain Areas following TC Practice

In the frontal lobe, increased grey matter thickness, spontaneous neural activities, and/or local connectivities of the medial prefrontal cortex, dorsolateral prefrontal cortex (DLPFC), medial orbitofrontal cortex (mOFC), precentral gyrus, superior and middle frontal gyri, and frontal operculum were all reported in TC practitioners (Table 2). Functionally, the medial prefrontal cortex is responsible for memory and decision making [47], the mOFC is for goal-directed decision-making [48], DLPFC is for top-down attentional and cognitive control [49], the precentral gyrus is the primary center for voluntary motor movement [50], the superior frontal gyrus is for self-awareness of individual personality [50], and the right middle frontal gyrus is a convergence site of attention networks for higher order cognition and motor-related information processing [51]. The frontal operculum plays an important role in a network controlling the process of cognitive tasks [52]. With these together, TC practice might be able to improve neuropsychological and related neuromuscular behaviors such as memory, attention, cognitive attention, decision-making, sensorimotor integration, motor execution and control, and individual self-awareness through influence on these structures in the frontal lobe. How these different structures within the frontal lobe work in a coordinated way is not clear, but an improved functional specialization in frontal lobe structures might be an explanation. For instance, a VHMC study showed reduced homogeneity in the middle frontal gyrus and precentral gyrus [23], which may indicate an increased functional specialization of these two structures after TC practice.

In the parietal lobe, the right post-central gyrus is the only area that showed increased cortical thickness and spontaneous neural activity [38,39], while increased local connectivities were seen in the precuneus and inferior parietal lobule (angular and supramarginal gyri) [32]. Functional considerations of these structures, like the post-central gyrus for primary somatosensory processing, the precuneus for executive function, default network of self-consciousness, and mental imagery strategies and episodic memory retrieval [53], and inferior parietal lobule for recognition memory, language, and perception of emotion [54], may indicate that TC practice is able to improve sensory integration of higher-order motor execution, memory, emotion, and mental imagery strategies for motor actions [32,37,38]. Further, these TC studies [32,37,38] showed that TC experience is positively associated with increased neural activity in the right post-central gyrus [38], but negatively with decreased synchrony in bilateral precuneus as indicated by decreased VMHC value [23]. So, it is possible to assume that the longer one practices TC, the more improved general sensory is shown in certain parts (e.g., the left side) of the body, which might be through decreased synchrony between the left and right precuneus. However, whether and how such an assumption is holdable surely needs more future studies.

The temporal lobe and its superior, middle, and inferior temporal gyri showed increased volume of grey matter [22,25,39,40],spontaneous neural activity [43], and local functional connectivity [32] after TC practice. The same changes were also seen in the medial temporal lobe [22,40,45]. Comparatively the left temporal lobe showed more changes [22,25,32,39,43] than the right one (mainly the right middle temporal gyrus) [40]. The temporal lobe is functionally responsible for emotion, memory, and awareness of special sensation, and the left (dominant) side is more involved in language understanding [55,56]. Thus, it is understandable that TC could be a good exercise choice to improve emotion, memory, auditory and visual sensory, and even language perception. The medial temporal lobe that includes the hippocampus and para-hippocampus will be discussed in the paragraph of the limbic system below.

The occipital lobe showed increased oxyhemoglobin (HbO2), total hemoglobin (cHb) [29] and local connectivity [32] following TC intervention. Also, increased thickness of grey matter was noticed in the middle occipital gyrus [25], lingual sulcus, and medial occipito-temporal gyrus [42]. With consideration of functions of the occipital lobe [57], reactions to TC practice in the middle occipital gyrus and occipital cortex in general may hint that the occipital lobe could be morphologically changed to some extent [36,39], and likely participate in improving cognition and anti-memory decline [26,29], as well as improving spatial recognition and perception of objects [57] after TC practice.

In parts of the limbic system, studies demonstrated increased 1) grey matter in the insula [39,40], medial temporal gyrus [40], left thalamus [31], and hippocampus [22,31,40]; 2) increased spontaneous neural activity in hippocampus [22], fusiform gyrus [22], and para-hippocampus [22]; 3) increased extent of interconnectivity in left thalamus [16]; 4) increment of N-acetylaspartate/creatine ratio (indicating neuronal growth) in posterior cingulate gyrus [35]; and 5) increased functional specialization in anterior cingulate cortex [38]. On the other hand, decreased grey matter was found decreased [20] and decreased neural connectivity was identified in the anterior cingulate cortex and dorsolateral prefrontal cortex-angular gyrus network [37]. The insula has been regarded as a limbic system structure in respect to visceral sensation and autonomic control, but it also takes part in functions of pain processing, empathy, social cognition, attention, and decision making [60]. The medial temporal lobe (including hippocampus, para-hippocampus, and amygdala) is associated with emotion learning and behavior, as well as memory encoding, consolidation, storage, and retrieval [59,60], particularly for episodic and spatial memory [60]. A decrease in size of the posterior cingulate gyrus has been reported to play a role in cognition by influencing attentional focus by 'tuning' whole-brain metastability [61]. Additionally, the fusiform gyrus is responsible for object and face recognition [62] and semantic memory [63], and the thalamus is a relay hub for multiple sensory information and even memory [64,65]. However, reduction of grey matter in the hippocampus was recently reported when TC intervention was combined in an exercise program (30-40 minutes per total session) including TC-inspired exercise, dancing, and cognitive game [20], in which the TC time for each session was not long enough [20]. With respect to these studies about TC effects on the limbic system [20,22,31,35,39,40], generally speaking, they may indicate that TC is likely able to improve the practitioners' emotion, memory, visceral and somatosensory capability, decision making, pain processing, and attention. TC may also be able to subsequently reduce the cognitive decline through the limbic system including the medial temporal lobe [66] if the TC practitioners have practiced over 5 years [22,31] or have practiced in longer duration (60 minutes each) on a daily basis [38].

In the basal ganglia and cerebellum, responses to TC exercise include increased grey matter in the putamen [40], and increased neural activity [43,44] and local connectivity in the cerebellum [32]. Literature has suggested that the putamen is functionally responsible for movement execution, working memory [67], and cognition [68]. Besides motor learning and coordination, the cerebellum is also for cognition and emotional processing (particularly the posterior cerebellar lobe) [69]. Injury to the cerebellum may cause cerebellar cognitive affective syndrome [70]. This information indicates that TC may improve motor execution, working memory and cognition through the putamen and cerebellum.

Inter-regional Connectivity after TC Practice

In addition to increased functional connectivity in each individual brain region (Table 2), there are also many inter-regional connectivities influenced by TC practice (Table 3, among which there are more increased such connectivities (see the left column of Table 3) than those decreased (see the right column of Table 3). We speculate that the increased inter-regional connectivities may suggest functional integration of different brain regions while the decreased inter-regional connectivities may indicate functional specialization of different regions. With consideration of morphological changes in each individual brain region after TC exercise, these individual brain regions might be able to functionally respond to TC practice differently depending on functions executed by these regions.

Functional Consideration

Given involved brain regions detailed in Tables 2 and 4, we can easily see that many of them are functionally and positively associated with neuropsychological behaviors. These behavior improvements were assessed with different neuropsychological instruments. For examples, following TC interventions, positive correlations were reported in improvement of 1) reduced risk-taking behavior as assessed by a series of risk-taking tasks [31]; 2) decreased error-making assessed with the switch-non-switch task [41]; 3) cognitive performance assessed by Category fluency test and attention network test [23,45]; 4) emotional regulation and stability assessed by Five Facets Mindfulness Questionnaire and Barratt Impulsiveness scale [31,36]; 5) depression by Beck Depression Inventory [19]; 6) vitality (energy and fatigue) assessed with SF-36 [19]; 7) memory as assessed by Wechsler Memory Scale [40,41] including working memory and episodic (long-term) memory [22,43]; and even knee pain as assessed by Knee Injury & Osteoarthritis Outcome Score [15,27,28]. These findings suggest that TC can be utilized not only as a physical but also a cognitive exercise, which may work by modulating both the local regional morphologies and inter-regional brain connectivity networks to improve the brain's neural functions.

Study Limitations

There are several limitations that should be mentioned. First, due to the barrier to resources in non-English language, we were not able to access articles that were published in non-English literatures. Second, 10 out of 21 qualified studies are randomized control trials, but others include 8 cross-sectional studies, 2 single group pre- and post-TC comparisons, and 1 single-case report may reduce the level of evidence for this review study. Third, seed-based analysis is often used in resting state MRI in which a neural region of interest (ROI) is selected to determine how other regions interested by the investigators may correlate to the ROI. However, the obvious downside of such a method is that it depends on the investigators' assumption for the ROI selection [71]. If a different ROI was picked, the involved brain regions might vary.

Conclusions

In the last 10 years, as neuroimaging techniques develop, more morphological changes of the human brain after TC practice have been investigated and identified in the frontal, temporal, parietal, and occipital lobes, insula, limbic system, basal ganglia, cerebellum, and brainstem, with the frontal and temporal lobes having more changes than other regions. These changes include increased cortical thickness or grey matter volume, altered local spontaneous neural activity, as well as changed inter-regional functional connectivities. Also, many of these changes are associated with improvements of many neuropsychological behaviors such as cognitive attention, memory, depression, vitality, risk-taking task, error-making tests, and even pain reduction. All of these imply that TC can be a great exercise program to improve the practitioners' neural dysfunctions. However, so far, many brain structures have been found to be affected by TC exercise, but why and how only these structures are involved in response to TC practice are still not fully understood. Future studies are needed to assess how the structures are involved and how functionally some of these structures are integrated and/or specialized post-TC interventions.

Author Contributions

All five authors had substantially contributed to the conception and design of the article and interpreting the relevant literature. HL drafted the article and revised it critically with YS, SA, CN and CH for important intellectual content.

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