



## Brain Structural Response and Neurobehavioral Changes in the Elderly after Tai Chi Practice - A Literature Review

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### Abstract

Tai Chi (TC) has been often provided to older adults by rehabilitation professionals for medical dysfunction and anti-aging healthcare. In last decade, there has been an increase in the number of studies examining the effects of TC on brain as assessed by neuroimaging including near infrared spectroscopy (fNIRS), and structure and functional magnetic resonating imaging (sMRI & fMRI). Thus, the primary purpose of this literature review is to evaluate how TC practice may affect the brain in the elderly as assessed by neuroimaging techniques, and followed by corresponding neurobehavioral changes as the secondary purpose. A comprehensive literature search was conducted using a variety of keywords with different search engines to search from the last ten years until January 15, 2022. Studies were included if they investigated topographic brain responses after TC practice in the elderly population. A total of 12 original studies with 15 articles met the criteria and were included for the review process. The results showed increased volume of cortical grey matter, improved neural activity and homogeneity, and increased neural connectivity in different brain regions, including the frontal, temporal, and occipital lobes, cerebellum, and thalamus. Intriguingly, the longer one practices TC, the more his/her brain regions may be altered. Such neural findings after TC practice are often associated with neurobehavioral improvements in attention, cognitive execution, memory, emotion, and risk-taking behaviors. TC is a promising exercise that is able to improve structural capability and neurofunctional activity in the brain in the elderly. These improvements appear to be associated with the time-length of TC practice.

**Keywords:** Tai Ji; Exercise; Central nervous system; Aged; Neuroimaging

### Introduction

Clinically, Tai Chi (TC) is one of the most commonly used exercises frequently provided by rehabilitation professionals for older adults [1]. TC is originally from ancient Chinese Martial arts and it integrates breathing, meditation, and body movement to achieve a great sense of inner peace and well-being in a calm, relaxed, and meditative way [1]. Over years, TC has been recognized as an effective mind-body exercise

intervention to improve physical performance, prevent falls, increase social participation, and enhance cognition activities, particularly for the elderly population who are experiencing neural degeneration due to the aging process and/or medical dysfunctions [1,2].

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.

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Functional near-infrared spectroscopy (fNIRS) is a cost-effective, wearable neuroimaging technology that can safely assess the real-time brain activity during physical performance by monitoring the hemodynamic response (HbO<sub>2</sub>) in the brain cortex using near-infrared light sources [3]. Structural magnetic resonance imaging (sMRI) is a non-invasive imaging technique that can examine the structural characterization of the brain in normal or pathological conditions [4]. Functional Magnetic Resonance Imaging (fMRI) is an imaging technique often used to assess two or more different states in an experimental functional condition. In fMRI, fractional amplitude of low-frequency fluctuations (fALFF) is a resting state fMRI indicator and the fALFF technique is often used to assesses the spontaneous neural activity of specific regions in the brain [5]. The regional homogeneity (ReHo) technique in fMRI is to assess local spontaneous coherence or intra-regional synchronization of neural activity [6]. The functional connectivity and diffusion tensor imaging (DTI) technique are often used to estimate white matter connectivity and integrity respectively in the brain [7]. Therefore, the purpose of this literature review was to review and examine if and how TC exercise might affect the brain after TC practice as assessed through these neuroimaging techniques, and how these TC effects may be associated with changes of neurobehavioral and cognitive functions.

## Methods

### *Search strategy*

TC-related literature that investigated TC's effects on structural 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). The searched time period is from January 2012 to January 15, 2022. The PubMed search strategy was based on the PICO approach. Both the term (tw) and MeSh (mh) search keywords were used to find the qualified articles. Published reviews and all relevant studies and their reference lists were also reviewed manually in search for other pertinent publications.

### *Study selection*

Studies identified in the search were screened for inclusion. Articles that met the following inclusion criteria were selected. 1. studies investigating the effects of TC on brain response. 2. studies assessing

the responses with fNIRS, sMRI, and/or fMRI as the primary outcome assessments. 3. participants were older adults ( $\geq 60$  years older). 4. randomized control trials, single-group pre- and post- comparison, and cross-sectional studies. 5. studies published in peer-reviewed English journals or English version of Chinese journals from last 10 years until January 15, 2022. However, an article could be excluded if it met one of the following exclusion criteria. 1. The study was case study, a review, study protocol, or a prospective article. 2. The Tai Chi intervention was a part of a combined exercise program for the intervention group. 3. The article was published in a non-English language, or published in English journals before December 31, 2022.

### *Data Extraction*

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

### *Outcome of Interests*

The interest from this review were: what TC parameters were provided to older adults to practice, how different parts of an aging human brain might react to the TC practice in neuroimaging approach, whether some neurobehavioral response might correspond to the neuroimaging changes, and if these brain reactions and neurobehavioral response might correlate to the time length of practicing TC. The outcome of these interests was measured with analysis of TC exercise parameters, sMRI, fMRI, rsFC, fNIRS, as well as instruments and questionnaires for neurobehavioral assessments.

## Results

Twelve studies were qualified for this review, but some authors published more than one article out of a single study, which made the final 15 articles qualified and retrieved for the final review (Table 1). There were six randomized control trials (RCTs) with seven articles [8,11,16,19-22], and six cross-sectional studies with eight articles [9,10,12-15,17,18]. In the six RCT studies, the intervention group or one of the intervention groups used TC as the intervention, while in the six cross-sectional studies, comparisons were

conducted between people who practiced TC over three years [17] or five years [9,10,12-15,18] with people who received usual care without any exercise

[12,13,18], or did exercise of walking [9,10], aquatic aerobics [17], or other exercises with matched physical activity level [14,15].

**Table 1.** Tai Chi studies assessed with neuroimaging techniques

Authors	Research Design	Subjects	Interventional Parameters	Assessment instruments
Adcock, Fankhauser, et al (2020)[8]	RCT	All healthy elderly individuals <ul style="list-style-type: none"> <li>IG – n =15 (77±6.4 y.o.)</li> <li>CG – n=16 (70.9±5.0 y.o.)</li> </ul>	IG – TC at home; 3/wk, 30-40 min/each for 16 wks CG – normal daily living with usual care	sMRI Victoria Stroop test Trail making test Wechsler memory scale
Yue, Zou, Mei et al (2020)[9] Yue, Yu, Zhang et al (2020)[10]	Cross-sectional	<ul style="list-style-type: none"> <li>42 healthy elderly females</li> <li>IG – n=20 TC practitioners (62.9±2.38 y.o.)</li> <li>CG – n=22, walking as the exercise (63.27±3.58 y.o.)</li> </ul> Both groups: 90 min/each, 5/week, over 6 years of experience	NA	fMRI
Yang, Chen, Shao, et al (2020)[11]	RCT	IG – n = 13 CG – n = 13 All healthy elderly individuals (>60 y.o.)	IG - TC: 45 min/each, 3/wk, for 8 wks, 24-form Yang style CG - usual care	fNIRS Flanker task test
Tsang, et al (2019)[12]	Cross-sectional	8 practitioners (over 7 years of experience) and 8 non-practitioners All: 60-75 y.o.	NA	fNIRS
Xie, et al (2019) [13]	Cross-sectional	32 ordinary vs 25 long-term (>5 years) Chen-style TC practitioners (all 60-70 y.o.)	NA	fNIRS
Liu, Li, Liu, Sun, et al (2020)[14] Liu Li, Liu, Guo et al (2019)[15]	Cross-sectional	52 community-dwelling older adults (60-70 y.o.) IG – n = 26 (10 years or more TC experience) CG – n = 26 (non-TC practitioners, but matched in physical activity level)	Both groups were asked to accomplish a sequential risk-taking task	sMRI and fMRI rsFC Beck depression inventory NEO five-factor inventory Five facets mindfulness questionnaire Sequential risk-taking task Mindful attention awareness scale Barratt impulsiveness scale
Wu, Tang, Goh, et al (2018)[16]	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 Intra-extra dimensional (IED) set shift task
Port, Santaella, et al (2018)[17]	Cross-sectional	8 TC practitioners (>60 y.o.) 8 water aerobics practitioners (>60 y.o.)	NA	fMRI Stroop Word Color Task N-back task
Liu, Wu, Li, Guo, (2018)[18]	Cross-sectional	IG – TC, n = 26 (10.44±5.48 years of TC experience) (65.19±2.30 y.o.) CG – age and sex matched group (63.92±2.87 y.o.) (no TC experience)	NA	fMRI Beck depression inventory NEO five-factor inventory Five facets mindfulness questionnaire Mindful attention awareness scale

Zheng, et al (2015)[19]	RCT	Elderly community dwellers IG – n = 17 (68.59 y.o.) CG – n = 17 (71.65 y.o.)	IG – TC: 60 mins/ each, 3/week for 6 wks 24 form Yang style CG – two 120-min health-related lectures in 6 wks	fMRI Paired associative learning test Category fluency test
Yin, et al (2014) [20] Li, Zhu, Yin, Niu, et al (2014) [21]	RCT	45 older community-dwellers IG – n = 26 CG – n = 19	IG – TC: 60 mins/ each, 3/week for 6 wks 24 form Yang style CG - daily routine, 2 120-min healthcare education	MRI MoCA Paired-associative learning test Digit span forward and backward tasks Category fluency test Trail making test Social support rating scale Satisfaction with life scale
Mortimer, et al (2012)[22]	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 along a 400-meter track IG3 - Social interac- tion: 60 min for any topics No interventions CG – usual care	sMRI and fMRI Mattis dementia rating scale; Category (verb) fluency test

CG: control group; fMRI: functional magnetic resonance imaging; fNIRS: functional near infrared spectrum; IG: interven-  
tional group with Tai Chi as the intervention; min: minute(s); MOCA: Montreal Cognitive Assessment; NA: not applicable;  
RCT: randomized control trial; sMRI: structural magnetic resonance imaging; TC: Tai Chi; wk(s): week(s); y.o.: years old.

*Tai Chi Exercise parameters*

Exercise parameters were reported in six RCT studies with seven articles in which subjects are 60 years and older. The frequency of TC exercise in each study was 3/week [8,11,16,19-22], the session length ranged from 30-45 minutes [8,11] to 50-60 minutes [16,19-22] respectively, and the duration varied from 6 weeks [19-21], 8 weeks [11 12], 12 weeks [16], 16 weeks [8], or even 40 weeks [22]. It seems that at least three times per week, and 50-60 minutes or above each time are the most common TC exercise parameters provided to older adults in longitudinal TC studies. Also a minimum of 6 weeks is the TC exercise duration by TC researchers to investigate TC effects on the human brain based on these analyzed RCT studies.

*Tai Chi effects on brain*

In the elderly, TC could affect the neural activity, the grey matter volume, and the neural functional connectivity as shown in Table 2. Neural activity was assessed indirectly with the fNIRS to measure the brain tissue oxyhemoglobin (HbO<sub>2</sub>) [3], or directly with the fALFF to measure the power of local spon-

taneous neuronal activity [5]. The local intra-regional synchronization of neural activity was evaluated with the ReHo technique: increased ReHo indicates integration of neural activity, while the decreased ReHo indicates the specialization of neural activity [6]. In four RCT studies with TC practiced 6 weeks [19,20], 8 weeks[11], or 12 weeks [16], increments of HbO<sub>2</sub> were found in the prefrontal cortex during the attention test time [11]; increased fALFF was identified in the left superior frontal cortex, right middle frontal cortex, and anterior cerebellum during the time of task-switching [16] and cognitive execution function [20]; and increased ReHo was noticed in the left superior and middle temporal gyri along with the posterior lobe of cerebellum [19]. Further, in three cross-sectional studies [10,12,13] practitioners with many years of TC practice demonstrated increments of HbO<sub>2</sub> in the prefrontal cortex [12,13], and occipital cortex [13], as well as increased ReHo in fusiform gyrus and hippocampus [10]. However, compared with people who have practiced water aerobic exercise over three years, people who have practiced TC over the same amount of time showed decreased fALFF in right su-

terior frontal gyrus and right frontal pole during working memory assessment time [17] and also in the right intra-calcarine cortex, lateral occipital cortex, and occipital pole during attention assessment time [20]. Assessed with the structural MRI, change of grey matter volume (GMV) in an elderly tended to be associated with how long this individual has practiced TC. There were no GMV changes reported in those RCT studies with duration from 6-12 weeks [11,16,19-21].

However, in a 16-week RCT study, decreased GMV was found in the frontal cortex and hippocampus [8], but increased in the total brain after 40-week practice [22]. Further, cross-sectional studies showed that TC practitioners with more than 5-year practice had increased GMV in more brain areas: inferior temporal gyrus [10], medial temporal gyrus including hippocampus [10], frontal motor cortex [13], and thalamus [15].

**Table 2.** Brain Response after Tai Chi (TC) Practice

Local Neural Activity Assessed with HbO <sub>2</sub> , fALFF and Regional Homogeneity with ReHo			
Frontal	Temporal	Occipital	
<p>Prefrontal cortex (PFC)</p> <ul style="list-style-type: none"> <li>• ↑neural activity with ↑HbO<sub>2</sub> [11-13], positively correlated with improved inhibitory control of attention as assessed with Flanker Task test) [11].</li> </ul> <p>Superior frontal gyrus (SFG)</p> <ul style="list-style-type: none"> <li>• ↑neural activity with ↑fALFF in left SFG activity during task-switching assessed with Intra-Extra Dimension test [16], but ↓fALFF during working memory time (N Back Test) [17].</li> </ul> <p>Superior and middle frontal gyrus (SFG and MFG)</p> <ul style="list-style-type: none"> <li>• ↑neural activity with ↑fALFF in right MFG, along with ↑fALFF in SFG and anterior *cerebellum, positively correlated with cognitive execution function (assessed with Trail making test) and well-being assessed with Satisfactory with Life scale in older adults [20].</li> </ul> <p>Frontal pole</p> <ul style="list-style-type: none"> <li>• ↓fALFF neural activation in R-frontal pole during working memory time assessed with N Back task test [17].</li> </ul>	<p>Fusiform gyrus and hippocampus</p> <ul style="list-style-type: none"> <li>• *↑ReHo [10].</li> </ul> <p>Superior and middle temporal gyrus (STG &amp; MTG) [19]</p> <ul style="list-style-type: none"> <li>• ↑ReHo in left STG and left MTG (along with left posterior lobe of *cerebellum)</li> <li>• ↑ReHo in left STG is positively correlated with speech production assessed with category Fluency Test,</li> <li>• ↑ReHo in right MTG correlated with episodic memory assessed with paired associative learning Test.</li> </ul>	<p>Occipital cortex</p> <ul style="list-style-type: none"> <li>• ↑HbO<sub>2</sub> in occipital cortex [13].</li> </ul> <p>Intra-calcarine sulcus, Occipital cortex, and Occipital pole</p> <ul style="list-style-type: none"> <li>• ↓fALFF in right intra-calcarine sulcus, right occipital cortex, and right occipital pole during attention time (assessed with Stroop Word Color test) [17].</li> </ul>	
Tai Chi Effect on Grey Matter Volume (GMV)			
Frontal	Temporal	Thalamus	Brain
↓GMV in Frontal cortex [8].	<p>↑GMV in both Inferior temporal gyrus and Medial temporal gyrus [10].</p> <p>↓GMV in hippocampus [8], but ↑GMV in hippocampus [10,15] which is positively correlated with improved episodic memory [10].</p>	↑GMV in thalamus [15].	↑GMV in total brain [22].
Tai Chi Effect on Neural Functional Connectivity			
<ul style="list-style-type: none"> <li>• Greater brain white matter network in TC practitioners as assessed with diffusion tensor imaging (DTI) MRI technique [9].</li> <li>• ↑front-bilateral striatum connectivity, associated with improved emotional regulation and stability (less risk-taking and less feeling of regret) [14].</li> <li>• ↑Dorsolateral prefrontal cortex – Middle frontal gyrus connectivity; correlated with improved emotional regulation affected by decisions as assessed with five-facet mindfulness questionnaire and sequential decision task [18].</li> <li>• ↑medial prefrontal cortex – medial temporal lobe connectivity, positively correlated with cognitive execution function (assessed with Trail Making Test) and speech production (Category Fluency Test) [19,21].</li> </ul>			

↑: increased/increase; ↓decreased/decrease; & ↑ReHo: indicates improved functional integration of neural activity; \*: cerebellum is involved with either ↑fALFF in its anterior lobe [20] or ↑ReHo in the posterior lobe [19]; DTI: diffusion tensor imaging for white matter structure integrity; fALFF: fractional amplitude of low-frequency fluctuations for neural activity; fMRI: functional magnetic resonance imaging; fNIRS: functional near infrared spectrum; GMV: grey matter volume; HbO<sub>2</sub>: oxyhemoglobin; ReHo: regional homogeneity; sMRI: structural magnetic resonance imaging; TC: Tai Chi.

As of neural functional connectivity, Yue et al [9] reported in a cross-sectional study with a DTI technique that people who had practiced TC over six years exerted greater white matter network than those healthy elderly who just did walking as a daily exercise. In addition, with a pre-determined region (e.g., a nucleus) as a seed area in the fMRI, the neural functional connectivity fMRI has revealed: 1) increased medial prefrontal cortex – medial temporal lobe connec-

tivity during cognitive execution time and speech production assessment time in two RCT studies [19,20], 2) increased dorsolateral prefrontal cortex – middle frontal cortex connectivity during sequential decision making time in a cross-sectional study [18], and 3) increased bilateral frontal cortex – ventral striatum connectivity during risk-taking testing time also in another cross-sectional study [14].

**Table 3.** Effects of time duration of Tai Chi practice on brain

Time duration of Randomized Control Trials between TC learners and others without TC practice					Cross-sectional studies comparing people between over 3-year TC practice and Non-TC practice		
6 wks [19-21]	8 wks [11]	12 wks [16]	16 wks [8]	40 wks [22]	Compared with usual care or healthcare consultation [12-15,18]	Compared with walking [9,10]	Compared with water aerobics [17]
↑medial prefrontal cortex – medial temporal lobe connectivity [19,21].					↑HbO <sub>2</sub> in prefrontal cortex [12,13], and *occipital cortex [13].		
↑fALFF in right superior and middle frontal cortex, and anterior cerebellum [20].					↑Brain white matter network [9].		
↑ReHo in left Superior and middle temporal gyri, and posterior cerebellum [19].					↑ReHo in hippocampus and *fusiform gyrus [10].		
↑fALFF in left superior frontal cortex					*↓fALFF in right superior frontal cortex, frontal pole, intra-calcarine cortex, occipital cortex, and occipital pole		
↑HbO <sub>2</sub> in prefrontal cortex					↑GMV in hippocampus and *thalamus [15].		
↓GMV in frontal cortex and hippocampus					*↑front-ventral striate connectivity [14].		
↑GMV in total brain					*↑GMV in inferior temporal gyrus and medial temporal gyrus including hippocampus [10].		
					*↑dorsolateral prefrontal cortex – middle frontal gyrus connectivity [18].		

\*changes in new brain areas that have not been reported in Tai Chi learners who had short-term (<1 year) practice duration in RCT studies, but reported in Tai Chi practitioners who had long-term (≥3 years) practice in cross-sectional studies; fALFF: fractional amplitude of low-frequency fluctuations; GMV: grey matter volume; HbO<sub>2</sub>: oxyhemoglobin; TC: Tai Chi; wks: weeks

*Influence of time duration of Tai Chi practice on brain*

As shown in table 3, the time duration of six RCT studies ranges from 6 to 40 weeks. Brain responses mainly occurred in the frontal lobe, temporal lobe and cerebellum starting with increased neural activity, regional homogeneity, and medial prefrontal cortex-medial temporal lobe connectivity in 6-week TC practices [19-22], followed by increased HbO<sub>2</sub> in prefrontal cortex in the 8-week study [11], and altered grey matter volume in a 16-week and a 40-week RCT respective studies [8,22]. However, in those cross-sectional studies in which subjects had practiced TC for many years, increased HbO<sub>2</sub>, grey matter volume, and functional connectivity were found in more additional brain areas including the occipital cortex [13], thalamus [13], medial temporal gyrus [10], the frontal – ventral striatum connectivity [14], and the dorsolateral

prefrontal cortex – middle frontal gyrus connectivity [18]. When compared with people who received water aerobic exercise, TC practitioners with over 3-year TC practice experience showed even decreased neural activity in some frontal and occipital areas [17].

*Neurobehavioral assessment association with neuroimaging changes*

Many neurobehavioral tasks or tests had been conducted to assess attention, cognitive execution, dementia, emotional regulation and stability, error-making, memory, speech production, and well-being in the elderly TC learners and practitioners (Table 4). In TC learners from six RCT studies, 6 to 40 weeks of TC exercise are able to improve capability of selective attention [11], task-switching [19-21], dementia [22], attention set shifting (error-making) [16], episodic memory [19], speech [19,21], and satisfaction with life [20], which involved the prefrontal cortex [11],

frontal gyri [16,20,22], anterior cerebellum [20,22], superior and middle temporal gyrus [19], and the medial prefrontal cortex – medial temporal lobe connectivity [19,21], respectively. However, improvements of emotional regulation and stability [14,15,18], working memory [10,17], and ability to inhibit cognitive interference [17], along with more neural structures and functional connectivity involved, are just reported in those TC practitioners who have practiced TC

over three years. The emotional regulation improvements are associated with the increased neural activity in thalamus [15], as well as with the increased fronto-ventral striatum connectivity [14] and increased dorsolateral prefrontal cortex – middle frontal gyrus connectivity [18]. However, the improved working memory is associated with decreased neural activity in right superior frontal gyrus and frontal pole [17], and the improved ability to inhibit cognitive interference is associated with decreased neural activity in intra-cal-

**Table 4.** Neurobehavioral aspects assessed in association with neuroimaging changes in brain

		The neurobehavioral tests (tasks) used in qualified studies:
Attention	<ul style="list-style-type: none"> <li>Assessed with Flanker task test – improved selective attention and inhibitory control of attention are positively correlated with ↑neural activity in prefrontal cortex [11].</li> <li>*Assessed with Stroop word color test – improved attention ability to inhibit cognitive interference correlated with ↓neural activation in right intra-calcarine sulcus, right occipital cortex, and right occipital pole during attention time [17].</li> </ul>	<ul style="list-style-type: none"> <li>Barratt Impulsiveness Scale [14,15] – to assess impulsive personality traits.</li> <li>Beck depression inventory [14,15,18] – to assess characteristic attitude and symptoms of depression.</li> <li>Category fluency test [19-21] – to assess semantic memory.</li> </ul>
Cognitive execution	<ul style="list-style-type: none"> <li>Assessed with Trail making test and MoCA – improved visual attention and cognitive task-switching execution are positively associated with ↑neural activity with fALFF in right superior and middle frontal gyri and anterior cerebellum [20] or ↑GMV in total brain [22], or ↑medial prefrontal gyrus – medial temporal lobe connectivity [19,21].</li> </ul>	<ul style="list-style-type: none"> <li>Digit span forward and backward task [20,21] - to assess verbal and visuospatial short-term/working memory.</li> <li>Five facets mindfulness questionnaire [14,15,18] – to assess mindfulness with regard to thoughts, experiences, and actions in daily life.</li> </ul>
Dementia	<ul style="list-style-type: none"> <li>Assesses with Mattis dementia rating scale – improved dementia score is positively correlated with ↑GMV in total brain [22].</li> <li>Assessed with Category verb fluency test – a test for screening dementia improved that is positively correlated with ↑GMV in total brain [22].</li> </ul>	<ul style="list-style-type: none"> <li>Flanker task test [11]– to assess the ability to inhibit non-relevant competing responses to a nonverbal stimulus.</li> <li>Intra-extra dimensional Set Shift (IED) task [16] – to assess cognitive flexibility, error-making decision, ability, and executive functions.</li> </ul>
Emotional regulation and stability	<ul style="list-style-type: none"> <li>*Assessed with Sequential risk-taking test and Barratt Impulsiveness Scale – improved meditation level and emotional stability (less risk-taking less feeling of regret) are positively correlated with ↑GMV in thalamus[15] and ↑fronto-ventral striatum connectivity [14].</li> <li>*Assessed with five-facet mindfulness questionnaire and sequential decision task - improved emotional regulation affected by decisions based on own feeling, perception, and thoughts is positively associated with ↑dorsolateral prefrontal cortex – middle frontal gyrus connectivity [18].</li> </ul>	<ul style="list-style-type: none"> <li>Mattis Dementia Rating Scale [22] – to screen dementia in attention, initiation to preservation, construction, conceptualization, and memory.</li> <li>Mindful attention awareness scale [15,18] – to assess a core characteristic of dispositional mindfulness.</li> <li>Montreal cognitive assessment (MoCA) [20,21] – to assess cognitive or thinking abilities including orientation, short-term memory, execution, language, and abstraction.</li> </ul>
Error-making	<ul style="list-style-type: none"> <li>Assessed with intra-extra dimensional Set Shift (IED) – improved attentional set shifting (error-making) with ↑neural activity in left superior frontal gyrus [16].</li> </ul>	<ul style="list-style-type: none"> <li>N-back task [17] – to assess working memory.</li> <li>NEO five-factor inventory [14,15,18] – to assess different traits of personality.</li> </ul>
Memory	<ul style="list-style-type: none"> <li>*Assessed with N Back Task- improved working memory of continuous performance correlated with ↓fALFF in right superior frontal gyrus and frontal pole during working memory time [17].</li> <li>Assessed with paired associative Learning Test – improved episodic visual memory and new learning are positively correlated with ↑ReHo in right middle temporal gyrus [190].</li> <li>*Assessed with Montreal Cognitive Assessment (MOCA) scale – improved episodic memory is not significantly correlated with ↑ReHo in left hippocampus [10].</li> </ul>	<ul style="list-style-type: none"> <li>Paired associative learning test [19-21] – to assess learning ability and working memory.</li> <li>Satisfaction with life scale [20,21] – to assess global cognitive judgments of one’s life satisfaction.</li> <li>Sequential risk-taking task [14,15] – to</li> <li>Social support rating scale – to assess dimensions of social support.</li> <li>Stroop word color task [17] - to assess the ability to inhibit cognitive interference when focusing on a specific stimulus.</li> </ul>
Speech production	<ul style="list-style-type: none"> <li>Assessed with category Fluency Test and MoCA – improved speech production is positively correlated with ↑ReHo in left superior temporal gyrus [19] or ↑medial prefrontal gyrus – medial temporal lobe connectivity [19,21].</li> </ul>	<ul style="list-style-type: none"> <li>Trail making test [8,20,21]– to assess visual attention and task-switching.</li> <li>Victoria Stroop test [8] – to assess cognitive execution including cognitive flexibility and inhibition, selective attention, and information process speed.</li> </ul>
Satisfaction with life	<ul style="list-style-type: none"> <li>Assessed with Satisfactory with Life scale – improved satisfaction with life is positively associated with ↑neural activity with ↑fALFF in right superior and middle frontal gyri and anterior cerebellum [20].</li> </ul>	<ul style="list-style-type: none"> <li>Wechsler memory scale [8] – to assess verbal, auditory, visual, short-term/working memory.</li> </ul>

\*neurobehavioral improvements reported in Tai Chi practitioners who had long-term (≥ 3 years) practice in cross-sectional studies; fALFF: fractional amplitude of low-frequency fluctuations; GMV: grey matter volume; ReHo: regional homogeneity; ↑: increased/increase; ↓: decreased/decrease.

carine cortex, occipital cortex, and occipital pole [17].

## Discussion

In the last decade, there has been increase in the practice of TC in elderly population. Previous studies showed that TC practice is associated with several brain morphological changes. Although several of those studies showed that TC practice is associated with neurobehavioral changes, the effects of TC practice on brain and neurobehavioral aspects have not been synthesized. This present review examined and synthesized the available literature regarding how TC exercise might affect the brain after TC practice as assessed through these neuroimaging techniques, and how these TC effects might be associated with neurobehavioral changes and cognitive functions.

### *Evidence of neuroplasticity and relevant TC exercise parameters*

The results from the present review study demonstrate that TC practice can alter (actually mostly, increase) local neural activity and homogeneity, increased grey matter volume, and increased functional connectivity between neural regions in the brain [8-22]. This may provide neuroimaging-based structural evidence that TC exercise could elicit the brain plasticity and promote neurobehavioral improvements in older adults. Moreover, biological evidence of TC effect on neural plasticity in aged population were previously reported [23,24]. Brain derived neurotrophic factor (BDNF), a neurotrophin for neural growth and maintenance, was found significantly increased in a group of elderly people who practiced TC with the parameters: 50-minutes per session, 3 times a week for 6-month [23]. Further, after 60 minutes each,  $\geq 2$ /week for 12 weeks of TC practice, NAA (N-Acetylaspartate), an important biomarker used to assess neuronal health, was found significantly increased as well in the brain [24]. When considering TC exercise parameters to achieve potential neuroplastic changes both morphologically and biologically, the TC exercise parameters at 50-60 minutes each time and 3 or more times a week for a minimum of 12 weeks seem to be the reasonable to use based studies for biological evidence [23,24] and neuroimaging evidence [8,11,16,19-22].

### *Comparison of effects between the short-term and long-term TC practices*

To our knowledge, comparison of TC effects on brain and neurobehavioral changes between long-term (over three years) and short-term (less than one year) TC practice has not been previously reported in any longitudinal studies. This present review provides an opportunity to look these effects indirectly (Table 3), since it happens to be that among all qualified studies, the time length of TC practice was less than one year

in all RCT studies [8,11,16,19-22]; while the time length was three years and longer in all cross-sectional studies [9,10,12,13-15,17,18]. Topographically, in those practicing TC less than 1 year as seen in RCT studies, the lateral frontal lobe, lateral temporal lobe, prefrontal cortex, and cerebellum can be identified as the TC-affected regions [8,11,16,19-22]. However, in those practicing TC over 3 years as seen in the cross-sectional studies, there are more brain regions involved including hippocampus, fusiform gyrus, occipital cortex, thalamus, ventral striatum, and dorsolateral prefrontal cortex [9,10,12,13-15,17,18]. Intriguingly, as shown in table 4, the short-term practice in RCT studies appears to have improvement in attention selection, cognitive execution, dementia, risk of error-making, episodic memory, speech, and self-satisfaction with life; while the long-term practice in cross-sectional studies seems to have additional improvements in ability of inhibiting cognitive interference during attention [17], emotional regulation and stability [14,15] and working memory [17]. These findings may reveal that TC effects on brain and neurobehavioral aspects are time-length associated. The longer one practices TC, the more brain regions (e.g., increased gray matter volume in hippocampus [10,15], thalamus [15]) and temporal lobe [10]), and the more additional neurobehavioral improvements (e.g., emotional control [14,15], and working memory [17]), can be identified in the long-term TC practitioners.

### *Altered functional neural connectivity for neurobehavioral changes*

As presented in tables 2 and 4, the associations between the functional connectivity among neural structures and relevant neurobehavioral changes were usually conducted with resting state functional MRI, in which a seed neural region is determined in order to see where other neural regions may make connectivity with the seed one. Since the frontal lobe is the common place related to neurobehavioral aspects and cognitive activities, the neural structures in the frontal lobe are often determined as a seed region for the investigation purpose of inter-connectivity between neural regions. So far, the connectivity between frontal-striatum [14], dorsolateral prefrontal cortex-middle frontal gyrus [18], and medial prefrontal cortex-middle temporal gyrus [19,21] have been conducted and found increased. These connections are in association with improved emotion control [14,18] and cognitive execution [19,21]. As more such connectivity studies are going to be carried out in the near future, a better and clearer picture of how these neural structures work alongside each other could be hopefully soon available.

### *TC on cognitive neural network*



Default mode network (DMN) is a network of interactive and interconnecting neural regions in the brain that engages in internally oriented cognition (e.g., attentional focus) [38]. Medial and superior prefrontal cortex, medial and lateral temporal lobes, and cerebellum are part of the DMN network [38]. On the other hand, the dorsolateral prefrontal cortex (DLPFC) is also a part of the cognitive control network (CCN) that is responsible for focused cognitive execution task, e.g., the target memory maintenance [39]. These herein mentioned frontal and temporal regions have increased neural activity and grey matter volume, and even the functional connectivity after TC practice as shown in table 2, so these may draw an inference that TC could affect both DMN and CCN related cognitive activities. For examples, the improvements of internally oriented cognitive behaviors such as attention, meditation level, emotion stability are noticed [14,15,18]. The improvements of externally focused cognitive tasks, for examples, abilities to inhibit cognitive interference during cognitive execution [11,17] or to avoid error-making [16], or to improve working memory [17] are also observed. Such cognitive improvements, as parts of neurobehavioral functions, are positively correlated with increased grey matter and neural activity in most component regions of the DMN and CCN as aforementioned [9,10,12,13-15,18]. However, interestingly, one of cross-sectional studies reported decreased neural activity in frontal and occipital areas in TC practitioners compared with people doing water-aerobic exercise when assessing the capability of working memory and the ability to inhibit cognitive interference and [17]. This may suggest that after long-term TC practice, TC practitioners might have developed more efficient cognitive performance with less neural activity needed in the brain.

#### *Neuroimaging response and related neurobehavioral improvements after TC practice*

In addition to cognitive aspect such as attention, execution, awareness, impulse-control, decision-making and judgment, and memory, neurobehavioral functions also consist of, language, sensory interpretation, and satisfaction [25,26]. As shown in the results of this review, neural regions in the frontal, temporal, occipital lobes, cerebellum, and thalamus are the main areas that respond to TC effect. Functionally, in the frontal lobe, the superior frontal gyrus is for self-awareness of individual personality [27]; the middle frontal gyrus is a convergence site of attention networks for higher order cognition and motor-related information processing [28]; the medial prefrontal cortex is for memory and decision making [29]; and the dorsolateral prefrontal cortex is for top-down attentional and cognitive control [30]. In the temporal lobe, the superior temporal gyrus is functionally for

language perception and social cognition [31]; the middle temporal gyrus is for semantic memory processing of familiar face, language, and voice [32]; the medial temporal lobe, including hippocampus, is associated with emotion learning and behavior, as well as memory encoding, consolidation, storage, and retrieval, particularly for episodic and spatial memory [33]; and the fusiform gyrus is for object and face recognition and semantic memory [34]. The cerebellum, besides motor learning and coordination, is also for cognition and emotional processing, and injury to the cerebellum may cause cerebellar cognitive affective syndrome [35]. The thalamus is a relay hub for multiple sensory information and even memory [36]. The occipital lobe participates in cognition improvement, anti-memory decline, and perception of objects [37]. In the present review, we noticed that TC is able to cause structural changes in the above-mentioned neural regions (Table 2), and is as well able to improve many of the neurobehavioral functions via its effects on different parts of the brain (Table 4). The studies included in this article are indicative that these neural regions above indeed involve in TC-affected neurobehavioral changes. However, up to date, how these different neural regions are structurally interconnected and/or functionally interacted for sure need further investigation.

#### *TC is a better body-mind exercise compared with some other exercises*

Numerous studies have revealed that TC is able to improve pain, balance, endurance, and muscle strength [40]. TC could show better results for physical health than other physical exercises, like the Keep-Fit exercise [41,42], particularly when considering the long-term TC practicing [42]. As of improving the mental health, this review article demonstrates that TC has better results as well. Compared with brisk walking [9,10] and aerobic exercise [17], TC can increase more grey matter and functional integration (evidenced with increased ReHo) in the hippocampus and temporal lobe [10], and can even likely improve the performance efficiency of neural activity (evidenced with decreased fALFF) in long-term TC practitioners [17]. These imply that TC is possibly a better mind exercise capable of improving neurobehavioral functions, indicated by altering neuroimaging manifestations in certain brain regions.

#### *Study limitations*

There are several limitations that should be noticed. 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, six out of 12 qualified studies are randomized control trials, while other 6 are cross-sectional studies. The

results from the six cross-sectional studies are not as high quality as those from the RCT studies based on their research methodology. Thus, the cross-sectional studies 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 [43]. If a different ROI was picked, the involved brain regions might vary. Fourth, tools for assessing the central nervous system may also include the electroencephalography (EEG), positron emission tomography (PET), and magnetoencephalography (MEG). However, up to this point, we have not seen any TC study using either PET or MEG for assessment. There are a few TC studies that applied EEG, but it was not considered by us as an imaging study technique for the brain, which might cause us missing valuable EEG data to complement the conclusions in this review article.

## Conclusions

In the last ten years, as neuroimaging techniques develop, more structural changes of the human brain after TC practice have been investigated and identified in the frontal, temporal, and occipital lobes, cerebellum, and thalamus, with the frontal and temporal lobes having more changes than other regions. These changes include increased cortical grey matter volume, altered local spontaneous neural activity, as well as increased inter-regional functional connections. The longer one practiced TC, the more brain areas may change. Many of these changes are associated with improvements of neuropsychological behaviors such as attention, cognitive execution, anti-cognition decline, emotional regulation and stability, avoidance of error-making, memory, speech production, and satisfaction with life. All of these indicate that TC can be a great exercise program to improve the neural dysfunctions in older adults practicing TC. Future studies are needed to assess how functionally the brain areas may be altered, integrated and/or specialized in longer longitudinal TC studies.

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## Conflict of Interests

No.

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