

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Effect of Baduanjin exercise on cognitive function in patients with post-stroke cognitive impairment: Study protocol for a randomized controlled trial
AUTHORS	Zheng, Yuhui; Zheng, Guohua; Xiong, Zhenyu; Ye, Bingzhao; Tao, Jing; Chen, Lidian

VERSION 1 – REVIEW

REVIEWER	Shin-Yi Chiou Imperial College London, United Kingdom.
REVIEW RETURNED	15-Jan-2018

GENERAL COMMENTS	<p>The purpose of this study is to investigate the effectiveness and safety of Baduanjin training on cognitive function of stroke survivors. It is a multi-centre, single blinded (assessors blinded), randomised controlled trial. The study protocol is straightforward and may possibly examine the aims of the study. However, there are a few points requiring clarification from the authors:</p> <ol style="list-style-type: none">1. The rationale for the protocol of intervention (i.e. intensity, duration) is unclear. As pointed out by the authors in the Introduction, the insufficient compliance may compromise the effect of the intervention on improving cognitive function and therefore the optimal protocol is required. How would the authors address this challenge?2. The description of Baduanjin exercise is vague. As stated by the authors, it is a mind-body exercise. Can the authors provide more details to address how are both physical and psychological components incorporated in this exercise?3. The study will be conducted in two centres and outcome measures will be performed by several people (i.e. neurologists, research assistants, medical staff). How is the fidelity of the study protocol checked?4. There are other factors affecting recovery of cognitive function (e.g. infarct side). Has a stratified randomisation technique been considered to account for the confounding factors? Or will this be addressed by statistical methods? In addition, are there other potential confounding factors noted? How would they be addressed?5. The cited literature used Addenbrookes's Cognitive Examination-Revised to assess cognitive function which is different from the assessment of the primary outcome in this study (i.e. MoCA). It would be more appropriate to perform power calculation based on the numbers obtained from the same primary outcome.6. Can the authors please make clear who are blinded in the trial? For example, will the research assistants involved in secondary outcome assessment also be involved in the procedure of participant retention as well as data entry?
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	<p>7. Does the intervention group undergo Baduanjin exercise training, in addition to the routine medical or rehabilitation treatment and health education? If so, please change the first sentence of the paragraph of the Intervention group to reflect this.</p> <p>8. Follow-up. The authors have planned to contact participants once every week via telephone after the completion of the intervention. Are there any assessments performed over the telephone? In the flow diagram, the follow-up assessment is only performed at 28 weeks.</p> <p>9. Will the amount of exercise that participants perform outside the time of the intervention be recorded? How would the authors plan to control this potential confounding factor?</p> <p>10. How often will the research assistants call the participants to motivate them to exercise? Are the participants able to reach the research assistants?</p> <p>11. Does the reward at the completion of the study apply to both groups? Please clarify.</p> <p>12. How long does the entire cognitive functional assessment take? Attention is related to cognitive function and long assessment time might fatigue participants (especially they are stroke survivors) and therefore affect the results. Would this be an issue?</p> <p>13. Please clarify the time points where the various secondary outcome measures will be carried out. The planned time points for the assessment stated in the text and in the figure 2 are different.</p> <p>14. Please clarify what is the calculation task that will be performed during walking.</p> <p>15. Please include gait parameters planned to collect during the gait assessment.</p> <p>16. Figure 1 some of the content in the text is obscured or unfinished. The time points and parameters of outcome assessments are not clear in the figure 1.</p>
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REVIEWER	Liye Zou Department of Sports Science and Physical Education, The Chinese University of Hong Kong, China
REVIEW RETURNED	29-Jan-2018

GENERAL COMMENTS	<p>It is a well-designed study, but the following things should be considered:</p> <p>1. Line 48-49, what does “a third of them may transform to dementia: mean? It does not make any sense to me. If you are trying to state that post-stroke patients with cognitive impairment are more likely to become dementia, please restate your sentence. Also, the introduction section is very difficult to follow through/understand (is usually not logical)</p> <p>2. My curiosity: do you really think that Baduanjin could improve cognitive function in this special population? From my understanding, exercise may be able to slow down the progression of cognitive degeneration in older adults or stimulate the cognitive abilities in children and adolescents (because their brain is not fully mature). For these post-stroke patients with cognition impaired (frontal lobe, particularly pre-frontal lobe is damaged already), can Baduanjin exercise rebuild the brain area? If not, I don't think the cognitive function of the special population can be improved.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

1. The rationale for the protocol of intervention (i.e. intensity, duration) is unclear. As pointed out by the authors in the Introduction, the insufficient compliance may compromise the effect of the intervention on improving cognitive function and therefore the optimal protocol is required. How would the authors address this challenge?

Author's response:

Baduanjin is a mind-body exercise with mild to moderate intensity exercise. It has been reported by many references. For example, Zou L, et al. A review study on beneficial effects of Baduanjin. *J Altern Complement Med.* 2017 Dec 11. doi: 10.1089/acm.2017.0241. Koh TC. Baduanjin -- an ancient Chinese exercise. *Am J Chin Med.* 1982;10:14-21. Tai J, et al. Tai Chi Chuan and Baduanjin Increase Grey Matter Volume in Older Adults: A Brain Imaging Study. *J Alzheimers Dis.* 2017;60(2):389-400. doi: 10.3233/JAD-170477. Previous studies have also reported that regular Baduanjin exercise has positive benefit in preventing age-related memory decline, delaying ageing of intelligence in older adults (Wang ST. Effect of Baduanjin on physiological age of intelligence for old people. *Journal of Clinical Rehabilitative Tissue Engineering Research.* 2007;11:7910-3. Ge S, Anli W. The influences of two different exercise means on the intellectual physiological age of the male elderly people. *Journal of Beijing Sport University.* 2008;31:1093-5.) . Above rationale of intervention is described in "Background" section of this manuscript. Please check them.

In this trial, we design the program of Baduanjin intervention that Baduanjin training will last 24 weeks with a frequency of 3 days one week and 40 min a day. The scheme of intervention has also been described in the section of Method. Please check.

Participants' compliance is a important factors to influence the effect of intervention. In order to ensure participants' compliance, the following quality control measures will be conducted in this trial:

- ① In the stage of recruitment, we will conduct the lecture about the benefit of Baduanjin training, and will carefully explain the objective and program of this study for the potential participants.
- ② In the stage of intervention period, we will employ the professional coaches to teach and supervise participants' Baduanjin training.
- ③ The study assistants will set up a WeChat group of Baduanjin training, and sent the training information to each participant.
- ④ We will provide the free medical examination to incite participants' participation positivity.

2. The description of Baduanjin exercise is vague. As stated by the authors, it is a mind-body exercise. Can the authors provide more details to address how are both physical and psychological components incorporated in this exercise?

Author's response:

As an important concept of traditional Chinese medicine theories, mind-body training emphasizes the interaction between the brain, the mind, and the body. The fundamental assumption is that individuals can regulate breathing, heart, and body activities by their own thoughts, resulting in enhancement in physical and mental health. Baduanjin (also called Eight Section Brocade) is a traditional Chinese mind-body exercise, characterized by slow, coordinative, sequential movements. The main forms of Baduanjin are eight separate exercises, with each exercise focusing on a different physical area and Qi meridian, which moves and activates all parts of the body. Baduanjin developed from the I-Ching philosophy regarding a balance between Yin and Yang. This set aims not only to strengthen musculo-skeletal fitness and circulation together with a Qi breathing training, but also to regulate emotions, representing body-mind effectiveness. Compared to the complex movements, such as Tai-Chi which is one of the most popular Chinese traditional Qigong exercises, Baduanjin is more easy-to-learn because it involves only eight separate movements. Each individual movement needs to be practiced on both the left and right sides of the body, while integrating deep rhythmic breathing, a meditative mind, and musculoskeletal stretching and relaxation.

3. The study will be conducted in two centres and outcome measures will be performed by several people (i.e. neurologists, research assistants, medical staff). How is the fidelity of the study protocol checked?

Author's response:

This study will be conducted at the Wufeng Community Centre in the Gulou District and the Cangxia Community Centre in the Taijiang District, Fuzhou City, Fujian, China. Participants are stroke patients from community, and those stroke patients have recovered from the acute attack and enter the community or family rehabilitation. Their routine medical or rehabilitative treatment will be performed by their care physicians according to the Chinese Medical Association's Guidelines for the Prevention and Treatment of Cerebrovascular Disease in China. The research assistant will record those treatment. The professional neurologists will be conducted the health education about the knowledge of the prevention and rehabilitation of stroke according to "Out of the Misunderstanding of Stroke Patients' Rehabilitation" (a bestseller book for health education after stroke from the Chinese Association of TCM)..... This study will be completed by the cooperation of several people (i.e. neurologists, research assistants, medical staff). In order to avoid or reduce the bias from researchers, we will convene them together and hold a project start meeting to understand the trial protocol.

4. There are other factors affecting recovery of cognitive function (e.g. infarct side). Has a stratified randomisation technique been considered to account for the confounding factors? Or will this be addressed by statistical methods? In addition, are there other potential confounding factors noted? How would they be addressed?

Author's response:

We agree with your comment very much. Due to the participants are the patients with post-stroke, there are too much confounding factors to influence the intervention effect. We also hope to avoid all of the confounding factors as far as possible. However, in fact, it is very difficult to recruit the stroke patients in China. Most of stroke patients are unwilling to participate any research project. If we design a ingenious trial protocol to avoid more confounding factors (e.g. stratified randomization), it will lengthen the research period and make the recruitment more difficult. Due the limitation of fund and research time, we can only use the simple randomization method to avoid the selection bias of participants, and reduce the influence of other potential confounding factors (such as location of infarction, basic medical treatment, course of disease, etc). Furthermore, we will record those cofounding factors to compare their balance between the intervention group and control group. If it is unbalance in certain cofounding factor between groups, we will adjust the bias effect by the rational statistical method.

5. The cited literature used Addenbrookes's Cognitive Examination-Revised to assess cognitive function which is different from the assessment of the primary outcome in this study (i.e. MoCA). It would be more appropriate to perform power calculation based on the numbers obtained from the same primary outcome.

Author's response:

Thanks for your comment. When we calculate the sample size, we did not find the references which it applied aerobic exercise as intervention method and MoCA as the primary outcome measure. Furthermore, we also found that there was an article indicating that ACE-R and MoCA are similarly in evaluating cognitive ability of stable cerebrovascular disease (Pendlebury S T, Mariz J, Bull L, et al. MoCA, ACE-R, and MMSE versus the National Institute of Neurological Disorders and Stroke-Canadian Stroke Network Vascular Cognitive Impairment Harmonization Standards Neuropsychological Battery after TIA and stroke[J]. Stroke, 2012, 43(2):464.). Therefore, we chose this article as the basis for calculating the sample size.

6. Can the authors please make clear who are blinded in the trial? For example, will the research assistants involved in secondary outcome assessment also be involved in the procedure of participant retention as well as data entry?

Author's response:

In this trial, it is impossible to blind the participants and exercise coaches because this trial investigates a non-pharmacological intervention. Other researchers who involve in outcome measurements, data entry and data management will be blinded in this study. We will employ at least four research assistants to be in charge of recruitment, intervention spot management and data entry, respectively. Most of outcome measurements will be performed by the blinded medical staff. A more clear description has been revised in the revised manuscript. Please check.

7. Does the intervention group undergo Baduanjin exercise training, in addition to the routine medical or rehabilitation treatment and health education? If so, please change the first sentence of the paragraph of the Intervention group to reflect this.

Author's response:

Besides Baduanjin exercise training, participants in the intervention group also receive routine medical or rehabilitative treatment and health education. We have revised the first sentence of the paragraph of the Intervention group according to your comments. Please check. Thanks!

8. Follow-up. The authors have planned to contact participants once every week via telephone after the completion of the intervention. Are there any assessments performed over the telephone? In the flow diagram, the follow-up assessment is only performed at 28 weeks.

Author's response:

During the additional 4 weeks follow-up period, the research assistants will ask all participants the information about subjective feeling, medications and daily activities by telephone or home visiting. At the end of 4 weeks follow-up, we will assign the professional staff to assess their primary and secondary outcomes. We have revised those vague information in the manuscript.

9. Will the amount of exercise that participants perform outside the time of the intervention be recorded? How would the authors plan to control this potential confounding factor?

Author's response:

Thanks for your comment. In order to exclude bias from the exceed activity of participants, we will also record the amount of exercise that participants perform outside the time of the intervention by activity log during the intervention and follow-up period. Therefore we inserted following sentences in the section of Method.

"In order to exclude bias from the exceed activity of participants, all participants in both intervention and control group will be required to record an activity log in the intervention period, in which the duration and intensity of their activity in a whole day will be classified into three sections including the duration of low-intensity, moderate-intensity, or high-intensity activities."

Please check them.

10. How often will the research assistants call the participants to motivate them to exercise? Are the participants able to reach the research assistants?

Author's response:

During the study period, we will set up a WeChat on the phone which will include all participants.

During the intervention period, research assistants who are in charge of the intervention spot will call or remind each participant in the intervention group to do Baduanjin exercise training according to the intervention scheme by the WeChat group. Participants can also reach the research assistants if they have some problem or need help by the WeChat group.

11. Does the reward at the completion of the study apply to both groups? Please clarify.

Author's response:

Every participant who complete the programme successfully will be rewarded, no matter which group they belongs to. We have clarified them in the revised manuscript.

12. How long does the entire cognitive functional assessment take? Attention is related to cognitive function and long assessment time might fatigue participants (especially they are stroke survivors) and therefore affect the results. Would this be an issue?

Author's response:

Thanks for your comment. We also take this issue into consideration. According to our pre-test, it took about 30-40 minutes to complete all the cognitive functional assessment. We will reasonably arrange the order of these assessment, or provide a short break so that those assessment does not fatigue participants.

13. Please clarify the time points where the various secondary outcome measures will be carried out. The planned time points for the assessment stated in the text and in the figure 2 are different.

Author's response:

We have modified the time points in manuscript. Executive ability, memory, attention, Processing speed and visuospatial ability will be measured at baseline, 8 weeks, 16 weeks and 24 weeks after intervention and at 28 weeks after a 4-week follow-up period. Gait stability, motor Function, balance function, activities of daily living and quality of life will be assessed at baseline, 24 weeks of intervention and 28 weeks after a 4-week follow-up period.

14. Please clarify what is the calculation task that will be performed during walking.

Author's response:

This is a gait analysis in two assigned conditions. Participants will be instructed to do two work concurrently (i.e. walk as usual and at same time execute a calculation task) when their gait are measured. The calculation task is that ask participants subtract 7 from 100, then subtract 7 from the outcome of last calculation, and so on, until participants finish the walking.

15. Please include gait parameters planned to collect during the gait assessment.

Author's response:

The gait parameters mainly comprise of step length (cm), stride length (cm), forward velocity (cm/s), cadence (steps/min), total support time (%), swing time (%), double support time (%), single support time (%) and step width (cm). All these parameters include the affected and unaffected side.

Above description has added in the revised manuscript. Please check!

16. Figure 1 some of the content in the text is obscured or unfinished. The time points and parameters of outcome assessments are not clear in the figure 1.

Author's response:

We have revised Figure1 in the manuscript according to your comments. Please check them.

Reviewer: 2

1. Line 48-49, what does "a third of them may transform to dementia: mean? It does not make any sense to me. If you are trying to state that post-stroke patients with cognitive impairment are more likely to become dementia, please restate your sentence. Also, the introduction section is very difficult to follow through/understand (is usually not logical)

Author's response:

Thanks for your comment. Indeed, we are trying to state that post-stroke patients with cognitive impairment are more likely to become dementia. According to the references that we have read (seen the following), approximately two-thirds of stroke survivors have some extent to cognitive impairment at five years post-stroke, and up to a quarter of those stroke survivors with cognitive impairment are more likely to transition to dementia. Maybe, our description misunderstand you. We have revise the sentence in the revised manuscript according to your comment. Thanks!

In Mellon L, et al.' study, they reported that over half of stroke patients (56.6%) were found to have cognitive impairment at six months post-stroke [Mellon L, Brewer L, Hall P, et al. Cognitive impairment six months after ischaemic stroke: a profile from the ASPIRE-S study. BMC Neurol 2015;15:1–9.]. Jin,

et al reported that 64% stroke survivors have cognitive impairment at the 5-year follow-up [Jin YP, Legge SD, Ostbye T, Feightner JW, Hachinski V. The reciprocal risks of stroke and cognitive impairment in an elderly population. *Alzheimers Dement*. 2006;2:171-8.]. Feigin VL, et al., reported that approximately two-thirds of stroke survivors have some form of neurological impairment at five years post-stroke [Feigin VL, Barker-Collo S, Parag V, Senior H, Lawes CM, Ratnasabapathy Y, et al. Auckland Stroke Outcomes Study. Part 1: Gender, stroke types, ethnicity, and functional outcomes 5 years post-stroke. *Neurology*. 2010;75(18):1597–607.]. Narasimhalu K, et al. also reported that those with moderate post-stroke cognitive impairment are six times more likely to transition to incident dementia compared with those without cognitive impairment [Narasimhalu K, Ang S, De Silva DA, et al. Severity of CIND and MCI predict incidence of dementia in an ischemic stroke cohort. *Neurology* 2009;73:1866–72.]. Sachdev PS, et al. reported that the dementia rate up to a quarter of patients (24.4%) were diagnosed among the stroke survivors with mild cognitive impairment in the 3 years following stroke [Sachdev PS, Chen X, Brodaty H, et al. The determinants and longitudinal course of post-stroke mild cognitive impairment. *J Int Neuropsychol Soc* 2009;15:915–23.].

2. My curiosity: do you really think that Baduanjin could improve cognitive function in this special population? From my understanding, exercise may be able to slow down the progression of cognitive degeneration in older adults or stimulate the cognitive abilities in children and adolescents (because their brain is not fully mature). For these post-stroke patients with cognition impaired (frontal lobe, particularly pre-frontal lobe is damaged already), can Baduanjin exercise rebuild the brain area? If not, I don't think the cognitive function of the special population can be improved.

Author's response:

Regular physical activity or exercise is benefit to improve cognitive ability in community older adults or stroke survivors. This opinion has been reported in many studies. For example, Blanchet S, et al reported that a short-term aerobic exercise intervention can improve the attention ability in chronic stroke survivors with cognitive impairment [Blanchet S, Richards CL, Leblond J, Olivier C, Maltais DB. Cardiorespiratory fitness and cognitive functioning following short-term interventions in chronic stroke survivors with cognitive impairment: a pilot study. *Int J Rehabil Res*. 2016;39(2):153-9.]. Moore SA, et al. reported the community-based exercise (19 weeks, 3 times/wk) is significant to improve the cognitive function and reduce gray matter atrophy in participants following stroke [Moore SA, Hallsworth K, Jakovljevic DG, et al. Effects of Community Exercise Therapy on Metabolic, Brain, Physical, and Cognitive Function Following Stroke: A Randomized Controlled Pilot Trial. *Neurorehabil Neural Repair*. 2015;29(7):623-35.]. El-Tamawy MS, et al. also reported that aerobic exercise can improve cognitive function of ischemic stroke patients [El-Tamawy MS, Abd-Allah F, Ahmed SM, Darwish MH, Khalifa HA. Aerobic exercises enhance cognitive functions and brain derived neurotrophic factor in ischemic stroke patients. *NeuroRehabilitation*. 2014;34(1):209-13.]. Baduanjin (also called Eight Section Brocade) is a traditional Chinese mind-body exercise with moderate exercise intensity, characterized by slow, coordinative, sequential movements. The main forms of Baduanjin are eight separate exercises, with each exercise focusing on a different physical area and Qi meridian, which moves and activates all parts of the body. Baduanjin developed from the I-Ching philosophy regarding a balance between Yin and Yang, which emphasizes the interaction between the brain, the mind, and the body. Previous studies(Tao J, Liu J, Egorova N, et al. Increased Hippocampus–Medial Prefrontal Cortex Resting-State Functional Connectivity and Memory Function after Tai Chi Chuan Practice in Elder Adults[J]. *Frontiers in Aging Neuroscience*, 2016, 8:25.) provide evidence that the bilateral hippocampus and the medial prefrontal cortex significantly increased in Baduanjin group compared to the control group. And the article(Tao J, Chen X, Egorova N, et al. Tai Chi Chuan and Baduanjin practice modulates functional connectivity of the cognitive control network in older adults[J]. *Scientific Reports*, 2017, 7:41581.) demonstrate the potential of Baduanjin exercises in preventing cognitive decline. Consequently, we speculate that regular Baduanjin exercise could be beneficial for cognitive function in patients with post-stroke cognitive dysfunction.

VERSION 2 – REVIEW

REVIEWER	Shin-Yi Chiou Imperial College London, UK.
REVIEW RETURNED	21-Mar-2018

GENERAL COMMENTS	<p>The authors have addressed most of my comments and made changes in the manuscript to improve the clarity of the study. I only have few more comments made on this revised manuscript, please see my comments below.</p> <p>Abstract. The description of the assessment at 28 weeks is confusing. Do the authors mean to assess participants 4 weeks after the completion of the intervention? Or do the authors mean to assess the participants 4 weeks after the completion of the intervention, and then assessment them again in 28 weeks? Please could the authors make this clearer by revising the description throughout the text?</p> <p>Introduction. Reference 14 did not compare the Baduanjin exercise with other forms of aerobic exercises, and therefore it isn't suitable to be used in support of the statement that Baduanjin exercise has less limitation than other aerobic exercises. Could the authors please find a different reference to avoid misleading? I realised that Baduanjin exercise is categorised as aerobic exercise by reading one of the references. If this is true, could the authors include this in the introduction to improve the clarity of comparing Baduanjin exercise with aerobic exercises?</p> <p>Methods. Although the authors addressed the rationale for Baduanjin exercise, they didn't actually address the rationale for the exercise protocol. The length of intervention reported in previous studies varies between 6 weeks and 1 year; the review study (Zou et al., 2017) did not conclude an optimal protocol for Baduanjin exercise. It is therefore unclear how the exercise protocol was determined. Could the authors please justify how would the effects of confounder, if there is any, be addressed using statistical approaches?</p> <p>Minor comments. In the discussion, Zhu HM et al. should be Zhu et al. Figure 1. 'Gait stability, motor 'Function', balance function,...', please change the motor function to lower cases. There is a space missing between life and will in the box.</p>
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REVIEWER	Liye Zou The Chinese University of Hong Kong, China
REVIEW RETURNED	24-Mar-2018

GENERAL COMMENTS	All issues are solved! I recommend for publication!
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

1. Abstract. The description of the assessment at 28 weeks is confusing. Do the authors mean to assess participants 4 weeks after the completion of the intervention? Or do the authors mean to assess the participants 4 weeks after the completion of the intervention, and then assessment them again in 28 weeks? Please could the authors make this clearer by revising the description throughout the text?

Author's response:

In this trial, participants will be receive 24 weeks Baduanjin exercise intervention or maintain 24 weeks usual physical activity. After intervention 24-week period, all participants will enter an additional 4-week no-supervise follow-up period. The assessment of global cognitive function and specific domain of cognitive function will be conducted at baseline, 8-, 16-, 24-week after intervention, and after an additional 4-week follow-up, while the motor function and quality of life will be measured at baseline, 24-week after intervention, and after an additional 4-week follow-up period.. We has revised the description of assessment throughout the text. Please check.

2. Introduction. Reference 14 did not compare the Baduanjin exercise with other forms of aerobic exercises, and therefore it isn't suitable to be used in support of the statement that Baduanjin exercise has less limitation than other aerobic exercises. Could the authors please find a differetn reference to avoid misleading? I realised that Baduanjin exercise is categorised as aerobic exercise by reading one of the references. If this is true, could the authors include this in the introduction to improve the clarity of comparing Badjuanjin exercise with aerobic exercises?

Author's response:

Thank you for your comment. Thought Baduanjin exercise consists of eight movement, it can be categorized as a moderate intensity aerobic mind-body exercise, which has been described by many references, such as Koch (an ancient Chinese exercise. Am J Chin Med. 1982;10:14-21.) and An BC, et al (An BC, Wang Y, Jiang X, et al. Effects of Baduanjin, exercise on knee osteoarthritis: a one-year study.Chinese Journal of Integrative Medicine. 2013;19(2):143-8.). In the An's paper, author described "Baduanjin, as another related form of fitness exercise, offers advantages more suited to the needs of physically weaker and more cognitively impaired elderly. It is easy to learn and low physically demanding".

We have revised the description of Baduanjin in the Introduction section. Please check.

3. Methods. Although the authors addressed the rationale for Baduanjin exercise, they didn't actually address the rationale for the exercise protocol. The length of intervention reported in previous studies varies between 6 weeks and 1 year; the review study (Zou et al., 2017) did not conclude an optimal protocol for Baduanjin exercise. It is therefore unclear how the exercise protocol was determined. Could the authors please justify how would the effects of confounder, if there is any, be addressed using statistical approaches?

Author's response:

As Zou et al's description in his review, an increasing studies have reported regular Baduanjin exercise has a positive benefit to improve cognitive function in different population, but it is unclear how long Baduanjin exercise should be practiced, and the length of intervention varied from 6 weeks to 12 months in the previous studies. In our previous studies (Tao J, et al. Tai Chi Chuan and Baduanjin Mind-Body Training Changes Resting-State Low-Frequency Fluctuations in the Frontal Lobe of Older Adults: A Resting-State fMRI Study. Tai Chi Chuan and Baduanjin Increase Grey

Matter Volume in Older Adults: A Brain Imaging Study.), we compared a 12-weeks Baduanjin or TaiChi intervention with control (usual physical activity), and found the 12-week Baduanjin exercise have a positive beneficial in prevention of memory deficit in the community older adults, but the effect of preventing memory deficit yet is weak. According to our previous studies and experts' suggestion, we design a 24-week Baduanjin exercise intervention in this trial, and expect to get a more positive results in the patients with post-stroke cognitive impairment.

4. In the discussion, Zhu HM et al. should be Zhu et al.

Author's response:

Thank you for your reminding. We have made corresponding modifications in our manuscript according to your comments.

5. Figure 1. 'Gait stability, motor 'Function', balance function,...', please change the motor function to lower cases. There is a space missing between life and will in the box.

Author's response:

We have revised the Figure 1 according to your comments. Please check them.Thank you!