Effectiveness of Traditional Chinese Medicine (TCM) treatments on the cognitive functioning of elderly persons with mild cognitive impairment associated with white matter lesions

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**Background:** Cerebral white matter lesion (WML) is a pathological change of the white matter which is considered an early sign of brain impairment in elderly individuals, so it is reasonable to administer early dementia prevention programs to individuals with WML. Traditional Chinese Medicine (TCM) has developed several approaches to prevent or delay the onset of dementia that have, as yet, not been formally tested.

**Aim:** Evaluate the effects of a 6-month TCM intervention for elderly persons with mild cognitive impairment and WML.

**Methods:** Eighty individuals 65 years of age or older with radiological evidence of WML and mild cognitive impairment based on the Montreal Cognitive Assessment (MoCA) were classified into the four main TCM constitutional types (qi deficiency, yang deficiency, phlegm dampness, or blood stasis) and randomly assigned to a treatment group or a treatment-as-usual control group. The treatment group participated in training focused on diet, lifestyle, exercises, and emotional regulation adjustment; they also received six monthly courses of moxibustion (heating acupoints by burning the moxa of dried mugwort), each of which involved 10 daily 15-minute sessions focused on three targeted acupoints (one of which was specific to the constitutional type). Changes in the MoCA and in the score of each of the four constitutional types were the main outcomes assessed.

**Results:** Two participants dropped out of each group over the 6 months, leaving 38 in each group. Based on repeated measures analysis of variance, the total MoCA score, four of the six MoCA subscales scores (visual space and executive function, naming, attention and calculation, and delayed memory), and all four of the TCM constitution type scores showed significantly greater improvement over the 6 months in the treatment group than in the control group.

**Conclusions:** This study shows that TCM interventions can improve both the cognitive functioning and the severity of symptoms considered in the TCM assessment of constitutional types among elderly individuals with mild cognitive impairment and WML. Long-term follow-up studies that use blinded evaluation of the outcome are needed to determine whether or not constitution-specific TCM treatments can prevent the onset of dementia.

**Keywords:** Traditional Chinese Medicine; white matter lesion; mild cognitive impairment; dementia; moxibustion; China

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1. Introduction
Cerebral white matter lesion (WML) is a pathological change of the white matter myelin in the cerebral cortex, paraventricular, and centrum ovale that occurs in up to 92% of individuals 65 to 75 years of age. Among individuals with WML, 64% have associated cognitive impairment, so the appearance of WML is considered an early marker of deteriorating brain function.

This study assess the effectiveness of Traditional Chinese Medicine (TCM) treatments based on the TCM classification of constitutional types for improving both cognitive function and TCM constitutional status in elderly individuals with WML. TCM constitutional types are commonly assessed using Wang’s ‘Rule of Nine.’ A previous report by Lin and colleagues found that the most common TCM constitutional types in persons with mild cognitive impairment were ‘qi deficiency’ (22%) (i.e., inability of qi and blood to nourish the body), ‘blood stasis’ (18%) (i.e., poor blood flow), ‘yang deficiency’ (17%) (i.e., lack of body warmth), and ‘phlegm dampness’ (11%) (i.e., blockage of other body fluids).

2. Methods
2.1 Subjects
The enrollment and management of study participants is shown in Figure 1. The 80 participants included in the study were inpatients and outpatients in the Departments of Brain Disorders and Mental Disorders at the Zhejiang Jinhua Hospital of Traditional Chinese Medicine from August 2013 to July 2014. They all met the inclusion criteria:

a) 65-79 years of age;
b) clear consciousness, the ability to hear and see, and the capability to participate in neuro-psychological testing;
c) diagnosed with WML by expert radiologists based on cranial magnetic resonance imaging (MRI) results showing a T2 weighted image and fluid-attenuated inversion recovery (FLAIR) with high signals;

Figure 1. Flowchart of the study
d) total score on the Chinese version of the Clinical Dementia Rating Scale (CDR)\(^6\) of 0.0 to 0.5 and a total score on the Chinese version of the Montreal Cognitive Assessment (MoCA)\(^6\) of under 26;
e) classified as one of the four most common Traditional Chinese Medicine (TCM) constitutional types – ‘qi deficiency’, ‘yang deficiency’, ‘phlegm dampness’, and ‘blood stasis’ – as assessed using a computerized tool provided by Yanhuang Oriental (Beijing) Health Technology Co. Ltd.;\(^7\)
f) no other current mental illness or recent suicide;
g) no serious medical illness;
h) had not used any psychoactive medications in the prior months;
i) signed an informed consent statement to participate in the study.

2.2 Interventions

The 20 participants in each of the four constitutional groups were randomly assigned to treatment and control groups (10 in each group) using a random number table. The treatment-as-usual control group participated in physical exercises and training to enhance brain function; they also received educational training, nutritional counseling, psychological and social support, and routine care of any co-occurring physical illnesses such as diabetes or hypertension.

In addition to this standard care, individuals in the treatment group also received ‘dialectic care’ and moxibustion to improve brain functioning that was specifically tailored to their TCM constitutional type. Dialectic care (aimed at balancing opposing forces) included training to help participants make environmental, lifestyle, and psychological adjustments; physical exercises; and dietary regulation. Moxibustion (i.e., the application of heat to acupuncture points by burning moxa made from dried mugwort) was administered to three acupoints for 15 minutes daily for 10 days and then the 10-day course of treatment was repeated each month for a total of 6 months. Two primary acupoints were used for all constitutional groups (‘bai hui’ and ‘zu san li’) and one additional acupoint was used for each of the four different constitutional types: ‘qi hai’ for the qi deficiency group; ‘shen yu’ for the yang deficiency group; ‘feng long’ for the phlegm dampness group; and ‘xue hai’ for the blood stasis group.

All patients in the control and treatment groups were followed up by phone every month for 6 months to reinforce the training.

2.3 Assessments

Three months after enrollment all participants returned to hospital to be evaluated by a clinician using MoCA. Six months after enrollment they returned to hospital to again be evaluated by a clinician using MoCA and to re-assess the scores for the various TCM constitutional types. The Chinese version of MoCA has good reliability and validity.\(^{6,8}\) The scores for each of the four constitutional types were assessed as follows: a trained TCM doctor assessed the individual’s symptoms using the ‘TCM Constitutional Type Scale’ developed by Wang\(^9\) and entered the results in a computer program\(^12\) which then generated scores for each constitutional type and an overall classification of the individual’s constitutional type based on the scores. The scores for each constitutional type were classified as ‘negative’ (under 30), ‘sub-threshold’ (30-60), and ‘positive’ (over 60).

2.4 Statistical methods

The changes in the MoCA total score and MoCA subscale scores over the three time-points (baseline, 3 months, and 6 months) were compared between the treatment and control groups using repeated measures analysis of variance. Before versus after comparison of the scores for each of the four TCM constitutional types between groups were conducted using analysis of variance with the baseline values as covariates. Within-group before versus after comparisons used paired t-tests. Comparison of categorical variables used chi-square tests. The analysis was conducted using SPSS version 19.0. Two-tailed statistical significance was set at \(p<0.05\).

3. Results

There were no statistically significant differences between the characteristics of the 40 participants assigned to the treatment group compared to those of the 40 participants assigned to the control group. The treatment group included 27 women (67.5%) versus 24 (60.0%) in the control group (\(X^2=0.67, p=0.68\)). The mean age of the treatment group was 71.2 versus 70.9 years in the control group (\(t=0.32, p=0.35\)). The mean years of formal education was 12.1 years in the treatment group versus 13.1 years in the control group (\(t=0.17, p=0.49\)). Among treatment group participants 36 (90.0%) were married versus 34 (85.0%) in the control group (\(X^2=0.27, p=0.68\)). In the treatment group 32 participants had high blood pressure, 11 had diabetes, 14 had hyperlipidemia, and 6 had coronary disease; in the control group 33 had high blood pressure, 13 had diabetes, 15 had hyperlipidemia, and 4 had coronary disease. As shown in Figure 1, only 4 participants dropped out over the 6-month trial – two from each group; so the analysis was based on the 38 individuals in each group who completed the study.

Comparison of total and subscale MoCA scores between the two groups before and after the TCM intervention is shown in Table 1. The repeated measures analysis of variance found that the total MoCA score and those of four of the six MoCA subscales (visual space and executive function; naming; attention and calculation; and delayed memory) showed significant improvement over time and that the improvement in the treatment group was significantly
greater than that in the control group. However, the scores of the language subscale and the abstract thinking subscale of MoCA did not show any significant change over time or any significant difference between the two groups.

The results of the before versus after change for each of the four TCM constitutional scores are shown in Table 2. For all four constitutional scores, there was a large, statistically significant decrease (improvement) in the scores in the treatment group over the 6 months and a small, non-significant decrease in the control group. Symptoms frequently seen in all four constitutional types – dizziness, shortness of breath, fatigability, feeling chilled, soreness, weakness, coldness of the waist and knees, and forgetfulness – were all less commonly reported at the end of the trial in the treatment group than in the control group. After adjusting for baseline values, the analysis of variance indicated that the improvement in the treatment group was significantly greater than that in the control group for all four constitutional types. Using the three ranges in constitutional scores for ‘negative’, ‘sub-threshold’, and ‘positive’ (under 30, 30 to 60, and over 60, respectively), 6 months of treatment resulted in the following changes in the classification of the 10 treatment group participants in the four constitutional groups: in the qi deficiency group, 1 person changed to negative and 5 changed to sub-threshold; in the yang deficiency group, 4 persons changed to sub-threshold; in the phlegm dampness group, 1 person changed to negative and 3 to sub-threshold; and in the blood stasis group, 1 person changed to negative and 6 to sub-threshold.

### Table 1. Comparison of mean (sd) Montreal Cognitive Assessment (MoCA) total and subscale scores at baseline and after 3 months and 6 months in 38 treatment group and 38 control group subjects

| scale/subscale | group       | baseline         | 3 months        | 6 months       | change over time in all subjects | compare groups at 6 months | compare change over time in groups |
|----------------|-------------|------------------|-----------------|----------------|----------------------------------|---------------------------|----------------------------------|
|                |             | F (p-value)      | F (p-value)     | F (p-value)    |                                  |                           |                                  |
| **total score**| treatment   | 18.85 (3.03)     | 19.20 (1.14)    | 20.21 (3.34)   | 4.97 (0.026)                      | 5.32 (0.012)               | 7.74 (0.004)                     |
|                | control     | 18.61 (2.70)     | 18.42 (2.81)    | 18.21 (2.52)   |                                  |                           |                                  |
| **visual space and executive capacity** | treatment | 1.84 (1.42) | 1.87 (1.17) | 1.95 (1.01) | 5.76 (0.029) | 5.21 (0.015) | 5.05 (0.019) |
|                | control     | 1.89 (1.13)      | 2.32 (1.25)     | 1.89 (0.84)    |                                  |                           |                                  |
| **naming**     | treatment   | 2.29 (0.69)      | 2.89 (0.51)     | 2.91 (0.27)    | 5.58 (0.018)                      | 6.01 (0.009)               | 5.93 (0.010)                     |
|                | control     | 2.29 (0.52)      | 2.42 (0.55)     | 2.45 (0.49)    |                                  |                           |                                  |
| **attention and calculating** | treatment | 4.42 (1.20) | 4.87 (0.90) | 4.85 (0.77) | 2.06 (0.085) | 2.37 (0.078) | 1.82 (0.092) |
|                | control     | 4.55 (1.11)      | 4.42 (0.92)     | 4.63 (0.57)    |                                  |                           |                                  |
| **language**   | treatment   | 1.42 (0.72)      | 1.71 (0.73)     | 1.74 (0.59)    | 1.96 (0.090)                      | 1.78 (0.095)               | 2.31 (0.082)                     |
|                | control     | 1.11 (0.73)      | 1.00 (0.74)     | 1.05 (0.57)    |                                  |                           |                                  |
| **abstract thinking** | treatment | 0.74 (0.69) | 1.05 (0.73) | 1.13 (0.36) | 2.03 (0.088) | 2.29 (0.083) | 1.88 (0.095) |
|                | control     | 0.66 (0.63)      | 0.63 (0.79)     | 0.68 (0.59)    |                                  |                           |                                  |
| **delayed memory** | treatment | 2.71 (1.04) | 3.63 (0.91) | 3.78 (0.83) | 4.69 (0.033) | 4.83 (0.026) | 4.57 (0.035) |
|                | control     | 2.85 (0.82)      | 2.61 (1.00)     | 2.76 (1.13)    |                                  |                           |                                  |
| **orientation** | treatment   | 5.16 (0.95)      | 5.58 (0.60)     | 5.60 (0.50)    | 6.32 (0.014)                      | 5.33 (0.025)               | 6.01 (0.017)                     |
|                | control     | 5.21 (0.78)      | 5.03 (0.79)     | 5.27 (0.52)    |                                  |                           |                                  |

* repeated measures F-tests compares 6-month result adjusting for baseline result
* comparison with baseline significant at p<0.05
* comparison with baseline significant at p<0.01
Table 2. Comparison of mean (sd) constitutional subtype scores at baseline and after 6 months between treatment and control groups in four Traditional Chinese Medicine (TCM) constitutional subtypes of individuals

| Constitutional subtype | Treatment group | Control group | Baseline mean (sd) | 6 months mean (sd) | Before vs after comparison: paired t-test (p-value) |
|------------------------|----------------|--------------|-------------------|-------------------|-----------------------------------------------|
| Yang deficiency        | 10             | 10           | 56.03 (12.61)     | 40.77 (5.54)      | 15.2 (0.027)                                 |
|                        |                |              | 56.15 (8.66)      | 54.50 (8.19)      | 3.6 (0.121)                                  |
|                        |                |              | 40.77 (5.54)      | 40.77 (5.54)      |                                              |
|                        |                |              | 56.15 (8.66)      | 54.50 (8.19)      |                                              |
| Qi deficiency          | 10             | 10           | 50.30 (7.54)      | 35.99 (6.65)      | 13.7 (0.031)                                 |
|                        |                |              | 49.99 (7.05)      | 48.56 (6.60)      | 2.7 (0.135)                                  |
|                        |                |              | 35.99 (6.65)      | 35.99 (6.65)      |                                              |
|                        |                |              | 49.99 (7.05)      | 48.56 (6.60)      |                                              |
| Blood stasis           | 9              | 10           | 46.78 (4.16)      | 33.24 (8.33)      | 17.2 (0.014)                                 |
|                        |                |              | 46.36 (4.60)      | 44.41 (5.20)      | 5.5 (0.096)                                  |
|                        |                |              | 33.24 (8.33)      | 33.24 (8.33)      |                                              |
|                        |                |              | 46.36 (4.60)      | 44.41 (5.20)      |                                              |
| Phlegm dampness        | 9              | 8            | 48.22 (3.87)      | 38.78 (5.32)      | 15.5 (0.025)                                 |
|                        |                |              | 47.68 (5.01)      | 46.01 (5.95)      | 6.0 (0.089)                                  |
|                        |                |              | 38.78 (5.32)      | 38.78 (5.32)      |                                              |
|                        |                |              | 47.68 (5.01)      | 46.01 (5.95)      |                                              |

*a F-test compares final result while adjusting for baseline results (used as covariates)*

4. Discussion

4.1 Main findings

We found substantial benefits in this 6-month TCM intervention for mild cognitive impairment in individuals classified in one of the 4 most common TCM constitutional types. Individuals who received this intervention reported improvement in a wide range of distressing symptoms. This reduction in the prevalence and severity of physical symptoms decreased individuals’ overall discomfort, increased their willingness and ability to participate in social and educational activities, and, thus, reinforced their engagement in the types of activities that are known to delay cognitive impairment in elderly individuals.[9] These results confirm the findings of a 2010 study which reported that a comprehensive TCM intervention can improve cognitive functioning and associated symptoms of individuals with mild cognitive impairment associated with leukoaraiosis.[10]

The practice of TCM is based on the belief that the inherent weaknesses in each type of constitution, the rising and falling of vital Qi, and the prevalence of different types of pathogens collectively determine the onset, severity, course, and outcomes of illnesses. Thus a person’s constitution (as defined by TCM) determines his or her body’s susceptibility to pathogenic factors. But these constitution-specific susceptibilities are not immutable; Dr. Wang, who created the widely used classification criteria for the nine basic TCM constitutional types, including the four most common assessed in this study, suggests that a combination of relative stability and dynamic variability in constitutional characteristics is most adaptive.[3]

The TCM care provided in this study targets the specific weakness of each of the four main constitutional types and, thus, increases the individual’s resistance to the progressive cognitive decline that is often associated with aging, particularly in individuals with WML. The TCM treatment regimen involves training about environmental and lifestyle adjustments, physical exercises, emotional regulation, and diet. It also involves moxibustion treatments specifically focused on nourishing Qi (the life force), warming and activating meridians (the channels in the body via which Qi is transmitted), conditioning viscera, scattering ‘cold dampness’, promoting blood circulation (to reduce blood stasis), and strengthening the body’s resistance to pathogenic factors. Using moxibustion on the two acupoints relevant for all four constitutional types (‘bai hui’ and ‘zu san li’) helps in the circulation of Qi and blood to the brain,[11] relieving uneasiness of the mind and tranquilizing the body in ways that enhance cognitive functioning and raise an individual’s spirits. Use of moxibustion on the constitutional type-specific acupoints improves the treatment effect by dealing with the specific imbalances relevant for the particular constitutional type.

4.2 Limitations

There are several factors that need to be considered when evaluating these results. The outcome evaluations were conducted by evaluators who were aware of the treatment status of the participants, so this may have led to biases in the results. The treatment group received many more clinical interactions (they had 60 moxibustion sessions), so this increased interaction with clinicians may have had positive effects on their
functioning unrelated to the treatment itself. There were only 10 individuals in the treatment and control arms of each of the four TCM constitutional groups, so the small sample size may have limited the robustness of the results. The sample included both inpatients and outpatients which may have confounded the results. And the psychometric properties of the four constitutional measures used as one of the main outcomes have not been rigorously assessed.

4.3 Importance

This study suggests that a TCM treatment based on intensive training and support combined with 60 sessions of moxibustion over a period of 6 months can substantially improve cognitive function in elderly individuals with mild cognitive impairment associated with WML. If this finding is confirmed in future studies, this could have important implications for retarding the onset and progression of dementia. However, the lack of blinding of the outcome measure and the large difference in the number of clinical contacts between the treatment and intervention groups indicates that subsequent studies that include effectively blinded evaluation of the outcome and mock treatments in the control group (to balance the number of clinical contacts between groups) will be needed to confirm these important results. Studies that continue for at least 3 years will be needed to demonstrate the long-term preventative effects of these TCM treatments. Other studies will be needed to distinguish the independent effects of the intensive training and moxibustion (are they both needed or is one sufficient?). Finally, the similar interventions administered to the four separate TCM constitutional groups and the very similar outcomes for the four groups suggests that further work is needed to demonstrate the value in classifying individuals into these groups and providing group-specific treatments.

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Conflict of interest statement

The authors declare that they have no conflict of interest related to this manuscript.

Informed consent

All participants provided written informed consent.

Ethical review

This study was approved by the Ethic Committee of Zhejiang Jinhua Hospital of Traditional Chinese Medicine.
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