Neuropsychological features in post-stroke cognitive impairment with no dementia patients with different Traditional Chinese Medicine syndromes

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Abstract

OBJECTIVE: To investigate neuropsychological features of post-stroke cognitive impairment with no dementia (PSCIND) patients with different Traditional Chinese Medicine (TCM) syndromes.

METHODS: We recruited 50 patients with PSCIND between April 2012 and March 2013. Patients were divided into different groups according to TCM classifications. Patients were assessed using neuropsychological tests, including cognitive screening (mini-mental state examination), memory testing (auditory verbal learning test), executive/attention (shape trails test, stroop color-word test (SCWT), reading the mind in the eyes test, the digit ordering test-A (DOT-A), and symbol digit modalities test), language (action naming test, Boston naming test, famous face test, similarity test, and verbal fluency test), and visuospatial functioning (complex figure test (CFT)).

RESULTS: We found no significant differences between patients with and without a diagnosis of turbid phlegm blocking the upper orifices on neuropsychological test performance. Patients diagnosed with upper hyperactivity of liver Yang syndrome scored significantly lower on the SCWT-C executive test and the CFT-delayed recall memory test. Patients with excess syndrome scored significantly lower on the SCWT-C executive test, and significantly higher on the DOT-A executive test.

CONCLUSION: Neuropsychological characteristics differ between PSCIND patients with different TCM classifications.

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Key words: Cognitive dysfunction; Stroke; Syndromes and signs; Neuropsychological tests

INTRODUCTION

Vascular cognitive impairment (VCI) is a type of cognitive impairment associated with vascular factors.1–3 VCI ranges from mild cognitive impairment (MCI) to dementia, and was first described by Hachinski.1 Because of differences in the curative effects and prognosis of
different types of dementia, many recent studies have focused on patients exhibiting vascular cognitive impairment-no dementia (VCIND). Previous studies of VCIND can be categorized according to their focus: (a) diagnostic methods, including functional magnetic resonance imaging (MRI), cognitive assessments, electroencephalography, and transcranial magnetic stimulation; (b) clinical characteristics including neuropsychological assessments and sleep macrostructure studies; (c) treatment; and (d) prevention. However, few studies have investigated the relationship between VCI and Chinese medicine, and only one study has examined the correlations between cognitive function and Traditional Chinese Medicine (TCM) syndrome classification in VCI patients. VCIND associated with stroke has been termed post-stroke cognitive impairment with no dementia (PSCIND). Previous studies have indicated that approximately one in six older people will suffer from stroke, and 30% will experience post-stroke cognitive impairment. However, relatively few studies have examined PSCIND, and no previous reports have studied the neuropsychological features of PSCIND with different TCM syndromes. In TCM, syndromes are pathological classifications describing a stage of disease progression, which can reflect the etiology, pathogenesis, nature of disease, symptoms, and trends of disease. It is currently unclear whether PSCIND patients with different TCM syndromes exhibit differences in cognitive function.

To examine cognitive impairment after stroke in more depth, we used a range of neuropsychological tests to investigate cognition in different cognitive domains, including memory, executive/attention, language, and visuospatial functioning. We diagnosed TCM syndromes to explore the neuropsychological features of different TCM syndromes in PSCIND patients. This study sought to elucidate the relationship between TCM syndromes and cognitive features in PSCIND patients, and to provide a basis for the prevention and treatment of PSCIND with TCM.

METHODS

Participants
This prospective, observational study received ethical approval from the institutional review board at the Yueyang Hospital of Integrated Traditional Chinese and Western Medicine. We recruited patients presenting to the neurology department outpatient clinics of Yueyang Hospital and Huashan Hospital between April 2012 and March 2013. All participants underwent brain MRI or computed tomography demonstrating strategic infarcts or subcortical small vessel infarcts, and reported an absence of anxiety, depression, other mental disorders, severe somatic disease, and visual or auditory disturbances in the previous month. Patients with cognitive complaints that were reported after the manifestation of infarcts answered questions about the occurrence of any cognitive problems, in the presence of a reliable caregiver.

Experienced neurologists diagnosed patients with PSCIND using the broad MCI diagnostic criteria recommended by the international working group on MCI. We used the National Institute of Neurological Disorders and Stroke-Canadian Stroke Network clinical and research standards to describe and study PSCIND. Based on this information, we generated the following operational criteria for PSCIND: (a) cognitive decline as reported by the patient or their caregiver; (b) objective evidence of cognitive decline as confirmed by neuropsychological tests (less than 1.5 SD below the mean); (c) intact general cognitive function and basic activities of daily living; (d) patient symptoms did not meet the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders (4th edition) for dementia; (e) etiology information indicated strategic infarcts or subcortical small vessel infarcts. All 50 patients were recruited using the PSCIND inclusion criteria, and comprised 24 men and 26 women with a mean age of (65 ± 6) years and a mean education duration of approximately 12 years. Of the 50 patients, 28 had a history of hypertension, and eight had a history of diabetes mellitus. According to the Oxfordshire Community Stroke Project diagnostic criteria, of the 50 patients with ischemic stroke, none exhibited total anterior circulation infarction, 14 (28%) exhibited partial anterior circulation infarction, three (6%) exhibited posterior circulation infarction, and 33 (66%) exhibited lacunar infarction.

All patients experienced only one cerebrovascular accident, and no patients reported a history of brain trauma, Parkinson’s disease, brain tumors, hydrocephalus, cerebral hemorrhage, or other brain diseases. All were receiving routine treatment for cerebral infarction and complications according to their condition. Informed consent was obtained from all participants.

Procedure
Participants completed a battery of cognitive assessment scales examining global cognition, executive function/attention, memory, language, and visuospatial function, and were assessed according to TCM syndrome classifications. All cognitive assessments have previously been tested for reliability and validity. The tests were administered by a qualified neurophysician who was trained to conduct neuropsychological assessments.

There is currently no TCM syndrome scale for PSCIND. The China Association of Traditional Chinese Medicine, Department of Internal Anti-aging Medicine, professional committee formulated the Vascular Dementia Syndrome Differentiation Scale (SDSVD), which is a TCM scale of vascular dementia. These standards are commonly used to assess VCI and...
The TCM syndrome analysis revealed that one-third of PSCIND patients. The SDSVD includes kidney essence deficiency, blood deficiency, turbid phlegm obstructing the orifices, endogenous heat, heat accumulation in the large intestine, blood stasis, and hyperactivity of liver Yang. Each TCM syndrome comprises a group of symptoms. If more than seven symptoms integral to the syndrome are observed, the syndrome diagnosis is established; if less than seven integral symptoms are observed, this indicates diagnosis of a different syndrome.

Neuropsychological assessment

The Mini-Mental State Examination (MMSE) (Chinese version): this test is similar to the English language version of the MMSE, and is scored out of 30. The shape trails test (STT) parts A and B: in the STT-A, the participant is asked to connect a series of Arabic numbers (1-25) in their numerical order. In the Chinese version of the STT-B, Arabic digits (1-25) are surrounded by either a square or a circle, and the participant is asked to connect the digits in a sequence such that the shapes surrounding the digits alternate. We recorded the time taken to complete the task. The Stroop color-word test (SCWT) (Chinese version): this test features cards on which the names of colors are written in various ink colors. The participant is instructed to name the ink color while ignoring the word. We analyzed the time taken to finish the task (SCWT-C time) and the accuracy for items for which the ink color was not consistent with the word meaning (SCWT-C correct). Reading the mind in the eyes (RME) test (Chinese version): in this test, the participant was asked to describe the emotions conveyed in 36 pictures of eyes taken from photographs of people of Chinese ethnicity. There was no time limit and the total possible score was 36.

Digit ordering test-A (DOT-A): the stimuli in this task comprised 12 groups of digits in non-numerical sequence. The participant was instructed to read the 12 groups of digits in numerical order. The highest total score was 12.

The symbol digit modalities test (SDMT): in this test, the participant was asked to match a series of symbols to corresponding digits according to a symbol-digit pairing illustration. We recorded the number of items correctly completed within 90 s. After 90 s, the participant was asked to recall the symbols that corresponded to each digit [known as SDMT-incidental learning (SDMT-IL)]; i.e., participants were not told in advance that they would be asked to recall the information].

The category verbal fluency test (VFT): the participant was asked to name as many animals or cities as they could in 1 min. They were also asked to conduct the exercise while alternating between animals and cities. We recorded the number of unique responses (VFT-animal, VFT-city, and VFT-alternating).

The auditory verbal learning test (AVLT): we employed the following testing procedure. The examiner read out 12 two-character words. Each group of 12 words contained three different categories with four words in each. The different word types were presented randomly with 1-s intervals between the words. Immediately after the entire list had been presented, the participant was asked to recall the words. This learning and recall phase was repeated three times. The participant was given a 5-min non-verbal test, and was then asked to recall the 12 words for the fourth time. Next, the participant completed another 20-min non-verbal task, and was then asked to recall the word list for the fifth time (AVLT-long delayed recall, AVLT-LR). Finally, the participant was shown the word list.

The Rey-Osterrieth complex figure test (CFT): participants were asked to copy a visual figure (CFT-copy), then to draw the figure from memory after approximately 25 min had passed (CFT-delayed recall, CFT-LR). We used the scoring standard established by Taylor in 1981, with a total possible score of 36. The Boston naming test (BNT) (30-item version): in this test, the participants were asked to name the subjects of 30 pictures with no time limit; the total possible score was 30.

The action naming test (ANT) (Chinese version): in this test, participants were asked to name 34 pictures depicting actions with no time limit; the total score was 34.

Famous face test (FFT) (Chinese version): the stimuli in this test comprised 20 photographs of famous Chinese people. The participants were asked to name the 20 individuals in the pictures with no time limit, with a total possible score of 20.

The similarity test (ST) (Chinese version): in this task, participants were asked to identify the similarities between two words (e.g., axe-saw, wood-alcohol). The total possible score was 26 points.

Data analysis

All analyses were performed using SPSS 16.0 (SPSS, Inc., Chicago, IL, USA). Continuous variables will be expressed using mean and standard deviation for normal distributions or median and interquartile range for non-normal distributions. Categorical variables will be described as frequencies or percentages. Between-group comparisons were performed using t-tests if the data followed the normal distribution or homogeneity of variance, and otherwise used Mann-Whitney tests. Only findings with a two-tailed P ≤ 0.05 were considered significant.

RESULTS

The TCM syndrome analysis revealed that one-third of patients were diagnosed with a single syndrome. From the seven TCM syndromes, those with turbid phlegm blocking the upper orifices and upper hyperactivity of liver Yang were diagnosed most often (42%). The third
most common syndrome was blood stasis blocking the collaterals (24%), and the fourth was kidney essence deficiency (20%). Overall, excess syndrome was most common, accounting for 54% of diagnoses. Next, we divided the 50 patients into two groups of patients diagnosed with the TCM syndrome of turbid phlegm blocking the upper orifices, and those diagnosed with other TCM syndromes, or patients diagnosed with upper hyperactivity of liver Yang and those diagnosed with other TCM diagnoses, or patients diagnosed with TCM excess syndrome and those diagnosed with other syndromes.

We compared patients diagnosed with the TCM syndrome of turbid phlegm blocking the upper orifices and those diagnosed with other TCM syndromes. There were no statistically significant differences in background information between the two groups ($P > 0.05$), and no differences in neuropsychological test scores ($P > 0.05$).

We compared patients diagnosed with upper hyperactivity of liver Yang and those diagnosed with other TCM diagnoses. There were no significant differences in background information between the two groups ($P > 0.05$). Patients diagnosed with upper hyperactivity of liver Yang scored significantly lower than patients with other TCM diagnoses on the SCWT-C executive tests ($P = 0.05$) and on the CFT-LR memory test ($P = 0.01$), suggesting that the executive function of upper hyperactivity of liver Yang was superior to that of patients with other TCM syndromes, but that they exhibited greater memory loss (Table 1).

We compared patients diagnosed with TCM excess syndrome and those diagnosed with other syndromes. There were no statistically significant differences in background information between the two groups ($P > 0.05$). Excess syndrome patients scored lower than patients with other syndromes on the SCWT-C executive function test, and significantly higher on the DOT-A executive function test ($P < 0.05$), suggesting that the executive function of PSCIND patients with excess syndrome is superior compared with those without this syndrome (Table 2).

**DISCUSSION**

Shi et al. reported that the three most common syndromes in VCI patients were kidney essence deficiency, turbid phlegm blocking the upper orifices, and blood stasis blocking the collaterals. These findings were consistent with our results, although the proportions of syndrome diagnoses differed. Because the current findings revealed a predominance of turbid phlegm blocking the upper orifices and upper hyperactivity of liver Yang patients, we categorized patients accordingly. There were no significant differences in neuropsychological test scores for patients diagnosed with turbid phlegm blocking the upper orifices and those without this diagnosis. However, patients diagnosed with upper hyperactivity of liver Yang scored significantly lower than those without this diagnosis on the SCWT-C and the CFT-recall memory test, indicating that the executive function of patients with upper hyperactivity of liver Yang was superior to those without this diagnosis, but that they experienced more memory loss.

In TCM, the liver is a forceful and firm viscera characterized by substantial Yin and functional Yang. If liver Yang is excessive, it can become hyperactive and con-

| Table 1 Comparison of neuropsychological test scores for liver Yang and other TCM syndromes |
|---------------------|---------------------|---------------------|
| Item                | CFT-LR              | SCWT-C (s)          |
|                     | $n$                 | $\bar{x} \pm s$     | $n$                 | Median (Min, Max) |
| Liver Yang          | 18                  | 12±6                | 21                  | 90 (68, 170)      |
| Other TCM syndromes| 23                  | 17±7                | 29                  | 126 (73, 300)     |
| **Statistic**       | 2.01                |                     | 2.56                |
| **$P$ value**       | 0.05$^*$            |                     | 0.01                |

Notes: TCM: Traditional Chinese Medicine; CFT-LR: complex figure test-delayed recall; SCWT: stroop color-word test; $\bar{x} \pm s$: mean ± standard deviation, ‘Independent samples $t$ test.

| Table 2 Comparison of neuropsychological test scores for excess syndrome and other TCM syndromes |
|---------------------|---------------------|---------------------|
| Item                | DOT-A               | SCWT-C (s)          |
|                     | $n$                 | $\bar{x} \pm s$     | $n$                 | Median (Min, Max) |
| Excess syndrome     | 26                  | 5.8±1.9             | 27                  | 93 (73, 170)      |
| Other TCM syndromes| 21                  | 4.4±2.7             | 23                  | 129 (68, 300)     |
| **Statistic**       | 2.09                |                     | 2.87                |
| **$P$ value**       | 0.04$^*$            |                     | 0.00                |

Notes: DOT-A: digit ordering test-A; SCWT: stroop color-word test; TCM: Traditional Chinese Medicine; $\bar{x} \pm s$: mean ± standard deviation, ‘Independent samples $t$ test.
sume Yin, resulting in excess in the upper body and deficiency in the lower body. Upper hyperactivity of liver Yang can disturb the mind, leading to symptoms like impatience. One possible reason for the higher level of executive function in patients with upper hyperactivity of liver Yang is a lack of nourishment to the brain stemming from the depletion of kidney Yin. This may manifest in poor memory.

Previous research on the association between TCM syndrome types and disease has tended to use clinical syndrome differentiation based on the Zang-fu viscera. In contrast, syndrome differentiation based on the eight principles is relatively straightforward. Further investigation of the cognitive characteristics of PSCIND linked to syndromes based on the eight principles could be useful for clinical diagnosis and treatment. Because of the limited number of cases, we divided PSCIND patients into excess and non-excess syndromes. Comparisons of these two groups indicated that excess patients performed better than non-excess patients on the SCWT-C executive test and the DOT-A executive test, suggesting that executive function of excess PSCIND patients was relatively better than that of non-excess PSCIND patients, although the overall level of executive function of the two groups was relatively low. The reason for this finding is unclear, and this pattern has not been reported previously. Patients with excess syndromes exhibit a predominance of pathogenic excess and the body is not obviously weak. This may explain why PSCIND patients with excess syndromes exhibited greater executive function.

The current study used a case-control design with comprehensive neuropsychological assessment, including tests of memory, executive attention, language, and visuospatial functioning, to compare the neuropsychological characteristics of patients with different TCM syndromes. One limitation of the current study was the small sample size. However, despite the preliminary nature of this study, we obtained several meaningful findings. Our results indicated that differences in TCM syndromes in PSCIND patients were associated with different neuropsychological characteristics. Future research would benefit from a larger sample size and a longer follow-up of PSCIND patients, and testing these patterns with prognoses for different aspects of cognition.

REFERENCES


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31 Guo Q, Zhao Q, Chen M, Ding D, Hong Z. A comparison study of mild cognitive impairment with 3 memory tests among Chinese individuals. Alzheimer Dis Assoc Disord 2009; 23(3): 253-259.


