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Effects of acupuncture on dementia
-A case series with a novel Sanjiao Acupuncture method-

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Abstract

[Objective] This study was aimed to explore the efficacy and usefulness of acupuncture which was technically defined by consistent manipulation on 9 needles at 6 acupoints in the body (Sanjiao method). The acupuncture treatment was done for patients with Alzhemier's disease (AD) or vascular dementia (VaD), and the identical treatment was performed on a group of the elderly who had lifestyle related disease (LS-D) with no detectable dementia.

[Methods] Totally 56 patients agreed to participate in the study, including 18 with AD, 12 with VaD, and 26 with LS-D with no obvious dementia. Sanjiao acupuncture treatment was done once a week for 3 months totaling 12 times. The treatment effect was assessed by scores of mini-mental state examination (MMSE) and Nishimura Scale of Activities of Daily Living (N-ADL). Their posttreatment scores were statistically compared to their pretreatment ones. Text dwelling analysis was made by the key words collected by interviews done at occasions of acupuncture.

[Results] In total 56 patients, the mean scores of MMSE before the treatment (21.4 ± 7.3) was significantly increased in the posttreatment (22.3 ± 7.0) ($p<0.01$). Particularly, significant improvement was shown in patients with VaD ($p<0.05$) and LS-D ($p<0.01$), although the improvement tended to be limited in patients with AD and patients who required higher nursing care levels ($\geqq 3$). The mean N-ADL scores in pretreatment stage (34.7 ± 13.1) differed significantly from the mean posttreatment score (34.9 ± 13.0) ($p<0.01$), showing favorable changes of the 56 patients. Physical, behavioral and psychological activities (BPSD) demonstrated by the text dwelling analysis were very well improved in each patient's group after the treatments of the acupuncture.

[Conclusion] The novel acupuncture treatment showed significant improvement of N-ADL and amelioration of BPSD, which would contribute to have a higher quality of daily lives of the patients and would bring better QOL to the family and care-givers as well. It would be possible to delay or even prevent the transition of LS-D into dementia. Thus, this acupuncture method would help curtail excessive medical expense in the ageing society.

Key words: Sanjiao acupuncture , Dementia, Lifestyle related disease, MMSE, N-ADL

I. Introduction

Oral drugs and percutaneous medications are now widely used for the treatment of dementia. Various non-drug therapies have been tested for preventing dementia as well. However, these trials have not been evidenced to a substantial level. In these days lifestyle related disease (LS-D) which adults and the elderly tend to suffer from, is believed to be one of the most potential precursors in the occurrence of dementia, including Alzheimer's disease (AD) and vascular dementia (VaD). Thus, prevention and treatment of LS-D would suppress the process of transition into dementia. Patients with LS-D and/or dementia are in frequent association with other complaints defined as geriatric syndrome, like headache, constipation, incontinence, lumbago and frailty. Dementia and geriatric syndrome certainly induce an apparent decrease or loss of the quality of life (QOL) in

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individual life. It is well known that acupuncture treatment based upon the yin-yang balance theory has been providing improvement and cure of complaints due to geriatric syndrome in the long history. Acupuncture treatment is recommended as a tool of integrated medicine by the World Health Organization.

In China dementia therapy with acupuncture has been extensively studied in both basic science and clinical fields[1-9]. However, such studies have been hardly found in Japan. Here, we report systemic studies taken by a group of well-trained acupuncturists, emphasizing efficiency and usefulness of a novel acupuncture method (Sanjiao) which had been developed by one of the present authors (HJ).

Ⅱ. Methods

1. Subjects

Total 56 patients (17 male and 39 female; mean age, 83±10, ranging 60–100 years) were enrolled as subjects following acceptance by the patients and their families/caregivers of the informed consent to participate the clinical studies. Eighteen patients had AD, 12 patients VaD, and 26 patients LS-D with no signs of dementia.

2. Diagnosis

Diagnosis of the subjects was established by attending doctors at nursery homes and one of the present authors (OK) as well. Patients in the LS-D group were suffering from a large variety of geriatric syndrome including hypertension, dyslipidemia, osteoporosis, diabetes mellitus and/or others. However, they never showed excessive cognitive loss or behavioral psychological symptoms of dementia (BPSD).

3. Treatment method

Twenty-two acupuncturists who had been qualified as masters of Sanjiao acupuncture method for dementia after the graduation of Education and Training Course (Gold-QPD) held by Gerontology Research Association Japan. They had followed a specific training course for the acupuncture technique described as Sanjiao acupuncture, and learned general medical knowledge of dementia and basic technique of nursing care for the elderly. Sanjiao acupuncture was originally described as anti-aging procedure by delaying aging processes by one of the present authors (HJ). Before and after the acupuncture treatments, they recorded scores of MMSE (mini-mental state examination) and checked living conditions of patients with N-ADL (activities of daily living after Nishimura). The standard procedure of the acupuncture was performed once a week for 3 months in total 12 times. We used total 9 needles (disposable stainless-steel M3; 0.2 mm diameter and 50 mm length, SEIRIN Co. Ltd.). Six acupuncture points were selected in the upper (heart and lungs), the middle (spleen and stomach), and the lower (liver and kidneys) energizers. They were Danzhong; CV17, Zhongwan; CV12, Qihai; CV6, Waiguan; TE5, Xuehai; SP10, and Zusanli; ST36. Specific manipulations on 9 needles are described in the Table 1, which was less stressful for the elderly and quite easy to perform as conducted in the supine position.

4. Evaluation method

To evaluate cognitive ability, MMSE was applied at occasions before the practice of acupuncture, and after the completion of 12 times' treatment. To reveal daily living skills, N-ADL which included 5 conditions, such as walking/sitting, dressing/undressing, bathing, eating and defecation with 10 points' scores each in total 50, was applied. The scores 10~9 points were considered normal, 8~7 borderline, 6~5 mild, 4~3 moderate and 2~0 severe degrees of burden. To notify behavioral changes of patients, interview/hearing was made from family or caregivers in relation to several items, including conversation, smile, and violated behavior due to loss of temper and others. Physical changes of patients were also written down about general pain, joint pain, tremor, headache, walking and so on. In addition, the conditions of nursing-care were defined as nursing care levels 1, 2, 3, 4 and 5 according to supports given by professional care-givers.

5. Statistical analysis

The means and standard deviations of the scores of MMSE and N-ADL scales were calculated.

And their scores before the treatment were compared

Table1. Sanjiao acupuncture Method

Acupuncture point	Angle	Depth(cm)	Maneuver
Danzhong;CV17	oblique	1〜1.5	twirling-tonifying needling
Zhongwan;CV12	Straight	〜3.0	twirling-tonifying needling
Qihai;CV6	Straight	〜3.0	twirling-tonifying needling
Waiguan;TE5	Straight	1〜1.5	neutral supplementation needling
Xuehai;SP10	Straight	〜3.0	neutral supplementation needling
Zusanli;ST36	Straight	〜3.0	twirling-tonifying needling

to those after 3 months' (12 times) treatments with a paired t-test. Assessment of MMSE was also done in 2 groups of the patients: one group with MMSE scores $\leqq$ 21 points (28 patients) and the other with scores $\geqq$ 22 (28 patients). The nursing-care levels of 41 patients were divided into 2 groups: 12 patients were nursing-care levels $\geqq$ 3 (implying that they need someone's help to take care of their surroundings), and the remaining 29 nursing-care levels $\leqq$ 2 indicating that they can live alone without particular help of care-givers. Moreover, correlations among age, and scores of MMSE, N-ADL and nursing-care levels were assessed by SPSS Statistics 17.0.

At the time of acupuncture treatments, language data of interviews were recorded and analyzed using the SPSS Text Analytics for Surveys (software for text mining). This statistical analysis was expected to reveal behavioral and psychological (BPSD) alterations of patients undetectable by the scores of MMSE, N-ADL or nursery care levels. Text mining is a method of analyzing a large amount of text data freely written at the interview of patients. We decompose the text into phrases and words (morphological analysis) and see how many phrases and words appear and how their correlation (co-occurrence network) and change in the time series are like. In this study, on the basis of positive and negative findings of both physical and mental aspects, we made estimation of the concept of sensitivity analysis for the purpose of understanding the patient image.

Ⅲ．Results

1. MMSE changes after Sanjiao acupuncture treatment

In all the 56 patients, the mean pretreatment MMSE score was 21.4 and their posttreatment score was 22.7. The difference between the two scores was significant ($p < 0.01$). Among the AD group, the mean MMSE score before the treatment was 17.6, and the posttreatment score was 18.3, in which no significant difference existed. The mean pretreatment scores of MMSE in VaD and LS-D groups were 17.1 and 26.0 respectively. Those after the treatments were 19.2 and 27.3, respectively. Significantly increased were the scores of VaD ($p < 0.05$) and LS-D ($p < 0.01$) groups, compared to their pretreatment scores.

Among all the patients, the MMSE scores of patients with MMSE scores $\leqq$ 21 (average 15.3) increased to 17.0 in average after the treatments ($p < 0.01$) . The patients with MMSE scores $\geqq$ 22 showed a significant increase of the scores from 27.4 to 28.4 in average ($p < 0.01$). In the patients with nursing-care levels $\geqq$ 3, the pretreatment mean score of MMSE was 15.8 and the posttreatment score was 16.5 in average, which was insignificant *(Table 2)*.

However, the MMSE score in the patients with nursing-care levels $\leqq$ 2 was 23.9 in average and their posttreatment score became 25.0, indicating statistical significance between the two scores ($p < 0.01$) *(Table 2)*.

Table 2. MMSE changes after the treatments

Comparison of MMSE in all 56 patients and in different groups of disease

MMSE	ALL N=56 before / after	p	AD N=18 before / after	p	VaD N=12 before / after	p	LS-D N=26 before / after	p
scores	21.4 / 22.7 ±7.3 / ±7.0	**	17.6 / 18.3 ±6.0 / ±6.9	n.s.	17.1 / 19.2 ±7.7 / ±6.4	*	26.0 / 27.3 ±5.1 / ±4.1	**

MMSE scores compared to the pre-treatment scores

MMSE	MMSE scores ≦ 21 N=28 before / after	p	MMSE scores ≧ 22 N=28 Before / after	p	nursing-care levels ≧ 3 N=12 before / after	p	nursing-care levels ≦ 2 N=29 before / after	p
scores	15.3 / 17.0 ±5.2 / ±5.4	**	27.4 / 28.4 ±2.5 / ±2.1	**	15.8 / 16.5 ±7.3 / ±7.9	n.s.	23.9 / 25.0 ±4.9 / ±5.0	**

Data are presented as means ± standard deviations

significant difference *$p < 0.05$ **$p < 0.01$

The scores of MMSE before and after the treatment are shown in Table 2.
All; all the patients examined, AD; Alzheimer's Dementia
VaD; Vascular Dementia, LS-D; Lifestyle related disease

2. N-ADL changes after Sanjiao acupuncture treatment

The mean N-ADL score in whole 56 patients was 34.7 before the treatment. After 3 months treatments, the score became 34.9, indicating significant differences ($p < 0.01$). In the patients with AD, pretreatment mean N-ADL scores 32.2 tended to increase to 32.3 after the treatment. N-ADL scores of VaD patients changed from 27.3 to 27.7, and those of LS-D raised from 39.8 to 40.1, respectively. However, they were not statistically significant.

In patients with MMSE scores ≦21, the pretreatment mean N-ADL score 28.3 was increased to 28.7 after the treatment, which indicates a significant difference ($p < 0.01$). However, in patients with MMSE scores ≧ 22 points, these scores changed from 41.1 to 41.2, indicating no significance.

In patients with nursing-care levels ≧ 3, the pretreatment mean N-ADL scores was 25.7 and the posttreatment 26.0, respectively. In patients with nursing-care levels ≦2, the pretreatment mean N-ADL score was 39.1 and posttreatment 39.3, respectively. There was no significant difference *(Table 3)*.

3. Correlations between the categories

Spearman's rank-correlation coefficients were evaluated for age, category of nursing-care level, MMSE, and N-ADL scores before the treatment. Significant negative correlations (-0.43) was found between category of nursing-care levels and MMSE scores. Also, significant negative correlation (-0.67) was found between category of nursing-care levels and N-ADL scores.

4. Physical, behavioral and psychological changes after Sanjiao acupuncture treatment

Categories of physical findings are shown by SPSS Text Analytics for Surveys *(Figure1)*. After the acupuncture treatment, as shown in vertical axis, the positive and favorable improvement was found in physical attitudes with regard to "pain", "stiff lower limbs", "lower back pain", "complaints in eyes, fingers and back, and abnormal tension" and so on. Negative changes were observed in physical conditions of "foot", "supine position", and "muscle tension". And "pruritus" was worsened when the body temperature was raised by such as in gymnastics. The horizontal axis indicates real number of patients claimed above.

The categories of psychological and behavioral findings are similarly shown in *Figure2*. After the treatment, psychological conditions were well improved in relation to "communication with care-givers", "smile to family members", "willingness to do something", "smooth expression of their intension and good impression to the others" and "mental tension and confidence". Negative attitudes of patients were found in the categories such as verbal abuse (shouting) and anxiety during communications and others.

Ⅳ. Discussion

1. Changes in MMSE and N-ADL after the treatment

Following the acupuncture treatment the mean scores of MMSE and N-ADL were significantly increased compared to those before the treatment among whole 56 patients. In patients with VaD or LS-D, the posttreatment MMSE scores were significantly increased, in contrast, MMSE increase was increased to a limited range among patients with AD.

Table 3. N-ADL changes after the treatments

Comparison of N-ADL in all 56 subjects and in different groups of disease

N—ADL	ALL N=56			AD N=18			VaD N=12			LS-D N=26		
	before	after	p	before	after	p	before	after	p	before	after	p
scores	34.7 ±13.1	34.9 ±13.0	**	32.2 ±15.4	32.3 ±15.4	n.s.	27.3 ±13.0	27.7 ±12.8	n.s.	39.8 ±9.1	40.1 ±9.0	n.s.

Comparison of MMSE according to the initial scores

N—ADL	MMSE scores ≦21 N=28			MMSE scores ≧22 N=28			nursing-care levels ≧3 N=12			nursing-care levels ≦2 N=29		
	before	after	p	before	after	p	before	after	p	before	after	p
scores	28.3 ± 13.6	28.7 ±13.5	**	41.1 ±9.1	41.2 ±9.0	n.s.	25.7 ±12.3	26.0 ±12.3	n.s.	39.1 ±11.5	39.3 ±11.3	n.s.

Data are presented as means ± standard deviations
significant difference *$p < 0.05$ **$p < 0.01$

The scores of N-ADL before and after the treatment are shown in Table 3.
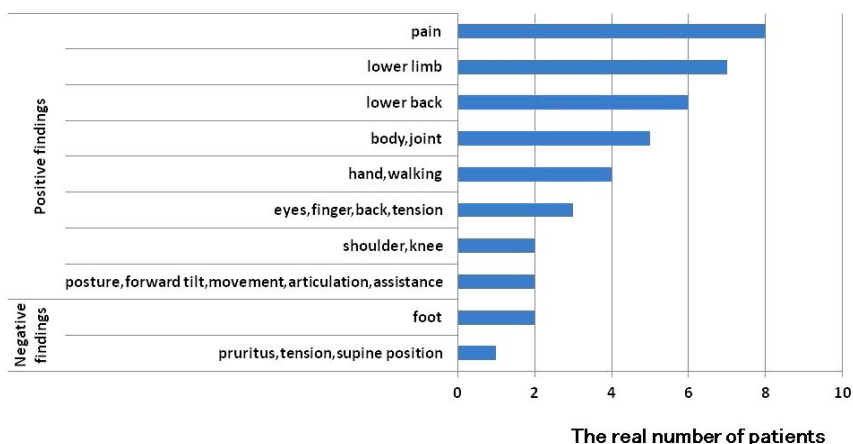
Figure 1. Physical findings
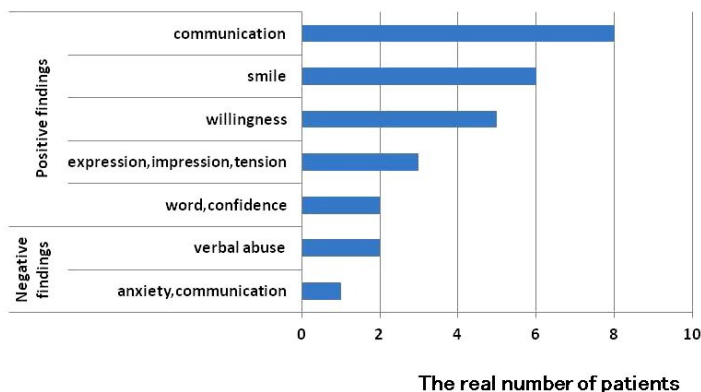The categories of physical findings are shown in Figure 1 (see the text).

Figure 2. Psychological findings
The categories of psychological findings are similarly shown in Figure 2 (see the text).

According to Sato et al.[10-14], mechanical skin irritation stimulates Meynert nuclei leading to the activation of neurons which results in acetylcholine release from the cerebral cortex. This process in turn increases cerebral cortex-blood flow where the brain function such as thinking and judgment in memory function is involved. The cerebral cortex and the hippocampus are very sensitive to a decrease of blood-flow. It is known that neurons results in death after a short period of ischemia[15,16]. The physical stimulation of acupuncture leads to cholinergic vasodilatation in the brain, which causes an increase of blood flow in the cerebral cortex and hippocampus. This may prevent neuronal death due to ischemia[17,18], which may be consistent with clinical improvement of the patients with Sanjiao acupuncture treatment as shown in the improvement of MMSE scores and physical and psychological activities.

One of the present authors (HJ) showed a 20% increase of lifespan in the senescence accelerated mouse.

These mice apparently showed cognitive improvements in Morris water maze test, including functions like spatial memory, relearning, thinking and analytical judgment abilities. Their neuropathological study indicated that acupuncture inhibits withdrawal of hippocampal neurons, suppresses reactive proliferation of glial cells while maintaining a neuronal/glia cell balance. Following acupuncture treatment done for AD and VaD patients, activities of daily living were improved significantly compared to those of the patients who received anti-cholinesterase medication. Memory retention, orientation, and calculating ability became apparently better in the VaD group than in the control group prescribed with Hydergine. Marked and sustained therapeutic effects were maintained especially in the patients with mild levels of VaD. This is in good accord with the present study of Sanjiao acupuncture therapy for dementia patients.

There was no good correlation between age, MMSE and/or N-ADL. No significant changes were observed in MMSE in the patients with nursing-care levels $\geqq$ 3, while a significant improvement of MMSE was found in those with nursing-care levels $\leqq$ 2. These results implicate that the Sanjiao acupuncture therapy shows significant help in maintaining and improving memory for patients who required lesser levels of nursing care.

Yamazaki et al.[19] conducted a study of 12-weeks acupuncture for patients with memory loss. One group of patients was given a guidance advice for lifestyle improvement alone and the other received acupuncture treatment with advices to their lifestyle as well. The patients' group with combined treatments of acupuncture and lifestyle advices showed a better improvement in MMSE scores and obtained a good sleep rest. Although the MMSE scores after the treatment were insignificant, improvement was expected to a limited range in patients with AD or in patients with nursing-care levels $\geqq$ 3 in the present study. These results imply that the acupuncture treatment may prevent an unexpected rapid decline of cognitive function as frequently seen among AD patients.

2. Physical, behavioral and psychological changes after the treatment

With acupuncture treatment for 3 months, Guo et al.[20] reported appreciable improvements of BPSD in the patients with AD, including insomnia, anxiety, frustration, disturbance in expression and communication with the caregivers. However, no therapeutic effects were present on the patients' cognitive function like memory and calculating ability. These results are in good accord with the present study, in which symptoms of physical pain and other geriatric syndrome were alleviated, and communication with caregivers and family members was drastically improved. Acupuncture treatment is an effective way of treatment for common complaints of the elderly, which in fact had been well appreciated in a long history and recommended by WHO in these days. Thus, the novel acupuncture method will contribute to improve BPSD and improve quality of life of patients with dementia and their family members.

3. Future issue

The present study showed rational effectivities of acupuncture treatment for patients with dementia and/or lifestyle disease[21]. As the number of patients examined is limited, we might need to add further experience. Cochran Review for acupuncture treatment might request to conduct a randomized controlled trial[22] in future. Excessive anxiety and irritabilities shown in BPSD of the dementia patients may lead to instant denial or discontinuation of the treatment. It is cardinal to keep them relaxed for the treatment and to give them and their care-givers trustful information of the treatment.

Conflict of interest

There is no conflict of interest.

References

1) Zhao L,Jia Y,Yan D,Zhou C,Han J,Yu J.Aging-related changes of triose phosphate isomerase in hippocampus of senescence accelerated mouse and the intervention of acupuncture. Neurosci Lett. 2013; 542: 59-64.

2) Li G, Cheng H, Zhang X, Shang X, Xie H, Zhang X, et al. Hippocampal neuron loss is correlated with cognitive deficits in SAMP8 mice. Neurol Sci. 2013 ;34(6): 963-9.

3) Li G, Zhang X, Cheng H, Shang X, Xie H, Zhang X, et al. Acupuncture improves cognitive deficits and increases neuron density of the hippocampus in middle-aged SAMP8 mice. Acupunct Med. 2012; 30(4): 339-45.

4) Zhao L, Shen P, Han Y, Zhang X, Nie K, Cheng H, et al. Effects of acupuncture on glycometabolic enzymes in multi-infarct dementia rats. Neurochem Res. 2011; 36(5): 693-700.

5) Zhu L, Yu J, Shi Q, Lu W, Liu B, Xu S, et al. Strain- and age-related alteration of proteins in the brain of SAMP8 and SAMR1 mice. J Alzheimers Dis. 2011; 23(4): 641-54.

6) Zhang X, Peng Y, Yu J, Liu C, Cheng H, Liu L, et al. Changes in histomorphometric and mechanical properties of femurs induced by acupuncture at the Shenshu point in the SAMP6 mouse model of senile osteoporosis. Gerontology. 2009; 55(3): 322-32.

7) Cheng H, Yu J, Jiang Z, Zhang X, Liu C, Peng Y, et al. Acupuncture improves cognitive deficits and regulates the brain cell proliferation of SAMP8 mice. Neurosci Lett. 2008; 432(2): 111-6.

8) Ding X, Yu J, Yu T, Fu Y, Han H. Acupuncture regulates the aging-related changes in gene profile expression of the hippocampus in senescence-accelerated mouse (SAMP10). Neurosci Lett. 2006; 399: 11-6.

9) Yu J, Zhang X, Liu C, Meng Y, Han J. Effect of acupuncture treatment on vascular dementia. Neurol Res. 2006; 28(1): 97-103.

10) Sato A, Sato Y. Regulation of regional cerebral blood flow by cholinergic fibers originating in the basal forebrain. Neurosci. Res. 1992; 14: 242-74.

11) Biesold D, Inanami O, Sato A, Sato Y. Stimulation of the nucleus basalis of Meynert increases cerebral cortical blood flow in rats. Neurosci. Lett. 1989; 98: 39-44.

12) Akaishi T, Kimura A, Sato A, Suzuki A. Responses of neurons in the nucleus basalis of Meynert to various afferent stimuli in rats. NeuroReport. 1990; 1: 37-9.

13) Kurosawa M, Sato A, Sato Y. Cutaneous mechanical sensory stimulation increases extracellular acetylcholine release in cerebral cortex in anesthetized rats. Neurochem. Int. 1992; 21: 423-7.

14) Adachi T, Meguro K, Sato A, Sato Y. Cutaneous stimulation regulates blood flow in cerebral cortex in anesthetized rats. NeuroReport; 1990. 1: 41-4.

15) Kirino T. Delayed neuronal death in the gerbil hippocampus following ischemia. Brain Res. 1982; 239: 57-69.

16) Pulsinelli WA, Brierley JB, Plum F. Temporal profile of neuronal damage in a model of transient forebrain ischemia. Ann Neurol. 1982; 11: 491-8.

17) Kagitani F, Uchida S, Hotta H, Sato A. Effect of nicotine on blood flow and delayed neuronal death following intermittent transient ischemia in rat hippocampus. Jpn J Physiol. 2000; 50: 585-95.

18) Hotta H, Uchida S, Kagitani F. Effects of stimulating the nucleus basalis of Meynert on blood flow and delayed neuronal death following transient ischemia in the rat cerebral cortex. Jpn J Physiol. 2002; 52: 383-93.

19) Yamazaki T, Sato M, Yano T, Sakurada K, Niwa F, Imanishi J. Randomized Controlled Study on Enhanced Cognitive Function with Acupuncture and Improvements in Life Style. The Japan Society for Oriental Medicine. 2012; 63(4): 229-37.

20) Guo Q, Maeda K, Yamamoto Y, Kawamata T. The effects of acupuncture in treating behaviors associated with psychological symptoms of dementia in Alzheimer's disease: three cases. Japanese journal of geriatric psychiatry. 2010; 21(4): 456-63.

21) Lee MS, Shin BC, Ernst E. Acupuncture for Alzheimer's disease: a systematic review. Int J Clin Pract, Jun. 2009; 63(6): 874-9.

22) Peng WN, Zhao H, Liu ZS, Wang S. Acupuncture for vascular dementia (Review). The Cochrane Collaboration, 2009.