

Rehabilitation of Stroke Patients Using Yamamoto New Scalp Acupuncture: A Pilot Study

Gabriella Hegyi, MD, PhD,¹ and Gyula P. Szigeti, MD, PhD²

Abstract

Objectives: The aim of this study was to investigate whether acupuncture, especially Yamamoto's New Scalp Acupuncture (YNSA), is of value in addition to standard poststroke motor rehabilitation.

Design: A prospective, assessor-blinded randomized control trial was carried out in an inpatient stroke rehabilitation unit with day hospital service. After inclusion, patients were stratified into control group and acupuncture group, randomly.

Outcome measures: The Barthel Index, the Rivermead Scale Index, and the Visual Analogue Scale were used to follow the efficacy of treatment.

Results: In the acupuncture group, all the sensory, motor, and functional scores improved significantly during the examination period until 2 years after injury. The Barthel Index is increased from 4 ± 2 to 95 ± 4 in the acupuncture group. This index also increased in the control group (from 4 ± 2 to 75 ± 4), but the changes were significantly less than in the acupuncture group. A significant spontaneous recovery during the 2-year follow-up was found, but the YNSA treatment facilitated the functional recovery. Improved moving function and more flexible joints and ligaments were observed in comparison to the patients' condition prior to treatment.

Conclusions: The data suggest that the YNSA is a useful method to treat stroke patients and enhance their quality of life.

Introduction

STANDARD TREATMENTS IN STROKE REHABILITATION are physiotherapy, occupational therapy, and speech therapy in addition to skilled medical and nursing care. Despite intensive inpatient rehabilitation in the stroke unit, more than 30% of acute stroke patients remain moderately to severely disabled at discharge. This reality drives people to search for other modalities of treatment (e.g., complementary and alternative therapies) in an attempt to further improve the outcome of stroke rehabilitation.

Acupuncture has been used in Traditional Chinese Medicine to relieve pain and cure a variety of diseases for more than 2500 years. Acupuncture has been used for stroke in China and Korea for centuries, but scientific studies on this topic have only recently started to emerge. Some but not all of these trials have suggested a positive effect on recovery. There are numerous reports in the Chinese literature about the efficacy of acupuncture in stroke rehabilitation. However, the result was rarely quantitatively expressed by properly validated measures, and intention-to-treat analysis was never mentioned.^{1–3}

Two (2) important reviews of acupuncture in stroke rehabilitation have been published in 1996.^{1,2} These reviews are open to criticism because the literature was not searched systematically² or inappropriate studies were not excluded.¹ Moreover, new data have been published since that time. In 2001 Park and colleagues published a systematic review of the previous publications.⁴ They focused only on the sham-controlled randomized clinical trials. They searched 25 databases and 12 major Korean traditional medicine journals. Based on the evidence of rigorous randomized controlled trials, they found there is no compelling evidence to show that acupuncture is effective in stroke rehabilitation. They suggested better-designed studies need to be done. Since that time, a few randomized controlled trials, reviews, and meta-analyses were performed, but the picture still is not clear.^{5–8}

In the previously cited studies, the traditional form of acupuncture was used to treat the patients, but in the last few decades some new forms of acupuncture were developed. One of these is Yamamoto's New Scalp Acupuncture (YNSA).^{9,10} After an intensive study of Chinese acupuncture, Dr. Yamamoto began to anesthetize patients when applying needles. He presented the YNSA points and the new scalp

¹University of Pécs, Institute of Complementary and Alternative Medicine, Pécs, Hungary.

²University of Debrecen, Medical and Health Science Centre, Department of Physiology, Debrecen, Hungary.

acupuncture method at the 1976 annual congress of the Japanese Ryodoraku Society. YNSA is most frequently used for neuromusculoskeletal diseases, dysfunctions, and pain that may be either acute or chronic in China. This acupuncture method is composed of two categories: Basic points and Ypsilon points. The Basic points are scalp acupuncture points used to treat pain and dysfunction of anatomical body parts that are directly related to the disease and dysfunctional process. Basic points are associated with small elevations or firmness in the subcutaneous tissue of the scalp at prescribed locations. YNSA also uses Ypsilon points, which relate to the 12 acupuncture meridians (LU, LI, KI, BL, HT, SI, LR, GB, PC, TB, SP, and ST). Since 1973, the YNSA method started to be applied to treat stroke patients worldwide; in our hospital, the method has been used since 1988.

Acupuncture therapy is usually done by the insertion of thin metal needles to the acupoints, and this is followed by slow manual twisting action of the acupuncturist. The needles, once correctly inserted into the acupoints, can also be stimulated electrically. The application of needles might even be a noxious stimulus causing autonomic hyperreflexia. Another acupuncture method is the YNSA, where small absorbable threads can make a continuous biostimulation of acupoints. Unfortunately, there is no information about the mechanism of the embedded acupuncture in the literature, but Drs. Shang and Fung described the same morphological changes in the connective tissue after electroacupuncture and embedded acupuncture.^{11,12} The most recent mechanism of action provided by electrical and embedded acupuncture therapy is believed to be different from traditional therapeutic electrical stimulation.

In 2010, a meta-analysis was published based on the previous studies. Wu published a systematic review and meta-analysis of randomized trials of acupuncture in post-stroke rehabilitation.¹³ He searched 7 English and 2 Chinese databases, and concluded that the randomized clinical trials demonstrate that acupuncture may be effective in the treatment of poststroke rehabilitation. Unfortunately, there are not enough studies in the field of electrical and embedded acupuncture therapy to do meta-analyses of this method in stroke patients in the meantime. So, what is the truth about acupuncture in stroke rehabilitation? The main objective of the present study was to try to make a strong hypothesis on whether acupuncture, especially the YNSA, has value in addition to standard poststroke motor rehabilitation.

Materials and Methods

Patients

Recruitment commenced between 2006 and 2009, after 50 patients had been enrolled (25 to receive acupuncture treatment and 25 for control). Fifty (50) consecutive patients admitted to the stroke rehabilitation unit were included in the study after informed consent. Inclusion criteria were the following: (1) patients with hemorrhagic or ischemic stroke, (2) admission within 6 weeks of stroke, (3) patients should have movement coordination problems including muscular atrophy, central paralysis, and also myasthenic symptoms, and (4) the degree of brain damage of stroke patients did not exceed 30% of damaged brain tissue. The last statement is important, because when the brain damage exceeds 30%, usually the dry needling treatment would not be successful.¹⁰

The size and anatomical location of stroke lesions is evaluated by magnetic resonance imaging using subtraction lesion analysis.¹⁴ Exclusion criteria were the following: (1) no motor deficit, (2) hemodynamic instability, (3) history of dementia, and (4) inability to give consent because of impaired cognition or receptive aphasia. The authors treated 25 patients with YNSA and the other 25 subjects were the nontreated control group (Fig. 1.) All patients gave informed consent to participate in the study, which was performed according to the guidelines of the local ethics committee. The participants were not informed of the possibility of being assigned to either acupuncture or no acupuncture group. Ethics Committee approval was granted and the trial was performed in accordance with the Declaration of Helsinki.

All the recruited patients went under rehabilitation program using the Hungarian standard rehabilitation protocol. Twenty-five (25) of the patients received additional acupuncture therapy using the dry needling method, and these patients were regarded as the acupuncture group. The other 25 patients without acupuncture therapy were regarded as the control group, and they only received necessary rehabilitation therapies. The average age was 58.6 ± 10.4 and 59.8 ± 9.6 years (in the acupuncture and control group, respectively). In both groups, 18 patients had ischemic and 7 had hemorrhagic stroke (Table 1).

Design and acupuncture protocol

A prospective, assessor-blinded randomized controlled trial was carried out in an inpatient stroke rehabilitation unit with day hospital service in Yamamoto Centre, Budapest, Hungary. After inclusion, patients were stratified into a control group and an acupuncture group. A simple randomization method was performed to create an acupuncture group and a control group.

YNSA is a special form of traditional acupuncture.^{9,10} The method is based on a somatotope of the scalp. In the same way as for ear or mouth acupuncture, the total organism is projected onto a defined area on the scalp. The locomotor system is situated on either side of the boundary between forehead and hair; the internal organs are represented by Y points on both sides of the temple region.⁹ According to the currently applicable official rules of YNSA, before treatment can begin an examination must be made of the lateral neck triangle by YNSA neck diagnostics.¹⁵ In the case of disorders affecting regions below the diaphragm, an inspection of the palms of both hands and palpation according to *Hegu* (Di 4) can be dispensed with. Neck diagnostics always start with palpation of the two kidney points. The diagnostics provide basic information about the side on which treatment should begin and, depending on the subjective perception of the person being treated, about whether needles should be applied to the frontal *yin* or dorsal *yang* treatment area. If the person being treated experiences sensitivity to pressure during palpation of the Kidney point, then treatment will be applied in the front *yin* area. Either the parietally located Y points can be used or exclusively the Cranial Nerve points located in the *yin* area. At the moment, there are no hard and fast rules concerning when Cranial Nerve points or Y points are to be used. The choice is up to the therapist. Cranial Nerve points and Y points can also be combined. If, for example, a treatment area has been destroyed by trauma or an

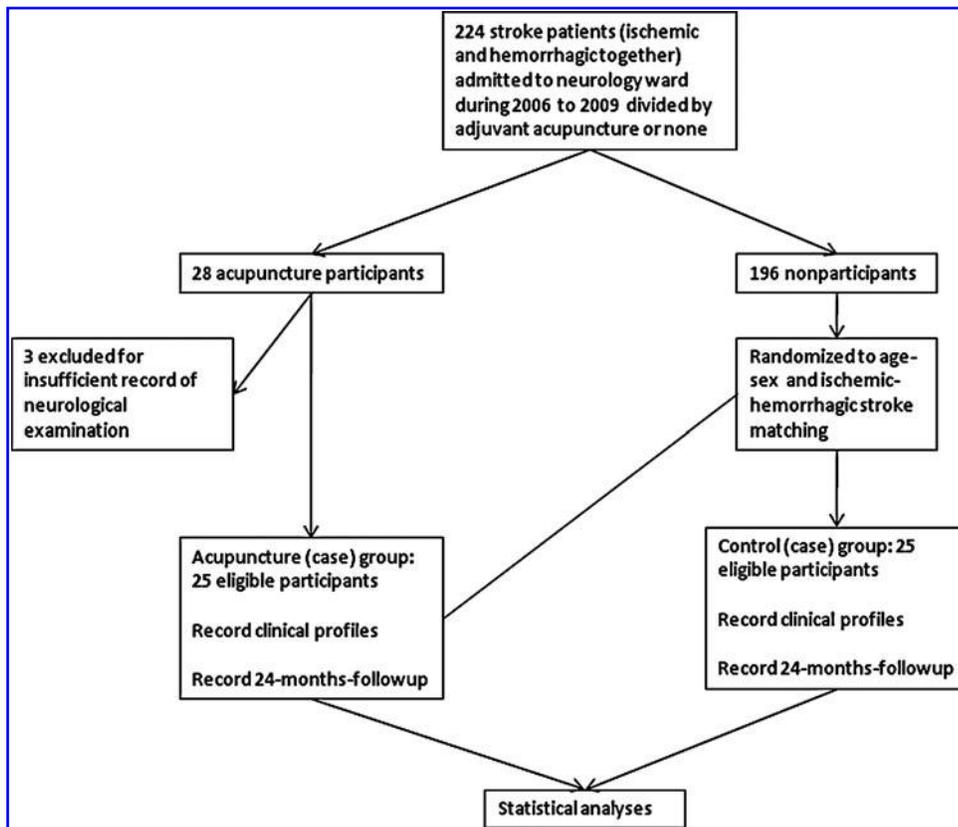


FIG. 1. Flow of participants through each stage of the trial.

operation, especially in treatment for apoplectic insult due to cerebral hemorrhage, or if the treatment is made more difficult due to the lack of a cranial vault or restricted by extensive scarring, then, depending on anatomical conditions, the points may be freely selected from both somatotopes. YNSA is not “ready-made” acupuncture but rather a treatment tailored to the individual patient.^{16,17}

The patients in the acupuncture group had been treated once in each month during the whole period of the clinical trial using the dry needling method with removable dry needles according to YNSA (Fig. 2). The “time release” dry needling system with the inserted and permanently entered

insertion with the help of a special needle was applied.¹⁸ The length of the special stainless-steel needle is 10.8 cm, and the diameter of the lumen is 0.7 mm. The threads (MAXOL-M Monofilamentum) were cut into 0.7–1-cm pieces and then applied with the needle. The threads were placed into this needle and the material was applied to the “acupoints.” Twelve (12) needles were inserted into every subject per session. The depth of thread insertion is 0.7–0.9 mm. There was no other needle manipulation performed. The insertions are applied once a month, based on the total absorption time of the previous threads being 4 weeks. The YNSA points (Cerebrum, Cerebellum, Basal Ganglia, Liver on the skull)

TABLE 1. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF TREATED PATIENTS, BY GROUP

Characteristics	Control group (standard rehabilitation therapy) (n = 25)	Acupuncture group (standard rehabilitation therapy with YNSA) (n = 25)	p (Fisher’s exact test for categorical variables, t-test for continuous variables [age])
Male gender, %	40	32	0.5
Mean age in years (SD)	59.8 (9.6)	58.6 (10.4)	0.8
Current smoking, %	36	40	0.7
High school or higher educational level, %	40	36	0.6
Depression (clinical diagnosis), %	0	4	0.2
Very intense pain at presentation, %	30	30	1
Lesion of brain tissue, %	15.8	17.1	0.7
Ischemic stroke vs all, %	72	72	1

YNSA, Yamamoto’s New Scalp Acupuncture; SD, standard deviation.

and additionally Kidney *Shu* back point bilaterally were stimulated by embedded filaments. The patients in the control group had not been treated by any form of acupuncture.

Physiotherapy

In our department, Institute of Complementary and Alternative Medicine, University of Pecs, as in many rehabilitation centers in Hungary, stroke rehabilitation was mainly based on the Dévényi-Pető method in an attempt to restore normal movement and improve strength. Each patient received certain modalities of treatment (3 times a week) as decided by the supervising senior physiotherapist according to the patient's need at different stages of recovery.

Measurements

Barthel Index (BI) is a validated and widely used instrument to measure disability in ADL.^{19,20} The original BI a disability profile scale developed by Barthel in 1965 to evaluate a patient's self-care abilities in 10 areas, including bowel and bladder control. The patient is scored from 0 to 15 points in various categories, depending on his or her need for help, such as in feeding, bathing, dressing, and walking. In the present study, the version used was the one described by Wade and Collin in 1988, which has a total BI score of 20.²¹ The severity of disability is classified as mild (BI15), moderate to severe (5BI15), and very severe (BI5).

Rivermead Mobility Index (RMI) is a measurement of mobility disability which concentrates on body mobility.²² The RMI comprises a series of 14 questions and one direct observation, and covers a range of activities from turning over in bed to running. Its validity as a measure of mobility after head injury and stroke was tested by concurrent measure-

ment of mobility using gait speed and endurance, and by standing balance. It is short, simple, and clinically relevant, and can be used in the hospital or at home.

Visual-Analogue Scale (VAS) is a subjective factor that describes the patient's general and physical status.²³

Data analysis

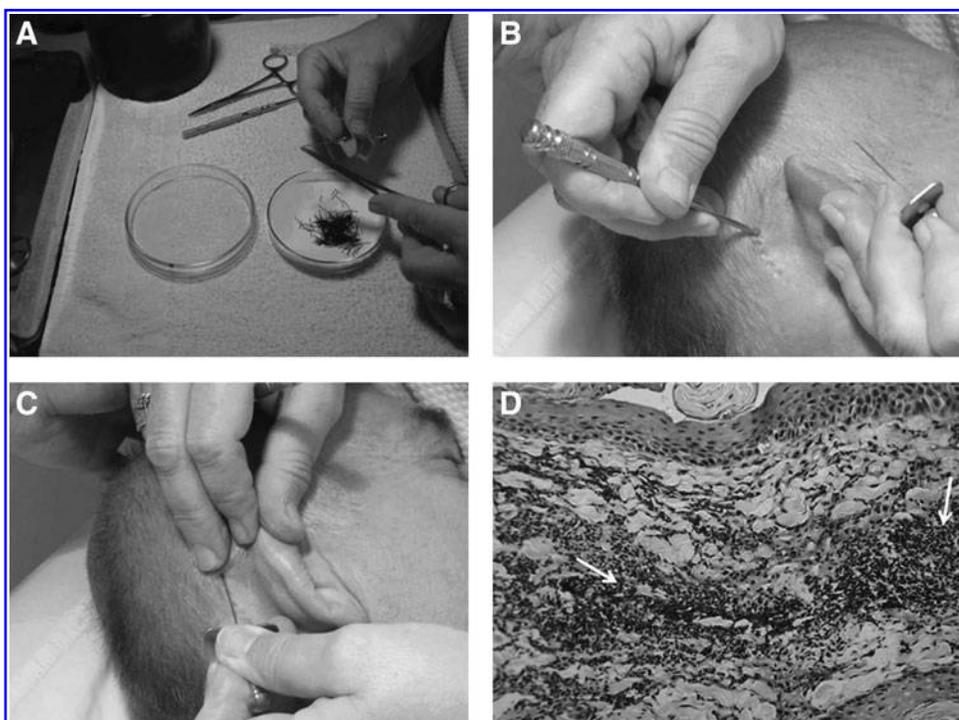
The sensory and motor assessment data were gathered during initial admission to the rehabilitation ward and 2 years after stroke. Statistical comparisons were performed based on these two time points. Categorical variables were analyzed using the χ^2 test or Fisher's exact test for small samples. Measurement data were analyzed using two-tailed *t*-tests. All recorded data were input using Epi Info software (CDC, Atlanta, GA) and statistically analyzed using SPSS 11.5 statistical software (SPSS, Chicago, IL). For all analyses, $p < 0.05$ was considered to be statistically significant. Chi-square analysis of the acupuncture group and control group was also performed to determine homogeneity between both groups in terms of age, gender, and pretreatment measurement outcomes.

The calculation of the sample size is based on the primary outcome measure. It was estimated that 23 patients were required in each group to detect a clinically relevant 2-point difference in Barthel, Rivermead, and Ritchie-Hegyí scores with a power of 80% and an α value of 0.05. Assuming a 20% dropout rate, it was planned to randomize 28 patients to each group. Unfortunately, 3 patients in both groups needed to be excluded for different reasons.

Results

During initial admission to the hospital, all of the 50 stroke patients were randomly distributed to the acupuncture and

FIG. 2. Procedure of Yamamoto's New Scalp Acupuncture (YNSA) treatment. **A.** Preparation of Maxom-M-Monofilament into special needle that contains lumen for embedding acupuncture. Procedure of insertion (**C**) after palpation (**B**) to find right topography. **D.** Changes of connective tissue structure 3 weeks after needle implantation ($\times 15$). The arrows show the two ends of previously inserted monofilament.



control group with 25 patients in each group as described in the Materials and Methods section. The neurologic and functional status of members of each group at the time of admission to the rehabilitation ward, discharge from the hospital, and 2-year postinjury follow-up examination are summarized in Figure 3. In the acupuncture group, all the sensory, motor, and functional scores improved significantly during the examination period until 2 years after injury.

The BI is increased from 4 ± 2 to 95 ± 4 in the acupuncture group. This index also increased in the control group (from 4 ± 2 to 75 ± 4), but the changes were significantly less than those of the acupuncture group (acupuncture versus control $p < 0.01$ at 24 months). The continuously increasing BI during the examination period showed an improvement of self-support ability in both groups, but the acupuncture treatment helped accomplish a faster and better recovery. The change of the other parameters under the examination period shows at least two important results. There was a significant spontaneous recovery during the 2-year follow-up; however, the YNSA treatment facilitated the recovery. The improved moving function (Rivermead scale, from 3 ± 2 to 29 ± 2 ; from 2 ± 1 to 20 ± 2 ; treated and control group, respectively, $p < 0.01$ at 24 months) and the more flexible joints and ligaments as compared to their condition before treatment were observed.

A subjective index (VAS from 27 ± 13 to 71 ± 12 ; from 20 ± 10 to 53 ± 7 ; treated and control group, respectively, $p < 0.05$ at 24 months) was also determined during the follow-up period. The VAS scale was also enhanced in all cases, but the members of the acupuncture group had more efficient function than the control group. In summary, according to the abovementioned results, changes of the indexes are better in the acupuncture group than in the control group.

The intervention was well tolerated by patients. Any "throw-out reaction" of monofilament and side-effect was not observed under the treatment. According to the results in this study, dry-needling elevated the microcirculation of the brain, which was verified by brain-scan investigation. Cerebral blood flow detected by single-photon emission computed tomography was increased by $15\% \pm 5\%$ after YNSA treatments.

Discussion

Stroke is the third major cause of death worldwide, and it is the most frequent cause of invalidity in old age. Apart from in-patient lysis treatment for a minority of those affected, no efficient methods of treatment addressing the cause of the insult are available for stroke patients. There is an 8.8% risk of cerebral hemorrhage after lysis therapy. As a valuable complement to this type of therapy, YNSA can be offered to all stroke patients who do not fulfill the criteria for lyses treatment.²⁴

The aim of this study was to examine the long-term effects of repeated embedded YNSA treatment on balance and activities of daily living in postacute stroke patients compared with the no-acupuncture group. "So, what is the truth about acupuncture in stroke rehabilitation?" was asked at the end of the Introduction section. In the authors' opinion at least two things are important to determine the efficacy of the acupuncture treatment in stroke rehabilitation. The most important is to enhance the life quality of the stroke patients

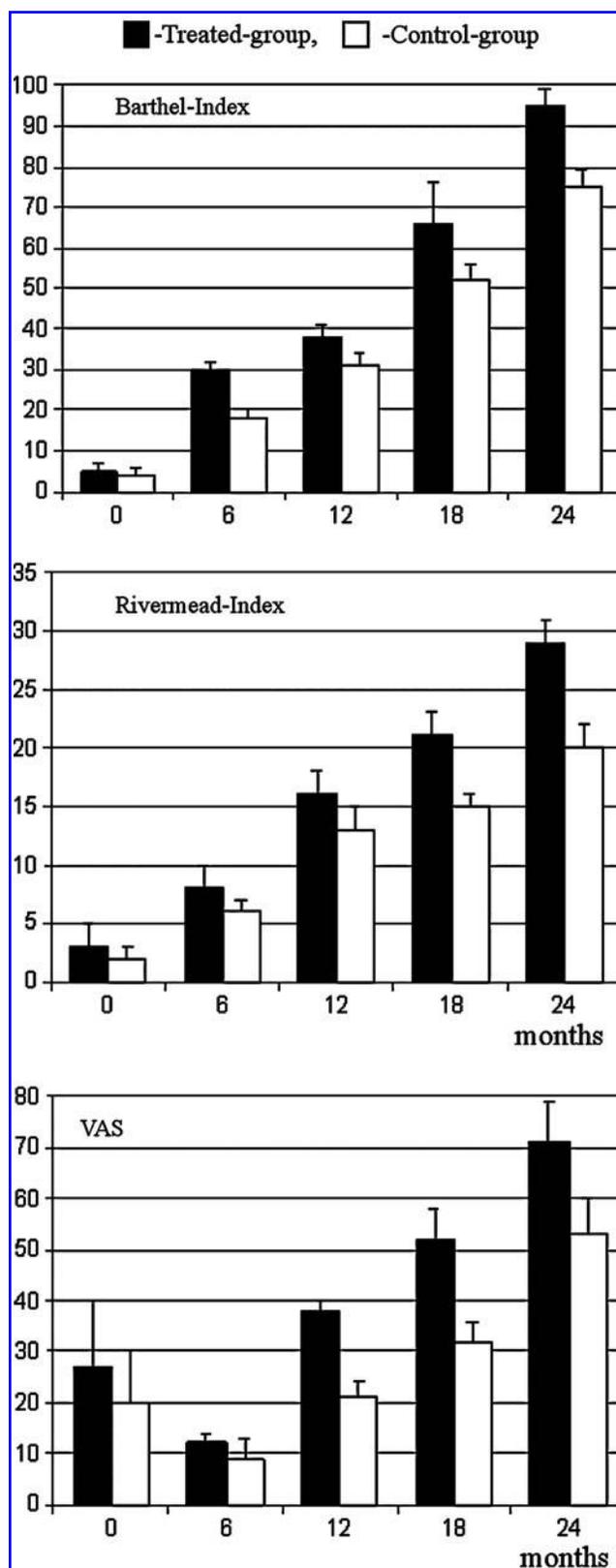


FIG. 3. Changes of Barthel Index, Rivermead Index, and Visual Analogue Scale (VAS) in acupuncture (black columns) and control (white columns) group.

during and after the acupuncture treatment. The second thing is to find the possible link between the acupuncture treatment and the cellular mechanisms that activated in the recovery period of stroke.

Previous studies have reported the ineffectiveness of sensory stimulation by acupuncture or transcutaneous electrical nerve stimulation, functional electrical stimulation, electromyographic feedback, force feedback or body weight supported treadmill training on balance in patients with stroke.²⁵ Recent evidences have shown that impairment-focused programs (biofeedback, electric stimulation, muscle strengthening) failed to generate functional improvements whereas therapies that administered functional training improved activity levels.²⁶ Unfortunately, there are no previous data published about the YNSA treatment in stroke survivors. However, in the current study, the generally used BI, the RMI, and the VAS were applied to determine the changes of life qualities of participants. The patients were followed in a 2-year period after the stroke. All of the four parameters were increased in the 24-month follow-up period in the acupuncture and control group; however, the changes were significantly greater in the acupuncture group than in the control group. The data suggest that the YNSA is a useful method to treat the stroke patients and enhance the quality of life.

Using BI, RMI, and VAS for the motor-status evaluation, the results showed that YNSA is effective in patients with stroke (ischemic and hemorrhagic) for motor recovery. To the authors' knowledge, this is the first study to demonstrate that YNSA has beneficial effects on body motor performance in patients with stroke. In terms of functional improvement, both the study group and the control group showed improvement in functional performance at follow-up assessments. However, there was a tendency for the study group to be superior to the control group in the total scores at follow-up stages, and at the end of the follow-up period it did reach statistical significance.

However, the link still must be found between the acupuncture and the cellular changes after stroke. Some evidence suggests that the acupuncture stimulation with needle can enhance the release of transmitters that can facilitate angio- and neurogenesis in the central neural system. In 2006, Li²⁷ and in 2009 Ding²⁸ and colleagues reported that electroacupuncture therapy could cause depolarization and enhance Ca²⁺ influx of neurons. Moreover, intracellular Ca²⁺ elevation may stimulate an autocrine neurotrophic mechanism, leading to the synthesis and release of neurotrophic factors.²⁷⁻³¹ Recently, in 2009 Longhurst described that electroacupuncture modulates the sympathoexcitatory reflex responses by decreasing the release of γ -aminobutyric acid.³² Carmichael reported that axonal sprouting and neurogenesis are induced in stroke rehabilitation.^{33,34} On a cellular level, the phenomenology of neural repair after stroke has been defined and unique regenerative environments in the poststroke brain identified. These data suggest that acupuncture facilitates some molecular and cellular mechanisms that have an important role in the angiogenesis, neurogenesis, and tonic neuronal inhibition in brain tissue. This it can be concluded that acupuncture, especially the YNSA, is a useful complementary tool to facilitate stroke rehabilitation.

Conclusions

These data suggest that the use of YNSA therapy with embedded threads after stroke can contribute to significant neurologic and functional recoveries. There are several limitations of this study. Because there was no sham control, it is not known how much the YNSA intervention contributed to the improvement of subjects in the acupuncture group because it is not known how much of the improvement was due to placebo effect. Further data exploration suggested that these complete case analyses are likely to provide valid statistical interferences.

Disclosure Statement

All authors and contributors declare that no conflict of interest exists.

References

- Ernst E, White AR. Acupuncture as an adjuvant therapy in stroke rehabilitation? *Wien Med Wochenschr* 1996;21: 556-558.
- Hopwood V. Acupuncture in stroke recovery: A literature review. *Complement Ther Med* 1996;4:258-263.
- Wong AMK, Leong CP, Su TY, et al. Clinical trial of acupuncture for patients with spinal cord injuries. *Am J Phys Med Rehabil* 2003;82:21-27.
- Park J, Hopwood V, White AR, Ernst E. Effectiveness of acupuncture for stroke: A systematic review. *J Neurol* 2001; 248:558-563.
- Sze FK, Wong E, Or KKH, et al. Does acupuncture improve motor recovery after stroke? A meta-analysis of randomized controlled trials. *Stroke* 2002;33:2604-2619.
- Shiflett SC. Does acupuncture work for stroke rehabilitation: What do recent clinical trials really show? *Top Stroke Rehabil* 2007;14:40-58.
- Kong JC, Lee MS, Shin BC, et al. Acupuncture for functional recovery after stroke: A systematic review of sham-controlled randomized clinical trials. *CMAJ* 2010;182:1723-1729.
- Vickers A, Wilson P, Kleijnen J. Acupuncture. *Qual Saf Health Care* 2002;11:92-97.
- Yamamoto T, Schockert T, Borojerdi B. Treatment of juvenile stroke using Yamamoto New Scalp Acupuncture (YNSA): A case report. *Acupunct Med* 2007;25:200-202.
- Schockert T, Schnitker R, Borojerdi B, et al. Cortical activation by Yamamoto new scalp acupuncture in the treatment of patients with a stroke: A sham-controlled study using functional MRI. *Acupunct Med* 2010;28:212-214.
- Shang C. Electrophysiology of growth control and acupuncture. *Life Sci* 2001;68:1333-1342.
- Fung PC. Probing the mystery of Chinese medicine meridian channels with special emphasis on the connective tissue interstitial fluid system, mechanotransduction, cells durotaxis and mast cell degranulation. *Chin Med* 2009;4:10.
- Wu H. Acupuncture and stroke rehabilitation. *CMAJ* 2010; 182:1711-1712.
- Alexander LD, Black SE, Gao F, et al. Correlating lesion size and location to deficits after ischemic stroke: the influence of accounting for altered peri-necrotic tissue and incidental silent infarcts. *Behav Brain Funct* 2010;6:6-15.
- Yamamoto T, Yamamoto H, Yamamoto MM. Yamamoto New scalp acupuncture. *Bad Kötzing: VGM*, 2005.
- Schockert T. YNSA: Individual therapy through neck diagnostic. *Komplement Integr Med* 2007;10:8-10.

17. Schockert T, Beissner F. Neurophysiological correlates of the effect of YNSA for patients with chronic pain of the locomotor system: Basic YNSA research by means of PET-CT. *Deutsch Ztschr Acup* 2010;2:8–13.
18. Hungarian patent No. 0000008/2001.
19. Mahoney FI, Barthel DW. Functional evaluation: The Barthel Index. *Md State Med J* 1965;14:61–65.
20. Granger CV, Dewis LS, Peters NC, et al. Stroke rehabilitation: Analysis of repeated Barthel index measures. *Arch Phys Med Rehabil* 1979;60:14–17.
21. Wade DT, Collin C. The Barthel ADL Index: A standard measure of physical disability? *Int Disabil Stud* 1988;10:64–67.
22. Endres M, Nyáry I, Bánhidi M, Deák G. RMI stroke rehabilitation: A method and evaluation. *Int J Rehabil Res* 1990;13:225–236.
23. Ahlsjö B, Britton M, Murray V, Theorell T. VAS disablement and quality of life after stroke. *Stroke* 1984;15:886–890.
24. Boroojerdi B, Yamamoto T, Schumpe G, Schockert T. Treatment of stroke-related motor impairment by Yamamoto New Scalp Acupuncture (YNSA): An open, prospective, topometrically controlled study. *Med Acup* 2005;9:24–28.
25. Geurts AC, de Haart M, van Nes IJ, Duysens J. A review of standing balance recovery from stroke. *Gait Posture* 2005;22:267–281.
26. van Peppen RPS, Kwakel G, Wood-Dauphinee S, et al. The impact of physical therapy on functional outcome after stroke: What's the evidence? *Clin Rehabil* 2004;18:833–862.
27. Li XB, Zeng YS, Chen YL, Chen YY, Guo JS, Chen SJ. Combination of gormor vessels electroacupuncture and transplanted neural stem cells promotes injured spinal cord tissue producing nerve growth active substances. *Acta Anatom Sin* 2006;37:622–626.
28. Ding Y, Yan Q, Ruan JW, et al. Electro-acupuncture promotes survival, differentiation of the bone marrow mesenchymal stem cells as well as functional recovery in the spinal cord-transected rats. *BMC Neurosci* 2009;10:35.
29. Cooper DMF, Mons N, Karpan JW. Adenylyl cyclases and the interaction between calcium and cAMP signaling. *Nature* 1995;374:421–424.
30. Ghosh A, Carnahan J, Greenberg ME. Requirement for BDNF in activity-dependent survival of cortical neurons. *Science* 1994;263:1618–1623.
31. Hansen MR, Zha XM, Bok J, Green SH. Multiple distinct signal pathways, including an autocrine neurotrophic mechanism, contribute to the survival-promoting effect of depolarization on spiral ganglion neurons in vitro. *J Neurosci* 2001;21:2256–2267.
32. Fu LW, Longhurst JC. Electroacupuncture modulates vIPAG release of GABA through presynaptic cannabinoid CB1 receptors. *J Appl Physiol* 2009;106:1800–1809.
33. Carmichael ST. Themes and strategies for studying the biology of stroke recovery in the poststroke epoch. *Stroke* 2008;39:1380–1388.
34. Carmichael ST. Targets for neural repair therapies after stroke. *Stroke* 2010;41(10 suppl):S124–S126.

Address correspondence to:

Gyula P. Szigeti, MD, PhD

University of Debrecen

Medical and Health Science Centre

Department of Physiology

P.O. Box 22

Debrecen H-4012

Hungary

E-mail: szgy@phys.dote.h