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## REFERENCES

1. Walach H. Generalized entanglement: A new theoretical model for understanding the effects of complementary and alternative medicine. *J Altern Comp Med* 2005;11:549–559.
2. Atmanspacher H, Römer H, Walach H. Weak quantum theory: Complementarity and entanglement in physics and beyond. *Found Phys* 2002;32:379–406.
3. Milgrom LR. Patient-practitioner-remedy (PPR) entanglement. Part 4: Towards classification and unification of the different entanglement models for homeopathy. *Homeopathy* 2004;93:34–42.
4. Hankey A. Are we close to a theory of energy medicine? *J Altern Complement Med* 2004;10:83–86.
5. Hankey A. CAM modalities can stimulate advances in theoretical biology. *Evid Based Comp Altern Med (eCAM)*. 2005;2:5–12.
6. Josephson B.D. Beyond quantum theory: a realist psycho-biological interpretation of reality revisited. *Biosystems* 2002;64:43–45.

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## STANDARDIZATION OF INDIVIDUALIZED TREATMENTS IN A RANDOMIZED CONTROLLED TRIAL OF ACUPUNCTURE FOR STROKE REHABILITATION

Dear Editor:

Considerable research in Asia and the West has evaluated the efficacy of acupuncture for stroke survivors.<sup>1–4</sup> The results of this research have been contradictory or equivocal. Most stroke studies in the West have used formulaic, fixed acupuncture protocols,<sup>5–7</sup> in contrast to the individualized treatments that are emphasized in the practice of Traditional Chinese Medicine (TCM). This approach may have introduced important biases in the evaluation of acupuncture and underestimated its benefits.<sup>8–11</sup>

In a randomized controlled trial of stroke survivors with persisting symptoms (>6 months),<sup>26</sup> we used treatment manualization, an approach<sup>11</sup> that permitted us to systematically administer individualized acupuncture protocols in the study. Treatment manualization provides replicability and standardization, while maintaining fidelity to traditional acupuncture treatment principles. The use of a treatment manual provided us with a clearly articulated theoretical framework, objective decision algorithms for diagnosis and treatment, and a protocol for training and evaluating practitioner competence and adherence to treatment.<sup>11,12</sup> It led to an objective, repeatable intervention with high internal va-

lidity tailored to the characteristics of individual patients. Manualization has been successfully employed in other clinical trials of acupuncture<sup>13–16</sup> and the general process has been described in detail elsewhere.<sup>11</sup> In the following, we illustrate the practical steps required to develop a manual using our chronic stroke trial as an example.

By using a survey, we identified a panel of 12 acupuncture experts within the New England School of Acupuncture faculty (total faculty = 70) with extensive training and clinical experience in treating stroke. Six faculty members agreed to participate in the manual development process. Four were trained in traditional Chinese acupuncture and two in Japanese-style acupuncture; four had received their training in Asia (three in China, one in Japan) and two in the United States. Their clinical experience ranged from 15 to 20 years.

In contrast to acupuncture for acute and subacute stages of stroke recovery, little research has investigated the potential benefits of acupuncture administered during the chronic stage.<sup>17–19</sup> Therefore, our manualization process aimed at enhancing the limited available research evidence. Our purpose was to define a conceptual framework, design an optimal treatment protocol for this population of stroke patients, develop an appropriate sham control, and set guidelines for treatment implementation. A researcher (RS) with extensive experience in the manualization process led the overall process.

We conducted a series of structured planning meetings using a focus group format<sup>20</sup> to develop and agree upon the content of the treatment manual. After an initial informational meeting, each expert independently completed a protocol questionnaire (PQ) that included questions on the TCM framework, specific acupuncture techniques, expected clinical outcomes, and adaptations required for research (Table 1). These results were synthesized and then presented to the panel along with a review of the literature evaluating acupuncture for stroke. The literature review employed conventional search engines (MEDLINE®, Cochrane, and Current Contents/Web of Science), as well as an internal database at NESAs Library that catalogs textbooks and articles from 63 alternative and complementary therapy (ACT) journals not indexed in MEDLINE. A total of 366 papers and books were identified that examined the use of acupuncture for stroke patients. Two members of our team reviewed this literature and excluded review papers and studies that did not explicitly describe treatment interventions or Oriental Medicine diagnoses. Studies were organized by treatment style (e.g., TCM, Korean, modern scalp) and techniques (e.g., manual stimulation versus electroacupuncture). A qualitative summary of the literature was presented to the expert panel, and representative articles of different styles and techniques were given to each expert to review.

Four styles of acupuncture were represented by the panel: Traditional Chinese Medicine (TCM)<sup>21</sup> and three styles of Japanese acupuncture: Meridian Therapy;<sup>22,23</sup> Manaka system,<sup>24</sup> and Yamamoto scalp acupuncture.<sup>25</sup> The team agreed on a TCM approach because greater clinical experience treating stroke with TCM was found within our expert panel and the research literature was more informative for TCM.

TABLE 1. PRACTITIONER QUESTIONNAIRE (PQ)<sup>a</sup>

Framework	<ul style="list-style-type: none"> <li>• What Chinese acupuncture (TCM) concepts would you use to evaluate and treat patients in the chronic phase of stroke? How would you classify these patients?</li> <li>• Describe complex clinical presentations you would expect to find? (Consider age, sex distribution, and nature of neurologic impairments and disabilities.)</li> <li>• Outline the treatment principles you would apply to each presentation.</li> <li>• Specify which acupuncture points you would select to address each clinical presentation and target each treatment principle (e.g., points on the yang channels of the affected limb with points to address the individual pattern, or scalp points and yang channel points).</li> </ul>
Treatment strategy	<ul style="list-style-type: none"> <li>• Describe the specific techniques (e.g., scalp versus body points, manual stimulation versus electrostimulation) you would use, including where and when.</li> <li>• Describe the ideal frequency and duration of treatment.</li> </ul>
Clinical outcomes	<ul style="list-style-type: none"> <li>• What areas of improvement would you expect to see from their treatments?</li> <li>• In what areas would you expect to see little or no change?</li> </ul>
Modifications to protocol for use in a randomized control trial (RCT)	<ul style="list-style-type: none"> <li>• What limitations and challenges do you foresee in applying the protocol in an RCT?</li> <li>• What modifications might you make to the protocol if you were to apply it in an RCT?</li> </ul>
Additional comments and recommendations	<ul style="list-style-type: none"> <li>• Please add any comments or recommendations regarding diagnosing and treating stroke from a TCM perspective.</li> </ul>

<sup>a</sup>Outline of the questionnaire that was completed independently by each expert panel participant to gather information about the conceptual framework and treatment strategies most often used in the treatment of stroke.

TABLE 2. BODY TREATMENTS<sup>a</sup>

	Acupuncture points	Treatment number									
		1	2	5	6	9	10	13	14	17	18
Hemiparesis											
<i>Upper affected limb</i>											
	LI 15	XX	XX	X	X	X	XX	X	XX	X	X
	LI 14		X	X	X	X	X			X	X
	LI 11	XX	XX	X	X	XX	X	XX	XX	XX	XX
	LI 10		X		X	X	X				
	LI 4	X	X	XX	X	XX	X	XX	X	XX	XX
	TH 14	X	XX	XX	XX	X	X	X	X	X	X
	TH 5	X	XX	X	XX	X	X		X	X	X
	TH 3			X	X		XX			X	X
	Baxie					X	X				
	SI 3			X	X	X					
<i>Lower affected limb</i>											
	GB 30	XX	X	XX	XX	X	X				
	GB 31		X		X	X					
	GB 34		X	X	X	XX		X	XX	XX	XX
	GB 39	XX	X	X	X	X					
	GB 40			X	X	X	X			X	X
	St 34	X			X	X		X	X	X	X
	St 36	X	X	XX	XX		XX	XX	X	X	X
	ST 42		X	X	X	XX	XX				
	LV3	X	X	X	X	X	X	XX	XX	XX	XX
Underlying pathogenic factor (healthy side)											
<i>Inter Liver wind</i>											
	Kd 3		X	X	X	X	X	X	X		
	Lv 8	X	X	X	X	X	X	X	X	X	X
	Sp 10	X	X	X	X	X					
	Lu 5	X		X							
	Lv 3		X		X		X				
<i>Internal fire (repletion or vacuity)</i>											
	Kd 6				X	X	X				
	UB 18	X			X		X				
	UB 23				X		X				
<i>Accumulation of Phlegm</i>											
	Sp 4	X	X		X						
	Sp 9	X	X	X	X		X	X		X	X
	St 40	X	X	X	X				X	X	X
	Lu 9	X			X	X	X				

(continued)

TABLE 2. BODY TREATMENTS<sup>a</sup> (CONTINUED)

Acupuncture points	Treatment number									
	1	2	5	6	9	10	13	14	17	18
UB 13			X			X				
UB 20		X	X		X					
UB 23		X	X		X	X				
Du 26		X								
P5	X									
Additional presenting symptoms										
Poor sleep	Ht 7	X	X							
Depression (withdrawal disease)	Du 20	X		X	X	X	X			
	Ht 7			X	X	X	X			
	P 7		X	X	X	X	X			

<sup>a</sup>Representative course of 10 body treatments for a subject randomized to the active acupuncture treatment group. X indicates acupuncture point manually stimulated during a given session. XX indicates acupuncture points electrically stimulated (5 minutes continuous stimulation followed by 15 minutes of intermittent stimulation, 25 Hz).

TABLE 3. SCALP TREATMENTS<sup>a</sup>

Treatment number	3	4	7	8	11	12	15	16	19	20
Scalp side areas	Right	Right	Right	Right	Right	Right	Right	Right	Right	Right
Upper motor	1st, 2nd	1st, 2nd	1st, 2nd	1st, 2nd	1st, 2nd	1st, 2nd	1st, 2nd	1st, 2nd	1st, 2nd	1st, 2nd
Sensory	1st, 2nd	1st, 2nd	1st, 2nd	1st, 2nd	1st, 2nd	1st, 2nd	1st, 2nd	1st, 2nd	1st, 2nd	1st, 2nd
Leg motor	1st, 2nd	1st, 2nd	1st, 2nd	1st, 2nd	1st	1st	1st	1st	1st	1st

<sup>a</sup>Representative course of 10 scalp treatments for a subject randomized to the active acupuncture treatment group. Various movements performed while the scalp needles were in place (e.g., walking, arm and or leg rotation, stretching). 1st, 2nd refer to fifths (regions) of scalp lines.

We continued the process with only those members of the expert panel who practiced TCM ( $n = 4$ ).

In a subsequent meeting, the diagnostic framework, structure of intake, treatment protocols, type of stimulation, and sham intervention were discussed. The final protocol consisted of general body acupuncture points using manual or electro stimulation (to treat paralysis, address the TCM pathologic factors, and support additional symptoms), combined with a modern system of "scalp" acupuncture (to increase muscle power and motor function).<sup>21,26,27</sup> Body and scalp acupuncture protocols were alternated (two body treatments a week followed by two scalp treatments the next week) for 10 weeks (20 total).

This information was collated into a working draft of the treatment manual, which was further refined with the input of the panel's two TCM practitioners with the most experience in treating stroke (CXM and ZZZ); these practitioners were also chosen to administer all treatments in our pilot study. Tables 2 and 3 summarize the active protocol for the 10 body and 10 scalp treatments in a representative study participant. A complete description of the sham protocols is presented elsewhere.<sup>28</sup>

Most acupuncture research in the West aims to evaluate the efficacy of acupuncture for biomedically defined conditions (e.g., stroke), and employs exclusively biomedically based screening and eligibility criteria. From the acupuncture perspective, people who meet these criteria include a heterogeneous population of patients for whom a single fixed treatment protocol will lack specificity and is unlikely to be optimally effective. The use of fixed acupuncture treatment protocols may be appropriate for some types of acupuncture research (e.g., single points to target specific physiologic processes)<sup>29,30</sup> or certain conditions (e.g., knee pain, emesis) for which fixed protocols have been proved effective.<sup>31-33</sup> However, for complex clinical conditions such as stroke, treatment individualization is the standard clinical approach, and the use of fixed protocols for these conditions lacks ecologic validity. Manualized protocols offer a solution for balancing the need for treatment individualization with objective standardization and replicability required for clinical trials. Manualization may have important applications in other areas of ACT research (e.g., massage, herbal medicine), which often tailor treatment to the individual.

## REFERENCES

1. Hopwood V. Acupuncture in stroke recovery: A literature review. *Complement Ther Med* 1996;4:258–263.
2. Naeser MA. Acupuncture in the treatment of paralysis due to central nervous system damage. *J Altern Complement Med* 1996;2:211–248.
3. Park J, Hopwood V, White AR, et al. Effectiveness of acupuncture for stroke: A systematic review. *J Neurol* 2001; 248:558–563.
4. Sze FK, Wong E, Kevin KH, et al. Does acupuncture improve motor recovery after stroke? A meta-analysis of randomized clinical trials. *Stroke* 2002;2604–2619.
5. Johansson BB, Haker E, von Arbin M, et al. Acupuncture and transcutaneous nerve stimulation in stroke rehabilitation: A randomized, controlled trial. *Stroke* 2001;32:707–713.
6. Wong AM, Su TY, Tang FT, et al. Clinical trial of electrical acupuncture on hemiplegic stroke patients. *Am J Phys Med Rehabil* 1999;78:117–122.
7. Gosman-Hedstrom G, Claesson L, Klingenstierna U, et al. Effects of acupuncture treatment on daily life activities and quality of life: A controlled, prospective, and randomized study of acute stroke patients. *Stroke* 1998;29:2100–2108.
8. Bensoussan A. Contemporary acupuncture research: The difficulties of research across scientific paradigms. *Am J Acupunct* 1991;19:357–365.
9. Hammerschlag R. Methodological and ethical issues in clinical trials of acupuncture. *J Altern Complement Med* 1998;4:159–171.
10. Lao L, Ezzo J, Berman B, et al. Assessing clinical efficacy of acupuncture: Considerations for designing future acupuncture trials. In: Stux G, Hammerschlag R, eds. *Clinical Acupuncture: Scientific Basis*. Berlin: Springer-Verlag, 2001:187–209.
11. Schnyer RN, Allen JJ. Bridging the gap in complementary and alternative medicine research: Manualization as a means of promoting standardization and flexibility of treatment in clinical trials of acupuncture. *J Altern Complement Med* 2002;8:623–634.
12. Wilson GT. Manual-based treatments: The clinical application of research findings. *Behav Res Ther* 1996;34:295–314.
13. Allen J, Schnyer R, Hitt S. The efficacy of acupuncture in the treatment of depression in women. *Psychol Sci* 1998; 9:397–401.
14. Schnyer R.N, Manber R, Fitzcharlers A. Acupuncture treatment for depression during pregnancy: Conceptual framework and two case reports. *Complement Health Pract Rev* 2003;8:40–53.
15. Manber R, Schnyer RN, Allen JJB, et al. Acupuncture: A promising treatment for depression during pregnancy. *J Affect Disord* 2004;83:89–95.
16. Kaptchuk TJ, Statson WB, David RB, et al. Sham device versus inert pill: A randomized controlled trial comparing two placebo treatments for arm pain due to repetitive use. *BMJ* 2006, in press.
17. Naeser MA, Alexander MP, Stiassny-Eder D, et al. Acupuncture in the treatment of paralysis in chronic and acute stroke patients—improvement correlated with specific ct scan lesion sites. *Acupunct Electrother Res* 1994;19:227–249.
18. Naeser MA, Alexander MP, Stiassny-Eder D, et al. Acupuncture in the treatment of hand paresis in chronic and acute stroke patients—improvement observed in all cases. *Clin Rehab* 1994;8:127–141.
19. Fink M, Gutenbrunner C, Rollnik J, et al. Credibility of a newly designed placebo needle for clinical trials in acupuncture research. *Placebo controls for acupuncture studies. Forsch Komplementarmed Klass Naturheilkd* 2001;8:368–372.
20. Powell RA, Single HM. Focus groups. *Int J Qual Health Care* 1996;8(5):499–450.
21. Shanghai College. *Acupuncture: A comprehensive text*. Shanghai: Shanghai College, 1984.
22. Denmai S. *Introduction to Meridian Therapy*. Seattle: Eastland Press, 1990.
23. Fukushima K. *Meridian Therapy*. Tokyo: Toyo Hari Medical Association, 1991.
24. Manaka Y. *Chasing the Dragon's Tail*. Brookline, MA: Paradigm Publications, 1995.
25. Yamamoto T, Yamamoto H. *Yamamoto New Scalp Acupuncture*. Tokyo: Japan Axel Springer Japan Publishing, 1998.
26. Jianwei Z, Fan Z. A research on scalp acupuncture for cerebral infarction. *J Trad Chin Med* 1997;17:194–197.
27. Hu HH, Chung C, Liu TJ, et al. A randomized controlled trial on the treatment for acute partial ischemic stroke with acupuncture. *Neuroepidemiology* 1993;12:106–113.
28. Wayne P, Krebs D, Macklin E, et al. Acupuncture for upper-extremity rehabilitation in chronic stroke: A randomized sham-controlled study. *Arch Phys Med Rehab* 2006;86:2248–2255.
29. Cho Z, Chung S, Jones J, et al. New findings of the correlation between acupoints and corresponding brain cortices using functional MRI. *Proc Natl Acad Sci* 1998;95:2670–2673.
30. Kong J, Ma L, Gollub RL, et al. A pilot study of functional magnetic resonance imaging of the brain during manual and electroacupuncture stimulation of acupuncture point (li-4 hegu) in normal subjects reveals differential brain activation between methods. *J Altern Complement Med* 2002;8:411–419.
31. Dundee JW, Ghaly RG, Fitzpatrick KT, et al. Acupuncture prophylaxis of cancer chemotherapy-induced sickness. *J R Soc Med* 1989;82:268–271.
32. Habek D, Barbir A, Habek J, et al. Success of acupuncture and acupressure of the pc 6 acupoint in the treatment of hyperemesis gravidarum. *Forsch Komplementarmed Klass Naturheilkd* 2004;11:20–23.
33. Berman BM, Lao L, Langenberg P, et al. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: A randomized, controlled trial. *Ann Intern Med* 2004;21; 141(12):901–910.

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