

Effects of Dǎoyīn Qìgōng in postpolio syndrome patients with cold intolerance

Efeitos do Dǎoyīn Qìgōng em pacientes com síndrome pós-pólio com queixa de intolerância ao frio

Paulo Eduardo Ramos¹, Gislaine Cristina Abe¹, Márcia Pradella-Hallinan^{1,2}, Abrahão Augusto Juvinião Quadros¹, Beny Schmidt¹, Acary Souza Bulle Oliveira¹

ABSTRACT

Postpolio syndrome (PPS) is characterized by progressive muscle weakness due to former infection with poliomyelitis and can be associated with other symptoms such as cold intolerance (CI). *Dǎoyīn Qìgōng* (DQ) is a technique in Traditional Chinese Medicine that impacts the circulation of energy and blood. **Objective:** It was to verify the effects of DQ in PPS patients complaining of cold intolerance. **Methods:** Ten PPS patients were assessed using the visual analogue scale (VAS) adapted for CI before and after intervention with DQ; patients practiced it in a sitting position for 40 minutes, 3 times per week over 3 consecutive months. Patients were reassessed three months after ceasing DQ. **Results:** There was a statistically significant difference in local and systemic VAS-Cold both at the end of DQ training and three months past the end of this. **Conclusion:** The DQ technique ameliorated CI complaints in patients with PPS.

Key words: Postpoliomyelitis syndrome, *Qìgōng*, breathing exercises, public health.

RESUMO

A síndrome pós-poliomielite (SPP) é caracterizada por instalação de nova fraqueza muscular às manifestações residuais da poliomielite, associada a outros sintomas, como intolerância ao frio (IF). O *Dǎoyīn Qìgōng* (DQ) é uma técnica da medicina tradicional chinesa que interfere na circulação da energia e do sangue. **Objetivo:** Foi verificar os efeitos do DQ em pacientes com SPP com queixa de intolerância ao frio. **Método:** Dez pacientes com SPP foram avaliados com a escala visual analógica (EVA) adaptada para IF antes e após intervenção com DQ, adaptados para a posição sentada, com duração de 40 minutos, 3 vezes por semana, durante 3 meses. **Resultados:** Verificou-se diferença estatisticamente significativa, na EVA-frio local e sistêmica, após o término do treinamento. **Conclusão:** O DQ é uma técnica que interferiu positivamente na queixa de IF em pacientes com SPP.

Palavras-Chave: síndrome pós-poliomielite, *Qìgōng*, exercícios respiratórios, saúde pública.

Post-polio syndrome (PPS) is characterized by progressive muscle weakness due to former infection with poliomyelitis and is often associated with other symptoms such as muscle fatigue, muscle and or joint pain, cold intolerance (CI) and sleep disorders¹⁻³. A Brazilian study of 167 patients who had previously been diagnosed with paralytic poliomyelitis and subsequently with PPS highlighted a CI frequency of 69.8%^{4,5}. The affected extremities are often unseasonably cold due to involvement of the sympathetic nerve cells, leading to vasoconstriction⁵. Until now, CI in patients with PPS had no defined etiology or specific rehabilitative or pharmacological treatment; muscle-strengthening exercises and

static magnetic fields seem to be beneficial, but these therapies warrant further research⁶. Guidelines for the treatment of symptoms include adequate clothing, distal/proximal massage and local heat for a short period of time^{5,7}.

From a clinical and histological perspective, the pathophysiology of PPS is associated with lower motor neuron dysfunction. One of the main mechanisms which may lead to this syndrome is overtraining. This activity favors the dysfunction of motor neurons which survive axon terminals which are completely destroyed. Compensatory mechanisms are triggered to reinnervate muscle tissue, thereby increasing the drive motor through stimulation of intact motor axons.

¹Department of Neurology and Neurosurgery, Department of Clinical Neurology, Division of Neuromuscular Disease Research, Clinic of Traditional Chinese Medicine, Universidade Federal de São Paulo (UNIFESP), São Paulo SP, Brazil;

²Department of Psychobiology, Sleep Institute, UNIFESP, São Paulo SP, Brazil.

Correspondence: Gislaine Cristina Abe; Universidade Federal de São Paulo; Rua Estado de Israel 899; 04022-002 São Paulo SP - Brasil; E-mail: gislaineabe@hotmail.com

Conflict of interest: There is no conflict of interest to declare.

Received 28 March 2012; Received in final form 18 April 2012; Accepted 25 April 2012

This mechanism occurs for the axons that are partially jeopardized. However, any exposure to stress will contribute to electrophysiological changes, which, in turn, challenge the nerve conduction velocity. This favors early degeneration of any remaining motor neurons⁸.

In the language of Traditional Chinese Medicine (TCM), CI is the main symptom of patients with a *yáng* (陽) deficiency; in TCM, the dynamic balance between *yīn* (陰) and *yáng* (陽) is one of the basic principles underlying homeostasis. In general, certain diseases are more likely to lead to imbalances that may cause susceptibility to cold⁹.

Dǎoyīn Qìgōng (DQ) (導引氣功), one of the various treatment techniques used in TCM, is a form of exercise that aligns gentle movements with controlled breathing. DQ has been practiced in China since ancient times to promote health, longevity and achieve spiritual immortality¹⁰⁻¹².

The objective of this study was to evaluate the effects of DQ in patients with PPS and CI complaints.

METHODS

Patients

The study included ten patients (three males, seven females) aged between 30 and 60 years with clinical diagnoses of PPS, according to criteria developed by Mulder¹³. Our study was conducted by the Division of Neuromuscular Disease Research with the approval of the Ethics Committee of UNIFESP, n° 529/09.

Allocation

Patients were randomly selected according to their record numbers. Patients signed a consent form after being informed about the study.

Inclusion criteria

We included patients diagnosed with PPS who complained of CI.

Exclusion criteria

Patients with medical histories featuring diseases that could mimic PPS, patients with diagnoses of stable polio sequelae, individuals with diagnoses of peripheral vascular disorders and individuals with well-established diagnoses of PPS that were likely to experience difficulties in the execution of the exercises.

DQ exercises used

We selected eight types of DQ exercises that had been adapted to the sitting position. The exercises were applied in sessions of 40 minutes, 3 times per week for 3 consecutive

months. We used the visual analogue scale (VAS)-Cold as an assessment instrument before and after intervention; the test was administered by an appraiser who did not attend the DQ training and was unaware of patient diagnosis.

Description of the exercises

Mángzhòng Wǔ Yuè Jié Zuò Gōng Tú (芒种五月節坐功圖)

1. Turn your palms outward and lift them above your head, drawing a circle in the air with both hands.
2. With your torso erect, shrink it as much as possible.
3. Lift the torso, stand erect, feeling the spine straight and your hands above your head holding up the sky.
4. Stretch your arms up as if to push up the sky.
5. Release your body, turn your palms down and repeat.

Dàshǔ Liù Yuè Zhōng Zuò Gōng Tú (大暑六月中坐功圖)

1. Keep your torso erect and your hands loose by your sides.
2. Rotate your torso and look over your left shoulder. Rotate your torso and look over your right shoulder.

Qīngmíng Sān Yuè Jié Zuò Gōng Tú (清明三月節坐功圖)

1. Get in a sitting position with back straightened.
2. The right hand flexes with the index and middle fingers stretched out as if arrowheads were about to be released.
3. Tilt your body to the left, stretching your right arm and pulling the elbow of your left arm back.
4. Release your right arm by bending it in front of your chest with fingers curled.

5. Shrink your left arm stretching the index and middle fingers.

6. Tilt your body to the right, stretching your left arm and pulling the elbow of right arm back.

Lìdōng Shíyuè Jié Zuò Gōng Tú (立冬十月節坐功圖)

1. Sit with your back straight and arms hanging down the sides.

2. Lift your right arm with the palm facing down.
3. At the same time, the left arm bends into the body with the palm facing down.

4. Stretch your right arm above your head and push down with your left palm.

5. Rotate your torso to the left, lowering your right arm while lifting your left arm.

6. Stretch your left arm above your head and push down with your right palm.

7. Rotate your torso to the right, lowering your left arm, then move back to the second movement.

Báilù Bā Yuè Jié Zuò Gōng Tú (白露八月節坐功圖)

1. In a sitting position, keep your back straight and hands on thighs.

2. Relax your back and try to lay your head three times on your right knee. Resume the initial position.

3. Relax your back and try to lay your head three times on your left knee. Resume the initial position.

4. Turn your torso clockwise and counterclockwise.
Jīngzhé èr Yuè Jié Zuò Gōng Tú (惊蛰二月節坐功圖)

1. Bend your body forward, shrinking the stomach, arms simulating a pendulum.

2. Raise your body and lift your arms up the level of your waist. Open them at the level of your head and bend your arms in front of your chest to enable both elbows to touch (breathe out slowly).

3. Release the remaining air and arms, bending your body forward, shrinking your stomach.

4. Return to the initial movement and repeat.

Qiūfēn Bā Yuè Zhōng Zuò Gōng Tú (秋分八月中坐功圖)

1. Keep in a sitting position, with back straight and arms on the side of the body.

2. Tilt and rotate your back slowly placing your neck against your shoulder.

3. Stretch your spine, pulling your shoulders back and craning your neck forward.

Lìqiū Qī Yuè Jié Zuò Gōng Tú (立秋七月節坐功圖)

1. Slowly bend your body forward, looking straight ahead with arms relaxed.

2. Bring your chin onto your chest.

3. Lift your body and lean back.

4. Turn your arms out with your palms facing back and then return to the initial movement.

Statistics

We used the test for equality of two proportions, the Anderson-Darling nonparametric test, Student's *t*-test and the Friedman test. The confidence interval was set at 95%, and *p*-values were set to *p*<0.05. The statistical software used in this analysis was SPSS V16, Minitab 15 and Excel Office 2007.

RESULTS

The mean age of participants was 48.3±4.21 years, with a mean schooling level of 13.2±1.57 years. Body mass index (BMI) averaged 23.67±1.77 (Table 1). No differences were found between male and female participants on the basis of BMI (*t*(8)=0.68, *p*=0.051), education (*t*(8)=1.94, *p*=0.08) and duration of PPS symptoms (*t*(8)=-0.20, *p*=0.84). Most participants (70%) were female. All patients (100%) presented with residual motor sequelae in the left leg, and 80% of patients showed motor paralysis in the right leg. There were significant differences between pre- and post-intervention assessments

Table 1. Demographics and study participation in ten patients.

Characteristics	Mean	Median	SD	CV (%)	CI
Age	48.3	50	6.8	14	4.21
Polio age (months)	15	11.5	10.79	72	6.69
Polio stability (year)	40.4	42.4	7.86	19	4.87
Time PPS (year)	6.7	6	3.02	45	1.87
Height (m)	1.55	1.5	0.07	5	0.04
Weight (kg)	56.2	57.6	4.49	8	2.78
Body-mass index	23.7	23.7	2.85	12	1.77
Years of schooling	13.2	15	2.53	19	1.57

SD: standard deviation; CV: variation coefficient; CI: confidence interval; PPS: postpolio syndrome (Anderson-Darling test).

Table 2. Generalized estimated equations' analysis of VAS-Cold during interventions in ten patients.

VAS	Mean	Median	SD	CI	<i>p</i> -value	
Systemic	Aval I	7.70	8.8	2.55	1.58	0.003
	Aval II	4.10	4.0	2.08	1.29	
	Aval III	3.70	4.0	2.31	1.43	
RUL	Aval I	5.85	6.0	3.07	1.91	0.019
	Aval II	2.90	3.0	1.91	1.19	
	Aval III	2.69	2.5	2.51	1.56	
LUL	Aval I	5.95	6.0	2.99	1.85	0.012
	Aval II	2.90	3.0	1.79	1.11	
	Aval III	2.64	2.5	2.58	1.60	
RL	Aval I	4.80	5.0	3.33	2.06	0.002
	Aval II	2.55	3.0	2.06	1.28	
	Aval III	2.54	2.0	2.53	1.57	
LL	Aval I	6.30	6.5	2.87	1.78	0.001
	Aval II	3.65	3.5	2.43	1.50	
	Aval III	3.23	3.3	2.64	1.64	

VAS: Visual Analog Scale; SD: standard deviation; CI: confidence interval; RUL: right upper limb; LUL: left upper limb; RL: right leg; LL: left leg (Friedman nonparametric test).

in local and systemic VAS-Cold values ($p \leq 0.019$). Significant differences persisted until the three-month post-intervention follow-up (Table 2 and Figure).

DISCUSSION

There is no defined etiology for CI complaints in patients with PPS. Studies show that the hypothalamus (the temperature regulation center) and the anterior horn of the spinal cord are also affected by poliovirus, which is one possible explanation for CI^{7,14-16}.

We found that all patients achieved statistically significant improvement in CI symptoms as a result of DQ practice compared to their previous complaints and were able to maintain these improvements. A study conducted in Brazil reported that CI, among other symptoms, is more prevalent among women (75%)⁸. In this study, our patients were predominantly female, which is consistent with other PPS studies conducted in Brazil^{4,5} as well as internationally¹⁷⁻¹⁹. In Brazil, the predominance of female patients is attributed to the fact that women seek health services more often than men (excluding one case in which gender predominance was reversed)²⁰. The average age of patients in this study was 48.3 years, that is similar to Brazilian and international studies in which an average age of 50 to 63 years was reported^{17,21,22}.

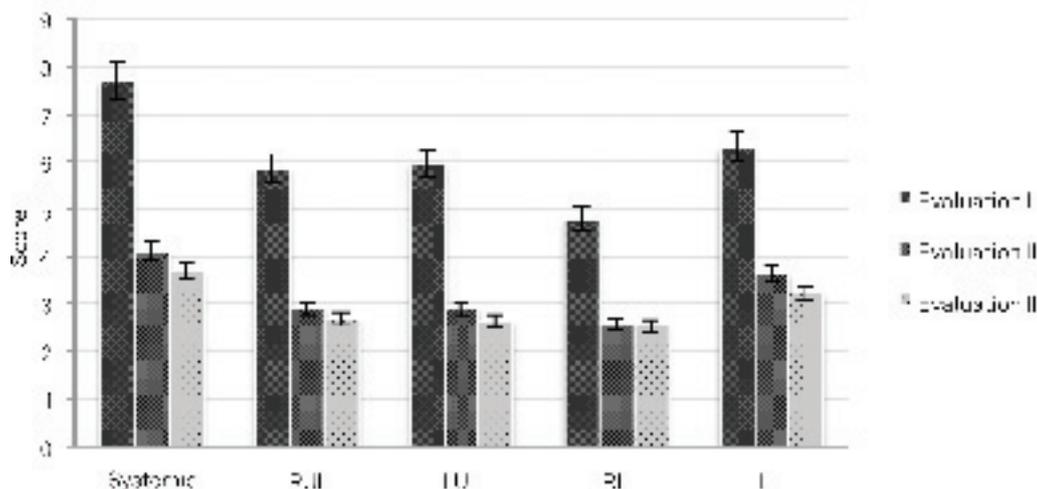
The level of patient schooling averaged 13.20 ± 1.57 years. Data from the Brazilian Institute of Geography and Statistics census (2000), regarding the general population of 25 years and older, show an average of 6.1 years of schooling. In the subset of individuals with some kind of disability, 10% experienced eight years of education²³. The body mass index of subjects averaged 23.67 ± 1.77 and did not appear to impact the assessment; this is an important fact because subcutaneous

tissue and fat compose the thermal insulation of the body and promote retention of body heat.

All processes that occur in an organism to maintain its proper functioning have certain environmental requirements, especially those relating to water and temperature. This is because the activity of proteins, enzymes, chemicals and physical reactions occur at speeds according to the temperature of the medium in which they are located. Human beings can be exposed to temperatures ranging from 13° to 65°C for several hours without any change in their internal temperature²⁴. Heat is a byproduct of all metabolic processes, including the metabolism of carbohydrates, fats and proteins. The body can increase heat production in response to low external temperatures or dissipate heat when temperatures are high. These external influences impact the body through radiation, conduction and convection. During physical activity, the metabolic rate increases and the biochemical transformations of nutrients promote muscle work (approximately 80% of body heat is produced in skeletal muscle), which together generate heat and raise body temperature²⁴.

The body loses heat through radiation, conduction, evaporation of water from the airways and skin along with excretion of feces and urine. Circulatory adjustments promote cutaneous vasodilation, which raises the temperature of the skin and favors the exchange of heat with the environment. The sympathetic vasoconstrictor nerves are the primary mediators of this response. Peripheral vasodilation is, therefore, a result of the inhibition of sympathetic tone. Heat can reduce this tone via an increase in the temperature of the central nervous system (CNS) or reflexively through the mediation of thermoreceptors in the skin²⁵.

The blood flow of an organ plays an important role in capturing and redistributing heat to cooler parts of the body. However, the ability to sense temperature and the efficiency



RUL: right upper limb; LUL: left upper limb; RL: right leg; LL: left leg.

Figure. Comparative reviews of VAS-Cold local and systemic, at the beginning and at the end, and after three months of no activity.

of thermoregulation to trigger a physiological response and resist exposure to cold declines with age, which is usually a factor in individuals with dementia or those who are sedentary²⁶⁻²⁸. Vasoconstriction and shivering, which are the primary means of maintaining body temperature during exposure to cold, are less efficient with this decline in vitality^{29,30}. In normal aging, such changes are part of the overall framework of physiological changes. However, individuals with PPS undergo these typically age-related changes precociously, experiencing such things as a substitution of lean mass for fat and hypersensitivity to cold²⁶. Several studies have demonstrated that Chinese exercises (*Qigōng* 氣功) have, as one function, a modulation of the autonomic nervous system (sympathetic)³¹⁻³⁵. Our study suggests that DQ provides an increase in internal temperature through the voluntary contraction of muscles in the pelvic cavity (during expiration) that are associated with diaphragmatic excursion (during inspiration). The literature has shown that physical activity may promote increased blood flow to skeletal muscle under conditions in which the activity significantly increases sympathetic vasoconstrictor muscle capacity. This process requires the involvement of vasodilators and sympatholytic signals capable of replacing the increased vasoconstriction with neural reflexes in the muscle³⁶⁻³⁸. The temperature generated by the triggered muscle activity may activate the release of adenosine triphosphate (ATP) within the vascular lumen of the arterial tree, providing oxygenation to the limb tissue (including skeletal muscle and skin) and an increase in intravascular ATP³⁸⁻⁴³. This phenomenon suggests that overheating the thermostatic preoptic area (POA) of the anterior hypothalamus increases the rate of heat loss from the body through two mechanisms: (1) evaporative heat loss by stimulating the sweat glands and (2) inhibition of the sympathetic centers in the posterior hypothalamus, which normally cause constriction of cutaneous vessels; this inhibition triggers vasodilatation and a consequent increase in heat loss. Because automatic physiological adjustments involve the autonomic

nervous system (ANS), there is a contribution from the connections between the hypothalamus, the parasympathetic nuclei of the brain stem and the intermediolateral sympathetic column of the spinal cord^{44,45}. Exercises that combine movement with breathing, such as yoga, cause significant increases in brain levels of gamma-aminobutyric acid (GABA) post-workout⁴⁶. One study demonstrated that the action of GABA in the mid-dorsal region of the POA causes an increase in the core temperature through stimulation of thermogenesis in brown adipose tissue⁴⁷.

Finally, the literature suggests that CNS plasticity may be induced by functional or motor tasks^{48,49}. Motor activities and neuroplasticity have been researched in humans in recent decades. Four weeks of daily training sessions for functional tasks allow activation of the primary sensorimotor cortex, ipsilateral and contralateral premotor cortices and ipsilateral cerebellum^{48,50}. This plasticity occurs not only in the cortex, but it can also be seen in subcortical regions such as the thalamus and brain stem⁵¹. These cortical neural connections can be remodeled by our experiences and by learning^{49,52-55}.

Our hypothesis is that DQ positively influences the modulation and coordinated recovery of the balance of sympathetic and parasympathetic responses, thereby enhancing the neuroplasticity of these structures.

In conclusion, DQ exercises positively influenced CI symptoms in patients with PPS. The results remained constant three months after cessation of DQ training. Additional studies will be required to understand the mechanism of action of DQ, as well as the duration of its benefits.

ACKNOWLEDGMENTS

We thank Ms. Wu Pi Chun, Eneida de Souza Bulle Oliveira, Celso Antonio de Souza Mello and Bruna Terumi Sato Yonamine for their invaluable help. This project was undertaken by voluntary researchers without funding.

References

1. Codd MPM, Mulder DW, Kurland LT, Beard CM, O'Fallon WM. Poliomyelitis in Rochester, Minnesota 1935-55: Epidemiology and long-term sequelae – a preliminary report. In: Halstead LS, Weicher DO (eds). Late effects of poliomyelitis. Miami: Miami Symposia Foundation Inc.; 1985:121-133.
2. Dalakas M, Illa I. Post-polio syndrome: concepts in clinical diagnosis, pathogenesis, and etiology. *Adv Neurol* 1991;56:495-511.
3. Dalakas MC. Post-polio syndrome 12 years later. How it all started. *Ann N Y Acad Sci* 1995;753:11-18.
4. Quadros AAJ, Oliveira ASB. Síndrome pós-poliomielite (SPP): avaliação de 167 pacientes. XXII Congresso Brasileiro de Neurologia – V Encontro Luso-Brasileiro. Recife. *Arq Neuropsiquiatr* 2006;64:75.
5. Maggi F, Marques B, Fávero FM, et al. Intolerância ao frio: uma manifestação clínica da síndrome pós-poliomielite (SPP). XXII Congresso Brasileiro de Neurologia – V Encontro Luso-Brasileiro. Recife. *Arq Neuropsiquiatr* 2006;64:73.
6. Koopman FS, Uegaki K, Gilhus NE, Beelen A, de Visser M, Nollet F. Treatment for postpolio syndrome. *Cochrane Database Syst Rev* 2011; CD007818.
7. Bodian D. The generalized vertebrate neuron. *Science* 1962;137:323-326.
8. Oliveira ASB, Maynard FM. Síndrome pós-poliomielite: aspectos neurológicos. *Rev Neurociências* 2002;10:31-34.
9. Wang Q, Yao S. Molecular basis for cold-intolerant yang-deficient constitution of traditional Chinese medicine. *Am J Chin Med* 2008;36:827-834.
10. Abe GC, Ramos PE, Fontes SV, et al. Poliomielite e síndrome pós-poliomielite pela Medicina Tradicional Chinesa: do diagnóstico aos mecanismos fisiopatológicos. *Rev Neurociências* 2011;19:365-381.
11. 吉, 布. 導引術. 西安: 陝西師範大學出版社; 2007; 193-199.
12. 魏, 成. 天下氣功. 四川: 四川人民出版社; 1995; 79-86.

13. Mulder DW. Clinical observations on acute poliomyelitis. *Ann NY Acad Sci* 1995;753:1-10.
14. Bodian D. Histopathologic basis of clinical findings in poliomyelitis. *Am J Med* 1949;6:563-578.
15. Bodian D. Letter to the Editor. *Science* 1962;135:245-248.
16. Bodian D, Bergman RA. Muscle receptor organs of crayfish: functional-anatomical correlations. *Bull Johns Hopkins Hosp* 1962;110:78-106.
17. Farbu E, Gilhus NE, Barnes MP, et al. EFNS guideline on diagnosis and management of post-polio syndrome. Report of an EFNS task force. *Eur J Neurol* 2006;13:795-801.
18. Vasconcelos OM, Poehm EH, McCarter RJ, Quezado ZM. Potential outcome factors in subacute combined degeneration: review of observational studies. *J Gen Intern Med* 2006;21:1063-1068.
19. Fordyce CB, Gagne D, Jalili F, et al. Elevated serum inflammatory markers in post-poliomyelitis syndrome. *J Neurol Sci* 2008;271:80-86.
20. Pinheiro R, Viacava F, Travassos C, Brito A. Genero, morbidade, acesso e utilização de serviços de saúde no Brasil. *Ciênc Saúde Coletiva* 2002;7:687-707.
21. Vasconcelos OM, Prokhorenko OA, Kelley KF, et al. A comparison of fatigue scales in postpoliomyelitis syndrome. *Arch Phys Med Rehabil* 2006;87:1213-1217.
22. Davidson AC, Auyeung V, Luff R, Holland M, Hodgkiss A, Weinman J. Prolonged benefit in post-polio syndrome from comprehensive rehabilitation: a pilot study. *Disabil Rehabil* 2009;31:309-317.
23. IBGE. Tabela avançada do censo demográfico 2000: resultados preliminares da amostra. Available at: <http://www.ibge.gov.br/home/presidencia/noticias/08052002tabulacao.shtm> [cited 2002 May 8].
24. Vogelaere P, Pereira C. Termorregulação e envelhecimento. *Rev Port Cardiol* 2005;24:747-761.
25. Guyton AC, Hall JE. *Fisiologia humana e mecanismos das doenças*. 6 ed. Rio de Janeiro: Guanabara Koogan; 1998:516-518.
26. Horvath SM, Radcliffe CE, Hutt BK, Spurr GB. Metabolic responses of old people to a cold environment. *J Appl Physiol* 1955;8:145-148.
27. Watts AJ. Hypothermia in the aged: a study of the role of cold-sensitivity. *Environ Res* 1972;5:119-126.
28. Sugarek NJ. Temperature lowering after iced water. Enhanced effects in the elderly. *J Am Geriatr Soc* 1986;34:526-529.
29. Wagner JA, Horvath SM, Kitagawa K, Bolduan NW. Comparisons of blood and urinary responses to cold exposures in young and older men and women. *J Gerontol* 1987;42:173-179.
30. Khan F, Spence VA, Belch JJ. Cutaneous vascular responses and thermoregulation in relation to age. *Clin Sci (Lond)* 1992;82:521-528.
31. Cheung BM, Lo JL, Fong DY, et al. Randomised controlled trial of qigong in the treatment of mild essential hypertension. *J Hum Hypertens* 2005;19:697-704.
32. Lee MS, Rim YH, Jeong DM, Kim MK, Joo MC, Shin SH. Nonlinear analysis of heart rate variability during Qi therapy (external Qigong). *Am J Chin Med* 2005;33:579-588.
33. Griffith JM, Hasley JP, Liu H, Severn DG, Conner LH, Adler LE. Qigong stress reduction in hospital staff. *J Altern Complement Med* 2008;14:939-945.
34. Johansson M, Hassmén P. Acute psychological responses to Qigong exercise of varying durations. *Am J Chin Med* 2008;36:449-458.
35. Stenlund T, Birgander LS, Lindahl B, Nilsson L, Ahlgren C. Effects of Qigong in patients with burnout: a randomized controlled trial. *J Rehabil Med* 2009;41:761-767.
36. Niimi Y, Matsukawa T, Sugiyama Y, et al. Effect of heat stress on muscle sympathetic nerve activity in humans. *J Auton Nerv Syst* 1997;63:61-67.
37. Padilla J, Garcia-Villalón AL, Fernandez N, Monge L, Gómez B, Diéguez G. Effects of hyperthermia on contraction and dilatation of rabbit femoral arteries. *J Appl Physiol* 1998;85:2205-2212.
38. Pearson J, Low DA, Stöhr E, et al. Hemodynamic responses to heat stress in the resting and exercising human leg: insight into the effect of temperature on skeletal muscle blood flow. *Am J Physiol Regul Integr Comp Physiol* 2011;300:R663-R673.
39. González-Alonso J, Mortensen SP, Jeppesen TD, et al. Haemodynamic responses to exercise, ATP infusion and thigh compression in humans: insight into the role of muscle mechanisms on cardiovascular function. *J Physiol* 2008;586:2405-2417.
40. González-Alonso J, Olsen DB, Saltin B. Erythrocyte and the regulation of human skeletal muscle blood flow and oxygen delivery: role of circulating ATP. *Circ Res* 2002;91:1046-1055.
41. Kirby BS, Voyles WF, Carlson RE, Dinunno FA. Graded sympatholytic effect of exogenous ATP on postjunctional alpha-adrenergic vasoconstriction in the human forearm: implications for vascular control in contracting muscle. *J Physiol* 2008;586:4305-4316.
42. Rosenmeier JB, Hansen J, Gonzalez-Alonso J. Circulating ATP-induced vasodilatation overrides sympathetic vasoconstrictor activity in human skeletal muscle. *J Physiol* 2004;558:351-365.
43. Rosenmeier JB, Yegutkin GG, González-Alonso J. Activation of ATP/UTP-selective receptors increases blood flow and blunts sympathetic vasoconstriction in human skeletal muscle. *J Physiol* 2008;586:4993-5002.
44. Simon E, Pierau FK, Taylor DC. Central and peripheral thermal control of effectors in homeothermic temperature regulation. *Physiol Rev* 1986;66:235-300.
45. Morrison SF. Central pathways controlling brown adipose tissue thermogenesis. *News Physiol Sci* 2004;19:67-74.
46. Streeter CC, Whitfield TH, Owen L, et al. Effects of yoga versus walking on mood, anxiety, and brain GABA levels: a randomized controlled MRS study. *J Altern Complement Med* 2010;16:1145-1152.
47. Osaka T. Cold-induced thermogenesis mediated by GABA in the preoptic area of anesthetized rats. *Am J Physiol Regul Integr Comp Physiol* 2004;287:R306-R313.
48. Borella MdP, Sacchelli T. Os efeitos da prática de atividades motoras sobre a neuroplasticidade. *Rev Neurociênc* 2009;17:161-169.
49. Fisher BE, Sullivan KJ. Activity-dependent factors affecting poststroke functional outcomes. *Top Stroke Rehabil* 2001;8:31-44.
50. Lindberg P, Schmitz C, Forssberg H, Engardt M, Borg J. Effects of passive-active movement training on upper limb motor function and cortical activation in chronic patients with stroke: a pilot study. *J Rehab Med* 2004;36:117-123.
51. Jones EG, Pons TP. Thalamic and brainstem contributions to large-scale plasticity of primate somatosensory cortex. *Science* 1998;282:1121-1125.
52. Nudo RJ. Adaptive plasticity in motor cortex: implications for rehabilitation after brain injury. *J Rehabil Med* 2003;41:57-510.
53. Adkins DL, Boychuk J, Remple MS, Kleim JA. Motor training induces experience-specific patterns of plasticity across motor cortex and spinal cord. *J Appl Physiol* 2006;101:1776-1782.
54. Kelly C, Foxe JJ, Garavan H. Patterns of normal human brain plasticity after practice and their implications for neurorehabilitation. *Arch Phys Med Rehabil* 2006;87:S20-S29.
55. Johansson BB. Brain plasticity and stroke rehabilitation. The Willis lecture. *Stroke* 2000;31:223-230.