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BRAIN RESEARCH

Research Report

Effect of electroacupuncture on motor recovery in a rat stroke model during the early recovery stage

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ABSTRACT

The effect of acupuncture on motor recovery after stroke continues to be debated. This animal study was designed to determine whether acupuncture improves motor function following experimentally induced cerebral ischemia. In addition, we studied whether the outcome of motor function was associated with the expression of BDNF (brain derived neurotrophic factor), trkB (receptor, trkB) and infarct volume. Cerebral ischemia was induced by permanent middle cerebral artery occlusion (MCAO) or MCAO plus bilateral vertebral artery occlusion in Sprague–Dawley rats. The groups studied were a control, treadmill exercise, electroacupuncture and a combined treatment group with both treadmill exercise and electroacupuncture (ExEA). On postoperative day 16, Western blot analysis for BDNF and trkB and estimation of infarct volume were performed. The motor behavior scores were measured 2 and 16-days postoperatively. Comparison of the motor scores among the groups showed that the motor scores in the exercise only group and ExEA group were higher than in the control group on postoperative day 16. No statistical significance was found among the groups in the Western blot analysis and the infarct volume. This study demonstrates no significant additional effect of electroacupuncture on the motor recovery in rats following mild cerebral ischemia during the early recovery stage. Further studies in a rat model with moderate to severe cerebral ischemia, assessment and reassessment for more extended periods after the cerebral ischemia will be required.

1. Introduction

The incidence of stroke in the US is between 500,000 and 730,000 annually and stroke results in significant morbidity, mortality and disability (EJ and RL, 2000). In addition, approximately 67% of survivors become functionally dependent (O'Mahony et al., 1999). However there is no single aid to recovery available for the rehabilitation of patients after stroke.

Acupuncture has been used for stroke recovery in East Asia for centuries. However, scientific studies on this topic have only recently started to merge with Western scientific methods. Although positive effect of acupuncture have been

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Abbreviations: BDNF, brain derived neurotrophic factor; trkB, receptor,trkB; MCAO, middle cerebral artery occlusion; ExfsEA, combined treatment with both treadmill exercise and electroacupuncture

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reported in a few early studies on stroke patients (Ernst and White, 1996; Hopwood, 1996), most of the recent studies including randomized controlled trials, meta-analyses and systematic reviews have reported that there was no significant positive effect of acupuncture on motor recovery in stroke patients (Gosman-Hedstrom et al., 1998; Park et al., 2001; Sze et al., 2002a; Sze et al., 2002b; Wu et al., 2006; Zhang et al., 2005).

A study of the effect of acupuncture on human stroke patients is complicated by the inability to control for several important confounding factors. The procedure of sham needling, which has been used in blinded studies, can exert a mechanical stimulation and excite nociceptive primary afferents (Moffet, 2006). and has been associated with neurochemical effects (Downs et al., 2005; Jeun et al., 2005). In this situation, the sham needling group is not a control group but rather an real acupuncture intervention group, which may result in parallel effects observed from the real as well as the sham acupuncture groups. This can result in the interpretation of the acupuncture intervention as ineffective in stroke patients compared with the sham intervention. In addition, the type of stroke, its severity and the interval after the stroke and before treatment is started also might significantly influence the results of acupuncture studies (Shiflett, 2007), but control of these confounding factors is difficult in human studies. Therefore, the effect of acupuncture on motor recovery has not been determined to date in well-controlled studies in stroke patients and animal studies provide useful models where important factors can be controlled. However, there have been few animal studies on the effect of acupuncture on motor recovery after cerebral ischemia. And the acupuncture literature has very limited information on the association between motor recovery and neurotrophic factors, although recent studies have reported an association between neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and its receptor, trkB (trkB) with motor recovery after cerebral ischemia (Ferrer et al., 2001; Kim et al., 2005; Miyake et al., 2002; Ploughman et al., 2005; Schabitz et al., 2004). Severity of the cerebral ischemia might also be a major confounding factor (Shiflett, 2007), but the animal studies concerning the severity of cerebral ischemia are very rare. To our knowledge, only one animal acupuncture study reported on functional recovery, using an objective measurement tool, and the association with the neurotrophic factor, Vascular endothelial growth factor (VEGF) in a rat stroke model (Wang et al., 2003). In addition, although exercise and acupuncture is commonly prescribed to stroke patients simultaneously in Far East Asia, combined effect of exercise and acupuncture on the functional recovery of stroke was controversial in the previous studies (Hu et al., 1993; Johansson et al., 2001; Wong et al., 1999).

Therefore, the purpose of the present study was to investigate the efficacy of electroacupuncture during motor recovery after cerebral ischemia. Furthermore, we hypothesized that the neurotrophic factors which are BDNF and its receptor trkB and infarct volume might be related with the motor recovery by interventions in this study (exercise or electroacupuncture or combined intervention with exercise and electroacupuncture). Finally, we tested whether a combined intervention with exercise and electroacupuncture is more beneficial than acupuncture or exercise alone, for the motor recovery of rats after cerebral ischemia.

2. Results

2.1. Motor behavior scores

All rats in this study showed mild cerebral ischemia based on Garcia's scores on postoperative day (POD) 2 in both middle cerebral artery occlusion (MCAO) and middle cerebral artery occlusion plus bilateral vertebral artery occlusion (MCBVAO) rats (Table 1). ANOVA (analysis of variance) indicated no significant differences of Garcia's scores on POD 2 between the 4 groups (control, exercise, electroacupuncture and exercise plus electroacupuncture group) in MCAO rats ($p=0.689$). And ANOVA results also showed no significant differences of Garcia's scores on POD 2 between the 4 groups in MCBVAO rats ($p=0.854$). The differences of Garcia's scores on POD 2 between MCAO and MCBVAO rats were not significant by independent t-test ($p=0.854$). Therefore we combined the Garcia's scores in MCAO and MCBVAO rats to reveal the therapeutic effects of exercise, electroacupuncture and exercise plus electroacupuncture (ExEA). The differences of Garcia's scores on POD 16 (posttreatment score) between the groups were significant after adjustment for Garcia's score on POD 2 as covariate ($p=0.004$). Post-hoc contrast test revealed that Garcia's scores on POD 16 in the exercise and ExEA group were better than control group ($p=0.001$, 0.043 respectively) but were not better in the electroacupuncture group (Fig. 1). The differences of Garcia's scores on POD 16 between exercise and ExEA group were not significant (post-hoc contrast test, $p=0.127$) (Fig. 1).

2.2. Expression profiles of BDNF and trkB in the Western blot analysis

Two bands were observed for BDNF, either as a mature (14 kDa, BDNF14) or immature (32–47.5 kDa, BDNF30) protein.

Table 1 – Garcia's scores on postoperative day 2

	MCAO	MCBVAO	Total
Con	15.17±1.03 (13–16, $n=12$)	15.50±0.58 (15–16, $n=4$)	15.25±0.93 (13–16, $n=16$)
Ex	14.87±1.30 (13–17, $n=15$)	15.63±0.52 (15–16, $n=8$)	15.13±1.14 (13–17, $n=23$)
EA	14.80±1.66 (12–17, $n=15$)	15.20±1.32 (12–16, $n=10$)	14.96±1.51 (12–17, $n=25$)
ExEA	15.27±0.70 (14–17, $n=15$)	15.38±1.19 (13–16, $n=8$)	15.30±0.88 (13–17, $n=23$)
Total	14.93±1.37 (12–17, $n=57$)	15.40±1.00 (12–16, $n=30$)	15.15±1.16 (12–17, $n=87$)

Values are mean±standard deviation of Garcia's score on postoperative day 2. Values in the bracket represent the range of score and number of rats. MCAO, middle cerebral artery occlusion; MCBVAO, MCAO plus bilateral vertebral artery occlusion; Con, control; Ex, exercise; EA, electroacupuncture; ExEA, exercise plus electroacupuncture.