ELSEVIER

Neuroscience Letters 279 (2000) 149–152

Neuroscience Letters

www.elsevier.com/locate/neulet

The difference between electroacupuncture only and electroacupuncture with manipulation on analgesia in rats

J.H. Kim[a], B.I. Min[b,*], D. Schmidt[a], H.J. Lee[c], D.S. Park[d]

[a]Department of East-West Medicine, Graduate School, Kyung Hee University, Seoul, South Korea
[b]Department of Physiology, Kyung Hee University, 1 Hoeki-Dong, Tongdaemoon-Gu, Seoul, 130-701, South Korea
[c]Department of Meridianology, College of Oriental Medicine, Kyung Hee University, Seoul, South Korea
[d]Department of Acupuncture and Moxibustion, College of Oriental Medicine, Kyung Hee University, Seoul, South Korea

Received 13 October 1999; received in revised form 3 December 1999; accepted 3 December 1999

Abstract

Plain acupuncture uses manipulation (rotation or varying the depth of insertion of the needle) to increase its effect. However, in commonly used electroacupunture (EA), variable manipulations have not been used. This study was performed to investigate the possibility of an increase in analgesic effect by adding manipulation to EA. The pain index used was the Tail–Flick latency (TFL) of the rat, which was lightly anesthetized with thiopental sodium (intraperitoneally). Four types of manipulation were used. Rotation and varying the depth of the needle (RN and VN) was employed using two different types of manipulation during each 20 min stimulation of EA. Each manipulation persisted for 1 min out of every 5 min (long - duration and long - interval: LDLI) or 12 s every 1 min (short - duration and short - interval: SDSI). EA produced an increase in TFL; peak value was 49.7 ± 12.2% of the pre - EA and occurred immediately after cessation of 20 min of EA stimulation. Performing RN or VN combined with EA also increased TFL more than just EA and a greater peak increase in TFL was observed with a SDSI - RN and SDSI - VN as compared to a LDLI - RN and LDLI - VN (77.5 ± 13.8, 79.2 ± 19.8 and 67.3 ± 14.0%, 65.6 ± 23.7% of the pre - EA, respectively). These results indicate that manipulation combined with EA produces a more potent antinociception than when only EA is applied.

Keywords: Acupuncture analgesia; Electroacupuncture; Variable manipulations and stimulation conditions; Tail–Flick test

Since ancient times, one of the most famous physical techniques for relieving pain has been acupuncture [10]. Numerous studies show that acupuncture stimulation increases experimental pain threshold in various animal species [1,6]. The acupuncture analgesic effect has been mediated by descending inhibitory system and endogenous opioid [7]. Also, it has been suggested that acupuncture control the activities of the autonomic nervous system and have a suppressive effect on stress responses [8,12,17]. Recent studies have shown that electroacupuncture (EA) has different analgesic effects according to the parameters of stimulation [16]. Traditionally, plain acupuncture uses manipulation (rotation or varying the depth of insertion of the needle) to increase its effect [18]. However, in EA, manipulation has not been used. This study was performed to investigate the possibility of an increase in analgesic effect by complementing manipulation to EA using rats.

Male Sprague–Dawley rats weighing 250–300 g were housed in cages in a temperature (20 ± 2°C) and light/dark (08:00–20:00h light, 20:00–08:00h dark) controlled room and given lab chaw and tap water ad libitum. The rats were slightly anesthetized with thiopental sodium (40 mg/kg) at a level of anesthesia in which the corneal blink and tail flick reflexes were present, but no spontaneous movements or vocalizations occurred [13,16,20]. Supplemental injections of thiopental sodium were not given after the beginning of the tail flick testing protocol. Using this method the rats were kept under a stable anesthesia during the 90 min of the testing period. The intensity of the light bulb was set so the baseline reaction time was 2 ± 0.3 s [19]. The light was turned out as soon as the rat flicked its tail and the time lapse between the onset of irradiation and the flick of the tail could be read directly from the digital display to an accuracy of 0.1 s. The latency was measured from the time of application of a heat spot (4 mm in light

* Corresponding author. Tel.: +82-2-961-0286; fax: +82-2-964-2195.
E-mail address: mbi@nms.kyunghee.ac.kr (B.I. Min)

0304-3940/00/$ - see front matter
PII: S0304-3940(99)00994-5

spot) in a marked part of the rat's tail. The experiment was performed in the daytime. Thirty minutes after anesthesia was given, five measurements in a 2-min interval were conducted in order to determine the baseline latency of the particular rat. When TFL (Tail–Flick Latency) exceeded 7 s during an experimental procedure, the light bulb was switched off to minimize tissue damage of the tail. The degree of analgesia was expressed as a percentile change in TFL and was determined as follows [5,19]

$$\text{Acquired TFL change} = \frac{\text{post.acup. TFL} - \text{control TFL}}{\text{control TFL}} \times 100\%$$

Through the slight preanesthesia, the baseline was not constant, but showed some decrease as time progressed. In order to level this effect out, the following equation was used when determining the results: Acquired TFL change (%) - TFL change (%) of simple anesthetized rat.

The Zusanli (ST36) point which is located at the anterior tibial muscle and about 10 mm below the knee joint was chosen for the manual acupuncture and also for the electro-acupuncture. This point has been used in clinical practice for tooth pain relief as well as for stomach pain relief and it has been also known to produce an analgesic effect in the tail as related to the noxious thermal Tail–Flick response [9].

For EA, train-pulses (3 Hz, 0.3-ms pulse width, 0.2–0.3 mA) were applied to the inserted needle for the period of insertion. The other needle (anode) was inserted into the anterior tibial muscle at a point 5 mm distal to the first one. Anodal and cathodal leads from a electric stimulator were connected to the two acupuncture needles. For combining manipulation with EA, manipulation was performed during the acupuncture period.

Four types of manipulation were used. Rotation or varying the depth of insertion of the needle was used during each 20 min stimulation period. In RN, the stainless acupuncture needle was inserted vertically through the skin to a depth of about 5 mm, and then rotated manually right and left three times per second. In VN, the needle was sunk and lifted three times per second within a depth of about 3–8 mm. Each manipulation persisted for 1 min in every 5 min (long-duration and long-interval: LDLI) and 12 s in every 1 min (short-duration and short-interval: SDSI).

EA produced an increase in TFL; peak increases were 49.7 ± 12.2% of the pre-acupuncture control, respectively, and occurred immediately after cessation of 20 min of acupuncture (Fig. 1). Performing manipulation combined with EA increased TFL more than EA itself by showing a greater peak increase in TFL. However there were no significant differences between the two types of manipulation used (Fig. 1). Performing both RN and VN combined with EA also increased TFL more than EA itself and a greater peak increase in TFL was observed with a SDSI-RN and SDSI-VN as compared with a LDLI-RN and LDLI-VN (77.5 ± 13.8, 79.2 ± 19.8 and 67.3 ± 14.0%, 65.6 ± 23.7% of the pre-acupuncture control, respectively) (Table 1). These results indicate that manipulation enhances effects of antinociception EA produced, where an enhancement is greater for the latter than for the former and that for both cases a SDSI-RN and SDSI-VN produces a greater enhanced antinociception than a LDLI-RN and LDLI-VN.

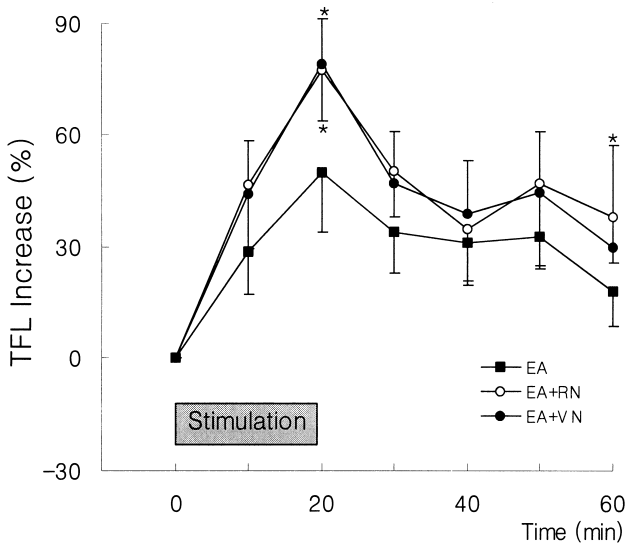

Fig. 1. EA ($n = 6$), group of electroacupuncture where train-pulses (3 Hz, 0.3-ms pulse width, 0.2–0.3 mA) were applied for 20 min into a Zusanli (ST36) acupuncture point which is located at the anterior tibial muscle about 10 mm below the knee joint; EA+RN ($n = 6$), group of EA combined with rotation methods; EA+VN ($n = 6$), group of EA combined with varying the depth of the needle methods. *$P < 0.05$ analyzed by ANOVA and Bonferroni test for comparison of EA with EA+RN or EA+VN groups. Both manipulations enhanced the analgesic effect of EA without any significant difference between rotation and varying the depth of the needle method.

The analgesic effect of EA is closely related to the parameters such as intensity, frequency, and the duration of the stimulation [16]. Low frequency with high intensity analgesia produces accumulative long lasting effects [2]. In this experiment the EA (3 Hz, 0.3-ms pulse width, 0.2–0.3 mA) group showed significant TFL increase continued for 30 min in the recovery period (Fig. 1). Higher intensity stimulation produces greater analgesic effect [16]. However there is a lot of controversy on the methods for optimal analgesia. EA combined with manipulation methods increased TFL more than EA itself by showing a greater peak and longer lasting increase in TFL (Fig. 1). Peak increase in TFL of EA with SDSI-VN (79.2 ± 19.8%) is higher than Tageshige's experiment of 60% TFL increase by EA for 60 min [19].

An additional sensory-modulation method with an alternate electrical stimulation overcame adaptation effect [14]. So it is assumed that the manipulation breaks adaptation to constant EA stimulation. It may also induce more potent inflammatory responses by its mechanical tissue injury and that the subsequent excitation of the nociceptors might last for a longer period [15]. There may also be

Table 1
Changes of increase in tail – flick latency during and after applications of electroacupunture only and electroacupunture combined with manipulation methods (values are means ± SD)

Group	No. of animal	TFL Increase (%)					
		Stimulation		Recovery			
		10	20	30	40	50	60 min
EA with manipulation							
EA only	6	28.7 ± 10.6	49.7 ± 12.2	33.9 ± 10.9	31.1 ± 5.6	32.5 ± 8.5	18.0 ± 7.3
LDLI-RN	6	32.0 ± 12.5	67.3 ± 14.0	51.3 ± 16.9	39.2 ± 15.0	39.2 ± 15.5	25.6 ± 5.6
LDLI-VN	6	32.4 ± 22.9	65.6 ± 23.7	48.6 ± 14.9	41.9 ± 19.1	40.2 ± 18.5	24.7 ± 17.9
SDSI-RN	6	46.4 ± 17.2	77.5 ± 13.8[a]	50.2 ± 2.4	34.6 ± 14.9	46.8 ± 21.9	38.1 ± 12.3[a]
SDSI-VN	6	44.2 ± 14.0	79.2 ± 19.8[a]	41.0 ± 13.7	38.9 ± 14.1	44.3 ± 16.6	29.8 ± 27.2

[a] $P < 0.05$, analyzed by ANOVA and Bonferroni test for comparison of EA with different test groups.

changes in the membrane potentials and excitations of various nociceptors such as polymodal receptors innervated by both A and C fibers [11,15]. Both manipulation techniques enhanced the analgesic effect of EA without any significant difference between rotation and varying the depth of insertion of the needle. In both cases, SDSI produces a greater enhanced analgesic effect than LDLI. All receptors can react to any manipulation. The discharge patterns of different receptors were alike when stimulated with the same manipulation, but there were different patterns when varying manipulation methods were used on the same receptor [3,4]. Different interval and duration showed different results over the same stimulation times.

It is suggested that performing manipulation with variable methods enhance the EA analgesic effect, and a SDSI RN or VN combined with EA seems to be one of the most effective ways to produce analgesia.

This study was supported by grants from the Ministry of Health and Welfare of Korea.

[1] Anderson, S.A., Ericson, T., Holmgreen, E. and Lindquist, G., Electro acupuncture effect on pain threshold measured with electrical stimulation of teeth. Brain Res., 63 (1973) 393–396.
[2] Cheng, S.S.R. and Pomeranz, B., Monoaminergic mechanism of electroacupuncture analgesia. Brain Res., 215 (1981) 77–92.
[3] Dong, Q., Dong, X., Chen, D., Li, H. and Zhang, S., The relation between acupuncture manipulations and responsive discharges of cutaneous receptors. Chen Tzu Yen Chiu, 17 (1992) 221–229.
[4] Dong, Q., Dong, X., Li, H., Chen, D. and Xian, M., The relations between acupuncture manipulations & responsive discharges of deep receptors. Chen Tzu Yen Chiu, 18 (1993) 75–82.
[5] Grossman, M.L., Basbaum, A.I. and Fields, H.L., Afferent and efferent connections of the rat tail flick reflex: A model used to analyse pain control mechanism. J. Comp. Neurol., 206 (1982) 9–16.
[6] Ha, H., Wu, R.S., Contreras, R.A. and Tan, E.C., Measurement of pain threshold by electrical stimulation of tooth pulp afferents in the monkey. Exp. Neurol., 61 (1979) 260–269.
[7] Han, J.S. and Terenius, L., Neurochemical basis of acupuncture analgesia. Annu. Rev. Pharmacol. Toxicol., 22 (1982) 193–220.
[8] Han, S.H., Yoon, S.H., Cho, Y.W., Kim, C.J. and Min, B.I., Inhibitory effect of electroacupuncture on stress responses evoked by tooth-pulp stimulation in rats. Physiol. Behav., 66 (1999) 217–222.
[9] Hand, P.J., Sheu, S.C. and Ha, H., Autoradiographic deoxyglucose study of some central effects of acupuncture: a compilation of the First International Symposium on Acupuncture and Moxibustion, Taipei, Taiwan, R.O.C., 1983, pp. 30–45.
[10] Hsu, D.T., Acupuncture: a review. Reg. Anesth., 21 (1996) 361–370.
[11] Kawakita, K., Polymodal receptor hypothesis on the peripheral mechanisms of acupuncture and moxibustion. Am. J. Acupunct., 21 (1993) 331–338.
[12] Kimura, A. and Sato, A., Somatic regulation of autonomic functions in anesthetized animals-neural mechanisms of physical therapy including acupuncture. Jpn. J. Vet. Res., 45 (1997) 137–145.
[13] McCarthy, M.M., Beyer, C. and Komisaruk, R.R., Barbiturate induced analgesia: permissive role of a GABAa agonist. Pharmacol. Biochem. Behav., 32 (1989) 897–900.
[14] Melzack, R., Jeans, M.E., Stratford, J.G. and Monks, R.C., Ice massage and transcutaneous electrical stimulation: comparison of treatment for low-back pain. Pain, 9 (1980) 209–217.
[15] Okada, K., Oshima, M. and Kawakita, K., Examination of the afferent fiber responsible for the suppression of jaw-opening reflex in heat, cold, and manual acupuncture stimulation in rats. Brain Res., 740 (1996) 201–207.
[16] Romita, V.V., Suk, A. and Henry, J.L., Parametric study on electroacupuncture like stimulation in a rat model: effects of intensity, frequency, and duration of stimulation on evoked antinociception. Brain Res Bull., 42 (1997) 289–296.
[17] Sato, A. and Sato, Y., Reflex modulation of catecholamine secretion and adrenal sympathetic nerve activity by acupuncture-like stimulation in anesthetized rat. Jpn. J. Physiol., 46 (1996) 411–421.
[18] Takakura, N., Ogawa, H., Iijima, S., Nishimura, K., Kanamaru, A., Sibuya, M. and Homma, I., Effect of acupuncture at the Hoku point on vibration-induced finger flexion reflex in man: comparison between press needle technique, electroacupuncture, and in-situ technique. Am. J. Chin. Med., 23 (1995) 313–318.

[19] Takeshige, C., Differentiation between acupuncture and non-acupuncture points by association with analgesia inhibitory system. Acupunct. Electro-Therap. Res., 10 (1985) 195–203.

[20] Wang, Q., Mao, L. and Han, J.S., Characterization of inhibition of spinal nociceptive reflex by stimulation of the arcuate nucleus of the hypothalamus in the pentobarbital-anesthetized rat. Pain, 41 (1990) 101–108.