# Effects of Acupuncture on Serum Cortisol Level and Dopamine Beta-hydroxylase Activity in Normal Chinese

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Abstract: Serum cortisol levels were determined in 40 normal Chinese and dopamine beta-hydroxylase activities were measured in 22 normal subjects before and after acupuncture treatment. All subjects were studied twice with an interval of one week or more. In the self-control study, the subjects were needled at 5 non-acupuncture loci. In the experimental study, they were needled at the following 5 traditional acupuncture loci — right side GB-20, both sides EH-6, and both sides St-36. Blood samples were withdrawn before acupuncture and 15 and 45 min. after acupuncture. No change of serum dopamine beta-hydroxylase activity was observed. Serum cortisol levels increased significantly after needling on the traditional acupuncture loci. After acupuncture for 15 and 45 min., the cortisol increase was 28 and 50%, respectively, as compared to the self-control studies. The beneficial effect of acupuncture in the treatment of functional disorders, therefore, may be mediated by cortisol or other hormones and neurohormones.

IN ADDITION TO ITS ANALGESIC EFFECT, acupuncture has many regulatory effects. In the latter aspect, acupuncture has been clinically used to treat rhinorrhea, nasal obstruction, allergic rhinitis, bronchial asthma, epigastric distress, diarrhea, constipation, drug abstinence symptoms and menopausal syndrome. Most of these disorders are due to hyperactivity or hypoactivity of the autonomic nervous system. On the other hand, some of the disorders, such as allergic rhinitis and bronchial asthma, can be controlled by the administration of steroid hormones. Results of some animal and clinical studies suggest the involvement of the autonomic nervous system and the endocrinological system in the action of acupuncture (1-6).

Blood dopamine beta-hydroxylase (EC 1.14.17.1) is released from the sympathetic ganglion, and its activity reflects the sympathetic activity (7). Blood cortisol is the major steroid hormone secreted by the adrenal gland in man (8). In this paper, we present 40 normal male volunteers who participated in an acupuncture study. Before

ACUPUNCTURE ON SERUM CORTISOL LEVEL AND DOPAMINE BETA-HYDROXYLASE and after acupuncture treatment their blood samples were consecutively withdrawn for direct determination of serum dopamine beta-hydroxylase activity and serum cortisol concentration in order to enlighten the mechanism of action of acupuncture.

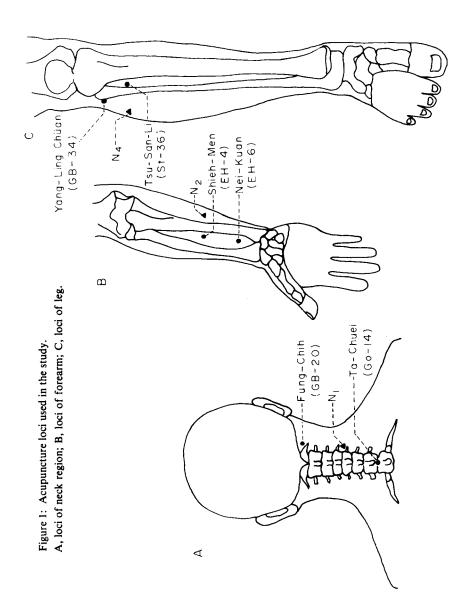
#### Methods

Acupuncture Loci. Two groups of loci were used for needling in this study, 5 traditional acupuncture loci and 5 equivalent non-acupuncture loci (Figure 1). The 5 traditional acupuncture loci were: right side Fung-Ch'ih (GB-20); both sides Nei-Kuan (EH-6); and both sides Tsu-San-Li (St-36). The 5 non-acupuncture loci which served as control points for the above mentioned acupuncture loci were: N<sub>1</sub>, the mid-point between the right side Fung-Ch'ih and Ta-Chuei (Go-14); N<sub>2</sub>, the place about 1.5 cm internal to right Chieh-Men (EH-4); N<sub>3</sub>, an equivalent point to N<sub>2</sub> on the left arm; N<sub>4</sub>, the site 2 cm inferior and external to right Yang-Ling Chüan (GB-34); and N<sub>5</sub>, and equivalent point to N<sub>4</sub> on the left leg.

Acupuncture Treatment. Our subjects were 45 normal male volunteer medical students 20-25 years of age, and 6 male medical staff 32-43 years of age. However, only 40 subjects completed the whole course of study. All subjects were studied twice with an interval of one week or more. In the self-control study, the subjects were needled at the non-acupuncture loci. In the experimental study, they were needled at the 5 traditional acupuncture loci just described. The self-control and experimental studies were distributed randomly. We usually investigated two subjects in a day, one for the self-control study and another for the experimental study. There were 11 subjects who finished only one study. Therefore, finally we had 40 subjects who completed the study program.

On the day of investigation, the subject came to the study room at 10:30 AM and rested for about 30 minutes. Needling was started at 11:00 AM. The needles were twirled for 3 seconds at intervals of 5 minutes with a frequency of 2 twirls per second, and they were removed 45 minutes after treatment. Venous blood samples, 7 ml, were taken just before acupuncture, and 15 and 45 minutes after acupuncture. The subject sat in a chair during the course of study. Whenever he felt faint, he was immediately assisted and was laid in a supine position. The study, however, went on without interruption.

Laboratory Measurement. Blood samples were left to coagulate for 60-90 minutes at room temperature, and sera were separated by centrifugation at 3,000 rpm for 15 minutes. The serum samples were then stored at -25°C for cortisol and dopamine beta-hydroxylase assay within 24 hours. Dopamine hydroxylase activity was determined by the method of Nagatsu and Udenfriend (9). The concentration of serum cortisol was measured fluorometrically according to Mattingly modified by Koch et al. (10). In our preliminary assays, serum cortisol concentrations were similarly either determined by the radioimmunoassay or by the flourometric method. We used the fluorometric method for convenience in our laboratory. Statistical analysis was performed using the student's t-test.



## Results

**Dopamine Beta-hydroxylase.** Serum dopamine beta-hydroxylase activity showed no significant change before and after acupuncture treatment (Table 1).

Serum Cortisol. The mean serum cortisol level of the normal Chinese determined in the late morning (11 AM) was 11.6  $\mu$ g/100 ml. It is interesting to note that the 64

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TABLE I.
Serum dopamine beta-hydroxylase activity in the course of acupuncture study.

Time after acupuncture (min)		0	15	45
DBH activity <sup>a</sup> : (IU/Liter)	Self-control Experimental		28.5 <u>+</u> 13.7 30.7 <u>+</u> 14.7	

aValues represent the mean + S.D. of 22 subjects.

TABLE II.
Serum cortisol concentrations after acupuncture in normal Chinese.

Time after acupuncture (min)		0	15	45
I. Subjects withou	ut fainting:			
Cortisol <sup>a</sup> : (ug/100ml)	Self-control (34) Experimental (34)		13.4 <u>+</u> 4.2 17.1 <u>+</u> 5.3 <sup>b</sup>	
Increase (%) <sup>C</sup>			28	50
II. Subjects with t	fainting:		28	50
	fainting: Self-control (6) Experimental (6)		13.9 <u>+</u> 3.1 23.6 <u>+</u> 7.8 <sup>b</sup>	13.5 <u>+</u> 3.8

<sup>&</sup>lt;sup>a</sup>Values represent the mean <u>+</u> S.D. The numbers in parenthesis indicate the number of subjects studied in each group.

bp<0.001, as compared to each self-control study.

<sup>&</sup>lt;sup>C</sup>The increase expressed as % represents the percent increase of cortisol of the experimental study in comparison with the self-control one.

basal level of the serum cortisol for an individual showed no remarkable change when it was determined at the same time period of a day. This was observed in the cortisol determinations for the self-control and the experimental studies of an individual with an interval of one week or more (Table 2 and Figure 2).

Cortisol Response. The level of cortisol increased significantly after needling on the traditional acupuncture loci (Table 2). After acupuncture for 15 and 45 minutes, the increase was 28 and 50%, respectively, as compared to the self-control study.

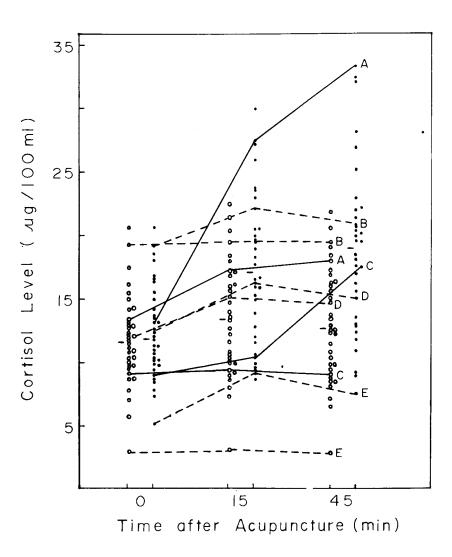


Figure 2: Serum cortisol response after acupuncture. Self-control values, Experimental values, — The mean of each column of data, A B C D E denote 5 representative subjects.

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The increase was much greater in subjects with fainting during the course of study, and the increase was 70 and 118%, respectively, 15 and 45 minutes after acupuncture. Although there was slight elevation of the serum cortisol level during the course of the self-control study, the increase was insignificant, and the 45 minute cortisol level was slightly reduced as compared to the 15 minute level.

Although the increase of serum cortisol occurred mainly in the first 15 minutes of acupuncture, the response was variable. As shown in figure 2, the cortisol level of subjects A & C continued to rise 15 minutes after acupuncture, but started to reduce in subjects B, D & E. The extent of response was also variable. The 15 minute cortisol level increased 108% in subject A, and only 8% in subject D, as compared to the cortisol concentration before acupuncture (Figure 2).

#### Discussion

The basal serum cortisol level of our volunteers in the late morning was  $11.6 \pm 3.8$   $\mu g/100$  ml (Table 2). This value is close to  $11.8 \pm 3.7$   $\mu g/100$  ml as reported by Lee et al. (11) using competitive protein binding assay. Needling of the traditional acupuncture loci caused a significant increase in serum cortisol concentration. The cortisol response was even greater in subjects with fainting during the course of acupuncture study (Table 2). To some extent, acupuncture effect, therefore, is similar to stress effect. Liao et al. (3, 4) reported that adrenocortical hormone production was increased as a result of electroacupuncture stimulation of the Tsu-San-Li locus in rabbits. Carasso et al. (12) reported that plasm ACTH level was slightly increased at 10 minutes after initiation of acupuncture needling on 3 normal subjects and 7 patients, but was unable to demonstrate any effect on cortisol level. As explained by the authors, this might be due to insufficient acupuncture stimulation in their research design.

In this study, the incidence of acupuncture induced fainting was high, 15% (Table 2). All the faintings were observed only in the experimental studies and occurred mostly 10-15 minutes after acupuncture treatment. This is probably related to the simultaneous utilization of 5 strong (in the sense of needle sensation) traditional acupuncture loci at a time and the inexperience in acupuncture of our volunteer subjects.

As compared to the 15 minute cortisol level, the slight reduction of the 45 minute level observed in the self-control studies (Table 2) and in some experimental studies (Figure 2) is concordant with normal diurnal variation to be expected during morning hours.

Alterations of serum dopamine beta-hydroxylase activity were not detected in this study. Probably, the alteration occurred in the first 15 minutes after initiation of acupuncture which we did not examine, and the detection method with a wide coefficient of variation of 46-49% in this study seemed unable to determine a small change of the enzyme activity during the course of acupuncture treatment.

Cortisol has anti-allergic, anti-inflammatory and metabolic regulatory effects (8). In this study, we showed that acupuncture treatment increased the blood cortisol level. This may account for the beneficial effect of acupuncture in the treatment of

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mild inflammatory and functional disorders. Synthesis and secretion of cortisol are controlled by the hypothalamus and the pituitary gland. There are studies to suggest acupuncture has an effect on the central control system though no definite conclusion has been obtained yet (2, 5, 13, 14).

Lin et al demonstrated that acupuncture stimulation of Ta-chuei (Go-14) or Chu-Chih (LI-11) produced a fall in oral temperature, while acupuncture of either the Nei-Kuan or Tsu-San-Li locus produced a slight decrease in oral temperature (15,16). Thus, it is possible that each acupuncture locus may have its own specific effect or action. In this study, we used a combination of 5 acupuncture loci in order to induce a maximal response. However, further studies are needed to delineate a possible specific action of each acupuncture locus with respect to the control of cortisol level or the control of other biochemicals and to examine possible interactions of each acupuncture locus.

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### References

- 1. Chen, G. Neurohumors in acupuncture. Am. J. Chinese Med., 3:27-34, 1975.
- Kawakami, M., Seto, K., Terasawa, E., Yoshida, K., Miyamoto, T., Sekiguchi, M. and Hattori, Y.
   Influence of electrical stimulation and lesion in limbic structure upon biosynthesis of adrenocorticoid in the rabbit. Neuroendocrinology, 3:337-348, 1968.
- Liao, Y.Y., Seto, K., Saito, H., Fujita, M. and Kawakami, M. Effect of acupuncture on adrenocortical hormone production: I. Variation in the ability for adrenocortical hormone production in relation to the duration of acupuncture stimulation. Am. J. Chinese Med., 7:62-371, 1070
- Liao, Y.Y., Seto, K., Saito, H., Fujita, M. and Kawakami, M. Effects of acupuncture on adrenocortical hormone production. (II) Effect of acupuncture on the response of adrenocortical hormone production to stress. Am. J. Chinese Med., 8:160-166, 1980.
- Liao, Y.Y., Seto, K., Saito, H. and Kawakami, M. Effect of acupuncture on adrenocortical hormone production in rabbits with a central lesion. Am. J. Chinese Med., 9:61-73, 1981.
- Lee, S.H., Yin, S.J., Hsu, M.S. and Sim, C.B. Preliminary observation of humoral response in man by acupuncture treatment. *Chinese Med. J.*, 24:127-131, 1977.
- 7. Axelrod, J. and Weinshilbaum, R. Catecholamines. N. Engl. J. Med., 287:237-245, 1972.
- 8. Mulrow, P.J. The adrenal cortex. Ann. Rev. Physiol., 34:409, 1972.
- Nagatsu, T. and Udenfriend, S. Photometric assay of dopamine beta-hydroxylase activity in human blood. Clin. Chem., 18:980-984, 1972.
- Koch, T.R., Edwards, L. and Chilcote, M.E. Nonspecific interferences in the fluorometric determination of plasma cortisol. Clin. Chem., 19:258, 1973.
- Lee, Y.S., Hsu, C.J. and Chen, F.W. Plasma cortisol in normal subjects and patients with various diseases. J. Formosan Med. Assoc., 76:311-319, 1977.
- Carasso, R.L., Fishman, Y., Vakil, E., Kisch, E.S. and Pelled, O. Endocrinological effects of acupuncture — A preliminary report. Acupuncture Research Quarterly (Taipei), 5:123-128, 1981.
- 13. Lee Peng, L.H., Yang, M.M.P., Kok, S.H. and Woo, Y.K. Endorphin release: a possible mechanism of acupuncture analgesia. *Comp. Med. East and West*, 6:57-60, 1978.
- 14. Malizia, E., Audreucci, G., Paolucci, D., Crescenzi, F. and Fraioli, F. Electroacupuncture and

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peripheral beta-endorphin and ACTH levels. Lancet, 2(8141):535-536, 1979.

- Lin, M.T., Liu, G.G., Soong, J.J., Chen, Y.F. and Wu, K.M. Effects of stimulation of acupuncture loci Ta-Chuei (GU-14), Nei-Kuan (HC-6) and Tsu-San-Li (S-36) on thermoegulatory function of normal adults. Am. J. Chinese Med., 7:324-332, 1979.
- Lin, M.T., Chandra, A., Chen-Yen, S.M. and Chen, Y.F. Needle stimulation of acupuncture loci Chu-Chih (LI-11) and Ho-Ku (LI-4) induces hypothermia effects and analgesia in normal adults. Am. J. Chinese Med., 9:74-83, 1981.