

Endocrinological Effects of Acupuncture — A Preliminary Report

R.L. Carasso, Y. Fishman, E. Vakil, E.S. Kisch and O. Pelled

On theoretical grounds, it is to be expected that acupuncture will induce changes in hormonal function.

In ten patients subjected to acupuncture for thirty minutes, heart rate and blood pressure were monitored and blood levels of ACTH, cortisol, TSH, GH, prolactin, plasma renin activity and urinary samples of VMA were determined before, during and after the completion of acupuncture.

Except for minor changes in systolic blood pressure, no significant changes were encountered in any of the variables tested.

INTRODUCTION

One of the current theories to explain the mechanism of action of acupuncture invokes the mediation by opioids, like enkephalins. These substances have a morphine-like action on opiate sensitive brain centers, and might play a role in the anaesthetic effects of acupuncture. Their action, as that of acupuncture, is antagonized by the narcotic antagonist naloxone (2). Like morphine, opiod substances are known to affect several endocrine hormones.

The pituitary gland was implicated as playing a role in the chain of events initiated by

acupuncture, and hypophysectomy in mice was reported to abolish those effects (4).

Moreover, the precursor molecule of the enkephalins is β -lipotrophin; both this substance and ACTH, are derived from a larger common precursor molecule also found in the pituitary gland. Secretion of β -lipotrophin and ACTH occur in parallel following stress (1). Another theory holds that acupuncture acts by a general stress effect.

For all these reasons we expected to encounter endocrinological effects of acupuncture in man. We examined hormones

* Departments of Neurology and Endocrinology, Ichilov Hospital, Municipal Governmental Medical Center, Tel-Aviv, Israel, The Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel, and the Department of Psychology, Bar-Ilan University, Ramat-Gan, Israel.

* Correspondence, proofs and requests for reprints to: Dr. R.L. Carasso, Dept. of Neurology, Ichilov Hospital, Tel-Aviv, Israel

such as ACTH, cortisol, prolactin, GH, as well as several other hormones known to react to morphine-like substances.

PATIENTS AND METHODS

Three volunteers and seven patients attending the acupuncture clinic for the first time, were informed of the procedures and their consent was obtained. At 09.00 a.m., half an hour before the start of acupuncture, after voiding urine, the subjects were requested to lie down, and remain supine all through the procedure. A butterfly needle was inserted in an antecubital vein; patency was assured with a dilute heparin solution. Heart rate and blood pressure were monitored at specified times, and blood samples were taken to be processed according to the protocol given in Table 1.

Acupuncture needles were placed at Ni-Kuan and Ho-Ku points, and in some cases also at another specific needling point. Exactness of needle placement was determined with a Multi-Purpose-Therapy Apparatus Type 71-3 made in the People's Republic of China.

Needles at Ho-Ku points were electrically stimulated with the same apparatus at 40 Hz. At no time was this stimulation experienced as painful.

The experimental group consisted of 10 persons (6 males and 4 females) whose average age was 34 years (range 25-46).

Heart Rate (HR) and Blood Pressure (BP)

Full data for HR were available for six subjects:

Time (min.)		-20	0	10	30	45	60
	mean	82.5	79.5	76.3	79.8	83.8	79.0
HR (beats/min.)	SD	8.7	8.6	8.7	13.3	8.4	12.5

The changes in heart rate at 10 min. and at 45 min. were not significant.

Hormonal assays were performed for cortisol, ACTH, prolactin, GH, PRA, and TSH assays were also performed using the customary radioimmunoassay methods, with commercial kits. VMA in urine was determined by a spectrophotometric method (3).

Six normal subjects, not subjected to acupuncture, served as a control group. We followed a protocol on these, similar to, but more restrictive than in the acupuncture group.

Statistical analysis was performed using non-parametric tests: the Wilcoxon test for two related samples, and the Friedman two-way-analysis of variance for more than two related samples. These tests are suitable for small groups with abnormal distribution of results.

RESULTS

As the aim of this report was not specifically directed towards achievement of analgesia, no attempt was made to assess its level in each individual subject. The results obtained with one patient in the acupuncture group who was in an evident state of stress during the preparations and the needling procedure itself, have not been included in this report. The ACTH results of one volunteer who had very high ACTH values in all samples, have been omitted, since the volunteer was in no apparent stress, and since his cortisol levels were normal throughout, his other data have been retained.

Endocrinological Effects of Acupuncture - A Preliminary Report

Blood pressure data were available in eight subjects:

Time (min.)		- 20	0	10	30	45	60
	mean	116.9	118.1	111.9	109.4	113.1	116.3
Systolic BP (mmHg)	SD	9.9	8.8	9.9	9.4	10.3	8.3

The decreases in systolic blood pressure at 10 and 30 min. were statistically significant ($p = 0.01$; $p < 0.05$).

Time (min)		- 20	0	10	30	45	60
	mean	76.9	78.1	80.6	78.8	76.3	74.4
Diastolic BP (mmHg)	SD	5.9	7.5	8.6	8.7	7.4	7.4

None of the changes in diastolic BP were statistically significant.

ACTH

Full data on nine subjects were available:

Time (min.)		- 20	0	10	20	30	45	60
	mean	33.2	31.9	40.8	31.2	34.6	35.1	30.9
acup. (n=9)	SD	12.5	8.9	17.6	7.6	19.5	14.3	12.2
ACTH (nanograms/ml)	mean	32.6	30.5	34.3	29.7	30.0	31.6	32.4
contr. (n=5)	SD	6.4	6.3	6.2	4.2	8.3	9.4	7.5

Although the rise of ACTH in the acupuncture group at 10 min. was suggestive of increased activity, this was derived from the values of only three patients who peaked at that time. None of the fluctuations in ACTH levels were significant according to the Friedman test.

Plasma cortisol

The experimental data on nine acupuncture subjects were used:

Time (min.)		- 20	0	10	20	30	45	60
	mean	9.0	8.7	8.2	8.0	6.5	5.9	5.4
acup. (n=9)	SD	3.6	5.0	4.9	4.3	3.5	2.4	2.7
Cortisol (g/dl)	mean	16.0	13.4	12.5	12.0	10.5	9.7	7.5
contr. (n=6)	SD	3.5	3.8	5.7	7.1	5.3	5.7	4.0

The decrease in cortisol levels in the acupuncture group was statistically significant ($p < 0.01$).

However, such a decrease is concordant with normal diurnal variation to be expected during morning hours. The control group exhibited a similar fall in cortisol values. Acupuncture did not therefore, affect the physiological pattern of cortisol levels.

Prolactin

This hormone decreased from $8.6 \text{ ng/ml} \pm 6.3 \text{ SD}$ at zero time to $6.4 \pm 4.8 \text{ SD}$ ($n=8$) at the completion of acupuncture. This decrease, although of statistical significance ($p=0.02$), corresponds to the physiological fall of prolactin levels during morning hours. Acupuncture did not interfere with this normal pattern.

GII

Eleven out of sixteen assays ($n=8$) were below the lower limit of detection of the method, making any interpretation of data impossible.

TSH

In five out of eight subjects studied there was no change in TSH determined at -20 minutes and $+30$ minutes. This number of subjects is too small for relevant statistical evaluation.

Plasma Renin Activity (PRA)

PRA was determined at zero and $+30$ minutes in six subjects. A decrease in PRA from $1.02 \text{ ng Angiotensin I/ml/hr} \pm 0.6 \text{ (SD)}$ to 0.73 ± 0.5 was found. This is in accordance with normal diurnal fall during morning hours.

VMA

VMA was quantitatively measured in the urine at -30 and $+60$ minutes in eight patients. VMA rose from a mean of $3.9 \text{ mg/L} \pm 1.1$

(SD) to 4.2 ± 1.5 . This rise was statistically non-significant. Hemoglobin, erythrocytes, hematocrit, leucocytes and differential white counts were determined 3 times at zero, $+30$ and $+60$ minutes. No significant changes were observed.

DISCUSSION

If acupuncture were to realize its effects through a simple stress mechanism, or via opiod mediators (2) who in turn affect several different hormone systems (6,7,8), then in either case, a response of the typical stress hormones, cortisol, ACTH, GII and prolactin was to be expected. This expectation pertains even more specifically to ACTH, as a close relationship has been reported for β -endorphin and ACTH, both originating from a common precursor substance, and both being secreted concomitantly by the pituitary gland (1). Since, at the time of the study, we unfortunately, were not able to measure the endorphins directly, we had to content ourselves with the determination of ACTH levels.

The apparent peak in ACTH which we noticed in a few subjects at 10 min, after inflation of acupuncture needling was of no statistical significance, but still was of considerable interest. These ACTH peaks give rise to several speculations. They might be stress induced, but the cortisol slope in the acupuncture group was similar to that of the control group, making a simple stress effect an unlikely explanation.

Another possibility is that the initial rise of ACTH was cut short by the concomitant secretion of opiod substances by the pituitary

from the same precursor substance. Opioids are known to inhibit ACTH release (7). Yet another explanation is that following acupuncture the pituitary precursor substance common to ACTH and β -endorphin undergoes differential cleavage, and β -endorphin is liberated while ACTH remains inactive, attached to remnants of the larger precursor substance. This might account for the clinical analgesic effect without a major increase in ACTH. On the same theoretical grounds, an increase in prolactin levels during acupuncture was anticipated in our series. However, we observed a decrease in prolactin as may be expected from its normal fall during morning hours. It might be argued that the stimulus applied in our subjects may have been insufficient to achieve measurable changes, as some authors (2) suggest that acupuncture needling has to be painful in order to achieve maximal results.

Isolated increase in VMA after acupuncture

described by Riederer et al (5) could not be confirmed by us. None of the other hormones or physical variables tested in this preliminary study gave results that encourage further experimentation with present techniques. We, therefore, saw no point in extending the work to include a sham-acupuncture group, or a naloxone-acupuncture group, although a larger number of subjects might bring out small differences that we failed to elicit in this study. Further experimental work in this area must include direct measurements of opioid mediator substances. This is presently being carried out.

ACKNOWLEDGEMENT

Our special thanks are due to the Hematology, Chemistry, Endocrinology and Radioimmunoassay laboratories of the Ichilov Hospital for performing the various tests reported here.

REFERENCES

1. β -endorphin and Adrenocorticotropin are Secreted Concomitantly by the Pituitary Gland. Guillemin, R., Vargo, Th., Rossier, J., Minick, S., Ling, N., Rivier, C., Vale, W. and Bloom, F. Science, 197, 1367-1369, 1977.
2. Antagonism of Acupuncture Analgesia in Man by the Narcotic Antagonist Naloxone. Mayer, D.J., Price, D.D. and Rafii, A. Brain Res., 121, 368-372, 1977.
3. Determination of 3-methoxy-4-hydroxymandelic Acid in Urine. Pisscho, J.J., Crout, J.R. and Abraham, D. Clin. Chim. Acta, 7, 285-291, 1962.
4. Acupuncture Reduces Electrophysiological and Behavioral Responses to Noxious Stimuli: Pituitary is Implicated. Pomerantz, B., Cheng, R. and Law, P. Experimental Neurology, 54, 172-178, 1977.
5. Manipulation of Neurotransmitters by Acupuncture. Riederer, P., Tenk, H., Werner, M., Bischko, J., Rett, A. and Krisper, M. Neural Transmission 37, 81-94, 1975.
6. Rivier, V., Vale, W., Ling, N., Brown, M. and Guillemin, R. Stimulation *in vivo* of the Secretion of Prolactin and Growth Hormone by β -endorphin. Endocrinology 100, 238-243, 1977.
7. Hormonal and Metabolic Responses to an Enkephalin Analogue in Normal Man. Stubbs, W.A., Delisala, G., Jones, A., Jeffcoate, W.J., Edwards, C.R.W., Ratter, S.J. and Besser, G.M. Lancet II, 1225-1227, 1978.

R.L. Carasso ET. AL.

8. Effect of the Synthetic Enkephalin Analogue FK 33-824 in Man. Von Graffenried, B., Del Pozo, E., Roubicek, E., Poldinger, W., Burmester, P. and Kerp, L. Nature 272: 729-730, 1978. (14)

In Memorium

Professor Chun Chung Wu, M.D., an associate editor of the Acupuncture Research Quarterly and professor of Internal Medicine at the National Taiwan University, died of hepatoma on September 22nd, 1981. He was 57.

Known as a "loner" for his stubborn dedication to Chinese acupuncture in the face of a completely western medical orientation at the National Taiwan University Hospital, Dr. Wu first became interested in the art nine years ago after a conference in West Germany. At the conference he realized that while the rest of the world was becoming more and more interested in acupuncture, the Chinese themselves were gradually losing a precious part of their own heritage through mere lack of attention. He spent the rest of his life in an attempt to correct this, and much of the recent wave of domestic interest in acupuncture is due to his efforts.

His death is a great loss and sorrow to us, and the entire acupuncture world is grieved at the news. Dr. Wu is survived by 2 sons and a daughter. (15)