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Increased Cerebrospinal Fluid Levels of Endorphins after Electro-Acupuncture

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In modern Chinese acupuncture, low frequency electrical stimulation of the inserted needles is often used instead of the classical method of manual twirling (Kaada *et al.* 1974, Bonica 1974). As confirmed in Western investigations (Andersson *et al.* 1973, Chapman *et al.* 1975) the pain threshold of healthy volunteers is increased with the procedure. Moreover, electro-acupuncture performed via surface electrodes has been found to be more effective than that via needles (Andersson *et al.* 1973), probably because the amount of current passed can be larger and the seemingly necessary muscle twitches in adjacent regions therefore are stronger (Andersson *et al.* 1976 b). Despite these results, attempts to use acupuncture for the long term relief of chronic pain have been largely unsuccessful (Andersson *et al.* 1976 a, Gaw *et al.* 1975). However, by modifying the stimulation technique to reinforce muscle contractions, electro-acupuncture via surface electrodes can give satisfactory relief of chronic pain (Eriksson and Sjölund 1976).

The mechanism behind acupuncture analgesia remains unclear. However, naloxone, a specific opiate antagonist (Martin 1967), counteracts the increase in pain threshold in healthy individuals found after classical needle acupuncture (Mayer *et al.* 1975) as well as the analgesia from electro-acupuncture in patients with chronic pain (Sjölund and Eriksson 1976). A similar effect has recently been reported with mice receiving electro-acupuncture (Pomeranz and Chiu 1976). These results suggest the activation of an inhibitory mechanism releasing endogenous morphinelike substances (endorphins; Hughes *et al.* 1975, Terenius and Wahlström 1975 a). Since it is now possible to determine the concentrations of several endorphins in human cerebrospinal fluid (CSF; Terenius and Wahlström 1975 b), we have investigated whether electro-acupuncture via surface electrodes (Eriksson and Sjölund 1976) changes the endorphin content of the CSF during the period of analgesia experienced by the patients.

Nine patients (Table I) suffering from chronic pain volunteered for the study. They underwent lumbar puncture twice, once while experiencing pain and without any analgesic measures during the previous 12–18 h, and once after electro-acupuncture via surface electrodes (Eriksson and Sjölund 1976) for 45 min. Within 30 min after stimulation the CSF was collected. The CSF (10 ml/test) was drawn into cooled tubes, frozen within 30 min and stored at −20°C for later analysis. Prior to this the CSF was thawed and centrifuged at 1 000 *g* for 10 min. The endorphin analysis was performed essentially as described earlier (Terenius

TABLE I. Endorphin content of lumbar CSF while experiencing pain (Control) and after electro-acupuncture (Stimul.).

Patient no.	Age (yrs)	Pain cause	Duration	Analgesia from stimulation	Endorphin content of lumbar CSF			
					Fraction I		Fraction II	
					Control	Stimul.	Control	Stimul.
1	65	Posttraumatic neuralgia thigh	4 yrs	Full	<0.4[a]	0.8	2.4	2.2
2	59	Mononeuritis of saphenous nerve	1 month	Full	0.5	1.3	2.9	0.9
3	49	Herniated disc L4–L5	5 yrs	Partial	0.9	2.0	0.9	2.4
4	48	Operated spinal AV malformation (L5 pain)	21 yrs	Full	<0.4	2.6	0.6	5.2
5	84	Herpes zoster Th 5	8 yrs	Full	<0.4	<0.4	0.6	1.2
6	78	Trigeminal neuralgia	16 yrs	Partial	<0.4	<0.4	4.9	0.6
7	75	Trigeminal neuralgia	7 yrs	None	<0.4	<0.4	3.8	3.0
8	74	Trigeminal neuralgia	12 yrs	Full	<0.4	0.5	2.4	3.5
9	64	Trigeminal neuralgia	5 yrs	Full	0.5	0.6	1.3	1.0

[a] Picomol of Met-enkephalin/ml.

et al. 1976). Four to five ml ultrafiltered CSF was run through a Sephadex G10 column eluted with 0.2 M acetic acid. Two fractions, I and II, were collected, lyophilized and assayed for opiate receptor affinity against tritium-labelled dihydromorphine. A calibration curve with authentic Met-enkephalin was run in parallel and the endorphin content was expressed as picomoles/ml of Metenkephalin.

The two chromatographic fractions (I and II) account for more than 75% of the total endorphin activity of the human CSF as measured in the receptor binding assay (Wahlström *et al.* 1976). In patients with no pain and apparently healthy, the CSF concentrations of these fractions, expressed as picomoles of Met-enkephalin/ml, are 1.4 ± 0.4 (mean $\pm$S.E.) pmol/ml (I) and 5.2 ± 1.8 pmol/ml (II) respectively (Terenius *et al.* 1976). From the present results (Table I) it appears that the lumbar CSF content of fraction I is very low in all patients while experiencing pain, confirming earlier observations on patients with trigeminal neuralgia (Terenius and Wahlström 1975 b). No systematic change is seen with fraction II. During stimulation analgesia a marked rise of endorphin fraction I in lumbar CSF is seen in patients no. 1–4, while this is not the case in the other patients. Again, the content of endorphin fraction II does not seem related to the analgesic effect.

The relation between CSF endorphin concentration and activity in endorphin systems is not clear although a direct correlation is likely. If so, the low endorphin fraction I in all patients experiencing chronic pain is remarkable. These low levels might be due to an inherent hypoactivity in the systems releasing endorphin (Terenius and Wahlström 1975 b) or to a high consumption of released endorphins. A normalization of the endorphin fraction I content of lumbar CSF with stimulation is seen only in the patients having lumbar pain (no. 1–4) and therefore undergoing stimulation of lumbar segments (Andersson *et al.* 1976 b, Eriksson and Sjölund 1976). On the other hand, patient no. 5, suffering from a post-herpetic neuralgia engaging the fifth thoracic segment unilaterally and the 4 patients with trigeminal

neuralgia were stimulated close to their respective painful areas. They did not exhibit any change of endorphin fraction I content in lumbar CSF despite the analgesia induced in 4 cases (Table I). This suggests a local release of endorphins during acupuncture, indicating that the site of action for pain relief by the endorphins is at least partly at the segmental level (*cf.* Le Bars *et al.* 1975, Duggan *et al.* 1976, Yaksh and Rudy 1976). An increase in CSF endorphins might well have been observed in patients no. 5, 6, 8 and 9 if fluid at higher levels had been analyzed.

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