# EFFECT OF PERCUTANEOUS TRANSCEREBRAL ELECTRICAL STIMULATION DURING ELECTROANESTHESIA ON CSF AND PLASMA β-ENDORPHIN LEVELS

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The discovery of opiate receptors, of endogenous peptide ligands possessing morphinomimetic properties when administered by the intragastric or systemic routes, and of enzymes concerned in their synthesis and intrasynaptic inactivation has led investigators to conclude that enkephalinergic and endorphinergic opiate systems performing a protective and antinociceptive function exist in the CNS of man and other vertebrates [7-9, 12]. It can accordingly be postulated that during percutaneous transcerebral electrical stimulation (ES) activation of the opiate systems of the brain will be observed, and this lies at the basis of the analgesic action of this procedure.

To discover the role of endorphinergic opiate systems of the brain in the mechanisms of electroanesthesia, which is widely used in clinical practice [1-4], the concentration of β-endorphin was studied in the cerebrospinal fluid (CSF) and blood plasma of patients before and after a 30-min session of percutaneous transcerebral ES in the electroanesthesia (EA) mode.

## EXPERIMENTAL METHOD

Ten cardiac surgical patients (three women and seven men) aged from 27 to 42 years and weighing from 52 to 76 kg were investigated. All patients were admitted to the hospital for treatment of acquired rheumatic heart disease (eight patients had mitral and two had combined mitral and aortic disease).

Percutaneous transcerebral ES was carried out before the beginning of the operation through silver surface electrodes 30 mm in diameter, located on the root of the nose (active electrode), on the mastoid processes, and on the occipital region of the scalp (inert electrodes), by means of the apparatus for EA developed at the A.V. Vishnevskii Institute of Surgery, Academy of Medical Sciences of the USSR (type 300-01). High-frequency (167 kHz) bipolar square pulses, modulated by a low frequency (77 Hz) were used. The amplitude of the current was 250-300 mA.

Under local anesthesia lumbar puncture was performed on the patients in a special ward and a catheter introduced into the spinal canal. This procedure, adopted at the A.V. Vishnevskii Institute of Surgery as an essential condition for monitoring the CSF dynamics, is aimed at the prevention or immediate treatment of hypoxic brain damage arising in patients undergoing operations under assisted circulation conditions.

After puncture and before the beginning of ES, samples of CSF and blood were taken from all patients, and this was repeated 30 min after the beginning of ES. No other manipulations were carried out during the procedure. With this approach the influence of all other factors than percutaneous ES on changes in the CSF and venous blood plasma levels of β-endorphin in the patients could be ruled out.

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Blood from the cubital vein was taken into plastic tubes containing EDTA (1 mg/ml, final concentration) and the protease inhibitor phenylmethylsulfonyl fluoride (0.5 mM, final concentration) (from Sigma, USA). The plasma was frozen on dry ice and kept at −70°C until use. CSF was collected in plastic tubes containing protease inhibitor and processed as plasma. The β-endorphin levels in CSF and plasma were determined by radioimmunoassay (RIA) using commercial kits from Immuno Nuclear Corporation (USA). To separate β-endorphin from β-lipotropic hormone and ballast proteins of CSF or plasma, the samples of CSF and plasma were extracted on Sepharose, covalently bonded with antibodies against β-lipotropin, and the β-endorphin was then purified on microcolumns with ODS-silicic acid, as described in the instructions for RIA kits for β-endorphin [11].

## EXPERIMENTAL RESULTS

An appreciable quantity of β-endorphin was found in the plasma and CSF of the patients before ES: 5.0 ± 2.5 and 4.8 ± 1.5 pg/ml respectively. Percutaneous transcerebral ES for 30 min under EA conditions caused a significant rise in the level of this neuromodulator in both CSF (19 ± 2 pg/ml; $P < 0.01$) and plasma of the patients (52 ± 20 pg/ml; $P < 0.05$).

β-Endorphin found in the plasma in known to be of pituitary origin, whereas β-endorphin in CSF is of intracerebral (largely hypothalamic) origin [10]. The increase in the concentration of plasma β-endorphin, which is secreted along with ACTH of the anterior lobe of the pituitary [13], after ES is evidence of a possible stress component in the mechanism of development of EA and of the participation of the pituitary and endorphinergic systems of the brain in the antinociceptive action of the EA procedure.

Akil et al. and Amano et al. [5, 6] showed that during direct focal ES of brain structures rich in opiate receptors in patients with a severe pain syndrome, analgesia reversible by naloxone is observed. A marked rise in the β-endorphin level in the CSF also was recorded under these circumstances. These findings are evidence of activation of the intracerebral β-endorphinergic system, leading to the appearance of analgesia.

There is, however, no evidence at present that activation of the intracerebral β-endorphinergic antinociceptive system is observed during percutaneous transcerebral ES. Elevation of the β-endorphin level which we demonstrated during percutaneous transcerebral ES under EA conditions thus indicates common mechanisms of development of analgesia arising during this procedure and during direct focal ES of opiatergic brain structures.

It is of course impossible to be absolutely certain that endorphinergic systems alone are responsible for the development of EA, but these results showing an increase in β-endorphin secretion into the CSF and blood plasma in response to percutaneous transcerebral ES, obtained for the first time, suggest that this mechanism does participate in the realization of the analgesic component of EA.

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