

# EFFECTS OF AMITRYPTILIN ADMINISTRATION ON RAT SERA AND BRAIN BETA-ENDORPHINS

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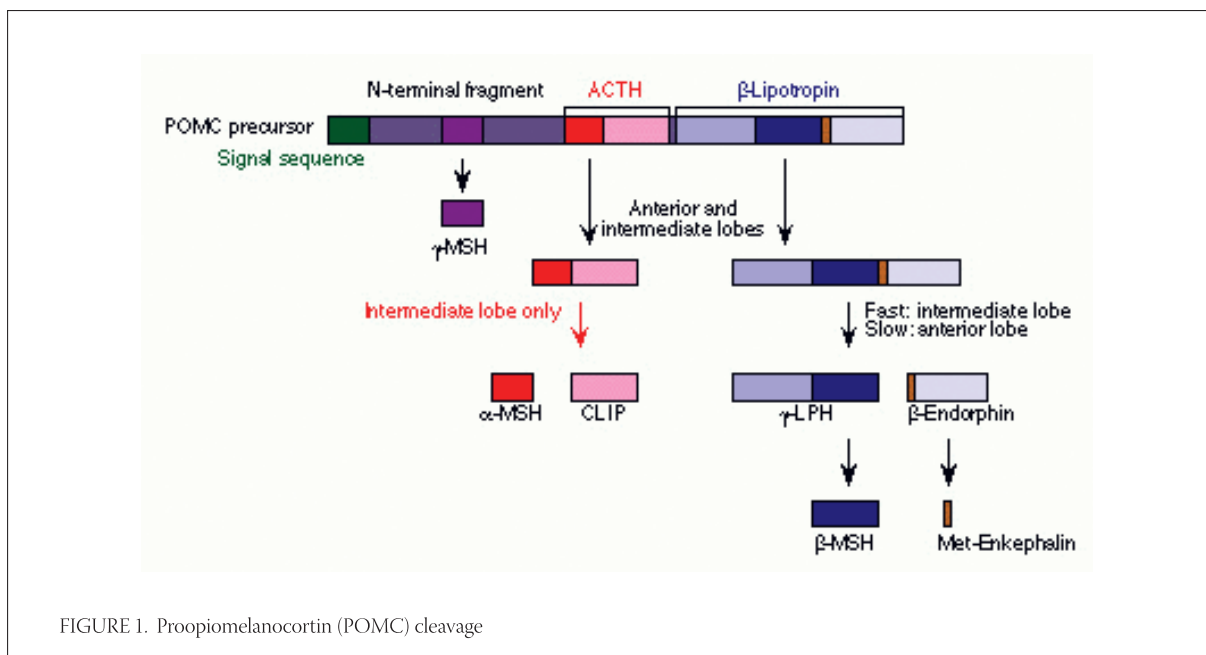
## ABSTRACT

The aim of our study was to establish the influence of antidepressive drugs on serum and brain beta-endorphins in experimental animals. Experiment was performed on albino Wistar rats. Antidepressant Amitryptilin was used, and for quantification of sera and brain beta-endorphins RIA technique. Our results showed difference between sera and brain beta-endorphins concentration in Amitryptilin pretreated animals, vs. those in serum and brain of control group treated with 0,95% NaCl. This study shows that use of psychoactive drugs have influence on sera and brain beta-endorphins concentration. Beta-endorphins could be of great importance, used as markers for evaluation of antidepressant drug effects.

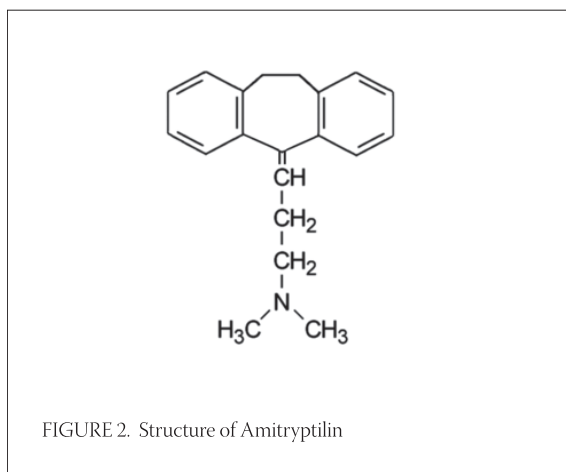
KEY WORDS: amitryptilin, beta-endorphins, rat, sera, brain

## INTRODUCTION

A scientific interest is for a long period based on influence of morphine-like psychoactive drugs, especially in expression of therapeutic effects in treatment of psychiatric disorders, anxiety, and depression. The endogenous opioid system consists of widely scattered neurons that produce three opioids:  $\beta$ -endorphin, the met- and leu-enkephalins, and dynorphins. These opioids act as neurotransmitters and neuromodulators at three major classes of receptors, termed  $\mu$ ,  $\delta$  and  $\kappa$ , and produce analgesia. Like their endogenous counterparts, the opioid drugs, or opiates, act at the same receptors to produce both analgesia and undesirable side effects. (1). Plasma  $\beta$ -endorphin is endogenous opioid peptide derived from proopiomelanocortin (Figure 1). It has a polypeptide structure, made of 31 amino acid, placed in beta-LPH C-terminal part, with high opiate activity, 3-5 times efficiently competing for opiate linking parts. Some facts are suggesting that beta-endorphin has a role in change of behaviour, appetite control, and development of obesity and



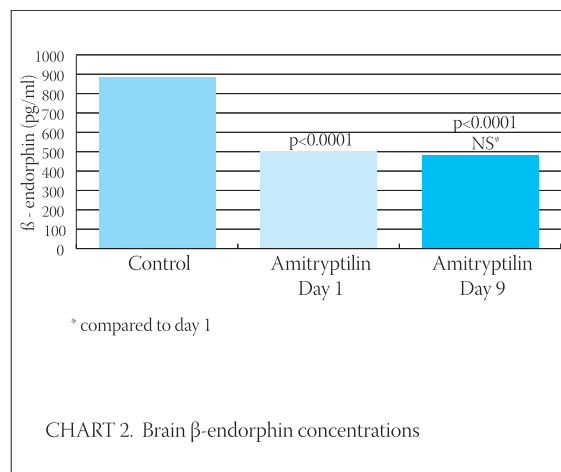
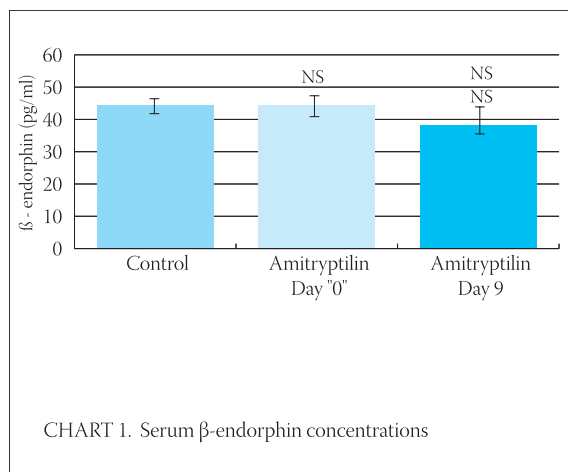
schizophrenia. It is produced as well as ACTH, when adrenalectomy is performed, related to stress or administration of CRH, meaning both substances are produced by the same adenohypophyseal cells from the same glycoprotein precursor (2, 3).  $\beta$ -endorphin in brain is turned to  $\gamma$ -endorphin with neuroleptic qualities, with  $\alpha$ -endorphin originating from the last in low pH, expressing psycho stimulative effects, with number of proteolytic stages between changing process (4). A wide range of techniques have been described, investigating various characteristics of human and rat specific antibodies.  $\beta$ -endorphin radioimmunoassays are widely performed following physical, emotional and environmental challenges in rat. (5). Findings in the field of psycho-pharmaceutics gave us a lot of knowledge about their positive and side effects, as well as for brain function and nature of psychotic diseases; signal substances and their impact on health and illness



of the brain (6). Desipramine and paroxetine, used in animal depression models, did not significantly affect the extracellular levels of beta-endorphin in nucleus accumbens, but chronic antidepressant treatment did normalize serotonin-induced release of beta-endorphin, as well as behavioural manifestation of depressive behaviour (7). Amitriptyline (Figure 2.) is a tricyclic antidepressant, chemically similar to antipsychotic drugs, giving him sedative effects. Main antidepressive act is based on relieving of agitation and anxiety.

## MATERIAL AND METHODS

Albino Wistar rats, weight 250 gr. were used, divided in groups of 6, with each animal control to itself. Amitriptyline was administrated to experimental (2mg/kg/day), and 0.95% NaCl solution to control group. Blood samples were collected from great tail vein, before beginning, and after 0 and 9th day of amitriptyline administration. Before brain samples were collected, all animals were properly sacrificed. Collection of brain samples was performed immediately for control group, and after 1<sup>st</sup> and 9<sup>th</sup> day of amitriptyline administration in treated animals. For analysing  $\beta$ -endorphin levels we used RIA technique, for quantification of human serum and brain  $\beta$ -endorphin (Nichols Institute, San Juan, Capistrano, USA), and for radioactivity level  $\beta$ -counter with gamma-radiation source (LKB Wallac – Sweden).  $\beta$ -endorphin concentration is directly proportional to radioactivity measured in samples. Concentration is given in pg/ml for serum, and in pg/g for brain  $\beta$ -endorphin values. Counting mean value, standard deviation and standard error we



performed statistic evaluation of obtained results. The level of significance was determined by use of Student's T test, with values  $p < 0,05$  considered as significant.

## RESULTS AND DISCUSSION

Our data, presented by charts, show sera  $\beta$ -endorphin values, before beginning, and after 0 and 9<sup>th</sup> day of Amitryptilin administration. Obtained values for each day were compared to the other, and to those of control group. There was no significant difference between rat sera  $\beta$ -endorphin for certain days, showing lowest values of sera  $\beta$ -endorphin concentration on day 9

## CONCLUSION

- Sera  $\beta$ -endorphin values after a continuous Amitryptilin treatment of animals are a bit lower then those in control group
- Brain  $\beta$ -endorphin values after a continuous Amitryptilin treatment of animals are significantly lower then those in control group
- Endogenous  $\beta$ -endorphin s can be used in evaluation of psychoactive drug therapy
- Evaluation of  $\beta$ -endorphin sera level could be of great importance used as markers for investigation of psychoactive drug effects

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