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Participation Of The Opiate Peptides In The Systemic Mechanisms Of Reintegration

Dr. Faig CEFEROV[1], Dr. Faruk BAĞIRICI[2]

(1) Department of Physiology, Azerbaijan Medical University, Baku, Azerbaijan
(2) Department of Physiology, Faculty of Medicine, University of Ondokuz Mayıs Samsun, Turkey

✔ Sunulan çalışmada, lateral hipotalamusun tahribi durumunda, beslenme davranışının santral düzenlenmesinde opioid peptidlerin rolü araştırıldı. Deneyler, vücut ağırlıkları 200–250 gram olan beyaz erkek sıçanlarda yapıldı. Deney hayvanları, her bir grupta 15 hayvan bulunan 3 gruba ayrıldı. Tüm hayvanlarda nükleus lateralis elektrokoagulasyon metodu ile tahrip edildi. Birinci gruptaki hayvanların lateral ventriküllerine serum fizyolojik, ikinci gruptakilere β-lipotropin ve üçüncü gruptakilere β-endorfin enjekte edildi. Vücut ağırlıkları, günlük alınan gıda ve su miktarları tüm hayvanlarda düzenli olarak kaydedildi. Ayrıca, hayvanların çevreye uyumu, gıda alımı, beslenme aktivitesi, konfor (temizlenme) davranışı ve uyanıklık düzeyi gibi serbest davranış özellikleri de gözlendi. Araştırılan maddelerin etkileri 15 gün süreyle hergün kaydedildi ve kontrol grubuyla karşılaştırıldı.

Hipotalamik yapıların harabiyeti durumunda, β-lipotropin ve β-endorfinin bozulan bu fonksiyonların merkezi sinir sisteminde yeniden düzenlenmesine, motive edici ve düzeltici yönde katkıda bulunduğu tesbit edildi.

Anahtar Kelimeler: Opioid peptidler, hipotalamus, davranış.

✔ In the present study, participation of opiate peptides in the central mechanisms of food motivation under conditions of destruction of lateral hypothalamus was examined. The experiments were carried out on 3 groups of white rats (body mass 200–250 g.), 15 animals each group. The lateral hypothalamus were destructed by the way of electrocoagulation. In first group, physiological saline solution was administrated into lateral ventriculus. In second group β-LPT and in third group β-endorphine were injected into lateral ventriculus respectively. Body mass, amount of the daily food and water were registered in all animals regularly as well as indices of the free behaviour: orientation–investigatory, food getting and nutritive activity, comfort behaviour, the level of wakeness. Effects of the action of investigated substances were registered everyday for 15 days and were compared with the control groups.

It was established that β-lipotropin and β-endorphine selectively including mativatiogenic and integrative activity under conditions of the destruction of the hypothalamic structures take part in the systemic mechanims of the reintegration of disturbed functions.

Key words: Opiate peptides, hypothalamus, behaviour.

High physiological activity of the opiates points on their essential role in the regulation of different vegatative and behavioural functions of human and animals. It was found that endogenic opiates not only participate in forming of motivations, emotions and memory, they also are able to restore disorders of motivational–emotional sphere and memory caused by trauma and intracerebral interventions[2,6,8,14,21,22,25]. Direct evidences of motivations and integrative functions of some peptides in systemic organisations of food behaviour were obtained and their exogenous administration are re-

sulting in changing of character of the food behaviour of animals[5,12,13,16,23,24].

Among endogenic opiate peptides with spectrum of action β-lipotropin (β-LPT) and its derivations (α, β, γ-endorphines, β-MSG, met-encephalines and etc.) are particularly interesting. They widely spread in different structures of brain, especially in nuclear structures of the hypothalamus. Nucleus arcuatus of hypothalamus is believed to be a main β-LPT synthesis and containing, nucleus lateralis β-LPT-reception zone of brain [1,3,4,7,9,10,11,15,17,18]. Therefore, in present study, possible participation of β-LPT and β-endorphine in mechanisms of compansation of biologic motivations and physiologic functions connected with it after destructions of arcuatus and lateralis was investigated. This question was not studied till now.

MATERIALS AND METHODS

Experiments were carried on 45 male rats (range w. 200-250 g.) divided into 3 groups (15 in each group). In first (control) group, nucleus lateralis were destructed and physiological saline solution (in volume 3-5 µl.) was administered into lateral ventriculus; in second and 3-rd groups nucleus lateralis was destructed and intraventricular microinjections of β-LPT and β-endorphine. Hypothalamic structures were destructed by electrocoagulation (anode current-50 mA, 5 sec.) oriented stereotaxically according to coordinates of atlas of rat brain under deep anaeshesia with nembutal[19]. Above mentioned peptides were administered into lateral ventriculus using implanted canulas in concentrations of $95,5x10^{-6}$ mmol (β-LPT) and $269x10^{-6}$ mmol (β-endorphine) in volume 3-5 µl of physiological saline solution using "Hamilton" microinjector (Switzerland).

Animals were kept in individual boxes with foodmeter and drincometer.After adaptation period of animals to the boxes (10-12 days) for both initial period (10-12 days), and affecting period (15 days), volume of food and water, diuresis, mass and temperature of body and behavioural indices food and drinking activity, orientive-investigative, comfort, duration of spontaneous sleeping were registered every day. End of experiments, animals were decapitated and brain was taken out and then by microscopic investigation of brain sections zones of structures were determined by protoexpress method and at brain section colorated by Nissle, reconstruction was done taking in affection results of morphologic analysis. Figure 1 shows the reconstruction of brain section with localization zones of destruction in n.lateralis. Results of experiments were statistically analysed using standart biometrical methods with Students-t Test[20].

RESULTS AND DISCUSSION

It was estimated that at 9-12 days after destruction of n.lateralis, the weight of rats were decreased (in average 16.9%), volumes of consuming food (in average 24.7%) and water (26.8%) were also decreased. The most common results of destruction of hypothalamic n.lateralis were decreasing food actions (27.5%) and oriented investigative activity (40.0%), increase of level of wakeness (17.1%), drinking activity (42.1 %), and increasing comfort forms of behaviour (licking, cleaning) in average of 93.4% (Fig. 2).

Thus, destruction of hypothalamic structures is accompanied not only with the "switching off" food motivation, also with the negative dynamics of functions, connected with its activity.

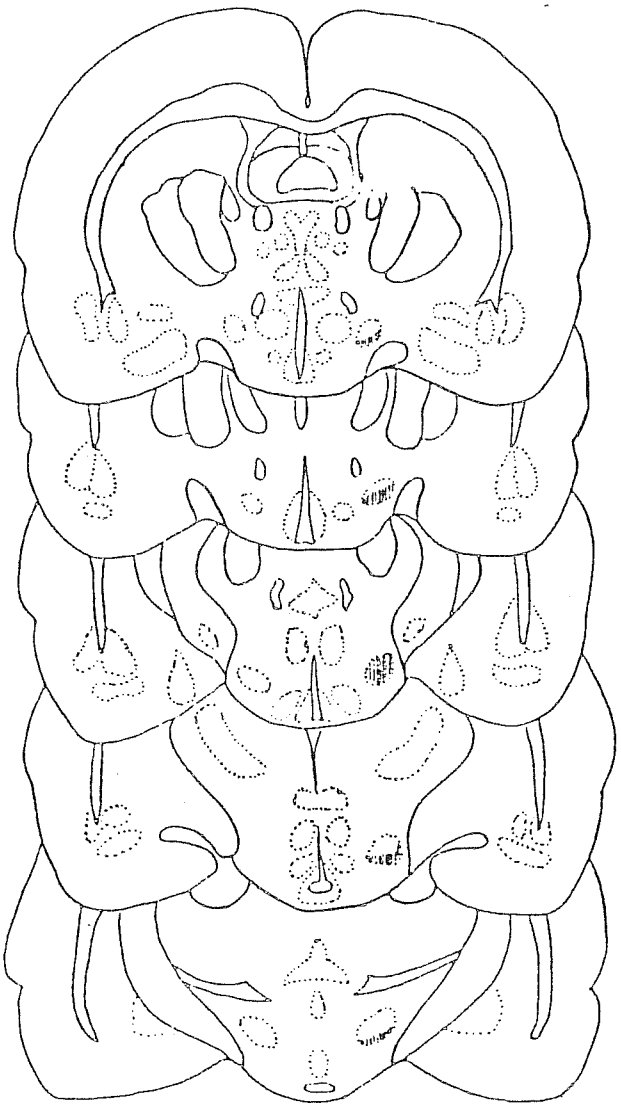

Fig 1: Brain cuts reconstruction with localization of lesion zone in hypothalamic lateral nucleus. 5–Level of cut; cut thickness is 10 μm. Lesion zone spreads for 600–1300 μm^2.

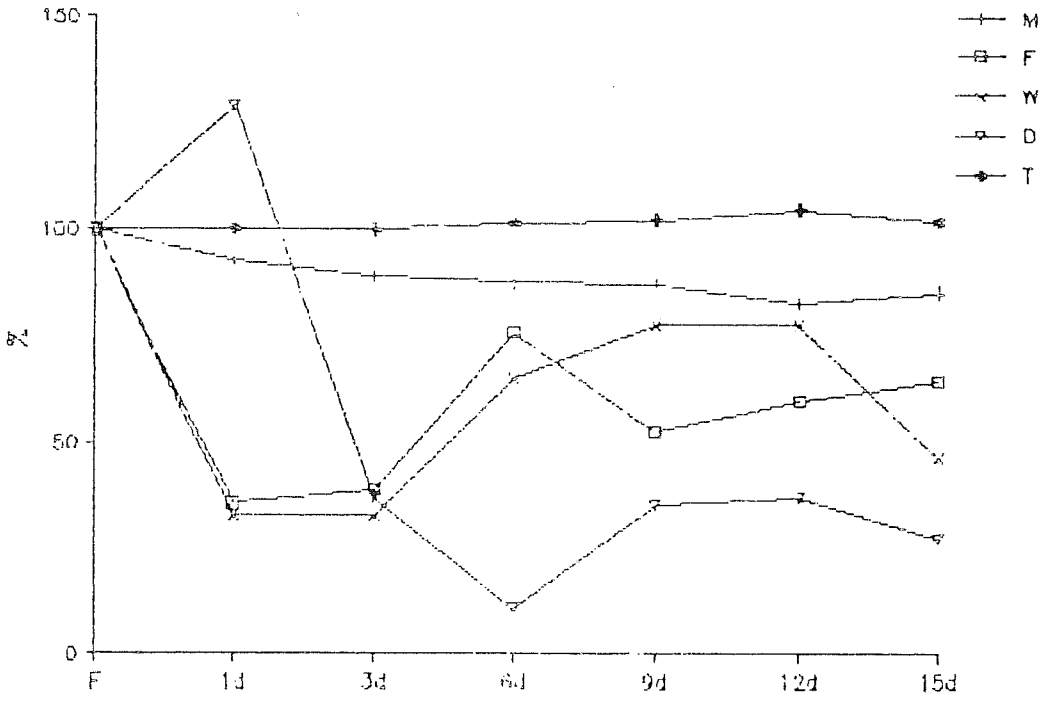

Fig 2: Dynamic changes of vegetative measures after hypothalamic letaral nucleus lesions.
Designations: M–mass; F–food; W–water; D–diuresis; T–temperature.
ox–coordinates –days of investigations (F–back–ground).
oy–coordinates –changes percentage.

Analysis of the obtained data showed that intraventricular administration of β–LPT and β–endorphine after destruction structures of hypothalamus was effective for restoring of broken functions. It was found that β–LPT administration not just restored indices of food behaviour and accompanied function, it even was higher than initial indices. These rats were very active in moving and drinking behaviour was dominating in food activity. Comfort behaviour and oriented–investigative activity were depressed (Fig. 3).

Administration of β–endorphine in the lateral hypothalamus destructed rats was able to restore only food activity, but not consuming water. At the same time, these animals had high level of comfort behaviour, spontaneous sleep and oriented–investigative activity was depressed (Fig. 4).

As our experiments showed, destruction of hypothalamic structures (n.lateralis) by electrocoagulation results in forming of central–peripherial syndromes, which are very difficult to prognose and their compensation have not sufficient guarantees. Pointed syndromes contain both of depressing and strengthening of functions. Expression and duration of changes and further "expanding of behavioural forms" allowed to estimate that after destruction of motivatiogenic structures not only vegetative food functions could be broken, also some beha-

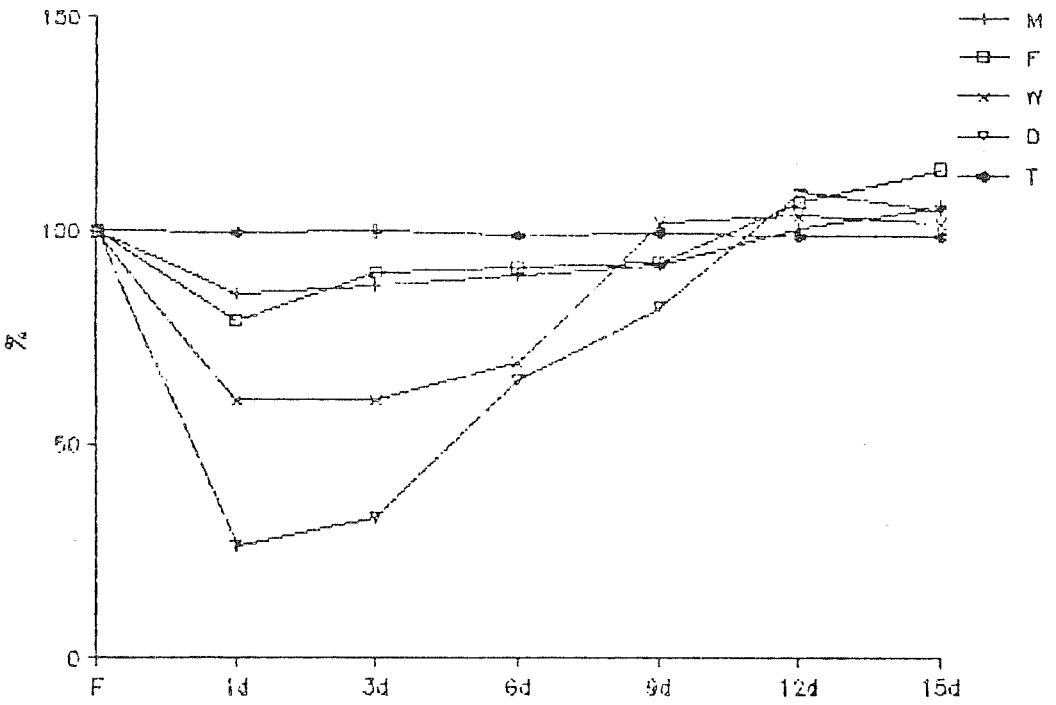

Fig 3: Dymanic changes of vegatative measures in intracerebroventricular administrations of β-LPT after hypothalamic lateral nucleus lesions.
Designations: M-mass; F-food; W-water; D-diuresis; T-temperature.
ox-coordinates -days of investigations (F-back-ground).
oy-coordinates -changes percentage.

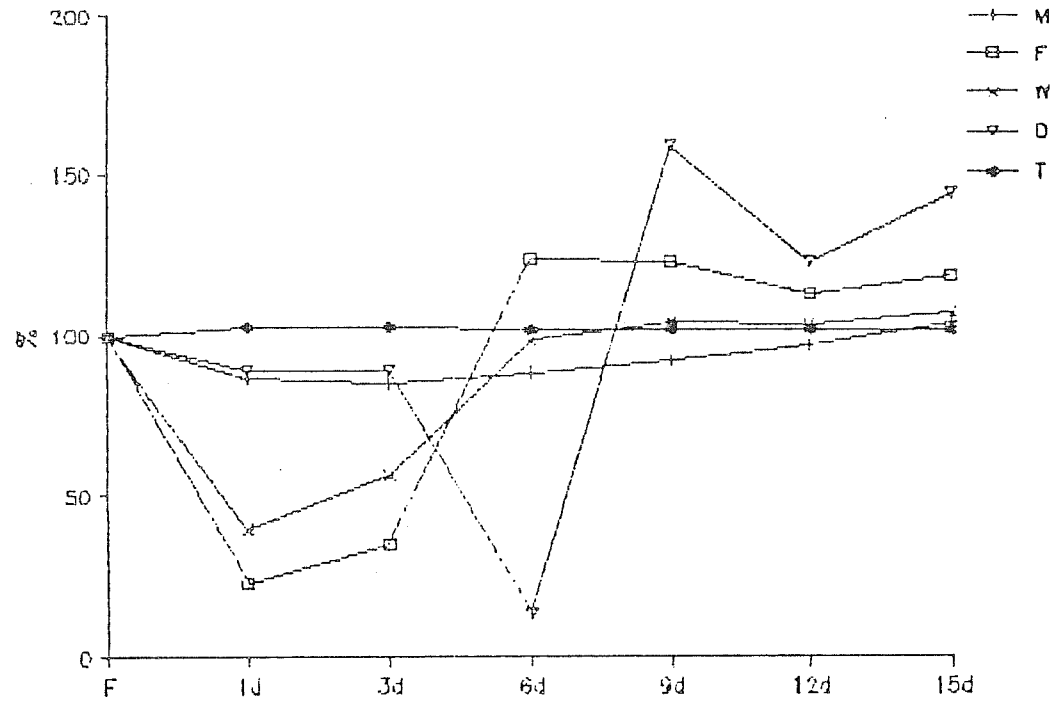

Fig 4: Dinamics of changes of vegatative measures in intracerebroventricular administrations of β-LPT endorphine after hypothamic lateral nucleus leesions..
Designations: M-mass; F-food; W-water; D-diuresis; T-temperature.
ox-coordinates -days of investigations (F-back-ground).
oy-coordinates -changes percentage.

vioural indices unconnected with food behaviour might be increased.

We have observed that intraventricular administration of β-LPT and β-endorphine compansate destroyed food behaviour and other accompanied functions. But the character of compensative effects of opiate peptides is not the same. Possibly, destruction of motivatiogenic structures in our experiments broke synthesis of β-LPT and β-endorphine in presence of specific opiate receptors in other structures of brain and organism, which were sufficient for compensation or realisation of its main adaptive functions in case of exogenic administration.

In conclusion, on the base of obtained data we can suppose systematic character of participation of the opiate peptides in the compensation of metabolic and behavioural disorders, caused by intrahypothalamical intervention. In this case, β-LPT and β-endorphine, selectively manifest their motivatiogenic, integrative and conforming properties.

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