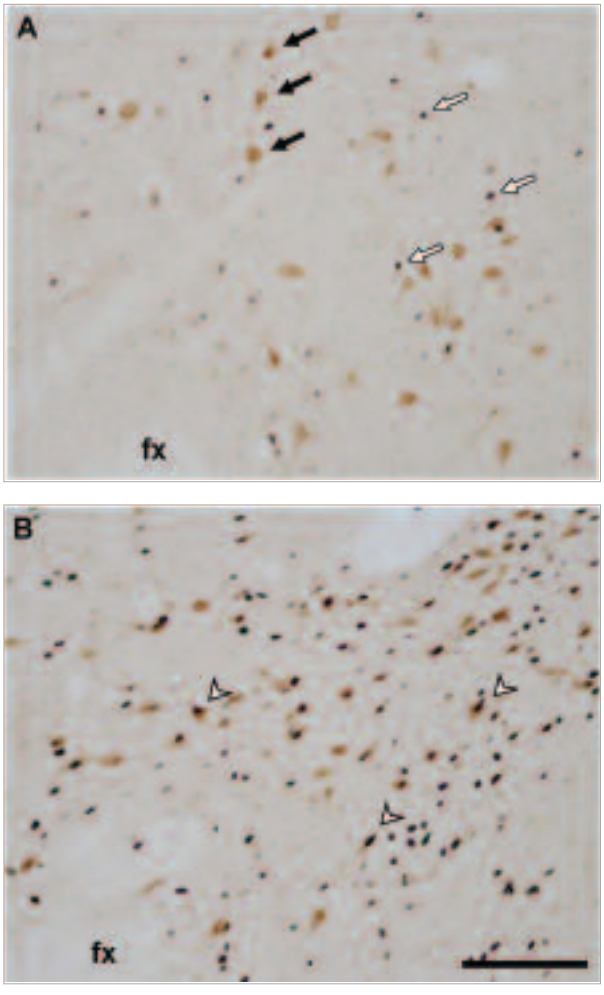
PEPTIDERGIC PATHWAYS INVOLVED IN THE ORGANIZATION OF FEEDING BEHAVIOR

Jackson Cioni BITTENCOURT

Institute of Biomedical Sciences / University of São Paulo (USP)

Feeding behavior is an essential part of the energy balance control. It allows the maintenance of health and an adequate body weight. In the last years, the description of leptin action as a lipostatic or satiety factor in the hypothalamus originated a burst of information about its action in food intake control and related disorders (obesity and anorexia). In parallel, an increasing number of peptides and receptors implicated in energy homeostasis have invaded the field. In this regard, melanin-concentrating hormone (MCH) has been related to the tonic control of feeding. MCH neurons are located in the hypothalamus, which made it a natural candidate for neuroendocrine, autonomic and behavioral control of the homeostasis and species subsistence. Accordingly, various findings support MCH action on feeding behavior: 1) MCH mRNA is abundant in fasted animals or obese (ob/ob) mice; 2) MCH administration in the cerebral ventricles or in specific hypothalamic nuclei that express MCH receptor (MCH -IR) induces hyperphagia and increases body weight; 3) MCH knockout mice shows decreased body weight due to hypophagia and rise in energy expenditure; 4) MCH-IR knockout mice are lean albeit hyperphagic; 5) administration of MCH-IR specific antagonists decreases body weight gain. Intriguingly however, the brain sites where MCH may act by inducing feeding, and the cell biology of these putative systems are not completely understood. It is important to point out that feeding is a complex behavior that includes homeostatic and hedonistic mechanisms, embracing from hunger sensation to motor activity, exploratory behavior, emotional responses, anxiety, memory and learning processes. Therefore, this study attempts to investigate MCH action in various feeding aspects and the related circuitry. Initially, we plain to analyze MCH participation in spatial orientation in the search for food, using a maze paradigm and different types of food: only nutritional or with hedonic value. In addition, by using the same paradigm we propose to investigate the animal performance following lesion, or injection of MCH or anti-MCH in specific brain nuclei previously identified. In these regions, we intend to investigate the neurochemistry, the occurrence of synaptic terminals by using electron microscopy, and describe the synaptic characterization. Finally, we aim to look into MCH's role in complex systems of search for food that include predatory behavior.



Colocalization of ƒos and orexin immunoreactivity (ƒos-ir and orx-ir) in diencephalic territory. Brightfield photomicrography of immunoperoxidase material stained for ƒos protein and orexin. A, ƒos-ir cells localized in the lateral hypothalamic area (LHA) (white arrows) and orx-ir cells (black arrows) in the control animals; B, cells colocalizing ƒos-ir and orx-ir (arrowheads) in the LHA region of animals during the predatory hunting behavior. Abbreviations: fx, fornix. Bar = 200µm

SUMMARY OF RESULTS TO DATE AND PERSPECTIVES

The participation of the lateral hypothalamic area (LHA) and the neuropeptide orexin in the predatory hunting behavior: for the first time, orexin was shown to be co-localized with *fos* protein in the neurons of the LHA after rats had been exposed to free cockroaches in the cage. The number of neurons in the LHA presenting the *fos* protein (a protein that is used as a marker for activated cells) significantly increased in the experimental model, as compared to the control animals, for which we did not observe the same results. This finding suggests that the LHA functions as an integrative center, also participating in the arousal system for this kind of behavior, and also indicates orexin as a neuromodulator.

In order to study the spatial memory participating in the feeding behavior and the involvement of some of the orexigenic peptides, such as the melanin-concentrating hormone and orexin (both present at hypothalamic territories), we were developed an experimental model that makes use of the already known "dry maze". To our knowledge, this is the first time such an apparatus is employed for studying the spatial memory participating in this type of behavior. Despite the fact that we have not yet concluded these experiments, we have already established a protocol to study the feeding behavior. The validation of such method is under way.

MAIN PUBLICATIONS

Elias CF, Sita LV, Zambon BK, Oliveira ER, Vasconcelos LA, Bittencourt JC. 2008. Melanin-concentrating hormone projections to areas involved in somatomotor responses. *J Chem Neuroanat*. **35(2)**:188-201.

Sita LV, Elias CF, Bittencourt JC. 2007. Connectivity pattern suggests that incerto-hypothalamic area belongs to the medial hypothalamic system. *Neuroscience*. **148(4)**:949-69.

Rondini TA, Rodrigues Bde C, de Oliveira AP, Bittencourt JC, Elias CF. 2007. Melanin-concentrating hormone is expressed in the laterodorsal tegmental nucleus only in female rats. *Brain Res Bull*. **74(1-3)**:21-8.

Attademo AM, Rondini TA, Rodrigues BC, Bittencourt JC, Celis ME, Elias CF. 2006. Neuropeptide glutamic acid-isoleucine may induce luteinizing hormone secretion via multiple pathways. *Neuroendocrinology*. **83(5-6)**:313-24.

Bittencourt JC, Celis ME. 2008. Anatomy, function and regulation of Neuropeptide EI. *Peptides*. (review - in press).

Jackson Cioni BITTENCOURT

Instituto de Ciências Biomédicas
Universidade de São Paulo (USP)
Departamento de Anatomia
Av. Prof. Lineu Prestes, 2415 Ed. B-III Lab 105
Cidade Universitaria
CEP 05508-900 – São Paulo, SP – Brasil

+55-11-3091-7300
jcbitten@icb.usp.br