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María Paula Cornejo, Franco Barrile, Pablo Nicolás De Francesco, Enrique Leo Portiansky, Mirta Reynaldo, Mario Perello

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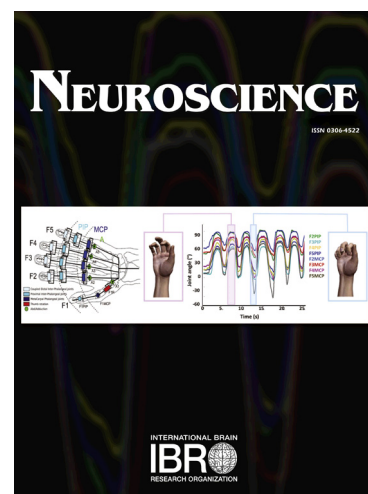
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**GHRELIN RECRUITS SPECIFIC SUBSETS OF DOPAMINE AND GABA NEURONS OF
DIFFERENT VENTRAL TEGMENTAL AREA SUB-NUCLEI**

María Paula Cornejo¹, Franco Barrile¹, Pablo Nicolás De Francesco¹, Enrique Leo Portiansky², Mirta Reynaldo¹, Mario Perello¹

¹Laboratorio de Neurofisiología del Instituto Multidisciplinario de Biología Celular, Consejo Nacional de Investigaciones Científicas y Técnicas de Argentina, Universidad Nacional de La Plata y Comisión de Investigaciones Científicas–Provincia de Buenos Aires, 1900 La Plata, Buenos Aires, Argentina.

²Laboratorio de Análisis de Imágenes, Facultad de la Ciencias Veterinarias, Universidad Nacional de La Plata y Consejo Nacional de Investigaciones Científicas y Técnicas de Argentina, 1900 La Plata, Buenos Aires, Argentina

Running title: Neuroanatomical aspects of ghrelin action in the VTA

Corresponding Author:

Dr. Mario Perelló

Laboratory of Neurophysiology, Multidisciplinary Institute of Cell Biology

Calle 526 S/N entre 10 y 11-PO Box 403

La Plata, Buenos Aires, Argentina 1900

Phone +54 221 4210112

Email: marioperello@yahoo.com or mperello@imbice.gov.ar

ABSTRACT

Ghrelin is a stomach-derived hormone that regulates rewarding behaviors and reinforcement by acting on the ventral tegmental area (VTA). The VTA is a complex midbrain structure mainly comprised of dopamine (DA) and gamma-aminobutyric acid (GABA) neurons that are distributed in several VTA sub-nuclei. Here, we investigated the neuroanatomical distribution and chemical phenotype of ghrelin responsive neurons within the VTA. In wild-type mice, we found that: 1) ghrelin binding cells are present in most VTA sub-nuclei but not in its main target, the nucleus accumbens (Acb); 2) systemically-injected ghrelin increases food intake but does neither affect locomotor activity nor the levels of the marker of neuronal activation c-Fos in the VTA sub-nuclei; 3) centrally-injected ghrelin increases food intake, locomotor activity and c-Fos levels in non-DA neurons of all VTA sub-nuclei; 4) intra-VTA-injected ghrelin increases food intake, locomotor activity and c-Fos levels in non-DA neurons of all VTA sub-nuclei; 5) both centrally- and intra-VTA injected ghrelin increases c-Fos levels in DA neurons of the parabrachial pigmented VTA sub-nucleus. In genetically modified mice in which a subset of GABA neurons expresses the red fluorescent protein tdTomato, we found that centrally-injected ghrelin increases c-Fos levels in GABA neurons of the interfascicular VTA sub-nucleus. These results suggest that ghrelin can recruit specific subsets of VTA neurons in order to modulate food intake and locomotor activity.

Keywords: mesolimbic pathway, locomotor activity, food intake, dopamine, GABA

INTRODUCTION

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