CGRP UPTAKE INTO PERIVASCULAR CAPSAICIN-SENSITIVE NERVE TERMINALS

A. Sams-Nielsen¹, C. Orskov², and I. Jansen-Olesen¹

¹Department of Pharmacology, The Royal Danish School of Pharmacy, Copenhagen, Denmark;

²Department of Medical Anatomy, The Panum Institute, University of Copenhagen, Denmark

INTRODUCTION

Specific mechanisms, providing reuptake of catecholamine and amino acid neurotransmitters (e.g., serotonin and glutamate) into cells of the central nervous system are well known, whereas neuronal uptake of neuropeptides have not previously been reported.

Our recent studies provide evidence that the 37 amino acid neuropeptide, calcitonin gene-related peptide (CGRP) undergo uptake into capsaicin-sensitive perivascular terminals of sensory nerve fibres.

The experimental design of our studies are based on current knowledge about capsaicin, which potently causes depletion of CGRP from specific sensory nerve terminals, and on the notion that extra cellular CGRP may be loaded into CGRP-depleted nerve terminals.

METHODS AND RESULTS

Release of CGRP from perivascular nerve terminals was obtained by capsaicin-induced vanilloid receptor-stimulation and detected as CGRP receptor-mediated dilation of isolated segments of the guinea pig basilar artery.

Following repeated capsaicin challenges, CGRP-depleted segments were incubated with CGRP. This caused significant reappearance of capsaicin-induced vasodilatory responses. These responses were dependent on duration and concentration of the preceding CGRP incubation and were inhibited by the CGRP receptor antagonist, CGRP₈₋₃₇.

Incubating the artery segments with ¹²⁵I-CGRP allowed subsequent detection of capsaicin-induced ¹²⁵I-release.

The CGRP redepletion was significantly reduced when CGRP₈₋₃₇ was present during the preceding CGRP incubation and presynaptic CGRP receptors may therefore be involved in neuronal CGRP uptake.

CONCLUSION

Perivascular capsaicin-sensitive sensory nerve terminals can be reloaded by extracellular CGRP. The mechanism of CGRP uptake may involve presynaptic CGRP receptors.