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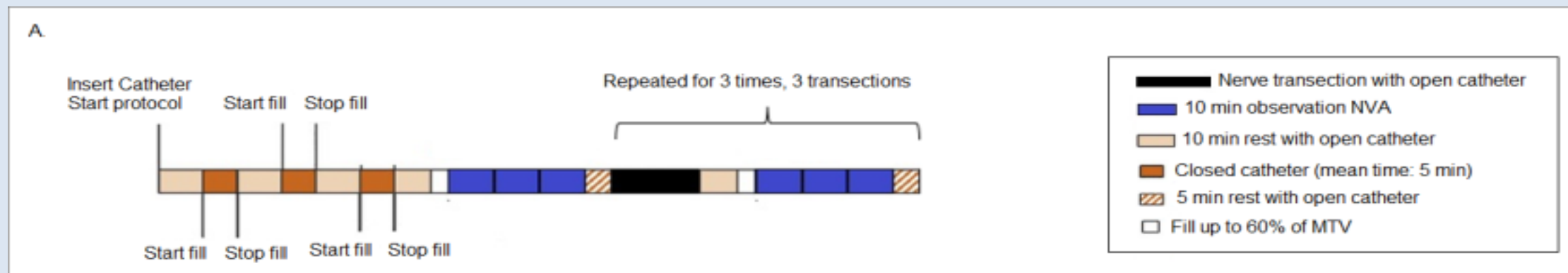
INTRODUCTION

Bladder afferent outflow plays a critical role in bladder pathology. Abnormal outflow results in altered sensation, leading to increased voiding frequency, urge and often incontinence. β_3 -adrenoceptor agonists were thought to treat these symptoms by mimicking sympathetic nerve activity and directly relaxing the detrusor (1). However, also other sites of action should be considered. It has been suggested that the peripheral ganglia might play a modulatory role in bladder physiology (2). The present study used immunohistochemical techniques to identify structures in the major pelvic ganglion (MPG) of the rat that might be involved in such neural circuitry. To further explore the role of the pelvic plexus in the control of bladder activity, we evaluated isovolumetric non-voiding activity (NVA) in a rat model in which the MPG's were cut bilaterally.

METHODS

Functional study

- 10 male Sprague-Dawley rats
- Urethane anesthesia (1.5 g/kg, i.p.)
- PE-50 catheter through the dome
- Bladder filled to 60% micturition threshold volume
- Observation NVA: control and after pelvic, hypogastric and MPG transection



Immunohistochemistry:

Primary antibodies immunoreactive (IR) to: tyrosine-hydroxylase (TH), vesicular acetylcholine transporter (VAChT), calcitonin-gene related peptide (CGRP), nitric oxide synthase (NOS)

RESULTS

- No significant changes in the integral and amplitude after consecutive hypogastric and pelvic nerve transection
- The control integral and amplitude didn't change after complete decentralization.
- A significant increase in the integral and amplitude of NVA was observed after MPG transection, when compared with the decentralized and control condition.
- The frequency of NVA did not change

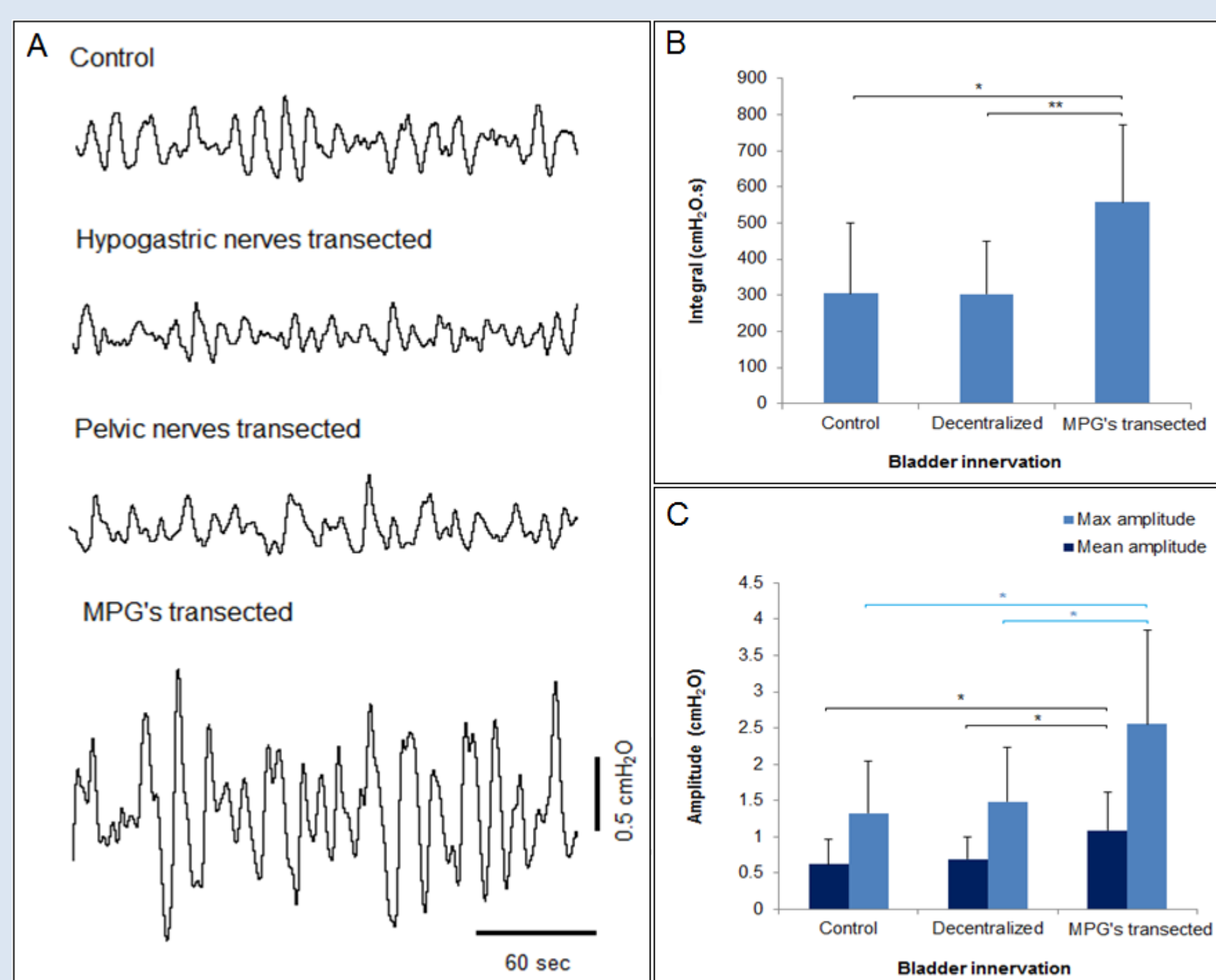


Figure 1. The effect of different nerve transections on isovolumetric non-voiding activity (NVA). Original record (A) and the mean effect of MPG transection on the integral (B) and amplitude (maximum and mean) (C) of NVA when compared with the decentralized and control condition measured from 10 rats. * $p < 0.05$; ** $p < 0.01$

- Adrenergic (TH) large cells and SIF cells were found in the MPG. The remainder are cholinergic (VAChT) large neurons with cholinergic inputs. All three types of neurons are surrounded by CGRP-IR sensory fibres.
- Also large NOS cells were observed and some had NOS-IR inputs, but none of them showed CGRP-IR synapses

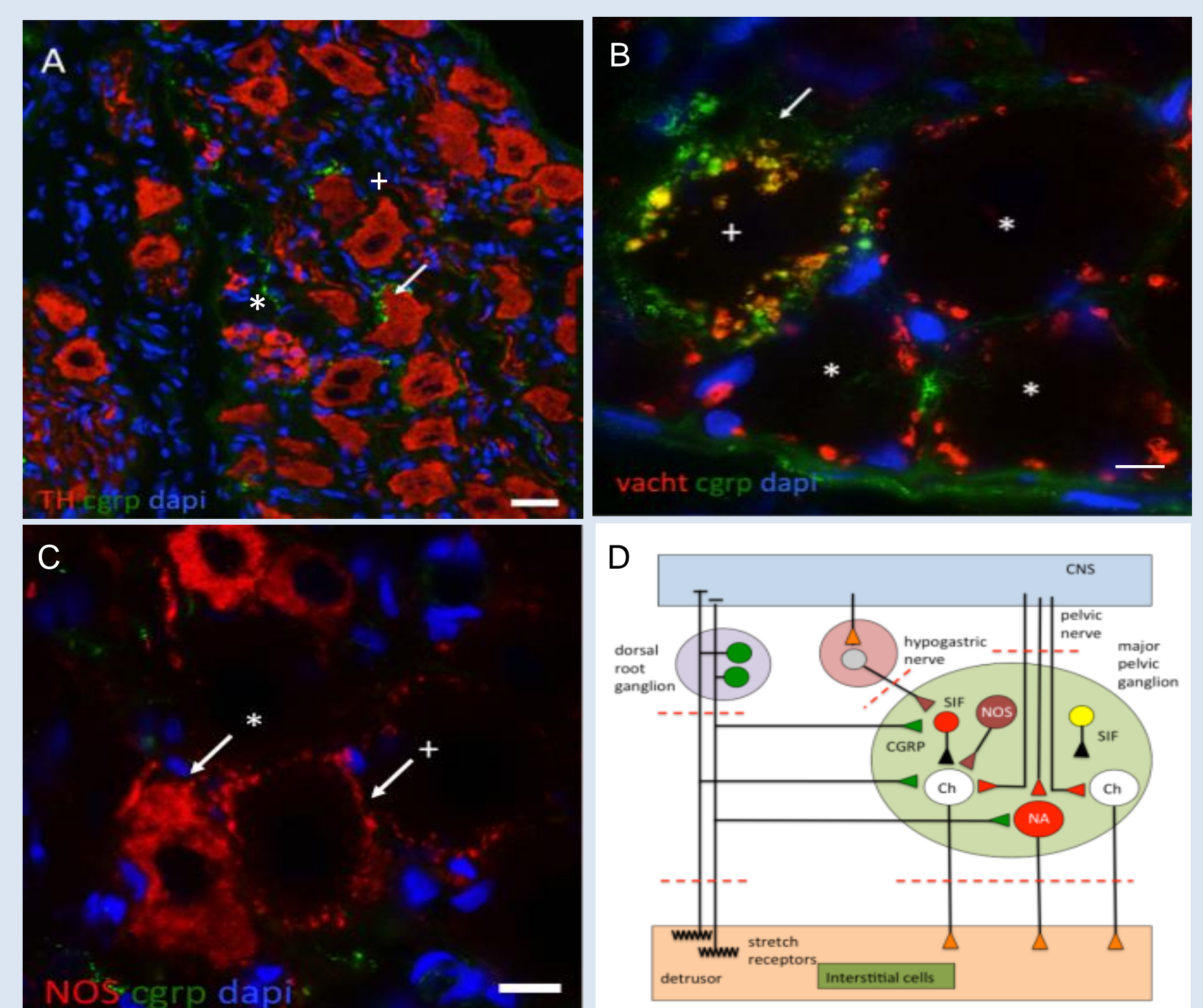


Figure 2. Illustration of the complex interactions between sensory, cholinergic and adrenergic systems in the major pelvic ganglion (MPG). A demonstrates large adrenergic (red: TH-IR) neurons (+) and SIF cells (*). Both cells are sometimes surrounded by CGRP-fibres (green, arrow). B illustrates large cholinergic neurons (*) that receive cholinergic input (red: vachT-IR). Some of these neurons (+) also receive CGRP-IR fibers (green, arrow). C demonstrates NOS (red)-positive (*) and NOS-negative (+) cells surrounded by NOS-IR fibres, not by CGRP-IR (green) fibres. Calibration bars: A, 30 μ m; B, 15 μ m; C, 10 μ m. D illustrates the reflex pathways and intra-ganglionic elements involved in the motor-sensory regulation of the bladder. The dotted lines represent the transections that have been performed by our functional study.

CONCLUSIONS

Local inhibitory reflexes are found in the MPG that may function to modulate NVA during the filling phase

A site of action for anticholinergic and β_3 -adrenergic drugs?

REFERENCES

1. Sacco E, Bientinesi R. Mirabegron: A review of recent data and its prospects in the management of overactive bladder. *Therapeutic Advances in Urology* 4: 315-324.
2. de Groat WC, Booth AM. Synaptic transmission in pelvic ganglia. In: Maggi CA (ed) *Nervous control of the urogenital system*. Harwood academic publishers. 1993