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Muscarinic receptor expression in spinal cord transected rats with early anticholinergic treatment

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Introduction & Objectives: We have previously demonstrated that early administration of fesoterodine fumarate (FF) in spinal cord transected (SCT) rats prevents the onset of detrusor overactivity [1]. The aim of this study was to examine the variation of expression and distribution of bladder muscarinic receptors due to the effect of FF in SCT rats.

Materials & Methods: The bladders of Sprague-Dawley rats were harvested 6 weeks after they were allocated to different treatment groups – Group 1: normal controls; Group 2: SCT controls; Group 3: SCT rats + FF 0.18 mg/kg/d; Group 4: SCT rats + FF 0.12 mg/kg/d; Group 5: SCT rats + FF 0.18 mg/kg/d + 72-h wash-out period; Group 6: SCT rats + FF 0.12 mg/kg/d + 72-h wash-out period. SCT was performed at T10. FF was continuously administered from post-op day 1. RT-PCR and immunofluorescence staining was done to investigate the presence and distribution of the receptors in the bladder. The variation of expression of the muscarinic receptors (M1 to M5) between each study group was evaluated by qPCR with specific sets of primers. Comparisons between groups were conducted using a Single Factor ANOVA and two-way T-tests.

Results: RT-PCR demonstrated that all 5 muscarinic receptors were present in the bladder tissue (Fig 1A). Immunofluorescence revealed the presence of the 5 subtypes of muscarinic receptors in the urothelial cells, while smooth muscle cell bundles only express M2 and M3 in their periphery (Fig 1B). Previously, immunoblotting only displayed changes in the levels of receptors M2 and M3. Similarly, analysis of M2 and M3 receptors from qPCR data indicate a statistical significance ($p<0.05$) in variation of expression in study groups relative to control and SCT rats (Fig

1C).

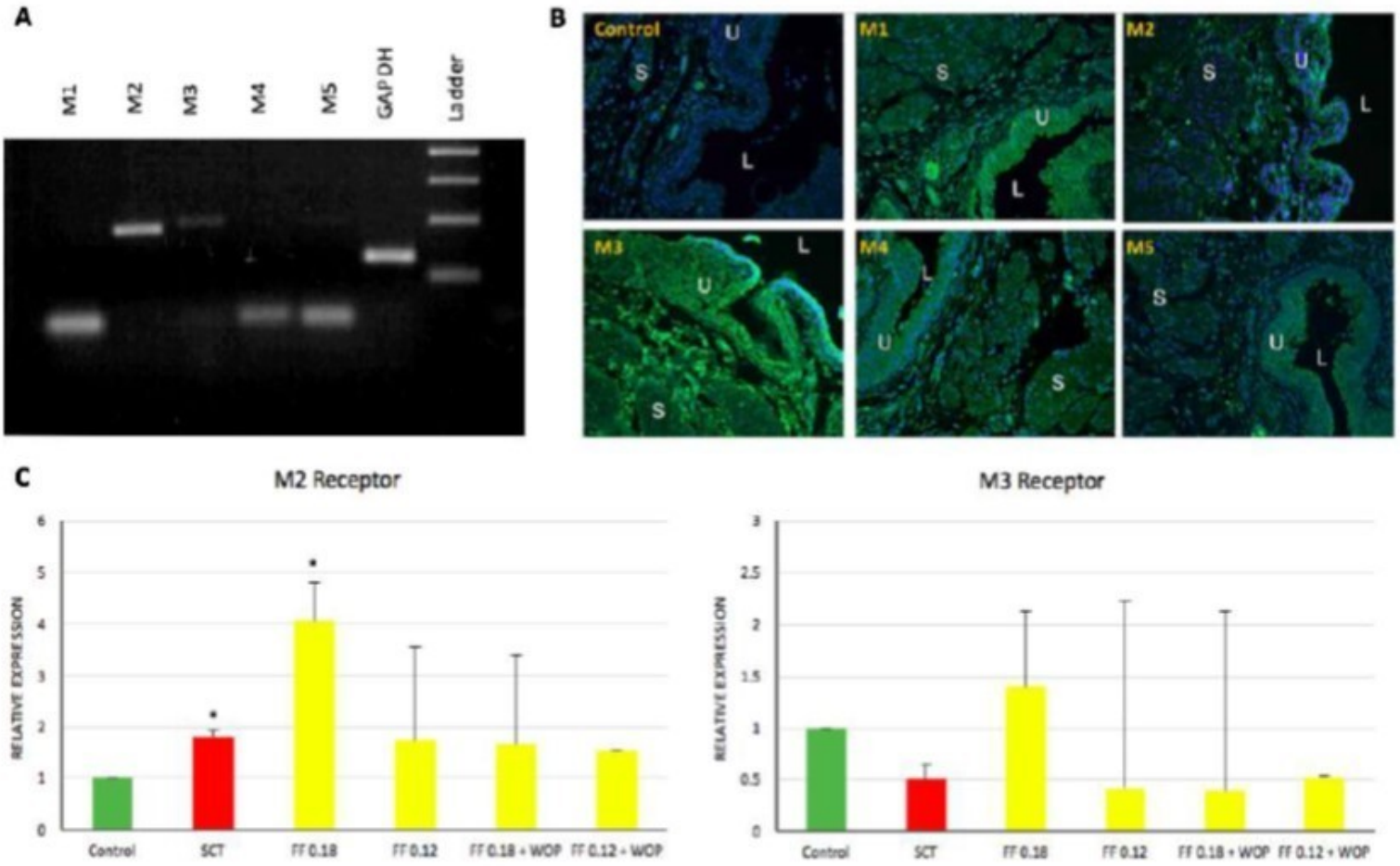

Figure 1. Analysis of Muscarinic Receptors, A- RT-PCR for each muscarinic receptor in the bladder tissue. B- Immunofluorescence of bladder with anti-muscarinic receptor staining (10x). C- Relative expression of M2 and M3 receptors compared to GAPDH, (* - $p<0.05$ compared to Control) among all study groups. WOP – Wash-Out Period. L – Lumen. U – Urothelium. S – Smooth Muscle Cells.

Conclusions: Early FF administration in a SCT rat model increases the expression of M2 muscarinic receptors in the bladder. This relative increase, along with previous results, could explain the cystometric changes previously described by early administration of FF in our model.

1. Biardeau X, et al. Early fesoterodine fumarate administration prevents neurogenic detrusor overactivity in a spinal cord transected rat model. PLoS One. 2017 Jan 6;12(1).