Mechanism of Increased Detrusor Contractility Induced by Mast Cell Activator Compound 48/80 in Murine Urinary Bladder

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The Tykocki Lab

Advancing Bladder Research

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INTRODUCTION:

- Compound 48/80 increases bladder wall compliance and detrusor contractility.
- Similar changes in compliance are seen in LUTS due to fibrosis[1].
- The rate of rise of each transient contraction is responsible for driving sensory outflow[2].
- Underlying mechanism of effects of Compound 48/80 in the bladder is unexplored.

We hypothesize that Compound 48/80 causes the release of prostaglandins and matrix metalloproteases to increase wall compliance and detrusor contractility.

METHODS: Pentaplanar Reflected Image Macroscopy

- All procedures followed institutional guidelines and were approved by the Institutional Animal Care and Use Committees of MSU.
- Transient pressure events, bladder volume, intravesical pressure, bladder wall stress and strain were measured simultaneously.

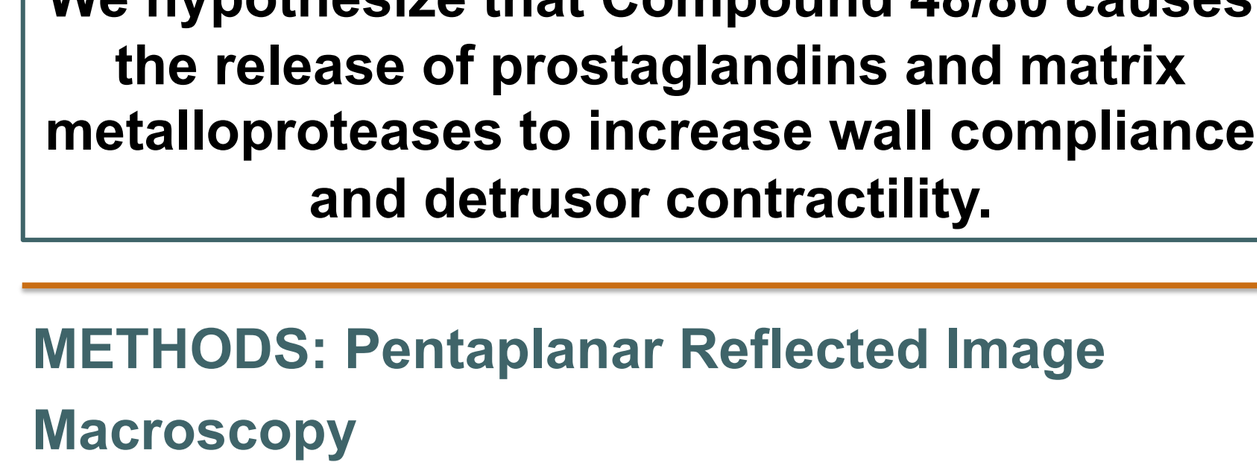

Fig. 1 (A) The PRIM system chamber. **(B)** Tracing of area and thickness in a frame of *ex vivo* filling and **(C)** model of bladder as an ellipsoid of radii c and e.

RESULTS

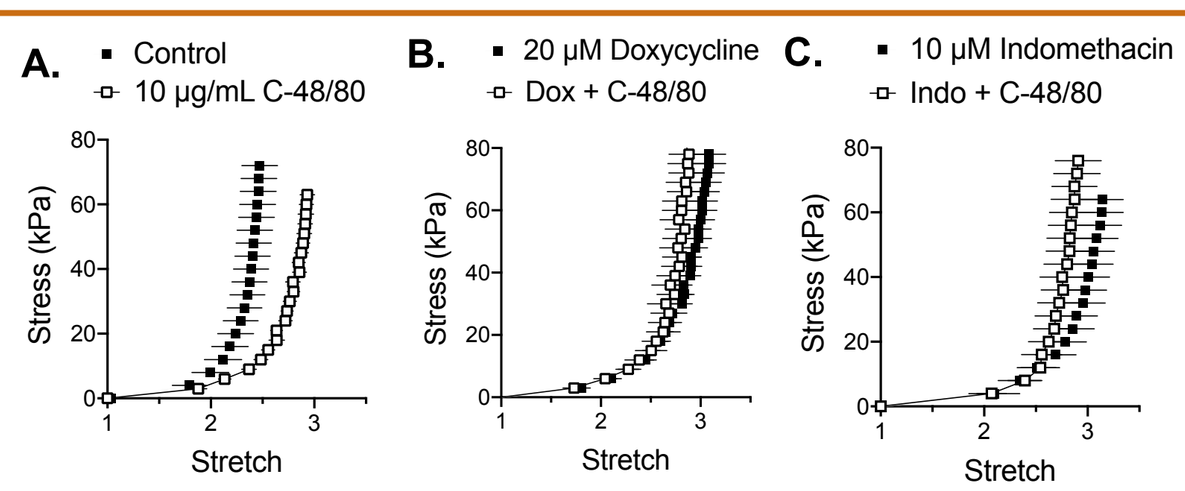

Fig. 2 (A) Compound 48/80 increases bladder wall compliance. This increase is blocked by MMP inhibitor Doxycycline **(B)** and COX inhibitor, Indomethacin **(C).**

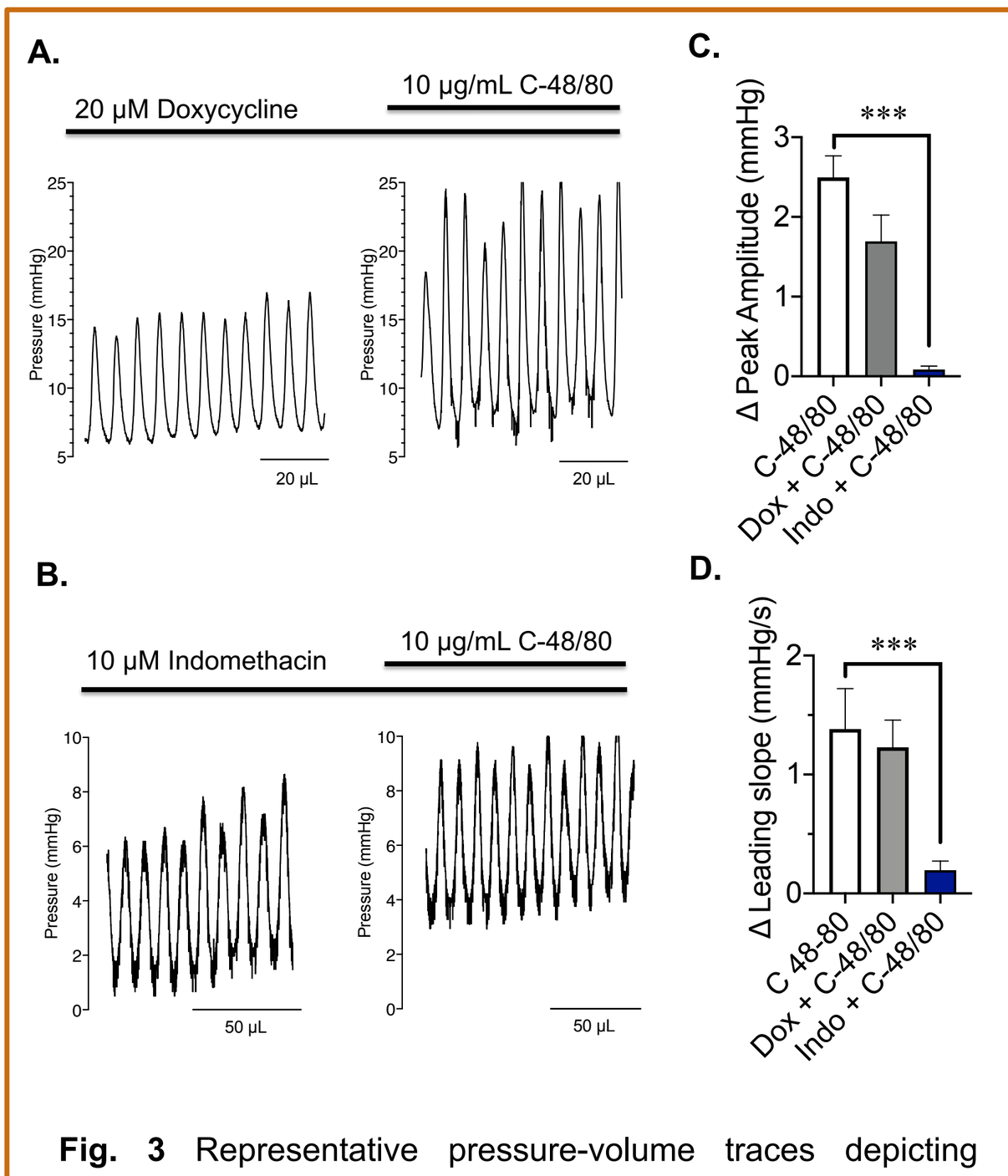

Fig. 3 Representative pressure-volume traces depicting effects of C-48/80 on transient contractions in the bladder in presence of doxycycline **(A)** and Indomethacin **(B).** Indomethacin abolishes but doxycycline does not abolish the increase in peak amplitude and leading slope caused by 10 µg/mL Compound 48/80 **(C-D).**

REFERENCES

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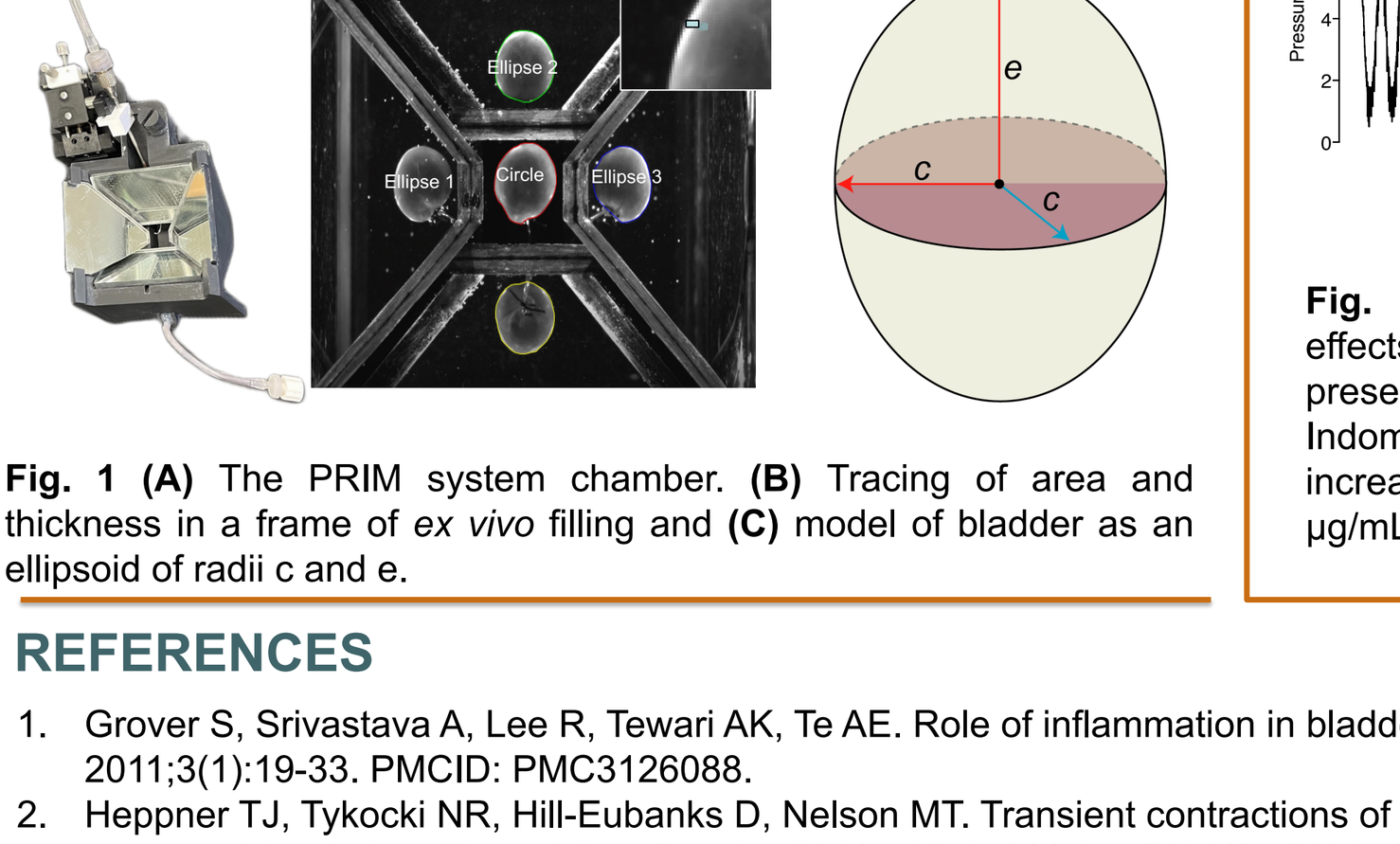
2. Heppner TJ, Tykocki NR, Hill-Eubanks D, Nelson MT. Transient contractions of urinary bladder smooth muscle are drivers of afferent nerve activity during filling. *J Gen Physiol*. 2016;147(4):323-35. PMCID: PMC4810069.

CONCLUSIONS



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