

Sacral Neuromodulation in Rats: Parameters and Pathways

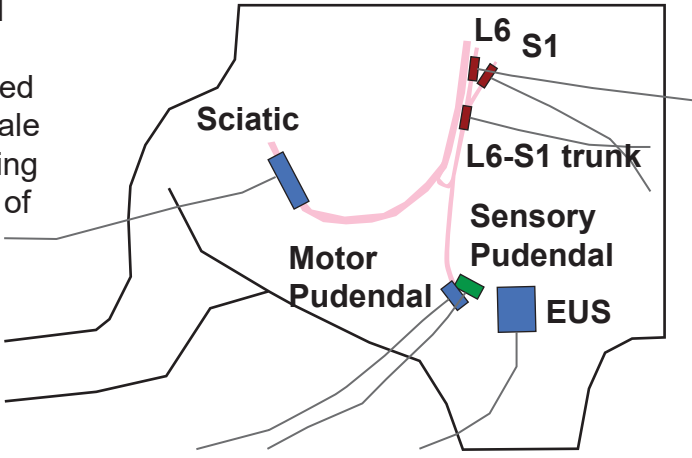
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Introduction and Objective: The neural pathways mediating the effects of sacral neuromodulation remain unclear. We conducted acute cystometry and mapping studies in female rats to determine the neural pathways mediating stimulation outcomes and quantify the effects of stimulation parameters.

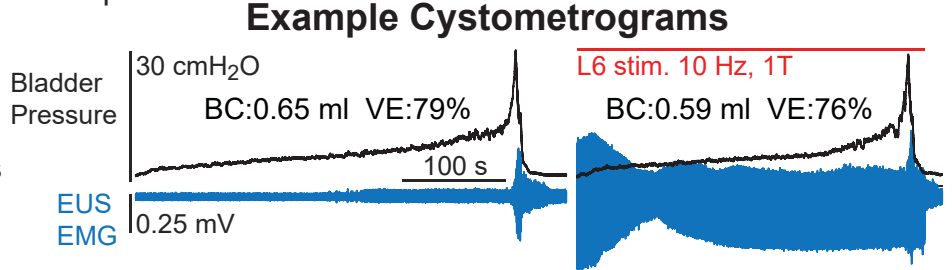
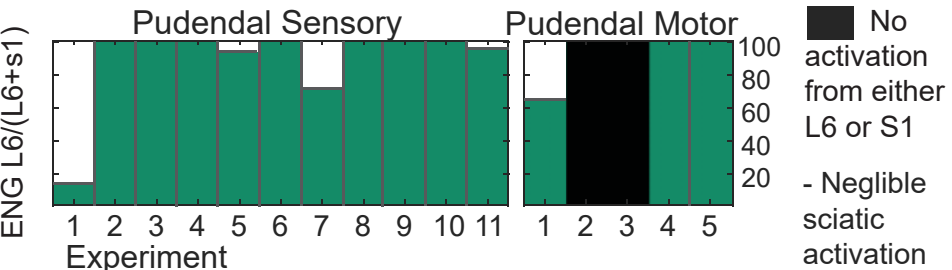
Stim Record Both

Methods:

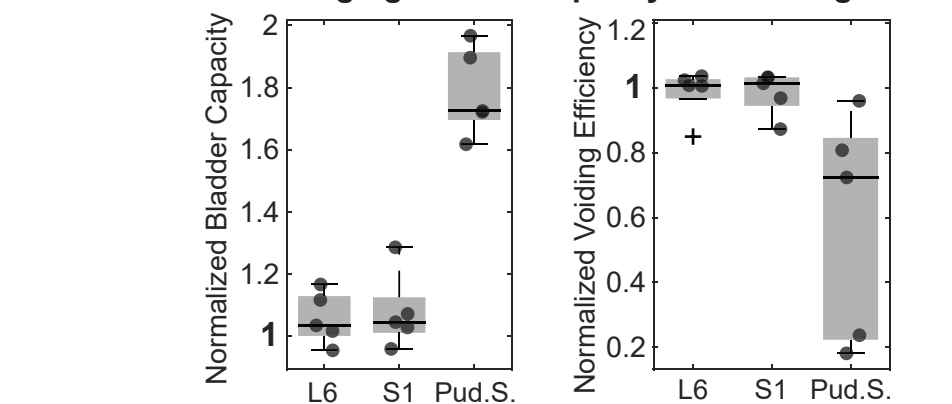
- female Charles-Dawley rats
- urethane anesthetized 1.2 g/kg SC
- motor movements used to detect L6, S1, and L6-S1 thresholds (1T)
- gallamine (paralytic) used during mapping to eliminate EMG contamination of neural recordings
- single fill cystometry conducted, with continuous stimulation at 10 Hz
- EUS EMG recorded during cystometry and used for paralytic validation and detection of sensory pudendal stimulation reflex threshold



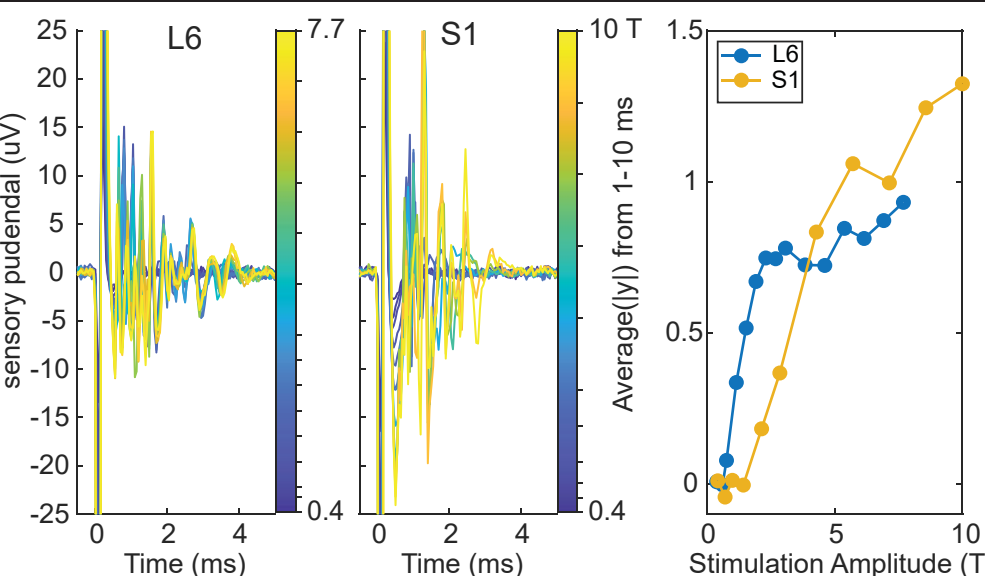
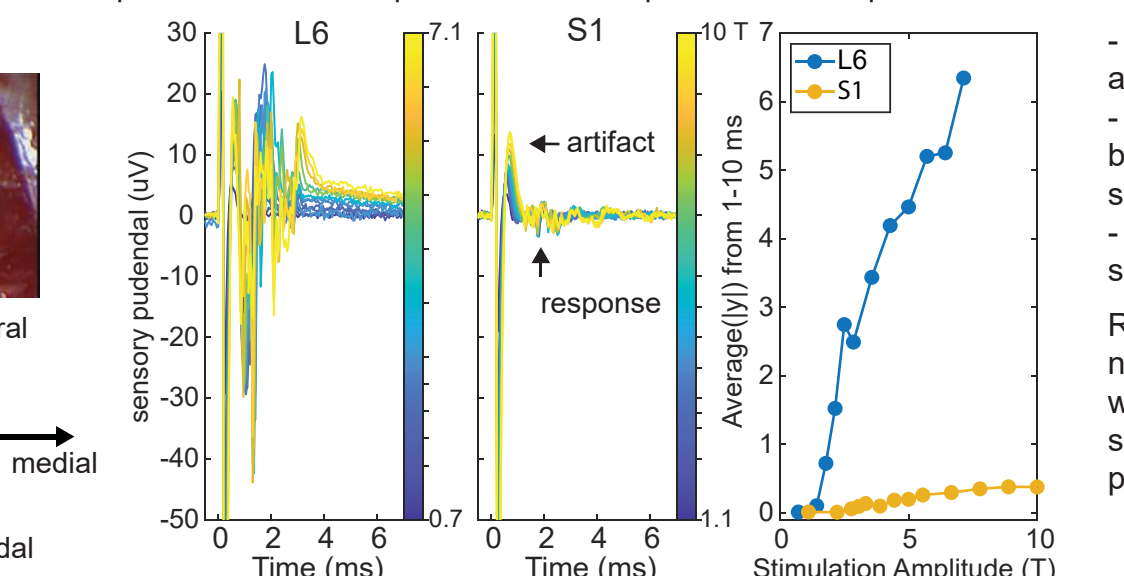
#2: S1 contributes minimally to the Pudendal Sensory Nerve based on ENG recordings (summarized here at 3T)



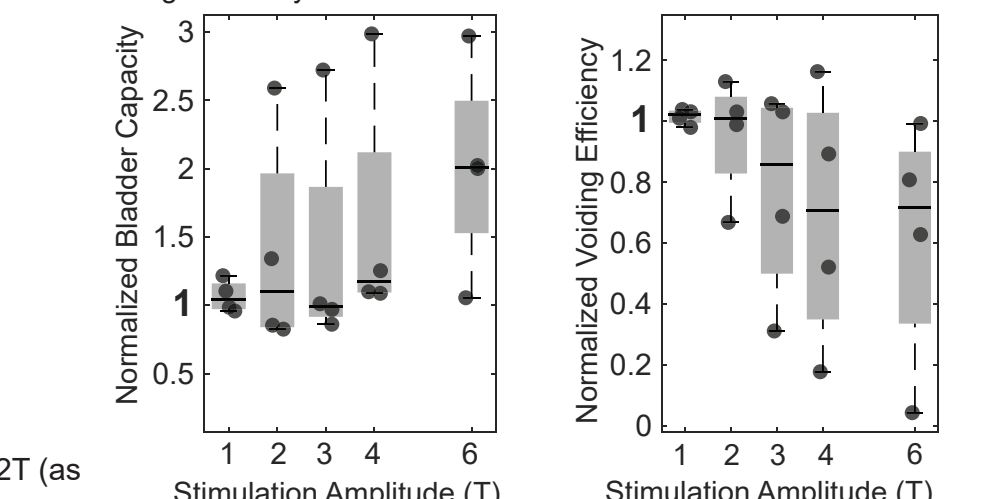
#3: 1-1.5T stimulation, chosen for being clinically relevant, was insufficient for changing bladder capacity and voiding efficiency.



Closer inspection indicates that neural recruitment does not saturate at 2T (as expected based on other nerves), but continues increasing at higher amplitudes. Here are representative examples from two experiments.



Recruitment observations match changes in bladder capacity and voiding efficiency from L6-S1 trunk stimulation.



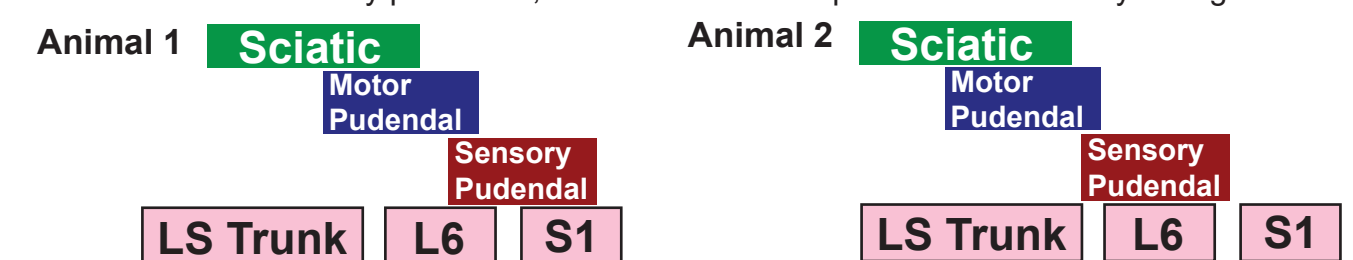
Conclusions

- S1 appears to contribute minimally to sensory pudendal activation.
- Neither L6 nor S1 stimulation at 1-1.5T, 10 Hz reliably changed bladder capacity or voiding efficiency whereas sensory pudendal stimulation reliably increased bladder capacity.
- Bladder capacity and voiding efficiency changes had not yet saturated at 4T as evidenced by changes at 6T.

Recent work in humans suggests that threshold amplitude sacral neuromodulation may not immediately impact urinary function in women with incontinence¹, consistent with our observations, and suggesting that low-amplitude sacral neuromodulation acts via a plasticity-dependent pathway.

¹Groenendijk et al. (2020) Neurourol Urodyn
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Model: After the first two mapping experiments the following model emerged
Relative order likely preserved, but location with respect to the roots may change.



Hypothesis: Efficacy of S1NS in increasing bladder capacity and increasing voiding efficiency correlates with relative activation (representation) of sensory pudendal nerve.

However, testing this hypothesis was limited by both anatomical and physiological challenges.

#1: Visually, the L6-S1 trunk receives only minor input from S1.

