

Improved Recovery from A Dual Nerve and Muscle Injury with Increased Frequency of Pudendal Nerve Stimulation

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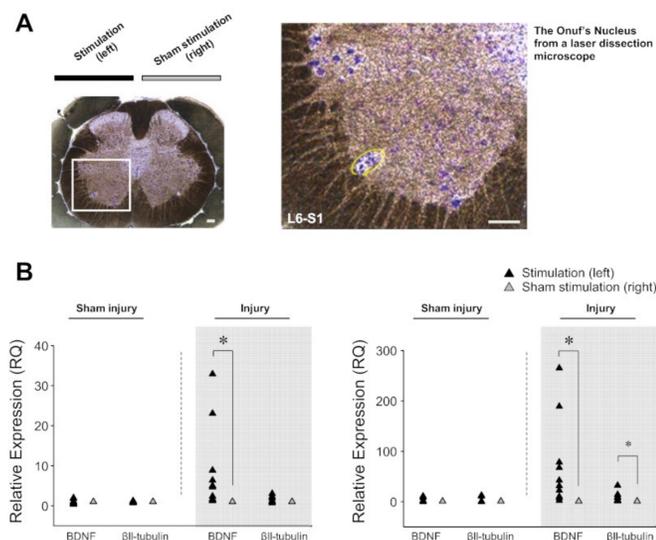
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Introduction

- Stress Urinary Incontinence (SUI) is the leakage of urine due to an increase in abdominal pressure that affects approximately 30% of women¹
- During childbirth the pudendal nerve (PN) and the muscle it innervates, the external urethral sphincter (EUS), are injured
- After childbirth women develop post-partum SUI associated with increased motor latency²
- While most women recover within one year, many will redevelop symptoms within 5 years, suggesting the PN does not regenerate properly after vaginal childbirth
- Current treatments do not address the underlying pathophysiology
- A dual nerve and muscle simulated childbirth injury model has been shown to have a delayed recovery compared to either injury alone⁴
- BDNF immunohistochemistry staining of the of the EUS showed⁵:
 - Decrease in BDNF after muscle injury alone
 - Increase in BDNF after nerve injury alone
 - Dysregulation of BDNF after the dual injury
- BDNF is not upregulated after a dual injury, suggesting its involvement in impaired regeneration of the PN following vaginal childbirth.

Regenerative Electrical Stimulation

- Electrical Stimulation (ES) has been known to increase neurite sprouting⁶
- In the early 2000's it was shown that ES upregulates BDNF and TrkB
- The Damaser lab has previously shown that BDNF is upregulated following a dual injury and twice weekly stimulation possible aiding in PN regeneration.⁷

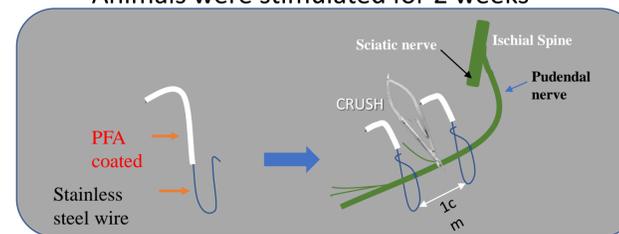


- Our hypotheses is that daily ES will improve recovery to a greater extent than less frequent stimulation**

Methods

Injury model

- Sprague-Dawley rats received a PN crush (PNC) and vaginal distension (VD) or a sham injury with or without electrode implantation with ES or with sham ES.
- 1 hour after the procedure, animals received 1 hour of ES (0.3mAmp, 20 Hz, 0.1ms) followed by either daily or 4 times a week stimulation under isoflurane anesthesia. Sham ES consisted of 1 hour of isoflurane anesthesia
- Animals were stimulated for 2 weeks



Groups:

- Sham No Implant** = Sham Injury + no electrodes
- Sham + Sham Stim** = Sham Injury + Sham ES
- PNC +VD + Sham Stim** = PNC + VD + Sham ES
- PNC + VD + 4/wk ES** = PNC + VD 4 times a week ES
- PNC + VD + daily ES** = PNC + VD daily ES

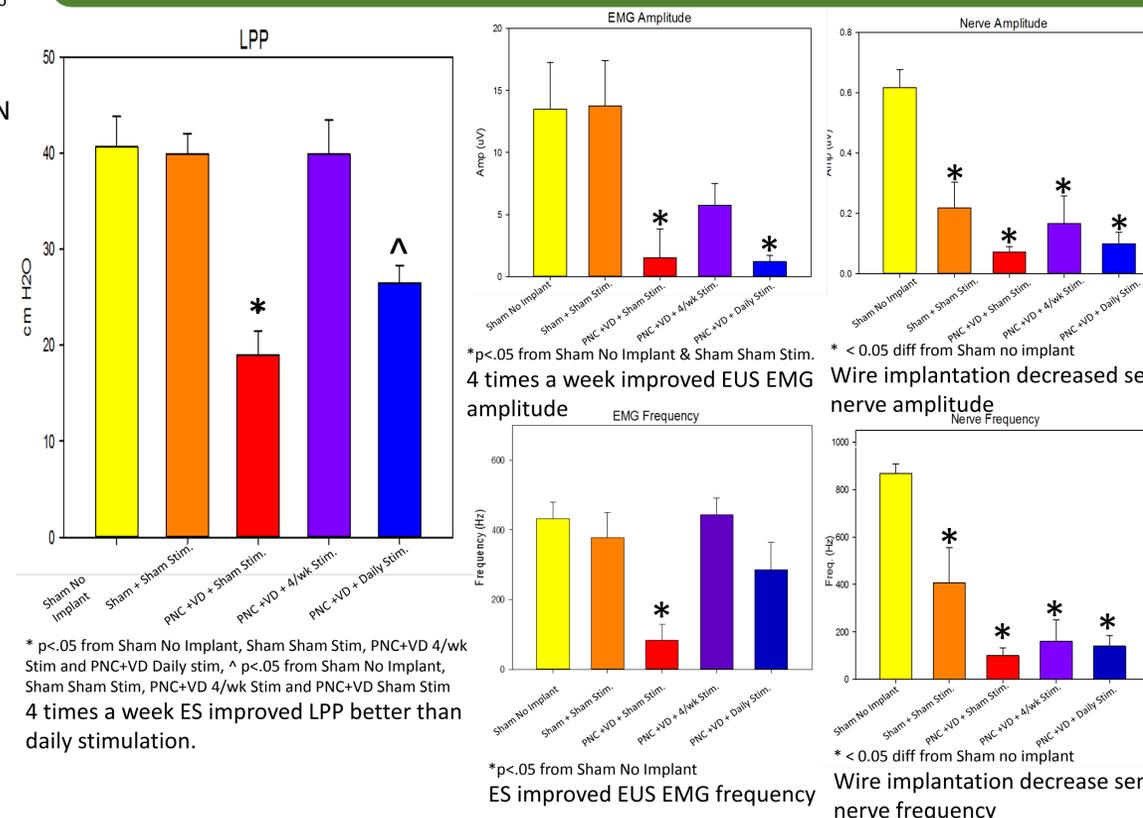
Functional outcome and Endpoint assessments 4 weeks after injury

- Leak Point Pressure (LPP) testing with simultaneous EUS electromyography (EMG) followed by Pudendal Nerve Sensory branch potential recordings.

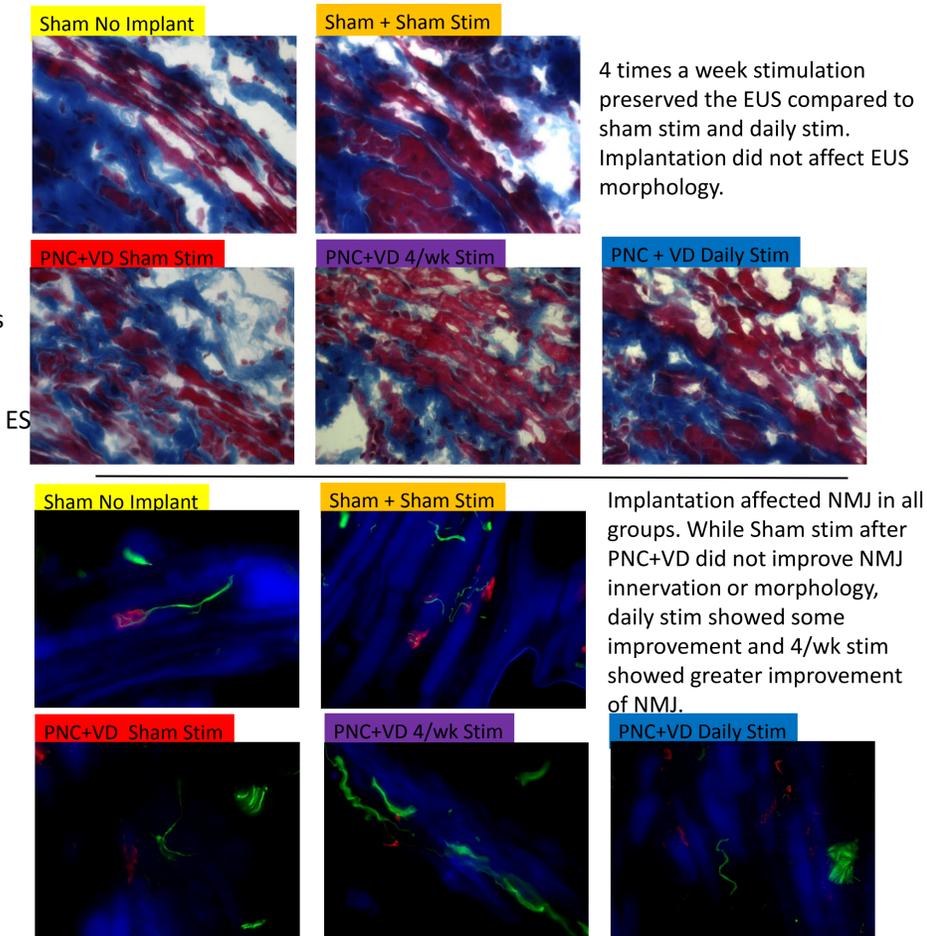
Histological Outcomes

- Masson's and Neuromuscular Junction (NMJ) staining of the EUS

Results



Results



Conclusion

- While ES accelerated LPP recovery, 4 times a week improved recovery better than daily stimulation, supported by the improvement in EMG amplitude and frequency
- Electrode implantation decreased sensory nerve amplitude and frequency, supported by the reduction in innervated NMJs
- Daily stimulation may have been too frequent, causing some damage to the PN and reduced accelerated regeneration.
- ES is a possible treatment for SUI, but electrode implantation is not advisable clinically after childbirth
- Future work will investigate clinically feasible stimulation routes

Acknowledgements

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