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CORRELATION OF SACRAL NERVE LEAD TARGETING AND UROLOGICAL EFFICACY: MOTOR MAPPING, ELECTRODE POSITION, AND STIMULATION AMPLITUDE

Hypothesis / aims of study

Sacral neuromodulation (SNM) is a clinically used therapy for refractory urge frequency and urge incontinent patients. Recent preclinical work in a large animal model [1] has focused on quantifying objective responses to SNM in order to examine questions of efficacy and durability. One simple hypothesis regarding therapy efficacy is that lead placement and locations are critical for delivering effective chronic therapy. The goal of this preclinical study was to retrospectively evaluate the relationship between implanted sacral lead locations, motor threshold values, motor response area (motor mapping), and acute urological efficacy. If acute location and physiological measurements are correlated, this model can be used to test and track therapy durability over time.

Study design, materials and methods

Twelve female polypay sheep were implanted with bilateral InterStim® devices (Model 3058) connected to quadripolar leads (model 3889) placed in the S2-4 foramina with S3 as the ideal target. CT scans were obtained immediately post-op and ≥ 12 months post-implantation. Three-dimensional rendering was performed on the CT images with MedCAD points placed on the S1 and S3 spinous processes, anterior S1 promontory, right and left lumbosacral joints, and at the center of each lead contact. This allowed determination of spatial coordinates for each contact relative to pelvic anatomy coordinates to compare contact locations between animals. Using a recently established sheep model [1], acute cystometry was performed to test responses to sacral nerve stimulation (0.21ms pulse-width, 10Hz) at maximum tolerable amplitude (MTA). MTA was determined by increasing stimulation amplitude in 0.1V increments until the sheep lifted the ipsilateral leg; amplitude was then decreased until the sheep placed the leg back on the floor. Motor threshold values were obtained by visual identification of the first motor response to 0.1V increases in stimulation amplitude. Using motor threshold responses, motor mapping was accomplished by responses being assigned to a map of the sheep's hindquarters subdivided into bilaterally symmetric regions.

Results

Similar to clinical results with InterStim patients [2], sheep can be categorized as either responders (n=6; 50%) or non-responders (n=6; 50%) based on ≥50% increase in bladder capacity to acute SNM. Using these criteria, there was a significant difference in motor mapping areas between responders and non-responders (Figure 1: chi-square; $p<0.05$) with peri-anal motor contractions more correlated with a urological response than activation of leg areas. Also, MTA values correlated with volume increases in bladder capacity (Pearson correlation; $p<0.05$) such that higher voltages lead to larger bladder capacity increases, and finally, lead contact position correlated with urological response (ANOVA; $p<0.05$). Using a generalized Procrustes analysis, the 3-dimensional distribution of all eight contacts (L0-3 and R0-3) across 17 leads placed in S3 in 12 animals (the remaining leads were in either S2 or S4) were aligned to a transformed sheep sacral projection to position all contact locations in the same three dimensional space allowing for comparison across animals. Figure 2 shows that the variability of distribution of the contacts was greater in the distal locations [0 and 1; left mean distance from center = 7.3 ± 1.8 mm (standard deviation; SD) ; right mean distance from center = 6.8 ± 1.3 m] than in the proximal locations (2 and 3; left mean distance from center = 5.8 ± 0.86 mm; right mean distance from center = 4.3 ± 0.35 mm) (ANOVA; alpha = 0.05; $F_{(3, 64)} = 20.55$; $p< 0.0001$).

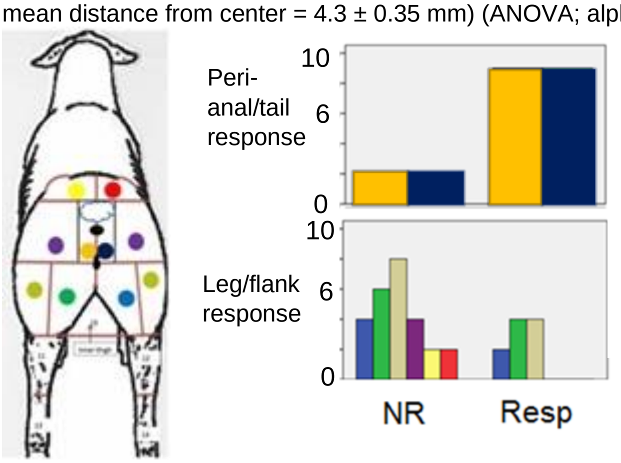

Figure 1. Motor mapping of first motor response to sacral nerve stimulation. Motor threshold responses were mapped to one or more of 8 bilaterally symmetric regions (color coded in the left panel to match the bar graphs in the right panel). Right panel shows the sum of motor responses in the peri-anal areas (upper panel, blue and gold columns) of non-responders (NR; left two columns) and responders (Resp; right two columns) and the other leg areas (lower panel) of NR (left 6 columns) and Resp (right 3 columns).

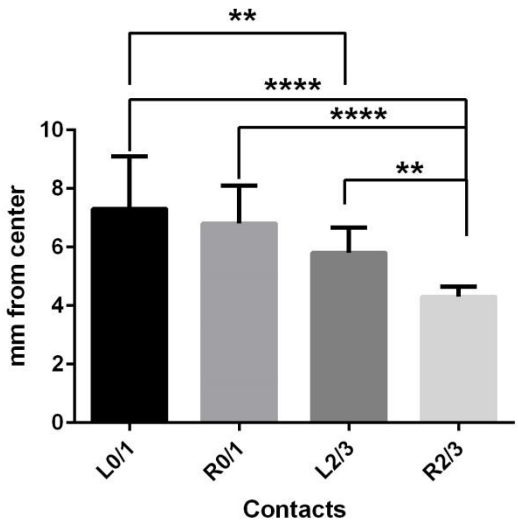

Figure 2. Distance of each contact from best fit center on Procrustes-transformed 3D coordinate system. Error bars = standard deviation. Asterisks denote significance using Tukey's multiple comparisons post-hoc analysis: ** = $p < 0.001$; **** = $p < 0.0001$.

<u>Interpretation of results</u>

1. Sheep that were categorized as responders showed a motor response in peri-anal areas significantly more often than non-responders.
2. Maximum tolerable amplitude weakly correlated with increased bladder capacity: higher amplitude stimulation = larger bladder capacity increase.
3. Activation of lead contacts proximal to the sacral foramen produced more reliable urological results than did activation of distal contacts.

<u>Concluding message</u>

These results suggest that an appropriately positioned lead will elicit motor responses from specific, identifiable muscle groups and is essential for effective sacral neuromodulation therapy. Future work will characterize changes in lead location over time to provide a temporal correlation of this relationship.

<u>References</u>

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<u>Disclosures</u>

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