Published in final edited form as:

Am J Gastroenterol. 2023 December 01; 118(12): 2242–2246. doi:10.14309/ajg.0000000000002394.

Pathoetiology of Levator Ani Syndrome and its treatment with Translumbosacral Neuromodulation Therapy

Yun Yan[1], **Askin Erdogan**[1], **Enrique Coss Adame**[1], **Satish SC Rao**[1]

[1]Division of Neurogastroenterology/Motility, Medical College of Georgia, Augusta University, Augusta, GA

Abstract

Introduction: The pathoetiology and treatment of levator ani syndrome (LAS) remains unclear.

Methods: We evaluated pathophysiology using translumbosacral motor evoked potentials (MEP), and anorectal manometry in LAS patients and compared with healthy controls. A cohort underwent Translumbosacral Neuromodulation Therapy (TNT).

Results: Lumbar and sacral MEP latencies were prolonged in 32 LAS patients compared to 31 controls ($p<0.013$), with higher prevalence of anal neuropathy ($p=0.026$). TNT improved anorectal pain ($p=0.003$), and neuropathy ($p<0.02$) in 13 LAS patients.

Conclusions: LAS patients demonstrate significant lumbo-sacral neuropathy that may cause anorectal pain. TNT improved anorectal pain and neuropathy, providing a novel therapeutic option.

Graphical Abstract

Please address correspondence to: Satish S.C. Rao, M.D., Ph.D., FRCP (LON), Division of Gastroenterology and Hepatology, 1120 15th Street, AD 2226, Augusta, GA, 30912, Office: 706-721-2238, FAX: 706-723-0382, srao@augusta.edu.

Contributions of each author:

Satish Rao – Project director and principal investigator, study concept and design, data analysis and interpretation, conducting neurophysiology test, anorectal ultrasound and translumbosacral neuromodulation therapy, manuscript preparation, overall supervision and critical revision

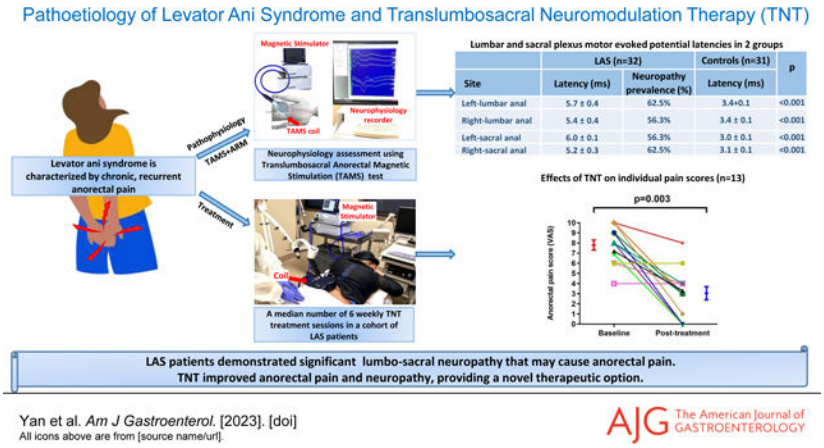
Yun Yan-Manuscript preparation, data collection and analysis, table, and figure.

Askin Erdogan-Data collection and figure

Enrique Coss Adame-Data collection

All authors have approved the final version of the manuscript submitted

Conflicts of Interest: All authors declare no conflicts of interests with this study



Keywords

TAMS; Neuromodulation therapy; Levator ani syndrome; Neuropathy; anorectal

Introduction:

Levator ani syndrome (LAS) is characterized by chronic, recurrent, anorectal pain, typically described as “heavy pressure”, or sharp or “sitting on a golf ball” like sensation, with a prevalence of 6%[1]. Its etiology is unknown, although levator ani spasm, anal hypertonia, dyssynergic defecation[1] and prior pelvic surgery have been implicated[1]. Whether patients with LAS have an underlying neuropathy or anorectal sensorimotor dysfunction(s) or altered morphology has not been systematically assessed. Further, there are no effective treatments for LAS[1].

We aimed to evaluate the pathophysiologic role of lumbosacral neuropathy and/or anorectal sensori-motor dysfunction in LAS patients. Also, we performed an exploratory trial of translumbosacral neuromodulation therapy (TNT) based on observations that TNT improved neuropathy in patients with fecal incontience[2].

Methods

Consecutive patients with LAS (Rome III)[3] and health controls were evaluated over 10 years, and included in this retrospective case-control study. All patients and controls had detailed digital rectal examination[4], neurophysiological evaluation using Translumbosacral Anorectal Magnetic Stimulation (TAMS) test[5], anorectal sensori-motor evaluation with anorectal manometry and balloon expulsion test[6] and anal ultrasound. Subsequently, a cohort of LAS patients who had failed standard treatment approaches were enrolled in an open labeled, proof of concept trial of TNT therapy[2]. The study was approved by Augusta University Institutional Review Board (1323091). Information regarding inclusion and exclusion criteria, study protocols, measurements, and statistical analysis are provided in supplementary section.

Results

Demographics

Thirty-two LAS patients and 31 healthy controls participated. Demographic features are summarized in Supplement Table 1. Only 22/31 controls underwent anorectal physiology. Digital rectal examination reproduced pain in one or more levator ani muscle quadrants, but the most painful quadrant varied across subjects (Supplement Table 1). The mean pain severity score in each of the 4 quadrants was similar, although slightly more severe posteriorly ($p>0.05$). A cohort of 13 patients (48.6 ± 1.7 years, F/M=9/4) received a median number of 6 TNT treatment sessions (range 2 – 8).

Lumbar and sacral plexus neurophysiology

Bilateral translumbo-anal and translumbo-rectal, transsacro-anal and transsacro-rectal MEP latencies were significantly prolonged in LAS patients than controls ($p<0.013$, Table 1, Fig.1A). Neuropathy was patchy, on average involved 3.4/8 loci. Anal neuropathy (84.4%) was more prevalent ($p=0.026$) than rectal neuropathy (59.4%).

Anorectal manometry

LAS patients had lower maximum and sustained squeeze pressures than controls ($p<0.0001$, Table 1). Anal residual pressure was higher ($p=0.002$), and defecation index was lower ($p<0.0001$) in LAS patients than controls suggesting dyssynergia. Balloon expulsion time was prolonged in LAS patients than controls ($p=0.006$). Eleven (34.3%) patients met criteria for dyssynergic defecation[1]. Rectal sensory thresholds were similar between groups.

Anal endosonography

The proportion of LAS patients with external anal sphincter (EAS) and internal anal sphincter (IAS) defects were comparable to controls (Supplement Table 1). The thickness of puborectalis was minimally higher ($p<0.023$) than controls, but IAS and EAS were similar (Supplement Table 1).

Effects of TNT

Thirteen patients, with a mean pain severity score of 7.9/10 participated. (Supplement Fig. 1). After TNT, pain scores improved significantly (7.9 ± 0.5 vs. 3.0 ± 0.7, $p=0.003$) (Supplement Fig. 1). Overall, 10/13 (76.9%) patients reported ≥30% improvement and 9/13 (69%) had ≥50% improvement and 3 had complete resolution. Although stool consistency improved ($p=0.028$), other bowel symptoms were unchanged (Supplement table 2). Baseline MEP latencies were prolonged in LAS patients compared to controls ($p<0.004$, Table 2). After TNT, the bilateral lumbo-anal and sacro-anal MEP latencies significantly improved ($p<0.01$, Table 2, Fig. 1B,C), with normalization of MEPs in 5 subjects. TNT was well tolerated, without adverse events.

Discussion

We found that patients with LAS demonstrated bilateral lumbar and sacral plexus neuropathy that affected the anal region more commonly than the rectal site. Further,

in a pilot study TNT improved anorectal pain together with improvement in neuropathy. These findings suggest that a neuropathophysiological dysfunction could be an underlying mechanism for anorectal pain in LAS.

The innervation of the levator ani muscle is complex involving both the autonomic and somatic nerves[7]. The autonomic nerves arise from the inferior hypogastric plexus (S1-S4 ganglion), the pelvic splanchnic nerves (S1 to S4), and the hypogastric plexus lumbar splanchnic nerves (L2-L4) [7]. The somatic innervation includes the pudendal nerve (S2-S4)[7] and the levator ani nerve (S3, S4)[7]. Here, we used translumbosacral anorectal magnetic stimulation (TAMS) test, as it provides a comprehensive assessment of the entire spino-anorectal nerve innervation and thereby provide mechanistic insights regarding the complex neurophysiology in LAS[5]. The prolonged bilateral, translumbo-anorectal, and transsacro-anorectal MEP latencies suggest that lumbosacral neuropathy could be a significant mechanism for anorectal pain in LAS patients.

Previous studies have suggested that the pathophysiology of LAS may involve anal hypertonia, levator ani spasm, and dyssynergic defecation[1]. We found that anal sphincter pressures were lower than healthy controls suggesting that anal hypertonia is unlikely. Rectal hypersensitivity is also unlikely as the rectal sensory thresholds were similar to controls. Thicker anal sphincters have been suggested anecdotally[1], but anal sphincter thickness was similar to controls. We found dyssynergic defecation in 34.3% of LAS patients, unlike 87% as reported previously[1], possibly due to differences in geographic prevalence or testing methods.

Current treatments for LAS remain unsatisfactory. Uncontrolled studies suggest that sitz baths, muscle relaxants, diathermy, tricyclic antidepressants, and sacral nerve stimulation (SNS) may be helpful[8]. A randomized controlled study showed that biofeedback therapy was more effective than electrogalvanic stimulation and anorectal massage and sitz baths[1]. Two retrospective studies of botulinum toxin showed short term relief in 43%−56% of patients, but a randomized double blind trial showed that it was ineffective[9]. Vaginal diazepam was also ineffective[14]. These observations suggest that relieving levator ani spasm is ineffective and that a myopathy is less likely in the pathogenesis of pain in LAS.

In contrast, three small case series showed improvement of pain with sacral nerve stimulation (SNS)[10–12], although postoperative complications including infection, pain, and device replacement were observed[10–12]. Nevertheless, neuromodulation may be helpful.

Our pilot study with TNT showed significant improvement of anorectal pain in 76.9% of patients along with improvements in the lumbar and sacral plexus neuropathy. This suggests that neuromodulation therapy, a noninvasive outpatient procedure that is safe and well tolerated may be useful in LAS patients.

Our study limitations include assessment of a small number of LAS patients. Also, although all healthy subjects had TAMS test, they were younger and some did not have manometry, limiting the interpretation of anorectal sensori-motor physiology. However, unlike other studies, we used Rome III criteria and examined a well characterized group of patients[3]. Also the treatment assessment was short-term, and its durability is unknown.

In conclusion, our study reveals that patients with LAS demonstrate significant lumbar and sacral plexus neuropathy associated with anorectal pain. TNT improved anorectal pain, and lumbosacral neuropathy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgement:

This work was supported in part by NIH grants 5R21 DK104127-02, 1U01DK115575-01 and 5R01DK057100-10. We sincerely thank Ms. Anne DeWitt and Arie Mack for excellent nursing support and Ms. Helen Smith for superb secretarial assistance.

References

1. Rao SS, Bharucha AE, Chiarioni G, et al. Anorectal Disorders. Gastroenterology 2016;150:1430–1442.
2. Rao SS, Xiang X, Sharma A, et al. Translumbosacral neuromodulation therapy for fecal incontinence: a randomized frequency response trial. Am J Gastroenterol 2021;116:162–170. [PubMed: 32740081]
3. Bharucha AE, Wald AM. Anorectal disorders. Am J Gastroenterol 2010;105:786–94. [PubMed: 20372131]
4. Rao SSC. Rectal Exam: Yes, it can and should be done in a busy practice! Am J Gastroenterol 2018;113:635–638. [PubMed: 29453382]
5. Yan Y, Sharma A, Herekar AA, et al. Translumbosacral Anorectal Magnetic Stimulation Test for Fecal Incontinence. Diseases of the Colon & Rectum 2022;65:83–92. [PubMed: 34670958]
6. Tetangco E, Yan Y, Rao S. Performing and analyzing high-resolution anorectal manometry. Neuro Gastro Latam Rev 2018;2:123–32.
7. Aurore V, Rothlisberger R, Boemke N, et al. Anatomy of the female pelvic nerves: a macroscopic study of the hypogastric plexus and their relations and variations. J Anat 2020;237:487–494. [PubMed: 32427364]
8. Atkin GK, Suliman A, Vaizey CJ. Patient characteristics and treatment outcome in functional anorectal pain. Dis Colon Rectum 2011;54:870–5. [PubMed: 21654255]
9. Rao SS, Paulson J, Mata M, et al. Clinical trial: effects of botulinum toxin on Levator ani syndrome--a double-blind, placebo-controlled study. Aliment Pharmacol Ther 2009;29:985–91. [PubMed: 19222415]
10. Falletto E, Masin A, Lolli P, et al. Is sacral nerve stimulation an effective treatment for chronic idiopathic anal pain? Dis Colon Rectum 2009;52:456–62. [PubMed: 19333046]
11. Govaert B, Melenhorst J, van Kleef M, et al. Sacral neuromodulation for the treatment of chronic functional anorectal pain: a single center experience. Pain Pract 2010;10:49–53. [PubMed: 19735362]
12. Dudding TC, Thomas GP, Hollingshead JR, et al. Sacral nerve stimulation: an effective treatment for chronic functional anal pain? Colorectal Dis 2013;15:1140–4. [PubMed: 23692279]

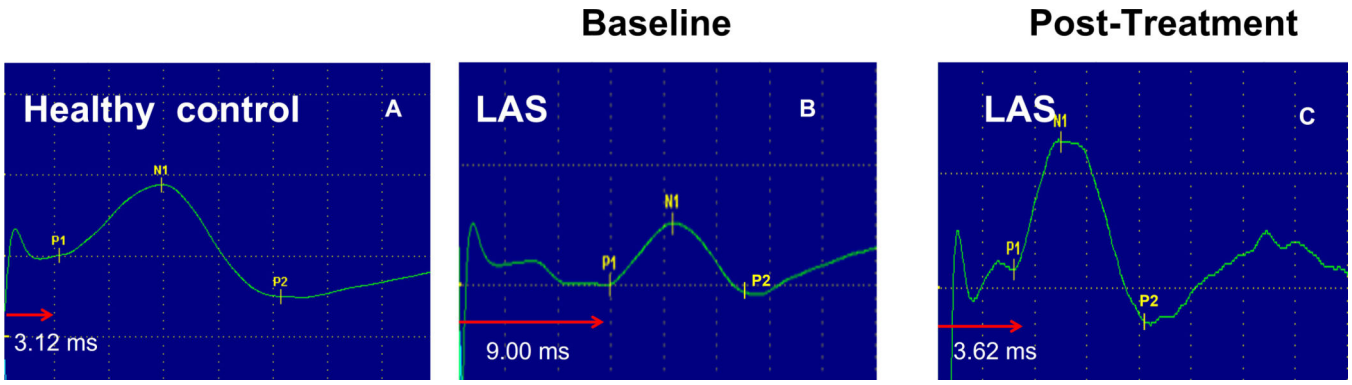


Figure 1.

Typical MEP responses from a healthy subject (A) and baseline (B) and post-TNT treatment (C) in a patient with levator ani syndrome showing significant decrease in the P1 latency time, and suggesting improvement in the lumbosacral neuropathy.

Table 1.

Motor evoked potential (MEP) latencies and the prevalence of neuropathy at each site and anorectal sensorimotor findings in levator ani syndrome (LAS) patients and healthy controls. (Mean ± SEM)

	LAS (n=32)	Healthy controls (n=31)		p
Neurophysiology assessment with MEP latencies and prevalence of neuropathy				
	Latency	Neuropathy %	Latency	
Lumbar				
Left-lumbar anal (ms)	5.7 ± 0.4	62.5%	3.4+0.1	<0.001
Right-lumbar anal (ms)	5.4 ± 0.4	56.3%	3.4 ± 0.1	<0.001
Left-lumbar rectal (ms)	3.8 ± 0.3	31.3%	2.9 ± 0.1	0.013
Right-lumbar rectal (ms)	3.9 ± 0.3	18.8%	3.2 ± 0.1	0.149
Sacral				
Left-sacral anal (ms)	6.0 ± 0.1	56.3%	3.0 ± 0.1	<0.001
Right-sacral anal (ms)	5.2 ± 0.3	62.5%	3.1 ± 0.1	<0.001
Left-sacral rectal (ms)	3.9 ± 0.3	21.9%	2.9 ± 0.2	0.001
Right-sacral rectal (ms)	3.9 ± 0.3	28.1%	3.0 ± 0.1	0.005
Anorectal physiology	**LAS (n=32)**		**Healthy controls (n=22)**	**p**
Anorectal pressure				
Anal resting pressure (mm Hg)	78.7 ± 5.3		93.0 ± 5.0	0.09
Maximum squeeze pressure (mm Hg)	155.1 ± 12.5		261.1 ± 11.6	<0.0001
Sustained squeeze pressure (mm Hg)	94.2 ± 6.9		146.0 ± 8.7	<0.0001
Rectal straining pressure (mm Hg)	52.8 ± 3.6		67.1 ± 5.8	0.05
Anal residual pressure (mm Hg)	79.2 ± 5.8		51.9 ± 4.7	0.002
Defecation index	0.7 ± 0.1		1.7 ± 0.3	<0.0001
Rectal sensory thresholds				
First sensation (ml)	19.0 ± 3.3		20.0 ± 1.7	0.067
Constant sensation (ml)	61.6 ± 10.4		60.9 ± 6.3	0.324
Desire to defecate (ml)	114.4 ± 13.3		107.7 ± 10.4	0.78
Urge to defecate (ml)	190.0 ± 14.8		174.5 ± 14.0	0.649
Maximum tolerable volume (ml)	220.1 ± 14.8		241.1 ± 14.7	0.314
Balloon expulsion time (s)	91.4 ± 21.5		28.9 ± 9.4	0.006

Table 2:

The bilateral lumbar and sacral MEPs in healthy controls compared with these at baseline and post treatment from a cohort of LAS patients who underwent Translumbosacral Neuromodulation Treatment. (Mean ± SEM)

	Healthy controls (n=31)	LAS patients		p	p
		Baseline (n=13)	Post-Treatment (n=13)	LAS vs control	Pre vs Post treatment
Lumbar					
Left-lumbar anal (ms)	3.4+0.1	6.6 ± 0.6	3.3 ± 0.3	<0.001	0.002
Right-lumbar anal (ms)	3.4 ± 0.1	6.4 ± 0.5	3.6 ± 0.3	<0.001	0.003
Left-lumbar rectal (ms)	2.9 ± 0.1	3.4 ± 0.3	3.1 ± 0.2	0.123	0.433
Right-lumbar rectal (ms)	3.2 ± 0.1	3.9 ± 0.4	3.2 ± 0.2	0.080	0.209
Sacral					
Left-sacral anal (ms)	3.0 ± 0.1	6.7 ± 1.0	4.0 ± 0.3	<0.001	0.002
Right-sacral anal (ms)	3.1 ± 0.1	5.2 ± 0.5	3.7 ± 0.3	<0.001	0.01
Left-sacral rectal (ms)	2.9 ± 0.2	4.2 ± 0.4	3.3 ± 0.4	0.001	0.021
Right-sacral rectal (ms)	3.0 ± 0.1	3.8 ± 0.3	3.6 ± 0.4	0.004	0.477