



Case Studies in Female Sexual Health

Persistent Genital Arousal Disorder/Genitopelvic Dysesthesia (PGAD/GPD)

Irwin Goldstein, MD, IF
Sexual Medicine, Alvarado Hospital

Disclosures

IG - No relevant disclosures

PGAD/GPD IS A MONSTER

EDITORIAL

SEXUAL MEDICINE REVIEWS

Making a Difference: Persistent Genital Arousal Disorder

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17 yo woman with lifelong PGAD

“PGAD feels as though I am being molested every waking moment of every hour by my own body”

**Essentials of
Female Sexual
Health**
June 4th, 2021

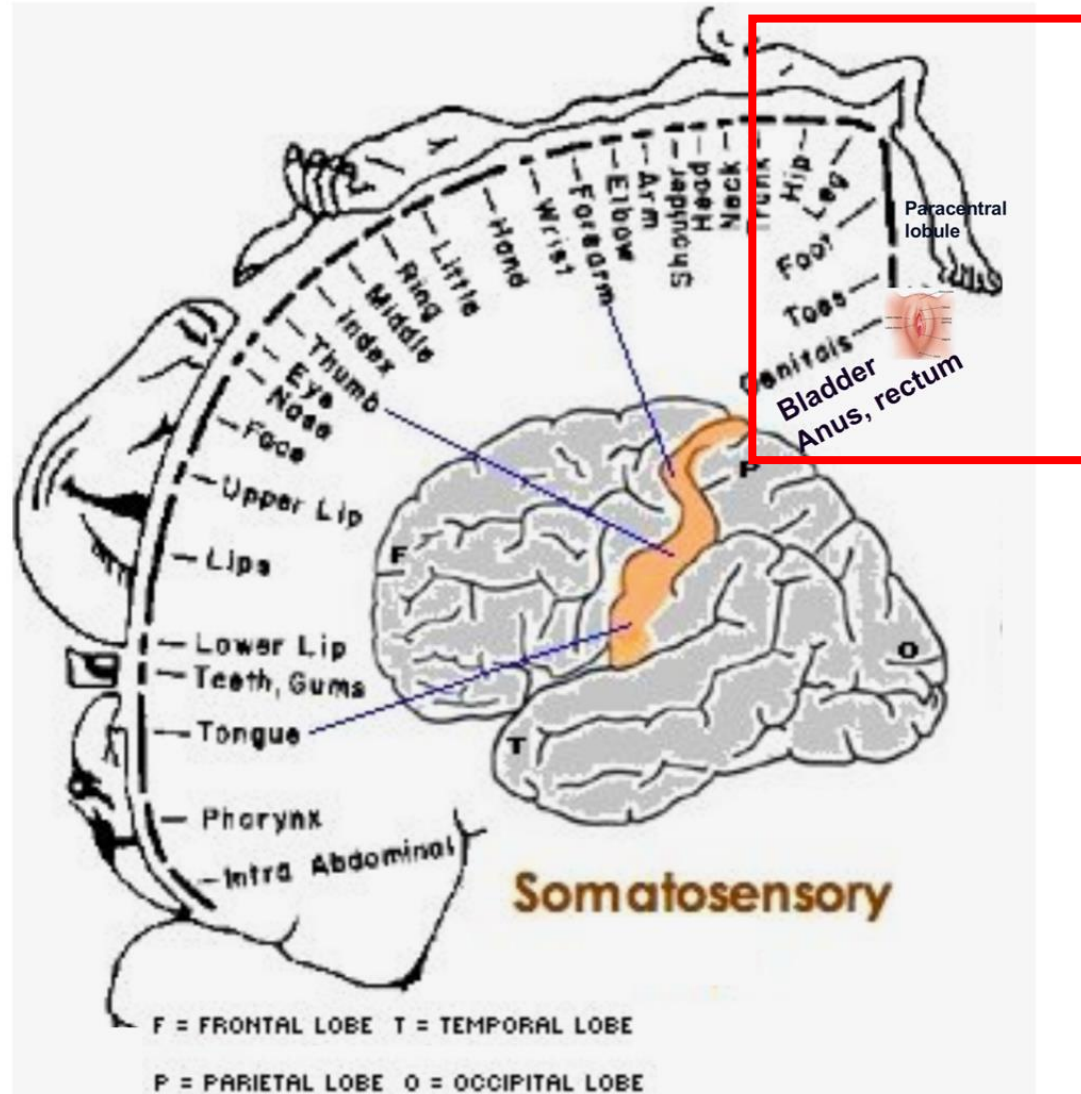
International Society for the Study of Women's Sexual Health (ISSWSH) Review of Epidemiology and Pathophysiology, and a Consensus Nomenclature and Process of Care for the Management of Persistent Genital Arousal Disorder/Genito-Pelvic Dysesthesia (PGAD/GPD)

Irwin Goldstein, MD,^{1,2} Barry R. Komisaruk, PhD,³ Caroline F. Pukall, PhD,⁴ Noel N. Kim, PhD,⁵
Andrew T. Goldstein, MD,⁶ Sue W. Goldstein, BA, CSE,² Rose Hartzell-Cushanick, PhD, EdS,²
Susan Kellogg-Spadt, PhD, CRNP,^{7,8} Choll W. Kim, MD, PhD,⁹ Robyn A. Jackowich, PhD,⁴ Sharon J. Parish, MD,¹⁰
April Patterson, PT, MSPT,¹¹ Kenneth M. Peters, MD,¹² and James G. Pfaus, PhD¹³

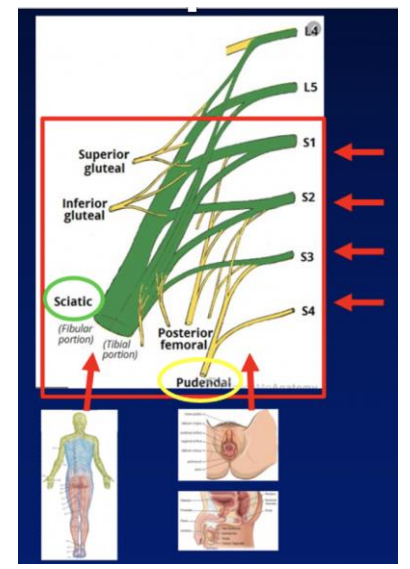
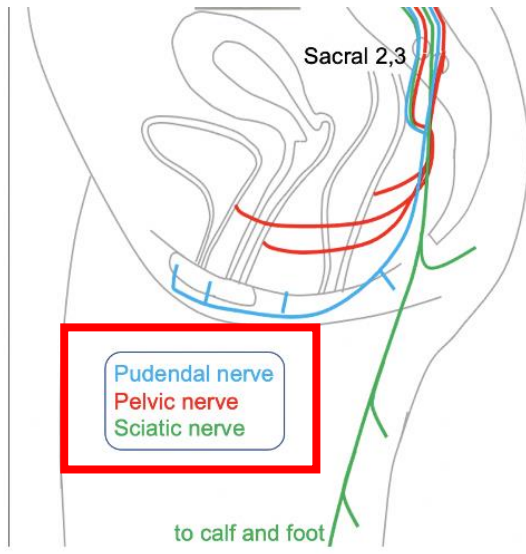
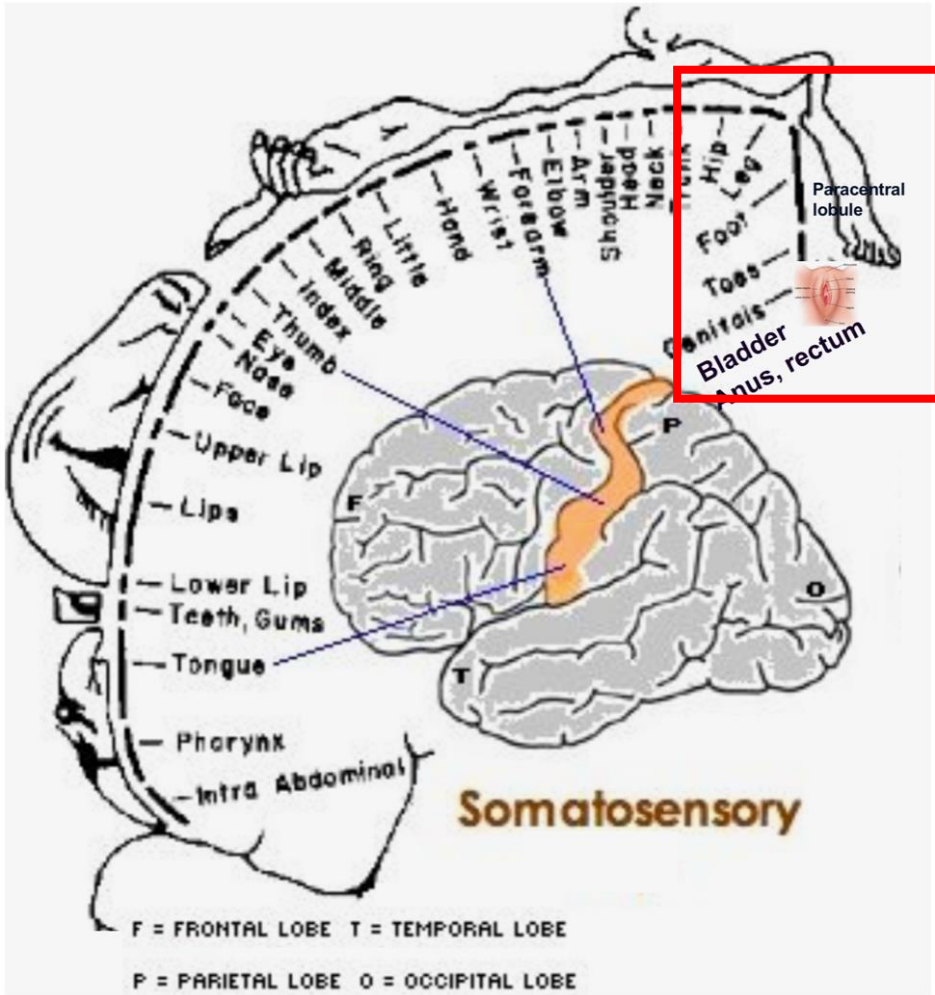


- Multinational epidemiological data suggest a substantial number of women worldwide (approximately 0.6-3%) may be affected by PGAD/ GPD.
- 1.6 million women in the US

What is the Paracentral Lobule of the Somatosensory Cortex



Paracentral lobule is region that processes sensory information from sacral roots



Sciatic nerve (L4, L5, S1, S2, S3)

Gluteal region – inferior, medial lateral cluneal n (S1 – S3)

Posterior thigh – posterior, lateral femoral cutaneous n (S1 – S3)

Posterior calf – medial lateral sural cutaneous n, saphenous n (S1 – S3)

Heel, lateral foot – tibial n, lateral plantar n (S1 – S3)

Pudendal nerve (S2, 3, 4)

Dorsal n – clitoris
 Perineal n – vulva, vestibule
 Inferior rectal n – perianal region

Visceral afferent Pelvic nerve (S2, 3, 4) (pressure sensation)

Anus/Rectum
 Bladder/urethra
 Vagina

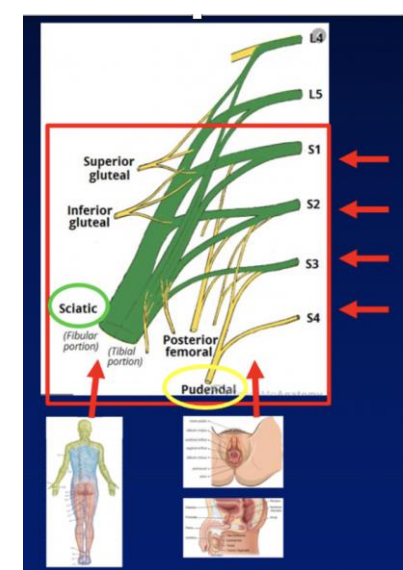
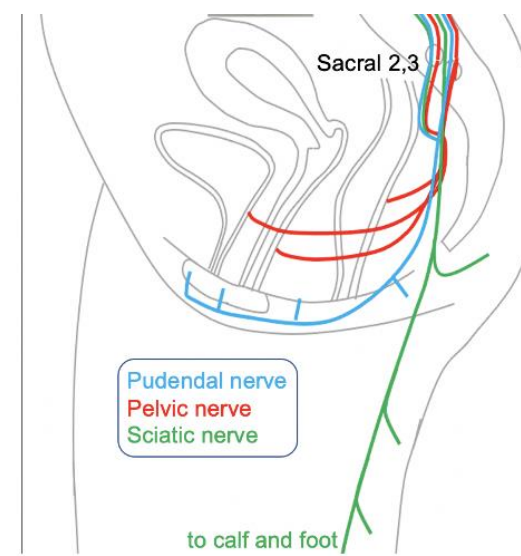
If a woman

..... has persistent or recurrent, unwanted or intrusive, distressing sensations of **genital arousal** (eg, feelings of being on the verge of orgasm and of lubrication and swelling, tingling, throbbing, contractions, not associated with concomitant sexual interest, thoughts, or fantasies that persist for >3 months)

..... experiences these unwanted sensations in the clitoris but may also experience these unwanted sensations in other genito-pelvic regions (eg, mons pubis, vulva, vestibule, vagina, urethra, perineal region, bladder, and/or rectum)

..... experiences these unwanted sensations as other types of genito-pelvic dysesthesia (eg, buzzing, burning, twitching, itch, **pain**)

..... experiences these unwanted sensations in gluteal region, posterior thigh region, posterior calf region, foot region



Pudendal nerve (S2, 3, 4)

Dorsal n – clitoris
Perineal n – vulva, vestibule
Inferior rectal n – perianal region

Visceral afferent Pelvic nerve (S2, 3, 4) (pressure sensation)

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Sciatic nerve (L4, L5, S1, S2, S3)

Gluteal region – inferior, medial lateral cluneal n (S1 – S3)

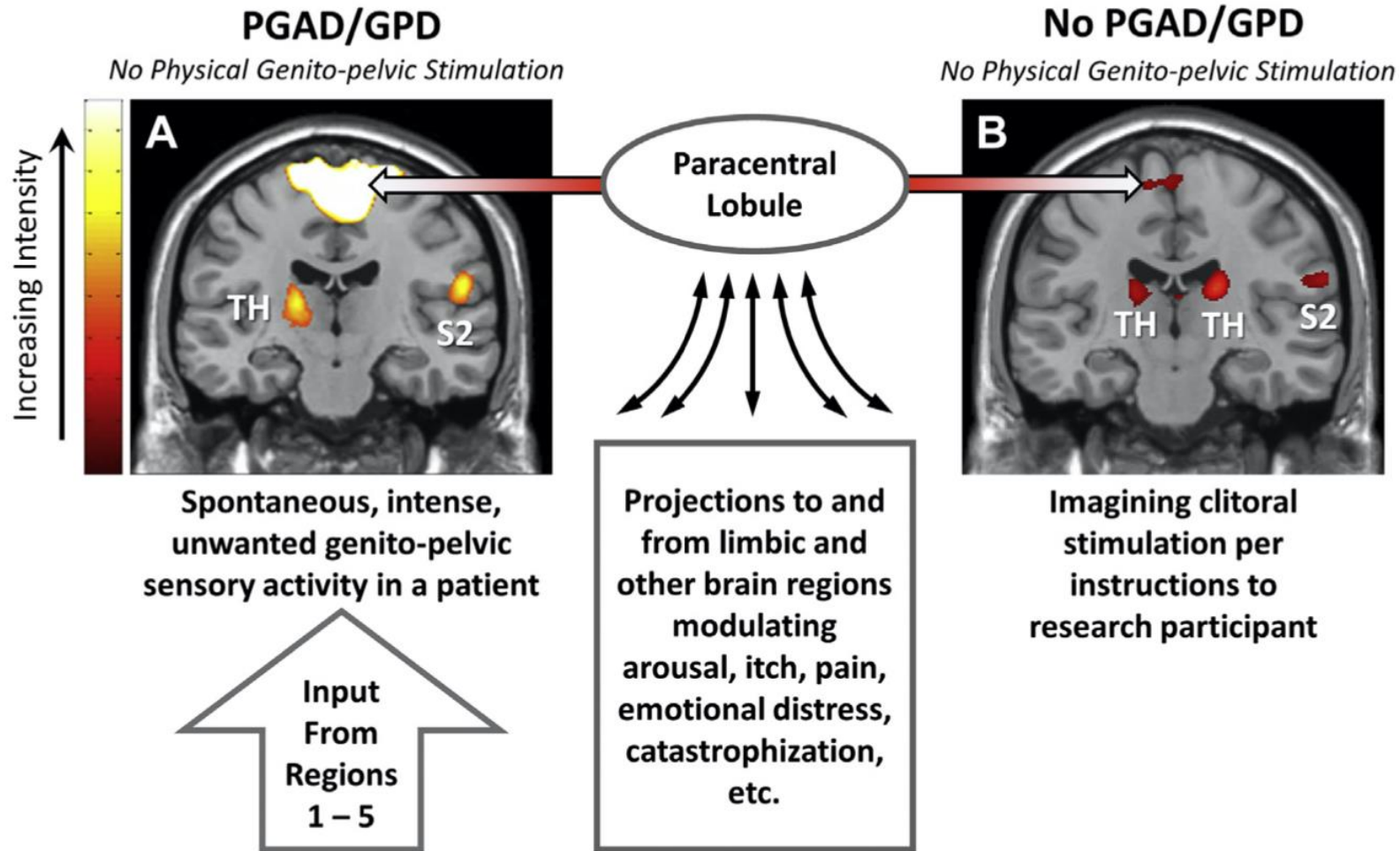
Posterior thigh – posterior, lateral femoral cutaneous n (S1 – S3)

Posterior calf – medial lateral sural cutaneous n, saphenous n (S1 – S3)

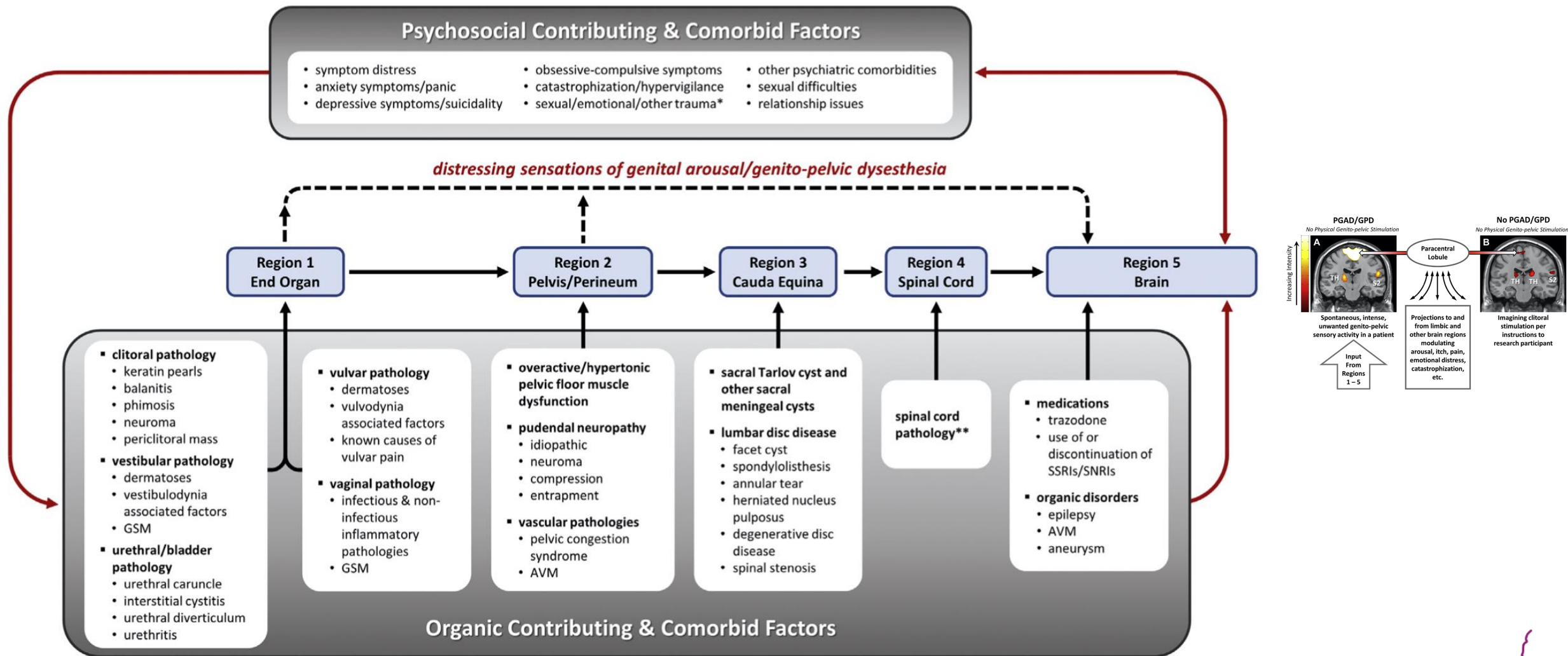
Heel, lateral foot – tibial n, lateral plantar n (S1 – S3)

This woman's fMRI would reveal:

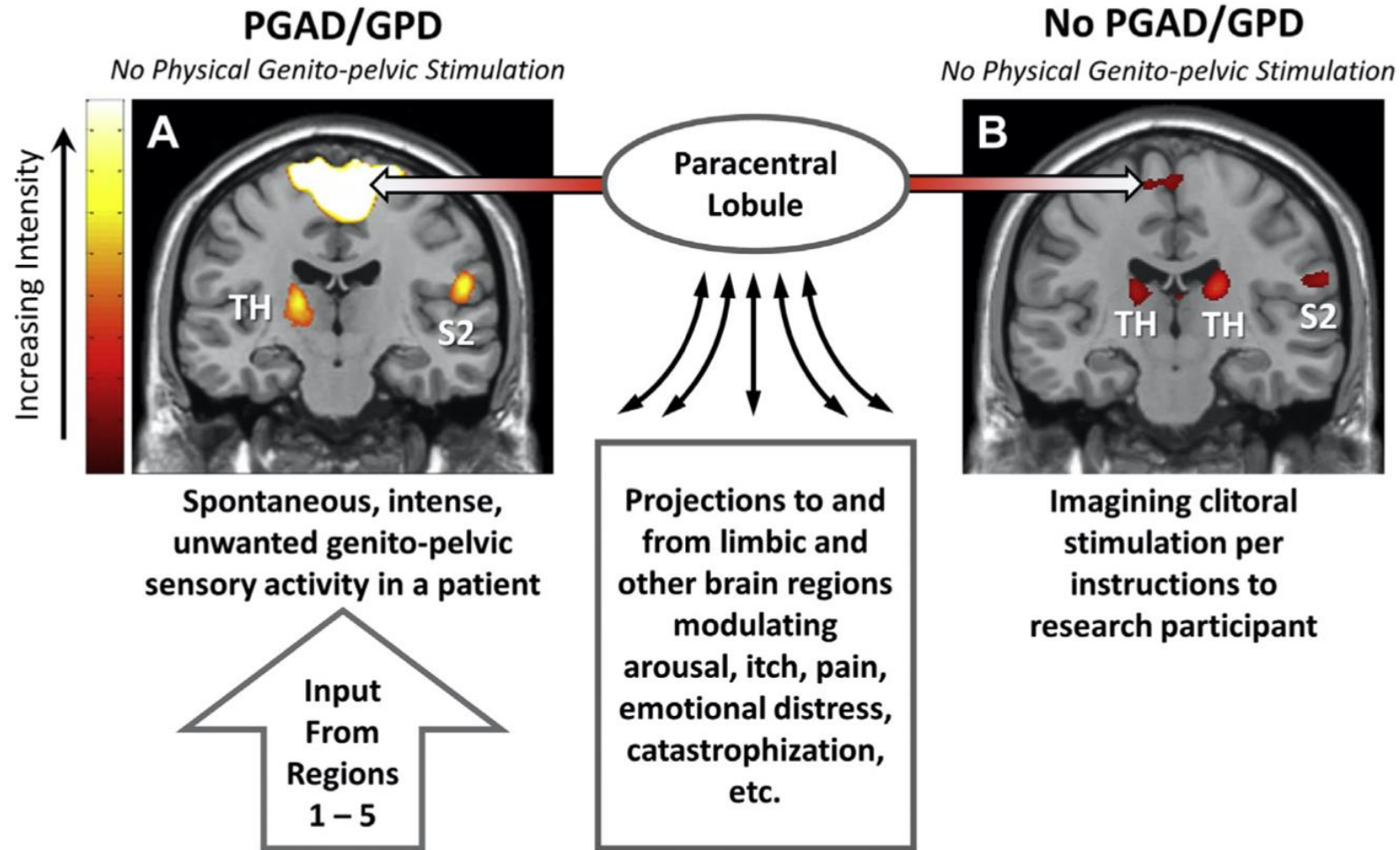
spontaneous intense unwanted genito-pelvic sensory activity (A vs B) in paracentral lobule of somatosensory cortex that processes sensory information from sacral roots



WHAT IS TRIGGERING the excess sensory information to paracentral lobule in brain



It is one role of the provider to REDUCE THE INTENSITY OF THE TRIGGER (S) that is/are resulting in spontaneous intense unwanted genito-pelvic sensory activity (A vs B) in paracentral lobule of somatosensory cortex that processes sensory information from sacral roots



Pharmacologic treatment strategies for Region 5

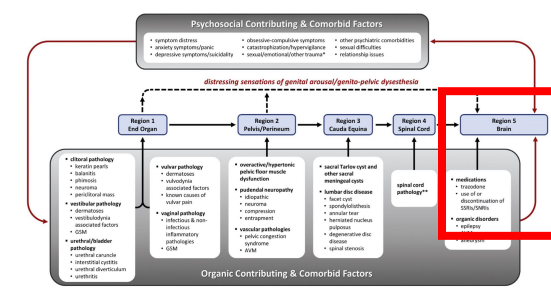


Table 6. Off-label medications, targeted symptoms, and primary mechanisms of action

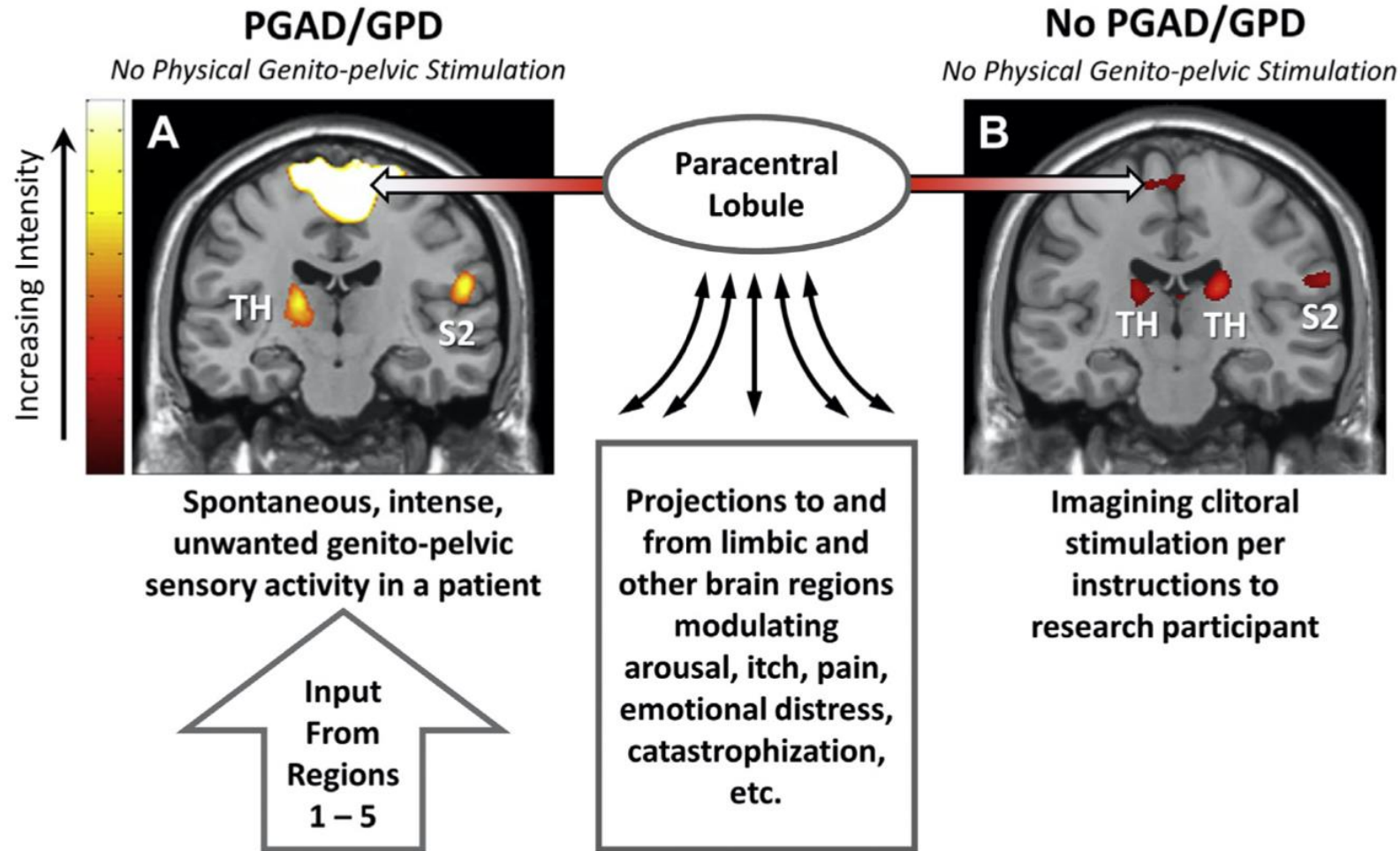
Commonly used medications	Symptoms associated with PGAD/GPD*					Primary mechanism of Action†						
	Genito-pelvic arousal	Genito-pelvic Itch/Pain	Mood problems	Restless legs	Pelvic floor dysfunction	GABA (Inhibitory)	Opioid	5-HT	NE	DA	ACh	Ion channels
Gabapentin	+	+				+						
Pregabalin	+	+				+						
Clonazepam	+					+						
Carbamazepine	+	+										-
Zolpidem	+					+				-		
Lamotrigine	+											-
Oxcarbazepine	+											-
Topiramate	+					+						-
Tramadol		+						+				
Hydrocodone		+						+				
Duloxetine		+	+						+	+		
Paroxetine		+	+						+	+		
Nortriptyline		+	+						+	+		
Clomipramine		+	+						+	+		
Amitriptyline			+						+	+		
Desipramine			+							+		
Varenicline	+			+						+/-	+	
Paliperidone			+							-		
Risperidone			+							-		
Pramipexole				+						+/-		
Baclofen Suppository					+	+						
Diazepam Suppository					+	+						
Botulinum Toxin A					+						-	

*Symptoms: Drug is effective against symptom (+).

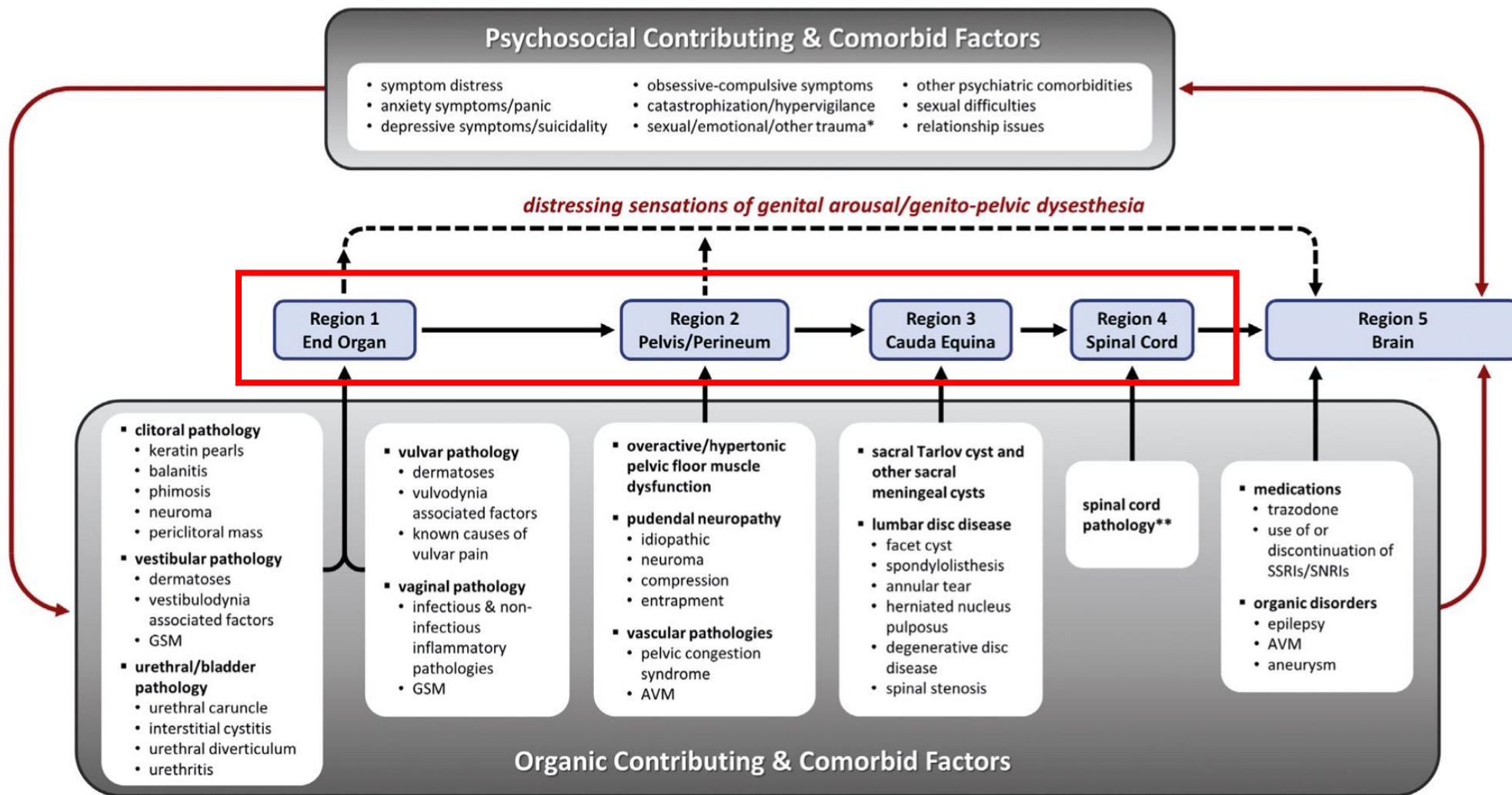
†Drug action: Drug increases neurotransmitter (+); drug decreases neurotransmitter or channel (-).



It is one role of the provider to IDENTIFY THE TRIGGER (S) that is/are resulting in spontaneous intense unwanted genito-pelvic sensory activity (A vs B) in paracentral lobule of somatosensory cortex that processes sensory information from sacral roots



WHAT IS TRIGGERING the excess sensory information to paracentral lobule in brain



History

- 31 y o woman presented with persistent distressing extreme itch, sensitivity, rawness, and dryness in genito-pelvic region x 2 ½ years
- Dysesthesia located at labia, vestibule, clitoris, buttocks, anus, inner/back of thighs, back of legs but no visual symptoms
- Yeast infection medications (fluconazole), multiple topical steroid medications, antihistamines, and local anesthetic agents to genitals for years provided no relief
- Amitriptyline, Duloxetine, Tramadol reduced the intensity of the extreme itch
- Aggravation of extreme itch by certain circumstances (eg, sitting, car driving, music or sounds, general anxiety, stress, or nervousness)
- Despair, emotional lability, catastrophization, and suicidal ideation - she was in counseling regularly
- 3 ½ years ago, 2 x week high intensity interval CrossFit strength and conditioning workouts – she may have hurt herself, low back pain – she was benefiting from regular pelvic floor PT

Validated Instruments

PGAD/GPD is a MONSTER

- Total Desire Domain score: 1.8.
- Total Arousal Domain: 2.7.
- Total Lubrication Domain: 5.1.
- Total Orgasm Domain: 3.2.
- Total Satisfaction Domain: 2.8.
- Total Pain Domain: 6.
- FSFI score: 15.6.
- SDS-R score: 31/52.
- PHQ-9 score: 16.
- PSS score: 23/40.
- Sensory score: 15/33.
- Affective score: 6 /15.
- PPI score: 4/5.
- V-Q: 12.

Physical Examination of Regions 1 and 2- Including Anesthesia Testing

Clitoral and Vestibular Anesthesia Testing – negative – extreme itch persisted

Pudendal nerve block x 2 – negative - extreme itch persisted

Clinically significant GPD symptom reduction was never realized

Topical anesthetic applied to glans clitoris & prepuce



Topical anesthetic applied to vestibule



Pudendal nerve block at ischial spine (transvestibular approach)



Subcutaneous anesthetic injection to prepuce



Cotton swab testing to anesthetized vestibule



Pudendal nerve block at ischial spine (transvestibular approach)

Blood Tests

Test	01/23/17	Units	Range
Calculated Free Testosterone [SDSM code]	0.416	ng/dL	6-8
Vitamin D 25-OH Total	22	ng/mL	30-100
Thyroid Stimulating Hormone (TSH)	1.43	uIU/mL	0.40-4.50
Testosterone, Total, Serum	45	ng/dL	2-45
Prolactin	5.0	ng/mL	3.0-30.0
Progesterone	<0.5	ng/mL	<1.0
Sex Hormone Binding Globulin	86	nmol/L	17-124
Follicle-Stimulating Hormone (FSH, Follitropin), Serum	7.9	mIU/mL	2.5-10.2
Luteinizing Hormone (Lutropin), Serum	10.5	mIU/mL	1.9-12.5
Estradiol	198	pg/ml	<350

Quantitative Sensory Testing – dorsal and perineal nerve branches of pudendal nerve (S2-4)

Test	Control (rt index finger)	Glans Clitoris	Right Labia Minora	Left Labia Minora
Vibration	3 volts	4 volts	5 volts	5 volts
Cold	22 degrees	17 degrees	17 degrees	15 degrees
Warmth	28 degrees	36 degrees	36 degrees	38 degrees

Consistent with mild neuropathy of the afferent dorsal and perineal branches of the pudendal nerve

Biothesiometry of glans clitoris



Temperature testing of glans clitoris



Sacral Dermatome Testing – Sciatic nerve branches (S2, S3)

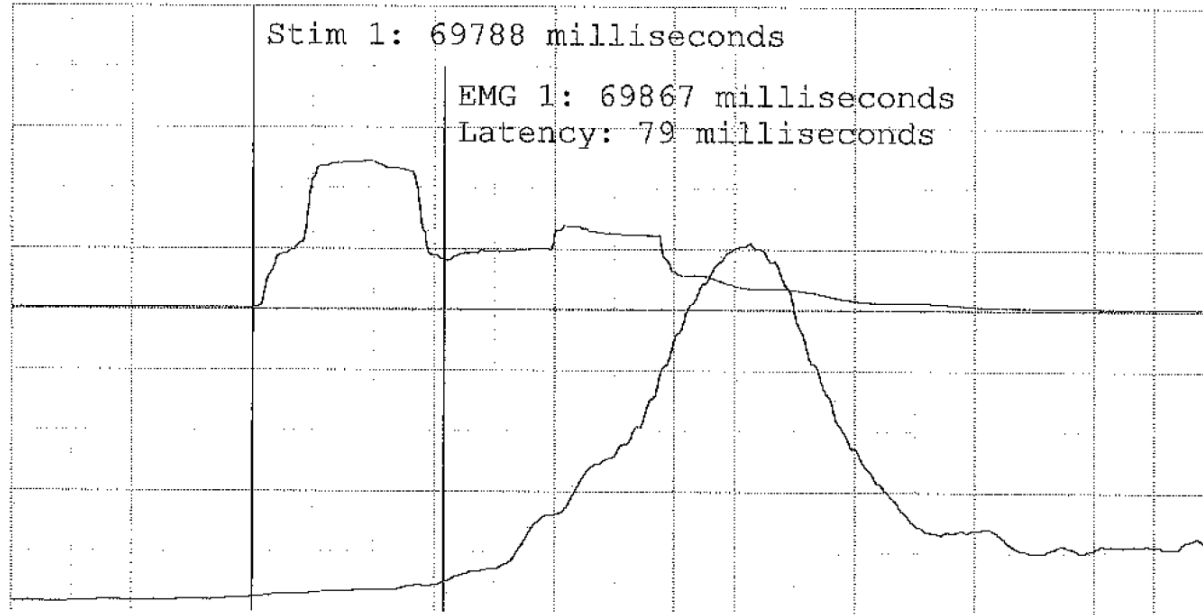
Test Site	Right	Left
Control	3 volts	
S4 Gluteal	16 volts	15 volts
S3 Gluteal	18 volts	16 volts
S2 Gluteal	17 volts	18 volts
S1 Gluteal	16 volts	20 volts
S2 Thigh	22 volts	18 volts
S1 Thigh	18 volts	28 volts
S2 Calf	17 volts	16 volts
S1 Calf	20 volts	19 volts

Abnormal vibratory perception threshold values consistent with moderate sensory neuropathy of sciatic afferent sacral nerve roots

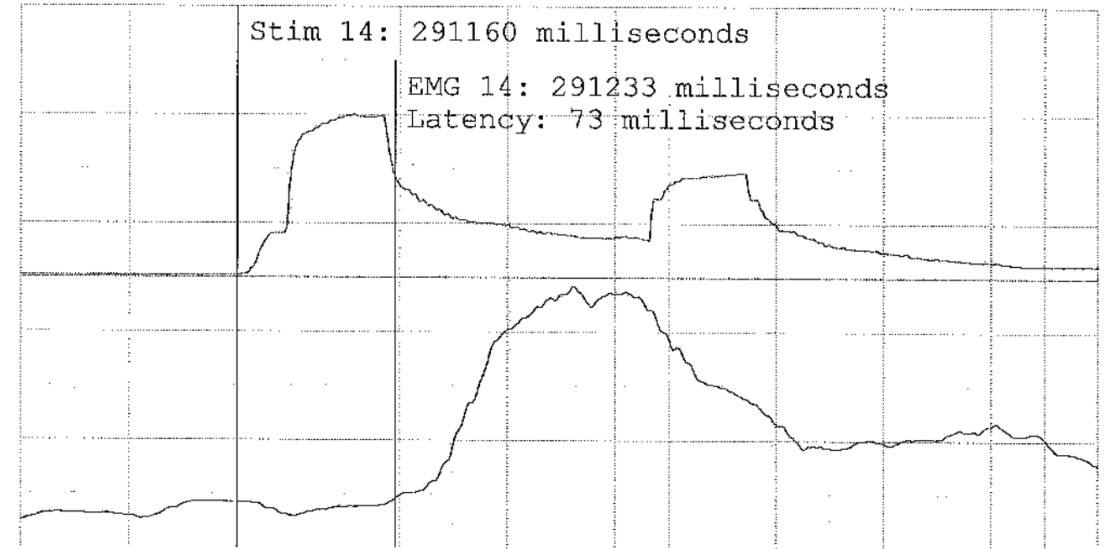
Biothesiometry of right gluteal S2



Bulbocavernosus Reflex Testing – afferent dorsal nerve, afferent pudendal nerve, cauda equina, efferent pudendal nerve



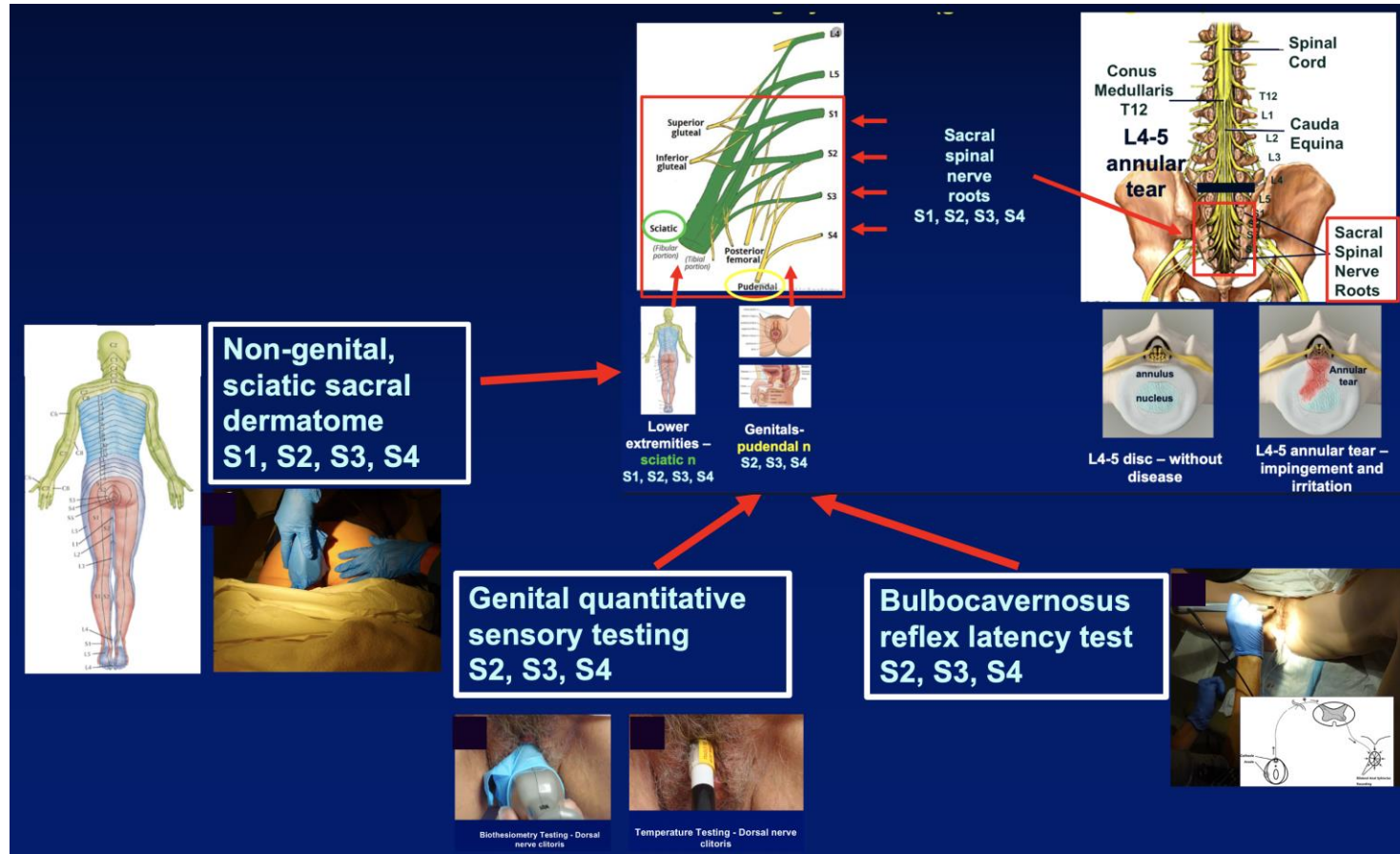
LEFT



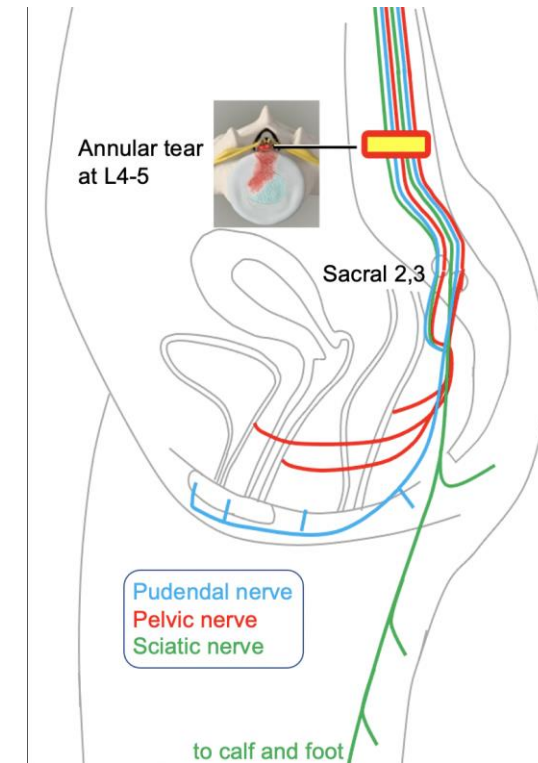
RIGHT

Right and Left bulbocavernosus reflex latency values > 45 msec consistent with pathology in sensory and motor S 2, 3 and 4 sacral roots of the cauda equina

Non-Invasive Neurogenital testing: Genital Sacral and Non-Genital (Sciatic) Sacral Testing

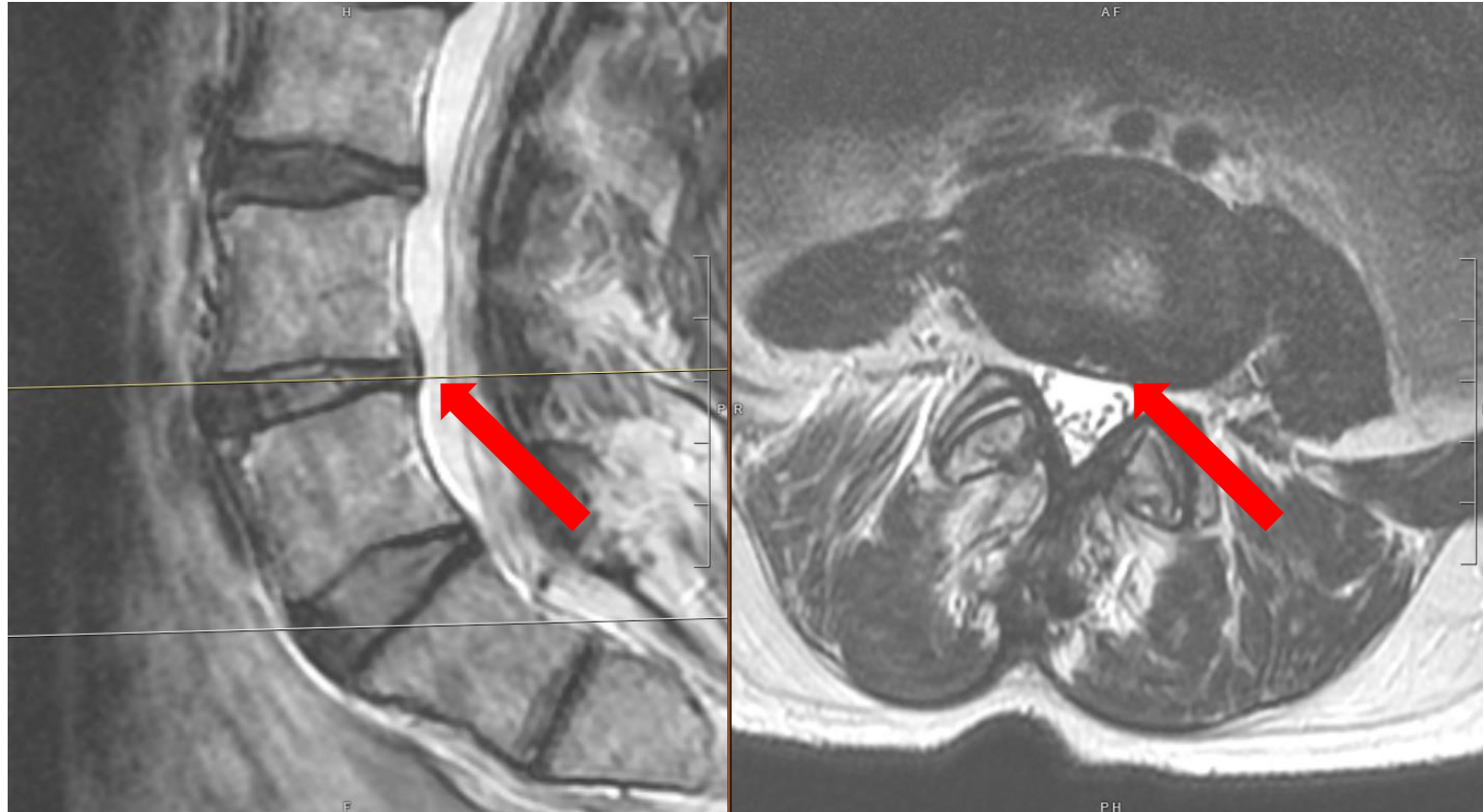


Lumbar disc disease CAN CAUSE GPD



Region of pathology	Genital Quantitative Sensory Testing (QST)*	Non-genital Sacral Dermatome Testing	Bulbocavernosus (BC) Reflex Latency Testing**
End organ – Region 1	abnormal	normal	abnormal
Perineum/Pelvis – Region 2	abnormal	normal	abnormal
Cauda Equina – Region 3	abnormal	abnormal	abnormal
Spinal cord*** – Region 4	abnormal	abnormal	normal
Brain – Region 5	abnormal	abnormal	normal

Lumbar MRI

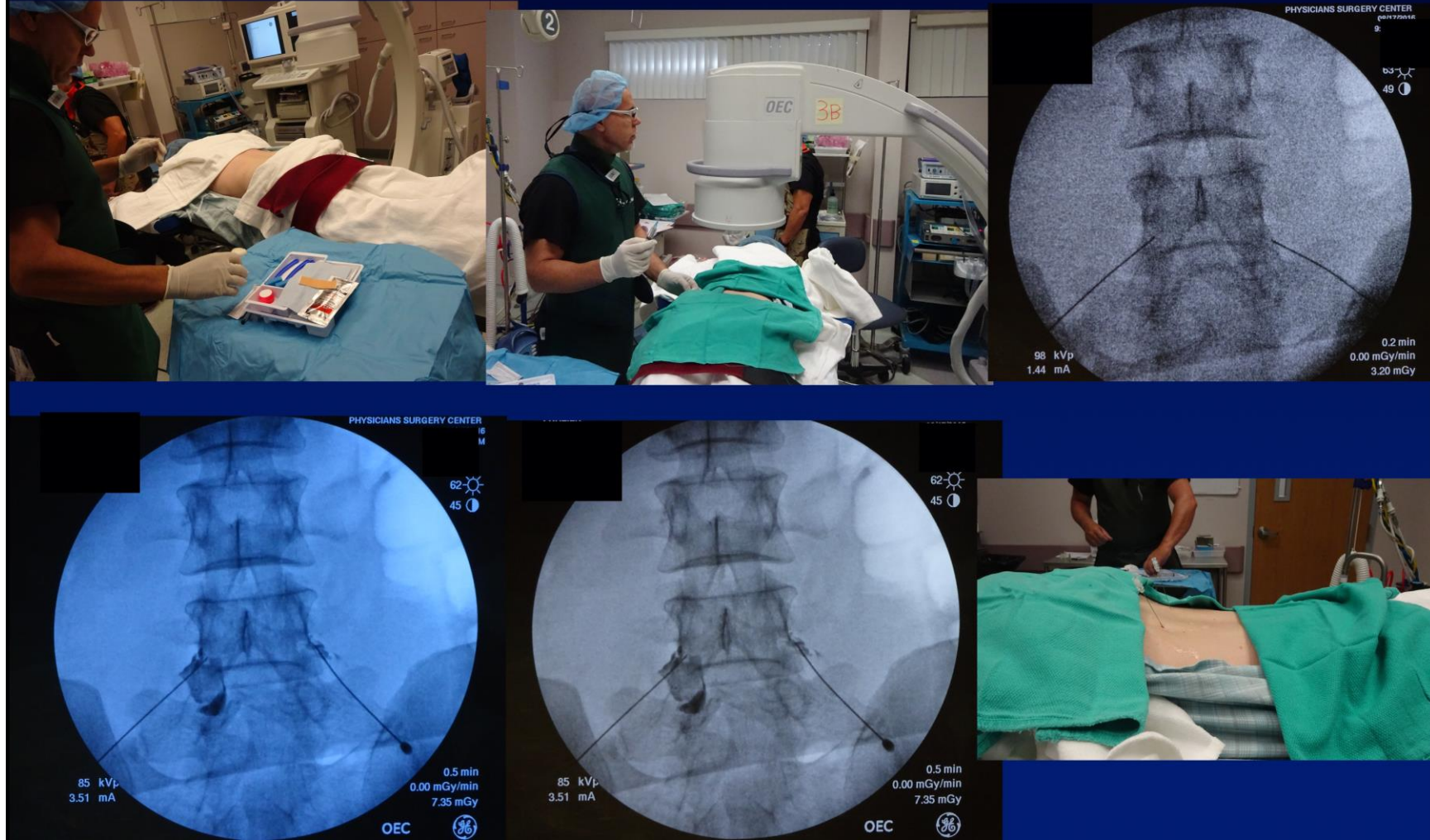


L4-L5 annular tear seen on sagittal and axial views

TRANSFORAMINAL EPIDURAL SPINAL INJECTION (TFESI)

**Positive
TFESI –
Clinically
significant
symptom
reduction**

**TFESI leading
to PGI-I (2 -
much better),
and 50%
Reduction in
“itching
symptoms”**



**In highly selected patients consider
lumbar endoscopic surgery...**

LESS *Procedure*

Post-op

Three months post-op:

The extreme itch feeling is completely gone

“I can wear leggings again”

Result is durable at 2 years follow-up

GPD/PGAD treated by LESS

N=20

GPD/PGAD

HNP/annular tear

Treated by LESS

25% Male

75% Female

Age 42 (18-68y)

F/U 16mos (13-37 mos)

PGI-I Response

7 *Very Much Better*

6 *Much Better*

3 *Little Better*

3 *No better*

0 *Little Worse*

0 *Much Worse*

1 *Very Much Worse*

GPD/PGAD treated by *LESS*

80% Improved

65% Much Improved

And...

**If (+) Injection response:
87% Improved**

**If (-) injection response:
50% Improved**

PGI-I Response

7 *Very Much Better*

6 *Much Better*

3 *Little Better*

3 *No better*

0 *Little Worse*

0 *Much Worse*

1 *Very Much Worse*

Summary

- PGAD/GPD is a diverse biopsychosocial condition
- Common underlying neurologic basis attributable to spontaneous intense activity in the paracentral lobule of the somatosensory cortex.
- A process of care diagnostic and treatment strategy was developed to guide the clinician, whenever possible, by localizing the symptoms as originating in any of five regions: (i) end organ, (ii) pelvis/perineum, (iii) cauda equina, (iv) spinal cord, and (v) brain.
- Psychological treatment strategies were considered critical and should be performed in conjunction with medical strategies.
- Pharmaceutical interventions may be used based on their site and mechanism of action to reduce patients' symptoms and the associated bother and distress.