CONTEMPORARY PHARMACOLOGY OF ORGASM

2:00 – 2:15 PM

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Past President, International Society for the Study of Women's Sexual Health
Past President, Sexual Medicine Society of North America
Editor Emeritus, Editor-in-Chief, *Sexual Medicine Reviews*
Editor Emeritus, *The Journal of Sexual Medicine*
Editor Emeritus, *International Journal of Impotence Research*

dr.irwingoldstein@gmail.com

DISCLOSURES

- NO DISCLOSURES

DISCLAIMER

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- PHARMACOLOGIC TREATMENT STRATEGIES FOR SYMPTOM CONTROL OF FOD ARE BASED ON EXPERT OPINION
- SEE PACKAGE INSERT FOR DOSE RANGES, ADVERSE EVENTS, TOXICITY, DRUG INTERACTIONS, CONTRAINDICATIONS, POTENTIAL FOR ABUSE, AND OTHER SAFETY INFORMATION

CONTEMPORARY PHARMACOLOGY OF ORGASM

ISSWSH Orgasm Consensus Panel

2016 ISSWSH Definition of Orgasm

Proposed 2025 ISSWSH Definition of Orgasm [not yet consensed]

Three Phases of Orgasm

Pre-Orgasm Phase FOD: Failure to Excite, Failure to Inhibit

Pre-Orgasm/Orgasm Phase FOD: Delayed Orgasm; Minimal Excitation/Minimal Inhibition Premature/Muted Orgasm

Orgasm Phase FOD: Orgasmic Anhedonia

Post-Orgasm Phase FOD: Post-Orgasm Illness Syndrome

Proposed Pharmacologic Management of FOD [not yet consensed]

Conclusion

ISSWSH ORGASM CONSENSUS PANEL

The ISSWSH Executive Committee selected co-chairs to organize a panel to develop consensus regarding Female Orgasm Disorder (FOD) including:

- nomenclature of orgasm
- physiology of orgasm
- epidemiology and pathophysiology of FOD
- classification and evidence-based diagnosis and treatment of FOD

The co-chairs identified international multidisciplinary experts in:

- clinical psychology
- sex therapy
- basic science
- neurophysiology
- gynecology
- urology
- psychiatry
- physiology
- pharmacology
- endocrinology
- reproductive endocrinology
- sexual medicine
- sexuality education
- pelvic floor physical therapy

ISSWSH ORGASM CONSENSUS PANEL


Barry R. Komisaruk, PhD


Annamaria Giraldi, MD, PhD


Irwin Goldstein, MD


Lori Brotto, PhD


Sue W. Goldstein, BA, CSE, CCRC


Michael Adams PhD


Estela Citrin, MD


Anita Clayton, MD


Debby Herbenick PhD


Emmanuele A. Jannini, MD


Sheryl Kingsberg, PhD


Roy Levin, PhD


Tierney Lorenz, PhD


Mijal Luria, MD


Melanie Morin, DPT


Sara Nasserzadeh, PhD


Kwangsung Park, MD, PhD


James Pfaus, PhD

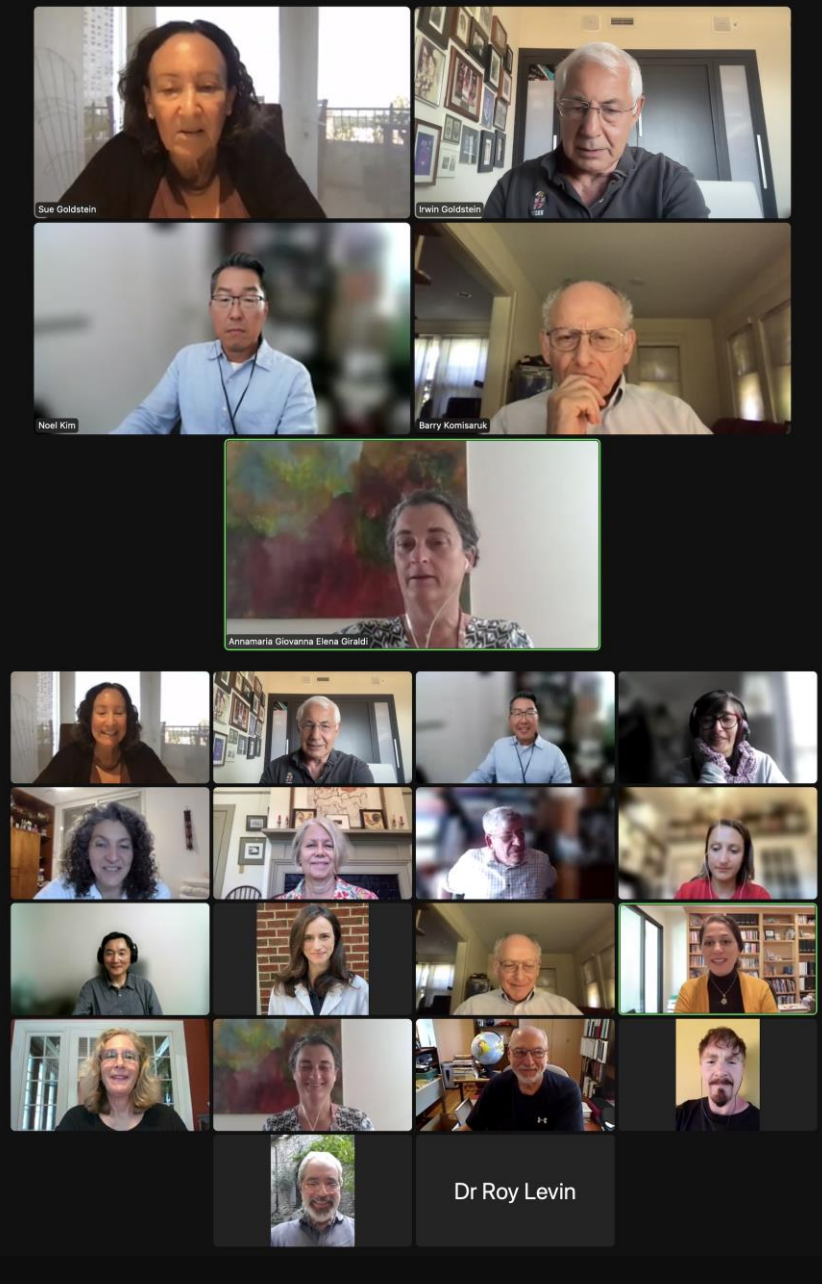

James Simon, MD


Linda Vignozzi, MD


Nan Wise PhD


Noel N.Kim, PhD

ISSWSH ORGASM CONSENSUS PANEL



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2016 ISSWSH ORGASM DEFINITION

A variable, transient, peak sensation of intense pleasure, creating an altered state of consciousness, usually with an initiation accompanied by involuntary rhythmic contractions of the pelvic striated circumvaginal musculature, often with concomitant uterine and anal contractions, and myotonia that resolves the sexually induced vasocongestion and myotonia, generally with an induction of well-being and contentment.

Toward a More Evidence-Based Nosology and Nomenclature for Female Sexual Dysfunctions Part II
Sharon J. Parish, Andrew T. Goldstein, Sue W. Goldstein, Irwin Goldstein, James Pfaus, Anita H. Clayton, Annamaria Giraldi, James A. Simon, Stanley E. Althof, Gloria Bachmann, Barry Komisaruk, Roy Levin, Susan Kellogg Spadt, Sheryl A. Kingsberg, Michael A. Perelman, Marcel D. Waldinger, and Beverly Whipple J Sex Med 2016;13:1888-1906 (pg 1898)

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PROPOSED 2025 ISSWSH DEFINITION OF ORGASM:
NOT YET CONSENSED

The 2025 ISSWSH consensus panel on orgasm in women addressed limitations of previous definitions by incorporating into a new proposed definition the:

I. repetitive genital and/or non-genital sensory stimulation that elicits the progressive positive feedback "climb" of excitation

II. myotonia that involves more than the pelvic floor including multiple somatic/visceral body regions

III. intense pleasure of orgasm that involves sensory awareness of both genital/non-genital stimulation and proprioceptive response to the whole-body myotonia and the subsequent cessation of the stimulation with de-activation and resolution of excitation

IV. identification of three phases of orgasm that allows for categorization of orgasm disorders

New definition should be more clinically relevant for patient management.

NEW PROPOSED ISSWSH 2025 DEFINITION OF ORGASM:
NOT YET CONSENSED

Orgasm is a feeling of intense pleasure that

- (pre-orgasm phase) is generated by repetitive genital and/or non-genital stimulation increasing physiologic arousal and whole body myotonia resulting in awareness and appreciation of a progressive positive feedback increase “climb” in excitation
- (orgasm phase) reaches a peak of positive feedback excitation surpassing the orgasm threshold, followed by release and relaxation of whole-body myotonia, cessation of the stimulation and de-activation/resolution of the excitation that is perceived as intensely pleasurable ending with satiety and/or contentment or continuation/re-activation of the stimulation leading to further orgasm(s)
- (post-orgasm phase) and return to the baseline pre-orgasm state

Orgasm may be accompanied by concomitant ejaculation

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Pre-orgasm phase:

Involves repetitive stimulation of:

- **genital somatic (clitoris, vulva) region and/or**
- **genital visceral (vagina, vestibule, prostate) region and/or**
- **non-genital (nipple, toes, ear) regions**

resulting in a "climb" of excitation

Includes awareness and appreciation of a progressive positive feedback increase (climb) in excitation involving:

- **whole-body myotonia**
- **respiratory and heart rate**
- **genital and/or non-genital tissue glandular secretion/lubrication (vestibule, vagina, cervix, Bartholin mucus, epinephrine, tears, salivation)**
- **engorgement / vasocongestion (clitoris, vulva, face, chest)**
- **pupil dilation, nipple engorgement**

Orgasm phase:

Involves:

- **peak of positive feedback excitation surpassing the orgasm threshold**
- **release and relaxation of whole-body myotonia**
- **cessation of genital/non-genital stimulation**
- **de-activation and resolution of the excitation, perceived as intensely pleasurable, ending with satiety and/or contentment**

Individuals who experience multiple orgasms desire/need to continue to have additional orgasms

Orgasm may be accompanied by concomitant ejaculation

Post-orgasm phase:

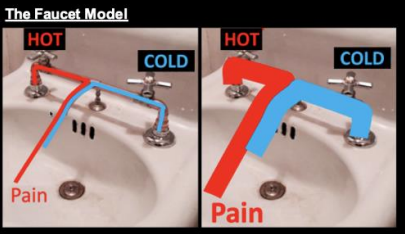
After orgasm

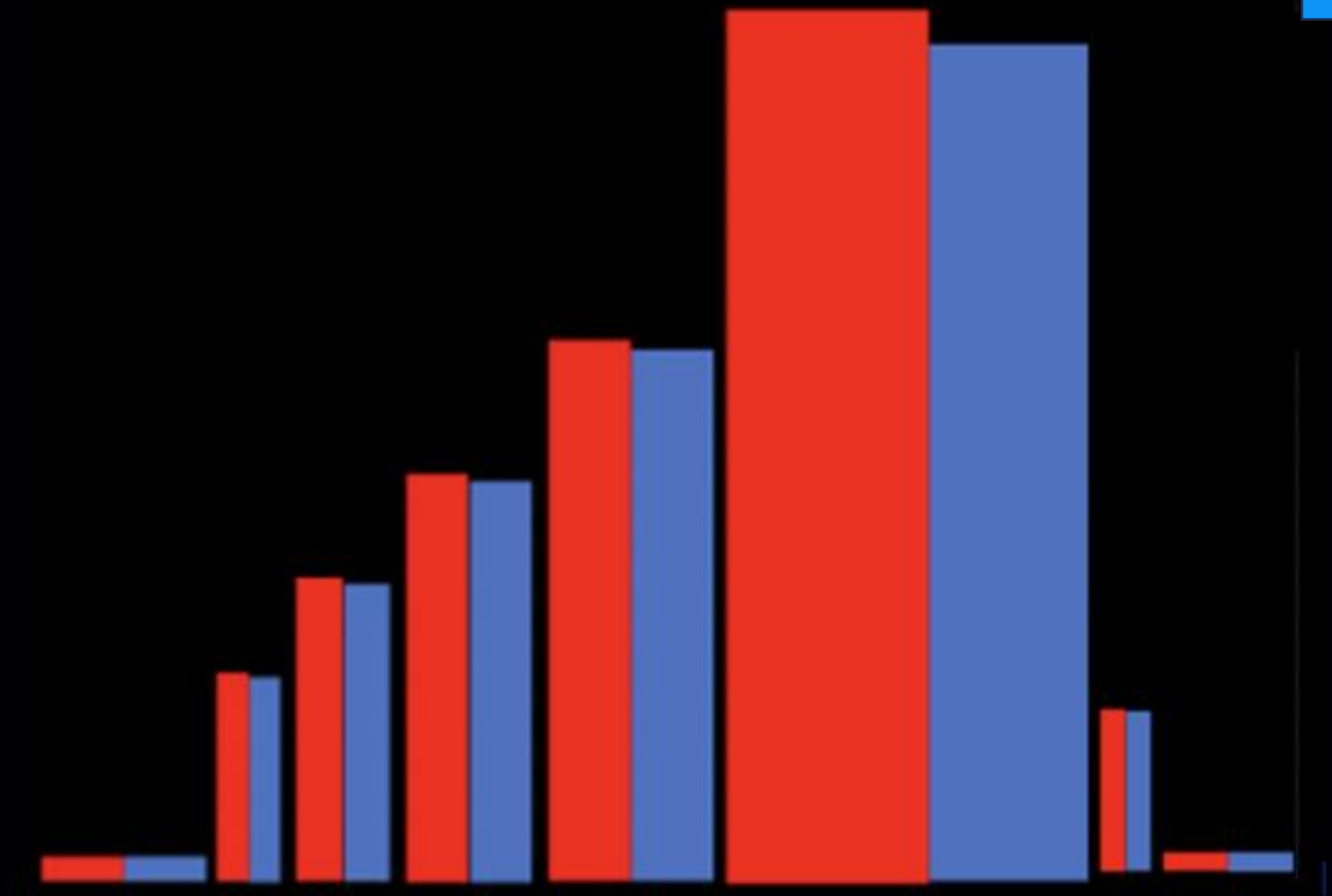
- **return to the baseline pre-orgasm state**

Three Phases of Orgasm

Excitation

Inhibition





Pre-orgasm phase

Orgasm phase

Post-orgasm phase

Three Phases of Orgasm

Orgasm phase: peak of excitation surpasses orgasm threshold, release/relaxation of myotonia, cessation of stimulation, de-activation/resolution of excitation perceived as intensely pleasurable ends with satiety/contentment.

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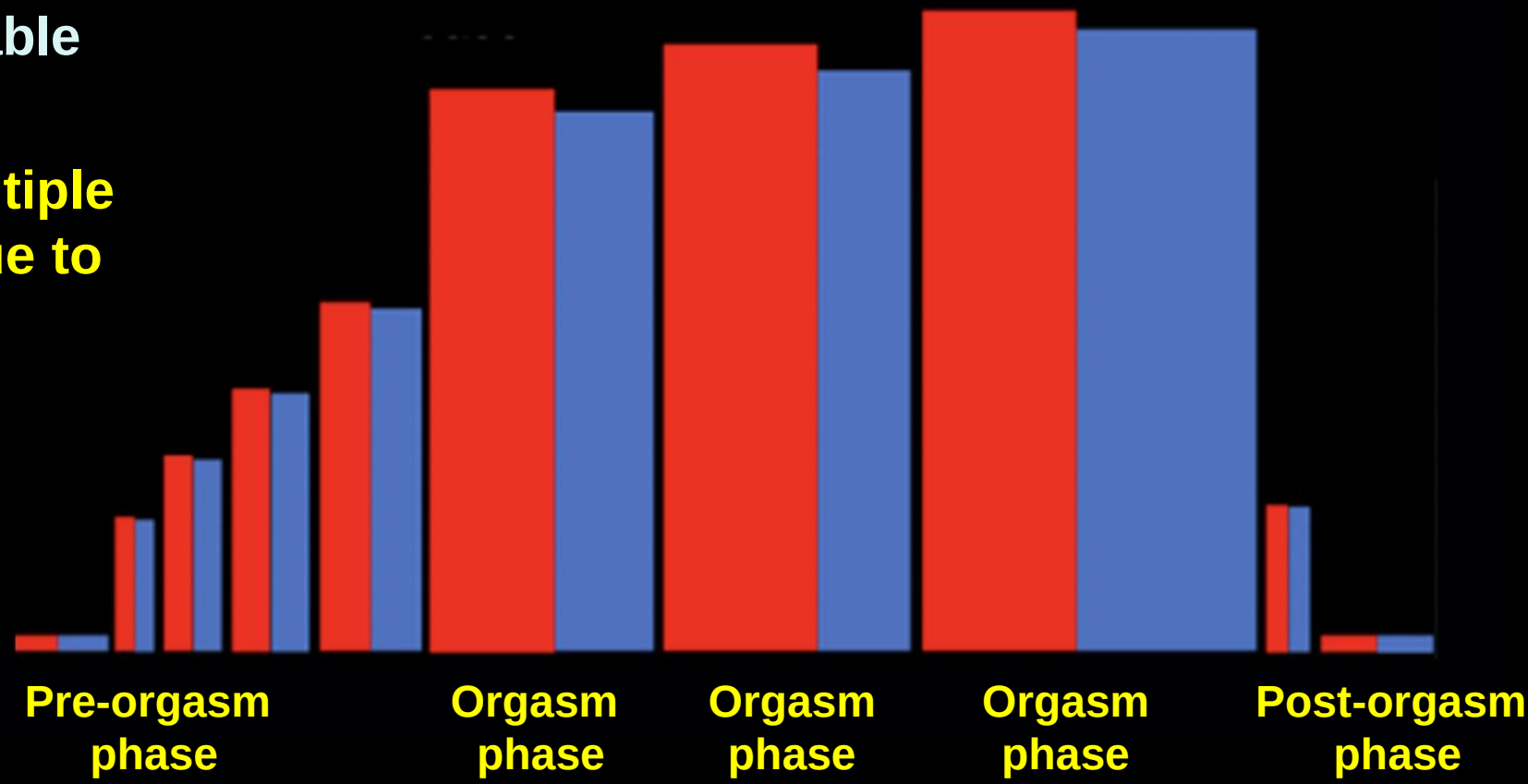

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Proposed Pharmacologic Management of FOD [not yet consensed]

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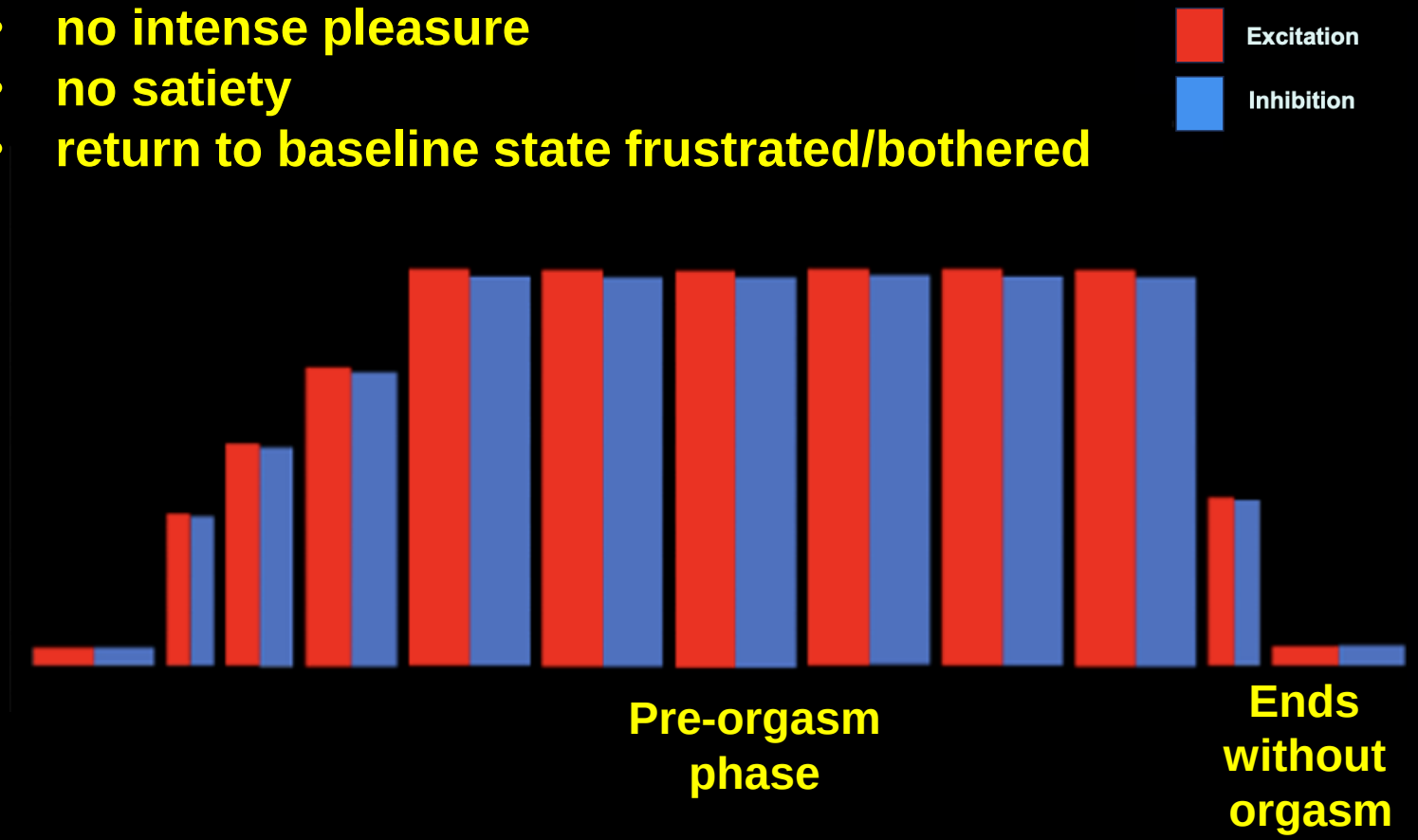
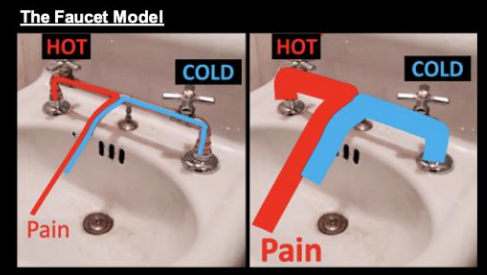
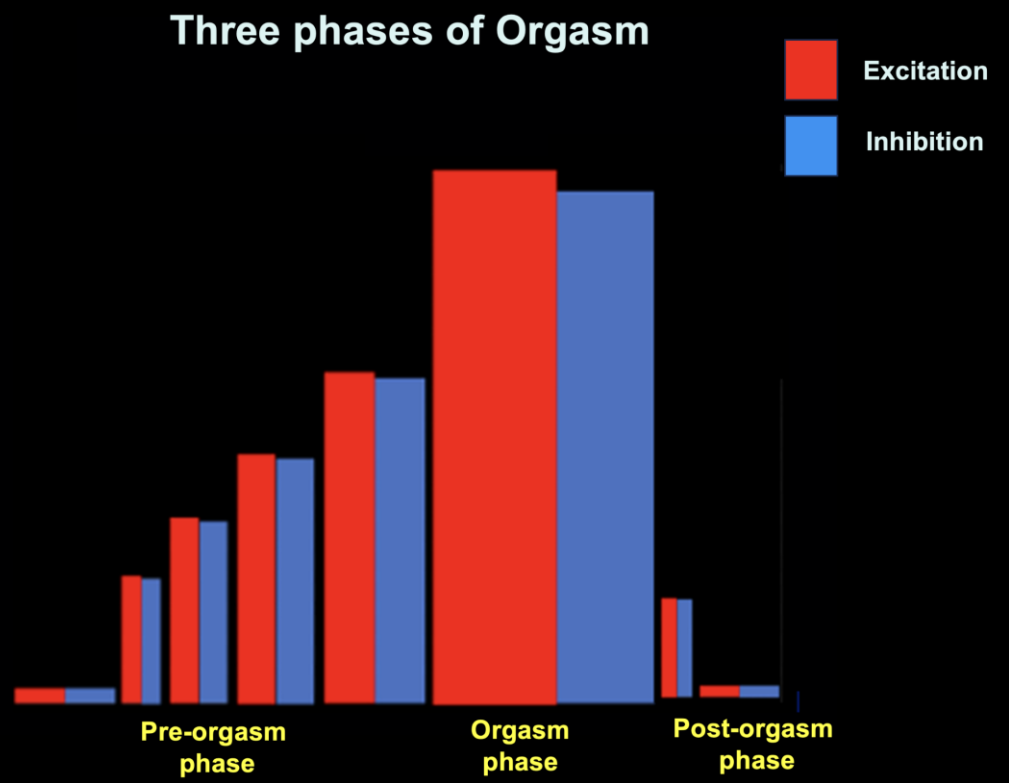
Pre-orgasm Phase: "Failure to Excite" FOD

- unable to experience initiation and/or progressive increase in "climb" of excitation
- peak of excitation never surpasses orgasm threshold
- minimal awareness of myotonia resolved
- no intense pleasure
- no satiety
- return to baseline state frustrated/bothered



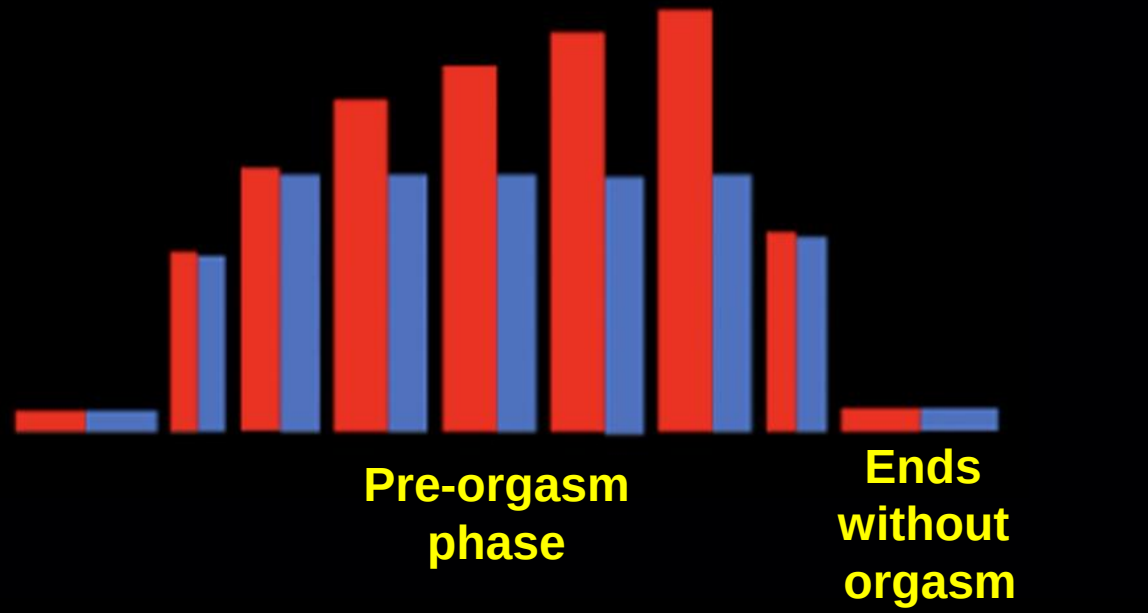
Without Female Orgasm Disorder





Pre-orgasm Phase: "Failure to Inhibit" FOD

- failure to inhibit increased genital/non-genital sensitivity leading to aversive discomfort during progressive increase in "climb" of excitation
- peak of excitation never surpasses orgasm threshold
- minimal awareness of myotonia resolved
- no intense pleasure
- no satiety
- return to baseline state - frustrated/bothered



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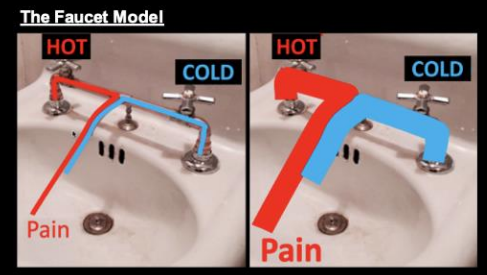
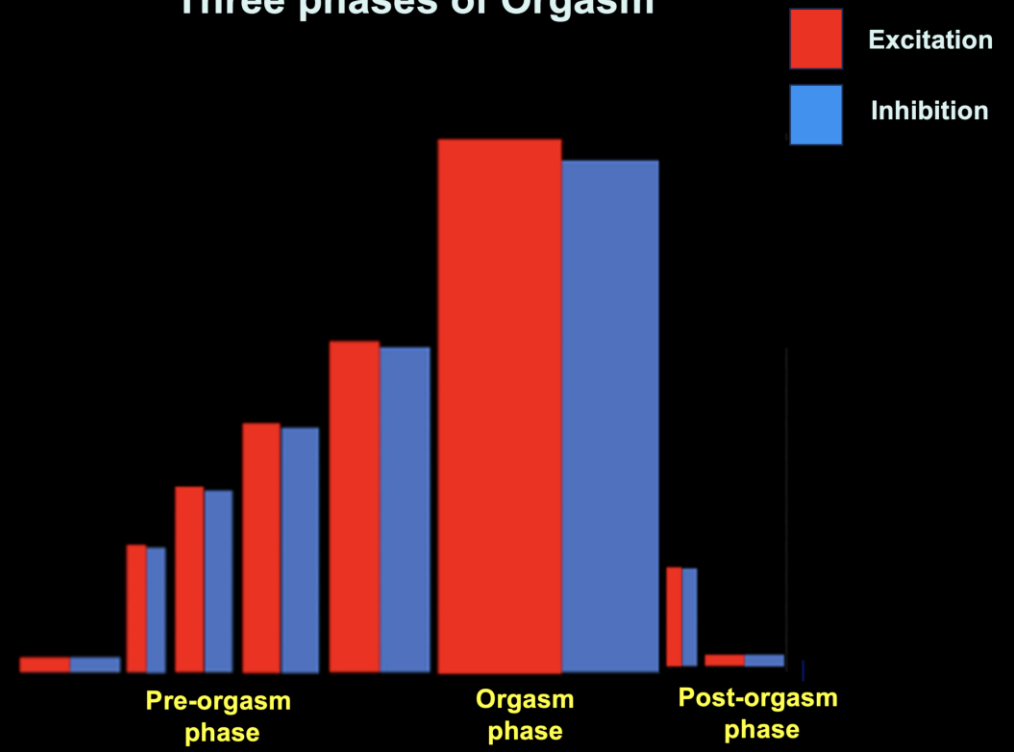


Three phases of Orgasm



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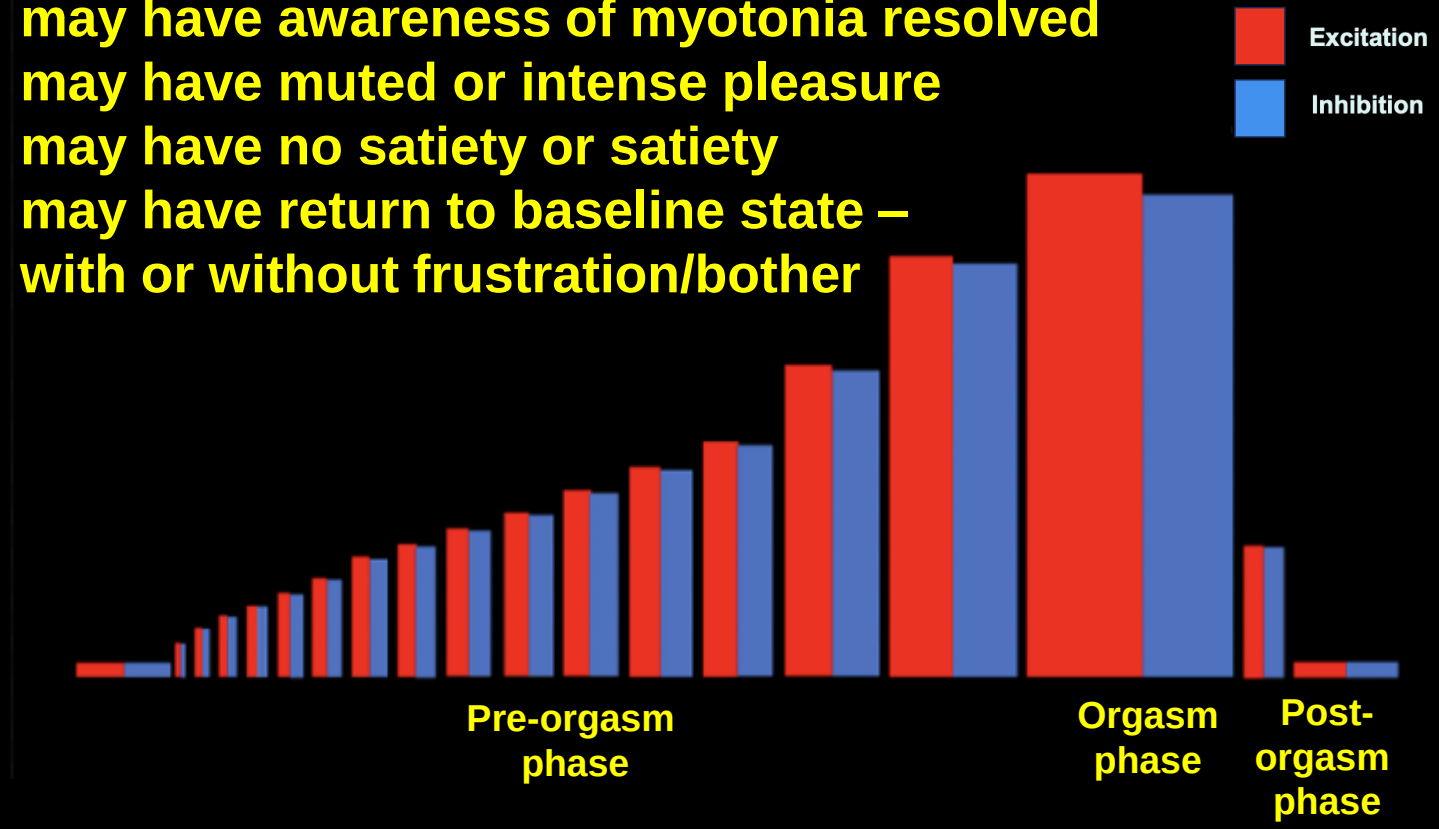
Proposed Pharmacologic Management of FOD [not yet consensed]

Conclusion

Pre-orgasm/Orgasm Phase: Delayed Orgasm FOD

- marked delay in progressive increase in "climb" of excitation
- peak of excitation may eventually surpass orgasm threshold, but not always
- fatigue is common
- may have awareness of myotonia resolved
- may have muted or intense pleasure
- may have no satiety or satiety
- may have return to baseline state – with or without frustration/bother



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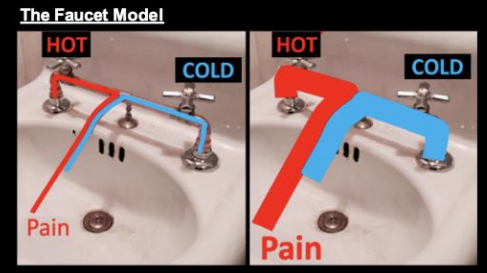
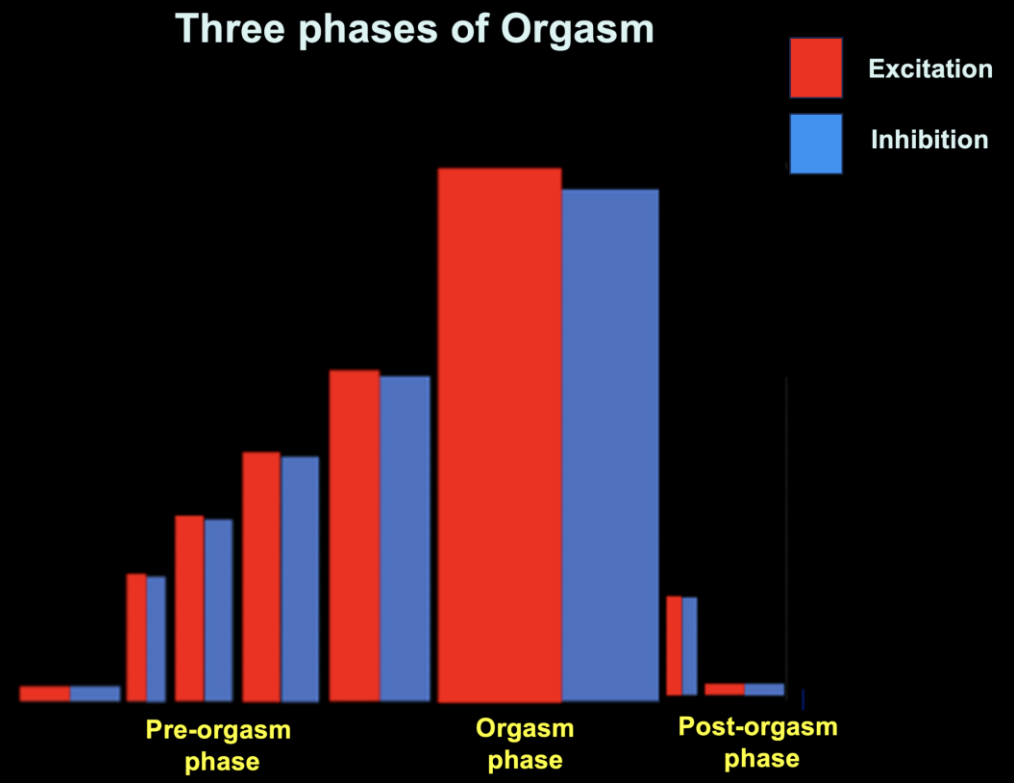
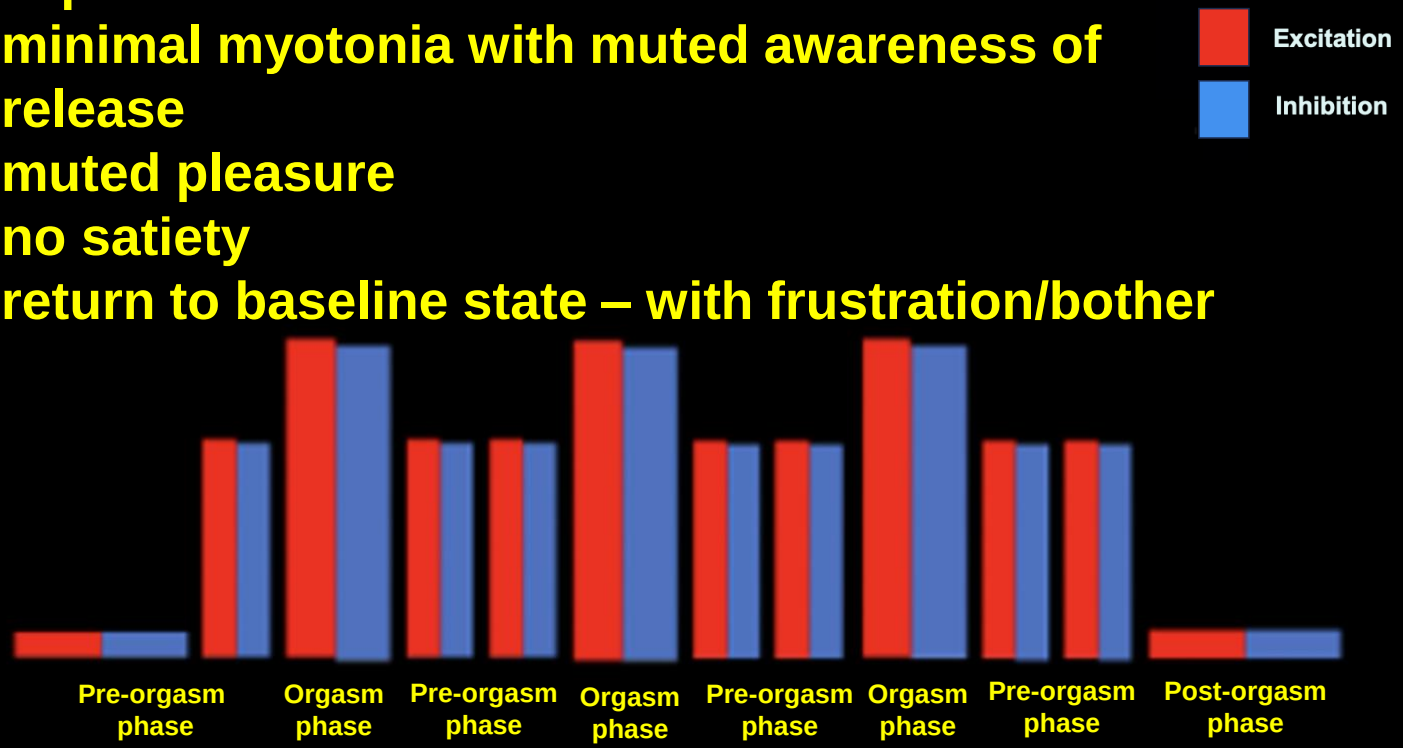




Pre-orgasm/Orgasm Phase: Minimal Excitation/Minimal Inhibition Premature/Muted Orgasm FOD

- minimal excitation, minimal inhibition
- peak of excitation surpassed at very low orgasm threshold
- “blips” of repeated muted premature orgasm experienced
- minimal myotonia with muted awareness of release
- muted pleasure
- no satiety
- return to baseline state – with frustration/bother



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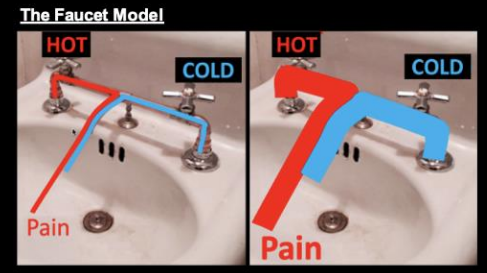

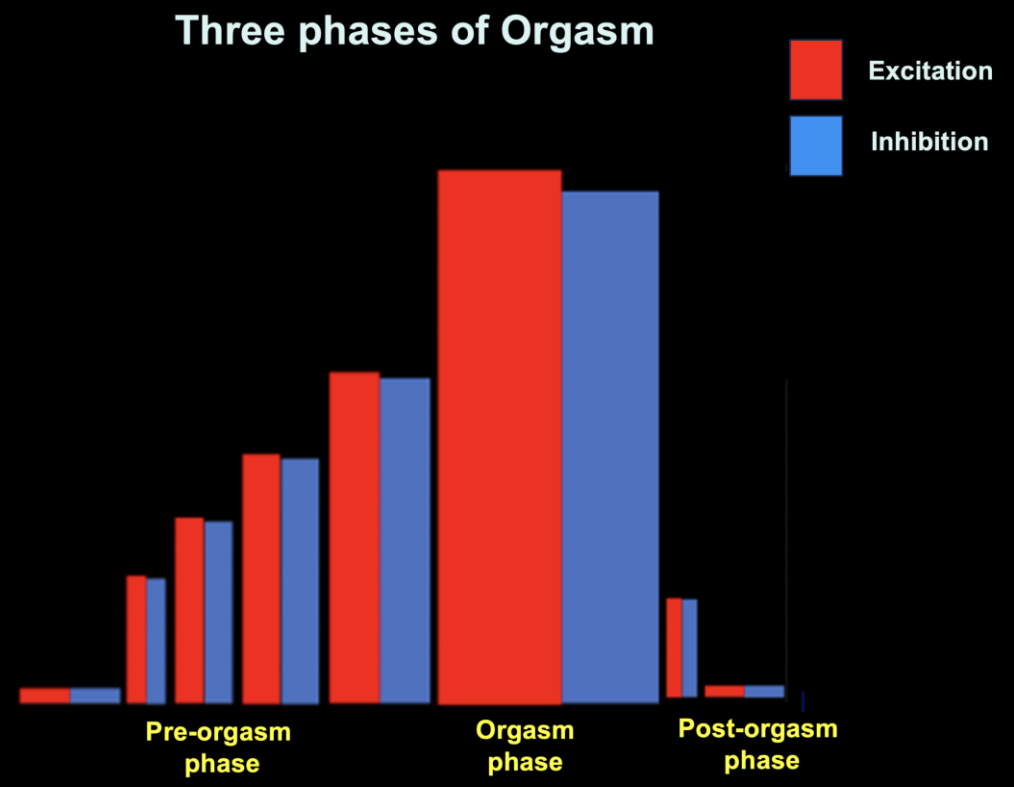

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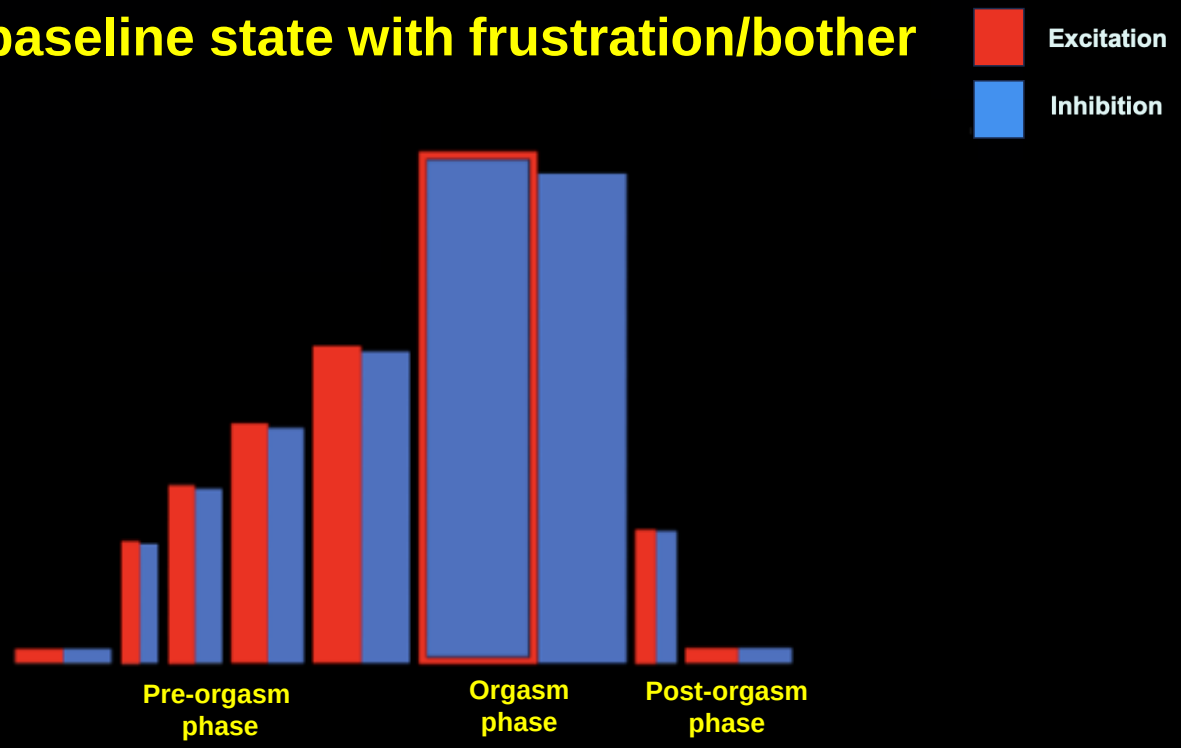
Orgasm Phase:
Orgasmic Anhedonia FOD

- **Orgasm phase: peak of excitation surpasses orgasm threshold, release/relaxation of myotonia, cessation of stimulation, de-activation/resolution of excitation**

NO PLEASURE EXPERIENCED

- **no satiety**
- **return to baseline state with frustration/bother**



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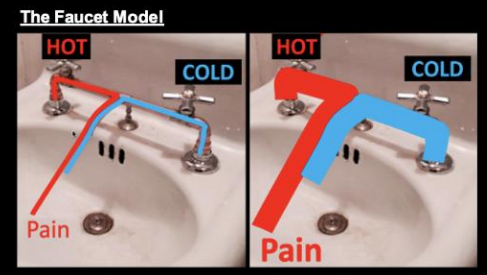

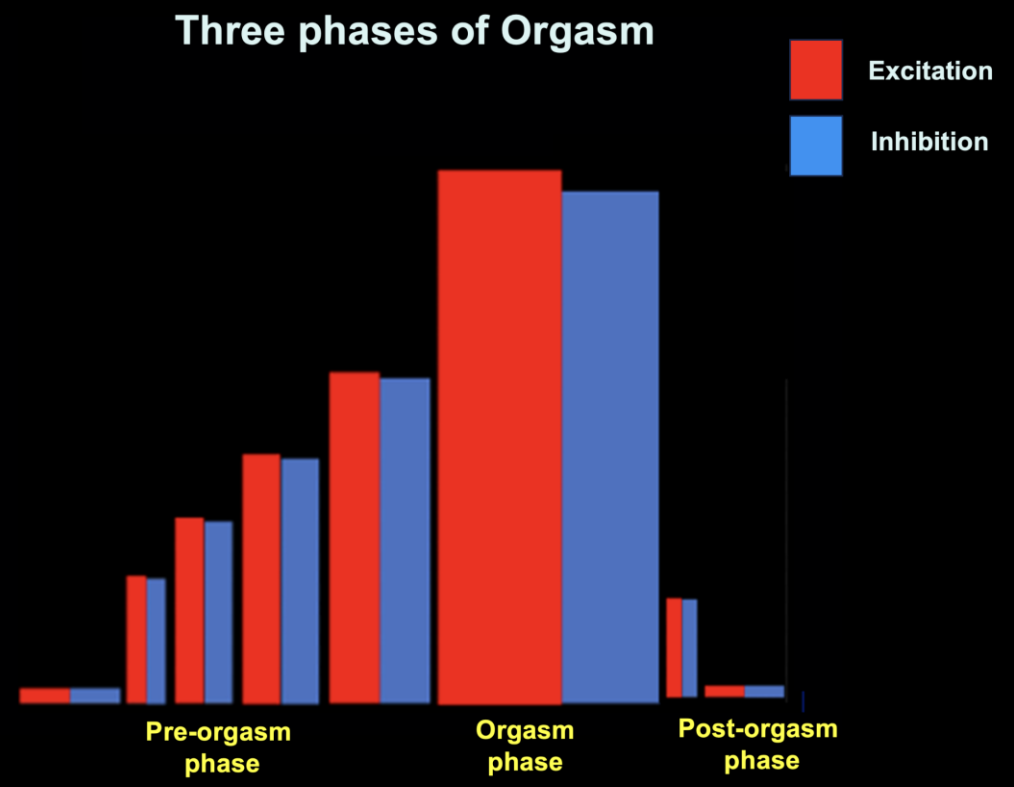

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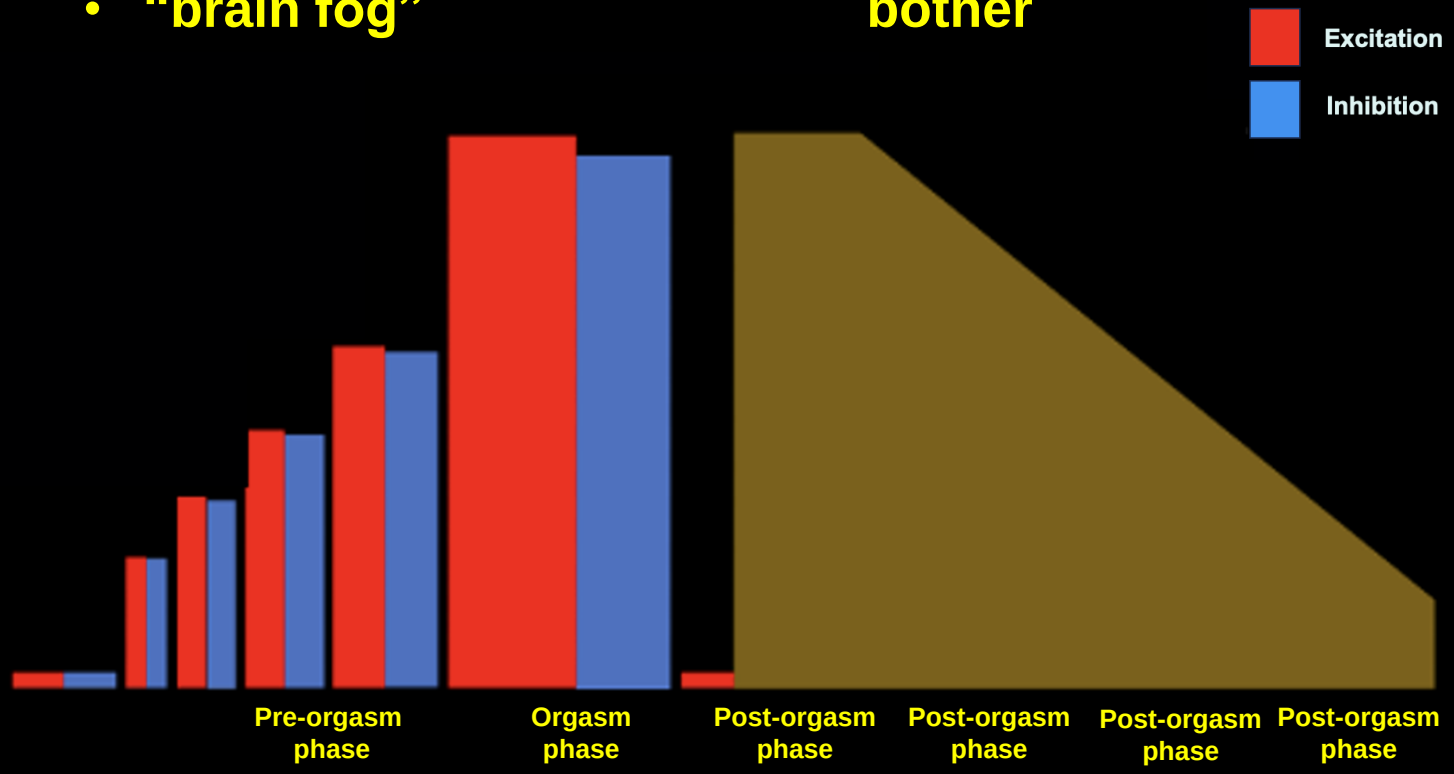
Post-Orgasm Phase:
Post-Orgasm Illness Syndrome (POIS) FOD

- marked protracted return (range days to weeks) to baseline state with
  - malaise
  - fatigue
  - “brain fog”
- low energy
- lack of motivation
- extreme frustration/ bother



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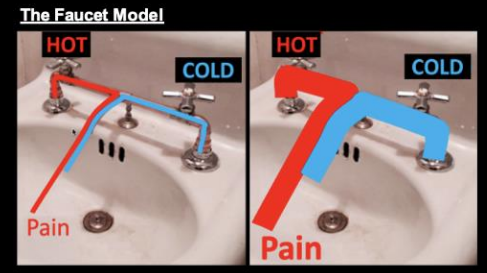

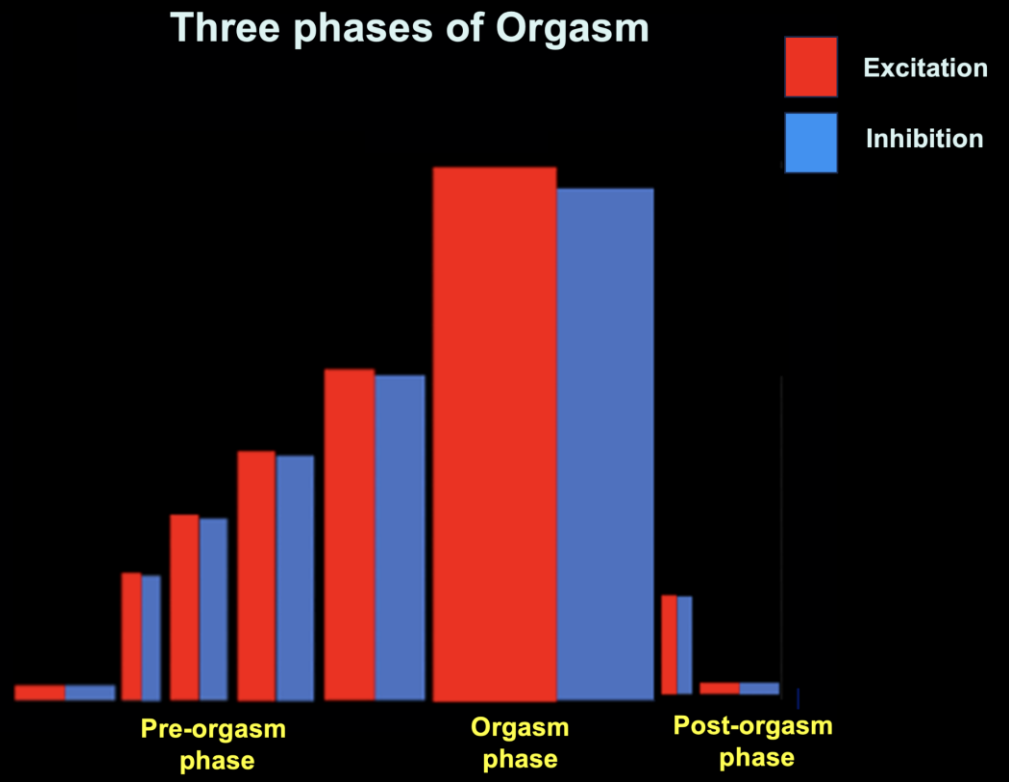

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PROPOSED PHARMACOLOGIC MANAGEMENT OF FOD ASSOCIATED WITH FAILURE OF/MINIMAL EXCITATION

NOT YET CONSENSED

Failure of/Minimal Excitation			
Category	Medication	Dose	Administration
CNS stimulant	caffeine	100 mg PO	1 hour before*
	dexmethylphenidate hydrochloride	2.5 mg PO	1-4 hours before*
	dextroamphetamine and amphetamine mixed salts	2.5 mg and increase by 2.5 mg up to 10 mg PO	1-6 hours before*
	methylphenidate	5 mg PO	1-2 hours before*
	lisdexamfetamine	10 mg PO	1-6 hours before*
Dopamine	bremelanotide	1.75 mg (0.3 ml) subcutaneous autoinjector administered to abdomen/thigh	1 hour before
	cabergoline	0.5 mg PO twice weekly	chronic
	pramipexole	0.375 mg PO daily	chronic
	ropinirole	0.25 mg PO 3 times/day	chronic
Dopamine/ norepinephrine	bupropion	75 mg PO in morning	chronic
Oxytocin	oxytocin lozenges	500 units sublingual	1 hour before
PDE5 inhibitor	sildenafil	20 mg PO	1 hour before
	tadalafil	5 mg PO	1 hour before
Serotonin antagonist	buspirone	10 mg PO twice daily	chronic
	flibanserin	100 mg PO nightly	chronic
Testosterone	1% testosterone gel	1/10th of a generic 50mg testosterone tube (0.5 ml; 5mg) to back of calf	2 hours before

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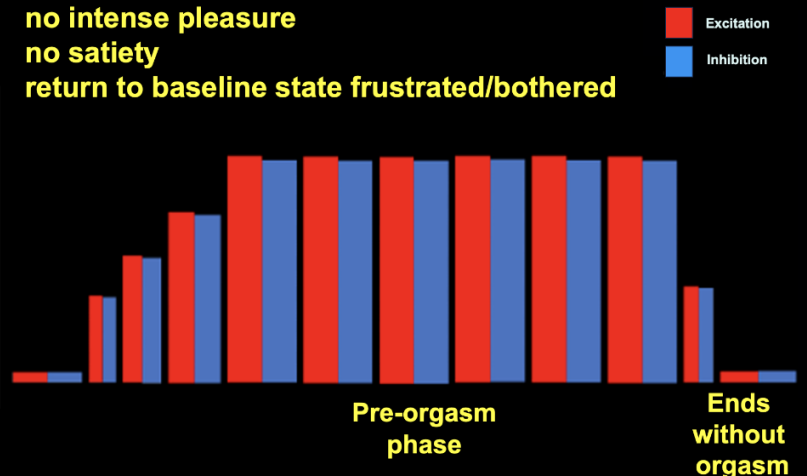
Pre-orgasm Phase: "Failure to Excite" FOD

- unable to experience initiation and/or progressive increase in "climb" of excitation
- peak of excitation never surpasses orgasm threshold
- minimal awareness of myotonia resolved
- no intense pleasure
- no satiety
- return to baseline state frustrated/bothered



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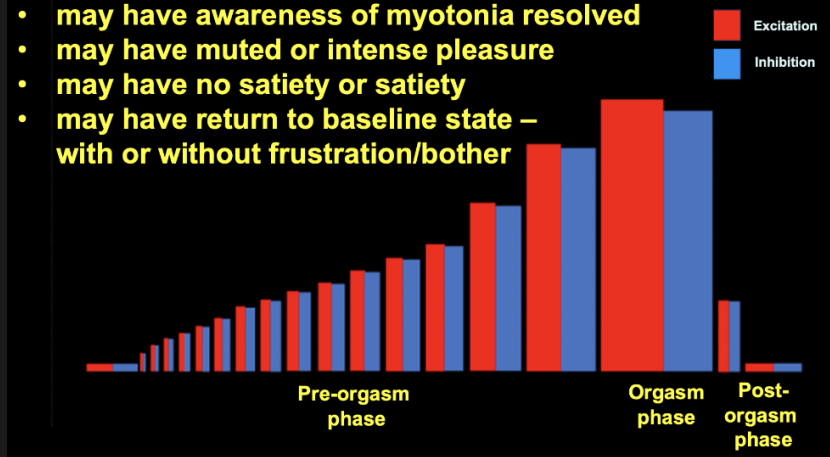

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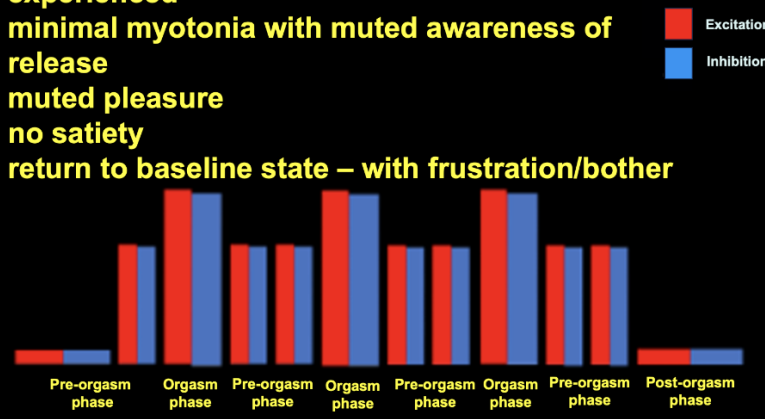
- minimal myotonia with muted awareness of release
- muted pleasure
- no satiety
- return to baseline state – with frustration/bother



PROPOSED PHARMACOLOGIC MANAGEMENT OF FOD ASSOCIATED WITH FAILURE OF/MINIMAL INHIBITION

NOT YET CONSENSED

Failure to Inhibit			
SSRI	dapoxitene	30 – 60 mg PO	1 hour before
	paroxetine	10 mg PO	1 hour before
	sertraline	25 mg PO	1 hour before
Analgesics	acetaminophen	1000 mg PO	1 hour before
	ibuprofen	600 mg PO	1 hour before

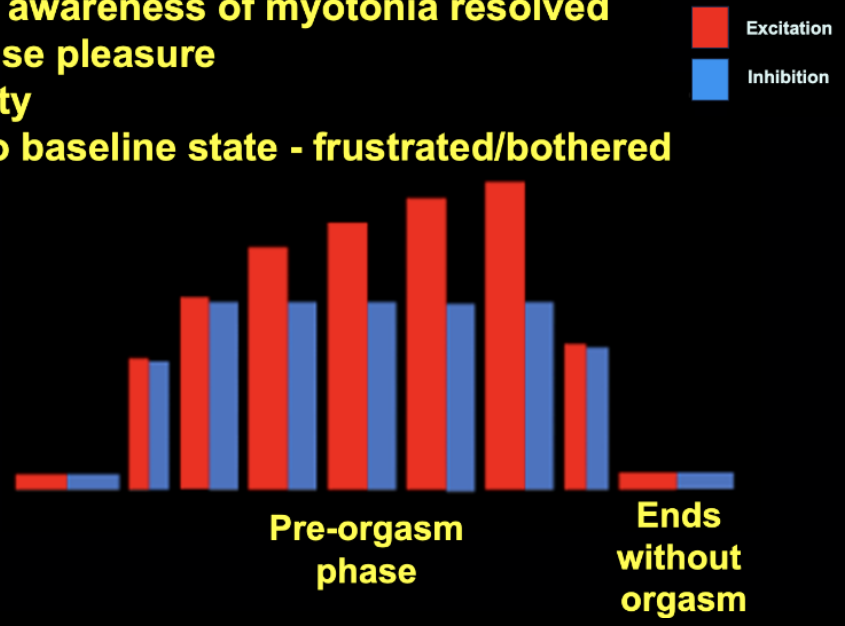
PHARMACOLOGIC TREATMENT STRATEGIES FOR SYMPTOM CONTROL OF FOD ARE OFF-LABEL
PHARMACOLOGIC TREATMENT STRATEGIES FOR SYMPTOM CONTROL OF FOD ARE BASED ON EXPERT OPINION
SEE PACKAGE INSERT FOR DOSE RANGES, ADVERSE EVENTS, TOXICITY, DRUG INTERACTIONS, CONTRAINDICATIONS, POTENTIAL FOR ABUSE, AND OTHER SAFETY INFORMATION

PROPOSED PHARMACOLOGIC MANAGEMENT OF FOD ASSOCIATED WITH FAILURE OF/MINIMAL INHIBITION

NOT YET CONSENSED

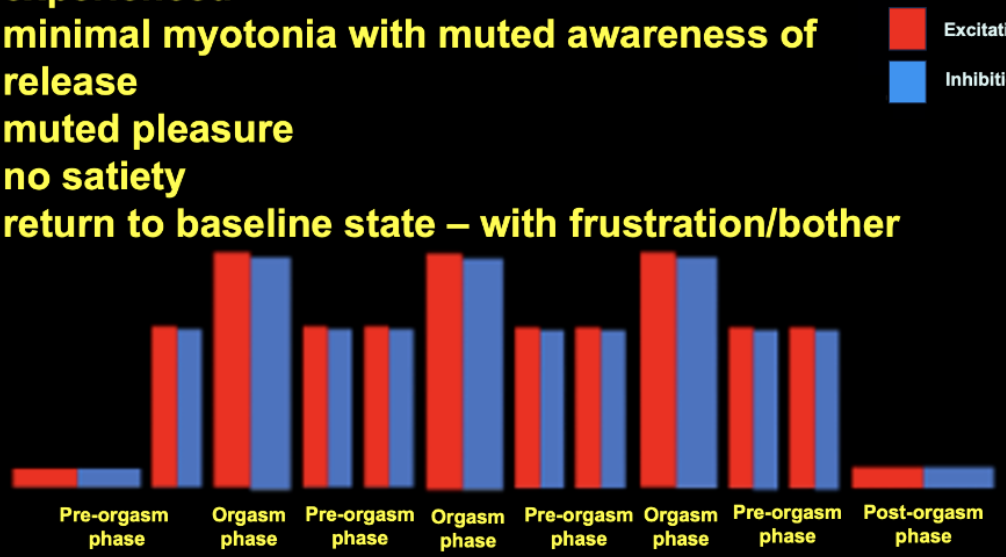
Pre-orgasm Phase: "Failure to Inhibit" FOD

- failure to inhibit increased genital/non-genital sensitivity leading to aversive discomfort during progressive increase in "climb" of excitation
- peak of excitation never surpasses orgasm threshold
- minimal awareness of myotonia resolved
- no intense pleasure
- no satiety
- return to baseline state - frustrated/bothered



Pre-orgasm/Orgasm Phase: Minimal Excitation/Minimal Inhibition Premature/Muted Orgasm FOD

- minimal excitation, minimal inhibition
- peak of excitation surpassed at very low orgasm threshold
- "blips" of repeated muted premature orgasm experienced
- minimal myotonia with muted awareness of release
- muted pleasure
- no satiety
- return to baseline state – with frustration/bother



PROPOSED PHARMACOLOGIC MANAGEMENT OF FOD ASSOCIATED WITH ORGASMIC ANHEDONIA

NOT YET CONSENSED

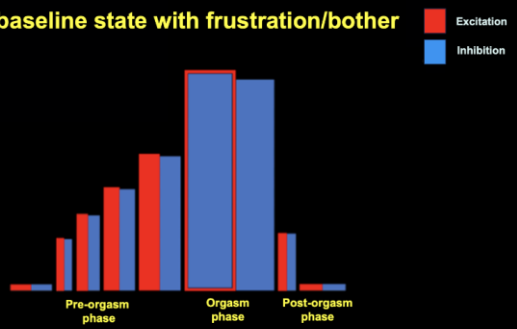
Failure to Achieve Pleasure			
Opioid antagonist	low dose naltrexone	4.5 mg PO	1 hour before
	naloxone nasal spray	4 mg sprayed into one nostril	during sexual activity
GABA antagonist	ashwagandha	250 mg PO	1 hour before

Orgasm Phase:
Orgasmic Anhedonia FOD

- **Orgasm phase: peak of excitation surpasses orgasm threshold, release/relaxation of myotonia, cessation of stimulation, de-activation/resolution of excitation**

NO PLEASURE EXPERIENCED

- **no satiety**
- **return to baseline state with frustration/bother**



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PROPOSED PHARMACOLOGIC MANAGEMENT OF FOD ASSOCIATED WITH ORGASMIC ANHEDONIA

NOT YET CONSENSED

ELSEVIER

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ORIGINAL ARTICLE

Naltrexone-Induced Augmentation of Sexual Response in Men

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Background. To ascertain the role of endogenous opioids in sexual response, naltrexone, an opiate receptor antagonist, was administered to men, and its effect on selected self-report measures of sexual response to masturbation was recorded.

Methods. The data are based on results from 20 healthy, sexually active (alone or with a partner) men, aged 20–29 years, who ingested naltrexone (25 mg/day × 3) or placebo in a randomized, double-blind crossover design. There was at least a 14-day interval between drug and placebo treatment. Between 18 and 22 h after the most recent dose of drug or placebo, subjects viewed sexually explicit videos in privacy for 2 h. They were instructed to masturbate and have as many orgasms as desired. The following three different self-report measures of their responses were recorded: number of orgasms; intensity of sexual arousal, and orgasmic intensity.

Results. Under the naltrexone condition, the volunteers experienced a significantly greater mean number of orgasms (3.4 ± 0.2 SEM) than under the placebo condition (2.6 ± 0.3). The total number of orgasms was 67 under the naltrexone condition and 51 under the placebo condition. At the first orgasm, the measure of intensity of arousal was significantly greater in the naltrexone (3.9 ± 0.2) than placebo (3.4 ± 0.2) condition, and the measure of orgasmic intensity was significantly greater in the naltrexone (3.7 ± 0.2) than in the placebo (3.0 ± 0.3) condition.

Conclusions. The present study provides evidence that endogenous opioids modulate orgasmic response and the perceived intensity of sexual arousal and orgasm in men. The findings suggest that naltrexone could be clinically useful in cases of inhibited sexual desire and erectile dysfunction.

PROPOSED PHARMACOLOGIC MANAGEMENT OF FOD ASSOCIATED WITH ORGASMIC ANHEDONIA

NOT YET CONSENSED

Increase Excitation			
Category	Medication	Dose	Administration
CNS stimulant	caffeine	100 mg PO	1 hour before*
	dexmethylphenidate hydrochloride	2.5 mg PO	1-4 hours before*
	dextroamphetamine and amphetamine mixed salts	2.5 mg and increase by 2.5 mg up to 10 mg PO	1-6 hours before*
	methylphenidate	5 mg PO	1-2 hours before*
	lisdexamfetamine	10 mg PO	1-6 hours before*
Dopamine	bremelanotide	1.75 mg (0.3 ml) subcutaneous autoinjector administered to abdomen/thigh	1 hour before
	cabergoline	0.5 mg PO twice weekly	chronic
	pramipexole	0.375 mg PO daily	chronic
	ropinirole	0.25 mg PO 3 times/day	chronic
Dopamine/ norepinephrine	bupropion	75 mg PO in morning	chronic
Oxytocin	oxytocin lozenges	500 units sublingual	1 hour before
PDE5 inhibitor	sildenafil	20 mg PO	1 hour before
	tadalafil	5 mg PO	1 hour before
Serotonin antagonist	buspirone	10 mg PO twice daily	chronic
	flibanserin	100 mg PO nightly	chronic
Testosterone	1% testosterone gel	1/10th of a generic 50mg testosterone tube (0.5 ml; 5mg) to back of calf	2 hours before

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PROPOSED PHARMACOLOGIC MANAGEMENT OF FOD ASSOCIATED WITH POST-ORGASM ILLNESS SYNDROME

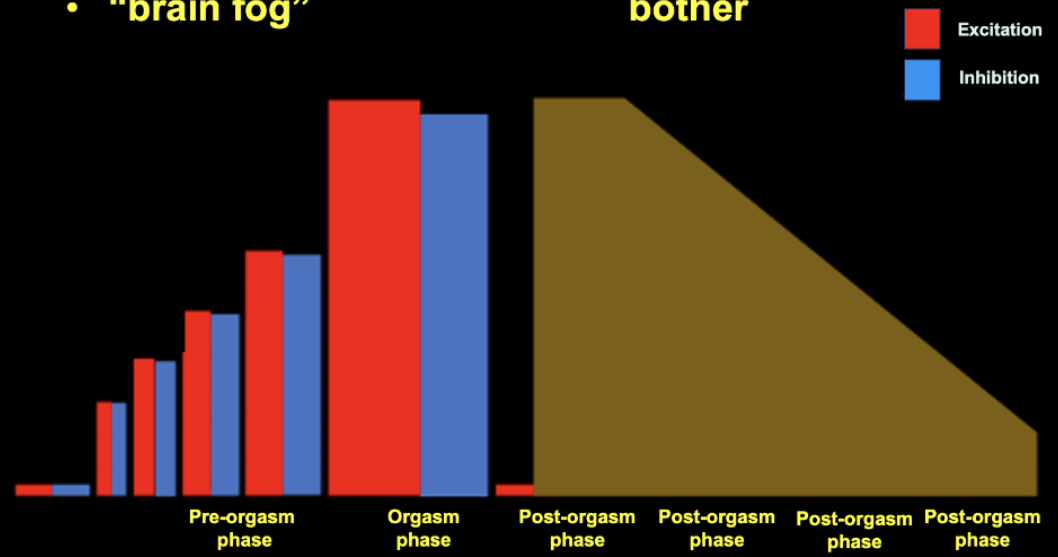
NOT YET CONSENSED

POIS is hypothesized to be associated with marked protracted states of:

ELEVATED SEROTONIN
LOW DOPAMINE
LOW OXYTOCIN
LOW ADRENALIN

Post-Orgasm Phase:
Post-Orgasm Illness Syndrome (POIS) FOD

- marked protracted return (range days to weeks) to baseline state with
  - malaise
  - fatigue
  - "brain fog"
- low energy
- lack of motivation
- extreme frustration/ bother



PROPOSED PHARMACOLOGIC MANAGEMENT OF FOD ASSOCIATED WITH POST-ORGASM ILLNESS SYNDROME

NOT YET CONSENSED

Post-Orgasm Illness Syndrome			
Category	Medication	Dose	Administration
CNS stimulant	caffeine	100 mg PO	1 hour before/after orgasm, repeat as tol
	dextroamphetamine and amphetamine mixed salts	2.5 mg and increase by 2.5 mg up to 10 mg PO	1-6 hours before/after, repeat daily
Dopamine	bremelanotide	1.75 mg (0.3 ml) subcutaneous autoinjector administered to abdomen/thigh	1 hour before/after, repeat as needed (4/month)
	cabergoline	0.5 mg PO twice weekly	Start after, one dose
Dopamine/ norepinephrine	bupropion	75 mg PO in morning	Start after, daily
Oxytocin	oxytocin lozenges	500 units sublingual	Start after 1 hour before, repeat daily
Serotonin antagonist	buspirone	10 mg PO twice daily	Start after, daily
Testosterone	1% testosterone gel	1/10th of a generic 50mg testosterone tube (0.5 ml; 5mg) to back of calf	2 hours before, daily
Antihistamines	Hydroxyzine	25-50 mg PO	Start after daily

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CONTEMPORARY PHARMACOLOGY OF ORGASM

ISSWSH Orgasm Consensus Panel

2016 ISSWSH Definition of Orgasm

Proposed 2025 ISSWSH Definition of Orgasm [not yet consensed]

Three Phases of Orgasm

Pre-Orgasm Phase FOD: Failure to Excite, Failure to Inhibit

Pre-Orgasm/Orgasm Phase FOD: Delayed Orgasm; Minimal Excitation/Minimal Inhibition Premature/Muted Orgasm

Orgasm Phase FOD: Orgasmic Anhedonia

Post-Orgasm Phase FOD: Post-Orgasm Illness Syndrome

Proposed Pharmacologic Management of FOD [not yet consensed]

Conclusion

TAKE HOME MESSAGES

1. ISSWSH ORGASM CONSENSUS PANEL ON FOD IS ONGOING [NOT YET CONSENSED]: APPRECIATE FEEDBACK ON ALL PRESENTATIONS

2. PROPOSED 2025 ISSWSH DEFINITION OF ORGASM INVOLVES ENHANCED PHYSIOLOGIC DESCRIPTION OF THREE PHASES OF ORGASM

3. 2025 ISSWSH DEFINITION ENABLES RECOGNITION OF AT LEAST SIX DIFFERENT DISORDERS OF FOD: AN INDIVIDUAL MAY HAVE HYBRID FOD

4. PHARMACOLOGIC STRATEGIES TO TREAT FOD BASED ON SUSPECTED FOD PATHOPHYSIOLOGIES

5. MORE RESEARCH ON ORGASM / FOD NEEDED

6. PROPOSED PHARMACOLOGIC MANAGEMENT OF FOD IS OFF-LABEL; BASED ON EXPERT OPINION

7. WHEN PRESCRIBING DRUGS, SEE PACKAGE INSERT FOR DOSE RANGES, ADVERSE EVENTS,TOXICITY, DRUG INTERACTIONS, CONTRAINDICATIONS, POTENTIAL FOR ABUSE, AND OTHER SAFETY INFORMATION