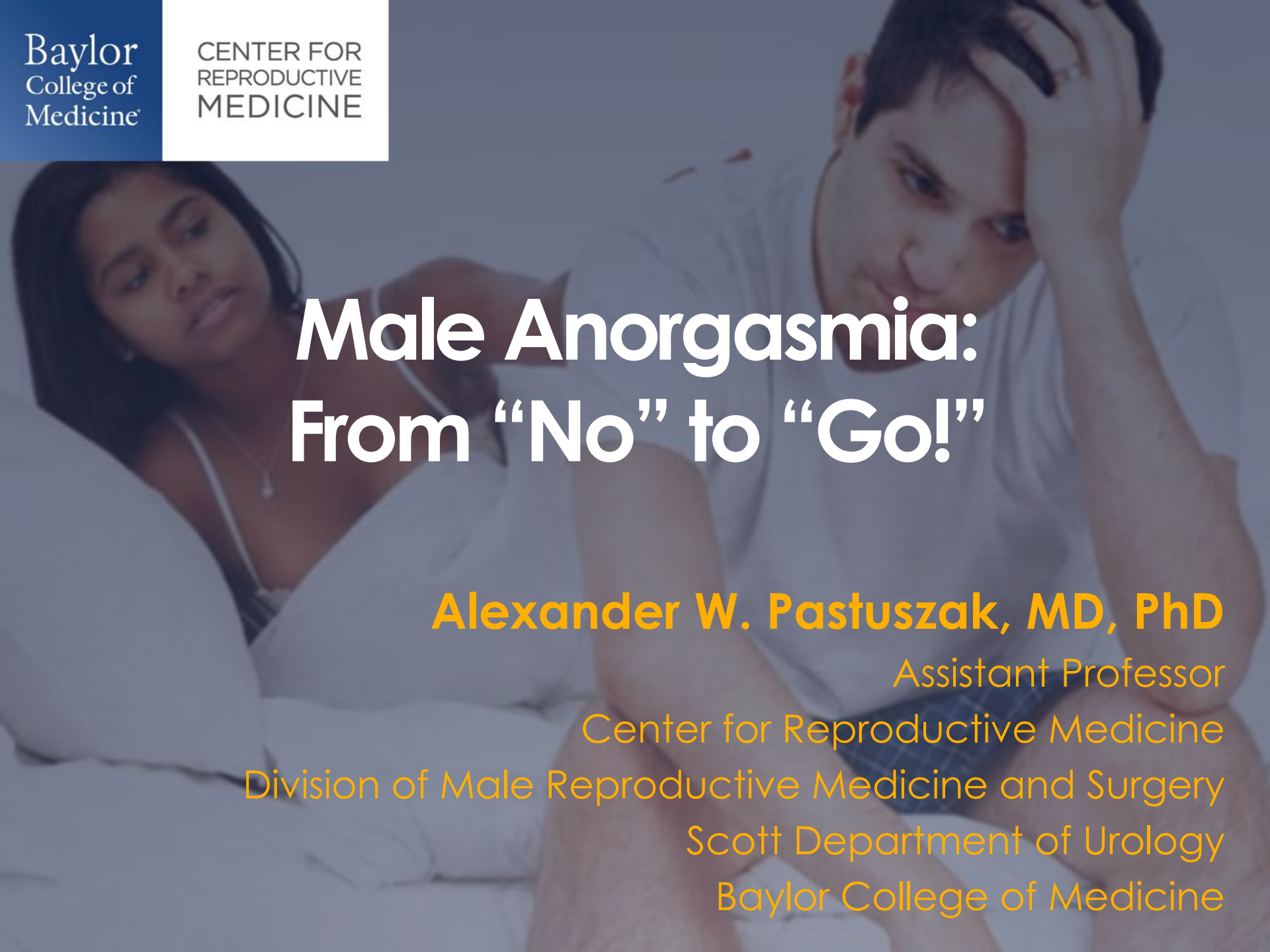

Baylor College of Medicine

CENTER FOR REPRODUCTIVE MEDICINE

Male Anorgasmia: From "No" to "Go!"

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Disclosures

- Endo – speaker, consultant, advisor
- Boston Scientific / AMS – consultant
- Woven Health – founder, CMO

Objectives

- Understand what delayed ejaculation (DE) and anorgasmia are
- Review the anatomy and physiology relevant to these conditions
- Review what is known about the causes of DE and anorgasmia
- Discuss management of DE and anorgasmia

Definitions

Delayed Ejaculation (DE) / Anorgasmia

- The persistent or recurrent delay, difficulty, or absence of orgasm after sufficient sexual stimulation that ***causes personal distress***

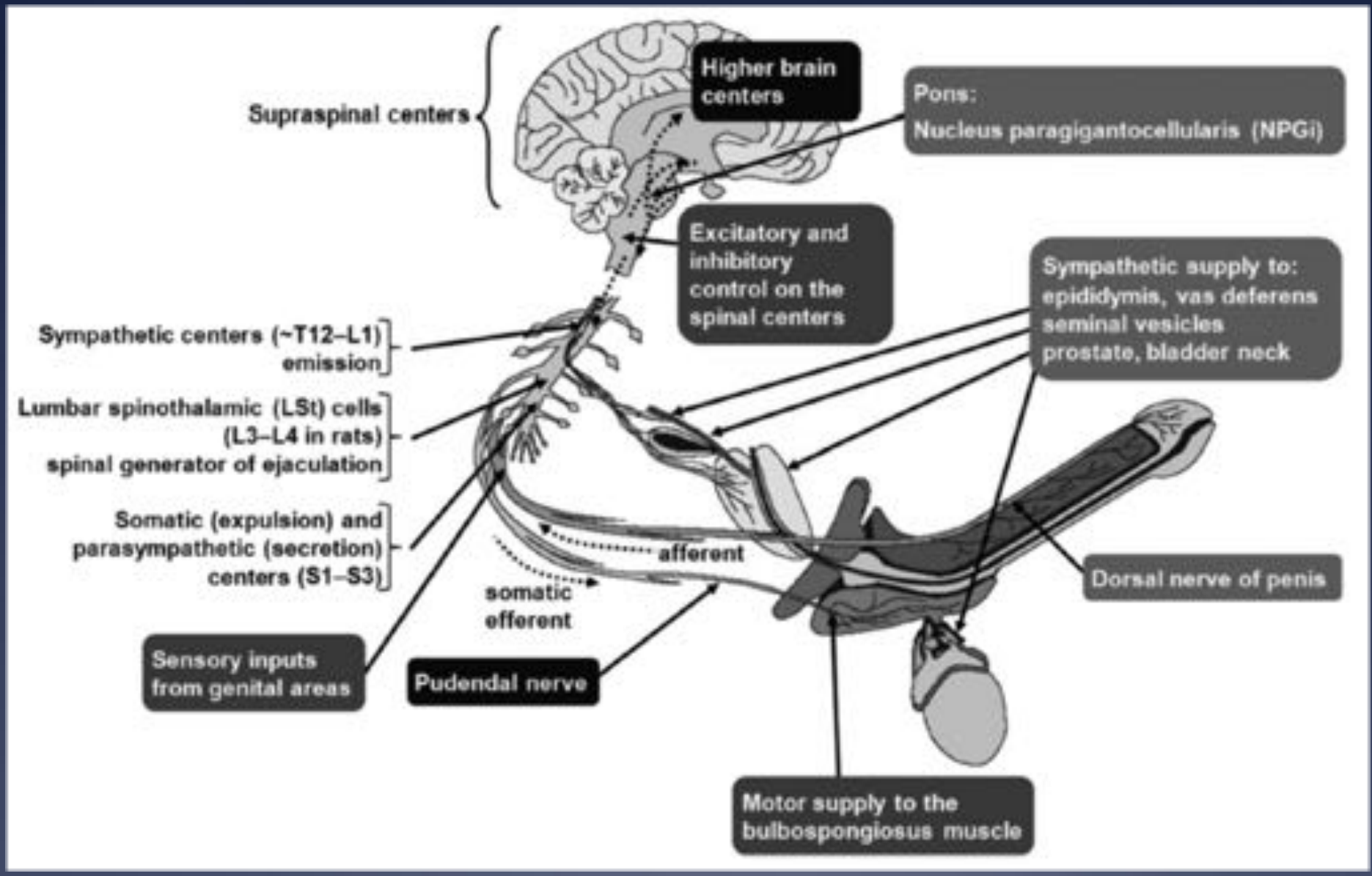
Intravaginal Ejaculatory Latency Time (IELT)

- **Normal** (median) → 5.4 minutes (0.55-44.1 minutes)
- **DE** → mean IELT + 2 SD = 25 minutes

- **Incidence** → 2-11%
  - Depends in part on definition used

J Sex Med. 2005; 2: 492.
Int J Impot Res. 2012; 24: 131.

Ejaculation



J Sex Med. 2011; 8 (Suppl 4): 310.

Neurochemistry

Sexual Response Areas of the Brain

- Pons
  - Nucleus paragigantocellularis

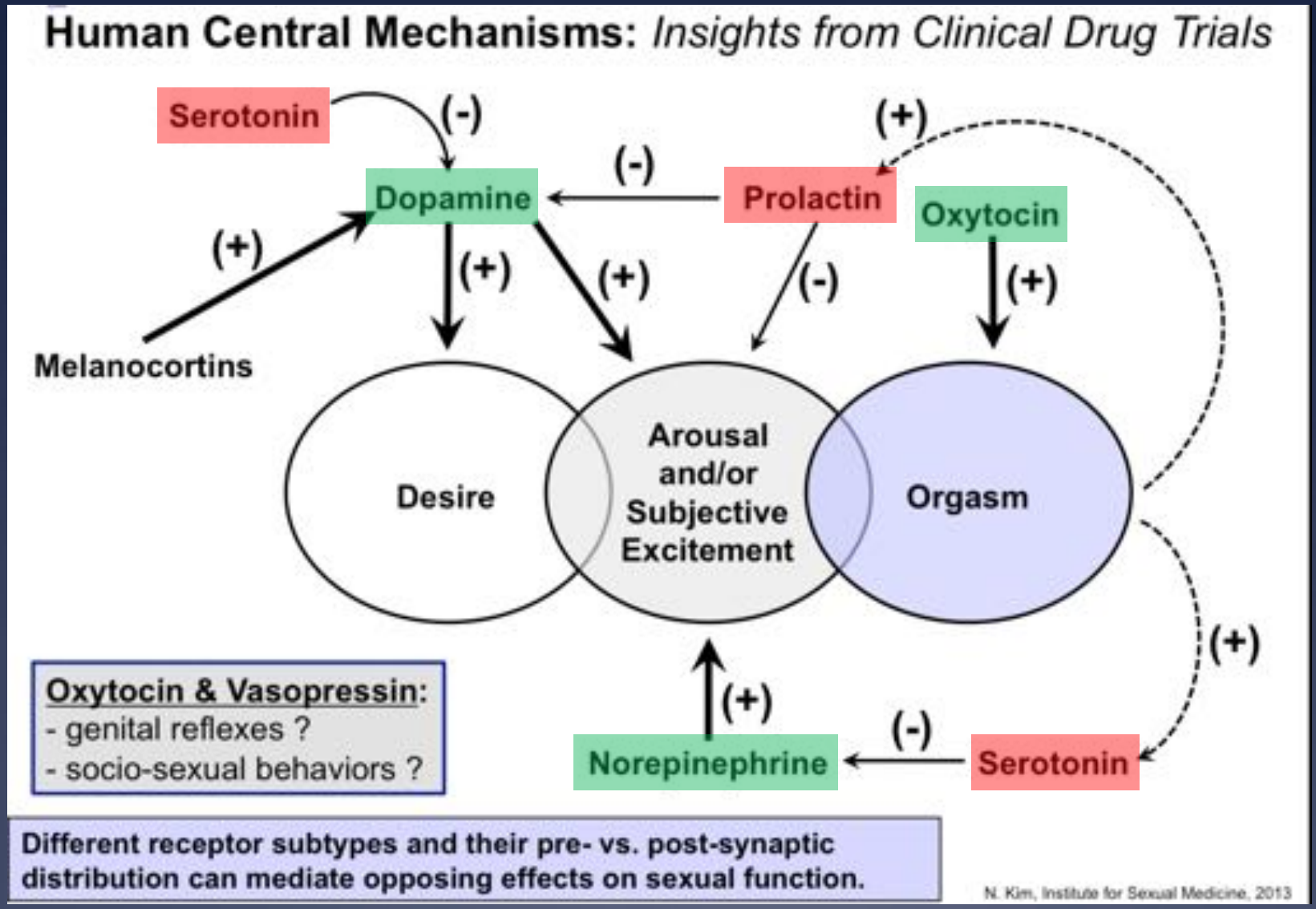
Neurochemicals

- *Norepinephrine, serotonin*:
  - Inhibit libido, erectile response, ability to climax
- *Dopamine* - promotes the above
- *Prolactin* – involved in the refractory period

SSRIs - increase serotonin / norepi & cause sexual dysfunction!

- Anorgasmia is most common symptom

Neurochemistry of Sexual Function



Normal Hormonal Function

Testosterone

- AR ubiquitous → including pelvic floor
- High T – PE; Low T = DE in some men
  - T levels vary in men with DE

Thyroid Hormone

- Similar to T levels in effect → high thyroid = PE; low thyroid = DE

Prolactin

- May be surrogate of serotonergic activity
- High Prl → low T and PE
- Suppressed during orgasm → spikes after

Oxytocin

- Surges during ejaculation, orgasm, and detumescence
- Increases ejaculation, paternal nurturing, sexual desire, and long-term romantic bonds

Causes of Anorgasmia

IELT Determinants:

- Genetics

Table 1. Medications Associated With Ejaculatory Dysfunction[2,5,10,24,27]

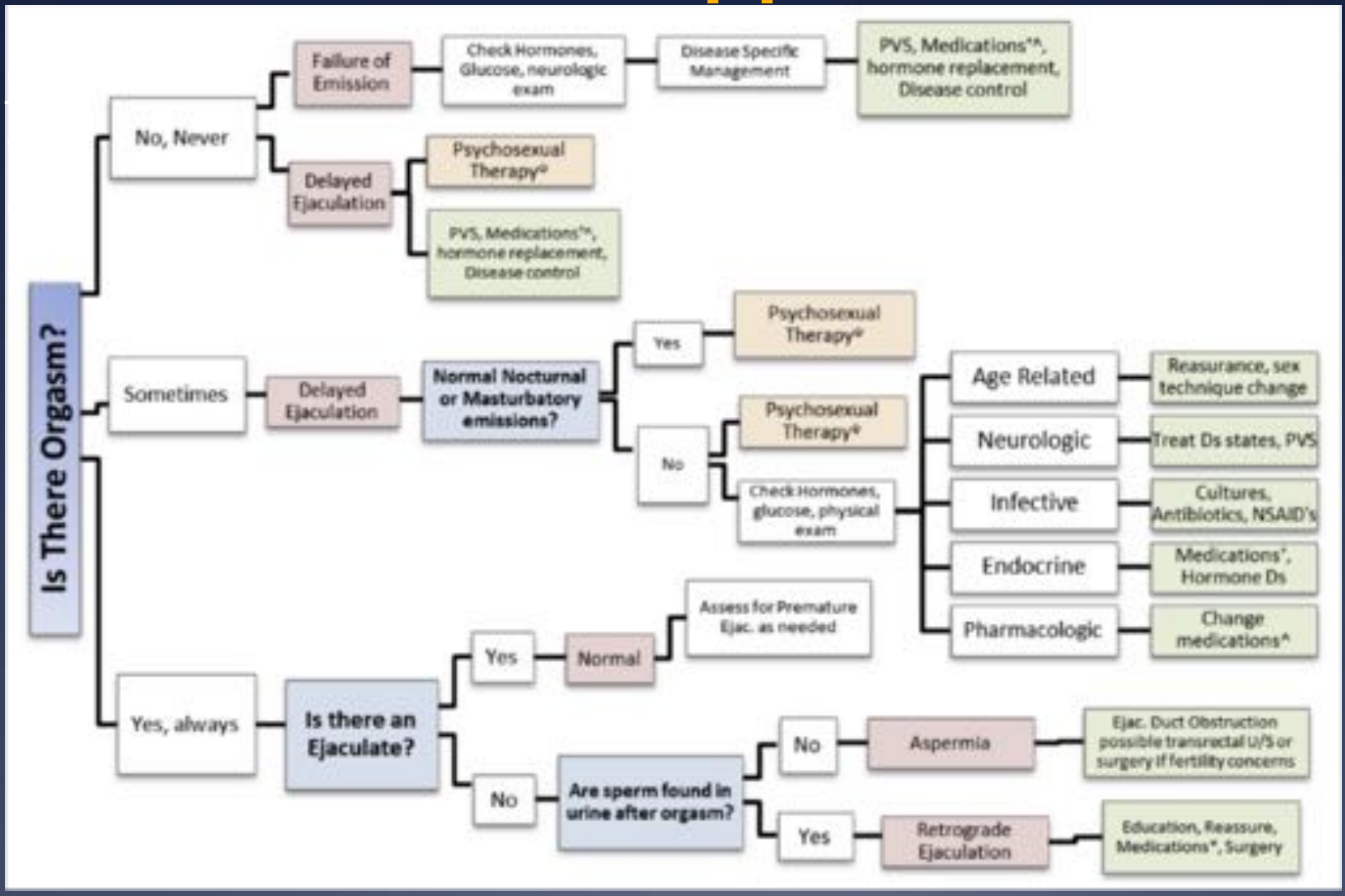
Alcohol	Clomipramine	Mebanizine	Phenelzine sulfate
Alprazolam	Desmethylimipramine	Mesoridazine	Prazosin
Aminocaproic acid	Fluoxetine	Methadone	Protriptyline
Amitriptyline	Fluvoxamine	Methyldopa	Reserpine
Amoxapine	Guanadrel	Naproxen	Sertraline
Baclofen	Guanethidine	Nortriptyline	All SSRIs
Bethanidine	Haloperidol	Pargyline	Thiazide Diuretics
Butaperazine	Hexamethonium	Paroxetine	Thioridazine
Chlordiazepoxide	Imipramine	Perphenazine	Trazadone
Chlorimipramine	Iproniazid	Phenothiazine	Trifluoperazine
Chlorpromazine	Isocarboxazid	Phenoxybenzamine	
Chlorprothixene	Lorazepam	Phentolamine	

SSRIs = selective serotonin reuptake inhibitors.

- Neurologic disorders (i.e. MS, DM)
- Endocrine disorders (i.e. low T, high Prl, thyroid)
- Medications

J Sex Med. 2006; 3: 104.
Sex Med Rev. 2016; 4: 167.

Treatment Approaches



Sex Med Rev. 2016; 4: 167.

Psychological & Sexual Therapy

When Should I See a Sex Therapist?

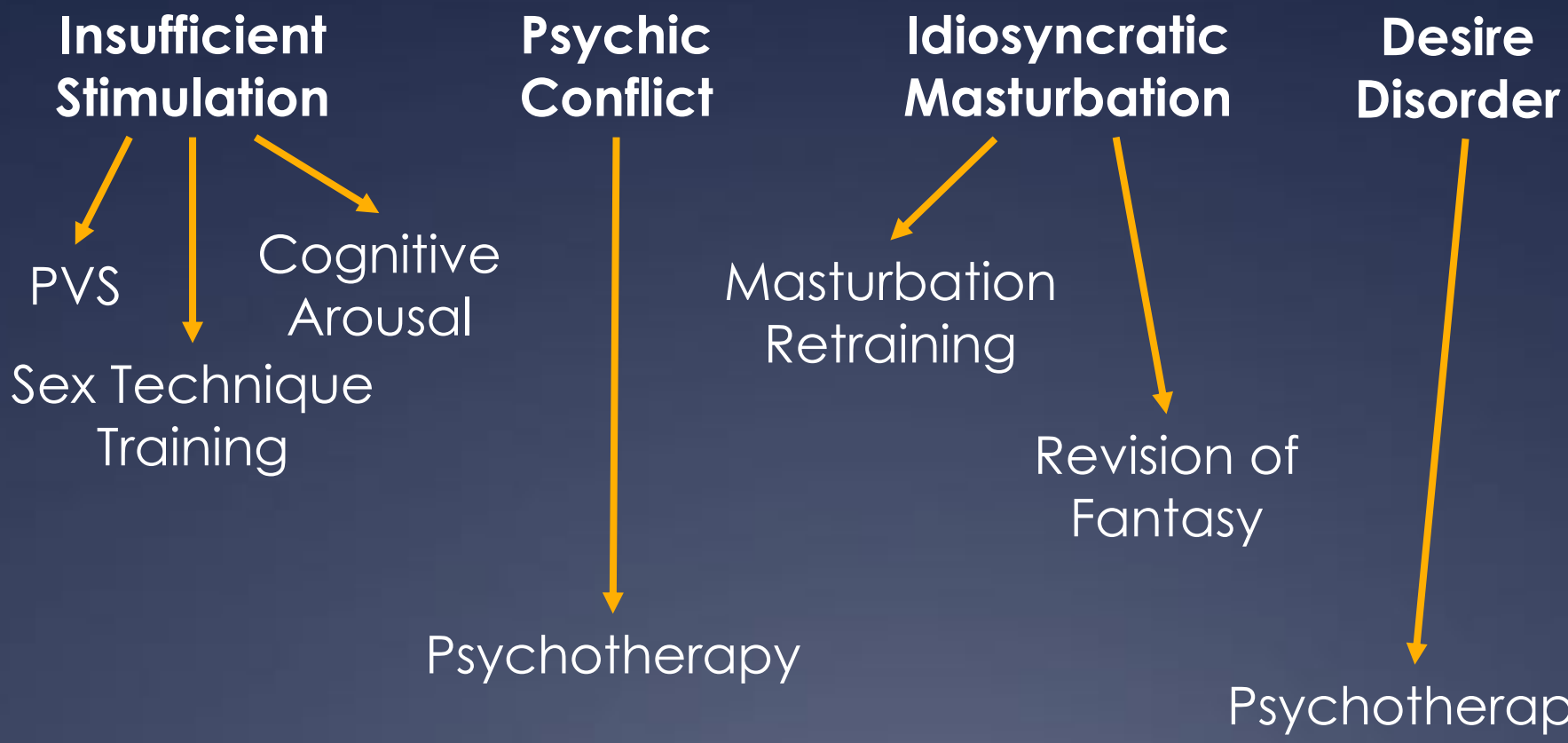
- No organic cause of DE
- Psychosexual factors suspected

General Principles

- Involve patient's partner
  - Set expectations
  - Educate on sexual response cycle
  - Improve communication between partners

Sex Therapy - Approaches

Theories of Psychological DE and Treatment



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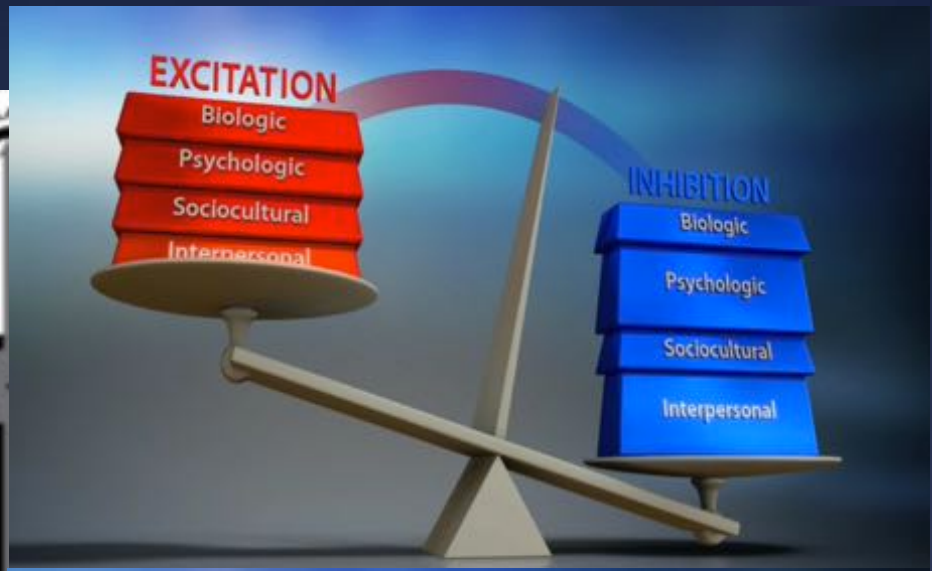
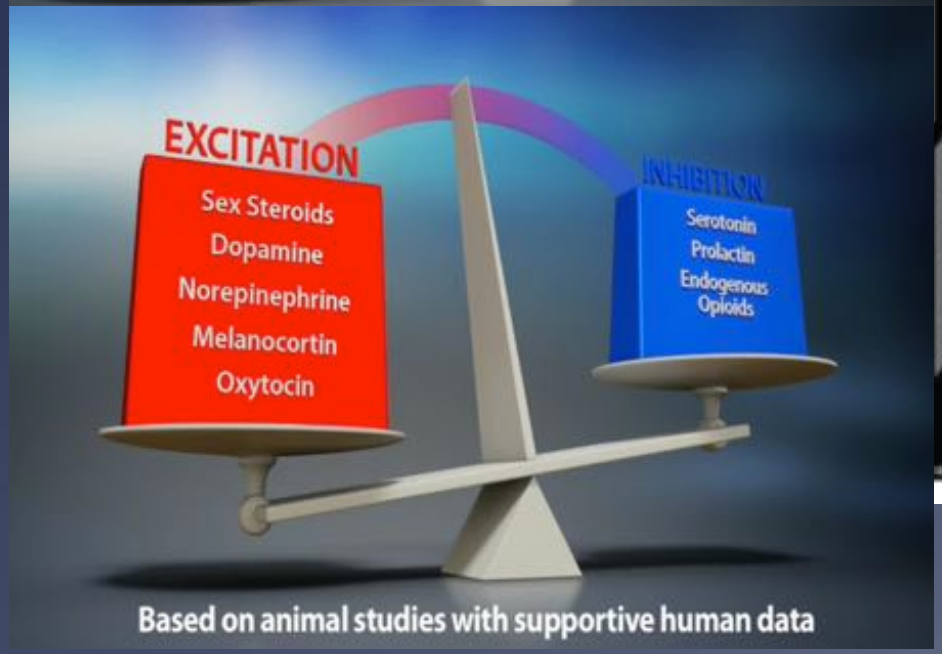
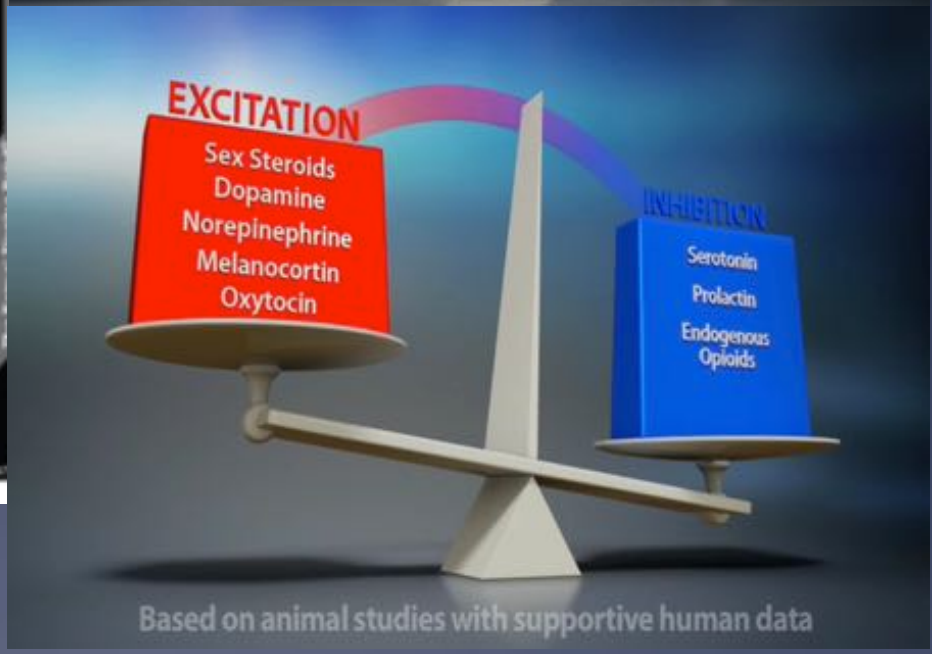
The Sexual Tipping Point Model







J Sex Med. 2009; 6: 629.

Pharmacotherapy

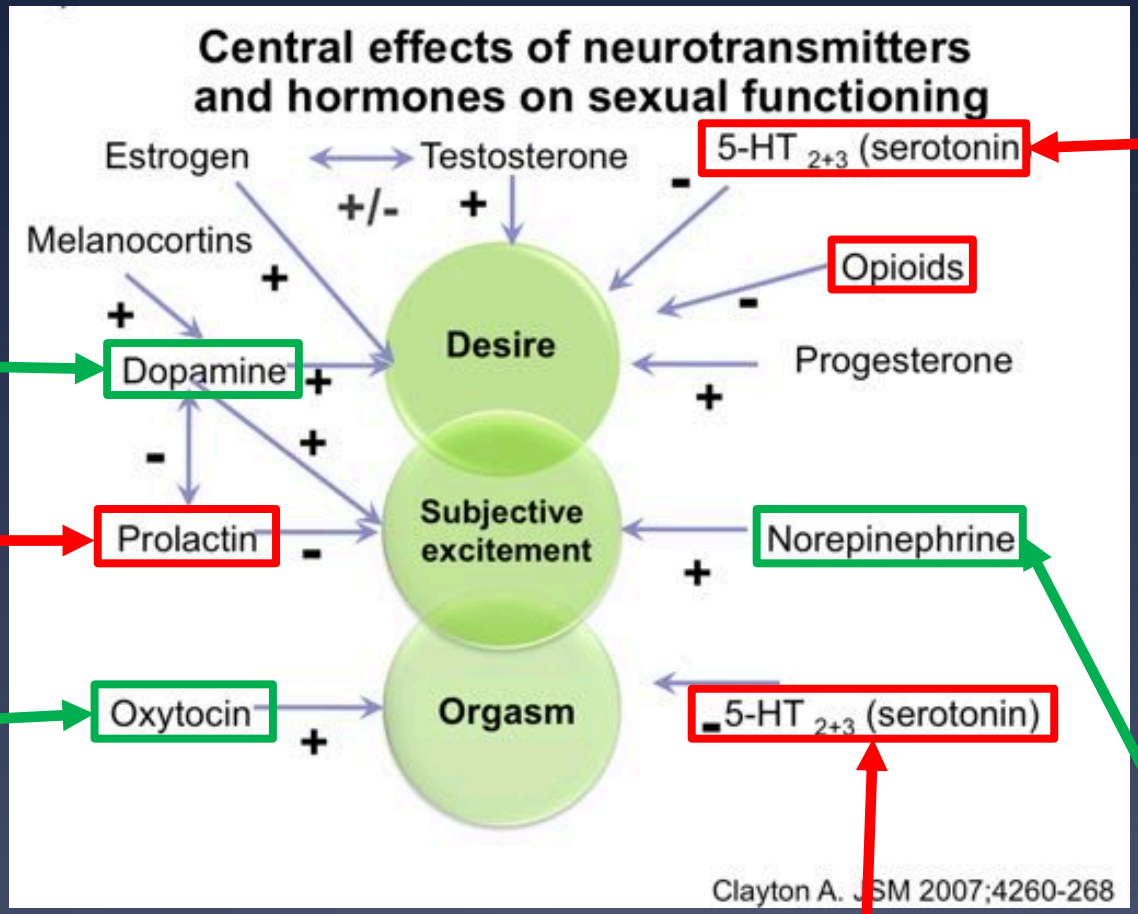
There is NO MEDICATION FOR DE that is currently approved by the U.S. FDA

Pharmacotherapies

- There are no clinical trials demonstrating efficacy
- Studies are small, underpowered, retrospective, and not controlled
- Disparities in outcomes likely reflect different populations

Cabergoline	Bupropion
Oxytocin	Cyproheptadine
Buspirone	Pseudoephedrine
Ephedrine	Midodrine
Yohimbine	Amantadine
Apomorphine	Bethanechol
Loratadine	Reboxitine

Pharmacotherapy



Buspirone

Bupropion
Apomorphine
Amantadine

Cabergoline

Oxytocin

Buspirone

Ephedrine
Pseudoephedrine
Midodrine

Pharmacotherapy – General Principles

- DE with concurrent ED should be treated with PDE5 inhibitors
- Penile vibratory stimulation can be helpful → 72% success with 3 x 1 minute rest / application cycles
- Most helpful drug effect → switch to **bupropion** from SSRI
- **Cabergoline** is another top choice for medical management

Treatment of SSRI-Induced DE

- Use when SSRI is likely cause of DE
- Can also switch to different SSRI in same class
- DE treatment with meds up to 70% effective

Drug	PRN Dosage	Daily Dosage
Cyproheptadine	4-12 mg (3-4h prior to sex)	--
Bethanechol	20 mg (1-2 hours prior to sex)	--
Amantadine	100-400 mg (for 2 days prior to sex)	75-100 mg BID / TID
Bupropion	--	75 mg BID / TID
Buspirone	--	5-15 mg VID
Loratadine	--	10 mg Daily

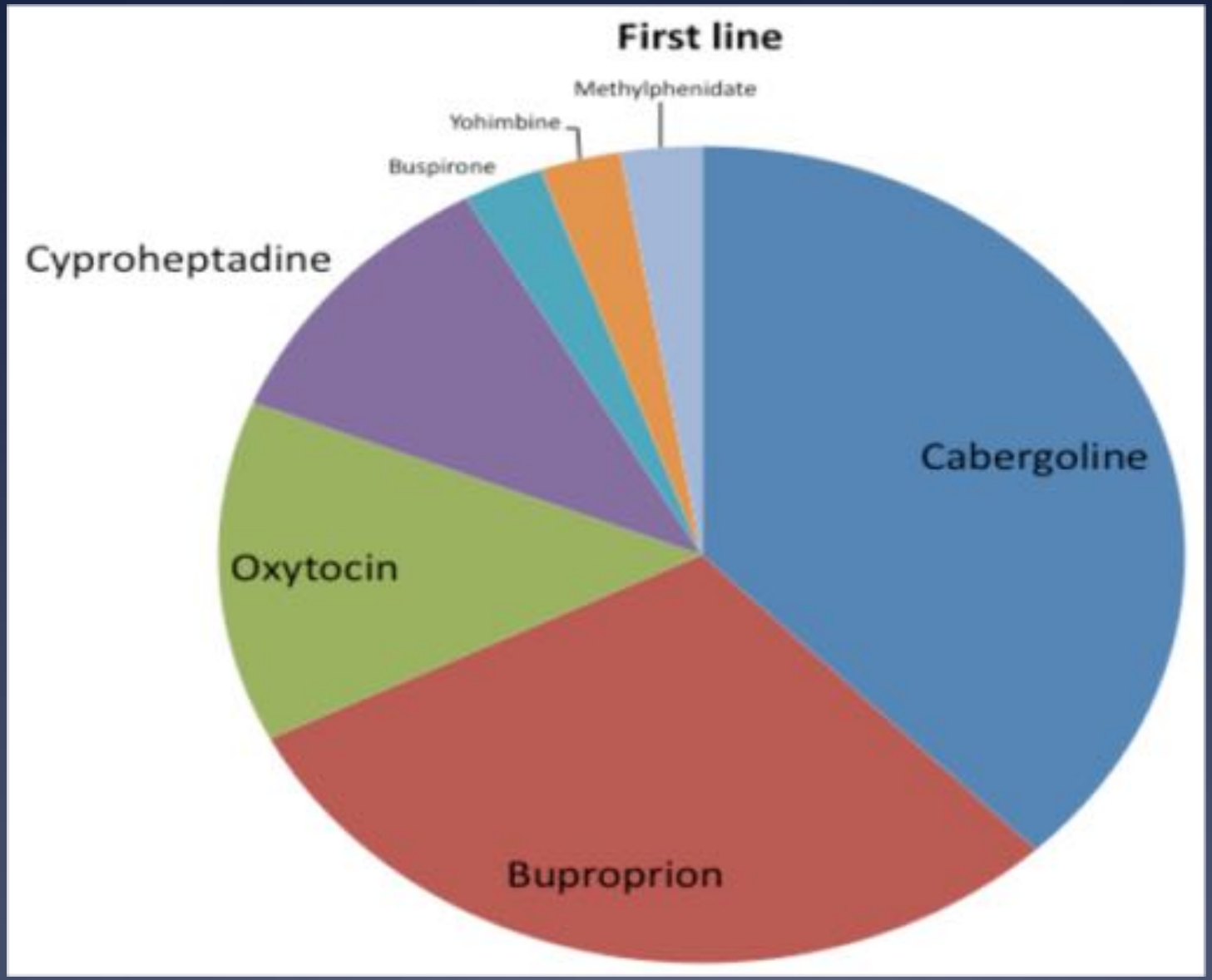
Sex Med Rev. 2016; 4: 167.
Andrology. 2015; 3: 626.

Treatment of DE – No SSRI

Drug	PRN Dosage	Daily Dosage
Oxytocin	24 IU intranasal / SL during sex	--
Pseudoephedrine	60-120 mg (120-150 min prior to sex)	--
Ephedrine	15-60mg (1 hour prior to sex)	--
Midodrine	5-40mg Daily (30-120 min prior to sex)	--
Apomorphine	0.5-1.5mg intranasal (20 min prior to sex)	--
Yohimbine	--	5.4 mg TID
Cabergoline	--	0.25-2 mg BIW
Reboxetine	--	4-8 mg
Imipramine	--	25-75 mg Daily

Sex Med Rev. 2016; 4: 167.

First Line Meds Used by SMSNA



Medication Considerations

If patient is on SSRI

- Switch to **bupropion** 75 mg PO BID / TID
  - SUICIDALITY, chest pain, palpitations, blurred vision
- If cannot switch → **cyproheptadine** 4-12 mg 3-4 h before sex
  - Nausea, dizziness, urinary retention, photosensitivity,
- Next, try **loratadine** 10 mg QD
  - Drowsiness, fatigue, HA, dry mucous membranes, pharyngitis

If patient is NOT on SSRI

- Check prolactin levels
- Prolactin high / normal → **cabergoline** 0.25-2 mg BIW
  - Nausea, dizziness, fatigue, abdominal pain, anxiety
- Prolactin low / low normal → **oxytocin** 24 IU intranasal

Backup Agents

- **Yohimbine** 5.4 mg TID
  - Urinary retention, hyperglycemia, tachycardia, irritability, tremor, nausea, dizziness, HA, flushing, diaphoresis, HTN

Sex Med Rev. 2016; 4: 167.

Bupropion and Anorgasmia

- **Used for SSRI-induced sexual dysfunction**

Ashton & Rosen 1998:

- 47 men with SSRI-induced sexual dysfunction
- 75 vs. 150mg bupropion 1-2h prior to sex → 75mg TID x 2 weeks if not responding

RESULTS:

- 31/47 (66%) of patients had improvement
- 18/47 (38%) of patients improved with Prn use
- Side effects → discontinuation in 7/47 (15%)

Other studies have had mixed results
Fixed dose bupropion may work better than prn

J Clin Psychiatry. 1998; 59: 112.

Cyproheptadine and Anorgasmia

- Histamine, 5HT, and AChR antagonist
- **Used for SSRI-induced sexual dysfunction**

Ashton, Hamer & Rosen 1997:

- 596 patients on SSRI
- SSRI-associated sexual dysfunction in 97 (16%)
- 45 treated with yohimbine, amantadine, or cyproheptadine

RESULTS:

- Yohimbine more effective than amantadine or cyproheptadine

Only other studies are case reports
Partial response to cyproheptadine reported

J Clin Psychiatry. 1997; 23: 165.

Cabergoline and Anorgasmia

- D2 receptor agonist → lowers prolactin
- Decreases refractory period in men

Hollander et al. 2016:

- 131 men treated with cabergoline 0.5mg BIW for orgasmic disorder
- Duration and subjective treatment response noted

RESULTS:

- 87/131 (66%) reported improvement in orgasm
- 44/131 (34%) reported no change
- Not impacted by testosterone level / therapy, age, h/o prostatectomy

Sex Med. 2016; 4: e28.

Oxytocin and Anorgasmia

- Oxytocin surges during orgasm in men
- Decreases ejaculatory latency in animals

Burri et al. 2008:

- DB, PC, balanced crossover study
- 10 healthy men treated with oxytocin 24 IU intranasal → washout period
- Examined oxytocin, catecholamine levels, sexual arousal

RESULTS:

- Increased oxytocin and catecholamine levels
- 8/10 men with increased sexual arousal

Psychoneuroendocrinology. 2008; 33: 591.

Yohimbine and Anorgasmia

- Used to treat ED and sexual dysfunction
- Acts on spinal cord adrenergic receptors → ejaculation
- Success with treatment of SSRI-induced DE

Adniyi et al. 2007:

- 29 men with orgasmic dysfunction
- Treated with 20 mg yohimbine → 50 mg if not effective

RESULTS:

- 19/29 (66%) men reached orgasm
- 3 needed PVS to reach orgasm

Asian J Androl. 2007; 9: 403.

Summary

- Orgasmic function is dependent on interplay of numerous neurohormonal and physical factors
- Norepinephrine, serotonin, dopamine, and prolactin are the primary neurohormones involved
- DE/anorgasmia can be caused by many meds, in particular SSRIs
- Treatment should include psychosexual and medical therapy
- Medical therapies are poorly studied and not FDA approved


Thank you!
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