Sexual Pharmacology

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Envision SRH

Objectives

List three commonly used medications with known sexual side effects

Describe the impact of serotonin on sexual response

Discuss the indication and current use of flibanserin

Inadequate Data and Guidelines

- Most trials do not ask enough about sexual side effects
- Tools for assessing sexual effects are inadequate
- Discrepancies between best practices by "sexual medicine" vs. other specialties
- Most data on neurotransmitters is from animal studies

Controversies involving treatments for sexual difficulties

Stakeholders interpret science for us in ways that support their political or ideological views, economic interests, or skill sets

Levine, S. B. (2015). *Arch Sex Behav,*

Serendipity

Much of "drug discovery" has been serendipitous

Sexual effects are often not recognized until enough participants in clinical trials or patients in treatment offer the information

- SSRI fluoxetine
- PDE-5 inhibitor sildenafil

Pfaus, J. G. (2009). *J Sex Med*

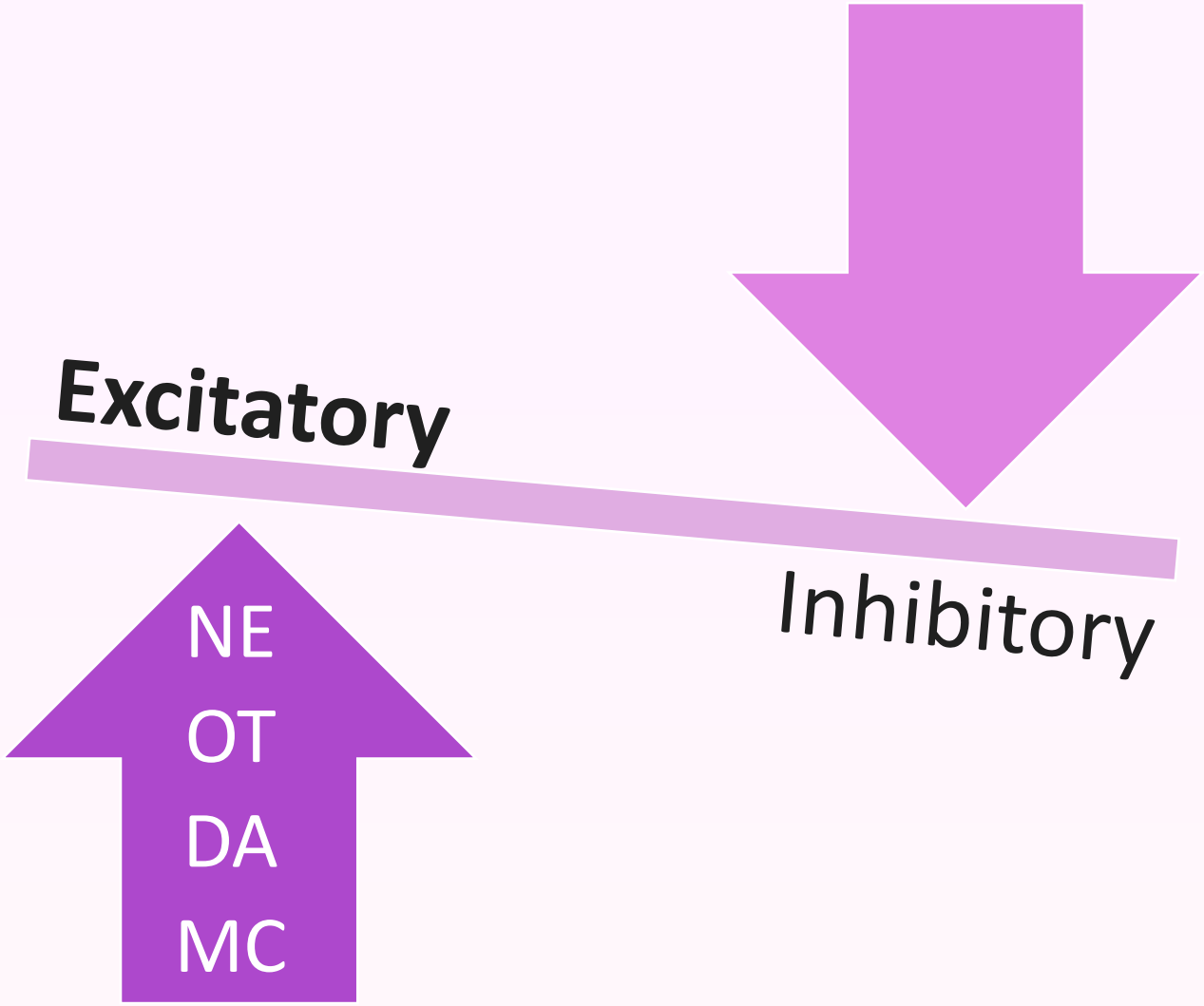
Mechanisms of Sexual Excitation

Sexual excitation involves the activation of neurotransmitters

- Noradrenaline (NE) and oxytocin (OT) stimulate sexual arousal
- Dopamine (DA) and melanocortins (MCs) stimulate attention and desire in response to sexual cues and stimulation

Pfaus, J. G. (2009). *J Sex Med*

Excitation and Inhibition



Mechanisms of Sexual Excitation

Nitric oxide increases blood flow in the genitals

Sexual excitation can be primed:

- Internally by steroid hormone actions
- Externally by sexual incentives
- Externally by drugs that activate excitatory neurochemical systems

Pfaus, J. G. (2009). *J Sex Med*

Dopamine Agents

- Pramipexole
- L-DOPA
- Amantadine
- Methylphenidate
- Dextroamphetamine
- Bromocriptine
- Bupropion (also NE)

Moll, J. L. (2011). *J Sex Med*

Amplification of brain DA risks

- Drug dependence/addiction
- Obsessive-compulsive or hypomanic episodes
- Anxiety
- Sensitization of psychosis

Pfaus, J. G. (2009). *J Sex Med*

Mechanisms of Sexual Inhibition

Brain opioid, endocannabinoid, and serotonin systems blunt the action of excitatory mechanisms

This occurs normally at the end of the sexual response cycle during a period of "sexual satiety" or refractoriness (e.g., after orgasm)

Pfaus, J. G. (2009). *J Sex Med*

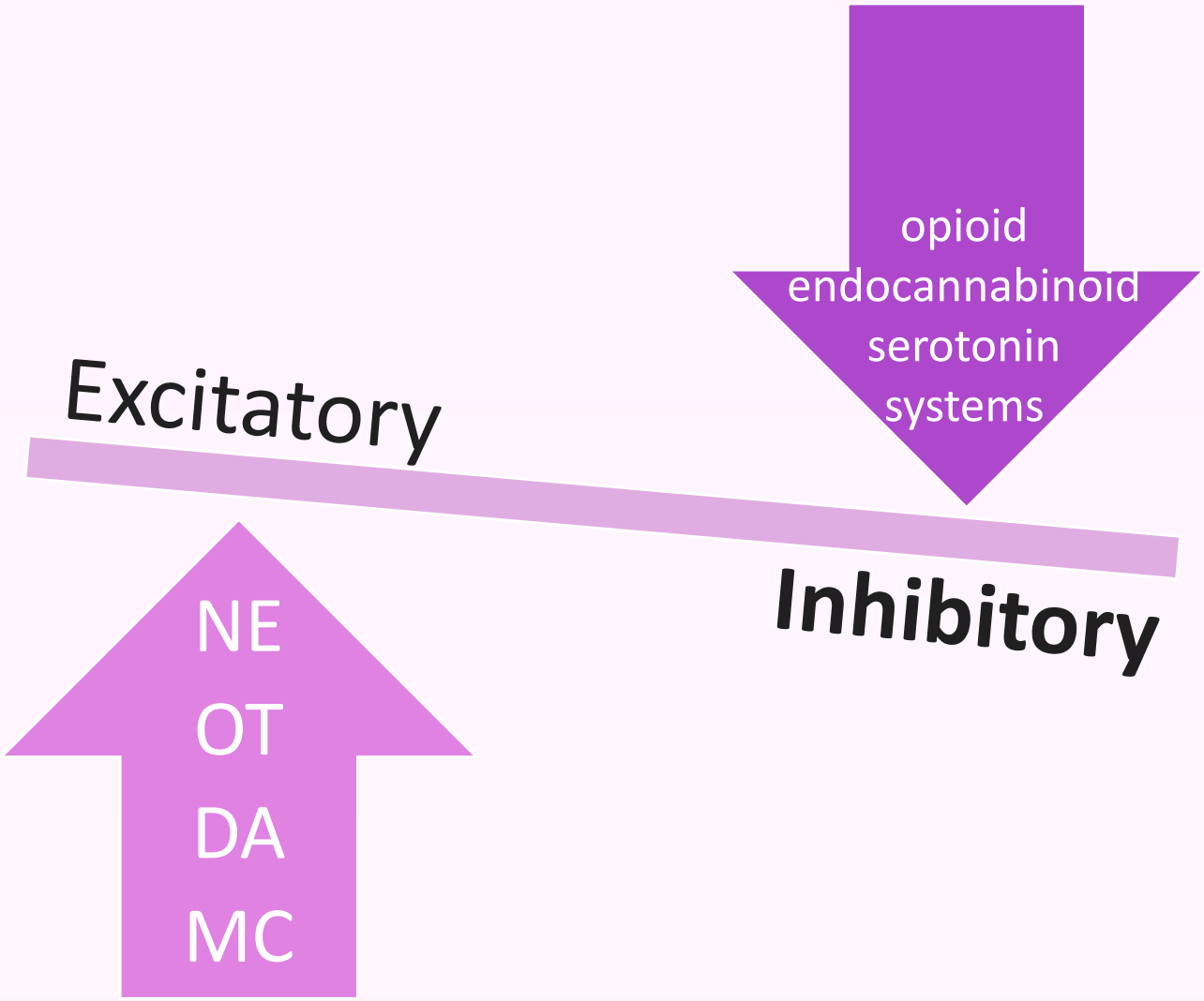
Mechanisms of Sexual Inhibition

Endocannabinoids (ECBs) mediate sedation

Serotonin (5-HT) induces refractoriness and sexual satiety

Moll, J. L. (2011). *J Sex Med*
Pfaus, J. G. (2009). *J Sex Med*

Excitation and Inhibition



Mechanisms of Sexual Inhibition

Inhibition of brain opioid, endocannabinoid, or serotonin systems risks

- Anxiety
- Dysphoria
- Depression

Pfaus, J. G. (2009). *J Sex Med*

Sexual Inhibition

Inhibitory mechanisms can be activated when sexual excitatory mechanisms are blunted:

- Endogenously
- Exogenously due to drugs that directly diminish excitatory influences

Pfaus, J. G. (2009). *J Sex Med*

Sexual Inhibition

Can occur if the endogenous inhibitory mechanism is activated by:

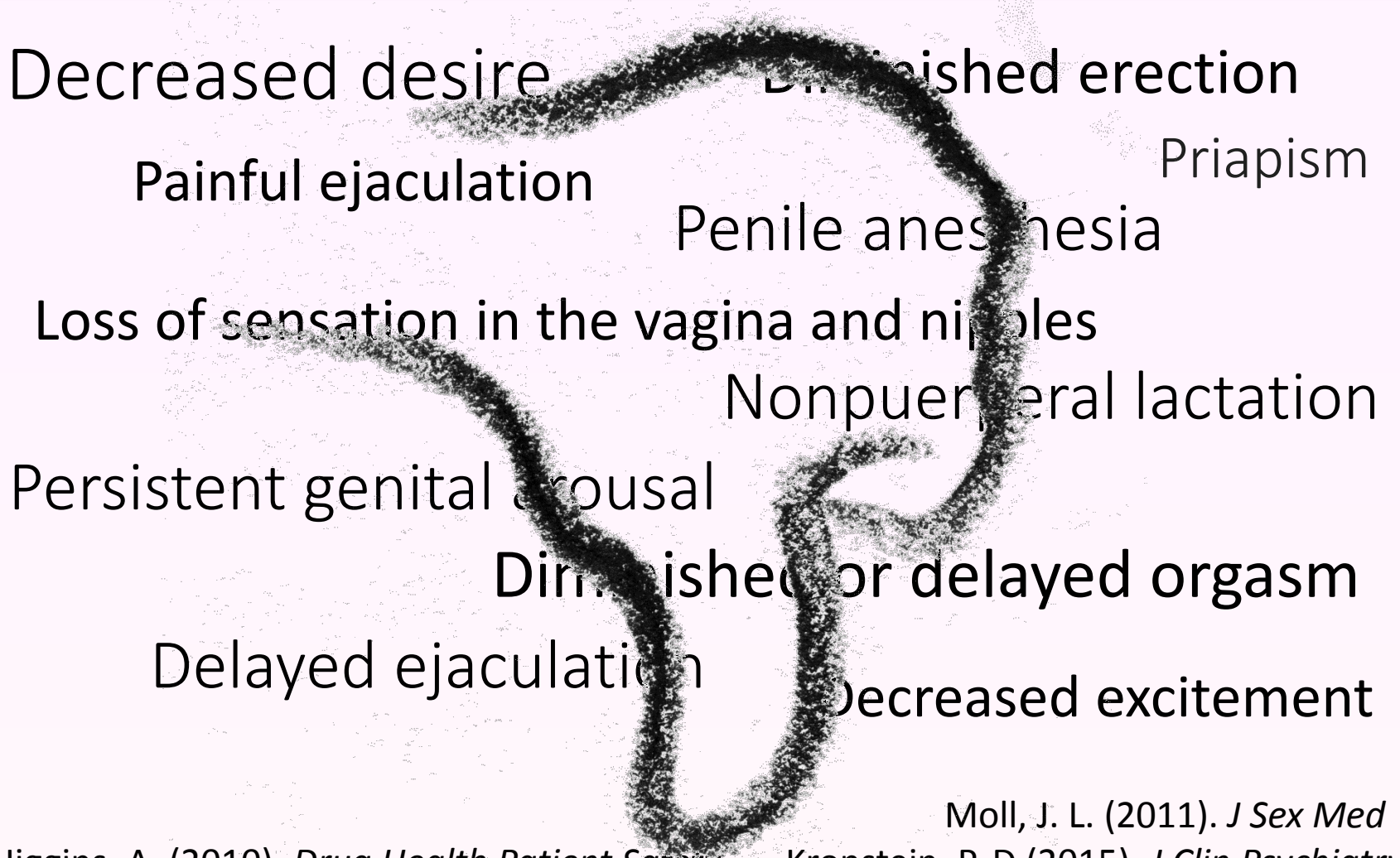
- A situational variable (stress)
- Drugs that augment their actions

SSRIs	TCAs
SNRIs	Lithium

Higgins, A. (2010). *Drug Health Patient Safety*

Moll, J. L. (2011). *J Sex Med*
Pfaus, J. G. (2009). *J Sex Med*

Sexual Complaints w/ Antidepressants



Higgins, A. (2010). *Drug Health Patient Safety*

Moll, J. L. (2011). *J Sex Med*

Kronstein, P. D (2015). *J Clin Psychiatry*

Antidotes

- Bupropion (DA, NE)
- PDE-5 inhibitors (NO)
- Exercise (increase in SNS)
- Maca root, Rosa damascena oil
- T, Ephedrine, Ginko biloba - mixed results

Taylor, M. J., (2013). *Cochrane Database Syst Rev, 5*, Nurnberg, H. G., (2008). *Jama,* Lorenz, T. A (2012). *Ann Behav Med,* Clayton, A. H (2004). *J Clin Psychiatry,* Farnia, V., (2015) *Neuropsychiatr Dis Treat,* Fooladi, E., (2014). *J Sex Med,* Pereira, V. M., (2014). *CNS Neurol Disord Drug Targets*

Antipsychotics

Negative effects

- Decrease DA transmission
- Increase prolactin levels via negative feedback

Elnazer, H. Y.(2015). *Hum Psychopharmacol*
Kennedy, S. H. (2009) *Clin Psychopharmacol*

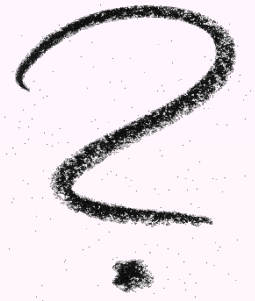
Neuroleptics

Negative effects

- Mood stabilizers
- Anticonvulsants

Insufficient evidence

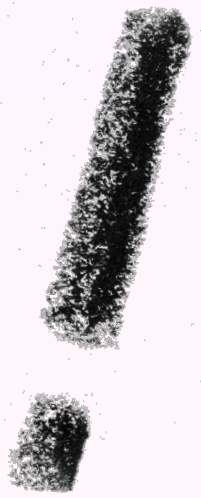
- Anxiolytics drugs



Schmidt, H. M (2012). *Cochrane Database Syst Rev*
La Torre, A. (2014) *Pharmacopsychiatry*
Elnazer, H. Y. (2015). *Hum Psychopharmacol*

Antidotes Neuroleptics

- Switching from enzyme-inducing to non-enzyme-inducing anticonvulsant drugs
- Adding a PDE-5 inhibitor



Schmidt, H. M (2012). *Cochrane Database Syst Rev*
La Torre, A. (2014) *Pharmacopsychiatry*
Elnazer, H. Y. (2015). *Hum Psychopharmacol*

Cardiovascular Medications

Negative effects

- Diuretics
- Beta-blockers

La Torre, A. (2015) *Pharmacopsychiatry*

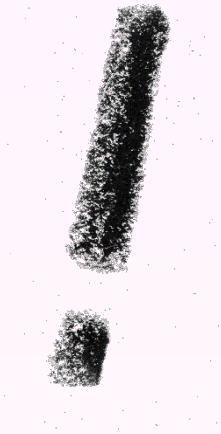
Cardiovascular Medications (continued)

Neutral

- ACE inhibitors
- calcium antagonists

Possible beneficial effects

- Angiotensin receptor blockers



La Torre, A. (2015) *Pharmacopsychiatry*

Smoking

The frequency of FSD was significantly higher In current smokers than nonsmokers

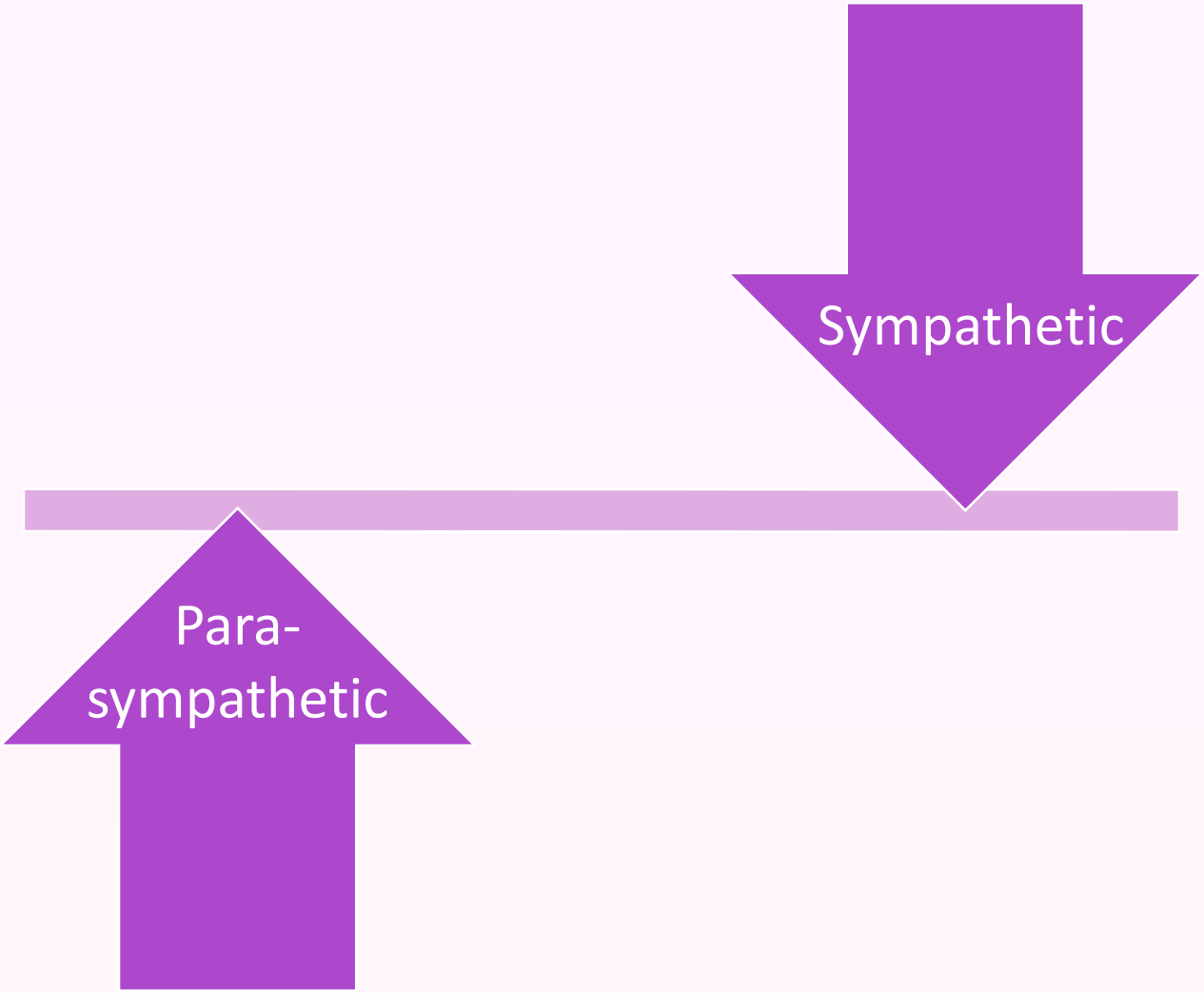
Choi, J., (2015). *Obstet Gynecol Sci*

Sympathetic / Parasympathetic

- Activation of the sympathetic nervous system sets the stage for sexual excitation
- Drugs that reduce sympathetic tone inhibit
- Drugs that increase parasympathetic tone inhibit

Pfaus, J. G. (2009). *J Sex Med*

Inhibition



Feminism or Capitalism?

Flibanserin Proposed MOA

- A multifunctional serotonergic agent
- A serotonin 1A agonist and a serotonin 2A antagonist
- Theoretically works by enhancing downstream release of dopamine and norepinephrine while reducing serotonin release

Abbreviated Flibanserin History

- Initially developed as an antidepressant
- 2009 FDA denied HSDD application approval after unanimous advisory committee vote
- 2013 FDA again denied approval citing safety concerns
  - hypotension, syncope
  - potential for drug interactions with alcohol or CYP3A4 inhibitors

Abbreviated Flibanserin History

Strong push for approval

2015 additional safety information was submitted to FDA

- Reviewed by scientific advisory committee
- Voted 18 to 6 in favor of recommending approval provided certain risk management options were implemented

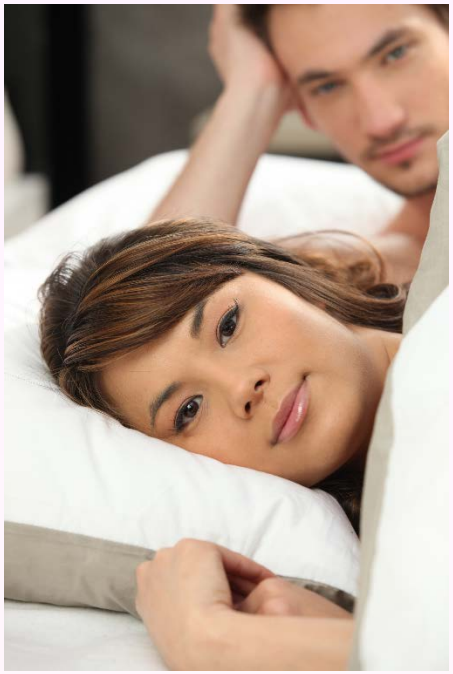
Risk Eval and Mitigation Strategy (REMS)

- Healthcare providers and pharmacists must be trained, assessed and certified
- Patient/provider agreement form
- No direct-to-consumer advertising in the first 18 months
- Label warning

  women must cease using flibanserin if there are no improvements in 8 weeks

Flibanserin plus therapy

Efficacy is not evident until 8 weeks



This period can be used to address personal and relational barriers that contribute to the low sexual desire, and which may interfere with flibanserin adherence

Brotto, L. A. (2015). *Arch Sex Behav*

Post Marketing Commitments

Three clinical trials

- Is there a safe amount of alcohol to consume while taking flibanserin?
- What is the risk of hypotension and syncope associated with high and low levels of alcohol consumption?

The earliest these studies will be completed is 2018.

Flibanserin and CYP3A4

Use of moderate or strong CYP3A4 inhibitors is contraindicated in patients taking flibanserin

Concomitant use increases flibanserin concentrations, which can cause severe hypotension and syncope

Flibanserin and Hepatic Impairment

Flibanserin is contraindicated for use in patients with any hepatic impairment

Flibanserin exposure increased 4.5-fold in patients with hepatic impairment

Drugs that Decrease Exposure

Rifampin decreased flibanserin exposure by 95%

Meta-Analysis

- 3,414 women
- Four randomized controlled trials
- SSE change 0.59

"Flibanserin is an effective and safe treatment for HSDD in women. 100 mg/d appears to provide a good balance between efficacy and side effects"

Gao, Z. (2015). *J Sex Med*

Another Meta-Analysis

- 5914 women
- The same four trials + 4 more (3 unpublished)
- SSE change 0.49

"Treatment with flibanserin resulted in 1/2 additional SSE/mo while statistically and clinically significantly increasing the risk of dizziness, somnolence, nausea, and fatigue."

Jaspers, L., (2016). *JAMA Intern Med*

Female Sexual Interest/Arousal Disorder

In the DSM V, HSDD was replaced by female sexual interest/arousal disorder (FSIAD) which merges arousal and desire disorders

FSIAD has no FDA-approved treatments. The FDA has recognized the condition as an area of unmet medical need.

Testosterone Peri and Post Menopause

The addition of testosterone to hormone therapy improved:

- Sexual function scores
- Number of satisfying sexual episodes

Somboonporn, W., Davis, (2005). *Cochrane Database Syst Rev*
Tungmunsakulchai, R (2015). *BMC Womens Health*
Davis, S. R.(2015). *Lancet Diabetes Endocrinol*

Endocrine Society Clinical Practice Guideline

Testosterone therapy for HSDD

- A 3-6 month trial of a dose of T for postmenopausal women to treat HSDD
- Goal: a mid-normal premenopausal T value to avoid pharmacological T administration

Wierman, M. E., (2014). *Clin Endocrinol Metab*

Endocrine Society Clinical Practice Guideline

Recommends against

- Routinely measuring testosterone in women for diagnosis
- Making a clinical diagnosis of androgen deficiency syndrome in healthy women

Wierman, M. E., (2014). *Clin Endocrinol Metab*

Ovulation

Women report more sexual interest mid-cycle

Mid-cycle women shown to have more

- Initiation of sexual activity
- Receptiveness to sex
- Self stimulation
- Sex

Prasad, A (2014) *Horm Behav*
Brown, S., (2011). *Arch Sex Behav*

Future Treatments for women: Topical

- Topical sildenafil
- Vaginal DHEAS
- Very low dose vaginal estrogen 4mcg
- Topical alprostadil: a prostaglandin analogue that increases genital vasodilatation

Belkin, Z. R (2015). *Expert Opin Investig Drugs*

Future Treatments for women

- SERMs
- Bremelanotide: stimulates melanocortin receptors
- Flibanserin for post menopause
- Apomorphine: a nonselective dopamine agonist
- Testosterone pulse
- Testosterone nasal

Belkin, Z. R (2015). *Expert Opin Investig Drugs*

Future Combinations

- Bupropion plus testosterone pulse
- Topical sildenafil plus pulse testosterone

Belkin, Z. R (2015). *Expert Opin Investig Drugs*

Thank you!

References

Brotto, L. A. (2015). Flibanserin. *Arch Sex Behav, 44*(8), 2103-2105. doi:10.1007/s10508-015-0643-9

Clayton, A. H., Warnock, J. K., Kornstein, S. G., Pinkerton, R., Sheldon-Keller, A., & McGarvey, E. L. (2004). A placebo-controlled trial of bupropion SR as an antidote for selective serotonin reuptake inhibitor-induced sexual dysfunction. *J Clin Psychiatry, 65*(1), 62-67.

Elnazer, H. Y., Sampson, A., & Baldwin, D. (2015). Lithium and sexual dysfunction: an under-researched area. *Hum Psychopharmacol, 30*(2), 66-69. doi:10.1002/hup.2457

Farnia, V., Shirzadifar, M., Shakeri, J., Rezaei, M., Bajoghli, H., Holsboer-Trachsler, E., & Brand, S. (2015). Rosa damascena oil improves SSRI-induced sexual dysfunction in male patients suffering from major depressive disorders: results from a double-blind, randomized, and placebo-controlled clinical trial. *Neuropsychiatr Dis Treat, 11*, 625-635. doi:10.2147/ndt.s78696

References

Fooladi, E., Bell, R. J., Jane, F., Robinson, P. J., Kulkarni, J., & Davis, S. R. (2014). Testosterone improves antidepressant-emergent loss of libido in women: findings from a randomized, double-blind, placebo-controlled trial. *J Sex Med, 11*(3), 831-839. doi:10.1111/jsm.12426

Gao, Z., Yang, D., Yu, L., & Cui, Y. (2015). Efficacy and Safety of Flibanserin in Women with Hypoactive Sexual Desire Disorder: A Systematic Review and Meta-Analysis. *J Sex Med, 12*(11), 2095-2104. doi:10.1111/jsm.13037

Higgins, A., Nash, M., & Lynch, A. M. (2010). Antidepressant-associated sexual dysfunction: impact, effects, and treatment. *Drug Healthc Patient Saf, 2*, 141-150. doi:10.2147/dhps.s7634

Jaspers, L., Feys, F., Bramer, W. M., Franco, O. H., Leusink, P., & Laan, E. T. (2016). Efficacy and Safety of Flibanserin for the Treatment of Hypoactive Sexual Desire Disorder in Women: A Systematic Review and Meta-Analysis. *JAMA Intern Med*. doi:10.1001/jamainternmed.2015.8565

References

Kennedy, S. H., & Rizvi, S. (2009). Sexual dysfunction, depression, and the impact of antidepressants. *J Clin Psychopharmacol, 29*(2), 157-164. doi:10.1097/JCP.0b013e31819c76e9

Kronstein, P. D., Ishida, E., Khin, N. A., Chang, E., Hung, H. M., Temple, R. J., & Yang, P. (2015). Summary of findings from the FDA regulatory science forum on measuring sexual dysfunction in depression trials. *J Clin Psychiatry, 76*(8), 1050-1059. doi:10.4088/JCP.14r09699

La Torre, A., Giupponi, G., Duffy, D., Conca, A., & Catanzariti, D. (2015). Sexual dysfunction related to drugs: a critical review. Part IV: cardiovascular drugs. *Pharmacopsychiatry, 48*(1), 1-6. doi:10.1055/s-0034-1395515

La Torre, A., Giupponi, G., Duffy, D. M., Pompili, M., Grozinger, M., Kapfhammer, H. P., & Conca, A. (2014). Sexual dysfunction related to psychotropic drugs: a critical review. Part III: mood stabilizers and anxiolytic drugs. *Pharmacopsychiatry, 47*(1), 1-6. doi:10.1055/s-0033-1358683

References

Kennedy, S. H., & Rizvi, S. (2009). Sexual dysfunction, depression, and the impact of antidepressants. *J Clin Psychopharmacol, 29*(2), 157-164. doi:10.1097/JCP.0b013e31819c76e9

Kronstein, P. D., Ishida, E., Khin, N. A., Chang, E., Hung, H. M., Temple, R. J., & Yang, P. (2015). Summary of findings from the FDA regulatory science forum on measuring sexual dysfunction in depression trials. *J Clin Psychiatry, 76*(8), 1050-1059. doi:10.4088/JCP.14r09699

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References

Levine, S. B. (2015). Flibanserin. *Arch Sex Behav, 44*(8), 2107-2109. doi:10.1007/s10508-015-0617-y

Lorenz, T. A., Harte, C. B., Hamilton, L. D., & Meston, C. M. (2012). Evidence for a curvilinear relationship between sympathetic nervous system activation and women's physiological sexual arousal. *Psychophysiology, 49*(1), 111-117. doi:10.1111/j.1469-8986.2011.01285.x

Lorenz, T. A., & Meston, C. M. (2012). Acute exercise improves physical sexual arousal in women taking antidepressants. *Ann Behav Med, 43*(3), 352-361. doi:10.1007/s12160-011-9338-1

Moll, J. L., & Brown, C. S. (2011). The Use of Monoamine Pharmacological Agents in the Treatment of Sexual Dysfunction: Evidence in the Literature. *J Sex Med, 8*(4), 956-970. doi:10.1111/j.1743-6109.2010.02190.x

References

Nurnberg, H. G., Hensley, P. L., Heiman, J. R., Croft, H. A., Debattista, C., & Paine, S. (2008). Sildenafil treatment of women with antidepressant-associated sexual dysfunction: a randomized controlled trial *Jama* (Vol. 300, pp. 395-404). United States.

Pereira, V. M., Arias-Carrion, O., Machado, S., Nardi, A. E., & Silva, A. C. (2014). Bupropion in the depression-related sexual dysfunction: a systematic review. *CNS Neurol Disord Drug Targets, 13*(6), 1079-1088.

Pfaus, J. G. (2009). Pathways of sexual desire. *J Sex Med, 6*(6), 1506-1533. doi:10.1111/j.1743-6109.2009.01309.x

Pfaus, J. G. (2015). Treatment for hypoactive sexual desire. *Cell, 163*(3), 533. doi:10.1016/j.cell.2015.10.015

Schmidt, H. M., Hagen, M., Kriston, L., Soares-Weiser, K., Maayan, N., & Berner, M. M. (2012). Management of sexual dysfunction due to antipsychotic drug therapy. *Cochrane Database Syst Rev, 11*, Cd003546. doi:10.1002/14651858.CD003546.pub3

References

Taylor, M. J., Rudkin, L., Bullemor-Day, P., Lubin, J., Chukwujekwu, C., & Hawton, K. (2013). Strategies for managing sexual dysfunction induced by antidepressant medication. *Cochrane Database Syst Rev, 5*, Cd003382. doi:10.1002/14651858.CD003382.pub3

Torre, A. L., Giupponi, G., Duffy, D., Conca, A., Cai, T., & Scardigli, A. (2016). Sexual Dysfunction Related to Drugs: a Critical Review. Part V: alpha-Blocker and 5-ARI Drugs. *Pharmacopsychiatry, 49*(1), 3-13. doi:10.1055/s-0035-1565100

Selected Bibliography

Baksh, S. N., Gellad, W. F., & Alexander, G. C. (2016). Maximizing the Post-Approval Safety of Flibanserin: A Role for Regulators, Clinicians, and Patients. *Drug Saf*. doi:10.1007/s40264-015-0389-2

Gellad, W. F., Flynn, K. E., & Alexander, G. C. (2015). Evaluation of Flibanserin: Science and Advocacy at the FDA. *Jama, 314*(9), 869-870. doi:10.1001/jama.2015.8405

Jayne, C., Simon, J. A., Taylor, L. V., Kimura, T., & Lesko, L. M. (2012). Open-label extension study of flibanserin in women with hypoactive sexual desire disorder. *J Sex Med, 9*(12), 3180-3188. doi:10.1111/j.1743-6109.2012.02942.x

Jin, J. (2015). JAMA PATIENT PAGE. Flibanserin for Treating Low Sexual Desire in Women. *Jama, 314*(12), 1312. doi:10.1001/jama.2015.11769

Joffe, H. V., Chang, C., Sewell, C., Easley, O., Nguyen, C., Dunn, S., . . . Beitz, J. (2016). FDA Approval of Flibanserin--Treating Hypoactive Sexual Desire Disorder. *N Engl J Med, 374*(2), 101-104. doi:10.1056/NEJMp1513686

Selected Bibliography

Katz, M., DeRogatis, L. R., Ackerman, R., Hedges, P., Lesko, L., Garcia, M., Jr., & Sand, M. (2013). Efficacy of flibanserin in women with hypoactive sexual desire disorder: results from the BEGONIA trial. *J Sex Med, 10*(7), 1807-1815. doi:10.1111/jsm.12189

Levine, S. B. (2015). Flibanserin. *Arch Sex Behav, 44*(8), 2107-2109. doi:10.1007/s10508-015-0617-y

McCarthy, M. (2015). US drug agency approves drug for low sexual desire in women. *Bmj, 351*, h4522. doi:10.1136/bmj.h4522

McCartney, M. (2015). Margaret McCartney: Flibanserin for low sexual desire is not feminism. *Bmj, 351*, h5650. doi:10.1136/bmj.h5650

Stahl, S. M. (2015). Mechanism of action of flibanserin, a multifunctional serotonin agonist and antagonist (MSAA), in hypoactive sexual desire disorder. *CNS Spectr, 20*(1), 1-6. doi:10.1017/s1092852914000832

•Selected Bibliography

Stahl, S. M., Sommer, B., & Allers, K. A. Multifunctional Pharmacology of Flibanserin: Possible Mechanism of Therapeutic Action in Hypoactive Sexual Desire Disorder. *J Sex Med, 8*(1), 15-27. doi:10.1111/j.1743-6109.2010.02032.x

Thorp, J., Jr., Palacios, S., Symons, J., Simon, J., & Barbour, K. (2014). Improving prospects for treating hypoactive sexual desire disorder (HSDD): development status of flibanserin. *Bjog, 121*(11), 1328-1331. doi:10.1111/1471-0528.12878

Thorp, J., Simon, J., Dattani, D., Taylor, L., Kimura, T., Garcia, M., Jr., . . . Pyke, R. (2012). Treatment of hypoactive sexual desire disorder in premenopausal women: efficacy of flibanserin in the DAISY study. *J Sex Med, 9*(3), 793-804. doi:10.1111/j.1743-6109.2011.02595.x

Tiefer, L., Laan, E., & Basson, R. (2015). Missed Opportunities in the Patient-Focused Drug Development Public Meeting and Scientific Workshop on Female Sexual Dysfunction Held at the FDA, October 2014. *J Sex Res, 52*(6), 601-603. doi:10.1080/00224499.2014.1003362

Selected Bibliography

Woloshin, S., & Schwartz, L. M. (2016). US Food and Drug Administration Approval of Flibanserin: Even the Score Does Not Add Up. *JAMA Intern Med*. doi:10.1001/jamainternmed.2016.0073

Bibliography

Ahrold, T. K., & Meston, C. M. (2009). Effects of SNS activation on SSRI-induced sexual side effects differ by SSRI. *J Sex Marital Ther, 35*(4), 311-319. doi:10.1080/00926230902851322

Appa, A. A., Creasman, J., Brown, J. S., Van Den Eeden, S. K., Thom, D. H., Subak, L. L., & Huang, A. J. (2014). The Impact of Multimorbidity on Sexual Function in Middle-Aged and Older Women: Beyond the Single Disease Perspective. *J Sex Med, 11*(11), 2744-2755. doi:10.1111/jsm.12665

Baksh, S. N., Gellad, W. F., & Alexander, G. C. (2016). Maximizing the Post-Approval Safety of Flibanserin: A Role for Regulators, Clinicians, and Patients. *Drug Saf*. doi:10.1007/s40264-015-0389-2

Bancroft, J. (2002). The medicalization of female sexual dysfunction: the need for caution. *Arch Sex Behav, 31*(5), 451-455.

Bancroft, J., Graham, C. A., Janssen, E., & Sanders, S. A. (2009). The dual control model: current status and future directions. *J Sex Res, 46*(2-3), 121-142. doi:10.1080/00224490902747222

Bibliography

Basson, R., Brotto, L. A., Petkau, A. J., & Labrie, F. (2010). Role of androgens in women's sexual dysfunction. *Menopause, 17*(5), 962-971. doi:10.1097/gme.0b013e3181d59765

Belkin, Z. R., Krapf, J. M., & Goldstein, A. T. (2015). Drugs in early clinical development for the treatment of female sexual dysfunction. *Expert Opin Investig Drugs, 24*(2), 159-167. doi:10.1517/13543784.2015.978283

Bhat, I. A., Shannon, K. D., Ara, A., & Coe, I. (2015). Ninety-six hours ordeal of priapism induced by paroxetine--A case report and literature review. *Int J Psychiatry Med, 50*(3), 326-334. doi:10.1177/0091217415610312

Blaicher, W., Gruber, D., Bieglmayer, C., Blaicher, A. M., Knogler, W., & Huber, J. C. (1999). The role of oxytocin in relation to female sexual arousal. *Gynecol Obstet Invest, 47*(2), 125-126. doi:10075

Bloemers, J., van Rooij, K., Poels, S., Goldstein, I., Everaerd, W., Koppeschaar, H., . . . Tuiten, A. (2013). Toward personalized sexual medicine (part 1): integrating the "dual control model" into differential drug treatments for hypoactive sexual desire disorder and female sexual arousal disorder. *J Sex Med, 10*(3), 791-809. doi:10.1111/j.1743-6109.2012.02984.x

Bibliography

Bossio, J. A., Suschinsky, K. D., Puts, D. A., & Chivers, M. L. (2014). Does menstrual cycle phase influence the gender specificity of heterosexual women's genital and subjective sexual arousal? *Arch Sex Behav, 43*(5), 941-952. doi:10.1007/s10508-013-0233-7

Bradford, A. (2013). Listening to Placebo in Clinical Trials for Female Sexual Dysfunction. *J Sex Med, 10*(2), 451-459. doi:10.1111/j.1743-6109.2012.02941.x

Bradford, A., & Meston, C. M. (2006). The impact of anxiety on sexual arousal in women. *Behav Res Ther, 44*(8), 1067-1077. doi:10.1016/j.brat.2005.08.006

Brotto, L. A. (2015). Flibanserin. *Arch Sex Behav, 44*(8), 2103-2105. doi:10.1007/s10508-015-0643-9

Brown, S., Calibuso, M., & Roedl, A. (2011). Women's Sexuality, Well-Being, and the Menstrual Cycle: Methodological Issues and Their Interrelationships. *Arch Sex Behav, 40*(4), 755-765. doi:10.1007/s10508-010-9630-3

Bui, E., & Klein, A. (2014). *Women with epilepsy : a practical management handbook*. Cambridge, United Kingdom: Cambridge University Press.

Bibliography

Buisson, O., & Jannini, E. A. (2013). Pilot echographic study of the differences in clitoral involvement following clitoral or vaginal sexual stimulation. *J Sex Med, 10*(11), 2734-2740. doi:10.1111/jsm.12279

Burger, H. G., Dudley, E. C., Cui, J., Dennerstein, L., & Hopper, J. L. (2000). A prospective longitudinal study of serum testosterone, dehydroepiandrosterone sulfate, and sex hormone-binding globulin levels through the menopause transition. *J Clin Endocrinol Metab, 85*(8), 2832-2838. doi:10.1210/jcem.85.8.6740

Burrows, L. J., Basha, M., & Goldstein, A. T. (2012). The effects of hormonal contraceptives on female sexuality: a review. *J Sex Med, 9*(9), 2213-2223. doi:10.1111/j.1743-6109.2012.02848.x

Cappelletti, M., & Wallen, K. (2016). Increasing women's sexual desire: The comparative effectiveness of estrogens and androgens. *Horm Behav, 78*, 178-193. doi:10.1016/j.yhbeh.2015.11.003

Chan, J. S., Olivier, B., de Jong, T. R., Snoeren, E. M., Kooijman, E., van Hasselt, F. N., . . . Oosting, R. S. (2008). Translational research into sexual disorders: pharmacology and genomics. *Eur J Pharmacol, 585*(2-3), 426-435. doi:10.1016/j.ejphar.2008.02.098

Bibliography

Chen, J., Geng, L., Song, X., Li, H., Giordan, N., & Liao, Q. (2013). Evaluation of the efficacy and safety of hyaluronic acid vaginal gel to ease vaginal dryness: a multicenter, randomized, controlled, open-label, parallel-group, clinical trial. *J Sex Med, 10*(6), 1575-1584. doi:10.1111/jsm.12125

Choi, J., Shin, D. W., Lee, S., Jeon, M. J., Kim, S. M., Cho, B., & Lee, S. M. (2015). Dose-response relationship between cigarette smoking and female sexual dysfunction. *Obstet Gynecol Sci, 58*(4), 302-308. doi:10.5468/ogs.2015.58.4.302

Clayton, A. H., Warnock, J. K., Kornstein, S. G., Pinkerton, R., Sheldon-Keller, A., & McGarvey, E. L. (2004). A placebo-controlled trial of bupropion SR as an antidote for selective serotonin reuptake inhibitor-induced sexual dysfunction. *J Clin Psychiatry, 65*(1), 62-67.

Corazza, O., Martinotti, G., Santacroce, R., Chillemi, E., Di Giannantonio, M., Schifano, F., & Cellek, S. (2014). Sexual enhancement products for sale online: raising awareness of the psychoactive effects of yohimbine, maca, horny goat weed, and Ginkgo biloba. *Biomed Res Int, 2014*, 841798. doi:10.1155/2014/841798

Bibliography

Davis, S. R., & Braunstein, G. D. (2012). Efficacy and safety of testosterone in the management of hypoactive sexual desire disorder in postmenopausal women. *J Sex Med, 9*(4), 1134-1148. doi:10.1111/j.1743-6109.2011.02634.x

Davis, S. R., & Wahlin-Jacobsen, S. (2015). Testosterone in women--the clinical significance. *Lancet Diabetes Endocrinol, 3*(12), 980-992. doi:10.1016/s2213-8587(15)00284-3

Davis, S. R., Worsley, R., Miller, K. K., Parish, S. J., & Santoro, N. Androgens and Female Sexual Function and Dysfunction—Findings From the Fourth International Consultation of Sexual Medicine. *J Sex Med, 13*(2), 168-178. doi:10.1016/j.jsxm.2015.12.033

Dawson, S. J., Sawatsky, M. L., & Lalumiere, M. L. (2015). Assessment of Introital Lubrication. *Arch Sex Behav, 44*(6), 1527-1535. doi:10.1007/s10508-015-0519-z

Derogatis, L. R., Komer, L., Katz, M., Moreau, M., Kimura, T., Garcia, M., Jr., . . . Pyke, R. (2012). Treatment of hypoactive sexual desire disorder in premenopausal women: efficacy of flibanserin in the VIOLET Study. *J Sex Med, 9*(4), 1074-1085. doi:10.1111/j.1743-6109.2011.02626.x

Bibliography

Derzko, C., Elliott, S., & Lam, W. (2007). Management of sexual dysfunction in postmenopausal breast cancer patients taking adjuvant aromatase inhibitor therapy. *Curr Oncol, 14 Suppl 1*, S20-40. Retrieved from http://www.current-oncology.com/index.php/oncology/article/download/178/151

Dording, C. M., Schettler, P. J., Dalton, E. D., Parkin, S. R., Walker, R. S., Fehling, K. B., . . . Mischoulon, D. (2015). A double-blind placebo-controlled trial of maca root as treatment for antidepressant-induced sexual dysfunction in women. Evid Based Complement Alternat Med, 2015, 949036. doi:10.1155/2015/949036

Elnazer, H. Y., Sampson, A., & Baldwin, D. (2015). Lithium and sexual dysfunction: an under-researched area. *Hum Psychopharmacol, 30*(2), 66-69. doi:10.1002/hup.2457

Farnia, V., Shirzadifar, M., Shakeri, J., Rezaei, M., Bajoghli, H., Holsboer-Trachsler, E., & Brand, S. (2015). Rosa damascena oil improves SSRI-induced sexual dysfunction in male patients suffering from major depressive disorders: results from a double-blind, randomized, and placebo-controlled clinical trial. *Neuropsychiatr Dis Treat, 11*, 625-635. doi:10.2147/ndt.s78696

Bibliography

Flibanserin for the treatment of hypoactive sexual desire disorder in premenopausal women: advisory committee briefing document. 4 June 2015. www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM449090.pdf.

Fooladi, E., Bell, R. J., Jane, F., Robinson, P. J., Kulkarni, J., & Davis, S. R. (2014). Testosterone improves antidepressant-emergent loss of libido in women: findings from a randomized, double-blind, placebo-controlled trial. *J Sex Med, 11*(3), 831-839. doi:10.1111/jsm.12426

Gao, Z., Yang, D., Yu, L., & Cui, Y. (2015). Efficacy and Safety of Flibanserin in Women with Hypoactive Sexual Desire Disorder: A Systematic Review and Meta-Analysis. *J Sex Med, 12*(11), 2095-2104. doi:10.1111/jsm.13037

Gellad, W. F., Flynn, K. E., & Alexander, G. C. (2015). Evaluation of Flibanserin: Science and Advocacy at the FDA. *Jama, 314*(9), 869-870. doi:10.1001/jama.2015.8405

George, W. H., Davis, K. C., Heiman, J. R., Norris, J., Stoner, S. A., Schacht, R. L., . . . Kajumulo, K. F. (2011). Women's sexual arousal: effects of high alcohol dosages and self-control instructions. *Horm Behav, 59*(5), 730-738. doi:10.1016/j.yhbeh.2011.03.006

Bibliography

Georgiadis, J. R. (2012). Doing it ... wild? On the role of the cerebral cortex in human sexual activity. *Socioaffect Neurosci Psychol, 2*, 17337. doi:10.3402/snp.v2i0.17337

Georgiadis, J. R., Kringelbach, M. L., & Pfaus, J. G. (2012). Sex for fun: a synthesis of human and animal neurobiology. *Nat Rev Urol, 9*(9), 486-498. doi:10.1038/nrurol.2012.151

Gori, A., Giannini, M., Craparo, G., Caretti, V., Nannini, I., Madathil, R., & Schuldberg, D. (2014). Assessment of the Relationship Between the Use of Birth Control Pill and the Characteristics of Mate Selection. *J Sex Med, 11*(9), 2181-2187. doi:10.1111/jsm.12566

Gracia, C. R., Sammel, M. D., Charlesworth, S., Lin, H., Barnhart, K. T., & Creinin, M. D. (2010). Sexual function in first-time contraceptive ring and contraceptive patch users. *Fertil Steril, 93*(1), 21-28. doi:10.1016/j.fertnstert.2008.09.066

Greco, T., Graham, C. A., Bancroft, J., Tanner, A., & Doll, H. A. (2007). The effects of oral contraceptives on androgen levels and their relevance to premenstrual mood and sexual interest: a comparison of two triphasic formulations containing norgestimate and either 35 or 25 microg of ethinyl estradiol. *Contraception, 76*(1), 8-17. doi:10.1016/j.contraception.2007.04.002

Bibliography

Guida, M., Di Spiezio Sardo, A., Bramante, S., Sparice, S., Acunzo, G., Tommaselli, G. A., . . . Nappi, C. (2005). Effects of two types of hormonal contraception--oral versus intravaginal--on the sexual life of women and their partners. *Hum Reprod, 20*(4), 1100-1106. doi:10.1093/humrep/deh686

Hamilton, L. D., & Meston, C. M. (2011). The role of salivary cortisol and DHEA-S in response to sexual, humorous, and anxiety-inducing stimuli. *Horm Behav, 59*(5), 765-771. doi:10.1016/j.yhbeh.2010.12.011

Harte, C. B., & Meston, C. M. (2008). The inhibitory effects of nicotine on physiological sexual arousal in nonsmoking women: results from a randomized, double-blind, placebo-controlled, cross-over trial. *J Sex Med, 5*(5), 1184-1197. doi:10.1111/j.1743-6109.2008.00778.x

Heard-Davison, A., Heiman, J. R., & Kuffel, S. (2007). Genital and subjective measurement of the time course effects of an acute dose of testosterone vs. placebo in postmenopausal women. *J Sex Med, 4*(1), 209-217. doi:10.1111/j.1743-6109.2006.00406.x

Higgins, A., Nash, M., & Lynch, A. M. (2010). Antidepressant-associated sexual dysfunction: impact, effects, and treatment. *Drug Healthc Patient Saf, 2*, 141-150. doi:10.2147/dhps.s7634

Bibliography

Hoberman, J. M. (2005). *Testosterone dreams : rejuvenation, aphrodisia, doping*. Berkeley: University of California Press.

Jaspers, L., Feys, F., Bramer, W. M., Franco, O. H., Leusink, P., & Laan, E. T. (2016). Efficacy and Safety of Flibanserin for the Treatment of Hypoactive Sexual Desire Disorder in Women: A Systematic Review and Meta-Analysis. *JAMA Intern Med*. doi:10.1001/jamainternmed.2015.8565

Jayne, C., Simon, J. A., Taylor, L. V., Kimura, T., & Lesko, L. M. (2012). Open-label extension study of flibanserin in women with hypoactive sexual desire disorder. *J Sex Med, 9*(12), 3180-3188. doi:10.1111/j.1743-6109.2012.02942.x

Jin, J. (2015). JAMA PATIENT PAGE. Flibanserin for Treating Low Sexual Desire in Women. *Jama, 314*(12), 1312. doi:10.1001/jama.2015.11769

Joffe, H. V., Chang, C., Sewell, C., Easley, O., Nguyen, C., Dunn, S., . . . Beitz, J. (2016). FDA Approval of Flibanserin--Treating Hypoactive Sexual Desire Disorder. *N Engl J Med, 374*(2), 101-104. doi:10.1056/NEJMp1513686

Bibliography

Katz, M., DeRogatis, L. R., Ackerman, R., Hedges, P., Lesko, L., Garcia, M., Jr., & Sand, M. (2013). Efficacy of flibanserin in women with hypoactive sexual desire disorder: results from the BEGONIA trial. *J Sex Med, 10*(7), 1807-1815. doi:10.1111/jsm.12189

Kennedy, S. H., & Rizvi, S. (2009). Sexual dysfunction, depression, and the impact of antidepressants. *J Clin Psychopharmacol, 29*(2), 157-164. doi:10.1097/JCP.0b013e31819c76e9

Komisaruk, B. R., Wise, N., Frangos, E., Liu, W. C., Allen, K., & Brody, S. (2011). Women's clitoris, vagina, and cervix mapped on the sensory cortex: fMRI evidence. *J Sex Med, 8*(10), 2822-2830. doi:10.1111/j.1743-6109.2011.02388.x

Kronstein, P. D., Ishida, E., Khin, N. A., Chang, E., Hung, H. M., Temple, R. J., & Yang, P. (2015). Summary of findings from the FDA regulatory science forum on measuring sexual dysfunction in depression trials. *J Clin Psychiatry, 76*(8), 1050-1059. doi:10.4088/JCP.14r09699

Labrie, F., Derogatis, L., Archer, D. F., Koltun, W., Vachon, A., Young, D., . . . Moyneur, E. (2015). Effect of Intravaginal Prasterone on Sexual Dysfunction in Postmenopausal Women with Vulvovaginal Atrophy. *J Sex Med, 12*(12), 2401-2412. doi:10.1111/jsm.13045

Bibliography

La Torre, A., Conca, A., Duffy, D., Giupponi, G., Pompili, M., & Grozinger, M. (2013). Sexual dysfunction related to psychotropic drugs: a critical review part II: antipsychotics. *Pharmacopsychiatry, 46*(6), 201-208. doi:10.1055/s-0033-1347177

La Torre, A., Giupponi, G., Duffy, D., & Conca, A. (2013). Sexual dysfunction related to psychotropic drugs: a critical review--part I: antidepressants. *Pharmacopsychiatry, 46*(5), 191-199. doi:10.1055/s-0033-1345205

La Torre, A., Giupponi, G., Duffy, D., Conca, A., & Catanzariti, D. (2015). Sexual dysfunction related to drugs: a critical review. Part IV: cardiovascular drugs. *Pharmacopsychiatry, 48*(1), 1-6. doi:10.1055/s-0034-1395515

La Torre, A., Giupponi, G., Duffy, D. M., Pompili, M., Grozinger, M., Kapfhammer, H. P., & Conca, A. (2014). Sexual dysfunction related to psychotropic drugs: a critical review. Part III: mood stabilizers and anxiolytic drugs. *Pharmacopsychiatry, 47*(1), 1-6. doi:10.1055/s-0033-1358683

Lazenka, M. F., Blough, B. E., & Negus, S. S. Preclinical Abuse Potential Assessment of Flibanserin: Effects on Intracranial Self-Stimulation in Female and Male Rats. *J Sex Med*. doi:10.1016/j.jsxm.2015.12.031

Bibliography

Levine, S. B. (2015). Flibanserin. *Arch Sex Behav, 44*(8), 2107-2109. doi:10.1007/s10508-015-0617-y

Lorenz, T. A., Harte, C. B., Hamilton, L. D., & Meston, C. M. (2012). Evidence for a curvilinear relationship between sympathetic nervous system activation and women's physiological sexual arousal. *Psychophysiology, 49*(1), 111-117. doi:10.1111/j.1469-8986.2011.01285.x

Lorenz, T. A., & Meston, C. M. (2012). Acute exercise improves physical sexual arousal in women taking antidepressants. *Ann Behav Med, 43*(3), 352-361. doi:10.1007/s12160-011-9338-1

Marazziti, D., Palego, L., Giromella, A., Mazzoni, M. R., Borsini, F., Mayer, N., . . . Cassano, G. B. (2002). Region-dependent effects of flibanserin and buspirone on adenylyl cyclase activity in the human brain. *Int J Neuropsychopharmacol, 5*(2), 131-140. doi:doi:10.1017/S1461145702002869

Marlowe, F. W., & Berbesque, J. C. (2012). The human operational sex ratio: effects of marriage, concealed ovulation, and menopause on mate competition. *J Hum Evol, 63*(6), 834-842. doi:10.1016/j.jhevol.2012.09.004

Bibliography

McCarthy, M. (2015). US drug agency approves drug for low sexual desire in women. *Bmj, 351*, h4522. doi:10.1136/bmj.h4522

McCartney, M. (2015). Margaret McCartney: Flibanserin for low sexual desire is not feminism. *Bmj, 351*, h5650. doi:10.1136/bmj.h5650

Meston, C. M. (2004). A randomized, placebo-controlled, crossover study of ephedrine for SSRI-induced female sexual dysfunction. *J Sex Marital Ther, 30*(2), 57-68. doi:10.1080/00926230490247093

Meston, C. M., Gorzalka, B. B., & Wright, J. M. (1997). Inhibition of subjective and physiological sexual arousal in women by clonidine. *Psychosom Med, 59*(4), 399-407. Retrieved from http://graphics.tx.ovid.com/ovftpdfs/FPDDNCOBLDKCMN00/fs046/ovft/live/gv023/00006842/00006842-199707000-00010.pdf

Meston, C. M., & Heiman, J. R. (1998). Ephedrine-activated physiological sexual arousal in women. *Arch Gen Psychiatry, 55*(7), 652-656. Retrieved from http://archpsyc.jamanetwork.com/data/Journals/PSYCH/5056/yoa7338.pdf

Bibliography

Meston, C. M., Rellini, A. H., & Telch, M. J. (2008). Short- and long-term effects of Ginkgo biloba extract on sexual dysfunction in women. *Arch Sex Behav, 37*(4), 530-547. doi:10.1007/s10508-008-9316-2

Moll, J. L., & Brown, C. S. (2011). The Use of Monoamine Pharmacological Agents in the Treatment of Sexual Dysfunction: Evidence in the Literature. *J Sex Med, 8*(4), 956-970. doi:10.1111/j.1743-6109.2010.02190.x

Moynihan, R. (2014). Evening the score on sex drugs: feminist movement or marketing masquerade? *Bmj, 349*, g6246. doi:10.1136/bmj.g6246

Moynihan, R., & Cassels, A. (2005). *Selling sickness : how the world's biggest pharmaceutical companies are turning us all into patients*. New York, NY: Nation Books.

Muin, D. A., Wolzt, M., Marculescu, R., Sheikh Rezaei, S., Salama, M., Fuchs, C., . . . Bayerle-Eder, M. (2015). Effect of long-term intranasal oxytocin on sexual dysfunction in premenopausal and postmenopausal women: a randomized trial. *Fertil Steril, 104*(3), 715-723.e714. doi:10.1016/j.fertnstert.2015.06.010

Bibliography

Nastri, C. O., Lara, L. A., Ferriani, R. A., Rosa, E. S. A. C., Figueiredo, J. B., & Martins, W. P. (2013). Hormone therapy for sexual function in perimenopausal and postmenopausal women. *Cochrane Database Syst Rev, 6*, Cd009672. doi:10.1002/14651858.CD009672.pub2

Nurnberg, H. G., Hensley, P. L., Heiman, J. R., Croft, H. A., Debattista, C., & Paine, S. (2008). Sildenafil treatment of women with antidepressant-associated sexual dysfunction: a randomized controlled trial *Jama* (Vol. 300, pp. 395-404). United States.

Olivier, B., & Waldinger, M. (2014). Guest editorial: pharmacology of female sexual behavior. *Pharmacol Biochem Behav, 121*, 1-2. doi:10.1016/j.pbb.2014.03.007

Orleans, R. J., Li, L., Kim, M. J., Guo, J., Sobhan, M., Soule, L., & Joffe, H. V. (2014). FDA approval of paroxetine for menopausal hot flushes. *N Engl J Med, 370*(19), 1777-1779. doi:10.1056/NEJMp1402080

Panay, N., Al-Azzawi, F., Bouchard, C., Davis, S. R., Eden, J., Lodhi, I., . . . Sturdee, D. W. (2010). Testosterone treatment of HSDD in naturally menopausal women: the ADORE study. *Climacteric, 13*(2), 121-131. doi:10.3109/13697131003675922

Bibliography

Panjari, M., & Davis, S. R. (2011). Vaginal DHEA to treat menopause related atrophy: a review of the evidence. *Maturitas, 70*(1), 22-25. doi:10.1016/j.maturitas.2011.06.005

Pastor, Z., Holla, K., & Chmel, R. (2013). The influence of combined oral contraceptives on female sexual desire: a systematic review. *Eur J Contracept Reprod Health Care, 18*(1), 27-43. doi:10.3109/13625187.2012.728643

Peixoto, M. M., & Nobre, P. (2014). Dysfunctional Sexual Beliefs: A Comparative Study of Heterosexual Men and Women, Gay Men, and Lesbian Women With and Without Sexual Problems. *J Sex Med, 11*(11), 2690-2700. doi:10.1111/jsm.12666

Pereira, V. M., Arias-Carrion, O., Machado, S., Nardi, A. E., & Silva, A. C. (2014). Bupropion in the depression-related sexual dysfunction: a systematic review. *CNS Neurol Disord Drug Targets, 13*(6), 1079-1088.

Pfaus, J. G. (2009). Pathways of sexual desire. *J Sex Med, 6*(6), 1506-1533. doi:10.1111/j.1743-6109.2009.01309.x

Pfaus, J. G. (2015). Treatment for hypoactive sexual desire. *Cell, 163*(3), 533. doi:10.1016/j.cell.2015.10.015

Bibliography

Poels, S., Bloemers, J., van Rooij, K., Goldstein, I., Gerritsen, J., van Ham, D., . . . Tuiten, A. (2013). Toward personalized sexual medicine (part 2): testosterone combined with a PDE5 inhibitor increases sexual satisfaction in women with HSDD and FSAD, and a low sensitive system for sexual cues. *J Sex Med, 10*(3), 810-823. doi:10.1111/j.1743-6109.2012.02983.x

Poels, S., Bloemers, J., van Rooij, K., Koppeschaar, H., Olivier, B., & Tuiten, A. (2014). Two novel combined drug treatments for women with hypoactive sexual desire disorder. *Pharmacol Biochem Behav, 121*, 71-79. doi:10.1016/j.pbb.2014.02.002

Prasad, A., Mumford, S. L., Buck Louis, G. M., Ahrens, K. A., Sjaarda, L. A., Schliep, K. C., . . . Schisterman, E. F. (2014). Sexual activity, endogenous reproductive hormones and ovulation in premenopausal women. *Horm Behav, 66*(2), 330-338. doi:10.1016/j.yhbeh.2014.06.012

Prause, N., Barela, J., Roberts, V., & Graham, C. (2013). Instructions to rate genital vasocongestion increases genital and self-reported sexual arousal but not coherence between genital and self-reported sexual arousal. *J Sex Med, 10*(9), 2219-2231. doi:10.1111/jsm.12228

Bibliography

Rosen, R. C. (2000). Sexual pharmacology in the 21st century. *J Gend Specif Med, 3*(5), 45-52.

Rosner, W., Auchus, R. J., Azziz, R., Sluss, P. M., & Raff, H. (2007). Position statement: Utility, limitations, and pitfalls in measuring testosterone: an Endocrine Society position statement. *J Clin Endocrinol Metab, 92*(2), 405-413. doi:10.1210/jc.2006-1864

Safarinejad, M. R., Hosseini, S. Y., Asgari, M. A., Dadkhah, F., & Taghva, A. (2010). A randomized, double-blind, placebo-controlled study of the efficacy and safety of bupropion for treating hypoactive sexual desire disorder in ovulating women. *BJU Int, 106*(6), 832-839. doi:10.1111/j.1464-410X.2010.09208.x

Satonin, D. K., Ni, X., Mitchell, M. I., Joly, H., Muram, D., & Small, D. S. Amount of Testosterone on Laundered Clothing After Use of Testosterone Topical 2% Solution by Healthy Male Volunteers. *J Sex Med, 13*(2), 187-193. doi:10.1016/j.jsxm.2015.12.007

Scheele, D., Striepens, N., Kendrick, K. M., Schwering, C., Noelle, J., Wille, A., . . . Hurlemann, R. (2014). Opposing effects of oxytocin on moral judgment in males and females. *Hum Brain Mapp, 35*(12), 6067-6076. doi:10.1002/hbm.22605

Bibliography

Schmidt, H. M., Hagen, M., Kriston, L., Soares-Weiser, K., Maayan, N., & Berner, M. M. (2012). Management of sexual dysfunction due to antipsychotic drug therapy. *Cochrane Database Syst Rev, 11*, Cd003546. doi:10.1002/14651858.CD003546.pub3

Schover, L. R., Baum, G. P., Fuson, L. A., Brewster, A., & Melhem-Bertrandt, A. (2014). Sexual Problems During the First 2 Years of Adjuvant Treatment with Aromatase Inhibitors. *J Sex Med, 11*(12), 3102-3111. doi:10.1111/jsm.12684

Shifren, J. L., Braunstein, G. D., Simon, J. A., Casson, P. R., Buster, J. E., Redmond, G. P., . . . Mazer, N. A. (2000). Transdermal testosterone treatment in women with impaired sexual function after oophorectomy. *N Engl J Med, 343*(10), 682-688. doi:10.1056/nejm200009073431002

Shifren, J. L., Davis, S. R., Moreau, M., Waldbaum, A., Bouchard, C., DeRogatis, L., . . . Kroll, R. (2006). Testosterone patch for the treatment of hypoactive sexual desire disorder in naturally menopausal women: results from the INTIMATE NM1 Study. *Menopause, 13*(5), 770-779. doi:10.1097/01.gme.0000243567.32828.99

Bibliography

Simon, J., Braunstein, G., Nachtigall, L., Utian, W., Katz, M., Miller, S., . . . Davis, S. (2005). Testosterone patch increases sexual activity and desire in surgically menopausal women with hypoactive sexual desire disorder. *J Clin Endocrinol Metab, 90*(9), 5226-5233. doi:10.1210/jc.2004-1747

Simon, J. A. (2010). Low sexual desire--is it all in her head? Pathophysiology, diagnosis, and treatment of hypoactive sexual desire disorder. *Postgrad Med, 122*(6), 128-136. doi:10.3810/pgm.2010.11.2230

Simon, J. A. (2011). Identifying and treating sexual dysfunction in postmenopausal women: the role of estrogen. *J Womens Health (Larchmt), 20*(10), 1453-1465. doi:10.1089/jwh.2010.2151

Somboonporn, W., Davis, S., Seif, M. W., & Bell, R. (2005). Testosterone for peri- and postmenopausal women. *Cochrane Database Syst Rev*(4), Cd004509. doi:10.1002/14651858.CD004509.pub2

Stahl, S. M. (2015). Mechanism of action of flibanserin, a multifunctional serotonin agonist and antagonist (MSAA), in hypoactive sexual desire disorder. *CNS Spectr, 20*(1), 1-6. doi:10.1017/s1092852914000832

Bibliography

Stahl, S. M., Sommer, B., & Allers, K. A. Multifunctional Pharmacology of Flibanserin: Possible Mechanism of Therapeutic Action in Hypoactive Sexual Desire Disorder. *J Sex Med, 8*(1), 15-27. doi:10.1111/j.1743-6109.2010.02032.x

Stanton, A. M., Pulverman, C. S., & Meston, C. M. (2016). Vagal Activity During Physiological Sexual Arousal in Women With and Without Sexual Dysfunction. *J Sex Marital Ther*, 0. doi:10.1080/0092623x.2015.1115793

Strufaldi, R., Pompei, L. M., Steiner, M. L., Cunha, E. P., Ferreira, J. A., Peixoto, S., & Fernandes, C. E. (2010). Effects of two combined hormonal contraceptives with the same composition and different doses on female sexual function and plasma androgen levels. *Contraception, 82*(2), 147-154. doi:10.1016/j.contraception.2010.02.016

Sungur, M. Z., & Gunduz, A. (2014). A comparison of DSM-IV-TR and DSM-5 definitions for sexual dysfunctions: critiques and challenges. *J Sex Med, 11*(2), 364-373. doi:10.1111/jsm.12379

Suschinsky, K. D., Bossio, J. A., & Chivers, M. L. (2014). Women's genital sexual arousal to oral versus penetrative heterosexual sex varies with menstrual cycle phase at first exposure. *Horm Behav, 65*(3), 319-327. doi:10.1016/j.yhbeh.2014.01.006

Bibliography

Taylor, M. J., Rudkin, L., Bullemor-Day, P., Lubin, J., Chukwujekwu, C., & Hawton, K. (2013). Strategies for managing sexual dysfunction induced by antidepressant medication. *Cochrane Database Syst Rev, 5*, Cd003382. doi:10.1002/14651858.CD003382.pub3

Thorp, J., Jr., Palacios, S., Symons, J., Simon, J., & Barbour, K. (2014). Improving prospects for treating hypoactive sexual desire disorder (HSDD): development status of flibanserin. *Bjog, 121*(11), 1328-1331. doi:10.1111/1471-0528.12878

Thorp, J., Simon, J., Dattani, D., Taylor, L., Kimura, T., Garcia, M., Jr., . . . Pyke, R. (2012). Treatment of hypoactive sexual desire disorder in premenopausal women: efficacy of flibanserin in the DAISY study. *J Sex Med, 9*(3), 793-804. doi:10.1111/j.1743-6109.2011.02595.x

Tiefer, L., Laan, E., & Basson, R. (2015). Missed Opportunities in the Patient-Focused Drug Development Public Meeting and Scientific Workshop on Female Sexual Dysfunction Held at the FDA, October 2014. *J Sex Res, 52*(6), 601-603. doi:10.1080/00224499.2014.1003362

Torre, A. L., Giupponi, G., Duffy, D., Conca, A., Cai, T., & Scardigli, A. (2016). Sexual Dysfunction Related to Drugs: a Critical Review. Part V: alpha-Blocker and 5-ARI Drugs. *Pharmacopsychiatry, 49*(1), 3-13. doi:10.1055/s-0035-1565100

Bibliography

Traish, A. M., Botchevar, E., & Kim, N. N. (2010). Biochemical factors modulating female genital sexual arousal physiology. *J Sex Med, 7*(9), 2925-2946. doi:10.1111/j.1743-6109.2010.01903.x

van Rooij, K., Poels, S., Bloemers, J., Goldstein, I., Gerritsen, J., van Ham, D., . . . Tuiten, A. (2013). Toward personalized sexual medicine (part 3): testosterone combined with a Serotonin1A receptor agonist increases sexual satisfaction in women with HSDD and FSAD, and dysfunctional activation of sexual inhibitory mechanisms. *J Sex Med, 10*(3), 824-837. doi:10.1111/j.1743-6109.2012.02982.x

Verze, P., Cai, T., Magno, C., Sabella, F., Cucchiara, V., Palmieri, A., & Mirone, V. Comparison of Treatment Emergent Adverse Events in Men With Premature Ejaculation Treated With Dapoxetine and Alternate Oral Treatments: Results From a Large Multinational Observational Trial. *J Sex Med, 13*(2), 194-199. doi:10.1016/j.jsxm.2015.12.017

Wahlin-Jacobsen, S., Pedersen, A. T., Kristensen, E., Laessoe, N. C., Lundqvist, M., Cohen, A. S., . . . Giraldi, A. (2015). Is there a correlation between androgens and sexual desire in women? *J Sex Med, 12*(2), 358-373. doi:10.1111/jsm.12774

Bibliography

Warnock, J. K., Clayton, A., Croft, H., Segraves, R., & Biggs, F. C. (2006). Comparison of androgens in women with hypoactive sexual desire disorder: those on combined oral contraceptives (COCs) vs. those not on COCs. *J Sex Med, 3*(5), 878-882. doi:10.1111/j.1743-6109.2006.00294.x

Wierman, M. E., Arlt, W., Basson, R., Davis, S. R., Miller, K. K., Murad, M. H., . . . Santoro, N. (2014). Androgen therapy in women: a reappraisal: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab, 99*(10), 3489-3510. doi:10.1210/jc.2014-2260

Woloshin, S., & Schwartz, L. M. (2016). US Food and Drug Administration Approval of Flibanserin: Even the Score Does Not Add Up. *JAMA Intern Med*. doi:10.1001/jamainternmed.2016.0073

Zimmerman, Y., Eijkemans, M. J., Coelingh Bennink, H. J., Blankenstein, M. A., & Fauser, B. C. (2014). The effect of combined oral contraception on testosterone levels in healthy women: a systematic review and meta-analysis. *Hum Reprod Update, 20*(1), 76-105. doi:10.1093/humupd/dmt038

CYP3A4

Enzyme also known as:

- HLP; CP33; CP34; CYP3A; NF-25; CYP3A3; P450C3; CYPIIIA3; CYPIIIA4; P450PCN1
- Involved in the metabolism of 50% of the drugs in use today

Strong CYP3A4 Inhibitors

- Ketoconazole, itraconazole, posaconazole,
- Clarithromycin, telithromycin
- Nefazodone (antidepressant)
- Atazanavir, darunavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir, tipranavir, boceprevir

Azithromycin OK

- Not all drugs within a class of medications are known to be inhibitors of CYP3A4
- All macrolides are known inhibitors of CYP3A4 with the exception of azithromycin

Moderate CYP3A4 Inhibitors

- Fluconazole, miconazole
- Ciprofloxacin, erythromycin
- Verapamil, diltiazem, amiodarone
- Amprenavir, fosamprenavir, delavirdine
- Conivaptan, grapefruit juice, cat's claw, echinacea, wild cherry, chamomile, licorice

Weak CYP3A4

- Oral contraceptives, cimetidine, fluoxetine, ginkgo, ranitidine
- The concomitant use of flibanserin with *multiple* weak CYP3A4 inhibitors may increase the risk of adverse reactions