UNDERSTANDING & TREATING IMPULSES, URGES & FANTASIES

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OBJECTIVES

Upon completion of this educational activity, learners should be better able to:

1. Discuss evidence for uncontrollable sexual urges and fantasies playing a role in problematic sexual behavior.
2. Enumerate the pharmacological treatments for sexual offenders.
3. Understand the proposed mechanisms of action of the medications used in the treatment of sexual offenders.
4. Review current algorithms for the treatment of sexual offenders.
   - (Understand levels of evidence that support these treatments.)
   - (Discuss ethical issues that make the use of the gold standard studies, the double-blind placebo-controlled trials difficult to undertake in this population.)

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WHERE ARE WE GOING?

1. The goal is to talk about pharmacotherapy for sex offenders.
2. But I talk about a lot of other stuff along the way. Why is this?
3. Make the case that non-paraphilic out of control sexual behavior is related to paraphilic out of control sexual behavior.
4. What is causing the problematic behavior in out of control sexuality
   a) Is it the fantasies or object of attraction?
   b) If not, what clues do we have about the source of the problem?
5. What is the neuroanatomical conceptualization of the problem.
6. What kind of evidence do we have that our treatments and why don't we have better evidence?
7. In this context, how do we treat these problems pharmacologically?

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START WITH DEFINITIONS

HYPERSEXUAL DISORDER VS. PARAPHILIAS

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A CONDITION WITHOUT A CONSENSUS

- Compulsive sexual behavior
- Sexual compulsivity
- Sexual addiction
- Paraphilia-related disorder
- Sexual impulsivity
- Hypersexual disorder

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AS CONCEPTUALIZED BY DSM-5 SUBCOMMITTEE

- Hypersexual Disorder
  - Proposed to avoid conceptual concerns
  - Criteria developed
  - Field trial implemented and published (RC Reid, et al.)
- Not in DSM-5 (rejected by Board of Trustees of the APA)
  - Pathologize normal behavior
  - Insufficient scientific evidence of distinct syndrome
  - Misuse of dx in forensic settings

(RC Reid, 2012)

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HYPERSEXUAL DISORDER CRITERIA

A. Over a period of at least 6 months, recurrent and intense sexual fantasies, sexual urges, and sexual behavior in association with **four or more** of the following five criteria:

1. Excessive time is consumed by sexual fantasies and urges, and by planning for and engaging in sexual behavior.
2. Repetitively engaging in these sexual fantasies, urges, and behavior in response to dysphoric mood states (e.g., anxiety, depression, boredom, and irritability).
3. Repetitively engaging in sexual fantasies, urges, and behavior in response to stressful life events.

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HYPERSEXUAL DISORDER CRITERIA

4. Repetitive but unsuccessful efforts to control or significantly reduce these sexual fantasies, urges, and behavior.
5. Repetitively engaging in sexual behavior while disregarding the risk for physical or emotional harm to self or others.

B. There is clinically significant personal distress or impairment in social, occupational, or other important areas of functioning associated with the frequency and intensity of these sexual fantasies, urges, and behavior.

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HYPERSEXUAL DISORDER CRITERIA

C. These sexual fantasies, urges, and behavior are not due to direct physiological effects of exogenous substances (e.g., drugs of abuse or medications), a co-occurring general medical condition, or to a manic episodes.

D. The person is at least 18 years of age.

Specify if masturbation, pornography, sexual behavior with consenting adults, cybersex, telephone sex, and strip clubs.

Source: http://www.dsm5.org

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DSM-5 PARAPHILIC DISORDERS

Diagnosis	Summary definitions
Exhibitionistic Disorder	Exposing one's genitals to an unsuspecting person or performing sexual acts that can be watched by others
Frotteuristic Disorder	Touching or rubbing against a non-consenting person
Voyeuristic Disorder	Urges to observe an unsuspecting person who is naked, undressing or engaging in sexual activities, or in activities deemed to be of a private nature
Fetishistic Disorder	Use of inanimate objects to gain sexual excitement
Pedophilic Disorder	Sexual preference for prepubescent children
Sexual Masochism Disorder	Wanting to be humiliated, beaten, bound or otherwise made to suffer for sexual pleasure
Sexual Sadism Disorder	In which pain or humiliation of a person is sexually pleasing
Transvestic Fetishism	Arousal from clothing associated with members of the opposite sex
Other Specified Paraphilic Disorder	Variety of paraphilic behaviors such as: partialism; zoophilia; necrophilia; klismaphilia; coprophilia; urophilia; infantilism; telephone scatologia.

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DSM-5 PARAPHILIA DISORDERS

- Feel personal distress about their interest, not merely distress resulting from society's disapproval

OR

- Have a sexual desire or behavior that involves another person's psychological distress, injury, or death, or a desire for sexual behaviors involving unwilling persons or persons unable to give legal consent

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AS CONCEPTUALIZED BY KAFKA

- Paraphilia-related disorder
  - Like DSM paraphilias except the sexual behavior is socially sanctioned.
    - Associated with significant distress or impairment
    - Persist for at least 6 months.
- Hypersexual desire-pathological and non pathological type
  - TSO > or = 7
  - Time/day on average 1 to 2 hours

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WHAT IS A "HIGH SEX DRIVE"?

- Kinsey (1953) (n = 5300)
  - 7.6% males TSO > 7 times/week for > 5 years
  - Masturbation primary outlet
- Atwood and Gagnon (1987) (n = 1077)
  - 5% high school males and 3% college males report daily masturbation
- Laumann et. al (1994) (n = 3159)
  - 3.1% of males masturbate at least once/day
  - 7.6% have sexual intercourse at least 4x/week

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HYPERSEXUALITY

- 89.3% cumulative TSO > 5
- 80.7% cumulative TSO > 6
- 76.2% cumulative TSO > 7

(Kafka, 1999)

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CONCEPTUAL ISSUES

- Fantasy-a mental image or pattern of thought that stirs a person's sexuality and can create or enhance sexual arousal. Can be volitional or intrusive thoughts. (H Leitenberg, K Henning, 1995)
- Urges/Craving/strong desire--refers to internal emotional states that derive from impulses and drives the individual toward a particular behavior.

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TREATMENTS

- Concerned about fantasies, which implicates concepts of deviant/non-deviant, acceptable/not acceptable, offense related
- Concerned about urges, which implicates concepts such as sexual behavioral control, impulsivity, and reward processing.

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FOCUSES ON FANTASY CONTENT

- Sexual offending behavior can often be driven by sexual interest (e.g. pedophilia, sexual sadism, voyeurism, etc.)
- Sexual content develops through conditioning, thus can be modified through conditioning

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CONDITIONING PARADIGM

- Behavioral interventions developed

Olfactory Aversion - classical counter-conditioning paradigm

Orgasmic reconditioning - classical conditioning paradigm

Masturbatory satiation - based on Hull (1943) concepts of motivation potential.

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CHANGING FANTASY CONTENT

- Covert sensitization: Usually involves adding to the fantasy content some type of negative consequence (e.g., being assaulted, being arrested, going to jail).
- Thought substitution

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EFFECTIVENESS OF TREATMENTS

- No evidence of long-term impact
- Early studies, as reviewed by Furby et al., 1989, showed little effect of the mainly behavioral interventions.
- Hall, 1995, best effects shown by cognitive behavioral and pharmacotherapy interventions.

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CONCEPTUAL PROBLEMS

- Classical conditioning is a weak behavioral paradigm.
- Punishment paradigms, such as olfactory aversion or covert sensitization, have short-term effects, but effects tend to wear off.
- The CS in a contiguity paradigm often is restricted to the training environment.

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CONCEPTUAL ISSUES (CONT.)

- Punishment paradigms often are restricted to certain discriminant stimuli.
- Procedures requiring the patient to switch fantasy content can not be controlled.
- Assumes that the UCS is orgasm.

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THEREFORE,

- The idea that the fantasies are the problem doesn't get us too far.

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DIFFERENCES BETWEEN PORN ONLY AND CONTACT

- 17% of online offenders known to have committed a hands-on sexual offense (Seto, Hanson & Babchishin, 2011)
- Child pornography offending is a stronger predictor of pedophilic interest than sexually offending against a child (Seto, Cantor & Banchard, 2006)
- Internet porn only offenders show less anti-social behaviors and attitudes than those with contact offenders (Lee et al., 2012)
- Child pornography offenders show fewer cognitive distortions and victim empathy deficits, and less emotional identification with children (Babchishin, Hanson & VanZuylen, 2015)
- Child pornography offenders with previous hands-on offenses showed more sexual regulation problems the those without hands-on offenses (Babchishin, et al., 2015)

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THEREFORE,

- Attraction to children and fantasies about children is not sufficient to explain pedophilic disorder.

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PREDICTORS OF OFFENDING IN MINOR ATTRACTED MALES

- More frequently working with children
- More frequently "falling in love" with children
- Attraction to males
- More attraction to children than adults*
- Experienced childhood sexual abuse
- Struggled to avoid committing a sexual offense*

*Predicted hands-on but not child pornography offenses.

(Bailey, Bernard, & Hsu, 2016)

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NON-OFFENDING MINOR ATTRACTED MALES

- An awareness that sexual activity with children is exploitative and harmful. (Mitchell & Galupo, 2018)
- **Deficits in inhibitory control** found in minor attracted individuals who have a history of offending and not in those without such a history (Massau, et al., 2017).

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THEREFORE,

- Factors associated with commission of hands-on sexual crimes are related to:
  - Attitudes and beliefs that interfere with motivation to inhibit behavior
  - Deficits in inhibitory mechanisms

Treatments that focus on **urges and inhibitory control** may be more useful than those that focus on fantasy content.

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FINDING FROM OUR RESEARCH

- Studied MSM who met criteria hypersexual disorder
- Comprehensive assessment of self-reported symptomatology
  - Compulsive Sexual Behavior Inventory (CSBI), (Coleman, et al., 2001)
    - Used to be 28 items, 3 scales
    - Now 13 items, control scale only
  - Sexual Symptom Assessment Scale (S-SAS) (Raymond, et al., 2007)
  - Sexual Excitation Scale/Sexual Inhibition Scales (Janssen, et al., 2002)
- Penile plethysmography with negative and anxious mood induction
- (Comprehensive neurocognitive evaluation)

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DIFFICULTIES WITH CONTROL OF URGES AND IMPULSES

- Findings from our current research on out of control sexual behavior
- Higher scores on CSBI associated with higher self reported urges and intrusive fantasies (r=0.57)

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ASSOCIATION OF URGES (S-SAS) WITH SES/SIS

	Unstandardized Coefficients		Standardized Coefficients		
	B	Std. Error	Beta	t	Sig.
Sexual Excitation Scale	.34	.075	.28	4.53	<.001
Sexual Inhibition Scale 1	.34	.092	.23	3.73	<.001
Sexual Inhibition Scale 2	-.28	.134	-.13	-2.07	.040

$R = .36, F_{3, 238}=11.5, p<.001$

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ASSOCIATION OF URGES AND IMPULSES WITH MOOD AND SUBSTANCE USE

	Unstandardized Coefficients		Standardized Coefficients		
	B	Std. Error	Beta	t	Sig.
Beck Depression Inventory II	.26	.086	.19	3.05	.003
Drug Use Disorders Test	.28	.069	.26	4.02	<.001
Alcohol Use Disorders Test	.20	.099	.13	2.03	.043

$R = .44, F_{3, 238}=18.6, p<.001$

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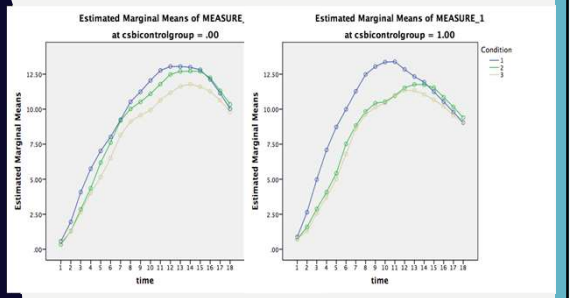
AROUSAL FOLLOWING INDUCTION MEDIAN SPLIT ON CSBI CONTROL SCALE



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AVERAGE SEXUAL RESPONSE IN NEUTRAL CONDITION

Coefficients[a]

Model		Unstandardized Coefficients B	Unstandardized Coefficients Std. Error	Standardized Coefficients Beta	t	Sig.
1	(Constant)	11.529	6.640		1.736	.084
	Age	-.172	.039	-.284	-4.376	.000
	Sexual Excitation Scale	.206	.059	.224	3.488	.001
	Sexual Inhibition Scale 1	-.133	.074	-.115	-1.798	.074
	Sexual Inhibition Scale 2	.115	.101	.073	1.148	.252
	Behavioral Inhibition Scale	-.485	.213	-.145	-2.283	.023

a. Dependent Variable: meanneutresponse

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UNDERLYING MECHANISMS FOR URGES AND IMPULSES

	Unstandardized Coefficients		Standardized Coefficients		
	B	Std. Error	Beta	t	Sig.
Sexual Excitation Scale	.34	.075	.28	4.53	<.001
Sexual Inhibition Scale 1	.34	.092	.23	3.73	<.001
Sexual Inhibition Scale 2	-.28	.134	-.13	-2.07	.040

$R = .36, F_{3, 238}=11.5, p<.001$

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URGES AND IMPULSES RELATED TO:

- Issues of reward processing, specifically:
  - high levels of sexual excitation
  - high emotional inhibitory processes
  - low negative outcome related inhibitory processes
- Depression
- Substance use and abuse

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ASSESSMENT

RATING SCALES

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CLINICAL TOOLS

- Sexual Symptom Assessment Scale (S-SAS)
  - (Raymond et al., (2007) Sexual Addiction and Compulsivity, 14:2, 119-129)
- Minnesota Impulse Control Inventory Questionnaire (MICI): Sexual Behavior Module
  - (Raymond, Coleman, Miner; (2003) Comprehensive Psychiatry, 44(5): 370-380)
- Compulsive Sexual Behavior Inventory (CSBI)
  - Used to be 28 items, 3 scales
  - Now 13 items, control scale only
  - (Coleman, et al., 2001; Miner, et al., 2005)

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CLINICAL TOOLS

- Sexual Outlet Inventory
  - Interview, 6 items
  - (Kafka, 1991)
- Yale-Brown Obsessive Compulsive Scale-Compulsive Sexual Behavior (YBOCS-CSB)
  - Interview, 10 items
  - (Morgenstern, 2004)
- Sexual Compulsivity Scale
  - Rating Scale, 10 items
  - (Kalichman, 1994)

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PHARMACOLOGICAL TREATMENT OF INTRUSIVE FANTASIES AND URGES

UNDERLYING MECHANISMS

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❖**An important caveat**

Medication alone is not sufficient to treat paraphilias or hypersexual disorder

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WHAT DO WE TREAT

- Hypersexual desire
  - Decrease urges/craving
  - Increase impulse control
  - Decrease preoccupation
- Co-morbid disorders
  - Depression
  - Anxiety
  - Bipolar disorder
  - Psychotic disorders
  - Substance abuse

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COMORBIDITY IN PEDOPHILIC DISORDER (N=45)

Disorder	Lifetime	
	N	%
Any Axis I Disorder	**42**	**93**
Any Mood Disorder	**30**	**67**
Depression	25	56
Any Anxiety Disorder	**29**	**64**
Social Phobia	17	38
Posttraumatic stress disorder	15	33

Raymond, et al., 1999

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COMORBIDITY IN PEDOPHILIC DISORDER (N=45)

Disorder	Lifetime	
	N	%
Any psychoactive substance use disorder	**27**	**60**
Alcohol	23	51
Cannabis	17	38
Any psychotic disorder	**1**	**2**

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COMORBIDITY IN PEDOPHILIC DISORDER (N=45)

Disorder	Lifetime	
	N	%
Any eating disorder (binge eating disorder)	**4**	**9**
Any impulse control disorder	**13**	**29**
Kleptomania	4	9
Pathological Gambling	5	11

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COMORBIDITY IN PEDOPHILIC DISORDER (N=45)

Disorder	Lifetime	
	N	%
Any additional paraphilia	**24**	**53**
Frotteurism	7	16
Voyeurism	12	27
Any sexual dysfunction	**11**	**24**
Premature ejaculation	7	16

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COMORBIDITY IN PEDOPHILIC DISORDER (N=40)

Disorder	Lifetime	
	N	%
Any Axis II Disorder	**24**	**60**
Cluster A	**7**	**18**
Paranoid	7	18
Cluster B	**13**	**24**
Narcissistic	8	20
Antisocial	9	23
Cluster C	**17**	**43**
Avoidant	8	20
Obsessive-compulsive	10	25

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MEDICATION CHOICES

- Selective serotonin reuptake inhibitors (SSRI)
  - Fluoxetine
  - Sertraline
  - Fluvoxamine
  - Citalopram (HD)
- Opiate antagonist
  - Naltrexone
  - Nalmafene
- Antiandrogens
  - MPA
  - CPA
- LHRH agonists
  - Lueprolide acetate
  - Triptoreline

All prescribed off-label for these disorders

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NEUROANATOMY SHORT COURSE

THE MONOAMINES

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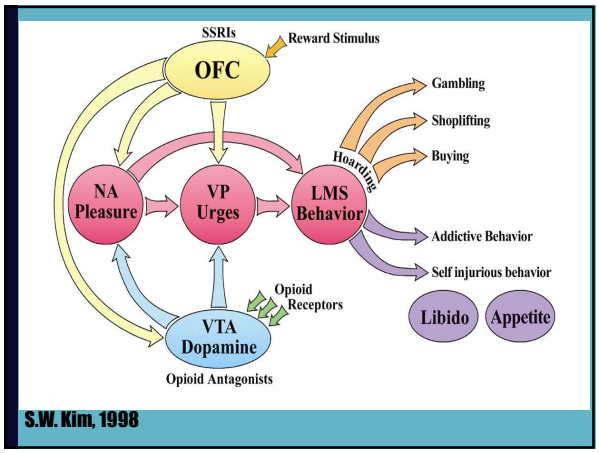

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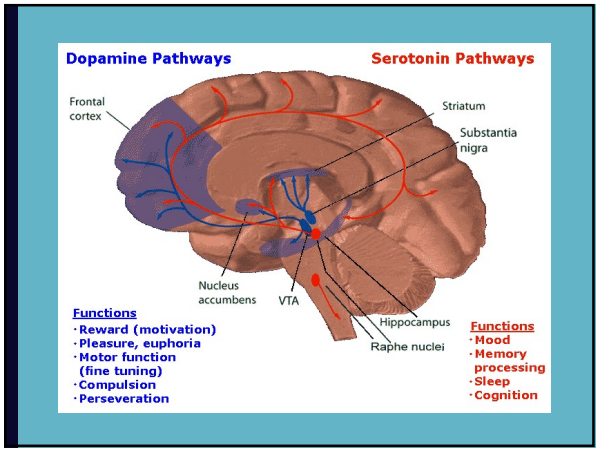

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SEROTONIN

- ↓Low levels :
  - –↑More aggressive behavior
  - –↑More impulsive behavior
  - –↑Higher risk of completed suicide in depression
  - –↑Increase sexual behavior in animal studies
- Location of action:
  - – Prefrontal Cortex (orbital frontal cortex)
  - – 14 receptor types
  - – 5-HT_{2A}

T Patti and L Vanderschurene, 2008

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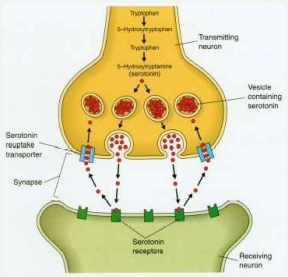
SEROTONIN



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NORADRENALINE

- Noradrenalin (desipramine and atomoxetine (Strattera)
  - ↓ Decreased impulsivity
  - ↑ Improved performance on the stop signal task
  - ↑ Increase delay aversion so more able to tolerate a delay before receiving a reward delay aversion so more able to tolerate a delay before receiving a reward (via stimulant tx)

Location of action:

- Prefrontal Cortex (orbital frontal cortex)
- Alpha-2 and Alpha-1 adenoreceptor

T Patti and L Vanderschurene, 2008

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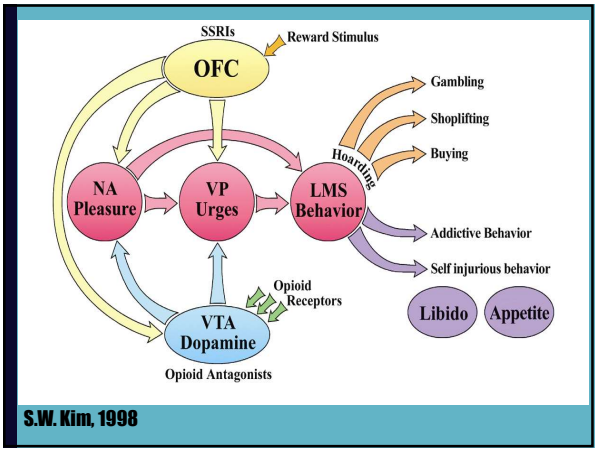

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DOPAMINE

- ↑High levels of dopamine
  - ↓Decrease impulsivity in ADD (via stimulant tx)
  - ↓ Performance on the stop signal task if baseline performance is low (via stimulant tx)
  - ↑Increase impulsivity in drug abuse
  - ↓Reduce delay aversion so more able to tolerate a delay before receiving a reward (via stimulant tx)
- Location of action
  - Nucleus Acumbens

T Patti and L Vanderschurene, 2008

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DOPAMINE
REWARD SYSTEM

- ↑ Mesolimbic dopamine pathway (ventral tegmental dopamine pathway)
- ↑ Pleasure, motivation, reward
- ↑ Motivation to seek reward

MA Bozarth, 1994 Pleasure: the politics and reality, pp5-14

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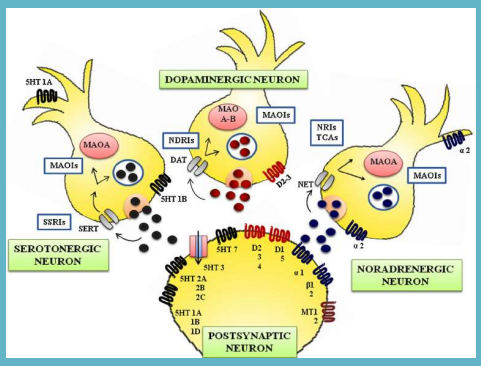

THE BRAIN ON MONOAMINES

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A GOOD WEBSITE

- https://neuroscientificallychallenged.com/

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EVIDENCE-BASED

(SUCH AS IT IS)

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LEVELS OF EVIDENCE

Level A

- GOOD research-based evidence to support the recommendation

- At least 3 moderately large, positive, randomized, double-blind, controlled trials (RCT) (with comparator)
- At least 1 of these is a well-conducted, placebo-controlled trial

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LEVELS OF EVIDENCE

Level B

- FAIR research evidence to support the recommendation
- At least 2 moderately large, positive, randomized, controlled trials (RCT) (comparator or placebo-controlled)

OR

- At 1 moderately large, positive, RCT that is placebo-controlled
- AND at least 1 prospective, moderately large (>50) open-label, naturalistic study

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LEVELS OF EVIDENCE

Level C

- MINIMAL research-based evidence to support the recommendation
- At least 1 double-blind study with the comparator treatment
- AND 1 prospective open-label/case series with >10 participant

OR

- Two prospective open-label/case series with >10 participants

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LEVELS OF EVIDENCE

Level D

- Evidence obtained from expert opinion
- AND at lease one prospective, open-label/case series with >10 participants

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SAMPLE BIAS

- Very few voluntary sex offenders or those seeking treatment for paraphilias
- Therefore, most participants are remanded to treatment
- Lots of hurdles to have adjudicated individuals in treatment studies
- Hard to know if the results generalize

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ETHICAL CONSIDERATIONS

- Use of outpatient sex offender treatment programs
- The gold standard for establishing treatment efficacy is the double-blind placebo-controlled trial.
- Hard to give a placebo to a sex offender because of the potential risk to the public if a subject is on placebo.

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PHARMACOTHERAPY

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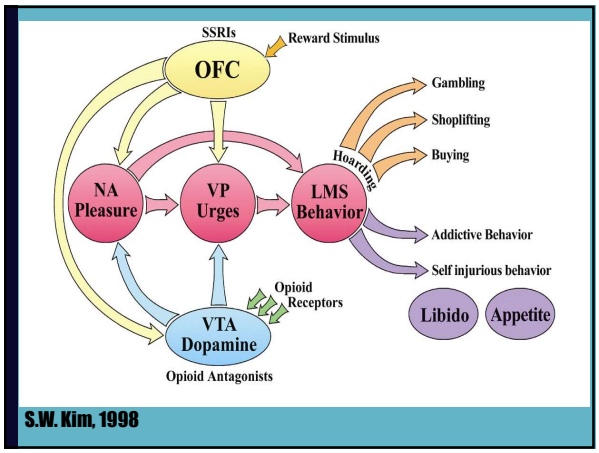

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ONE DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

One trial of citalopram (Celexa) in hypersexual disorder

Inclusion/Exclusion Criteria:

- 28 MSM and bisexual men.
- 18 years of age or older
- Sex with at least 2 male partners in the last 90 days
- Clinical Global Impressions scale (CGI) modified for CSB=moderate
- No psychiatric disorder that would interfere with participation (SI)
- No current or recent (past 90 days) tx with SSRI

(ML Wainberg, 2006)

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ONE DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

- Flexible dose of 20 to 60 mg vs placebo
- 12-week treatment
- Followed by a 2-week taper
- 2 dropped out at week 4 but were included in analysis.
- Rating Scales
  - YBOCS-CSB
  - CSBI
  - Timeline follow back procedure to daily sexual history

(ML Wainberg, 2006)

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ONE DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

- Reduced compared to placebo:
  - Desire/drive for sex
  - Frequency of masturbation
  - Hour of pornography per week
  - Severity was no different at end of tx (medication group started out with higher severity.
  - No decrease in partnered sexual behavior

(ML Wainberg, 2006)

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ONE DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

- Sexual risk decreased in both groups but no significant difference between groups
- Side effects-citalopram group
  - Delayed ejaculation
  - Mediated decrease in masturbation and pornograply
  - Did not mediate decreased sexual drive/desire
- Sexual satisfaction
  - Remained fairly stable and was not related to SSE

(ML Wainberg, 2006)

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CASE REPORTS
ANTIDEPRESSANT/ANXIOLYTICS

SSRI'S

- Citalopram (PSP-, CB+, HD+/-, K-)
- Fluoxetine – Prozac (T+/-, IED+, PSP+)
- Sertraline – Zoloft (PG -)
- Paroxetine – Paxil (PG +/-)
- Fulvoxamine – Luvox (PG +/-, CB-)
- Escitalopram – Lexapro (PG +, K -)

OTHER

- Nafazodone – Serzone
- Buspirone – Buspar
- TCA's
  - Clomipramine vs Anafranil (T +)
  - Desipramine – Norpramin (T-)

Key
CB=compulsive buying, K=kleptomania, IED=intermittent explosive disorder, PG=pathological gambling, T=trichotillomania, PSP=pathological skin picking

(Review by L Schreiber, 2011)

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CASE STUDY-WHEN IT WORKS

- Fluoxetine in the treatment of paraphilias
- RD, Perilstein, et.al., J Clin Psychiatry 52:4, 169-170

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POTENTIAL PROBLEM WITH SSRI'S

- Side effects
  - Headache
  - Nausea
  - Sexual side effects
    - Delayed orgasm
    - Decreased desire

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CASE STUDIES-WHEN IT MAKES MATTERS WORSE

- Two case studies from my clinic population
  - Rape fantasies treated with sertraline
  - Pedophilic disorder treated with paroxetine

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MORE CASE REPORTS
MOOD STABILIZERS

- Lithium carbonate – Lithobid (PG+)
- Carbamazepine – Tegretol
- Valproic acid – Depakote (IED+ with cluster B)
- Lamotrigene – Lamictal (PSP- /execpt in those with impaired cognitive flexibility)

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MORE CASE REPORTS
ATYPICAL ANTIPSYCHOTICS

- Risperdone- Risperdal
- Olanzapine- Zyprexa (PG-,T+)
- Quetiapine- Seroquel
- Ziprasidone-Geodon
- Aripirizole-Abilify

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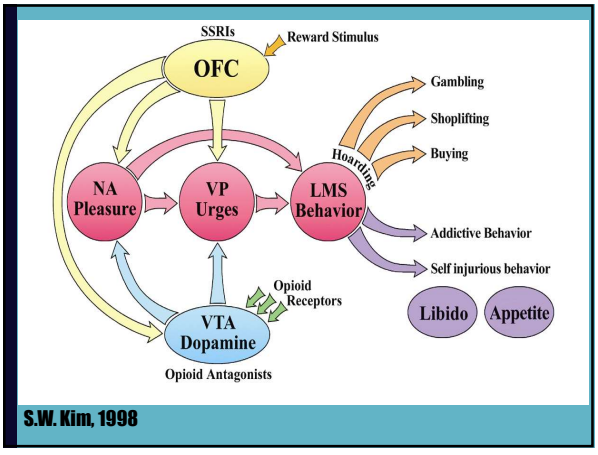

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PHARMACOTHERAPY
OPIATE ANTAGONIST

- Naltrexone - ReVia
- Dose 50 - 200 mg/day (higher doses divided)
- Contraindicated if regular use of nonsteroidal anti-inflammatory medications (NSAIDS)
  - drug interaction that can lead to liver damage.
- Monitor liver function tests
- Notify physician and stop before surgery!!
  - Case study from my clinical practice
- +/- Co-administration of *N*-acetyl cysteine

(NC Raymond, 2010; SW Kim, 2001)

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NALTREXONE-PROSPECTIVE STUDY

One open-label prospective study

- Twenty-one legally adjudicated, adolescent male sexual offenders on an inpatient unit.
- Ages 13 to17, mean 15.2 years
- Had been on the 36-bed unit an average of 1.2 year at onset
- 19 heterosexual, 1 homosexual, 1 bisexual

(Ralph S. Ryback, J Clin Psychiatry 65:7, 2004)

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NALTREXONE-PROSPECTIVE STUDY

Placed on naltrexone if they:

- Masturbated excessively (3 x per day or more)
- Felt they could not control their arousal (became sexually excited with erections spontaneously when seeing or thinking about children, girls, women or men)
- Spent more than 30% of their awake time in sexual fantasies
- Had sexual fantasies or behavior that regularly intruded into or interfered with their functioning in the tx program

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NALTREXONE-PROSPECTIVE STUDY

Comorbidity:

- 11 ADD or ADHD
- 6 sexually abused as a child
- 5 substance use disorder
- 4 intermittent explosive disorder
- 3 Frotteurism
- 3 PTSD
- Nearly every other DMS dx at in at least one person

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NALTREXONE-PROSPECTIVE STUDY

Concomitant Medications:

- 6 stimulants with guanfacine or clonidine
- 8 on antidepressants, mainly bupropion
- (no clear effect of SSRI's in this population)
- 5 were on mood stabilizers (valproate, lithium, oxcarbamazepine, topiramate)
- 1 risperidone
- 1 treatment for Tourette's

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NALTREXONE-PROSPECTIVE STUDY

Naltrexone dose:

- Average maintenance dose 170 mg per day
- Range 100 to 200 mg
- 50 mg for 4 days and then increased every 4 days until effective
- Tracked:
  - Behavioral changes
  - Sexual fantasies (deviant and nondeviant)
  - Masturbation
- Positive result if 30% decrease

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NALTREXONE-PROSPECTIVE STUDY

Of the 21 participants:

- 2 responded to 50 mg
- All but one noticed decreased arousal, masturbation, fantasies with 100 mg
- 11 increased to 200 mg in divided dosages—6 of these wore off after average of 3 months
- At 150 and 200 mg all but one reported benefit—the one later admitted he had been lying because it interfered with ability to fantasize and masturbate "about little kids"
- Improved self-esteem, self-mastery and control.

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PHARMACOTHERAPY
OPIATE ANTAGONIST

- Potential side effects:
  - **Nausea,** vomiting, diarrhea, or constipation, stomach pain or cramping
  - **Sedation**
  - Loss of appetite
  - Headache
  - Dizziness
  - Nervousness, irritability, or anxiety
  - Tearfulness. depressed mood

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MORE ON NALTREXONE
BEHAVIORAL ADDICTIONS/IMPULSE CONTROL DISORDERS

- Naltrexone in Pathological Gambling
  - 2 positive and 1 negative studies
  - Nalmefene (Revex) 1 positive and 1 negative
- Kleptomania
  - One positive study
- Alcohol
  - Nalmefene
  - Long-acting injectable naltrexone-Vivitrol

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N-ACETYL CYSTEINE (NAC)

- Modulates the glutaminergic system
- Protective for the liver
- Some independent/synergistic action with naltrexone
- Positive double-blind placebo-controlled trials in pathological gambling and trichotillomania
- Used in 1200 mg to 2400 mg or even 3000 mg doses.

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CASE REPORTS

- 42 year-old woman and 62 year-old man
- NC Raymond, et.al., International Clinical Phsychopharmacology, 2002 17:4, 201-205

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MORE NEUROANATOMY

HYPOTHALAMIC PITUITARY GONADAL AXIS

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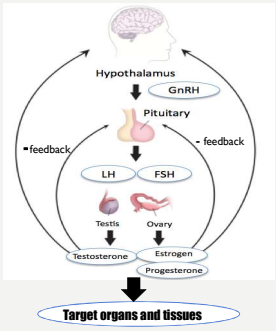
HYPOTHALAMIC PITUITARY GONADAL AXIS (HPG AXIS)



- GnRH-gonadotropin releasing hormone
- LH-Luteinizing hormone
- FSH-Follicle stimulating hormone
- GnRH agonist
  - Triptorelin
  - Leuprolide acetate (depo Lupron)

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ANTI-ANDROGENS

TREATMENT OF PARAPHILIA DISORDERS AND OCCASIONALLY HD

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CONTRAINDICATIONS

Drug	Contraindication
MPA/CPA	1. Thromboembolic disorders 2. Liver failure 3. Active pituitary pathology
Leuprolide	1. Osteoporosis 2. Active pituitary pathology

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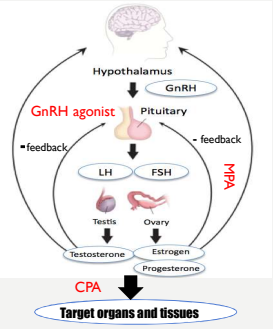
HYPOTHALAMIC PITUITARY GONADAL AXIS (HPG AXIS)



- HPA axis hormones
  - GnRH-gonadotropin releasing hormone
  - LH-Luteinizing hormone
  - FSH-Follicle stimulating hormone
- Anti-androgens
  - CPA cyproterone acetate
  - MPA medroxyprogesterone acetate (Provera)
- GnRH agonist
  - Leuprolide acetate (Lupron Depot)
  - Triptorelin (Triptodur)

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ANTI-ANDROGENS

- Cyproproterone acetate (CPA) (Europe and Canada)
- Mechanism of Action
  - True anti-androgen
  - Competitive inhibitor of testosterone at the binding sites
  - Acts as a progestin and suppressions of production of FSH and LH via negative feedback loop

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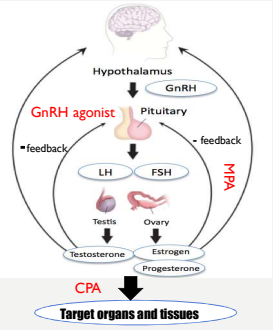
HYPOTHALAMIC PITUITARY GONADAL AXIS (HPG AXIS)



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  - LH-Luteinizing hormone
  - FSH-Follicle stimulating hormone
- Anti-androgens
  - CPA cyproterone acetate
  - MPA medroxyprogesterone acetate (Provera)
- GnRH agonist
  - Leuprolide acetate (Lupron Depot)
  - Triptorelin (Triptodur)

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ANTI-ANDROGENS

- Medroxyprogesterone acetate (MPA) (Provera)
- Mechanism of action:
  - Induces the testosterone reductase in the liver (increased the metabolismof testosterone)
  - Acts as a progestin and suppressions of production of FSH and LH via negative feedback loop

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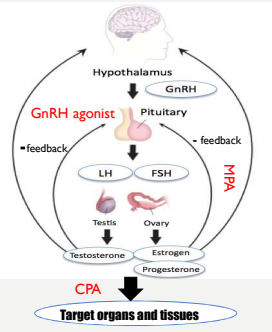
HYPOTHALAMIC PITUITARY GONADAL AXIS (HPG AXIS)



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  - Triptorelin (Triptodur)

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SIDE EFFECTS:

- Increase blood pressure
- Cardiac disease
- Tromboembolic events
- Hypergycemia
- Weight gain
- Gynecomastia
- Hot flashes
- Liver dysfunction
- Anemia
- Depression

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BASELINE TESTING—MPA AND CPA

1. Serum testosterone, luteinizing hormone, follicle stimulating hormone, and prolactin levels
2. Liver function tests
3. Complete blood count
4. Serum glucose
5. Blood pressure
6. Weight
7. EKG if suspicion of cardiac issues

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MONITORING DURING TX—MPA AND CPA

1. Serum testosterone monthly for 4 months then every 6 months
2. Serum luteinizing hormone and prolactin levels every 6 months
3. Monitor changes in blood pressure and weight
4. If serum testosterone suppressed significantly, then bone scan at baseline and annually
5. If hepatotoxicity suspected, then liver function tests (I would recommend every 6 to 12 months)

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ANTI-ANDROGENS

Long acting GnRH agonists

- Lueprolide acetate (Depo Lupron) long-acting LHRH agonist
- Triptoreline (Europe)

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ANTI-ANDROGENS

Lueprolide acetate (Depo Lupron), long-acting LHRH agonist

- Mechanism of action: Overstimulates the hypothalamus and decreases the release of GRH
- Side effects: osteopenia

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LUEPROLIDE ACETATE

- Anti-androgen side effects:
  - hot flushes
  - decrease body and facial hair
  - gynecomastia
  - weight gain
  - changes in blood pressure
  - decreased glucose tolerance
  - decrease testicular volume (hypogonadism that may be irreversible)

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LUEPROLIDE ACETATE

Flare phenomenon:

- Initial increase in testosterone levels
- Then drop to almost 0
- Peak-4 to 7 days (in cancer patients)
- Down to or below pre-injection level by 2 weeks
- MPA or CPA one week before and 1 to 2 weeks after starting is an option

Test done:

- 1 mg leuprolide subcutaneously with careful observation for allergy and anaphylaxis

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BASELINE TESTING—LEUPROLIDE

1. Serum testosterone
2. Luteinizing hormone
3. Follicle stimulating hormone levels
4. Serum urea and creatinine levels
5. Complete blood count
6. Bone-density scan
7. EKG

Can J Psychiatry (2000), 44(6):559663-6

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MONITORING DURING TREATMENT—LEUPROLIDE

1. Serum testosterone level and complete blood count monthly for 4 months then every 6 months
2. Serum luteinizing hormone level every 6 months
3. Serum blood urea nitrogen and creatinine levels every 6 months.
4. Bone-density scan yearly

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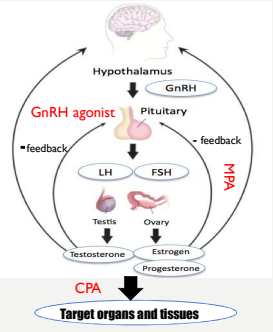
HYPOTHALAMIC PITUITARY GONADAL AXIS (HPG AXIS)



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  - CPA cyproterone acetate
  - MPA medroxyprogesterone acetate (Provera)
- GnRH agonist
  - Leuprolide acetate (Lupron Depot)
  - Triptorelin (Triptodur)

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CASE STUDY

- 41-year-old male with sexual attraction to males
- NC Raymond, et.al., *Sex Offender Treatment: Accomplishments, Challenges, and Future Directions. 2001, p 79-88*

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CONSENSUS GUIDELINES FOR TREATMENT OF PARAPHILIC DISORDERS

LEVEL OF EVIDENCE

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GUIDELINES

The World Federation of Societies of Biological Psychiatry Guidelines for the biological treatment of paraphilias

(F Thibaut, F de la Barra, H Gordon, P Cosyns, J Bradford, WFSBP Tasks Force on Sexual Disorders, World Journal of Biological Psychiatry ; 11: 604-655; 2010)

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AIMS OF TREATMENT

- Control paraphiliac fantasies and behaviors in order to decrease risk of recidivism
- Control sexual urges
- Decrease the level of distress of the paraphilic subject.

Int J Law Psych 36 (2013) 235-2406

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TREATMENT OF SEXUAL OFFENDERS
LEVEL 1

Aim: Control of paraphilic sexual fantasies, compulsions and behaviors without impact on unconventional sexual activity and on sexual drive

- Psychotherapy
  - Preferentially cognitive behavioral therapy if available (Level C)
  - No level of evidence for other forms of psychotherapy

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TREATMENT OF SEXUAL OFFENDERS
LEVEL 1

- Aim: control of paraphilic sexual fantasies, compulsions and behaviors without impact on conventional sexual activity and on sexual drive.
- Psychotherapy (preferentially cognitive behavioral therapy is available (Level C): no level of evidence for other forms of psychotherapy)

Int J Law Psych 36 (2013) 235-2406

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TREATMENT OF SEXUAL OFFENDERS
LEVEL 2

- Aim: control of paraphilic sexual fantasies, compulsions and behaviors with minor impact on conventional sexual activity and on sexual desire
- May be used in all mild cases ("hands-off" paraphilias with lower risk of sexual violence, i.e. exhibitionism without any risk of rape or pedophilia)
- No satisfactory results at Level I
- SSRIs: increase the dosage at the same level as prescribed in OCD (e.g. fluoxetine 40–60 mg/day or paroxetine 40 mg/day (Level C)

Int J Law Psych 36 (2013) 235-240

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TREATMENT OF SEXUAL OFFENDERS
LEVEL 3

- Aim: control of paraphilic sexual fantasies, compulsions and behaviors with a moderate reduction of conventional sexual activity and sexual desire
- "Hands-on" paraphilias with fondling but without penetration
- Paraphilic sexual fantasies without sexual sadism
- No satisfactory results at Level two after four to six weeks of SSRIs at high dosages
- Add a low dose of anti-androgen (e.g. cyproterone acetate 50–100 mg/day) to SSRIs (Level D)

Int J Law Psych 36 (2013) 235-240

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TREATMENT OF SEXUAL OFFENDERS
LEVEL 4

- Aim: control of paraphilic sexual fantasies, compulsions and behaviors with a substantial reduction of sexual activity and desire
- Moderate and high risk of sexual violence (severe paraphilias with intrusive fondling with limited number of victims)
- No sexual sadism fantasies and/or behavior (if present: go to Level 5)
- Compliant patient, if not: use IM form or go to Level 5

Int J Law Psych 36 (2013) 235-240

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TREATMENT OF SEXUAL OFFENDERS
LEVEL 4 (CONT.)

- No satisfactory results at Level 3
- First choice: full dosage of cyproterone acetate (CPA): oral, 200–300 mg/day or IM 200–400 mg once weekly or every two weeks
- Second choice: medroxyprogesterone acetate: 50–300 mg/day if CPA not available (Level C)
- If comorbidity with anxiety, depressive or obsessive-compulsive symptoms, SSRIs might be associated with cyproterone acetate

Int J Law Psych 36 (2013) 235-240

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TREATMENT OF SEXUAL OFFENDERS
LEVEL 5

- Aim: control of paraphilic sexual fantasies, compulsions and behaviors with an almost complete suppression of sexual desire and activity
- High risk of sexual violence and severe paraphilias
- Sexual Sadism fantasies and/or behavior or physical violence
- No satisfactory results at Level 3
- Long acting GnRH agonists, i.e. triptorelin or leuprolide acetate 3 mg/month or 11.25 mg IM every three months (Level C)

Int J Law Psych 36 (2013) 235-240

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TREATMENT OF SEXUAL OFFENDERS
LEVEL 5 (CONT)

- Testosterone levels measurements may be easily used to control the GnRH agonist treatment observance if necessary
- Cyproterone acetate may be associated with GnRH agonist treatment (one week before and during the first month of GnRH)
- Prevents flare up effects and to control the relapse risk of deviant sexual behavior associated with the flare up effect

Int J Law Psych 36 (2013) 235-240

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TREATMENT OF SEXUAL OFFENDERS
LEVEL 6

- Aim: control of paraphilic sexual fantasies, compulsions and Behaviors with a complete suppression of sexual desire and activity
- Most severe paraphilias (catastrophic cases)
- No satisfactory results at Level 5
- Use anti-androgen treatment i.e. cyproterone acetate (50–200 mg/day per po or 200–400 mg once meekly or every two weeks IM) or, medroxyprogesterone acetate (300–500 mg/week IM if CPA not available) in addition to GnRH agonists (Level D)
- SSRIs may also be added (Thibaut, et al., 2010)

Int J Law Psych 36 (2013) 235-240

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KEY POINTS—TREATMENT OF PARAPHILIC D/O

- Paraphilias are chronic and, in most cases, lifetime disorder.
- The combination of psychotherapy and pharmacotherapy is associated with better efficacy compared with either treatment as monotherapy.
- The gold standard treatment of severe paraphilias in adult males is antiandrogen treatment, especially GnRH agonists.
- Using an appropriate protocol to detect and treat any side effects, antiandrogen therapy constitutes no more or less of a risk than most other psychotropic drugs.***
- According to most authors, a minimal duration of treatment of 3 to 5 years for severe paraphilia with a high risk of sexual violence is necessary
- In juvenile sex offenders, behavioral therapy and SSRIs are the first treatment options. Also, consider naltrexone.

Psychiatr Clin N Am, 37: 173-181, (2014)

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FINAL THOUGHTS AND DISCUSSION POINTS

- Medication is a useful adjunct to psychotherapeutic interventions.
- Opioid antagonist medications act on urge states.
- Antiandrogen act on sexual drive.
- Sexual behavior is driven by sexual excitatory and inhibitory mechanisms.
- Psychotherapeutic interventions may be more effective if focused on behavioral inhibition and reinforcement contingencies which allow the individual to cope with urges.
- These targets appear to fit with the Good Lives Model and other intervention models currently guiding sex offender treatment.

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