Medication Treatment Sexual Offending in Developmental Disorders

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Sexual Offending or Paraphilic Disorders

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- Difficult to define the difference between sexual offending and paraphilic disorders
- Not all sexual offenders can be diagnosed as suffering from paraphilic disorder
- Whilst extreme manifestations of paraphilic disorder would inevitably constitute criminal acts, low level fantasies (where there is no acting out) are not in themselves criminal acts
- However, the risk and likelihood of escalation means those with low level fantasies pose concern which often drives therapeutic interventions
- Sexual offending not in itself a pathological disorder, but both DSM V and ICD 11 disease classification systems include diagnostic criteria for a range of paraphilic disorders
- Evidence relating to pharmacological interventions will target recognised paraphilic disorders

Classification Paraphilic Disorders

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Paraphilic Disorders Included ICD 11 or DSMV Diagnostic Schedules

	DSM V	ICD 11
Exhibitionistic Disorder	X	X
Voyeuristic Disorder	X	X
Pedophilic Disorder	X	X
Sexual Sadism Disorder	X	X
Frotteuristic Disorder	X	X
Sexual Masochism	X	
Transvestic	X	
Fetishistic	X	

Therapeutic Rationale

Control of Sexual Desire

- Substantial evidence supports testosterone as key in controlling male sexual desire
- Age related decline testosterone linked to reduced male libido
- Therapeutic replacement testosterone linked to increased male libido

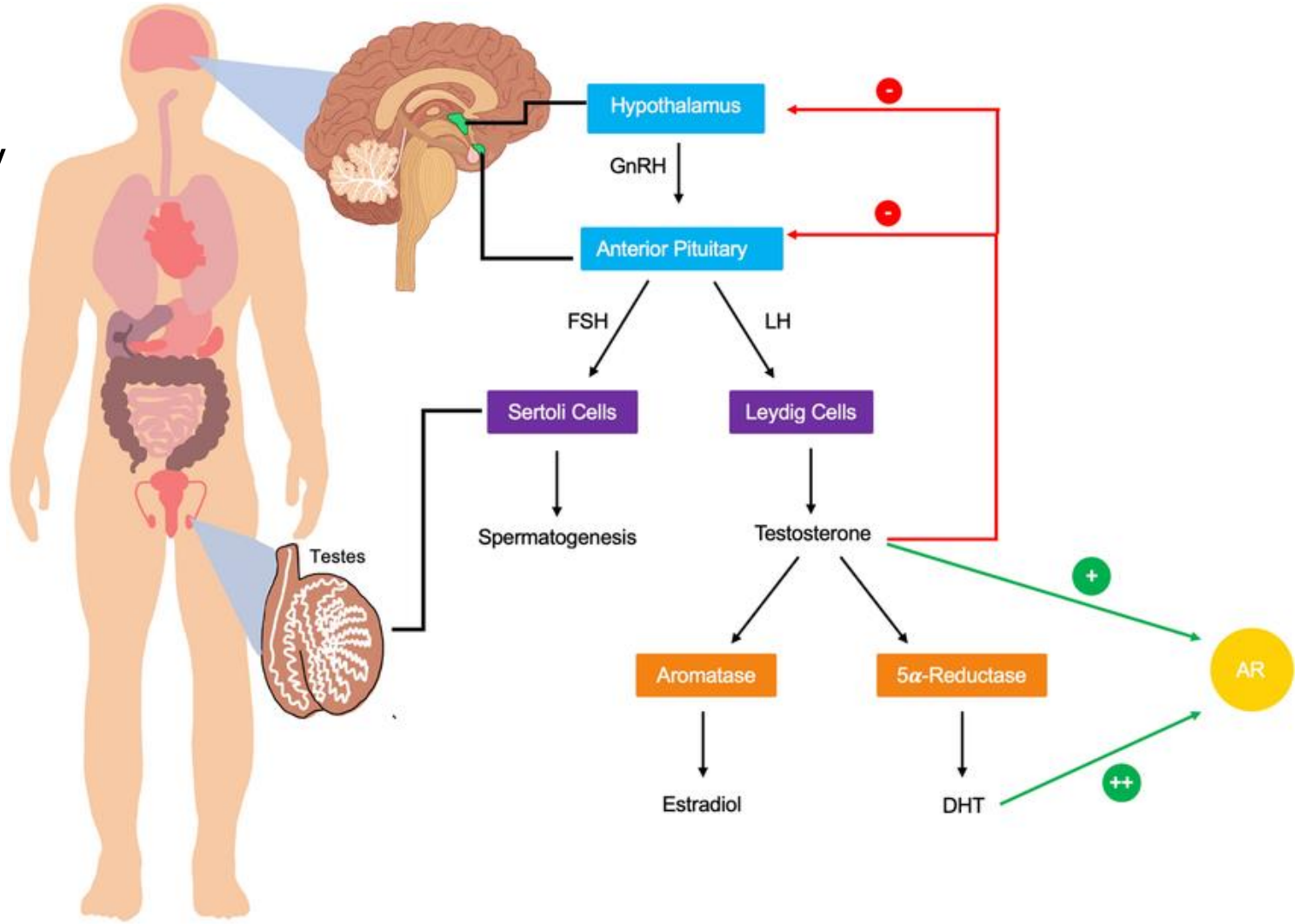
Other Hormones

- Raised prolactin associated with decreased libido
- Study demonstrated decreased libido associated with 10x increased risk of severe hyperprolactinaemia (>735 mU/L)
- Mechanism not understood, could be prolactin induced hypogonadism, either direct or mediated through action on dopamine
- Dopamine also plays role in regulating sexual desire
- Empirical evidence stems from observation reduced libido in Parkinson's disease and positive effect of DA agonists on sexual desire

Therapeutic Rationale

Control of Testosterone Release

- Sexual development and drive linked to testosterone production and activity
- Central control of testosterone production emanates from hypothalamus and anterior pituitary
- Release of FSH and LH triggered by levels of GnRH
- LH stimulates production of testosterone



Therapeutic Rationale

Hormonal Treatments

- Antiandrogens decrease circulating levels testosterone
- Also block cellular uptake of androgens by receptor binding mechanism
- Examples include:
    - Cyproterone
    - Medroxyprogesterone

Gonadotrophin hormone releasing hormone - GnRH Analogs

- Suppress release of leutinising from the pituitary gland
- This inhibits testosterone production
- GnRH also proposed to have central modulating effects on sexual behaviour
- Examples include:
    - Triptorelin
    - Goserelin

Therapeutic Rationale

SSRI's

- Serotonin inhibits sexual arousal, reduces orgasmic and ejaculatory capacity
- No dysfunction of serotonin metabolism or receptors has been identified in patients with paraphilias
- SSRIs reduce paraphilic behaviours by
  - Non-specific reduction in sexual interest
  - Reduced impulsiveness
  - Reduced obsessive compulsive symptoms
  - Indirect reduction serum testosterone levels

SSRIs and Reduced Sexual Libido

- Established side effect of SSRIs
- Immediate genital sensory changes bring about changes to orgasm, which results in reduced libido
- Concern growing that reduced libido persists beyond termination of therapy
- PSSD (Post SSRI Sexual Dysfunction) possibly linked to initial genital sensory changes, but extending beyond genital area
- No agreement as to how sensory changes caused, hypothesised due to changes in sodium channel activity

Therapeutic Rationale

Non-Hormonal Treatments

- Antipsychotics have historically been used
- Inhibition dopamine could have a direct action on sexual desire
- Many antipsychotics increase prolactin levels, which will also inhibit sexual desire and libido
- Many antipsychotics also have significant sedative effects

Benperidol

- Butyrophenone antipsychotic, related to haloperidol
- Licensed for the control of deviant antisocial sexual behaviour
- License does not necessarily indicate evidence of superior efficacy
- Currently unavailable (since Mar 2022) and no indication of when (or if) supplies will resume

Evidence Supporting Pharmacological Interventions

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Cochrane Review - Ashman et al 2008

- Interventions for learning disabled sex offenders
- Considered both pharmacological and non-pharmacological interventions
- No randomised controlled trial evidence found to guide the use of interventions for learning disabled sex offenders
- Studies found were excluded due to:
  - Non randomised trials
  - Participants were not both LD and sexual offending behaviour

Cochrane Review – Khan et al 2015

- Pharmacological interventions for those who sexually offended, or are at risk of offending
- Seven studies (138 participants) included All published before 1995
- Six studies examined effectiveness of three testosterone suppressing drugs – cyproterone, ethinyl oestradiol, medroxyprogesterone
- One study compared benperidol and chlorpromazine
- No studies found investigating newer drugs (specifically SSRIs or GnRH analogues
- Review unable to draw firm conclusions

Evidence Supporting Pharmacological Interventions

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

- Evaluated role of pharmacotherapy in treatment of paraphilias amongst males
- Based on extensive literature search across both literature databases and other sources
- Guidelines not specific for ID
- Acknowledged limitations of review
    - Mostly open studies or case reviews
    - Ethically difficult to conduct double blind studies
    - Social limitations on individuals requesting treatment
    - Small sample sizes
    - Subjective outcome measures, or outcome with poor indication of treatment success (e.g. testosterone level)

WFSBP Guidelines For Treatment Adolescent Sexual Offenders

Evidence Supporting SSRIs

- Several case reports and uncontrolled studies (mainly involving adults)
- Most reports highlighted benefits from fluoxetine or sertraline

Evidence Supporting Antipsychotics

- Most studies old (1970s)
- Study comparing benperidol, chlorpromazine and placebo amongst paedophiles with no significant difference
- Open study patients receiving fluphenazine depot found deviant sexual tendencies disappeared in 5 cases and were reduced in 4

Evidence Supporting Pharmacological Interventions

Evidence Supporting Antiandrogens Cyproterone or Medroxyprogesterone

- Cyproterone, 900 patients included in open or blinded studies, but limited trial designs.
  - Significant decrease self-reported sexual fantasies or masturbation, or disappearance deviant behaviour within 4-12 weeks
  - Doses 50-300mg oral, or 300-600mg IM 1-2 weekly. In most cases 100-200mg dose sufficient
- Medroxyprogesterone, most studies not controlled and given severe side effects observed benefit / risk ratio does not favour medroxyprogesterone

Evidence Supporting Antiandrogens GnRH analogues

- Small, open studies using goserelin, triptorelin or leuprorelin
- Observed efficacy very high,with most participants reporting absence of deviant behaviours whilst therapy continued.
  - Even amongst those reporting prior failure to respond to Cyproterone
- Long-acting injection formulation can make GnRH analogues preferential if treatment adherence an issue

Evidence Supporting Pharmacological Interventions

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Summary of Effects – SSRIs

- Most experience fluoxetine and sertraline
- Efficacy seen in reducing fantasies and paraphilic behaviours in paedophilia, exhibitionism, voyeurism and fetishism
- Systematic review found offenders with exhibitionism, compulsive masturbation and paedophilia showed most improvement

Summary of Effects – Cyproterone

- WFSBP guidelines reviewed 10 studies, 900 male subjects (20% paedophilia)
- 80-90% experienced significant decrease sexual fantasies or activity
- Cyproterone might be more effective than medroxyprogesterone, in terms of re-offending rates.

Summary of Effects – GnRH Analogues

- Smaller number of studies, compared with cyproterone, but found to be highly effective
- GnRH analogues might have advantages over cyproterone
  - Use where Cyp contra-indicated or ineffective
  - Apparent better side effect profile

Adverse Effects Pharmacological Therapy

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SSRIs

- Range of adverse effects reported with SSRIs, including:
  - Gastric Irritation, nausea
  - Anxiety, restlessness
  - Loss appetite, weight loss
  - Headache
  - Bleeding disorders
- Increasing concern regarding antidepressant withdrawal reactions, incident ranging from 27-86% patients
- Higher doses associated greater risk of withdrawal reaction

Antiandrogens

- Hot flushes, sweats
- Weight gain
- Mood changes
- Risk of meningioma (cyproterone)
- Risk hepatotoxicity (cyproterone)

GnRH Analogues

- Osteoporosis, reduced bone mineral density
- Mood changes, depression
- Initial transient increase testosterone
- QT interval prolongation (risk if co-administered antipsychotics)

Treatment Guidelines – Thibaut et al 2016

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- Suggested treatment algorithm based on literature for treatment adolescent sexual offenders
- Stratified treatment, representing more aggressive treatments for individuals posing higher risk
- In common with other reviews suggested treatments either SSRI, antiandrogens or GnRH analogues

	Aim to Control	Intervention
Level 1	• Paraphilic sexual fantasies, compulsions, and behaviours	• Cognitive Behavioural Therapy
Level 2	• Escalating paraphilic sexual fantasies, 'hands-off' and low risk of sexual violence	• SSRIs at OCD Treatment dose Fluoxetine 40-60mg daily
Level 3	• 'Hands-on' fantasies, with fondling, but without penetration • Paraphilic sexual fantasies, without sadistic elements	• Add low dose anti-androgen to SSRI treatment Cyproterone, oral, 50-100mg daily
Level 4	• Moderate or high risk of sexual violence • Severe paraphilias with more severe hands-on sexual activity	• High dose anti-androgen Cyproterone, oral, 200-300mg daily
Level 5	• High risk of sexual violence, severe paraphilias and sexual sadism	• Triptorelin 11.25mg every 3 months
Level 6	• Most severe paraphilias where complete suppression of sexual activity and desire is needed	• Triptorelin 11.25mg every 3 months Plus • Cyproterone, oral, 50-200mg daily

Summary

- Lack of robust evidence supporting any therapeutic intervention to control sexual offending behaviour
- Virtually no studies published in last 10-20 years
- Clear rationale for considering agents which reduce testosterone levels
- Concerns over immediate and long-term side effects of these agents

- SSRI antidepressants are associated with sexual effects
- Pharmacological explanation for some of these sexual effects
- Low grade evidence (mostly small, non-randomised studies) support use of SSRIs
  - Evidence not necessarily from studies involving ID patients
- Adverse effects of SSRIs should be considered before commencing therapy
  - Especially consider the risk of antidepressant withdrawal reactions