

SEXUAL DYSFUNCTION: DISORDERS AND DRUGS



Chittaranjan Andrade, MD
Professor in Psychopharmacology
National Institute of Mental Health and Neurosciences
Bangalore, India

OUTLINE

- ❑ Components of the sexual response
- ❑ Determinants of the sexual response
 - Psychosocial
 - Neurobiological
- ❑ Effect of psychiatric disorders on the sexual response
 - Focus on schizophrenia as a candidate disorder
- ❑ Effect of psychotropic drugs on the sexual response
 - Focus on antipsychotic drugs

COMPONENTS OF SEXUAL BEHAVIOR AND RESPONSE

❑ Desire

- Drive, libido, interest in sex-related activities
- Assessment based on reports of frequency and quality of sexual fantasies and desire to engage in sex-related activities

❑ Arousal

- Erection, vaginal lubrication

❑ Orgasm

NEUROLOGICAL STRUCTURES

- ❑ Nucleus accumbens (and DA)
 - Anticipation of reward
- ❑ Hypothalamus
 - Medial preoptic area (desire, motivation)
 - Paraventricular nucleus (genital response)
 - Ventromedial nucleus (receptivity)
- ❑ Autonomic nervous system
 - Parasympathetic (erection, lubrication)
 - Sympathetic (ejaculation, orgasm)

CHEMICAL PLAYERS

- ❑ Hormones, neurotransmitters, neuropeptides
 - Estrogen, testosterone (central, peripheral actions)
 - Prolactin (? through lowering DA)
 - DA (central action)
 - 5HT (central action; orgasm)
 - NE (central, peripheral actions; erection, orgasm)
 - Ach (peripheral action; erection)
 - Melanocortin (central action)

CHEMICALS AND DESIRE

- ❑ Centrally-driven
- ❑ Driven by
 - Neurotransmitters, neurohormones, neuropeptides
 - Psychosocial factors, including past experiences
- ❑ Background: sex hormones
 - Estrogen, testosterone, prolactin
- ❑ Foreground: DA as an important player
 - Anticipation of pleasure, reward

CHEMICALS AND AROUSAL

- ❑ Centrally- and peripherally-driven
- ❑ Background: sex hormones
- ❑ Central action: Facilitated by melanocortin
- ❑ Peripheral actions
 - Facilitated by Ach (parasympathetic actions)
 - Inhibited by NE (think of anxiety) acting on alpha-1
 - NO
- ❑ (Inhibited by 5HT)

NO AND AROUSAL

- ❑ L-arginine (amino acid)
- ❑ Converted by nitric oxide synthase to NO
- ❑ NO acts on Fe in the enzyme that converts GMP to cGMP
- ❑ cGMP relaxes smooth muscle in blood vessels
- ❑ Vasodilation results in erection, lubrication
- ❑ Action of cGMP is terminated by PDE5

CHEMICALS AND ORGASM

- ❑ Facilitated by NE
 - Descending fibres in the spinal cord
 - Act on alpha-1
 - Sympathetic actions
- ❑ Inhibited by 5HT
 - Descending fibres in the spinal cord
 - Act on 5HT2a, 5HT2c
- ❑ Possible involvement of DA, NO

SCHIZOPHRENIA AND SEXUAL DYSFUNCTIONS

- ❑ Issues related to attractiveness to spouse
 - Positive symptoms
 - Negative symptoms
 - Lack of personal hygiene
 - Obesity
 - Miscellaneous behaviors e.g. smoking

SCHIZOPHRENIA AND SEXUAL DYSFUNCTIONS: GENDER ISSUES

- ❑ Women have better adjustment
 - Later onset of illness, so better adjustment and more opportunities to have partners
 - Passive role
- ❑ Women have more children

SCHIZOPHRENIA: CAUSES OF SEXUAL DYSFUNCTIONS

- ❑ Positive symptoms and desire
- ❑ Negative symptoms and desire
- ❑ Social dysfunction and partner relationships
- ❑ Dyslipidemia, vascular insufficiency, erectile problems
- ❑ Metabolic syndrome, autonomic disturbances, abnormal arousal and orgasm
- ❑ Drugs (blamed)

IMPORTANCE OF ADDRESSING SEXUAL DYSFUNCTION IN SCHZ

- ❑ Improves QoL
- ❑ Less likely to result in medication non-adherence.
- ❑ Need to ask
 - Or assess using questionnaires

ANTIPSYCHOTICS AND SEXUAL DYSFUNCTION: 1

- ❑ Antipsychotic users
 - 12-38% have decreased desire
 - 7-46% have impaired arousal
 - 4-49% have orgasmic dysfunction
- ❑ Retrograde ejaculation
 - Mechanism, alpha-1 blockade
- ❑ Priapism as a rare AE
 - Mechanism, perhaps alpha-1 blockade

ANTIPSYCHOTICS AND SEXUAL DYSFUNCTION: 2

- ❑ Worst: Risperidone, neuroleptics
- ❑ Intermediate: Clozapine, olanzapine, quetiapine (in that order)
- ❑ Best: Aripiprazole
- ❑ Less information on other drugs, newer drugs

ANTIPSYCHOTICS AND SEXUAL DYSFUNCTION: 3

- ❑ DA blockade: Decreased desire
- ❑ M1 anticholinergic action: Erectile dysfunction
- ❑ Alpha-1 blockade: Delayed orgasm, retrograde ejaculation (peripheral)
- ❑ H1 blockade: Sedation and general dysfunction
- ❑ Hyperprolactinemia: Decreased desire
- ❑ Similar concerns with other psychotropics
 - ADs, BDZP etc.

ANTIPSYCHOTICS AND SEXUAL DYSFUNCTION: 4

□ General management

- Educate patient, partner
- Address psychosocial issues (e.g. relationships)
- Address medical issues (e.g. metabolic syndrome)
- Address behavioral issues (e.g. smoking)

□ Drugs

- Lower dose
- Change to drug with less action on target NTs
- Add aripiprazole
- Advise sildenafil or related drugs

ANTIDEPRESSANTS AND SEXUAL DYSFUNCTION:

1. Mechanisms

- ❑ Sedating drugs impair desire, arousal
 - Antagonism of H1, 5HT2
 - E.g. TCA
- ❑ Anticholinergic drugs impair erection
 - E.g. TCA, paroxetine
- ❑ Serotonergic drugs delay ejaculation
 - E.g. SSRIs, CMI
- ❑ Alpha-1 blockers may cause retrograde ejaculation
 - E.g. TCA

ANTIDEPRESSANTS AND SEXUAL DYSFUNCTION:

2. Management

- ❑ Prefer vilazodone, bupropion, mirtazapine, agomelatine, NE reuptake inhibitors, MAOIs
- ❑ Lower dose (may lower efficacy)
- ❑ Add bupropion
- ❑ Switch to drugs that do not cause sexual AEs
- ❑ Consider planned drug holidays
- ❑ Add cyproheptadine PRN (may sedate)
- ❑ Use sildenafil or related drugs

ANTIDEPRESSANTS AND SEXUAL DYSFUNCTION:

3. Caveats

- ❑ Switching drugs
 - Efficacy may be lost

- ❑ Drug holidays
 - Discontinuation syndrome
 - May encourage poor or non-adherence
 - If frequent, may result in breakthrough depression

E-LEARNING INITIATIVES



- ❑ Send a blank email to:
 - ❑ synergytimes-subscribe@yahoogroups.com
 - For Synergy Times, an e-newsletter on psychiatry and the allied medical and mental health sciences
 - ❑ eJCIndia-subscribe@yahoogroups.com
 - To join the Journal Club e-group of the Dept of Psychopharmacology and Indian Psychiatric Society.
- ❑ My email: andradec@gmail.com