Reviews and Mini Reviews

Sexual Dysfunction And Depression

By

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Research into sexual activity means investigating a complex human behavior in which a lot of variables may confound the outcome.

Why Psychiatrists should know about sexual dysfunction in depression?
Sexual dysfunction (SD) is often underestimated. It may be a symptom of depression itself, a cause of depression, a side effects of psychoactive agents including antidepressants and antipsychotics, or due to an underlying medical condition or subtance abuse. Independent SD depression may be seen too.

Impact of sexual dysfunction in depressed patients:
It may lead to loss of self-esteem, relationship difficulties, increased anxiety with the sexual partner, low physical and sexual satisfaction and adversely affects quality of life of patients.
Also drug regimen non-compliance and thus risk recurrence of depression, and an economic impact due to increased utilization of health services

Sexual disorder is a couple's problem:
It involves both partners in a sexual relationship. Relationship difficulties may contribute to or be a consequence of sexual dysfunction. Relationship causes SD stem from lack of trust or intimacy, power or dominance conflicts, loss of physical attraction to partner and/or communication difficulties between partners. Relationship consequences of SD include loss of physical affection, emotional distancing, extramarital affairs, and/or separation or divorce.

Psychiatric causes of sexual dysfunction:
In practice, one has to disentangle whether SD exists during a medical condition (endocrinal, cardiovascular, genitourinary, neurological, or urological), or has been induced by drugs of abuse, psychotropics, or non-psychotropics, or due to psychological factors and psychiatric causes, or combined factors.
A wealth of clinical literature suggests that a currently prevailing depression, or anxiety disorders, alcohol and substance abuse, psychoses, or medication used in psychiatric treatment may be psychiatric causes of SD.

Interface between sexual dysfunction and psychiatric disorders:
Neurotransmitters, hormones, and peptides play important roles in sexual functioning.
Levels of these substances may be altered by depression, or psychiatric medication.

Proposed roles of neurotransmitters in sexual functional:-

- Serotonin either centrally or peripherally was shown to have an established role in sexual functions. Central serotonin decrease dopamine in mesolimic region that can decrease sexual functioning at all stages, stimulates prolaction secretion that decreases desire. Stimulation of 5HT 2A, 1B and 1C receptors are inhibitory, while stimulation of 5HT 1A and 2C receptors are facilitatory to sexual performance. Periperal serotonin has a relation with vascular smooth muscles with no arousal enhancement, but minimal negative effect. It relaxes genital smooth muscles with inhibition of muscles contractions of orgasm. It causes genital anesthesia that decreases arousal and orgasm. In addition, peripheral serotonin presynaptically inhibits noradrenergic stimu- lation to cause delayed or inhibited orgasm.
- Norepinephrine, centrally antagonizes alpha 2 receptors with increased arousal and orgasm, and peripherally stimulates alpha 1 & 2 receptors in the penis that maintain baseline flaccid state. It also has hypogastric stimulation effect enhancing arousal and erection, helps closure of uretheral sphincter to prevent retrograde ejacu- lation, and the increased systemic circulating NE increases arousal and orgasm.
- Acetylcholine alters the balance of adrenergic and parasympathetic genital inputs that may initiate and facilitate arousal, increase secretory lubrication of genitals with increased comfort during sexual activity, and facilitates the synthesis and release of NO and VIP which cause vascular engorgement of the genitals during arousal.
- Dopaminergic pathways affect sexual functioning in its 4 sites. Tubero-infundibular DA causes tonic inhibition of prolactin. Nigrostriatal DA helps motor control for sexual behaviors. Mesolimbic DA is related to sexual motivation and reward (nucleus accumbens) and

- Incertohypothalamic DA potentiates erectile perfor- mance, and sexual motivation.

Hormones and sexual functions:-

Gonadotrophic releasing factor, testosterone, estrogen, progesterone, oxytocin, prolactin, and cortisol are effective in sexual functions

Peptides and others agets:

vasoactives intestional peptides (VIPs), histamine, GABA opioids, and Nitric acid were demonstrated as beneficial mediators in sexual functions.

Novel agents studied are arginine, substance P, vasopressin, angiotensin II, cholecystochinin 8, and alpha melanocite stimulating hormone.

The forementioned substances are believed to affect the different phases of sexual response cycle (i.e.desire, arousal, orgasm, and resolution).

Desire is FACILIATATED by DA, testosterone, oxytocin, and alpha 2 antagonism, and is INHIBITED by 5HT, PRL, opiods, GABA, and histamine-2 blockers.

Arousal is POTENSIATED by NO, VIPs, DA testosterone, oestrogen, oxytocin, and Ach/NE balance, and is HINDERED by opiods, B-blockers, GABA, and histamine-2 blockers. While **Orgasm** is POSITIVELY controlled by oxytocin, NE, and DA, and NEGATIVILY influenced by 5HT, GABA, and opioids.

Types of sexual problems common in depression:

Various disturbances of sexual functions were clinically encountered in depressives. They are considered here according to phases of sexual response cycle as; **desire** (deceased libido), **arousal** (inhibited sexual excitement, diminished genital sensation, erectile dysfunction "impotence", and failure to achieve / maintain vaginal lubrication), **orgasm** (delayed orgasm / ejaculation, retrograde ejaculation, partial / complete anorgasmia, and premature ejaculation), in addition to **pain syndromes** and **satisfaction** deficits.

Prevalence of SD:

- **In general population:** *(Montejo et al1997)*

	Males	Females
Frank et al. (1978) on 100 Comples.	40% (erectile or ej. dys.)	63% (arousal, orgasm)
National health & Soc. Life Survey (NHSLS, 1992) on ≥ 3000 people	31%	43%
Massachusettes male aging Study (Feldman et al. 1994) On 1290 males, 40-70 ys.	34.8%	---

- **In untreated depression**: *(Kasper etal.1992)*

Phase of sexual response	Reported prevalence
- reduced libido	40 - 75%
- arousal / erectile disorder	16 – 50%
- orgasmic dysfunction	15-22%

Kasper etal., 1992 estimated that 70-80% of SD is due to depression itself, the rest is caused by antidepressant therapy. SD are complete to moderate in severe depression (Feldman etal., 1994).

Sexual dysfunction and antidepressants:

- While treatment of depression can improve sexual functioning, antidepressant therapy may cause SD in terms of; erectile dysfunction, diminished or absent libido, arousal difficulties, and absent or delayed orgasm.
- Possible modernisms comprise; non-specific CNS effects (sedation), specific CNS effects (increased central serotonergic function may lead to diminished DA effect and inhibitory effects of 5HT2C), peripheral effects (NE / Ach balance), hormonal effects (increase PRL that diminishes desire, and testosterone inhibition), enzymatic effects (inducing hepatic metanolism of testosterone?), and effect on nitric oxide that mediates penile vascular changes.
- Reported SD with various antidepressants includes:

* MAOIs: non-selective MAOIs cause no problem with desire or arousal but affect orgasm and satisfaction. RIMAs induced SD is low.

* TCAs: (physicinans desk reference, 2000) they may cause decreased libido, erectile dysfunction, testicular hypertrophy, or painful ejaculation.

* SSRIs: montejo, et al., 1997 showed troubled sexual functions with all the class members.
Fluoxetine may cause decreased libido, erectile dysfunction, or anorgasmia. Citalopram may result into delayed ejaculation, and erectile dysfunction. Paroxetine (Ashton, etal., 1997 ; Montejo, etal., 1997) may induce decreased libido, and delayed ejaculation throught its greater sensitivity to 5HT relative to DA reuptake, increased anticholinergic effects, and inhibition of NO synthetase. Fluvoxamine, and sertraline showed relatively lower incidence of SD in the form of abnormal ejaculation and decreased libido.

* SARIs: (Dual serotonin 2 antaginists & serotonin reuptake inhibitors e.g. Trazodone & Nefazodone): are associated with lower incidence of erectile dysfunction and abnormal ejaculation.

* SNRIs: (e.g. venlafaxine) have relatively lower incidence of SD as anorgasmia, abnormal ejaculation, or erectile dysfunction.

* NaSSA (Norepinephrine & Specific Serotonergic Antidepressants e.g. Mirtazapine): have lower incidence of abnormal ejaculation and erective dysfunction because of its 5 HT 2A

* NRIs: (Norepinephrine Reuptake Inhibitors e.g. rebo- xetine) have lower incidence of SD.
* NDRIs (Norepinephrine & Dopamine Reuptake Inhibi- tors e.g. bupropion) showed lower incidence of erectile dysfunction, decreased libido, or abnormal ejaculation.
* Serotonin reuptake enhancers: Tianeptine enhances the reuptake of 5HT at the synapse without activating post-synaptic 5HT2A receptors responsible for sexual dys- function. Tianeptine did not have any adverse effects on Libido (Ducrocq, 1999) and when compared to the SSRIs, Tianeptine showed significantly less sexual dysfunction (Montejo et al, 2001).

Myths about SD in depression:
Rotschild (1995) coined out wrong beliefs that:
(i) depressed patients do not care about their sex problems, (ii) they will spontaneously report these problems to their doctors, (iii) they will not discontinue their medication if they experience SD, and (iv) all antidepressants cause SD.

Assessment of SD:
To assess sexual function changes with antidepressant therapy more accurately, one needs to:
- Establish baseline data of sexual function.
- Inform patients about possible SD specifically and directly before initiating therapy.
- Know that patients will not report to clinician voluntarily that there is a problem.
- Bring this matter by clinicians, not the patients.
- Include partners for facilitation, and
- Use reliable assessment.

Clinicians should have:-
- comprehensive sexual history.
- Pre-depression baseline sexual function.
- Pre-antidepressant sexual function.
- Check for;
  - Comorbid medical condition.
  - Concurrent medications.
  - Risk factors (age, smoking, alcohol / substance abuse, general health, sexual abuse, trauma, relationship difficulties, and
  - Response to drug given.

Management strategies for antidepressant induced SD:
Sexual side effects usually appear at 8 to 12 weeks. Since reliable assessment provides the best level of confidence in their presence, the principle is to:
- wait and see if the side effect goes away (development of tolerance)
- have drug holiday (of antidepressant dose reduction).
- Suggest timing of antidepressant administration in relation to the time of sexual activity!
- Adjust the concomitant non-psychotropic drugs (if possible).
- Conduct a stepwise technique of Optimization, Combi- nation, and Substitution.

Optimization:
By adding another drug to reduce SD produced by the antidepressant. The following table summarizes the major ones.

Drug	Action	Dose (1 hr. before sex.)	Effect
Cyproheptadine (Periactine)	5HT2	2-6mg	May reduce antidep. effect, induce sedation and fatigue (antihist. Side effect)
Dextroamphetamine (Dexedrine)	DA2 agonist	5mg	Lose dose may enhance high dose may inhibit orgasm.
Methylphenida (Ritalin)		5-25mg	dependence
Amantadine (symmetrel)	100-200mg		
Buspirone (Buspar)	5HTIA agonist (inh.PRL) DA2 agonist Alpa-2 Antag.	5-20 (PRN pr tid)	Fluoxetine & Parxoetine may inhibit its metanolism
Pindolol	Auto-receptor Agonist		
Yohimbine	Alpha-2 Antag.	4-5mg (PRN)	
Ginko Biloba (herbal)	Relaxes vas- smooth muscles and improves blood flow	60mg (BID)	Titrate slowly to reduce GI effects
L-arginine			
Bromocriptine			
Sildenafil (viagra)	NO mediated penile vascular relaxation	50-100mg	

Combination:
By adding another antidepressant with less sexual side effects to the existing one.

One to be added	action	dose (mg/d)	effect
Bupropion (wellabutrin)	DA2 reupt- ake inh.	75	may interact With fluoxetine causing serious adv. effects
Nefazodone (serzone)	5HT2 antag.	100-150	
Reboxetine (Edronax)	NE reupt- ake inh.	2-4	
Mirtazapine (Remeron)	Alpha-2 & 5HT2 antag.	15	take 1-2 wks for benefical effects.

Substitution:
By changing medication. Before switch;

- revise the patients response,
- consider ethical background, and
- choose the proper antidepressant drug with less SD effect [e.s. SARI (Nefazodone) , NaSSA (Mirtazapine), NDRI (Bupropion), NRI (Reboxetine), or serotonin enhancer (Tianeptine)]

In this review, the nature and extent of sexual problems that occur with antidepressant therapy were described. Their recognition and management depend on the awareness of the clinical team and their willingness to disuss this aspect of their patients lives. It is hoped that question about sexual function will become an accepted part of the doctors repertoire in assessing the effects of illness, surgery, or medications, in addition to measures to prevent such problems.

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Integration of Therapeutic Approaches in Working with Children

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Introduction:
Research on both primates and humans suggests that psychological influences result in permanent alterations of a neurobiological nature. Similarly, psychological interventions in a treatment context may have a profound impact on neurophysiology. Clinical case examples demonstrate that "biologically based" disorders may be rich in unconscious meaning. Clinical understanding of the meaning of symptoms may be instrumental in ensuring patients' compliance with pharmacotherapy regimens and in the removal of other resistances to treatment.

Knowing that the "decade of the brain" is well launched and remarkable discoveries from the neurosciences fill the pages of our journals, the time
may be ripe for a reexamination of the continued relevance of psychodynamic thinking to both clinician and researcher, especially in working with children and adolescents. Two trends in contemporary psychiatry have been increasing: 1) The "either-or" polarization of the psychodynamic and the biological. 2) The devaluation of psychodynamic understanding and therapy as increasingly irrelevant.