Sexual Dysfunction: A Neglected Area of Knowledge

By Angelos Halaris, MD

The human sexual response cycle is comprised of a series of physiologic functions, cognitions, emotions, and behaviors that involve the central and peripheral nervous systems and the muscular, vascular, and endocrine systems. These systems must be timely coordinated and integrated into the whole we commonly refer to as "sexual function" or "sexual response."

Certain aspects of sexual response are based on a series of reflexes that may not require an intact brain or intact neural axis to be activated. However, the brain exerts ultimate control over the entire sexual response. The processing and awareness of internal and external stimuli that generate the subjective experience of sexual desire are unique brain functions. The subjective sensation of sexual arousal, the awareness of the orgasmic response in its qualitatively diverse psychic manifestations, the experience of pleasure, and the formation of adult bonding are anchored in the brain. The relationship between brain and sexual function is illustrated when the brain is dysfunctional because certain psychiatric disorders impair sexual function.

The quest to identify a single "sex center" has been abandoned as knowledge has increased. We appreciate the complexity of sex physiology, anatomy, biochemistry, and behavior. Sexual behavior and function are an immensely complex series of events that encompass diverse parts of the brain and the nervous system. Different brain areas serve different functions. The cortex retains an integrative role mediating the awareness of emotions. The hypothalamus, striatum, and amygdala each play more specialized roles, although their precise functions are unknown.

Lifetime prevalence rates of sexual dysfunction are higher in women than in men. Mood disorders that frequently present with sexual dysfunction are almost twice as prevalent in women. Reproductive life events, which correlate highly with changes in sex steroids, are a contributory factor to these higher prevalence rates. Jill K. Warnock, MD, PhD, and C. Faye-Biggs, CCRC, convincingly illustrate the role of sex steroids by discussing several cases that cover hormonal changes following hysterectomy and oophorectomy. They discuss the need to make an accurate assessment of the nature of the sexual disorder the clinician is called upon to evaluate and treat. They review antidepressant-induced sexual dysfunction and the need to make an accurate assessment of the nature of the sexual disorder the clinician is called upon to evaluate and treat. They review antidepressant-induced sexual dysfunction and discuss the need to make an accurate assessment of the nature of the sexual disorder the clinician is called upon to evaluate and treat.

The last article deals with the pharmacologic management of sexual disorders and treatment-emergent sexual side effects resulting from psychotropic and non-psychotropic drug exposure. Robert Taylor Segraves, MD, PhD, reviews the disorders for which pharmacotherapy can be helpful. With respect to female arousal disorder, the effectiveness of sildenafil and other related agents under experimentation. Inferences from the mechanism of action of psychotropics and non-psychotropics and their side effects have provided clues about transmitter regulation of sexual function. The article by Angelos Halaris, MD, provides a "bird's eye view" of key neurochemical and neurohormonal aspects of sexual function and dysfunction.

The prevalence of sexual disorders is alarmingly high and is compounded by our restricted ability to provide expert evaluations and treatments to patients. Many clinicians lack even a minimal level of comfort and expertise to collect basic sexual information as part of a routine health care visit. Medical school and residency curricula have traditionally paid lip service to the teaching of sexuality. Most medical specialists are not experts at assessing sexual function and dysfunction. John Halvorsen, MD, MS, offers a simple, cohesive, and practical guide to assessing and treating common sexual problems. The "Level of Involvement Model" is exceptionally useful. It is desirable that all clinicians acquire the expertise to conduct, at the very least, a Level 1 examination.

The emphasis of this issue is on the neurobiology and pharmacology of sexual function and dysfunction. There was no intention to imply that psychological and social factors are of lesser importance. It is recognized that psychosocial factors almost always play a major role in most types of dysfunction and must therefore be properly assessed and included in the formulation of a comprehensive treatment plan. Developmental and sociocultural issues, intrapsychic conflicts, and relationship and interpersonal dynamics must be explored with diligence and sensitivity. The biopsychosocial model provides the context within which sexual dysfunction can be best understood and helped.
How to measure your patients’ depression
*Full antidepressant effect may take 4 to 6 weeks.

LEXAPRO is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs) or in patients with a hypersensitivity to escitalopram oxalate or any of the ingredients in LEXAPRO. As with other SSRIs, caution is indicated in the coadministration of tricyclic antidepressants (TCAs) with LEXAPRO.

Please see brief summaries of prescribing information for LEXAPRO and CELEXA at end of advertisement.
How to measure
Well-tolerated therapy
in a powerful SSRI

LEXAPRO 10 mg/day demonstrated comparable efficacy to CELEXA 40 mg/day\textsuperscript{1}

Significantly improved depression for many patients beginning at week 1 or 2\textsuperscript{*1}

Effectively treats anxiety symptoms associated with depression\textsuperscript{1}
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Enjoying life again

*Full antidepressant effect may take 4 to 6 weeks.

LEXAPRO is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs) or in patients with a hypersensitivity to escitalopram oxalate or any of the ingredients in LEXAPRO. As with other SSRIs, caution is indicated in the coadministration of tricyclic antidepressants (TCAs) with LEXAPRO.

Please see brief summaries of prescribing information for LEXAPRO and CELEXA at end of advertisement.
In the treatment of major depression

**LEXAPRO 10 mg/day significantly improved depression**

![Graph showing MADRS Total Score by Visit](image)

- Placebo (n=119)
- Citalopram 40 mg/day (n=126)
- LEXAPRO 10 mg/day (n=118)

**Study design:** 8-week, randomized, double-blind, placebo-controlled, fixed-dose (LEXAPRO 10 or 20 mg/day; citalopram 40 mg/day). U.S. multicenter trial in adult patients with DSM-IV diagnosed major depression (MADRS ≥22, lasting ≥4 weeks). Overall mean MADRS=28.9 at baseline.

**LEXAPRO 10 mg/day demonstrated comparable efficacy to CELEXA™ (citalopram HBr) 40 mg/day**

[Well-tolerated strength]

Lexapro
escitalopram oxalate
Well-tolerated strength

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How to measure
Well-tolerated therapy

Slept well

The most common adverse events reported with LEXAPRO vs placebo (approximately 5% or greater and approximately 2X placebo) were nausea, insomnia, ejaculation disorder, somnolence, increased sweating, and fatigue.

Please see brief summaries of prescribing information for LEXAPRO and CELEXA® (citalopram HBr) at end of advertisement.

In the comprehensive safety database*
Low drop-out rates due to adverse events³

Drop-Out Rates Due to Adverse Events

<table>
<thead>
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<th>% of Patients</th>
<th>LEXAPRO (n=715)</th>
<th>Placebo (n=592)</th>
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- LEXAPRO 10 mg/day had drop-out rates due to adverse events comparable to placebo³

Favorable side-effect profile
- Only one adverse event occurred at a rate above 10%³
- LEXAPRO patients experienced no clinically important change in body weight³

Simple 10 mg/day starting dose for all patients³
- 10 mg/day starting and maintenance dose for most patients

*Includes patients treated with 10 to 20 mg/day.
LEXAPRO™
(escalopram oxalate)

LEXAPRO™ (escalopram oxalate) TABLETS

Dosage and Administration

1. LEXAPRO™ is indicated for the treatment of depression in adults.

2. The recommended initial dose of LEXAPRO™ is 10 mg/day taken as a single dose in the morning, and increasing to 20 mg/day taken as a single dose in the morning or divided dosing (5 mg twice a day) at a rate of 5 mg/day every 1-2 days. The dose may be increased to 20 mg/day at 1-week intervals, if needed, based on clinical response and tolerance. The maximum recommended dose is 20 mg/day. LEXAPRO™ has been studied in doses up to 40 mg/day.

been associated with decreased cardioselectivity. Co-administration of Celexa and metoprolol has been demonstrated in two nonclinical studies. Theophylline - Combined administration with other antidepressants, Celexa should be introduced with care in patients with a history of hypertension, who have a higher rate of cardiovascular disease, or who have been receiving norepinephrine/epinephrine inhibitors in combination with a beta-blocker. Hypertension and tachycardia have been reported in patients who have recently discontinued SSRI treatment and have been treated with Celexa.

Contraindications

Celexa is contraindicated in children and in patients who have a significant impairment of hepatic metabolism, or who have a hypersensitivity to citalopram or any of the inactive ingredients of Celexa.

Drug Interactions

Metabolism of Citalopram

A systematic review of clinical literature revealed no clinically important changes in laboratory test parameters associated with Celexa. However, patients treated with Celexa in controlled trials experienced a weight loss of about 0.5 kg (2 pounds) during treatment. There were no clinically significant changes in vital sign measures, including supine blood pressure and pulse rate, and the incidence of abnormal electrocardiograms was similar in patients receiving Celexa and placebo. A comparison of supine and standing vital sign measures for Celexa and placebo treatments revealed no clinically significant changes from baseline in any of these measures. Physical dependence and psychological dependence have not been observed in patients treated with Celexa in controlled trials. Among 1063 depressed patients who received Celexa at doses ranging from 10 to 80 mg/day in controlled trials, only 11% of patients discontinued treatment because of treatment-associated events, compared with 9% for placebo.

Drug Interactions with Other CNS Drugs

Anxiety, hypomania, mania, and neuropsychiatric adverse events have been reported in patients treated with Celexa. Because of the potential for interaction, the use of antidepressants with significant sedative or anticholinergic properties should be approached with caution in patients who are receiving a monoamine oxidase inhibitor (MAOI).

Anxiolytics

Anxiolytics may enhance the tranquilizing effects of Celexa, and the concomitant use of both drugs may result in additive sedation, hypotension, respiratory depression, and possible electrical monitoring not in patients with a history of heart disease.

ADVERSE REACTIONS

The pharmacokinetics of citalopram is not affected by concomitant administration of citalopram with other drugs. However, coadministration of citalopram (40 mg) and ketoconazole did not significantly affect the pharmacokinetics of either citalopram or digoxin. Lithium - Coadministration of Celexa (40 mg/day for 10 days) and lithium (30 mmol/day for 5 days) in healthy volunteers had no significant effect on the pharmacokinetics of either citalopram or digoxin. However, a potential interaction may occur when Celexa and lithium are coadministered. Theophylline - Combined administration with other centrally acting drugs. Alcohol - Although citalopram did not potentiate the sedative effects of alcohol, the use of alcohol by depressed patients taking Celexa is not recommended. Use in Patients With Concomitant Illness

The concomitant administration of another CNS depressant may result in additive CNS effects. The concomitant administration of other psychotropic agents may result in additive anticholinergic effects, sedative effects, or other CNS depression.

Use in Patients With Hepatic Impairment

Coadministration of Celexa and metoprolol has been demonstrated in two nonclinical studies. Theophylline - Combined administration with other centrally acting drugs. Alcohol - Although citalopram did not potentiate the sedative effects of alcohol, the use of alcohol by depressed patients taking Celexa is not recommended.

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