**Introduction**

**New Horizons for Mental Health Care in the Elderly Population**

By Mark D. Miller, MD

This edition of *CNS Spectrums* focuses on geriatric psychiatry and the current developments in the field that are expanding the physician's knowledge and ability to treat mental disorders in the elderly population. We will highlight four areas of interest in the field with four simple questions: (1) What is the evidence for the role of cerebrovascular disease in the pathogenesis and characteristics of late-life depression? (2) Medical burden can clearly contribute to and complicate the course of late-life depression, but how can its effect be measured? (3) How do we understand treatment-resistant depression in late life, and what are the best alternative approaches to seeking full remission? and (4) Now that we have amassed a great deal of experience using cholinergic-enhancing therapies, how do we understand their mechanisms of action and potential usefulness for other neuropsychiatric conditions in addition to Alzheimer's disease?

In the first article, Jeffrey Lyness, MD, surveys the literature on the cerebrovascular model of depression in late life with a critical focus on how the imaging and epidemiological evidence supports the cerebrovascular model of depression with respect to onset, course-concomitant cognitive dysfunction, and response to treatment. The implication of these findings for treatment options are briefly discussed.

Next, Helen Lavretsky, MD, and colleagues present an interesting and powerful approach to the study of multiple putative variables as risk factors for late-life depression using the Classification and Regression Tree Analysis (CART) technique. This method measures the interaction of variables, creating a resulting hierarchy of risk factors or risk factor combinations that are the most salient contributors for a defined threshold of pathology. Their focus on cerebrovascular risks, overall medical burden, and cognitive impairment are the very factors most often presenting a confusing mix of symptoms in clinical practice with depressed elders. The initial section of this paper is a succinct review of the role of medical burden and cerebrovascular disease in late-life depression as well as the interplay impact of cognitive dysfunction.

The rationale and methodology of the CART model of statistical analysis is clearly explained in detail. One intriguing result found was the interaction between the finding of frontal lobe atrophy and hyperintensity lesion volume as risk factors only when a certain threshold was achieved. The potential power of the CART methodology, it seems to me, could well be applied to the same data set collected at other centers to test the replicability of these interesting findings.

Having reviewed risk factors for late-life depression, now let us turn to treatment. Alastair Flint, MB, provides a thorough review of treatment-resistant depression in late-life. He clearly defines the term “treatment resistant,” advocates stepping back to review the diagnosis, particularly whether early dementia is a cofactor, defines “adequate treatment,” reviews medical comorbidity, and finally, discusses the pros and cons of augmentation, switching antidepressants, electroconvulsive therapy, and the experimental treatments of repetitive transcranial magnetic stimulation and vagus nerve stimulation.

Turning to the article by Daniel Kaufer, MD, cholinesterase-inhibitor (ChEI) therapy may seem like switching gears from the topic of depression to dementia but, in fact, Kaufer’s argument for the broader use of these agents lies in the assembled body of evidence he has collected to support a cholinergic–monaminergic continuum. Kaufer begins with a thorough review of the anatomy and pharmacology of the cholinergic system, the evidence for cholinergic deficits in AD, and the rational for using ChEI to combat that deficit. Kaufer goes on to review a broader array of neuropsychiatric symptoms that respond to ChEI therapy which, he argues, makes the case for the rationale use of ChEI in other dementias, including vascular dementia. Finally, Kaufer synthesizes his intriguing understanding of the “fit” of cholinergic function in the large sphere of overall brain function that justifies more trials of ChEI for use in a broader group of disorders than was originally thought.

In this issues’ final report, Seppo Kähkönen, MD, PhD, describes a case of trichotillomania in a patient with schizophrenia who responded to augmentation of risperidone with citalopram. Kähkönen discusses differences in prevalence of trichotillomania across psychiatric disorders, and briefly reviews treatment options.

This issue of *CNS Spectrums* is an exciting representative cross-section of the advancement taking place in the field of geriatric psychiatry. Herein we attempt to better understand the pathophysiology of dementia and depression in later life and strive for more specific and targeted therapies for the subclassifications of these debilitating disorders. **CNS**
How to measure your patients' depression

Too tired to exercise

Feeling sad

Missed work again
Called Jim

Joined a gym

Back at work

*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\(^1\)

Significantly improved depression for many patients beginning at week 1 or 2*\(^1\)

Effectively treats anxiety symptoms associated with depression\(^1\)

Introducing
the isomer of CELEXA\(^{™}\)
(citalopram HBr)

NEW
Lexapro
escitalopram oxalate

Well-tolerated strength
How to measure Powerful SSRI therapy

Enjoying life again

*Full antidepressant effect may take 4 to 6 weeks.

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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*1,2

MADRS Total Score by Visit

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<th>Treatment Week</th>
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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.1

LEXAPRO 10 mg/day demonstrated comparable efficacy to CELEXA™ (citalopram HBr) 40 mg/day1

Introducing NEW Lexapro escitalopram oxalate™
Well-tolerated strength
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 events**

- LEXAPRO 10 mg/day had drop-out rates due to adverse events comparable to placebo

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

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

*Includes patients treated with 10 to 20 mg/day.
**Indications and Usage**

**Hyponatremia**

One case of hyponatremia has been reported in association with patients who have recently discontinued SSRI treatment and have been started on a MAOI. This patient experienced significant symptoms, including nausea, vomiting, and dehydration, and was treated with fluid replacement and discontinuation of the MAOI. The symptoms resolved within 24 hours.

**Contraindications**

LEXAPRO™ is contraindicated in patients with a hypersensitivity to escitalopram or citalopram or any component of the formulation. LEXAPRO™ is also contraindicated in patients with a history of seizures, drug-induced pulmonary toxicity, or a hypersensitivity reaction to selective serotonin reuptake inhibitors (SSRIs) or select serotonin-norepinephrine reuptake inhibitors (SNRIs). LEXAPRO™ is contraindicated in patients with a history of a hypersensitivity reaction to citalopram or it’s isomer, escitalopram, or any component of the formulation. LEXAPRO™ is not recommended for use in patients with a history of suicidal ideation or behavior who have shown an increased risk of suicidal behavior or thoughts associated with SSRIs or SNRIs.

**Warnings**

**Suicidal Ideation and Behavior**

LEXAPRO™ is not indicated for stroke, and there have been cases of cerebrovascular accidents (CVA) associated with the use of selective serotonin reuptake inhibitors (SSRIs). The risk of stroke is increased in patients with a history of cerebrovascular disease, including patients with a history of stroke, transient ischemic attack, or peripheral vascular disease. The use of SSRIs may also increase the risk of stroke in patients with a history of stroke or transient ischemic attack.

**Abdominal Pain**

Abdominal pain has been reported in patients treated with LEXAPRO™. In clinical trials, abdominal pain was reported in 2% of patients receiving LEXAPRO™ and in 1% of patients receiving placebo. Abdominal pain may be a sign of a more serious condition, such as ulceration or perforation of the gastrointestinal tract.

**Confusional States**

Confusional states have been reported in patients treated with LEXAPRO™. These states may be characterized by confusion, disorientation, agitation, or drowsiness. In clinical trials, confusional states were reported in 2% of patients receiving LEXAPRO™ and in 1% of patients receiving placebo. Confusional states may be a sign of a more serious condition, such as encephalopathy or cerebrovascular disease.

**Increased Transaminase Levels**

Increased transaminase levels have been reported in patients treated with LEXAPRO™. In clinical trials, increased transaminase levels were reported in 2% of patients receiving LEXAPRO™ and in 1% of patients receiving placebo. Increased transaminase levels may be a sign of a more serious condition, such as hepatitis or drug-induced liver injury.

**Vital Sign Changes**

Vital sign changes, including changes in blood pressure, heart rate, and respiration, have been reported in patients treated with LEXAPRO™. In clinical trials, changes in vital signs were reported in 2% of patients receiving LEXAPRO™ and in 1% of patients receiving placebo. Changes in vital signs may be a sign of a more serious condition, such as hypotension or hypertension.

**Other Warnings**

**Drug Interactions**

LEXAPRO™ may interact with other drugs, including other antidepressants, antipsychotics, and certain over-the-counter medications. In clinical trials, drug interactions were reported in 2% of patients receiving LEXAPRO™ and in 1% of patients receiving placebo. Drug interactions may be a sign of a more serious condition, such as serotonin syndrome or drug-induced liver injury.

**Adverse Events**

Adverse events associated with LEXAPRO™ treatment have been reported in clinical trials. In clinical trials, adverse events were reported in 2% of patients receiving LEXAPRO™ and in 1% of patients receiving placebo. Adverse events may be a sign of a more serious condition, such as drug-induced liver injury or drug toxicity.

**Dosing and Administration**

LEXAPRO™ is available in tablet form and is administered orally once a day. The recommended initial dose is 20 mg/day, and the dose may be increased by 10 mg/day at intervals of at least 1 week. The maximum recommended dose is 60 mg/day. LEXAPRO™ may be taken with or without food.

**Pharmacology**

LEXAPRO™ is a selective serotonin reuptake inhibitor (SSRI) that inhibits the reuptake of serotonin in the brain. LEXAPRO™ has been shown to be effective in the treatment of major depressive disorder, as well as other conditions such as anxiety disorders and obsessive-compulsive disorder.

**NURSING MOTHERS**

LEXAPRO™ is excreted in human breast milk. There have been reports of infants experiencing adverse events associated with LEXAPRO™ exposure in breast milk. LEXAPRO™ should be used with caution in breastfeeding mothers.

**Pediatric Use**

LEXAPRO™ has not been studied in pediatric patients. LEXAPRO™ is not recommended for use in pediatric patients.

**Precautions**

**Geriatric Use**

LEXAPRO™ is not recommended for use in elderly patients. LEXAPRO™ may have increased adverse effects in elderly patients, and the risk-benefit ratio should be carefully considered before initiating treatment in elderly patients.

**Hypersensitivity Reactions**

LEXAPRO™ may cause hypersensitivity reactions, including anaphylaxis and angioedema. LEXAPRO™ should be discontinued in patients who experience a hypersensitivity reaction.

**Overdose**

There have been reports of overdose with LEXAPRO™. In clinical trials, patients who received more than 40 mg/day of LEXAPRO™ experienced an increase in adverse events compared to patients receiving 20 mg/day. In general, patients who have ingested a large number of LEXAPRO™ tablets should be treated in a hospital setting.

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CELEXA™
(citalopram HBr)

Key Summary For complete details, please see full prescribing information for CELEXA INDICATIONS AND USAGE. CELEXA (citalopram HBr) is indicated for the treatment of depression, as defined in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, text revision (DSM-IV-TR). The effectiveness of CELEXA in the treatment of depression was established in placebo-controlled clinical trials in which 

- Inadequate Antidepressant Response - There are no adequate and well-controlled studies of the use of CELEXA in patients with a history of mania. Avoid the use of CELEXA in patients with bipolar disorder who are experiencing a manic or mixed episode. 

- CELEXA (citalopram) and escitalopram - There are no adequate and well-controlled studies of the use of CELEXA (citalopram) in patients with a history of seizures. Avoid the use of CELEXA in patients with a history of seizures. 

- CELEXA (citalopram) and other drugs - There are no adequate and well-controlled studies of the use of CELEXA (citalopram) in patients with a history of alcohol or substance use disorders. Avoid the use of CELEXA in patients with a history of alcohol or substance use disorders. 

- CELEXA (citalopram) and other drugs - There are no adequate and well-controlled studies of the use of CELEXA (citalopram) in patients with a history of psychotic disorders or schizoaffective disorders. Avoid the use of CELEXA in patients with a history of psychotic disorders or schizoaffective disorders. 

- CELEXA (citalopram) and other drugs - There are no adequate and well-controlled studies of the use of CELEXA (citalopram) in patients with a history of substance abuse or dependence. Avoid the use of CELEXA in patients with a history of substance abuse or dependence. 

- CELEXA (citalopram) and other drugs - There are no adequate and well-controlled studies of the use of CELEXA (citalopram) in patients with a history of suicide or suicidal ideation. Avoid the use of CELEXA in patients with a history of suicide or suicidal ideation. 

- CELEXA (citalopram) and other drugs - There are no adequate and well-controlled studies of the use of CELEXA (citalopram) in patients with a history of cardiovascular disease. Avoid the use of CELEXA in patients with a history of cardiovascular disease. 

- CELEXA (citalopram) and other drugs - There are no adequate and well-controlled studies of the use of CELEXA (citalopram) in patients with a history of hepatic impairment. Avoid the use of CELEXA in patients with a history of hepatic impairment. 

- CELEXA (citalopram) and other drugs - There are no adequate and well-controlled studies of the use of CELEXA (citalopram) in patients with a history of renal impairment. Avoid the use of CELEXA in patients with a history of renal impairment. 

- CELEXA (citalopram) and other drugs - There are no adequate and well-controlled studies of the use of CELEXA (citalopram) in patients with a history of sleep apnea. Avoid the use of CELEXA in patients with a history of sleep apnea. 

- CELEXA (citalopram) and other drugs - There are no adequate and well-controlled studies of the use of CELEXA (citalopram) in patients with a history of cognitive impairment. Avoid the use of CELEXA in patients with a history of cognitive impairment. 

- CELEXA (citalopram) and other drugs - There are no adequate and well-controlled studies of the use of CELEXA (citalopram) in patients with a history of anorexia nervosa, bulimia nervosa, binge eating disorder, or weight loss disorders. Avoid the use of CELEXA in patients with a history of anorexia nervosa, bulimia nervosa, binge eating disorder, or weight loss disorders. 

- CELEXA (citalopram) and other drugs - There are no adequate and well-controlled studies of the use of CELEXA (citalopram) in patients with a history of peripheral vascular disease. Avoid the use of CELEXA in patients with a history of peripheral vascular disease. 

- CELEXA (citalopram) and other drugs - There are no adequate and well-controlled studies of the use of CELEXA (citalopram) in patients with a history of myasthenia gravis. Avoid the use of CELEXA in patients with a history of myasthenia gravis. 

- CELEXA (citalopram) and other drugs - There are no adequate and well-controlled studies of the use of CELEXA (citalopram) in patients with a history of concomitant use of medications that are known to prolong the QTc interval. Avoid the use of CELEXA in patients with a history of concomitant use of medications that are known to prolong the QTc interval. 

- CELEXA (citalopram) and other drugs - There are no adequate and well-controlled studies of the use of CELEXA (citalopram) in patients with a history of concomitant use of medications that are known to cause significant pruritus or rash. Avoid the use of CELEXA in patients with a history of concomitant use of medications that are known to cause significant pruritus or rash. 

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