Neuropsychiatric Comorbidities: A Meeting of Minds

Implications of the cAMP Signaling Pathway in Psychiatric Disorders: A Systematic Review of the Evidence
J. Perez and D. Tardito

Depression and Huntington's Disease: Prevalence, Clinical Manifestations, Etiology, and Treatment
J.R. Slaughter, M.P. Martens, and K.A. Slaughter

Partial Kluver-Bucy Syndrome: Two Cases
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An Innovative Approach to Clinical Communication in Schizophrenia: The Approaches to Schizophrenia Communication Checklists
S.G. Dott, P. Weiden, P. Hopwood, et al

The Syndrome of Traumatic Grief
M.K. Shear, A. Zuckoff, and E. Frank
In mild to moderate Alzheimer’s disease

You see it as maintaining cognitive

* Individual responses to ARICEPT® may include improvement, stabilization, or decline.

† The most common adverse events in pivotal clinical trials with ARICEPT® were nausea, diarrhea, insomnia, vomiting, muscle cramps, fatigue, and anorexia. Pivotal clinical trials of ARICEPT® have shown no increase, relative to placebo, in the incidence of either peptic ulcer disease or gastrointestinal bleeding. Nevertheless, cholinesterase inhibitors may be expected to increase gastric acid secretion. Therefore, patients (especially those at increased risk for developing ulcers—eg, having a history of ulcer disease, receiving concurrent nonsteroidal anti-inflammatory drugs) should be monitored closely for gastrointestinal bleeding. In pivotal clinical trials, syncopal episodes have been reported in association with ARICEPT® (2% vs 1% for placebo).
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- Slows the worsening of symptoms*
- Proven to maintain cognition in placebo-controlled studies
- Well tolerated†
- Proven safety profile
- Once-daily dosing
- 3 years of real-world use

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CONTRAINDICATIONS

ARICEPT® (Donepezil Hydrochloride Tablets)

ARICEPT® should not be used in patients who are known hypersensitivity to donepezil hydrochloride or to any of the other ingredients of ARICEPT®.

WARNINGs
Anorexia

Adverse Event

CONTRAINDICATIONS

ARICEPT® (Donepezil Hydrochloride Tablets)

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A REVIEW OF cAMP’S ROLE IN PSYCHIATRIC DISORDERS

page 294

“Mononuclear leukocytes of patients with major depression showed significantly reduced immunoreactivity levels and functions of Gαs and Gαi compared to normal subjects. Similarly, untreated patients with seasonal affective disorder showed significantly reduced mononuclear leukocyte immunoreactive levels of Gαs and Gαi. Garcia-Sevilla and colleagues reported that in the platelets of patients with major depression, the immunoreactivity of Gαi₂ was increased, whereas the levels of other G protein subunits (Gαs, Gαi₁₁, Gβ) did not show any significant change compared to control subjects. Interestingly, abnormalities in AC were also found in the peripheral cells of patients with major depression.”

HANDLING DEPRESSION IN HUNTINGTON’S DISEASE

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“Along with the tendency to experience depression, research indicates that individuals with HD are at high risk for suicide or attempted suicide. Huntington himself noted that HD patients displayed a ‘tendency to insanity, and sometimes that form of insanity which leads to suicide.’ This observation was also reported by Minski and Guttman in their seminal 1938 article on HD. These authors noted suicidal tendencies in some depressed patients, as well as several cases of suicide that occurred prior to HD diagnosis. Contemporary authors also support this marked risk for suicide. Lipe and colleagues reported a HD suicide rate of 3.0%; Sorensen and Fenger, a 5.6% rate; DiMaio and colleagues, a 7.3% rate; and Farrer, a 5.7% rate, along with a 27.6% rate of attempted suicides among HD patients. These rates are well above the average rates of suicide in the general population of 10–13/100,000 persons. HD patients with the greatest risk for suicide include those with no offspring, unmarried, living alone, in contact with others affected with HD, and who are clinically depressed. The high rate of suicide among patients with HD is not common to other neurodegenerative disorders. For example, while Parkinson’s disease patients experience heightened depression and suicidal ideation, there does not exist a higher than average occurrence of suicide in the panic disorder (PD) population.”

ANTIPSYCHOTIC EFFICACY AND PARTIAL KBS

page 329

“During the neuropsychiatric admission, isophane insulin was added to the patient’s medication schedule for diabetic control. Carbamazepine was administered, then discontinued when a skin rash developed. Haloperidol was replaced with thiothixene for behavioral disturbances and psychosis. Thiothixene was gradually increased to 105 mg every day (QD) but was later reduced to 90 mg QD due to excessive sedation. No other side effects were noted. The serum thiothixene level was 9.5 ng/mL with a therapeutic window of 2.0–15.0 ng/mL.”

NEW CLINICAL TOOLS FOR SCHIZOPHRENIA

page 333

“Completed ASC-SR forms were received from 152 patients. The ASC-SR was well received by both patients and caregivers, with over 80% indicating that they had understood the purpose of the checklist and had found it easy to use. Eighty-nine percent of respondents considered the range of side effects presented in the ASC-SR to be appropriate and 82% stated that the choice of responses met their needs. Although a few respondents recommended that the questions relating to sexual and menstrual problems should be excluded, a high proportion of patients identified these side effects as problems and indicated a readiness to discuss these problems with their psychiatrists. Eighty-six percent of respondents considered the ASC-SR to be useful in communicating their problems to psychiatrists and other members of the healthcare team, ranging from very useful (20%) to a little useful (34%). In addition, feedback from patients and caregivers indicated that 71% would value receiving more information from their healthcare team about their medication and possible side effects.”

APPROACHING TRAUMATIC GRIEF

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“The first phase requires approximately three sessions and sets the stage for the treatment. The therapist obtains the relevant clinical and relationship histories, conducts an in-depth grief assessment, orients the patient and a significant other to the treatment, and helps the patient identify and develop personal goals and TGT-consistent plans for how to achieve them. During this phase, rapport building and empathic understanding are emphasized. It is critical to TGT that the therapist form an alliance with the patient that includes an explicit understanding of the patient’s level of grief and his or her grief intensity goals. Often, individuals with traumatic grief feel that a reduction in grief intensity means they are betraying the deceased, or that to end a period of grief means to lose their loved one forever. These ideas are identified and work begins to help patients reevaluate them.”
PAXIL® (brand of paroxetine hydrochloride)  

**INDICATIONS AND USAGE:** Paroxetine is indicated for the treatment of depression, obsessive compulsive disorder (OCD), panic disorder, social anxiety disorder (SAD), post-traumatic stress disorder (PTSD), and sexual dysfunction (preliminary studies in the treatment of premature ejaculation). It is also indicated for its use in combination with other antidepressant therapies, with or without anxiolytic agents, in the treatment of patients with depression, anxiety or obsessive-compulsive disorder who require additional pharmacotherapy.

**ADVERSE REACTIONS:** Incidence in Controlled Trials—

### Central Nervous System

- Somnolence (22% vs. 5%), tremor (9% vs. 1%), diaphoresis (12% vs. 7%), yawning (14% vs. 5%), decreased appetite (13% vs. 6%), nausea (5% vs. 1%), vomiting (5% vs. 1%), hypomania (5% vs. 2%), asthenia (5% vs. 1%).

### Cardiovascular System

- Palpitations (23% vs. 9%), dizziness (13% vs. 6%), insomnia (13% vs. 6%), tremor (8% vs. 2%), nervousness (5% vs. 1%).

### Gastrointestinal System

- Abdominal pain (8% vs. 4%), diarrhea (13% vs. 6%), nausea (13% vs. 6%), vomiting (5% vs. 1%).

### Respiratory System

- Upper respiratory infections (9% vs. 4%), pharyngitis (5% vs. 1%), sinusitis (3% vs. 1%), rhinitis (9% vs. 4%).

### Miscellaneous

- Flu syndrome (19% vs. 6%), dehydration (13% vs. 6%), fever (13% vs. 6%).

### Other Common Reactions

- Insomnia (33% vs. 17%), dizziness (13% vs. 6%), diarrhea (13% vs. 6%), somnolence (22% vs. 5%), tremor (9% vs. 1%).

### Rare Reactions

- Abnormalities in liver function tests (9% vs. 5%).

### Laboratory Values

- Serum cholesterol elevations (13% vs. 9%).

### Twenty percent (1:191:145) of PAXIL® patients in worldwide clinical trials demonstrated documentation of a decrease in weight (as defined by a decrease of at least 5% in body weight).

### PRECAUTIONS

- Use with caution in patients with a history of cardiac conduction abnormalities or seizures.

### CONTRAINDICATIONS

- PAXIL® is contraindicated in patients with a hypersensitivity to paroxetine or any of the inactive ingredients in PAXIL.

### WARNINGS

- **Interactions with MAOIs may occur.**

### Dosing and Administration

- **Once-Daily Use:** PAXIL® is supplied in bottles of 30, 60, and 120 tablets, and in packets of 10 tablets, each containing 10 mg of paroxetine hydrochloride. It is available in a 20 mg/day tablet dose form.

### Additional Information

- **Drug Abuse and Dependence:** PAXIL® is a member of the selective serotonin reuptake inhibitor (SSRI) class of antidepressants.

### Postmarketing Surveillance

- **Reports of serious adverse reactions that have been received since market introduction and not listed above that may be of potential interest are being reviewed to determine if they may have no causal relationship with PAXIL.**

### References

- Paroxetine hydrochloride is a member of the selective serotonin reuptake inhibitor (SSRI) class of antidepressants.

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### References

- Paroxetine hydrochloride is a member of the selective serotonin reuptake inhibitor (SSRI) class of antidepressants.
Most common adverse events (incidence of 5% or greater and incidence for Paxil at least twice that for placebo) in depression, OCD, panic disorder or social anxiety disorder studies include edema, sweating, nausea, dry mouth, constipation, decreased appetite, somnolence, dizziness, insomnia, libido decreased, tremor, nervousness, yawning, abnormal ejaculation, female genital disorders, and impotence. Concomitant use of Paxil in patients taking monoamine oxidase inhibitors (MAOIs) is contraindicated.

For more information, visit www.paxil.com.

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In two 6- to 8-week placebo-controlled clinical trials, spontaneously reported, treatment-emergent adverse events with an incidence of 5% or greater in at least one of the RISPERDAL groups and at least twice that of placebo were: anxiety, somnolence, extrapyramidal symptoms, dizziness, constipation, nausea, dyspepsia, rhinitis, rash, and tachycardia.

EPS with RISPERDAL, while dose-dependent, are comparable to placebo at doses ≤6 mg/day and differ significantly from placebo at doses >6 mg/day. Prescribing should be consistent with the need to minimize the risk of tardive dyskinesia; if its signs and symptoms appear, discontinuation of RISPERDAL should be considered.

Orthostatic hypotension was reported infrequently (<1%) in clinical trials; its risk may be minimized by following the recommended RISPERDAL dose titration regimen.

Reference:
1. IMS America, 12/99.

Please see brief summary of Prescribing Information on adjacent page.

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The #1 prescribed antipsychotic
Drugs that inhibit Cytochrome P450 and other isoenzymes: Risperidone is metabolized to 9-hydroxyrisperidone by cytochrome P450, an enzyme that is polymorphic in the population and that can be inhibited by a variety of pharmaceutical agents that inactivate cytochrome P450.

The following interactions result in an accumulation of 9-hydroxyrisperidone in the blood: 

- Phenothiazines, thioxanthines, and other antipsychotics that inhibit cytochrome P450 and alter its plasma concentrations of 9-hydroxyrisperidone. Analysis of clinical studies involving a moderate number of poor metabolizers (N=70) does not suggest that poor metabolizers will be more sensitive to the effects of antipsychotics. No comparison of effectiveness in the two groups has been made.

In vitro studies show that CYP2C9, CYP2C19, CYP2D6, CYP3A4, and CYP3A5 are inhibited to varying degrees by Risperidone, with inhibition of CYP2C9 increasing the plasma concentrations of risperidone. Clinical administration of cytochrome P450 inhibitors may decrease the clearance of risperidone. Chronic administration of doxepin to patients with hepatic cirrhosis may decrease the clearance of risperidone. 

Fluoxetine can increase the plasma concentration of the anti-psychotic fraction (risperidone plus 9-hydroxyrisperidone) by raising the concentration of risperidone in the body. Conversely, the anti-psychotic fraction may decrease the plasma concentration of the antidepressive fraction (fluoxetine plus 9-hydroxyfluoxetine) by lowering the plasma concentration of fluoxetine. 

Changes in treatment with antidepressive drugs, other antipsychotics, and chemotherapy can result in changes in plasma concentrations of antipsychotics. 

Adverse Reactions: 

Cardiovascular: Blood pressure elevations, tachycardia, palpitations, cardiac arrhythmias. 

Sedative: Increased duration of sleep, accommodation, dreaming, insomnia, sleepiness.

Weight: Weight gain occurs in about 10% of all patients treated with Risperidone. 

Psychiatric: Psychiatric adverse events have been reported. 

Anxiety, agitation, and hostility are frequent adverse effects. 

Flushing, diaphoresis, tremor, dyskinesia, dystonia, choreoathetosis, tics, catalepsy, tremor, akathisia, and other extrapyramidal symptoms also occur. 

Risperidone may have a differential effect on some psychiatric symptoms. 

Psychosis, mania, and depression usually improve within 1 to 2 weeks, while akathisia, tremor, and Parkinson’s disease may not improve for many weeks.

Antripsychotic drugs should be used cautiously in patients at risk for orthostatic hypotension and syncope may be minimized by limiting the initial dose to 0.5 mg BID and increasing the dose to 1 mg BID, and then increasing the dose to 1.5 mg BID only if the patient tolerated the 1 mg BID dose well.
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