Antinarcoplysis Drug May Improve ADHD

**Modafinil could prove an alternative to stimulants for addressing symptoms, phase III studies show.**

**By Mary Ellen Schneider**

**ATLANTA** — Results from new research point to a possible alternative to stimulants for the treatment of attention-deficit hyperactivity disorder (ADHD) symptoms in children and adolescents.

Modafinil is currently marketed by Cephalon under the brand name Provigil in 100-mg and 200-mg strengths. Provigil is indicated for the treatment of excessive sleepiness associated with narcolepsy, obstructive sleep apnea, narcolepsy syndromes, and shift work sleep disorder. The company, which funded the phase II trials, is seeking approval from the Food and Drug Administration to market modafinil in 85-mg, 170-mg, 255-mg, 425-mg and 425-mg strengths. If approved, the drug would be indicated for treatment of ADHD in children and adolescents aged 6-17 years.

The company is planning to launch the drug under the brand name Adderall by early 2006.

In one study, 189 patients with ADHD aged 6-17 years were randomized to a 7-week double-blind, fixed-dose treatment with either modafinil or placebo. This protocol was followed by a 2-week withdrawal period in which half of the modafinil-treated patients were placed on placebo without tapering, and half were continued on the drug, said Joseph Biederman, M.D., the lead investigator in the study and professor of psychiatry at Harvard University in Boston.

Modafinil was administered once daily, starting at 85 mg/day and was rapidly titrated over 7-9 days to dosages of either 140 mg/day for patients who weighed less than 30 kg or 2425 mg/day for patients who weighed 30 kg or more.

The results of the study were assessed using the school and home ADHD Rating Scale IV. Data were also collected on the comorbidities:

- Conduct disorder.
- Oppositional defiant disorder.
- Hyperactivity.
- Inattention.
- Sleep issues.
- Motor problems.
- Sensory stimulation and night terrors.
- Other medical conditions.

People do not truly outgrow ADHD; motor hyperactivity in childhood evolves into internal feelings of restlessness in adolescence and adulthood.

**Conduct disorder.** “I call these the thugs and ‘thugettes,’” Dr. Gillifan said. These children or teens have respect for societal norms—they genuinely do not care about the rights of others. The majority of child-onset cases of conduct disorder are temporary by adolescence the numbers are approximately equal.

**Oppositional defiant disorder.** By contrast, children with oppositional defiant disorders tend to be argumentative, but usually only within their immediate network of family and friends. Some kids negotiate that way, some derive satisfaction from engaging their parents in an argument.

**Hyperactivity.** More than 50% of adolescents with bipolar disorder have at least one coexisting psychiatric disorder. “In many areas, to get a child some time in a psychiatric hospital, you must have a diagnosis of bipolar disorder,” Dr. Gillifan noted. As a result, many clinicians lead with the bipolar diagnosis because they know the child needs to spend some time in an inpatient hospital. Features of bipolar disorder in children and adults are similar to characteristics of ADHD. The prolonged outbursts, which she described as “affective storms,” are bipolar rather than hyperactive.

**Inattention.** Symptoms of childhood-onset bipolar disorder include oversensitivity to sensory stimulation and night terrors as an infant, and high levels of anxiety and difficulty controlling anger as a school-aged child. Reports from family members might suggest that the child has a difficult temperament.

Treatment options for children and adolescents with ADHD and other conditions include Strattera (atomoxetine), Adderall (amphetamine mixed salts), and Concerta (methylphenidate), as well as Ritalin (methylphenidate HCI) and Deadrine (dextroamphetamine sulfate).

Underdosing is one of the most common reasons for discontinuing medication. Dr. Gillifan said, “Parents are often not used to titrating their children’s medications, since it is not used for ear infections or urinary tract infections. Families become impatient and say that the medication is not working; they may want to switch drugs instead of increasing the dose.” Medication can do some things, but other things must be done at the same time, she said. Nonmedication therapies for ADHD include biofeedback, sensory integration therapy, and relaxation techniques. Other problems include hobbies, sports that channel excess energy, and strategies for better academic performance, said Dr. Gillifan, a consultant to the speakers’ bureau for Pfizer, Ortho-McNeil, and Abbott, and a member of the speakers’ bureau for AstraZeneca.