

ADHD Drugs May Avert Later Psych Disorders

BY BRUCE JANCIN

ISTANBUL, TURKEY — Stimulant therapy for boys with attention-deficit/hyperactivity disorder protected them into young adulthood against development of depression, anxiety disorders, and disruptive behavior disorders in a landmark 10-year prospective case-control study.

Perhaps equally important, the stimulant-treated children were significantly less likely to repeat a grade in school than boys with ADHD who did not receive stimulant therapy in this naturalistic observational study, Dr. Joseph Biederman reported at the annual congress of the European College of Neuropsychopharmacology.

"School failure is a major issue. ...I tell my residents that the train of childhood passes through the station only once in life; if you miss that train you will not be able to recuperate," said Dr. Biederman, professor of psychiatry at Harvard Medical School, Boston.

Stimulant therapy neither increased nor decreased the risk of a subsequent drug, alcohol, or nicotine use disorder during 10 years of follow-up. This finding is at odds with the previously reported 4-year follow-up in this same patient population, which showed that stimulant therapy had a protective effect against substance use disorders.

The reason for the divergent findings regarding development of substance use disorders at 4 and 10 years follow-up is unclear. One possibility is that during the first 4 years, patients were still young enough to be under tight parental control. Another possible explanation is that

stimulants delay but do not stop subsequent substance use disorders.

The key take-away point is that these 10-year longitudinal data help alleviate widespread physician and parental concerns that prescribing stimulants to children with ADHD may predispose them to future substance use disorders. It's worth emphasizing that in this study, neither the age at which stimulant therapy began nor its duration was associated with subsequent substance use disorders, added Dr. Biederman, chief of the clinical and research program in pediatric psychopharmacology and adult ADHD at Massachusetts General Hospital, Boston.

The study involved 140 consecutive white boys with and 120 without ADHD who were a mean of 12 years old at study entry. Ten years later, 112 children with ADHD and 105 controls were available for reassessment. Eighty-two ADHD patients had been treated with stimulants for a mean of 6 years starting when they were on average 8.8 years old, and 30 were not treated with stimulants.

The study was undertaken because even though stimulants are the mainstay of ADHD treatment and have convincingly been shown to improve the disorder's core symptoms, little was known about stimulant therapy's impact, if any, on the risk of developing the psychiatric comorbidities for which patients with ADHD are at high risk.

Stimulant therapy turned out to have a profound protective effect. At 10 years' follow-up, it was associated with a highly significant 78% reduction in the relative risk of developing major depression, compared with those ADHD patients

who did not take stimulants, a 79% decrease in conduct disorder, an 85% reduction in the risk of having two or more anxiety disorders, and a 79% reduction in oppositional defiant disorder. Stimulant-treated patients were also 75% less likely to have repeated a grade.

Moreover, stimulant-treated patients were 53% less likely to be diagnosed with bipolar disorder during 10 years of follow-up, a trend that approached but did not achieve statistical significance.

"This issue is of high clinical importance considering the large and bidirectional



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DR. BIEDERMAN

comorbidity between ADHD and bipolar disorder and the concern that treatment with stimulants may activate children with bipolar disorder," Dr. Biederman observed.

One audience member asked how stimulant therapy could be effective both for control of ADHD symptoms and for preventing subsequent major depression, given that the neurobiology of the two disorders is quite different. Dr. Biederman agreed that it's a puzzle.

"I was very surprised by my own findings," he acknowledged. "The short answer is I don't know. The longer answer, if I were to speculate, is that I suspect that

the continued use of stimulant therapy allows the child to be more successful, minimizes friction at home, minimizes psychosocial vulnerabilities, and that in turn may reduce the risk of developing psychiatric comorbidities like depression.

"Doing well in school in the formative years, having the ability to succeed and experience self-esteem, may have allowed some of the students to take the right train."

He noted that this study carries a key message regarding the importance of medication adherence in ADHD.

"The adherence we have with stimulants, at least in the U.S., is among the worst in the entire field of medicine. One year out, 80% of children are no longer taking their medication. Given these data showing that treatment is so important to avert bad outcomes, adherence is extremely important," Dr. Biederman argued.

Another audience member commented that the study results cannot be considered definitive because participants were not randomized. Dr. Biederman replied that the days are long gone when a placebo-controlled study of stimulants in ADHD would be possible. "These data are the best we're going to have," he said.

Ten-year follow-up data from the investigators' parallel study of girls with ADHD are now being analyzed.

The ongoing longitudinal study is supported by the National Institutes of Health. Dr. Biederman disclosed receiving research support from and serving as a consultant and/or advisory board member to numerous pharmaceutical companies. ■

Atopic Dermatitis Linked to ADHD in German Studies

BY BRUCE JANCIN

BERLIN — Atopic dermatitis is strongly and independently associated with attention-deficit/hyperactivity disorder, three large German studies suggest.

If the relationship is causal—and that's an unsettled issue—atopic dermatitis would explain roughly 10% of all cases of ADHD, Dr. Jochen Schmitt estimated at the annual congress of the European Academy of Dermatology and Venereology.

Atopic dermatitis is the most common chronic inflammatory disorder in childhood, and ADHD is the most common psychiatric diagnosis. The nature of the relationship is a classic chicken-or-egg question.

"As dermatologists, we first think that eczema causes sleeping problems, and this then would maybe cause ADHD. But a close friend of mine who is a psychiatrist says, no, ADHD causes psychological distress and this distress is an exacerbating factor for eczema," explained Dr. Schmitt of Carl Gustav Carus Technical University in Dresden, Germany. "It's also possible that this is a syndrome, that eczema, ADHD, and sleeping problems are parts of one syndrome with another third or fourth underlying cause. And it's even possible that ... eczema triggers ADHD and vice versa and that sleeping problems could play a crucial role."



Dr. Schmitt first became interested in the relationship between atopic dermatitis and ADHD after learning of a Dutch group's hypothesis that some cases of ADHD are an allergic hypersensitivity disorder (*Pediatr. Allergy Immunol.* 2009;20:107-12).

Dr. Schmitt and his coinvestigators turned to a German administrative health care database containing complete information on the outpatient care of 600,000 residents of Saxony. They identified 1,436 subjects aged 6-17 years with atopic dermatitis and randomly selected an equal number of age- and gender-matched controls. In a multivariate logistic regression analysis, the investigators showed that a diagnosis of atopic dermatitis was independently associated with a 1.47-fold increased likelihood of prevalent ADHD (*JAMA* 2009; 301:724-6).

Next came a second cross-sectional study, this one involving KIGGS, a population-based nationwide German survey including 13,318 youths aged 3-17 years, of whom 1,952 had atopic dermatitis and 653 had ADHD. After adjustment for potential confounders, including parental smoking, breastfeeding, perinatal health problems, and atopic comorbidity, individuals with atopic dermatitis were 1.54-fold more likely to carry a diagnosis of ADHD than were those without atopic dermatitis.

Among the 6,484 children aged 3-11 years, Dr.

Schmitt and his colleagues found that those with atopic dermatitis and parent-reported sleep problems had a highly significant 2.67-fold increased likelihood of ADHD, compared with children without atopic dermatitis. But atopic dermatitis patients without sleep problems did not have a significantly increased rate of ADHD (*J. Epidemiol. Community Health* 2009 [doi:10.1136/jech.2009.093534]).

To move beyond the limitations imposed by cross-sectional data, Dr. Schmitt and his coworkers have most recently turned to the German Infant Nutritional Intervention Study (GINI-Plus), a 3,000-subject multicenter prospective investigation into environmental and genetic influences on the development of allergies.

In an as-yet-unpublished analysis of GINI-Plus data, the investigators found that physician-diagnosed atopic dermatitis during infancy was an independent risk factor for mental health problems at age 10 years. "Even those children who only had eczema during the first 2 years of life and cleared afterwards had an increased risk of mental health problems at age 10," Dr. Schmitt added.

He and his colleagues next plan to examine the relationship between severity of atopic dermatitis and ADHD risk. If the association between eczema and ADHD indeed proves to be causal, effective treatment of the dermatologic disorder would have potential as a strategy for the prevention of ADHD, he noted.

Dr. Schmitt disclosed having no financial conflicts of interest. The GINI-Plus study is funded by the German Federal Ministry of Education and Research. ■

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DR. SCHMITT