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DSM-5 proposals spark thousands of comments from professionals and the public. **2**

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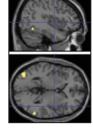
The Gulf oil spill might result



might result in many cases of subclinical or masked PTSD, Dr. Robert T. London argues. 10

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For Children on Antipsychotics, Metabolic Changes Occur Rapidly

BY BETSY BATES

FROM THE ANNUAL MEETING OF THE AMERICAN
PSYCHIATRIC ASSOCIATION

NEW ORLEANS — Worrisome and clinically measurable metabolic changes can be seen in just 12 weeks among children and adolescents who received antipsychotic medications in a National Institutes of Health–sponsored study, prompting serious concern among clinicians who learned of the results at the annual meeting of the American Psychiatric Association.

The results struck at the heart of a troubling dichotomy: an explosion of prescriptions of antipsychotic medications for children, but little evidence in real-world practice that young patients are being routinely screened for metabolic changes that have the potential to shorten life expectancy.

The ongoing Metabolic Effects of Antipsychotics in Children study has already enrolled more than 140 children aged 7-18 years who were already slated to be placed on antipsychotics in the community. Investigators closely monitored changes over 3 months in body fat



Dr. John W. Newcomer says his early data suggest that clinically measurable changes can occur in 12 weeks in children and teens taking antipsychotics.

using dual-energy x-ray absorptiometry (DEXA) and insulin sensitivity using gold-standard methods, as well as tracking clinically available measures such as

body mass index (BMI) percentile, and plasma glucose and lipids.

Body fat percentages rose in "not all, See Antipsychotics page 6

Patient Choice in Treatment of PTSD Might Boost Adherence

BY DAMIAN MCNAMARA

FROM THE NEW CLINICAL DRUG EVALUATION UNIT MEETING SPONSORED BY THE NATIONAL INSTITUTE OF MENTAL HEALTH

BOCA RATON, FLA. — Patients with posttraumatic stress disorder permitted to choose either 10 weeks of prolonged exposure therapy or sertraline had better adherence and treatment response, compared with others randomly assigned to the intervention they did not want.

"Our results highlight a need to rethink a 'one size fits all' approach to the

treatment of PTSD," Norah C. Feeny, Ph.D., said during a late-breaking research session at a meeting of the New Clinical Drug Evaluation Unit sponsored by the National Institute of Mental Health.

"We are fortunate we have good, efficacious treatments for PTSD," Dr. Feeny said. "But patient preference may affect efficacy down the line."

In this first head-to-head comparison between a validated cognitive-behavioral therapy and a selective serotonin reuptake inhibitor for PTSD, 61% of 200 participants at baseline said they would pre**40**ur results highlight a need to rethink* [standardized] approaches.

fer prolonged exposure. The remaining 39% indicated they would prefer treatment with sertraline.

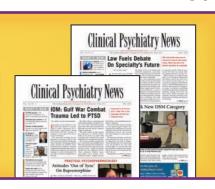
Dr. Feeny was somewhat surprised by these percentages because "prolonged exposure requires them to engage with material they want to avoid, such as combat, a motor vehicle accident, or sexual assault. Sertraline does not require engagement with this painful stimuli," said Dr. Feeny, director of the PTSD Treatment & Research Program at Case Western Reserve University, Cleveland. The NIMH and Pfizer, maker of Zoloft,

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Don't Wait a Year to Check Labs

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but certainly the majority of these children and youth," said Dr. John W. Newcomer, professor of psychiatry and medicine and Director of the Center for Clinical Studies at Washington University in St. Louis.

Mean increases were highly variable among children and adolescents taking antipsychotic medications, but have averaged almost 3 kilos, or 6.5 pounds, "of body fat, not just weight," in just 12 weeks, he said.

Some variance was seen in mean percent body fat accrual depending on which antipsychotic the children and adolescents received in the randomized open-label study. However, box plots revealed "substantial overlap" in the results, showing that each individual child's metabolic response to a given drug is somewhat unpredictable.

"You can find kids who take any one of these medications and potentially get a substantial increase in body fat, and you can also find kids who take any one of these agents who actually have very little change in body fat, although some medications are associated with a higher risk of substantial increase," Dr. Newcomer said.

Increases in BMI percentiles were "substantial" as well, and closely paralleled more sophisticated measures of body fat, such as DEXA. "The good news is, it's pretty easy to track the changes in adiposity," said Dr. Newcomer in an interview after the meeting.

"We used very fancy and expensive measures of body fat, but what pediatricians have in the front of every kid's chart (the BMI percentage table) does a darned good job of not only lining up where the child is at the baseline screen, but also in tracking changes over time." In a similar vein, the study found that simple blood cholesterol profiles—especially triglycerides and HDL—did a "halfway decent job" of estimating insulin sensitivity at baseline and then tracking changes through the early months of therapy, Dr. Newcomer added. "The point is... don't wait a year to check the labs," he said. "Don't not look."

What is troubling to many is the fact that many clinicians indeed are not looking

A Medicaid claims data study published earlier this year found that glucose screening was performed in just 31.6% and lipid testing in just 13.4% of 5,370 children aged 6-17 years prescribed antipsychotic drugs from July 1, 2004 to June 30, 2006 (Arch. Pediatr. Adolesc. Med. 2010;164:344-51).

Dr. Newcomer, a coauthor on the Medicaid claims research, said a growing number of "very eye-opening studies" about the enduring impact of childhood metabolic dysregulation and obesity should make clinicians weigh risks and consequences carefully when choosing drugs to prescribe for childhood schizophrenia, and perhaps even more so for use in disruptive behavior disorders and other nonpsychotic diagnoses.

"I have certainly learned that there are children at the end of the road of clinical options who are either not going to be in school or unable to participate without some heroic treatment measures, such as low-dose antipsychotic treatment, to help them to re-engage in education," he said.

At the same time, relatively brief pharmacologic interventions for children who do not have schizophrenia or bipolar disorder should leave "a metabolic footprint. . . as modest as possible," he said.

The Washington University study extended body weight findings from the nonrandomized SATIETY study published last year (JAMA 2009;302:1765-73), in which 272 4- to 19-year-olds prescribed antipsychotic drugs gained from a mean 4.4 kg (aripiprazole) to 8.5 kg (olanzapine) in a median of just 10.8 weeks on medication.

At the APA scientific session where interim data were released from the MEAC study, one audience member rose to call the findings "catastrophic."

"What you're showing us is very, very scary," he told Dr. Newcomer, who replied that the metabolic effects of other classes of drugs widely used in children, including benzodiazepines and high-dose anti-depressants, are also potentially concerning. "We're having this policy debate under a streetlamp as though second-generation antipsychotics are the only drugs that cause weight gain," Dr. Newcomer said. "Let's not kid ourselves."

One alternative raised at the session was intensive behavioral modification, such as a year-long, school-based program for disruptive children described by Dr. Jacob Venter, of Wellesley, Mass., and his colleagues at the same APA scientific session.

Dr. Newcomer pointed to the University of Arizona behavioral study as an example of how nonpharmacologic interventions can produce "some good results," even among children with severe behavioral dysregulation.

"The problem is, I don't know about your town, but in St. Louis, there is a 6-month waiting list to see a child psychiatrist," he told the audience.

By the time they can be seen, "These families are in great distress and sometimes aren't terribly interested in taking those referrals for behavioral treatments, either because they already tried some therapy or because they seek rapid change," he said. Families want the quick

responses they associate with medication, and when a trial of behavioral modification is suggested as a starting place, "We can't give it away."

As for trying to reduce prescribing of antipsychotic medications to children, particularly among those who do not have symptoms consistent with bipolar disorder or schizophrenia, Dr. Newcomer, who also chairs Missouri's Drug Utilization Review Board, was somewhat skeptical about the potential to substantially reduce that clinical practice.

"Like it or not, that horse is out of the barn. The clinical benefits can be obvious to parents, children, and their doctors, so there will continue to be interest in this therapeutic approach, even as we fully elaborate the risks. This is happening all over the country. The rates of prescriptions are going up. The off-label use is tremendous, suggesting a lot of unmet need," he said.

Indeed, a series of studies conducted by a team led by Dr. Mark Olfson at Columbia University, New York, has found that prescribing of antipsychotic medications by psychiatrists and primary care physicians has skyrocketed in the United States since the mid-1990s, with treatment of disruptive behavior disorders, including attention-deficit/hyperactivity disorder, playing a significant role in the increase.

In one recent example, Dr. Olfson reported that antipsychotic use by 2- to 5-year-olds covered by private insurance rose from 0.78 per 1,000 to 1.59 per 1,000 from 1999 to 2007. Less than half of the children in the study had received a mental health assessment, a psychotherapy visit, or a consultation with a psychiatrist.

Dr. Newcomer disclosed that he has served as a consultant to several pharmaceutical companies but reported no relevant financial conflicts of interest associated with his study.

Preference Matters

PTSD from page 1

funded the study. Zoloft is the brand name for sertraline.

A total of 97 participants were randomized to a "choice" group and 103 others to a "no choice" group. Therefore, some in the no-choice group received an intervention they did not want. This design allowed analysis of the degree to which patient preference affects treatment adherence and outcomes, Dr. Feeny said.

The prolonged exposure group received manualized therapy for 10 weekly sessions, each lasting 90-120 minutes. The sertraline group also received 10 weekly, 30-minute manualized education sessions (e.g., about common reactions to trauma).

Major Finding: Treatment response was 75% in the prolonged exposure group vs. 65% in the sertraline group, which was not a significant difference. However, prolonged exposure might have a slight advantage.

Data Source: Preliminary, intent-to-treat results for 200 participants in the 10-week Acute Treatment for Chronic PTSD study.

Disclosures: Dr. Feeny said she did not have any relevant disclosures.

"We know very little about how prolonged exposure and sertraline compare with each other," Dr. Feeny said. Although overall there were no significant differences in treatment response (75% in the prolonged exposure group vs. 65% in the sertraline group), "prolonged exposure may have a slight advantage in terms of the magnitude of change [from baseline]."

Patient preference for treatment, however, did make a difference, Dr. Feeny said. After 10 weeks, "those who received their choice were doing better in terms of responder status."

Participants in the no-choice group randomized to the intervention they did not want, referred to as the "discrepancy" cohort, were more likely to have a lower response. "People in the discrepancy group were doing worse on every index." For example, this group had lower adherence to their treatment—they were more likely to attend fewer sessions of prolonged exposure or took "substantially lower" doses of sertraline during the study.

All participants met DSM-IV criteria for chronic PTSD as their primary diagnosis and were aged 18-65 years (mean, 37 years). The cohort was primarily female, 76%. Most, 65%, were white, 22% were African American, and the remaining 13% identified with other ethnic groups. Participants were "quite chronic," enrolling in the study a mean of 12 years after their trauma. The most common traumatic events were adult sexual assault (31%), childhood assault (24%), and adult nonsexual assault (23%). If patients were multi-

ply traumatized, they were asked to choose a primary trauma in case they chose or were assigned to prolonged exposure.

Although patients could not be blinded in this or any behavioral versus medication protocol, raters were blinded to group assignment when interpreting the findings, Dr. Feeny said in response to a meeting attendee question. "In an attempt to be real-world, we were less concerned about blinding people to the interventions"

Dr. Feeny explained why she and her colleagues chose a novel, double-randomized treatment preference study design. Beyond the obvious lack of choice for patients in traditional randomized controlled trial, "if we just let people choose their own medications, there could be selection bias," she said. In an attempt to be as impartial as possible while allowing participants to make a more informed choice, they initially watched two videos. Each video featured clinicians who explained the rationale for each intervention, including efficacy information, procedures, and possible side effects. Wording of the two videos was matched as closely as possible.

Dr. Feeny only presented preliminary, intent-to-treat results of the 10-week Acute Treatment for Chronic PTSD study at the meeting. Two-year follow-up findings will be presented in the future, she added.

Dr. Feeny is a consultant or lecturer for multiple pharmaceutical companies, but none of her disclosures were relevant to this presentation.

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