Section Contents

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Predictors and Treatment Outcomes

This month's section of Focus on Childhood and Adolescent Mental Health offers a wide array of clinically relevant topics.

Interest in the use of dietary supplements to treat mood disorders has been on the rise. Wozniak and colleagues examined whether high EPA/DHA omega-3 fatty acids and inositol were effective in the treatment of pediatric bipolar spectrum disorders. Twenty-four children aged 5 to 12 years with *DSM-IV*–diagnosed mild to moderate bipolar spectrum disorders (bipolar disorder—I, II, or not otherwise specified) participated in the trial. Youths were randomly assigned to omega-3 fatty acids plus placebo, inositol plus placebo, or combined omega-3 fatty acids plus inositol. Fifty-four percent of youths completed the 12-week trial. The group who received combination treatment had a significantly greater reduction of manic symptoms as assessed by the percentage of subjects who had decreases in Young Mania Rating Scale score of 30% (defined as *response*) and 50% from baseline to endpoint.

The combination of omega-3 fatty acids and inositol was well tolerated. The most common adverse event was gastrointestinal problems. This study suggests preliminary support for the potential use of omega-3 fatty acids and inositol for the treatment of pediatric bipolar spectrum disorders. However, the sample size was small, more than half of the subjects discontinued treatment, and patients with severe illness were excluded from the study. A large controlled trial of omega-3 fatty acids and inositol that includes a placebo arm is warranted in order to determine the efficacy of these dietary supplements in the treatment of pediatric bipolar disorder.

The role of proinflammatory markers (PIMs) as a biomarker for bipolar disorder is of clinical interest. Goldstein et al examined whether PIMs were associated with the severity and burden of manic/hypomanic and depressive symptoms over the preceding 6-month epoch. PIMs that were assayed were serum levels of interleukin (IL)-6, tumor necrosis factor (TNF)-α, and high-sensitivity C-reactive protein (hsCRP). One hundred twenty-three adolescents and young adults (mean age = 20.4 years) who were part of the Course and Outcome of Bipolar Youth (COBY) study participated. Psychiatric symptoms over the preceding 6-month period were assessed. Higher IL-6 and hsCRP levels were significantly associated with longer duration of bipolar disorder. Earlier age at onset of bipolar disorder was also significantly associated with higher hsCRP. In analyses that controlled for differences in comorbidity and treatment, IL-6 was significantly associated with percentage of weeks with subthreshold mood symptoms, whereas high hsCRP was associated with severity of depressive symptoms. TNF-α was associated with psychotic symptom outcome but not mood outcome. This is the largest study to date of multiple PIMs in association with mood symptoms of bipolar disorder in adolescents and young adults. The authors recommend further study of PIMs for clinical outcomes such as illness course and treatment selection.

The predictors of clinical outcome in early-onset first-episode psychosis were evaluated by Parellada and colleagues. The sample consisted of 110 children and adolescents (mean age = 15.5 years) who were followed over a 2-year period of time. Clinical assessments, structural neuroimaging, and biological parameters (genetics and redox metabolism) were obtained at baseline. The primary outcome variables were global functioning, functional improvement, and presence of primary negative symptoms. The baseline clinical assessments predicted 2-year follow-up outcome better than the selected biomarkers in this sample of youth with a first episode of psychosis. The Strauss-Carpenter Outcome Scale was a good predictor of improvement and functioning. Youth who had more severe symptoms at baseline improved more than those with less severe symptoms. Those youth with primary negative symptoms at baseline continued to have negative symptoms over the course of the 2 years. The authors point to the need to identify symptoms and treat early in the course of a first episode of psychosis.

Attenuated psychosis syndrome (APS) is listed in *DSM-5* as a condition for further study and is also listed under other specified schizophrenia spectrum and other psychotic disorders in Section II. The proposed criteria are that delusions,

hallucinations, and/or disorganized speech be present in an attenuated form for at least once per week for the past month with symptoms having begun or worsened in the past year. The symptoms are distressing and disabling to the extent that clinical attention is warranted. The aim of Gerstenberg and coworkers' study was to determine the frequency and correlates of APS in psychiatrically hospitalized adolescents with nonpsychotic disorders. Diagnostic assessments and rating scales were administered to these adolescents. Of 89 nonpsychotic adolescents, 23.6% fulfilled criteria for APS on the basis of *DSM-5* and research criteria for attenuated positive symptom prodromal syndrome. Adolescents with APS had significantly more comorbid disorders than adolescents without this diagnosis. Adolescents with APS compared to non-APS adolescents were more likely to have major depressive disorder (61.9% vs 27.9%), oppositional defiant disorder/conduct disorder (52.4% vs 25.0%), and personality disorder traits (57.1% vs 7.4%). Prescribed psychotropic medications were not significantly different between these 2 groups. Adolescents with APS were more severely ill and had lower overall functioning. Given the high prevalence rate of APS in this sample, the investigators recommend that large, long-term prospective studies be conducted to further determine the outcome of youth with APS status.

Rosenberg and colleagues examined whether acute stress disorder (ASD) predicted posttraumatic stress disorder (PTSD) in children with large burn injuries. One hundred eighty-three children and adolescents participated in this study; of these, there were 85 matched pairs of youth with and without ASD. Youth with ASD received timely pharmacotherapy and psychotherapy for the management of anxiety during their inpatient hospitalization. Approximately 5 years postburn, there was no significant difference in the prevalence of PTSD in the group who had ASD (8.2%) compared to the non-ASD comparison group (4.7%). Variables such as prior ASD diagnosis, burn size, gender, ethnicity, age at time of study participation, and number of years postburn did not predict PTSD. On the basis of these findings, the investigators suggest that timely psychotherapy and pharmacotherapy for ASD may have been the factor that decreased the likelihood of development of PTSD.

Frank and colleagues conducted a literature review to determine why patients with attention-deficit/hyperactivity disorder (ADHD) do not adhere to long-term treatment. Thirty-eight studies were included in their analyses, and the majority of the sample included children and adolescents. Both stimulant and nonstimulant medication treatments for ADHD were included in their analyses. Overall, 46% of subjects discontinued treatment over a 1-year period. Of those, 19.9% discontinued because of their own wish to stop, belief that they did not need treatment, or symptom remission; 16.2% withdrew consent for treatment; 15.1% discontinued because of adverse events, in particular reduction in weight and appetite; and 14.6% discontinued because of less than optimal effect. Medication adherence was more likely with long-acting compared to short-acting stimulants. Psychosocial stressors were also associated with less medication adherence. The study suggests that medication adherence is an important topic for discussion in the treatment of patients with ADHD.

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