



# Focus on Childhood and Adolescent Mental Health

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*Le Xiao, Stephen J. Ganocy, Robert L. Findling, Kiki Chang, Melissa P. DelBello,  
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A Supervised Exercise Intervention for Youth at Risk for Psychosis:  
An Open-Label Pilot Study

*Derek J. Dean, Angela D. Bryan, Raeana Newberry, Tina Gupta, Emily Carol, and Vijay A. Mittal*

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## Findings of Interest

This section of Focus on Childhood and Adolescent Mental Health examines exercise as a psychosis prevention measure, the significance of persistent negative symptoms in first-episode psychosis, early treatment response in bipolar disorder, and trends in cannabis use.

Does exercise prevent psychosis in adolescents and young adults who are at ultrahigh risk for psychosis? A pilot study by Dean and colleagues provides preliminary information to address this question. Twelve adolescents and young adults between 16–24 years of age who were at ultrahigh risk for psychosis participated in a 12-week open-label exercise intervention. Eligible participants had a predominantly sedentary lifestyle with no more than 60 minutes of at least moderate physical activity per week for the past 6 months. Clinical interviews were administered before and after the exercise intervention to diagnose a prodromal syndrome and to track positive and negative symptom changes. Cognitive testing and structural and resting state functional connectivity magnetic resonance imaging scans were performed before and after the exercise intervention. Assessments of physical fitness and social and role functioning were also obtained. The exercise intervention consisted of either moderate or vigorous intensity aerobic exercise. Participants randomly assigned to the

moderate condition were required to exercise 2 days per week at 65% of their maximum oxygen uptake for a total of 24 sessions. Participants randomly assigned to the vigorous condition were required to exercise 3 days per week at 85% of their maximum oxygen uptake for a total of 36 sessions. Each exercise session was under the supervision of an exercise physiologist.

Nine of the 12 participants completed the exercise intervention; the 3 dropouts were in the vigorous condition. Participants showed improvement in social functioning, positive and negative symptoms, and cognition (working memory, verbal learning, visual learning, speed of processing, attention/vigilance, and reasoning and problem solving, but not social cognition). Increased functional connectivity was found between the left hippocampus and occipital cortex postexercise. There were no changes in hippocampal volume for either the right or left hippocampus. The investigators conclude that exercise interventions are feasible and may benefit individuals who are at ultrahigh risk for psychosis. The results suggest that exercise may lead to changes in the functional organization of the cortico-hippocampal networks. Given these preliminary positive findings, the investigators have begun recruitment for a randomized controlled trial to further examine the role of exercise in prevention of psychosis.

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Negative symptoms are often associated with poor outcome in schizophrenia. Puig and colleagues examined cognitive and social functioning in individuals with first-episode psychosis with and without persistent negative symptoms (PNS). These investigators also examined cognitive and functional correlates of PNS in early-onset versus adult-onset first-episode psychosis. Two hundred thirty-five patients with first-episode psychosis (51 early-onset, 184 adult-onset) and 240 healthy controls participated in a multicenter longitudinal study. Patients' ages were from 9 to 36 years. Ratings of global and social functioning were obtained, and cognitive assessments were performed. PNS were defined as (1) Positive and Negative Syndrome Scale score  $\geq 4$  for at least 1 of the following symptoms: blunted affect, emotional withdrawal, poor rapport, passive withdrawal, and lack of spontaneity and (2) the absence of or only mild depressive symptoms. These criteria had to be met at 2 months and maintained at 12 months or met at 6 months and maintained at 12 months to fit the definition of PNS.

During the first year, 16.2% ( $n=38$ ) of patients met criteria for PNS. Patients with an early onset of psychosis were more likely to meet criteria for PNS during the first year after first-episode psychosis compared to those with adult onset (odds ratio = 2.18). Those patients with PNS who had an early onset were more cognitively impaired than those individuals with a later onset. Independent of age at onset, patients who met criteria for PNS during the first year after first-episode psychosis had a selective deficit in executive functions and greater impairments in social and global functioning. PNS during the first year after first-episode psychosis was associated with the diagnosis of schizophrenia spectrum disorder at 12-month follow-up. On the basis of these findings, the investigators recommend early intervention for negative symptoms particularly during the period of adolescence. These interventions may decrease the likelihood of the social and executive dysfunction associated with PNS in first-episode psychosis.

Does early response to treatment predict ultimate response and remission for adolescents with bipolar disorder, manic or mixed episode? Xiao and colleagues conducted a post hoc analysis of a 3-week, randomized, placebo-controlled trial of olanzapine (2.5–20 mg/d) for adolescents 13–17 years old diagnosed with bipolar I disorder, manic or mixed episode. Data were obtained from 104 patients who received olanzapine in this trial. Early response and early nonresponse were defined as  $\geq 25\%$  and  $< 25\%$  reduction, respectively, in Young Mania Rating Scale (YMRS) score at week 1. Ultimate response was defined as  $\geq 50\%$  YMRS score reduction at study endpoint. Remission was defined as YMRS total score  $\leq 12$  (standard definition) or  $\leq 8$  (stringent definition) at endpoint.

Seventy-two (69.2%) of 104 patients were in the early response group at week 1. Early response patients were significantly more likely to achieve ultimate response at week 3 than early nonresponse patients (61.1% vs 21.9%, respectively). Early response patients were significantly more likely to achieve remission at study endpoint than nonresponse patients (45.8% vs 12.5% with remission defined as YMRS score  $\leq 12$  and 33.3% vs 3.1% for YMRS score  $\leq 8$ ). Early response patients also had

significantly greater improvement in overall global functioning than nonresponse patients. A threshold for early response of  $\geq 35.5\%$  reduction in YMRS score was found to have the best predictive validity for ultimate response and remission at endpoint. Baseline characteristics were similar between the early response and early nonresponse groups with the exception of higher scores for sleep and thought content in those with early response. Adverse events were similar between early response and early nonresponse patients except for dyskinesia in the early nonresponse group. Given these results, the investigators recommend that an early improvement measure be used as a tool to predict treatment outcomes in order to assist in clinical decisions for management of bipolar disorder in youth.

Trends in cannabis use disorders among adolescents in the United States were investigated by Han and colleagues. Data were obtained from 288,300 adolescents aged 12–17 years who participated in the 2002–2014 National Survey on Drug Use and Health conducted by the Substance Abuse and Mental Health Services Administration. Information about past-year use of tobacco, alcohol, cannabis, cocaine, hallucinogens, heroin, and inhalants, as well as nonmedical use of prescription pain relievers, sedatives, and stimulants, was collected. Data were also obtained about perceptions of cannabis use, including the perceived risk of smoking cannabis once or twice a week, perceived parental strong disapproval of using cannabis once a month or more, perceived strong disapproval by peers of using cannabis once a month or more, perceived state legalization of medical cannabis use, and perceived cannabis availability.

The prevalence of past-year cannabis use among adolescents decreased from 15.8% in 2002 to 13.1% in 2014. The prevalence of past-year cannabis use disorder among youth decreased from 4.3% in 2002 to 2.7% in 2014. The prevalence of tobacco use decreased from 23.6% in 2002 to 12.7% in 2014. Alcohol use decreased from 34.6% in 2002 to 24.0% in 2014. For those adolescents who used tobacco, the prevalence of past-year cannabis use increased from 51.9% in 2002 to 57.1% in 2014. For adolescent alcohol users, the prevalence of past-year cannabis use increased from 40.5% in 2002 to 43.0% in 2014. The prevalence of perceiving great risk of smoking cannabis decreased from 2002 to 2014 (51.5% to 37.4%, respectively). The prevalence of past-year cannabis use and the prevalence of cannabis use disorder were generally higher among racial/ethnic minorities. No gender differences were found in the prevalence of past-year cannabis use and cannabis use disorder. Given the strong association between decline in tobacco use and decline in cannabis use, the investigators suggest that tobacco control and prevention among adolescents may lead to decreased cannabis use in this age group.

We hope you enjoy this issue's Focus on Childhood and Adolescent Mental Health section.

Karen Dineen Wagner, MD, PhD  
kwagner@psychiatrist.com

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