declines from childhood to adulthood. Individuals with schizophrenia showed accelerated decline in ability to learn.)

In summary, we previously demonstrated that in childhood, when the normative trajectory of cognitive ability is one of growth, children who later develop schizophrenia exhibit slowed growth in fluid cognitive abilities (1). Here, we demonstrate that in adulthood, when fluid cognitive abilities start to normatively decline (4), individuals with schizophrenia in our cohort exhibited early degeneration and accelerated decline. Granted, these latter findings are based on only two tests, but to us, they blur the distinction between development and degeneration. Moreover, unlike fluid abilities, deficits in crystallized abilities were apparent as early as age 7 and remained stable to age 38 years (1, 2). Fluid abilities are thought to support the acquisition of crystallized skills, with the developmental trajectory of crystallized abilities lagging behind that for fluid abilities (5). Therefore, it is somewhat surprising that deficits in crystallized abilities emerged before deficits in fluid abilities and did not worsen over time. Whether different pathophysiological mechanisms underlie cognitive deficits in fluid and crystallized abilities in schizophrenia is a key question for future research.

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Management Issues During Pregnancy in Women With Bipolar Disorder

TO THE EDITOR: We read with interest the article by Clark et al. (1) on lamotrigine dosing in pregnant patients with bipolar I disorder. The authors report on the use of lamotrigine in eight patients with bipolar disorder, six of whom received concomitant psychotropic drugs including four women who were taking antidepressant drugs. Dosage adjustments of lamotrigine were made in response to hypomanic, manic, or depressive symptoms. It is not clear whether the dosages of concomitant psychotropic drugs remained the same during pregnancy. Of the three women requiring a dosage increase to manage symptoms, two were also taking antidepressants that can increase the recurrence of bipolar mood episodes both during and after pregnancy (2). There are no data suggesting that monitoring serum levels with corresponding adjustments to lamotrigine dosing will protect against antidepressant-led mood instability. Interestingly, the authors did not report a correlation between lamotrigine concentration and scores on rating scales for depression and mania. Thus, the conclusion that women with bipolar disorder who are treated with lamotrigine experience an increase in symptoms as a result of declining concentrations of this drug is not justified.

While lamotrigine has a role in the management of bipolar disorder during pregnancy, no data on its effectiveness in the prevention of postpartum mood episodes are currently available. Moreover, lamotrigine is generally not recommended for the acute treatment of mania (3).

Finally, the statement that pregnancy is a vulnerable period for recurrence of mood episodes is true for women treated at tertiary care centers with complex and often comorbid disorders and women who discontinue mood-stabilizing drugs. However, evidence from studies using nonclinical samples, retrospective studies, and studies on psychiatric hospitalization rates is suggestive of a positive effect of pregnancy on bipolar disorder (4).

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Response to Sharma and Sommerdyk

To the Editor: As Prof. Sharma and Ms. Sommerdyk highlight, optimizing medication management in pregnant women with bipolar disorder is an area with an urgent need for data to drive decision making. The objectives of the Treatment in Psychiatry article (1) were to combine a review of the data on the pharmacokinetic changes of lamotrigine in pregnant women with epilepsy with observations from our case series and to generate recommendations for lamotrigine dosing in pregnant women with bipolar disorder. Sharma and Sommerdyk raise an important point about whether women treated with lamotrigine in pregnancy experience an increase in mood symptoms as a result of declining lamotrigine concentrations. Serum level reductions of psychotropic medications as a result of dosage decreases or drug nonadherence are associated with episode recurrence and symptom worsening. Data on lamotrigine use in pregnant women with bipolar disorder are sparse; however, the literature on managing lamotrigine in women with epilepsy is relevant for guidance about pharmacokinetic changes during gestation. Women with epilepsy experience increased seizure frequency associated with declining lamotrigine levels during pregnancy. Similarly, if the bioavailability of lamotrigine for maintenance treatment of bipolar disorder is not sustained in the pregnant woman, she is at risk for symptom worsening. As Sharma and Sommerdyk recommend, careful symptom monitoring is essential in the gravid woman taking lamotrigine, since pregnancy may increase clearance and lower levels (2). Establishing a baseline serum level at the patient's therapeutic dose of lamotrigine and adjusting the dosage to maintain the baseline level increases the likelihood of preventive efficacy.

As we discussed (1), an association between lamotrigine serum levels and mania and depression scores was not found. In our naturalistic study from which the case series was derived, the individuals' lamotrigine dosages were managed by their community-based physicians. Serum levels were checked during scheduled study protocol visits rather than at the time their physician observed a change in symptoms and changed the dosage. A study designed to address these pharmacokinetic and pharmacodynamic questions for optimal management of lamotrigine dosing and prevention of relapse is underway in our center.

Whether lamotrigine prevents postpartum episodes remains to be investigated; however, continuing effective maintenance therapy prior to and during pregnancy is good clinical practice, and every woman with bipolar disorder requires close observation after birth regardless of medication status (3).

The predictors of episode recurrence during pregnancy may be related to the bipolar disorder variant rather than sample characteristics (tertiary care or community psychiatric setting). In a large-scale screening study for postpartum depression in an obstetrical population, 22.6% of women with positive screens were diagnosed with bipolar disorder (4). The majority of these women were symptomatic during pregnancy, with episode onset either before pregnancy (38%) or during pregnancy (33%) and continuing through 4–6 weeks postpartum (unpublished 2013 data from K. L. Wisner). Bergink et al. (5) reported that women with chronic bipolar disorder (such as the individuals in our case series) benefitted from continued lithium prophylaxis during pregnancy, while those with a history limited to postpartum episodes remained well during gestation without medication but relapsed postpartum. In sum, pregnancy is a vulnerable time for episode recurrence in many women with bipolar disorder.

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