offspring of parents with bipolar disorder and offspring of community comparison subjects (1).

The fact that the caregiver/teachers could not differentiate between high-risk and comparison offspring in the BIOS trial does not prove or disprove the reliability of our study because, as expected, the sample size of preschool children who had caregiver/teacher reports was small (N=51). Moreover, of these children, only eight had a disruptive disorder. Recent analyses showed that relative to healthy children, these eight children had significantly higher attention and externalizing scores, but these results need to be replicated in larger samples.

We agree that very little is known about bipolar disorder in preschoolers. Therefore, at the request of parents with bipolar disorder who participated in our school-age study (1), we decided to evaluate their preschool children for psychopathology, including the presence of DSM manic symptoms. After adjusting for several confounding factors (e.g., the child's ADHD symptoms), offspring of parents with bipolar disorder had significantly higher total scores on the Mania Rating Scale relative to offspring of comparison parents. Additionally, in adjusting for multiple comparisons, exploratory analyses showed that between-group differences in manic symptoms were mainly attributable to irritability, elation, decreased need for sleep, and mood lability. However, 96% of the severity scores for manic symptoms were classified as mild or less. Interestingly, these subclinical manic symptoms are similar to the prodromal manic symptoms retrospectively reported in the Amish study. We are in the process of following the children to evaluate the nature of these symptoms and whether they predict an increased risk for mood disorders.

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Schizophrenia and Childhood Adversity

TO THE EDITOR: In his editorial, published in the January 2010 issue of the *Journal*, John H. Gilmore, M.D. (1), argues for a developmental perspective in relation to schizophrenia. However, it is perhaps no longer accurate to argue that "most studies have focused on pre- and perinatal environmental risk factors" (1, pp. 8, 9). Recently, researchers have found a range of adverse events in childhood to be significant risk factors for developing psychotic symptoms and/or being diagnosed with schizophrenia, even after controlling for family history of psychosis or schizophrenia in some cases. These adverse events include early loss of a parent; parental poverty; bullying; witnessing parental violence; emotional, sexual, or physical abuse; physical or emotional neglect; and insecure attachment (2, 3).

These findings support the editorial's call for "a new concentration of efforts on childhood brain development" (1, p. 9). The Traumagenic Neurodevelopmental model (4) is based on findings that differences in the brains of many adults diagnosed with schizophrenia are also found in children who have been severely traumatized, especially in the first years of life. These include overactivity of the hypothalamic-pituitary-adrenal axis; dopamine, norepinephrine, and serotonin abnormalities; hippocampal damage; cerebral atrophy; ventricular enlargement; and reversed cerebral asymmetry. Thus, the heightened sensitivity to stress evidenced by dysregulation of the brain's stress regulation mechanisms is not necessarily inherited. It can be caused by childhood trauma.

Gene-environment interactions will be best understood in terms of new knowledge about how epigenetic processes turn gene transcription on and off through mechanisms that are highly influenced by socioenvironmental experiences (3). It will be important to integrate these epigenetic processes, especially those involving the stress regulating functions of the hypothalamic-pituitary-adrenal axis, with research about the psychological mechanisms (cognitive distortions, attachment, dissociation, etc.) by which specific types of childhood trauma can lead to specific types of psychotic experiences (2, 3).

While it can be tempting to ignore childhood adversity, out of fear of being accused of family-blaming, many childhood adversities occur outside the family and those that occur within families tend to be intergenerational and are therefore areas in which many families need assistance. Indeed, we were pleased to see the implications for prevention mentioned in the editorial. We also feel that it is important to note that one environmental enrichment program for children ages 3 to 5 years reduced schizotypal personality scores in adulthood (5).

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Dr. Gilmore Replies

To the Editor: I thank Drs. Read and Bentall for their interest in my editorial comments about brain development and the causes of schizophrenia. I am pleased they are in agreement with the overall argument made. They rightly point out that risk factors across the entire range of prenatal and postnatal development ultimately contribute to schizophrenia and call our attention to the literature regarding early childhood adversity. As they note, hypothalamic-pituitary-adrenal axis alterations and epigenetic regulation are likely candidate mechanisms that deserve study. Their discussion of the potential role of environmental enrichment is very important, since we realize that it may be difficult to prevent many of the multiple causes of schizophrenia but may be possible to identify and modify developmental trajectories of risk.

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Increasing the Age at Onset for ADHD?

To the Editor: In their commentary, published in the January 2010 issue of the *Journal*, Christian Kieling, M.D., et al. (1) presented the rationale for a DSM–5 proposal to increase the required age at onset for attention deficit hyperactivity disorder (ADHD) from age 7 years to 12 years. Unfortunately, the commentary did not include a risk/benefit analysis. The authors focus only on the benefit of reducing false negatives and ignore the considerable risk that eliminating this age of onset gatekeeper will result in a flood of new false positives for a diagnosis that may already be quite overinclusive.

Especially in adolescents and adults, real or perceived attention problems are so common and so nonspecific that ADHD can be easily overdiagnosed in those suffering from any number of other mental disorders and in those who are merely seeking performance enhancement (2–6).

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Drs. Christian Kieling, Renata Kieling, and Rohde Reply

To the Editor: On the behalf of all authors, we appreciate Dr. Frances' interest in our commentary documenting the rationale for changing the age at onset criterion for ADHD in DSM–5. Since the preparation of DSM–5, the implementation of an evidence-based approach to the development of diagnostic criteria has been an essential step toward strengthening the scientific bases of psychiatric nosology. Any modification in DSM is intended to be a consequence of comprehensive literature reviews, re-analyses of available data sets, and results from field trials (1).

Accordingly, our systematic review of the literature found no evidence for retaining the 7-year-old cutoff as a valid criterion for parsing individuals with and without ADHD. It is important to note that this recommendation derives from 31 studies (including the DSM–IV field trials) assessing a variety of outcomes in multiple settings across different countries (2). Prospective data of an existing data set corroborate these findings, revealing that extending the age at onset criterion to 12 years resulted in a negligible increase of 0.1% in the prevalence of ADHD (3). Results from upcoming field trials should finally assess the suitability and consequences of the proposed modification (4).

The lack of internal and external validity of the 7-year-old cutoff indicates that it impedes the accurate diagnosis of adolescents and adults for whom a comprehensive clinical assessment should identify other more valid criteria in order to reduce false positives (5). Indeed, from a statistical point of view, the inclusion of any additional arbitrary criterion leads to a reduction in the overall prevalence of a disorder. However, as highlighted by Wakefield and Spitzer (6), lower prevalence rates do not necessarily imply more valid diagnostic criteria. The shift from committee-recommended to evidence-based criteria in the development of DSM should be sustained to further increase the clinical validity of the manual.

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