Resolving the discrepancy in BIOS high-risk study findings

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Dear Dr Freedman

Birmaher and colleagues (1) discuss some factors that may explain why their findings (BIOS study) in preschool-age children of parents with bipolar disorder (BD) appear to contradict those of other studies. There are, however, other reasons for the obvious contradictions: the different methods of recruitment, assessment and symptom definition.

The BIOS study ascertained many high-risk families through advertisement, confirmed parental BD on cross-sectional assessment and allowed for psychiatric co-morbidity among the co-parents. This differs from some studies (2;3), in which the parent was diagnosed with BD based on structured interviews combined with all available clinical information and in which well biological co-parents were required; as well as from other studies which recruited parents largely from clinics or patient support groups(4;5).

Such variation in recruitment may explain high rates of co-morbid diagnoses in BIOS parents. Furthermore, the unexpectedly high rates of substance use, conduct disorders and ADHD in their female probands suggest that the offspring sample may be enriched for genetic susceptibility to these conditions.

Secondly, other studies that used only experienced clinicians to directly assess offspring did not report elevated rates of ADHD in high-risk children (2-6), unlike the BIOS study that employed parental reports. The find that the caregiver-teachers were not able to differentiate high-risk from control offspring raises questions about reliability of the diagnostic information.

Thirdly, the BD criteria in children are not developmentally sensitive and disorders evolve from non-specific to specific. Thus, labeling symptoms in preschoolers as “manic” may be premature until proven to be related to BD. In support, in the Amish study (2) the more “manic-like” symptoms appeared only

later in development; and other studies (2;4-7) failed to find a single case of prepubertal mania. Irritable mood, distractibility, increased activity, poor judgement and unusual energy in preschoolers may not be symptoms of mania, but rather indicators of risk for a variety of future outcomes or a mixture of developmentally appropriate behaviors that ill parents find challenging.

We share the view of Birmaher and colleagues that longitudinal observation over the entire risk period will clarify the natural history of BD in high-risk children.

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