

A Perspective on Prospective Research

Prospective follow-up studies are treasures, especially when used wisely. The three follow-up studies in this issue of the *Journal* allow us to settle some important issues, certainly raise a host of new ones, and, it is hoped, have in their data banks the ability to provide some further answers.

In the article by Schiffman et al., the intriguing methodology developed by Walker et al. (1) is used to code post hoc videotaped observations of the lunchroom interactions of children ages 11–13 for whom subsequent adult diagnoses are available. It is an inspired use of existing data. We don't know why videotapes were initially made, but it seems unlikely it was done originally to test neuromotor development. Managing open-faced Danish sandwiches at lunch can't have been the only methodology available to examine abnormal movements and social interaction in 1971. Nevertheless, although the conclusions are not stunning, they are consistent with myriad other studies—beginning with that of Barbara Fish (2, 3) and now including other prospective studies (4, 5)—that have said that people at risk for schizophrenia have motor oddities. However, beyond the implication of a very early, probably prenatal defect, no one ever explains how, if at all, neuromotor problems relate to a disorder characterized by communication, motivation, interaction, and “reality testing” deficits. Perhaps the signs are only transient, early signals. If so, it would be useful to examine the sensitivity and specificity of such findings, whether they relate to soft neurological signs, and whether they can be used in conjunction with other findings (teacher ratings, parent ratings [6]) to select a population of super high-risk youth for intervention.

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The fact that a videotape of a casual interaction can detect children at risk for schizophrenia because they smile, laugh, and initiate conversation less often than nonaffected peers is amazing. Although the study emphasizes that children were videotaped before the onset of schizophrenia, in fact they were only videotaped before the onset of *psychosis*. It is difficult to know when *schizophrenia* begins. Whether these subtle social features were prodromal (and the subsequent psychosis onset not far off), whether the symptoms were consistent with negative symptoms, and whether the parent with schizophrenia who conferred the risk status had similar symptoms would help us understand the significance of these behaviors. Moreover, one of the complications in understanding the reduced sociability in schizophrenia is disentangling the multiplicity of other symptoms occurring that might reduce a child's social interaction, e.g., their cognitive deficits (7), serious social anxiety, depression, or response to having a mentally ill parent.

Liu et al. in this issue use a relatively stable population, Indo-African and Creole inhabitants of a small island off the coast of Africa, to examine the impact of severe malnutrition on the development of behavior disorders in childhood and adolescence. There is a convincing difference in “antisocial behavior” scores between not horribly malnourished and very malnourished children. Still, in order to understand the real ramifications, it would be helpful to know the kinds of antisocial behaviors being manifested and the effect size between groups. It would be useful to know if there is an age interaction such that the impact of malnutrition increases or decreases with age and if the same subjects are accounting for the findings at all three time points. Given how substantially the sample size drops at age 17, and that subjects with behavior disorder

are likely to be the ones less easily found and agreeable to follow up, such questions may be difficult to answer with these data. Finally, recognizing the importance of both environment and heritability in families with little education (9), one wonders if the IQ mediation is explained by low parent IQ on subsequent child behavior. This is probably heritable and relates both to poor nutritional practice and less competent parenting.

The study by Lahey et al. validates the DSM-IV attention deficit hyperactivity disorder (ADHD) criteria as they apply to preschool children. It is reassuring to know that the predictive validity of diagnostic criteria for newly defined (as it would have been in 1995) ADHD, combined type, remained stable over time in about 80% of children. Current concerns that could be further addressed include the following:

1. Who are the children who *don't* need intervention and will outgrow the ADHD symptoms by mid-elementary school and beyond? How few symptoms are needed before one can reliably predict that this really *isn't* something that warrants intervention? Given the concerns about rising medication use in preschool children (10), it is as important to know when to treat as when *not* to treat.
2. The validity of "cross-situational impairment" in determining the presence of ADHD rests on how much impairment is "enough." For example, consider a 5-year-old who was clearly "impaired" in preschool and kindergarten but not treated by his pediatrician because parents said on interview and rating scales that the child was "fine" at home. It is important to note that the parents *observed* the ADHD behaviors, they just made excuses for them. The child ran out the door at age 2 because "we didn't bolt the door." He never went to the supermarket because he wouldn't stay in the cart. He was sat in front of the television at supper because he wouldn't sit through meals. So there was "some" impairment. Conversely, a parent can tear out her hair and the teacher deny problems, but then one observes the classroom and finds it is extremely well run, with the child mildly symptomatic but the teacher able to manage him.
3. Level of impairment also determines age at onset. An adolescent often presents with recent academic failure because he or she is disorganized, forgetful, and lies about homework assignments that remain undone. No one *complained* earlier but careful questioning reveals *some* symptoms of ADHD (inattentive and even hyperactive, the latter especially in preschool), and inspection of old report cards indicates comments like "Mary is a lovely girl but her overly social nature sometimes interferes with her work." Translation: Mary talks too much, butts into other children's activities, and doesn't finish her work.

I look forward to further treasures emerging from these and other patiently acquired longitudinal data.

References

1. Walker EF, Savoie T, Davis D: Neuromotor precursors of schizophrenia. *Schizophr Bull* 1994; 20:441-451
2. Fish B: Neurobiologic antecedents of schizophrenia in children: evidence for an inherited, congenital neurointegrative defect. *Arch Gen Psychiatry* 1977; 34:1297-1313
3. Fish B, Marcus J, Hans SL, Auerbach JG, Perdue S: Infants at risk for schizophrenia: sequelae of a genetic neurointegrative defect: a review and replication analysis of pandyismaturation in the Jerusalem Infant Development Study. *Arch Gen Psychiatry* 1992; 49:221-235
4. Schubert EW, McNeil TF: Prospective study of neurological abnormalities in offspring of women with psychosis: birth to adulthood. *Am J Psychiatry* 2004; 161:1030-1037
5. McNeil TF, Cantor-Graae E, Blennow G: Mental correlates of neuromotoric deviation in 6-year-olds at heightened risk for schizophrenia. *Schizophr Res* 2003; 60:219-228
6. Olin SC, Mednick SA: Risk factors of psychosis: identifying vulnerable populations premorbidly. *Schizophr Bull* 1996; 22:223-240
7. Munro JC, Russell AJ, Murray RM, Kerwin RW, Jones PB: IQ in childhood psychiatric attendees predicts outcome of later schizophrenia at 21 year follow-up. *Acta Psychiatr Scand* 2002; 106:139-142
8. Kumra S, Wiggs E, Bedwell J, Smith AK, Arling E, Albus K, Hamburger SD, McKenna K, Jacobsen LK, Rapoport JL, Asarnow RF: Neuropsychological deficits in pediatric patients with childhood-onset schizophrenia and psychotic disorder not otherwise specified. *Schizophr Res* 2000; 42:135-144

9. Bartels M, Rietveld MJ, Van Baal GC, Boomsma DI: Genetic and environmental influences on the development of intelligence. *Behav Genet* 2002; 32:237–249
10. Zito JM, Safer DJ, dosReis S, Gardner JF, Boles M, Lynch F: Trends in the prescribing of psychotropic medications to preschoolers. *JAMA* 2000; 283:1025–1030

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