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Diagnostic stability and bipolar disorder in youth

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Although juvenile bipolar disorder is practically a household concept now, this has not always been the case. From a scientific standpoint, for instance, there were no papers on manic depression/bipolar disorder in youth in the *Journal* in the 1960s, there were 3 in the 1970s (two case reports and a case series), 13 in the 1980s, and then a burst subsequently to 90 or so in the 1990s and over 100 in the last decade.

Interestingly, the diagnosis of manic-depression/bipolar disorder in youth has always been a conundrum and considerable effort has been and is being expended validating the condition. Current practice, and a number of articles published in the *Journal* reflect that the major diagnostic stress is the distinction between bipolar disorder and externalizing disorders i.e. attention deficit hyperactivity disorder, and comorbid oppositional defiant disorder. Historically, however, in both adult and child/adolescent psychiatry, the diagnostic confusion was not with behavior disorders. Rather, bipolar disorder in general, and mania in particular, was most often missed in people with psychosis. This was especially true in adolescents where the assumption had been that any psychosis represented schizophrenia. In one of the three *JAACP* articles of the 1970s (before the journal added “and Adolescent” to its name), Carlson and Strober1 pointed this out in a case series of 6 hospitalized teens initially diagnosed with schizophrenia who, upon re-examination of their index episode, and subsequent follow up, were rediagnosed with bipolar I disorder (BP I). Most of the papers in the *Journal* in the 1980s were concerned with lithium use, however the thread of bipolar disorder and schizophrenia was taken up again in 1993 in a larger study of 59 psychotic older children and adolescents (mean age 14± 2). The importance of the study by Werry and colleagues2،3 was that 57% of those initially diagnosed with schizophrenia, were rediagnosed with bipolar disorder at follow-up anywhere from 1 to 15 years later (mean, 4–5 years). The best predictor of outcome was premorbid adjustment and IQ. Clinical features at the time were not very discriminating. It was the longitudinal course that told the tale.

We do not know what ultimately became of the teens in either study, and if they continued to have BP I. We recently learned, though, that in a 10 year follow up of early episode patients ever diagnosed with bipolar disorder, diagnostic inconsistency occurred in half the

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She published her first paper on mania/bipolar disorder during her residency in 1973 and became a child and adolescent psychiatrist to better understand the developmental psychopathology of this condition. She was awarded the Blanche F. Ittleson award for Research and the New York Council on Child and Adolescent Psychiatry's Hulse Award. She is recent past president of the Society for Research in Child and Adolescent Psychopathology and will become Program Chair for the American Academy of Child and Adolescent Psychiatry in 2011.

sample4. In half of these, schizophrenia spectrum diagnoses were the alternative. Much of the diagnostic instability was predicated on change in course of illness. BPI became clearer over time in 17% (as people with psychotic depression developed mania for example), but in the rest, even though BPI seemed obvious early, other conditions emerged. The most powerful predictors of diagnostic instability (i.e. not maintaining a BPI diagnosis) were having any childhood psychopathology (O.R. 2.8, CI 1.4–5.6), specifically having a childhood externalizing disorder (OR 4.7, CI 2.5–8.9), and an insidious (vs acute or subacute) onset (OR 4.2, CI 1.6, 11.2). A non-research, discharge diagnosis of bipolar disorder by the treating clinician (3.2, CI 1.8, 5.9) predicted stability. Age of onset and age at index episode were not predictors. These observations suggest that the more acute and uncomplicated the diagnosis at outset, the more stable the diagnosis; poor premorbid adjustment in terms of childhood psychopathology and non-acute onset predicted diagnosis change. Prognostic implications were substantial as the consistently diagnosed bipolar group had significantly better functioning on GAF ($p<0.001$), spent less time symptomatic over their first 48 months of illness (26% Vs 47%) ($p<0.001$) and much less time psychotic (7% vs 31%) ($p<0.001$).

Interest in the stability of diagnosis of bipolar disorder in adults is surprisingly uncommon (4for review). The NIMH Collaborative Study of Depression5, which has served as a beacon for research on bipolar disorder in adults and children has dwelt on episode duration and percent time ill, but has never addressed what percent of the sample continues to have bipolar illness. The assumption is 100%. Since 55% presented with psychotic symptoms, it is quite possible that the assumption is erroneous.

Diagnostic stability has yet to be addressed in large scale studies of children and adolescents where psychotic symptoms range from a low of 16–22% in the Massachusetts General Hospital data set6 to 34.5% in the Course and Outcome of Bipolar Youth study7, and a high of 60.2% in the study by Geller and colleagues8. Granted most of these subjects have not been psychiatrically hospitalized. However, long term follow up studies of children with psychotic symptoms evidence a very high risk of developing schizophreniform disorders9. While these symptoms were ascertained in a general population, and without reference to whether or not mood symptoms were present, the question remains whether psychotic symptoms occurring in children diagnosed with bipolar disorder portend a different outcome, especially given the fact that their episodes are not acute, rates of comorbidity are extremely high, and all have complicated clinical pictures.

The relationship between child and adult psychopathology is multi-faceted and rarely linear whether the disorders are developmental, or so called “adult disorders” beginning in childhood10. There is no reason why bipolar disorder in youth should be different. The question is for whom is the condition homotypic, for whom is it heterotypic, and in whom does it completely remit? This is important to keep in mind because decisions being made about how to inform parents, and whether or not medication (mood stabilizer or antipsychotic) should be a lifetime commitment are predicated on the unsubstantiated certainty that bipolar disorder is unique in the annals of psychopathology and once any child is labeled with bipolar disorder, the condition is lifelong. Although I have focused on BP I with psychotic symptoms, interest is equally keen for young people with manic symptoms who do not have psychosis.

Clinically, it may be wise to be circumspect about diagnosis in patients with what appear to be symptoms of BPI, especially where there are high rates of childhood psychopathology, poor premorbid adjustment, insidious onset, and psychotic symptoms. Research-wise, I am hopeful that the *Journal* will be the recipient of manuscripts that examine the question of diagnostic stability over time. The methodology will need considerable thought given the

questions in the field about the generalizability of data from one research site to another. In addition, there is merit in doing follow up blind to original diagnosis, but there is equal merit in doing follow up cognizant of prior information so that questions can be asked about the course of specific comorbidities and symptoms.

The long and short of the story, however, is that until we have biological markers that make diagnosis unequivocal, we need to be sensitive to the possibility that diagnoses could change. Given the effort and care that has gone into making a diagnosis in clinical research studies, there is no reason for embarrassment if diagnosis does change in some subjects over the course of follow-up. It would be amazing if it didn't. The crime is only if the door is locked to the possibility that another condition might have evolved.

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