Mood disorders in children and adolescents: coming of age

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We have made considerable headway in our understanding of early-onset mood disorders since 30 years ago, when the prevailing theory was that a child's immature superego would not permit the development of depression. Awareness of early-onset depression has increased in North America with the publication of such texts as *Depression in childhood: diagnosis, treatment and conceptual models*.[1] To date, criteria for diagnosis of early-onset mood disorders remain essentially the same as those in adults, but with some developmental differences. In major depressive disorder (MDD), somatic complaints, behavioural problems, symptoms of separation anxiety and phobias appear more frequently in the younger age group, whereas endogenous symptoms increase with age.[2,3] Comorbidity with anxiety, behavioural disorders and substance abuse is common, emphasizing the importance of both accurate and comprehensive diagnosis.

Longitudinal studies of affectively ill parents show significantly higher rates of affective illness in their children. Weissman et al,[4] in a 10-year study of affectively ill parents and their children, found that prepubertal depression was more common in children with a depressed parent. By year 10, in addition to higher rates of depression, these children also experienced higher rates of phobias, panic disorder and alcohol dependence than the non-ill comparison group. Beardslee et al[5] noted in their 4-year follow-up study that children of affectively ill parents also had earlier onset as well as longer episodes of MDD, with greater comorbidity, than did children whose parents had a nonaffective psychiatric disorder or no current or past history of a psychiatric disorder.

People born in the past several decades are reported to be at greater risk for mood disorders and for onset at an earlier age.[6] Along with a widespread increase in mood disorders, suicide rates in youth have also risen. Increased risk of suicide has been associated with depression and bipolar disorder (BD), anxiety, substance abuse, personality disorder, family history of mood disorders or suicidal behaviour, exposure to family violence, impulsivity and access to lethal methods.[7]

Epidemiological research reviewed and summarized by Birmaher et al[8] indicates that the prevalence of major depression is 0.4% to 2.5% in children and 0.4% to 8.3% in adolescents. Lifetime prevalence rates for MDD in adolescents (15% to 20%) are comparable with the lifetime rate of MDD in adults, suggesting that adult MDD may often be adolescent MDD in a recurrent form. The mean length of an episode of early-onset MDD is 7 to 9 months, with a cumulative probability of recurrence of 40% by 2 years and 70% by 5 years. Dysthymic disorder (DD) has a point prevalence rate of 0.6% to 1.7% in children, and 1.6% to 8% in adolescents. Longitudinal studies of early-onset DD report a mean episode length of 4 years, with an increased risk of developing MDD (70%), substance abuse (15%) and BD (13%). Evidence of a 2- to 3-year time interval between the onset of DD and the

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development of MDD implies that early-onset DD is a "gateway" disorder, and as such provides an opportunity for early intervention and prevention.[9]

The diagnosis and treatment of BD in youth is receiving increasing attention. Approximately 20% of adult patients with BD have their first episode during adolescence, but it is often under- or misdiagnosed in youth despite increasing awareness. Accurate diagnosis is not always apparent, since, phenomenologically, adolescent BD frequently appears different from that in adults; adolescent BD is characterized by higher rates of the mixed form of BD, depressed mood, suicidal ideation and familial mood disorder, and lower rates of psychotic features.[10] Switch rates from MDD to BD in youth still in their teens or early 20s are reported to be from 20% to 30%, significantly higher than the 10% rate reported in adult unipolar depression. This suggests that early-onset MDD can be a serious and evolving form of affective illness.[11] There are few long-term prospective studies of bipolar disorder. Strober et al,[12] in a 5-year naturalistic prospective follow-up study of adolescent inpatients with bipolar disorder, has shown that 44% of patients who recovered from their initial episode had 1 or more relapses of a major affective disorder. The cumulative probability was highest (60%) in those who were cycling at entry. There is a paucity of controlled studies of the efficacy of lithium and anticonvulsants in acute and maintenance treatment of early-onset BD. Lithium is reported to be effective in cases that do not present with mixed affective features, a finding predominantly supported in the adult literature.[13]

Birmaher et al,[14] in their review of pharmacological treatment of early-onset MDD, summarize the overall lack of efficacy of tricyclic antidepressants relative to placebo. The authors report that the studies included small numbers, more mild to moderate depression, a treatment phase of only 6 to 8 weeks, and in some cases insufficient doses. They suggest that a longer period of study could show a greater effect. Placebo responses (50% to 70%) were higher than those found in adults (30% to 40%). This may be associated with unstable affective symptoms, the presence of mild to moderate depression, less melancholic depression and high comorbidity, especially with disruptive disorders. In their review of developmental factors affecting the response of children and adolescents to antidepressants, they note that selective serotonin reuptake inhibitors may be more beneficial than tricyclic antidepressants in this age group, since the noradrenergic system is not considered fully developed until early adulthood. Other age-specific reasons that may explain the lack of efficacy of medications proven effective in adults are the more efficient hepatic metabolism in children, the hormonal changes of puberty and the phenomenological differences from adult depression (e.g., greater transition to BD in this age group). Emslie et al,[15] in an 8-week double-blind study of fluoxetine in 96 children and adolescents, showed a 56% improvement rate relative to placebo (33%). However, in many patients the improvement was only partial, highlighting the continuing limitations of current antidepressant medication and the importance of psychosocial treatments in dealing with early-onset mood disorders.

The potential for high placebo response rates in assessing psychosocial treatment outcome in this population must also be considered. Renaud et al,[16] in their evaluation of cognitive, family and supportive psychotherapies in adolescent depression, address this issue and the possible contribution of spontaneous remission or nonspecific treatment response by differentiating and following the outcome of "rapid responders" to treatment. Rapid responders had better outcome at acute treatment, at 1-year follow-up, and in some cases at 2-year follow-up, and emerged as a group with less severe MDD than initial nonresponders. In the supportive therapy group, adolescents either responded quickly or not at all, contrasting with cognitive-behavioural therapy and family therapy, in which a substantial proportion eventually improved. The authors suggest that the use of a placebo run-in period or a brief course of supportive therapy might be a means to "wash out" nonspecific responders, permitting better evaluation of treatment-specific effects in adolescents.

As our understanding of mood disorders in children and adolescents comes of age, we are well aware that they occur frequently and often in a recurrent or evolving form. Our current knowledge of their natural course points to the importance of identifying those at risk and determining appropriate primary, secondary and tertiary prevention strategies. The often familial nature of these disorders creates an opportunity for early identification of those at risk and emphasizes the importance of family-based interventions. Despite the burgeoning research in the field of genetics and mood disorders, there is a relative paucity of studies that have investigated mood disorders from the "bottom up," using childhood probands. The interplay of biologic and psy-

chosocial processes in the development of these disorders requires further investigation. Increasing community awareness of the frequency and severity of these disorders, addressing alternative "youth-friendly" means of access to interventions to deal with the stigma of mental illness,[17] and advocating for a public health policy that incorporates prevention strategies, will continue to require emphasis.

The challenge when evaluating treatment outcome in early-onset mood disorders is to consider developmental differences, and not necessarily apply adult paradigms or research designs to the study of mood disorders in children. As we become more aware of the distinct differences between adult and early-onset mood disorders and their treatment response, it is apparent that our approach must be considered and evaluated from a developmental perspective. Geller et al[18] caution that treating MDD with antidepressant therapy in children with a potential bipolar disorder may precipitate or worsen rapid cycling. In their commentary on developmental pharmacodynamics, Carrey and Kutcher[19] emphasize the need for greater understanding of the impact of prescribing psychoactive medication on the developing central nervous system. We must be mindful of these caveats in our treatment of children and adolescents with mood disorders.

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