Overview of Pediatric Bipolar Disorder and Severe Mood Dysregulation

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DSM-IV sets out the criteria for bipolar disorder with two fundamental components—1) the presence for 4-7 days of episodes of irritable or elated mood that reflect a change from baseline functioning, and 2) the simultaneous occurrence of changes in behavior during the period of irritable or elated mood. Beginning in mid-1990s, developmental modifications in the practice of applying DSM-IV criteria resulted in a substantial increase in the diagnosis of pediatric bipolar disorder (PBD). The rise in the prevalence of this diagnosis in children and youth continued through the first decade of 2000, reaching a 44-fold increase in the prevalence by the end of the decade when compared to the rate at the beginning of the first decade. Two developmental modifications contributed to this change. One was that severe irritability alone was sufficient to waive the criterion for episodes of mood. A second was that “episodes” of bipolar disorder might be so brief in children that the duration criterion should be waived. As a result, frequent episodes of tantruming, aggression, and/or explosive behavior in context of chronic irritability became sufficient for many clinicians to consider a child to have PBD.

Recent work has suggested that children displaying a chronic pattern of irritability plus the relatively non-specific “B” symptoms of mania (e.g. pressured speech, flight of ideas, distractibility, recklessness, insomnia) have a different course, family history, and outcome from those with PBD. Such children have been described as suffering from Severe Mood Dysregulation (SMD). Data emerging from studies that compare children with SMD to those with PBD find, that, although they are as impaired as children with PBD, those with SMD have much less of a family history for bipolar disorder among first degree relatives. Also it appears that SMD is not the “leading edge” for development of classic bipolar disorder in adulthood. SMD does convey a significantly higher risk for developing depression in adulthood. Psychophysiological and imaging studies suggest that those with SMD may share some features with PBD, but on many tasks, such as those with emotion/attention, reversal learning, and response flexibility paradigms, performance of those with SMD differs from children with PBD.

One of the significant clinical implications of considering SMD to be a separate diagnostic entity from PBD is that these two conditions show different response to medications. A recent double blind placebo controlled trial showed that, in contrast to PBD, SMD did not respond to lithium carbonate. Further work suggests that certain agents should be used with extreme caution in BPD, such as stimulants for ADHD, or serotonin reuptake inhibitors for anxiety. If SMD is not the same as PBD, then judicious application of these agents for symptoms of ADHD or anxiety, respectively, could be an important consideration.

Currently there are FDA indications for lithium (>12 yo), aripiprazole, quetiapine, risperidone (all for >10 yo), and olanzapine (>13, as a second line drug) all for treatment of acute mania. Although divalproex is commonly use for acute mania and maintenance prophylaxis, there is little evidence for efficacy in children and
adolescents. The only double blind trial was a discontinuation study comparing lithium and divalproex. The results suggested equivalent efficacy of these agents.

A recent study of long acting divalproex (Wagner et al., 2010) for acute mania showed no difference from placebo. Other commonly used anticonvulsant-type agents, such as, topiramate, levotiracetam, and carbamazepine, have no studies employing double-blind placebo-controlled methods in children to support their use for acute mania or prophylaxis. A double blind placebo controlled trial of oxcarbazepine (Wagner et al., 2006) also failed to show a difference from placebo. Since SMD is a new designation, the indications and agents for treating it can only be sought from literature on symptom components. There is a great deal of evidence to suggest that symptoms of inattention, impulsivity, and restlessness will benefit from ordinary stimulants such as methylphenidate and dextro-amphetamine, and their different analogs, as well as weaker but relevant evidence for atomoxetine. In addition, there is emerging evidence that stimulants alone will decrease aggressive behavior in children with ADHD and aggression (Blader et al., 2010). Similarly, for anxiety, which may be very common in children with SMD, there is good evidence for efficacy of SSRI agents (Birmaher et al., 2003; RUPP, 2001; Rynn et al., 2001; Walkup et al., 2008). Fluoxetine has support for treating depression in children although the response rates are relatively weak (March et al., 2004). A recent study suggested that oppositional behavior in the context of depression may also respond to fluoxetine (Jacobs et al., 2010). For outbursts and aggression the data can only be drawn by analogy to autism spectrum disorders and direct studies of aggression in children. The data point to divalproex (Blader et al., 2009) and low doses of risperidone (Aman et al., 2001; McCracken et al., 2002 and others) or aripiprazole (Marcus et al., 2009; Owen et al., 2009) as potentially useful. There is no evidence for efficacy of other anticonvulsant drugs (See Huband et al., 2010).

There are reasons to believe that psychological treatments could be quite effective for SMD, in combination with medication or alone (Sukhodolsky, et al., 2009), but the data is very limited (Hassiotis et al., 2009). It is too soon to know which treatments will be most effective, but it is important to underscore that pharmacological treatment should not be the only one in a clinician’s armamentarium to treat these conditions. Hopefully more clinical trials and effectiveness studies will be forthcoming soon.

References


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