Review Article :

CHILDHOOD BIPOLARITY: A REVIEW

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ABSTRACT:

Mood disorder, in form of both depression and bipolar variant is known since antiquity though by different names at different time. Like most of the mental disorders the focus always hovered around the adult population and 'pediatric' or 'childhood' bipolar disorder remained neglected. Though, recent workers have identified 'childhood variant' as gateway to understand the pathophysiology of bipolar disorder better. Current review is an attempt to delineate the historical aspect of childhood bipolarity, highlight the difference from adult bipolarity and summarise the treatment with special reference to pediatric population.

Keyword: ***childhood bipolar disorder, pediatric bipolar disorder, treatment.***

Mood disorders have a long pedigree, traceable from classical antiquity to the modern era. Early clinical observations between the mid-19th and early 20th centuries accepted the presence of mania and clinical depression in children and adolescents, but from the 1930s to the recent past, BPD was widely considered rare before puberty. In 1838 Esquirol described three cases of prepubertal mania and melancholia. In the 1880s, Moreau de Tours described excited psychotic states in children, Ritti (1883) reported a paediatric case of circular psychosis (now BPD) starting at age 12, and Emminghaus (1887) and his contemporaries (Porot & Vicario-Kiener, 1961) noted many symptomatic similarities between adult and pediatric mania and melancholia. Between 1900 and 1910, Soukhanoff & Gannouchkine (1903) found an onset before age 15 in 18% of 84 BPD patients, and Friedman (1909) distinguished three types of pediatric BPD:

-periodic psychosis with brief alternating episodes of depression and manic excitement and short euthymic intervals;

-isolated episodes of depression or excitement, sometimes related to stress;

-and brief episodes of mild depression or excitement progressing to more typical cyclic BPD in adulthood.

Other authors, (Baruk & Gevaudan, 1937; Rumke, 1928; Ziehen, 1911) anticipating recent studies of secondary mania, (Baldessarini, *et al.*,1996) observed isolated episodes of mania in medical conditions such as fever or neurological disorders (epilepsy, chorea, mental retardation). In his seminal early textbooks, Ziehen (1911) classified BPD in children as involving single or recurring episodes of mania, or circular (bipolar) insanity, more commonly the latter. In the 1920s, Rumke (1928) described mania as the most frequent psychosis in children; and Homberger (1952) noted the frequent occurrence of anxiety and of mixed mood states in children with BPD. Since midcentury, several series of early onset BPD cases have been reported. In 18 cases of major mood disorder before age 16 years, Campbell (1952) found that a third represented BPD, that mild depression or mania were often misdiagnosed as other illnesses, and that many children severely ill with BPD had been diagnosed as schizophrenic. In children under age 11 with BPD, Spiel (1961) reported rapid mood shifts, irritability, anxiety or apathy, and disturbed sleep to be common, and Stutte (1963) found episodes to be shorter than in adults.

To expand and accelerate research on mood disorders, the National Institute of Mental Health (NIMH) (NIMH, 2001) developed a project to formulate a strategic research plan for mood disorder research. One of the areas selected for review concerns the development and natural history of these disorders. Expanded knowledge of pediatric-onset bipolar disorder identified was as a particularly pressing issue because of the severity of the disorder, the controversies surrounding its diagnosis and treatment, and the possibility that widespread use of psychotropic medications in vulnerable children may precipitate the condition. The Workgroup recommends that NIMH should establish a collaborative multisite multidisciplinary Network of Research Programs on Pediatric- Onset Bipolar Disorder and identify several pressing questions and three high-priority recommendations

for better understanding early-onset bipolar disorder. The first of these recommendations, to establish a Collaborative Network of Research Programs on Paediatric-Onset Bipolar Disorder, judged the most important of the seven recommendations made by the Workgroup. Questions identified include the following: How common is bipolar disorder in children? How does it differ from adult-onset bipolar disorder? What are the earlier signs and symptoms of paediatric bipolar disorder? What is the relationship of ADHD and other disruptive disorders to paediatric-onset bipolar disorder (Costello, 2002)?

While it is clear that relatively few children have a classic adult-like presentation of bipolar disorder (BD), children with severe irritability, hyperactivity and distractibility are exhibiting a "broad phenotype" of PBD (Leibenluft, Charney, Towbin et al., 2003; NIMH, 2001). Nonetheless studies of children with either classic BD symptoms or the "broad phenotype" suggest that PBD is both markedly impairing and treatment-resistant, increasing the demand for relevant information and research (Biederman, Faraone, Wozniak et al., 2005a)

Clinical Presentation

The Course of Bipolar Youth (COBY) study in the USA recruited 263 children with clearly episodic bipolar illness (Axelson, Birmaher, Strober et al., 2006). Of the children in the COBY study, 92% had euphoria and 84% had irritability, indicating that most youth with PBD have both symptoms. Over 2-year follow-up, patients (n = 152) had mixed mania or rapid cycling 29% of weeks, significantly more than BD adults (Birmaher, Axelson, Strober et al., 2006). In another sample of 90 children with clearly episodic BD, 86% had elevated mood, while 92% had irritability; also, 50% had a rapid cycling course, and periods of euthymia were identifiable but brief (Findling, Gracious, McNamara et al., 2001).

Thus conclusions can be drawn from the literature on the phenomenology and course of PBD. First, data from the COBY study and Findling, Gracious, McNamara et al. (2001), contradict frequent statements in the literature that children with BD do not have euphoria, because almost all patients in these studies experienced euphoria, in addition to irritability. studies support the contention that early-onset BD is associated with high episode frequency (Birmaher, Axelson, Strober et al., 2006; Findling, Gracious, McNamara et al., 2001. The data do not indicate that children with BD have a non-episodic illness, because several investigators have recruited sizable samples of children with clearly defined episodes meeting DSM-IV duration criteria. And consistent with the observation that children tend to cycle more frequently than adults with BD, all studies agree that PBD is a very impairing illness, leaving affected children symptomatic most of the time.

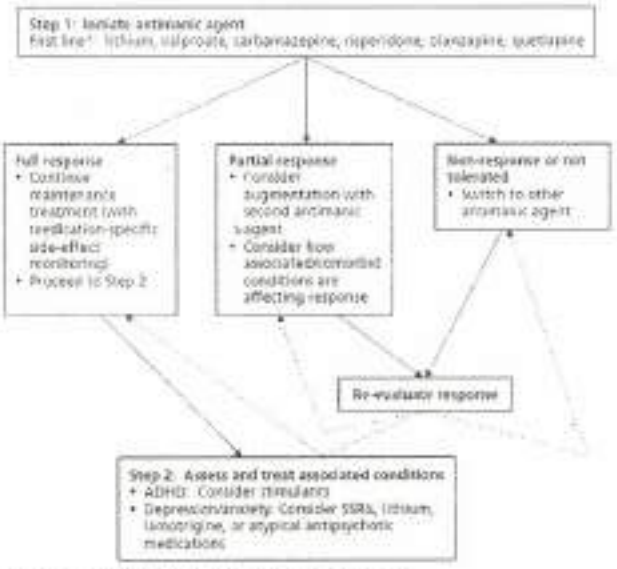
Assessment

When assessing comorbid illnesses, clinicians should diagnose such illnesses only if symptoms are present when the patient is not in an acute mood episode (Axelson, Birmaher, Strober et al., 2006; Dickstein, Rich, Binstock et al., 2005b). For example, a child with BD should be diagnosed with ADHD only if ADHD symptoms are present when he or she is euthymic or subsyndromally ill. Conversely, for a symptom such as distractibility to count toward the diagnosis of mania in a child with ADHD, the distractibility must worsen significantly during the putative manic episode. ADHD can be distinguished from mania in those children with ADHD alone do not have distinct episodes of mood change accompanied by DSM-IV-TR "B" criteria of mania. Similarly, BD youth with associated ADHD and oppositional defiant disorder (ODD) may have severe irritability, but irritability resulting from ADHD or ODD is distinct from manic irritability in that only the latter occurs, or worsens, during distinct time periods that last days or weeks and during which "B" mania criteria also occur. (DSM-IV-TR "B" symptoms of mania or depression (e.g., sleep and activity changes, increased distractibility)) adolescents should be assessed for substance abuse, because cocaine, amphetamine and a number of other illicit substances can cause symptoms resembling those of mania.

Treatment Guidelines For Paediatric Bipolar Disorder

These treatment guidelines arose out of a need first voiced by members of the Child and Adolescent Bipolar Foundation (CABF), who noted that clinicians who treat children and adolescents with bipolar disorders (BPDs) are in desperate need of guidelines regarding how to best treat these patients. In July 2003, a group of 20 clinicians and CABF members met over a 2-day period to develop these guidelines. There were four work groups: diagnosis, led by Mary Fristad; comorbidity, led by Boris Birmaher; and treatment, in two groups led by Karen Wagner and Robert Findling, respectively. These guidelines are not intended to serve as an absolute standard of medical or psychological care but rather to serve as clinically useful guidelines for evaluation and treatment that can be used in the care of children and adolescents with bipolar disorder. (Findling et al., 2005)

Clinicians attempting to prescribe evidence-based treatment for PBD are confronted by a dearth of randomized placebocontrolled trials (RCTs) that precludes designating any psychopharmacological or psychotherapeutic treatment as having "strong" evidentiary support. Given the paucity of pediatric data, clinicians often rely on data from adult BD. However, caution is urged in basing treatment on adult data, because youth sometimes respond differently from adults. children clearly meeting DSM-IV-TR criteria for bipolar disorder who, like adults with the illness, are typically too severely impaired to benefit from psychotherapeutic approaches without initial stabilization with pharmacotherapy. This is the population that is generally targeted in RCTs of medications. In children exhibiting the "broad phenotype" of PBD, whose major presenting problem is non-episodic irritability, psychosocial approaches, including interventions with the child, family and school environment, may be particularly important.



Pediatric bipolarity psycho-pharmacology algorithm. Kowatch *et al.* (2005a).

Pharmacotherapy of Mania

Mania should be the initial treatment focus in BD, because antimanic medications not only reduce manic symptoms but may also prevent activation secondary to antidepressants or psychostimulants. Currently available antimanic medications include: Lithium, Antiepileptic medications (AEDs, e.g. valproate and carbamazepine) and atypical antipsychotic medications. In general, relatively weak support exists concerning the efficacy of any of these agents in PBD. This complicates efforts to select any one agent as a first-line treatment and emphasizes the importance of thorough discussions with patients and their families concerning the available data on each agent's efficacy and safety. The detailed discussion of individual agent is beyond the scope of this review.

Pharmacotherapy of Depression in PBD

No RCT has targeted bipolar depression in children or adolescents.RCTs in adult bipolar depression demonstrate efficacy for lamotrigine, quetiapine and the combination of olanzapine plus fluoxetine (Altshuler, Suppes, Black et al., 2003). Of note, some evidence suggests that the risk of antidepressant-induced mania is higher in pre-pubertal children than in older adolescents or adults (Martin, Young, Leckman et al., 2004; Rey & Martin, 2006).

Treatment Of Comorbid Psychiatric Disorders

Most children and adolescents with BPDs have other coexisting (comorbid) psychiatric disorders, particularly ADHD, oppositional defiant disorder, conduct disorder, anxiety disorder, and, during adolescence, substance abuse. The treatment plan should be modified to include treatment of each disorder because comorbid conditions worsen the prognosis of BPD. Before treating the comorbid disorder(s), it is important to first stabilize the symptoms of BPD. Once the bipolar symptoms are stabilized, the need for treatment of comorbid disorders should be reviewed. If the symptoms of the comorbid condition(s) are negatively affecting the child's psychosocial or academic functioning, then treatment is warranted. Whenever appropriate, using psychosocial therapies to treat coexisting disorders is recommended (e.g. using CBT to manage depression).

Although it is important to treat most of the impairing comorbid symptoms as soon as possible, it is best to begin treatment for each comorbid disorder sequentially, one at a time after the BPD has been adequately treated. It is recommended to introduced medications one at a time, if possible, to discern the benefits and side effects of each agent.

Attention-Deficit/Hyperactivity Disorder

ADHD is one of the most common comorbid conditions, occurring in 70% to 90% of prepubertal children

and 30% to 40% of adolescents with BPD (Kafantaris *et al*, 1998;). Currently, the medications used to treat ADHD include the stimulants (methylphenidate and derivatives of amphetamine) and nonstimulants (atomoxetine, bupropion, the tricyclic antidepressants), and to a lesser extent the a2-agonists (clonidine and guanfacine) (Biederman *et al*, 2004). Of all these medications, stimulants are the agents of choice for ADHD uncomplicated by BPD. Apha 2-agonists are helpful for the aggressive behavior in children with ADHD (Connor *et al*, 2002).

Oppositional Defiant and Conduct Disorders

If a child has BPD and the behavior problems appear to be secondary to the mood disorder (mania, depression, or both), the panel recommended first optimizing the treatment of the BPD. medications used for the treatment of BPD such as lithium and divalproex (Steiner *et al*, 2003), the first generation of typical antipsychotics, and the atypical antipsychotics have been found useful for the management of behavior disorders, Importantly, many children with behavior disorders have ADHD; in these cases, the use of the stimulants may be warranted, particularly in the reduction of aggression. (Biederman *et al*, 2004).

Anxiety Disorders

Comorbid anxiety disorders can be treated using psychotherapy and/or pharmacological interventions. The SSRIs have also been found to be efficacious for the treatment of these disorders, but caution should be used because these agents may trigger manic, mixed, or rapid cycling episodes. Therefore, in most cases, particularly in patients with BPD-I, before attempting to use SSRIs to alleviate the anxiety disorder, it is advisable to first stabilize the BPD. The benzodiazepines have been shown to be efficacious for the treatment of adult anxiety disorders, but only a few studies with small samples have been conducted in children with anxiety (Bernstein & Shaw, 1997).

Substance Abuse

It is important to determine whether the mood symptoms were present before substance abuse began or if the mood changes are the result of substance abuse. If it is clear that the person has both substance abuse and BPD, both conditions need to be treated simultaneously without delay. A placebo-controlled trial in adolescents with comorbid BPD and substance dependence disorders showed that lithium was an efficacious treatment for both disorders (Geller *et al*, 1998). A number of family-related factors, such as parental alcoholism or other substance abuse, poor parent–child relationships, low parental support, inconsistent or ineffective discipline, and poor parent supervision and management of the teen's behavior, have been identified as risk factors for the development of substance abuse among teens.

Management of Suicidal Behaviors

First step is to evaluate whether the child is safe and whether the treatment needs to be carried out in an outpatient or inpatient setting. The data regarding long-term use of lithium are compelling: It is associated with an eightfold reduction in suicide and reported attempts in adults with BPD (Baldessarini & Jamison, 1999). Specific psychosocial therapies for the management of ongoing suicidality such as dialectic behaviour therapy, if available, should also be considered (Rizvi & Linehan, 2001).

Pervasive developmental disorders (PDD)

Patients with paediatric bipolar disorder and PDD should be initially treated with an atypical antipsychotic (e.g. risperidone), and mood stabilizers should be added as necessary. The use of other medication to target other PDD symptoms should be considered, taking into account that some medications may destabilize mood. Patients should be referred to an appropriate PDD programme when available.

Migraine or epilepsy

For those with paediatric bipolar disorder and seizures or migraines, the mood stabilizer chosen should be an anti-migraine agent (eg. carbamazepine, valproate).

Other Psychiatric and Medical Conditions

Youths with BPD who are experiencing significant tics and who have behavioural symptoms associated with PDD should be initially treated with an atypical antipsychotic, and other mood stabilizers should be added as necessary. For youths with seizures or migraines in addition to BPD, medications that target both disorders, such as divalproex, carbamazepine, and oxcarbazepine should be tried first. Female patients with significant premenstrual dysphoria may be offered SSRIs after mood stabilization with lithium, divalproex, or other mood stabilizers.

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