

# Attention deficit hyperactivity disorder and bipolar mood disorder in children and adolescents

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Attention deficit hyperactivity disorder (ADHD) is one of the most prevalent and widely studied disorders of childhood.<sup>1</sup> On searching the literature, thousands of articles are found on all aspects of this disorder, including its diagnosis, co-morbidities, longitudinal course and management.

Bipolar mood disorder (BMD) has traditionally been seen as an adult disorder and has only been described in children since the last decade of the 20th century.<sup>1,2</sup> In the past 10 years, the number of children being diagnosed with BMD has more than doubled, with more than 100 000 children in the USA receiving treatment for BMD in 2001 in spite of the uncertainties that still surround its diagnosis in children.<sup>3</sup>

The following problems regarding the diagnosis of BMD in children can be particularly vexing for clinicians working with these patients:

- Diagnostic validity and diagnostic criteria for BMD in children. The course in children, especially prepubertal children, seems to feature more rapid cycling and mixed episodes than in adults, with fewer children having a classic presentation.<sup>4</sup>
- There are considerable differences in the reported incidence of BMD between different studies and countries.<sup>4</sup>
- There is significant symptoms overlap between BMD and other disorders, such as ADHD, in children.<sup>5</sup>
- Co-morbidity in children with psychiatric illness seems to be the rule.<sup>6,7</sup>
- There is a lack of treatment studies to use as an evidence base for the treatment of BMD in children.<sup>8,9</sup>

ADHD and BMD can very easily be confused with one another and are frequently reported to be co-morbid conditions.<sup>2,3,10</sup> Community samples of children with ADHD show that affective illness is present in up to 60% of children diagnosed with ADHD.<sup>2</sup> Approximately 23% of children diagnosed with ADHD also meet the diagnostic criteria for BMD.<sup>2,3,7</sup> Prepubertal children with

BMD almost all also meet diagnostic criteria for ADHD, with this figure falling to 57% in adolescence.<sup>2,3,10</sup> In adults with BMD the comorbidity with ADHD is 13%.<sup>2</sup> Adding to the diagnostic confusion, it has also recently been recognised that children as young as 5 or 6 years of age may present with symptoms of BMD.<sup>4,10</sup>

The lay press also abounds with books and articles on childhood-onset BMD, as well as books related to ADHD. This leads to more and more parents diagnosing their own children and making the clinician's job even more complex.

## Diagnostic overlap between ADHD and BMD

There is significant diagnostic overlap between the diagnostic criteria for ADHD and BMD that can cause diagnostic uncertainty. A number of criteria are similar or produce similar results in terms of behaviour<sup>5</sup> (see Table 1 for selected diagnostic criteria).

There are additional clinical features commonly found in children suffering from ADHD that do not form part of the formal diagnostic criteria. These features may help to create a picture similar to that seen in BMD.<sup>5</sup>

- Low tolerance of frustration, leading to a picture of irritability
- Temper outbursts unwarranted by the situation
- Excessive insistence on requests being met immediately and difficulty in delaying gratification
- Symptoms vary according to different situations, leading to a picture similar to that of the mood swings seen in BMD.

## Neurobiology of attention and mania

The catecholamine neurotransmitters dopamine (DA) and norepinephrine (NE) have the best-documented roles in attention, concentration and associated cognitive functions (motivation, interest and focused arousal acting as the executive functions). The prefrontal noradrenergic pathways play an important role in sustaining and focusing attention, mediating energy, fatigue, motivation and interest. The mesocortical dopamine pathways are important for mediating cognitive functions such as verbal fluency,

**Table 1. Diagnostic criteria for ADHD and BMD**

ADHD	BMD
Difficulty sustaining attention	Distractibility
Often runs about or climbs excessively	Increase in goal-directed activities
Difficulty playing quietly	Seeking of potentially harmful pleasurable activities
Acting as if 'driven by a motor'	Decreased need for sleep
Blurts out answers	Pressure of speech
Difficulty in organising	Flight of ideas
Cannot wait turn	Insomnia
Often interrupts	Irritable mood

serial learning, sustaining vigilance and focusing attention, prioritising behaviour and modulating behaviour. A deficit of DA in the prefrontal cortex, which it has been suggested is the case in patients suffering from ADHD, may lead to inattentiveness. In states of 'hyperarousal' (as is postulated happens in the manic state) one likewise finds a decline in cognitive function due to an inability to concentrate.<sup>11</sup>

There are two interacting systems involved in attending and sustaining attention in the human brain. The posterior system, localised to the superior parietal cortex, the superior colliculus and the pulvinar, orientates to and engages with novel stimuli. It receives dense NE innervation from the locus coeruleus which inhibits the spontaneous activity of postsynaptic neurons, thereby increasing the signal-to-noise ratio of target neurons (i.e. orientation).

The anterior system in the prefrontal cortex and the anterior cingulate serves the executive system. It is modulated by ascending DA fibres from the ventral tegmental area. DA suppresses spontaneous activity of target neurons and reduces their responsivity to new inputs (i.e. better focusing).<sup>11</sup>

The neurobiological basis of mania is less well understood, but overactivity of DA, NA and/or serotonin (5HT) systems in the supra-orbital frontal cortex and glutamatergic overactivity are postulated to play a role.<sup>12,13</sup> Brain-derived neurotrophic factor (BDNF) is being investigated as a possible underlying factor in the development of mania.<sup>14</sup> BDNF is implicated in a variety of intracellular mechanisms that may be associated with the development of mania, e.g. mitogen-activated protein kinase, phosphatidylinositol 3-kinase and phospholipase C alpha signal pathways. Both lithium and valproate increase BDNF levels.

Glutamate has also been implicated in the development of mania.<sup>15</sup> Excess excitation from glutamate may lead to mania

or panic and may eventually lead to excitotoxicity and neuron damage.<sup>15</sup>

Children diagnosed with ADHD experience problems in the neurocognitive domains of motor control and working memory, difficulties with time perception, difficulties with inhibiting or delaying behavioural responses and ongoing processing and naming speed deficits.<sup>1</sup> Adult literature regarding BMD indicates neuropsychological problems experienced in the domains of working memory, spatial and sustained attention, problem solving, poor visual and spatial orientation and impaired executive functioning.<sup>1</sup>

Looking at the current knowledge regarding the neurobiological basis for both disorders, it is therefore clear that symptom overlap is to be expected.

### Clinical differentiation between ADHD and BMD in children

The first important aspect to take into consideration regarding the differentiation between BMD and ADHD in children is the family history regarding illness.<sup>6</sup> Although a negative family history of BMD does not exclude the diagnosis of BMD in children, the presence of this diagnosis in first-degree relatives strongly suggests that this may be the correct diagnosis.

In children with BMD there is more likely to be a history of discrete periods of elevated energy (90% of children diagnosed with BMD report this phenomenon) than in children diagnosed with ADHD.<sup>2</sup> Children with ADHD are always on the go and driven and do not show these periodic increases in energy and activity levels.

The symptom of irritability is for child psychiatry what the symptom of fever is for general paediatrics. It indicates a problem, but has no diagnostic value in and of itself. Other childhood psychiatric

disorders in which irritability may play a key role include the pervasive developmental disorders, mental retardation and adjustment disorders.<sup>3,10</sup> The mood of children presenting with BMD is more likely to be irritable than elated.<sup>3,10</sup> ADHD can likewise be associated with irritability and mood lability. For diagnostic purposes the quality of the irritability presents the key to differentiating the disorders. Children suffering from BMD have more frequent, more severe and more unpredictable mood 'swings'. An elevated mood, when present, helps to confirm a diagnosis of BMD, but its absence does not exclude the diagnosis.<sup>2,3,16</sup>

Depressed mood is more likely to be present in children presenting with BMD than children with ADHD.<sup>3,10</sup> One-third of children diagnosed with BMD will initially present with a depressive episode.<sup>10</sup> Children with BMD also have higher rates of co-morbid oppositional defiant disorder and anxiety disorders than children with ADHD.<sup>10</sup>

Grandiosity is seen in the majority of children with BMD (up to 4 out of 5 children being reported in the literature), but a significant number of children do not have this symptom.<sup>2,3</sup> Grandiosity is also often seen in other disorders that are associated with antisocial behaviour, such as conduct disorder.<sup>3</sup> In young children it may be difficult to distinguish between grandiosity and developmentally normal imagination. Adolescents with narcissistic personality constructs may also present with an inflated self-esteem. Fluctuations in grandiosity seem to be more promising in differentiating paediatric BMD from children suffering from ADHD.<sup>3</sup> Children with ADHD tend to have poor self-esteem and even if they are confident on the outside, interviewing them will often show up the self-doubts that they experience due to experiencing consistent failure. Children with co-morbid ADHD and conduct disorder may present with elevated self-esteem.

Hypersexuality (or an increased interest in sexual matters) is highly specific to paediatric BMD,<sup>3</sup> but this symptom is present in less than half of children diagnosed with BMD. When present in the absence of a history of sexual abuse this is a highly specific symptom for the diagnosis of BMD. A decreased need for sleep is similarly specific for BMD, but not very sensitive.<sup>2,3</sup> Decreased need for sleep needs to be differentiated from the bedtime resistance that often accompanies ADHD in children.

Flight of ideas is seen in about 57% of children with BMD,<sup>3</sup> and this symptom is specific to BMD.<sup>2</sup> The presence of psychosis in children should likewise prompt one to look for mood disorders as a possible cause of the psychosis, as mood disorders are a frequent cause of psychotic phenomena in children.<sup>3</sup> ADHD

is usually not associated with psychotic symptoms, although treatment with stimulant medication may lead to psychotic symptoms as a side-effect.<sup>8,9</sup>

Symptoms that are not helpful in differentiating between BMD and ADHD are difficulty in concentrating, high motor activity and aggression.<sup>3</sup> Aggression in ADHD more often than not takes the form of impulsive anger when needs are not met. In BMD more constant irritability seems to be present.<sup>2</sup> The aggression seen in BMD is more likely to be vicious, attacking and hostile (described as an emotional meltdown), and the anger outbursts may last for days.<sup>2</sup>

The course of ADHD is more chronic than that of BMD. Children suffering from BMD usually experience cycling mood changes.<sup>2</sup> These cycles, however, tend to be present over extended periods of time and are often ultradian (multiple cycles occurring within a 24-hour period).<sup>3</sup> The presentation of symptoms in ADHD is more stable over a period of time.<sup>3</sup> Both disorders change over time and it is important to realise that the earlier the onset of BMD, the less like that of classic bipolar disorder the presentation is.<sup>3</sup>

A family history can help in differentiating between BMD and ADHD, as in both disorders genetic factors have a significant contribution.<sup>2,3,10</sup>

Neurocognitive tests can help to fill in the picture if there is still uncertainty as to the correct diagnosis after taking a thorough history and doing a mental status examination. Children with BMD were found to be less impaired in the neurocognitive domains of processing speed, automatised naming speed, memory and executive functions than children diagnosed with ADHD.<sup>1</sup>

In personality structure and temperament, children with BMD are more likely to be high novelty seeking with lower reward dependence, lower persistence, less self-direction and lower cooperativeness than children with ADHD.<sup>3</sup>

It is clear from the above descriptions that no single symptom can be said to indicate the presence or absence of BMD or ADHD. The full clinical picture needs to be taken into consideration. A fluctuating course of later onset is more suggestive of BMD than of ADHD, in which symptoms must be present before the age of 7 years and where the course is more stable.<sup>5</sup> The presence of increased sexual interest is a great help in making the diagnosis of BMD, as is the symptom of grandiosity. Irritability is not a good indicator of difference, as it is the quality of the irritability that is important and this is difficult to judge in the clinical situation. Often time and continued consultations are necessary before a final diagnosis can be made with certainty.

## Management of co-morbid ADHD and BMD

As always in psychiatry, a biopsychosocial management approach should be followed. Although there are no proven psychosocial interventions for the management of BMD,<sup>17</sup> there are strategies that can be helpful. In general parents need to be equipped with knowledge regarding BMD and they need to be taught strategies for becoming effective mentors for affected children.<sup>17</sup> Adolescents diagnosed with BMD will also benefit from strategies that enable them better to understand their disorder, the medication used to treat it, and how to manage stress and promote good family relationships.<sup>17</sup> Psychosocial treatments may be of great benefit for treating co-morbid conditions such as anxiety disorders or disruptive behaviour disorders.<sup>6</sup>

Conversely, the management of ADHD with psychosocial methods have been shown to be successful and a number of approaches are available to clinicians.<sup>18</sup>

Lithium is the only mood stabiliser approved by the Food and Drug Administration of the USA for use in young people aged 12 years and older for acute mania and maintenance treatment of BMD.<sup>19</sup> However, the literature suggests that combinations of mood stabilisers are often needed to treat children with BMD.<sup>8,10,20</sup>

Second-generation antipsychotic medication is being used increasingly often as first-line treatment for children with BMD.<sup>10</sup> After mood symptoms have been stabilised, the addition of stimulant medication to treatment may help if symptoms of inattention are still present.<sup>10,19</sup> The combination of lithium carbonate and stimulant treatment has been shown to be both effective and safe for children with co-morbid ADHD and BMD.<sup>7,21</sup>

Carbamazepine is not often used for young people with BMD,<sup>8</sup> but may merit consideration as it can also be used as a second-line treatment for ADHD.<sup>9</sup>

The combination of psychopharmacology with behavioural and psychosocial interventions is generally necessary for the adequate treatment of both disorders.<sup>19,21</sup> Family interventions are very important for children suffering from both ADHD and BMD. Families in which mood disorders have been diagnosed show disrupted functioning, an increased rate of conflict within the family, and high expressed emotions.<sup>3</sup> If parents are also diagnosed with ADHD, they may be unable to structure their child's world adequately without help.

Where ADHD is thought to be the primary diagnosis, treatment with stimulant medication should be initiated. If the response

is poor, or if mood symptoms become more prominent, mood stabilisers can be added to the treatment.

## Conclusion

Differentiating between BMD in children and ADHD is a challenge to most physicians working in the field of child and adolescent psychiatry. However, by looking at the whole presentation and considering every piece of evidence it is possible to make an accurate diagnosis. It is only by differentiating correctly and treating these children adequately with the correct methods that we can ensure the best adult outcome.

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