The Development of New Diagnostic Criteria Sets for Pediatric-onset Bipolar Disorder: An Overview

Core Phenotype - Research Diagnostic Criteria

In 2001, the NIMH Roundtable on pre-pubertal Bipolar Disorder convened a panel of experts to review the growing literature on the prevalence and clinical presentation of pediatric bipolar disorder (PBD) and develop recommendations for future research (Special Communication, 2001). Members of the Roundtable suggested behavioral phenotypes for two groups of children: 1) those that met the adult DSM-IV criteria for mania/hypomania and 2) those that did not. The latter group presented differently from adults, but was severely impaired by symptoms of mood instability. (Biederman et al., 2000a,b; Carlson et al., 1998; Carlson and Kelly, 1998; Wozniak et al., 1995).

These experts additionally recommended that the DSM-IV diagnosis: bipolar disorder, not otherwise specified (BP-NOS) serve as a "working diagnosis" to categorize such children for further study, with the caveat that the dimensions of their impairment, such as attentional deficits, anxiety symptoms, aggression, thought disorder, cognitive impairment, disruptive behaviors, and substance use, be investigated using multiple rating instruments, including the Child Behavior Checklist (CBCL), which could then be calibrated across sites. Future studies were additionally encouraged to track the course of symptoms and features both specific and non-specific to PBD, such as hyperactivity and irritability/dyscontrol, to determine their status as symptoms of comorbid disorders, prodromal signs, or symptoms of bipolar disorder as it appears in youth.

Because researchers wishing to investigate the pathophysiology and genetics of PBD required inclusion and exclusion criteria that yielded more homogeneous groups for study, investigators at the NIMH intramural program went a step further in proposing the "Narrow," "Intermediate," and "Broad" phenotypes (Liebenluft et al., 2003). The DSM-IV diagnosis of mania requires elated or irritable mood lasting a week or longer accompanied by three additional symptom criteria (four, if mood is irritable only).

In an effort to clearly discriminate PBD from ADHD and other childhood disorders characterized by irritability, the proposed Narrow Phenotype includes those children with the "hallmark symptoms" of elevated mood or grandiosity and clear episodes meeting DSM-IV symptom and duration criteria, but excludes those diagnosed based on irritable mood alone. The Intermediate Phenotype includes those with episodes of shorter duration *and* those with "irritable (hypo)mania." The Broad Phenotype includes children who have explosive rages, aggression, hyperarousal (hyperactivity, distractibility) and chronic mood disturbance but meet neither DSM-IV symptom nor duration criteria, and excludes those who have discrete episodes and elated mood or grandiosity. The NIMH panel recommended that future studies use DSM-IV diagnoses as "descriptive data" and substitute the proposed phenotype definitions as inclusion/exclusion criteria (Liebenluft et al, 2003).

The "Core" phenotype developed by Dr. Demitri Papolos as defined in the Research Diagnostic Criteria places the DSM-IV manic or mixed episode in a broader framework of specific functional impairments directly related to the regulation of affect, drive, attention, arousal, and circadian rhythm, linked to defined neurobehavioral systems, and reflecting a neurobiological model informed by recent research. (Kalin & Shelton, 2000; Dolan 2002; LeDoux, 2000; Drevets, 1998; Blumberg et al. 2002; Papolos & Papolos, 2000; Xu et al., 2004).

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Juvenile Bipolar Disorder: Core Phenotype - Research Diagnostic Criteria

Must meet Criteria A-D for diagnosis

A. **Episodic and abrupt transitions in mood states accompanied by rapid alternations in levels of arousal, emotional excitability, sensory sensitivity, and motor activity. Variable mood states are characterized by the following features**: **manic/hypomanic** (mirthful, silly, goofy giddy, elated, euphoric, overly-optimistic, self-aggrandizing, grandiose); **depressed** (withdrawn, bored/anhedonic, irritable, sad, dysphoric, or overly pessimistic, self-critical).

   Episodes are defined by DSM-IV symptom criteria but not by DSM-IV duration criteria; manic/hypomanic or mixed episode required for diagnosis:

   1. **Manic or hypomanic episodes** are associated with elated/euphoric (silly-goofy-giddy), or angry/irritable mood states, and 3 of the following symptoms and behaviors (4 if irritable mood only): more talkative than usual, pressured speech; flight of ideas; subjective experience of thoughts racing; distractibility; diminished need for sleep; increase in goal directed activity; heightened interest, enjoyment, and enthusiasm for usual activities; excessive involvement in

pleasurable activities that have a high potential for painful consequences; overestimation of resources and capacities; over-valuation of self and others: more argumentative than usual; overbearing, bossy, in pursuit of personal needs or agenda. CBQ (11,12,25,26,28,29,30,36)*

2. **Depressive episodes** are associated with dysphoric/sad/irritable or anxious/fearful mood states with loss of interest and pleasure in previously enjoyed activities often resulting in expressions of boredom and excessive stimulus seeking behaviors; in addition to depressed mood or anhedonia, 4 or more of the following symptoms are present: decreased sense of self-esteem; slowed speech; paucity of thought; increased need for sleep or disrupted sleep; loss or increase in appetite; decrease or loss of energy; difficulty sustaining attention; diminished ability to concentrate or indecisiveness; psychomotor retardation; loss of initiative and motivation; under-estimation of resources and capacities; devaluation of self and others; negative interpretation of events and misattribution of other's behaviors; recurrent thoughts of death, recurrent suicidal ideation. CBQ (37-42,60)

3. **Mixed episodes** are associated with overlapping features of the primary mood states (manic/hypomanic, angry, depressed, anxious) accompanied by other associated symptoms of manic/hypomanic and depressive mood states. The presentation may include irritability, agitation, insomnia, appetite dysregulation, poor control over aggressive impulses, in addition to course modifiers such as aggression directed against self or others (e.g. suicidal thinking or attempts, aggressive displays, rages) or psychotic features. Mixed Episodes may be due to the direct effect of exposure to antidepressants, stimulant medication, electroconvulsive or light therapy, or other medical treatments (e.g. corticosteroids, sympathomimetic agents). CBQ (11,12,25,26,28,29,30,36,37-42,60)

B. **Poor modulation of drives (aggressive, sexual, appetitive, acquisitive) resulting in behaviors that are excessive for age and/or context.** This regulatory disturbance is associated with excessive **aggressive/fight-based behaviors** (critical, sarcastic, demanding, oppositional, overbearing "bossy", easily enraged, prone to violent outbursts), **and/or self-directed aggression** (head-banging, skin-picking, cutting, suicide), as well as, **premature and intense sexual feelings and behaviors** (precocious curiosity about sex and premature expression of sexual impulses, as well as inappropriate public displays), **appetite dysregulation** (excessive craving for carbohydrates and sweets, binge eating, purging, and anorexia), **and poor control over acquisitive impulses** (relentless pursuit of needs, buying excessively and hoarding). CBQ (10,34,35,46-49,51,53,55-60,63)

Episodic and abrupt transitions in mood states and poor modulation of drive are currently present most days and have been present for at lease the past 12 months without any symptom free periods exceeding 2 months in duration, and cause functional impairment in 1 or more settings (e.g., significant behavioral problems at home but not necessarily in the school setting).

C. **Four (or more) of the following disturbances have been present during the same12-month period:**

1. **Excessive anger and oppositional/aggressive responses to situation that elicit frustration.** Compared to his/her peers, the child exhibits difficulties in the postponement of immediate gratification, when parents set limits. In particular, when answered "no" to expressed wishes, when having to wait his/her turn, or when there are changes in planned activities or routines, this deficit results in maladaptive responses, such as seeming not to listen (purposeful), the display of disruptive, intrusive, and overbearing behaviors, or, in the extreme, temper tantrums and aggressive attacks, often followed by sullen withdrawal and expressions of remorse. CBQ (18,27,51)

2. **Poor self-esteem regulation.** At times is overly-optimistic, defiant arrogant, filled with bravado, and prone to self-aggrandizement, exaggeration of abilities, and has feelings of omnipotence, or, alternatively, is overly-pessimistic, self-critical, and overly sensitive to criticism or rejection, often responding to criticism with intense feelings of humiliation and shame. The child often expresses feelings of insecurity, worthlessness, and is capable of rapid and intense idealization and/or devaluation of self and others. CBQ (29,30,40-42)

3. **Sleep/wake cycle disturbances; at least one of the following: 1) Sleep discontinuity** (initial insomnia, middle insomnia, early morning awakening, hypersomnia) **2) Sleep arousal disorders** (sleep inertia, night-terrors and nightmares - often containing images of gore and mutilation, and themes of pursuit, bodily threat and parental abandonment, sleep-walking, confusional arousals, bruxism and enuresis); **3) Sleep/wake reversals** (a tendency toward periodic lengthening or shortening of sleep duration, often dependent on circadian and circannual changes in light/dark and temperature cycles, as well as, the availability of regular social zeitgebers). CBQ (3,5-9)

4. **Low threshold for anxiety.** A tendency to react with excessive anxiety and fearfulness in response to novel or stressful situations; transitions of context, loss, separation, or the anticipation of loss/separation from attachment objects, or loss of social status. Anxiety often arises from fear of harm to self in the form of anger, rejection, criticism, ostracism, or, alternatively, from the fear that he/she will harm others or self. This deficit can predispose to behavioral inhibition, or flight-based behaviors such as separation anxiety disorder, social phobias, and other anxiety disorders including panic-disorder, obsessive compulsive disorder and post-traumatic stress syndrome. CBQ (1,2,64)

5. **Disturbance in the capacity to habituate to sensory stimuli often when exposed to novel, repetitive or monotonous sensory stimulation.** A tendency to over-react to environmental stimuli and to become over-aroused, easily-excited, irritated, angry, anxious or fearful when exposed to novel sensory experiences, e.g., crowds, loud or unexpected sounds, (e.g., vacuum cleaners, ticking clocks, thunder and lightening), and dissonant sensations (e.g., shirt tags, fit of clothes or shoes, perceived foul odors). CBQ (21-24)

6. **Executive Function Deficits; One or more of the following:**
   Mental Inflexibility - Difficulty shifting cognitive set, planning ahead, planning strategically as seen in unrealistic estimates of energy resources and time requirements for the accomplishment of tasks (e.g. difficulty adjusting to changes in plans for the day such as planned trips and changes in venue), has difficulty giving up an idea or desire, no matter how unrealistic or unfeasible, has difficulty starting and completing school assignments without a great deal of prompting, often gets caught up on small details of an assignment and misses the larger picture. This executive dysfunction is often associated with working memory deficits, problems making transitions from one context to another, poor organizational skills, distractibility, excessive daydreaming, and performance deficits in school, particularly in the organization of thought for written expression. CBQ (17-20)
   Emotional Inflexibility - Impulsive, acts before thinking. Over-reacts to small events, rapidly shifts emotional state, can demonstrate sudden anger, resentment, and/or rage for greater than 15 minutes that is unresponsive to reason, discussion, or soothing, can become progressively unrestrained or silly, and does not appear to gain pleasure from mastering a skill. CBQ (1,24,27,31,36,53)
   Inflexibility of Motor Activity -The initiation of movement directed at the accomplishment of motor tasks is effortful (e.g.

has difficulty starting activities in the morning, and requires help in initiating any activity), is often restless and fidgety. Handwriting is poor, and has trouble initiating and completing written assignments. CBQ (3,16,39,43)

7. **A family history** of recurrent mood disorder and/or alcoholism, as well as other bipolar spectrum disorders. A history of bilineal familial transmission is commonly observed.

D. **Symptoms are not due to a general medical condition (e.g. hypothyroidism).**

*CBQ refers to the Child Bipolar Questionnaire – a 65-item screening inventory keyed to the Research Diagnostic Criteria.