Juvenile Bipolar Research Foundation

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Expert Diagnostic Workshop on Juvenile-Onset Bipolar Disorder

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Background

Designation of appropriate diagnostic criteria for juvenile-onset bipolar disorder has been the subject of considerable discussion and debate. There are a number of controversial issues that will require resolution before a consensus diagnosis can be established. With its complex cycling patterns, comorbidities, and the evolving developmental trajectories that contribute to the potential for different symptom complexes that change over time, juvenile-onset bipolar disorder does not easily fit into categories derived from adult studies. Expert opinion about diagnostic issues focused systematically on a common sample of juveniles with a range of symptoms associated with early-onset bipolar disorder can be of assistance in achieving consensus on what criteria should be accepted as definitive for juvenile-onset bipolar disorder.

Epidemiological studies rely on accurate diagnostic criteria to distinguish one condition from another to determine the true rates of the disorder in the general population. Genetic studies, our best hope of understanding the etiology of the illness, will likely succeed or fail depending on whether the field is able to characterize precisely-defined syndromes leading to definitive behavioral phenotypes that are consistently associated with specific genetic variations.

The Juvenile Bipolar Research Foundation (JBRF) has established an Expert Diagnostic Workshop to assemble clinically-expert opinion on what behavioral elements should define juvenile-onset bipolar disorder.

Method

The Juvenile Bipolar Research Foundation (JBRF) has assembled an internationally-recognized group of clinicians and researchers to participate in a concerted effort to foster the development of a consensus diagnosis for juvenile-onset bipolar disorder. JBRF has compiled a set of case histories of juveniles with a range of symptom expressions typical of youth with bipolar disorder. Additional presentations will be drawn from cases screened for participation in JBRF research studies. All case histories will be fictionalized to ensure the individual's confidentiality. The case material will be presented via the Internet, accessible at the JBRF web-site in a password protected area in a case presentation format.

Three distinct diagnostic systems for juvenile-onset bipolar disorder currently exist: [1] DSM-IV criteria; [2] NIMH-modified DSM-IV criteria, and [3] JBRF-proposed Research Diagnostic Criteria. Each of these three systems has advantages and disadvantages. The Expert Diagnostic Workshop asks expert diagnosticians to employ each system to rate individual case histories which will include symptom descriptions, characterizations of the most severe prior episode, and clinical and developmental histories that pertain to key behavioral criteria incorporated within the three different diagnostic systems. In addition, available for most cases will be relevant supplemental information, including medical history, family psychiatric history for first degree relatives, and treatment history.

Analytic Plan. For each of the three diagnostic symptoms, for each case/rater combination, item-level detail will be available. The DSM-IV rating system yields 26 item responses (yes/no) plus three diagnosis indicators (manic, hypomanic, depressive); the NIMH system yields 18 item responses and two diagnosis indicators; the Research Diagnostic Criteria yields 18 item responses and four diagnostic indications (manic, depressive, mixed, bipolar).

The analytic plan will focus on searching for concordance among these several dimensions. That is, within each diagnostic system, across all cases and raters, the analyses will identify the items that are [1] concordant or [2] discordant with overall summary judgments. Similarly, and secondarily, these concordance analyses will be repeated searching for concordant/discordant raters. Conditional logistic regression modeling methods, with adjustment for clustering across subjects and across raters, will be used in these analyses. There will be missing data in these datasets, as raters will have the option of not completing certain sections of the Expert Diagnostic Workshop procedure, but the conditional logistic modeling procedure is tolerant of such missing data.

These analytic procedures will be repeated while omitting discordant items and discordant raters. This procedure will identify, within each diagnostic system, a set of items and a group of raters that appear to be discordant. These aberrant items and non-conforming raters can then be dropped from subsequent analyses. Then, this reduced set of items/raters will be combined in analyses extending across all three diagnostic systems, to determine which diagnostic system appears to yield the most coherent and reproducible diagnostic indications. These results can also be used to inform the selection of items from each of the three diagnostic symptoms to form a consolidated/combined "best estimate" system. These summary analyses can be carried out separately in designated subsets, for example, separately for cases identified/not identified by one or more of the diagnostic systems as satisfying diagnostic criteria. Finally, provided that the Expert Diagnostic Workshop database develops sufficiently well so that a large number of diagnosticians provide data for a substantial number of cases, a validation subset of cases (25%, say), set aside specifically for this purpose, will be used to test the generalizability of these analyses.

Results

Definitions of Proposed Phenotypes

Narrow Phenotype (elated mood)

This phenotype is characterized by abnormal elevated mood states. A distinct episode of hypomania or mania of at least four days duration is required, during which time the child had elevated, elated mood or grandiosity. In addition, at least three other DSM-IV B symptom criteria must be met for diagnosis. In the absence of elated mood, three symptom criteria must be met in addition to grandiosity.

Symptom criteria include all 7 DSM-IV symptom criteria: inflated self-esteem or grandiosity, decreased need for sleep, more talkative than usual or pressure to keep talking, flight of ideas or subjective experience that thoughts are racing, increase in goal-directed activity or psychomotor agitation, and excessive involvement in pleasurable activities that have a high potential for painful consequences. If the child also meets criteria for ADHD, the symptom criteria of distractibility and psychomotor agitation count toward the diagnosis of mania only if in excess of the child's usual ADHD.

Broad Phenotype (angry, irritable mood, chronic hyperarousal, explosiveness)

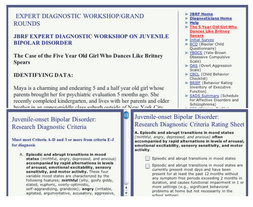
This phenotype is designed to capture children who have chronic irritability and hyperarousal. It is also called severe mood and behavioral dysregulation, and it differs from the narrow phenotype in that the child has no euphoria or grandiosity and no discernable episodes.

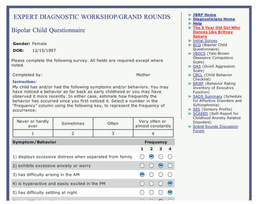
All of the following required: 1) Chronic explosiveness, i.e., the child exhibits marked reactivity to negative emotional stimuli at least 3 times a week, on average. For example, the child's response to frustration is associated with extended temper tantrums, verbal rages, and/or displays of aggression toward people or property; 2) Baseline abnormal mood (i.e., even between outbursts the child is angry or irritable); and 3) Chronic hyperarousal. To meet this last criterion, the child must have three of the following symptoms: distractibility, racing thoughts or flight of ideas, pressured speech, intrusiveness, agitation, and insomnia, nearly every day. In addition to the absence of elated mood or grandiosity, the presence of irritable mood distinguishes the broad phenotype from the narrow phenotype.

Core Phenotype (Episodic and abrupt transitions in mood state, and poor modulation of at least one drive state)

The hallmark features of this phenotype are episodic and abrupt transitions in mood state (mania/hypomania, depression, mixed state) and poor modulation of at least one drive (aggressive, sexual, appetitive, acquisitive). Descriptive definitions of mania/hypomania, depression, and mixed states remain essentially unchanged from DSM-IV. However, specifying daily, abrupt mood fluctuations and eliminating episode duration distinguish this phenotype from the others. These cardinal features must result in behaviors that are excessive or inappropriate for age and/or context and must be present on most days for at least 12 months to make the diagnosis.

Symptoms must not be due to the direct physiological effects of a substance or a general medical condition.
In addition, the child must exhibit four or more of the following disturbances;
1) Excessive anger and oppositional and aggressive responses to situations that elicit frustration;
2) Poor self-esteem regulation (self-aggrandizement, exaggeration of abilities, and feelings of omnipotence, or, alternatively, pessimistic, self-critical, and overly sensitive to criticism or rejection);
3) Sleep/wake cycle disturbances as exemplified by sleep discontinuity, sleep arousal disorders, or sleep/wake reversals; 4) Excessive anxiety and fearfulness in response to novel or stressful situations;
5) A disturbance in the capacity to habituate to novel, loud or unexpected sounds and dissonant sensations;
6) Executive function deficits as exemplified by mental, emotional, or motor inflexibility;
7) A family history of recurrent mood disorder and/or alcoholism, as well as other bipolar spectrum disorders.





Discussion

Before any large scale epidemiological and genetic studies can proceed in earnest, it is imperative that the field achieve consensus about one or several behavioral phenotypes defined as juvenile, childhood-onset or pediatric bipolar disorder. The Expert Diagnostic Workshop methods, if carefully applied, should lead to the specification of diagnostic procedures identifying definitive behavioral phenotypes in juvenile-onset bipolar disorder. The data that emerge from the diagnostic workshop system, coupled with expert deliberations and peer discussions, will potentially be of considerable importance in the collaborative efforts to achieve this consensus.