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Preliminary communication

Is there progression from irritability/dyscontrol to major depressive and manic symptoms? A retrospective community survey of parents of bipolar children

Emily L. Fergus[a], Rachel B. Miller[a], David A. Luckenbaugh[a], Gabriele S. Leverich[a], Robert L. Findling[b], Andrew M. Speer[a], Robert M. Post[a,*]

[a] *Biological Psychiatry Branch, National Institute of Mental Health, NIH, Bethesda, MD, USA*
[b] *Case Western Reserve University, Cleveland, OH, USA*

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Abstract

Background: Although previous studies have discussed age-related changes in the presentation of early onset bipolar illness, the developmental progression of early symptoms remains unclear. The current study sought to trace parents' retrospective report of yearly occurrence of symptoms in a sample of children with and without a diagnosis of bipolar disorder in the community. *Methods:* Parents retrospectively rated the occurrence of 37 activated and withdrawn symptoms causing dysfunction for each year of their child's life (mean age 12.6 ± 6.9). Children were divided into three groups based on parent report of diagnosis by a community clinician: bipolar ($n = 78$); non-bipolar diagnosis ($n = 38$); and well (no psychiatric diagnosis) ($n = 82$). Principal components analysis was performed to understand the relationship among the symptom variables and their potential differences among the three groups as a function of age. *Results:* Four symptom components were derived and these began to distinguish children with bipolar disorder from the other groups at different ages. Component II (irritability/dyscontrol), which included temper tantrums, poor frustration tolerance, impulsivity, increased aggression, decreased attention span, hyperactivity and irritability, began to distinguish bipolar children from the others the earliest (i.e., from ages 1 to 6). The other components (I, III, and IV) which included symptoms more typical of adult depression (I), mania (III), and psychosis (IV), distinguished the children with a bipolar diagnosis from the others much later (between ages 7 and 12). *Limitations:* The data were derived from retrospective reports by parents of their children's symptoms on a yearly symptom check list instrument which has not been previously utilized. Parents' ratings were not validated by an outside rater. Moreover, the children were diagnosed in the community and a formal diagnostic interview was not given. *Conclusions:* By parental report, the cluster of symptoms in the irritability/dyscontrol component may characterize the earliest precursors to an illness eventually associated with more classic manic and depressive components that are diagnosed and treated as bipolar disorder in the community. These retrospective survey data suggesting a longitudinal evolution of symptom clusters in childhood bipolar-like illness identify a number of areas for prospective research and validation.

Keywords: Bipolar disorder; Child; Adolescent; Early onset; Development

* Corresponding author. Room 3S239, Building 10, 10 Center Drive, MSC 1272, Bethesda, MD 20892, USA.

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1. Introduction

Although varying incidences of childhood onset bipolar illness have been reported (Kraepelin, 1921; Loranger and Levine, 1978; Lish et al., 1994; Suppes et al., 2001), the earliest presentations and how they evolve over time remain controversial. Extreme mood lability, irritability, and impulsivity have been repeatedly described as prominent symptoms of early bipolar illness (Carlson et al., 1998; Chang et al., 2000; Geller et al., 1998b, 2002a,b; Varanka et al., 1988; Carlson, 1983; Bowring and Kovacs, 1992; Weinberg and Brumback, 1992; Biederman et al., 2000). Furthering the idea of this choleric childhood presentation, aggression has been found to be a common symptom (Carlson, 1983; Geller et al., 1998a; Varanka et al., 1988), occasionally accompanied by homicidal and suicidal threats. Other prominent symptoms of early bipolar illness include: rapid and ultra-rapid cycling (Varanka et al., 1988; Strober, 1992; Geller et al., 1994, 1995, 1998a,b; Sanchez et al., 1999; Findling and Calabrese, 2000; Findling et al., 2001), racing thoughts (Geller et al., 1998b; Varanka et al., 1988; Weinberg and Brumback, 1992), and psychotic manifestations such as grandiose delusions and hallucinations (Sanchez et al., 1999; Geller et al., 1998b, 2000, 2002a,b; Varanka et al., 1988; Carlson, 1983; Weinberg and Brumback, 1992). There is a high comorbidity with attention deficit hyperactivity disorder (ADHD) (Biederman et al., 1996, 1998, 2000; Chang et al., 2000; Wozniak et al., 1995) and disruptive behavior disorder (Findling et al., 2001).

A few studies have discussed age-related changes in the presentation of bipolar illness based on cross-sectional observations of children at different ages, although it is uncertain what the developmental trajectory of these symptoms might be in the same children followed longitudinally. According to Carlson (1983), bipolar children between ages 15 months to 8 years experience symptoms of agitation, absence of depressed appearance, non-discrete episodes, and irritability instead of euphoria as the predominant mood symptom. For bipolar children between ages 9–12 years, she describes a more 'classically manic' symptomatology, including euphoria with irritability, discrete episodes, and grandiosity alternating with classical depressive symptoms. More generally, Geller et al. (1994) found that 100% of children in her sample under 13 years of age experienced rapid cycling compared with only 71% of children 13 years or older. She noted that the initial presentation of childhood bipolar illness is often bipolar II (BP-II), with more frequent depressions and brief, intermittent periods of mild mania, which then intensify as the child develops, becoming bipolar I (BP-I) with depressions alternating with moderate to severe mania, at times including psychosis (Geller et al., 1998b). A consensus group suggested in prepubertal children both the occurrence of classical BP-I and BP-II presentations, and another type characterized by extreme mood lability causing considerable dysfunction, which they suggested should be called BP-NOS (not otherwise specified) (National Institute of Mental Health Research Roundtable on Prepubertal Bipolar Disorder, 2001).

In order to take a preliminary look at the longitudinal evolution of symptoms potentially beginning to differentiate children with bipolar illness from others, we elicited cooperation from parents willing to rate the presence and severity of symptoms in each year of their child's life in those with and without a diagnosis of bipolar illness. The current study focused on the longitudinal course of symptom evolution. We utilized a principal component analysis in order to explore how the presence of moderate to severe symptoms grouped together and examined the developmental progression of each of the four components as they began to distinguish the children with a bipolar diagnosis in the community from those without. These retrospective survey data provide a series of ideas about the longitudinal progression of symptoms differentiating children with a bipolar diagnosis from others that can further be examined more rigorously prospectively.

2. Methods

The nature and rationale of the survey and the confidentiality of the information were described in advertisements and subsequent written material as part of the informed consent process, and only after parents requested participation in the study were the actual surveys sent. Parents were requested to rate

the presence and severity of each of 37 symptoms in each year of their child's life. Severity was rated as: 0 = not present; 1 = mild; 2 = moderate; 3 = severe, based on the degree of impairment that the symptom caused in the child's usual education, family, and social roles. These 37 signs and symptoms represented a wide range of activated or withdrawn symptoms described in the DSM-IV for a variety of childhood diagnoses. The survey forms are available from the corresponding author. The mean age of the children described was 12.6 ± 6.9. The study sample was separated into three groups based on the clinical diagnoses given in the community; bipolar disorder ($n = 78$); non-bipolar conditions ($n = 38$); and well (no diagnoses [$n = 82$]).

The non-bipolar group's diagnoses included disorders such as unipolar depression, ADHD, conduct disorder, obsessive–compulsive disorder, oppositional defiant disorder, and Tourette's syndrome. The non-bipolar diagnosed and the well (non-diagnosed) groups were comprised mostly of siblings of the bipolar children. A symptom was considered present in a given year only if it was rated by the parents as moderate (2) or severe (3) based on the degree of associated dysfunction.

In order to understand the interrelationships among the symptom variables, an exploratory principal components analysis (PCA) was performed with varimax rotation to improve the orthogonality of the relationships. Two variables (tics and mute) were endorsed by less than 5% of the sample; therefore, they were not included in this analysis. Bartlett's Test of Sphericity was significant ($\chi^2 = 3364.651$; df = 595, $P = 0.000$), indicating that there was enough overlap in the variance of the symptoms to group them. Further, Kaiser–Meyer–Olkin Measures (KMO) of sampling adequacy were used to confirm that the sample size was sufficient to perform the PCA. Kaiser (1974) suggested that values below 0.5 were unacceptable for this kind of measure, whereas values above 0.7 were 'middling' and above 0.8 were 'meritorious'. The overall KMO was 0.890 and individual KMOs ranged from 0.752 to 0.951. Only three individual variables fell below 0.8; therefore, the sample size appeared sufficient.

Initially, eight components with eigenvalues greater than 1 were extracted. In an attempt to simplify the components, we included a symptom in a component only when it had a loading of 0.5 or greater. After reducing the number of components to get a more coherent structure, the final solution included four components that explained a total of 50% of the variance. No variables loaded on more than one component, and six variables (i.e., compulsive behaviors, increased anxiety, physical complaints, no remorse, decreased sleep, and bed wetting) did not load on any components.

Only post-rotation component loadings and percentages of variance explained are reported. Reciprocals of the reproduced correlation matrix show the amount of variance not explained by the PCA solution. Values above 0.05 indicate unexplained variance. This matrix had 33% of its values above 0.05. Therefore, while the components account for a substantial proportion of the variance among the symptoms, there remained a good portion that was not explained by this solution.

The incidence of each symptom in a given component was compared in the children with a bipolar diagnosis and those without. For each symptom, the age when the bipolar group began to have between a 10, 20, 30, 40, or 50% greater incidence than the other two groups was graphed.

3. Results

The mean age for the diagnosed groups was similar; 13.7 years (± 6.6) for the bipolar children versus 13.6 years (± 6.9) for the non-bipolar children, but lower for the non-diagnosed children (11.1 years, ± 7.1, $P < 0.03$). Gender distribution was even in all three diagnostic groups.

The precursors to the PCA showed that the data fit the necessary requirements for the technique and yielded four components which we labeled: I, Depression; II, Irritability/Dyscontrol; III, Mania; and IV, Psychosis/Suicidality (Table 1). The depression component (I) explained 14.2% of the variance and included nine symptoms (severe fatigue, periods of sadness, increased sleep, low self-esteem, more withdrawn, suicidal thinking, change in appetite, cries easily, and excessive guilt). The irritability/dyscontrol component (II) explained 14.1% of the variance and included seven symptoms (temper tantrums, poor frustration tolerance, impulsivity,

Table 1
Principal components analysis of early intervention symptoms in children with and without bipolar diagnosis

Loading	Component 1: Depression	Component 2: Irritability/Dyscontrol	Component 3: Mania	Component 4: Psychosis/Suicidality
0.7	0.715 Periods of sadness	0.713 Impulsivity	0.705 Racing thoughts[a]	0.793 Suicidal gesture[a]
		0.712 Temper tantrums[a]		
0.6	0.691 Severe fatigue	0.689 Poor frustration tolerance	0.671 Extended mood elevations	0.623 Paranoid thoughts
	0.644 Low self-esteem	0.685 Increased aggression		0.619 Hear voices
	0.600 Increased sleep	0.675 Hyperactivity		0.606 Serious suicide attempt
		0.665 Decreased attention span[a]		
0.5	0.572 More withdrawn	0.524 Irritability[a]	0.599 Grandiosity/Delusions[a]	0.503 Obsessive thoughts
	0.568 Change in appetite		0.597 Pressured speech	
	0.544 Suicidal thinking		0.559 Bizarre behavior	
	0.536 Cries easily		0.549 Brief mood elevations	
	0.535 Excessive guilt			
0.4	0.491 Irritability	0.458 Compulsive behavior	0.435 Increased sleep	0.497 Suicidal thinking
	0.456 Increased anxiety	0.423 Brief mood elevation	0.426 Decreased sleep	0.406 Compulsive behaviors
	0.411 Physical complaints	0.408 No remorse	0.414 No remorse	
0.3	0.375 Decreased sleep	0.392 Inappropriate sexual behavior	0.344 Irritability	0.380 Bed wetting
	0.362 Poor frustration tolerance	0.373 Obsessive thoughts	0.341 Obsessive thoughts	0.372 Inappropriate sexual behavior
	0.308 Hear voices	0.316 Night terrors	0.331 Paranoid thoughts	0.355 Bizarre behavior
	0.302 Temper tantrums	0.307 Cries easily	0.327 Excessive guilt	0.337 Increased anxiety
				0.327 Night terrors
% Variance explained	14.2	14.1	11.0	10.2

[a] The six symptoms previously described in the age-independent stepwise logistic regression as differentiating bipolar from non-bipolar children (Fergus et al., 1999).

increased aggression, decreased attention span, hyperactivity, and irritability). The third component explained 11% of the variance and included six symptoms of mania (racing thoughts, extended mood elevation, pressured speech, grandiosity or delusions, bizarre behavior, and brief mood elevations). The fourth component, labeled psychosis/suicidality, explained 10.2% of the variance and included five symptoms (hearing voices, paranoid thoughts, suicidal gestures, suicidal attempts, and obsessive thoughts).

Comparison of incidence of symptoms within each of the four components gleaned from the PCA revealed the ages at which bipolar children experienced at least a 10% or greater incidence of the individual symptom than the other two groups (Fig. 1). From age 1 onward, at least one symptom in Component II (irritability/dyscontrol) was experienced more frequently by the bipolar children. By age three, the bipolar children experienced five of the seven symptoms in this component with at least 10% or greater incidence than the other groups. However, not even single symptoms from either Component I (depression) or Component III (mania) began to distinguish the bipolar children from the other two groups until ages 7 and 8, respectively. Symptoms from Component IV (psychosis/suicidality) did not begin to distinguish the children with bipolar illness from the others until age 9.

4. Discussion

4.1. Methodological limitations

A number of methodological issues limit the firmness of conclusions that can be drawn from the current analysis. The data were derived from a retrospective survey completed by parents, and the accuracy of recall of age of symptom emergence and severity would not be as precise as parental reports of the past 6 months (Youngstrom et al., 2001). Moreover, these survey descriptions were not validated by the child's doctor, clinician, or teacher. Importantly, the diagnoses used for group assignment were made in the community. However, when

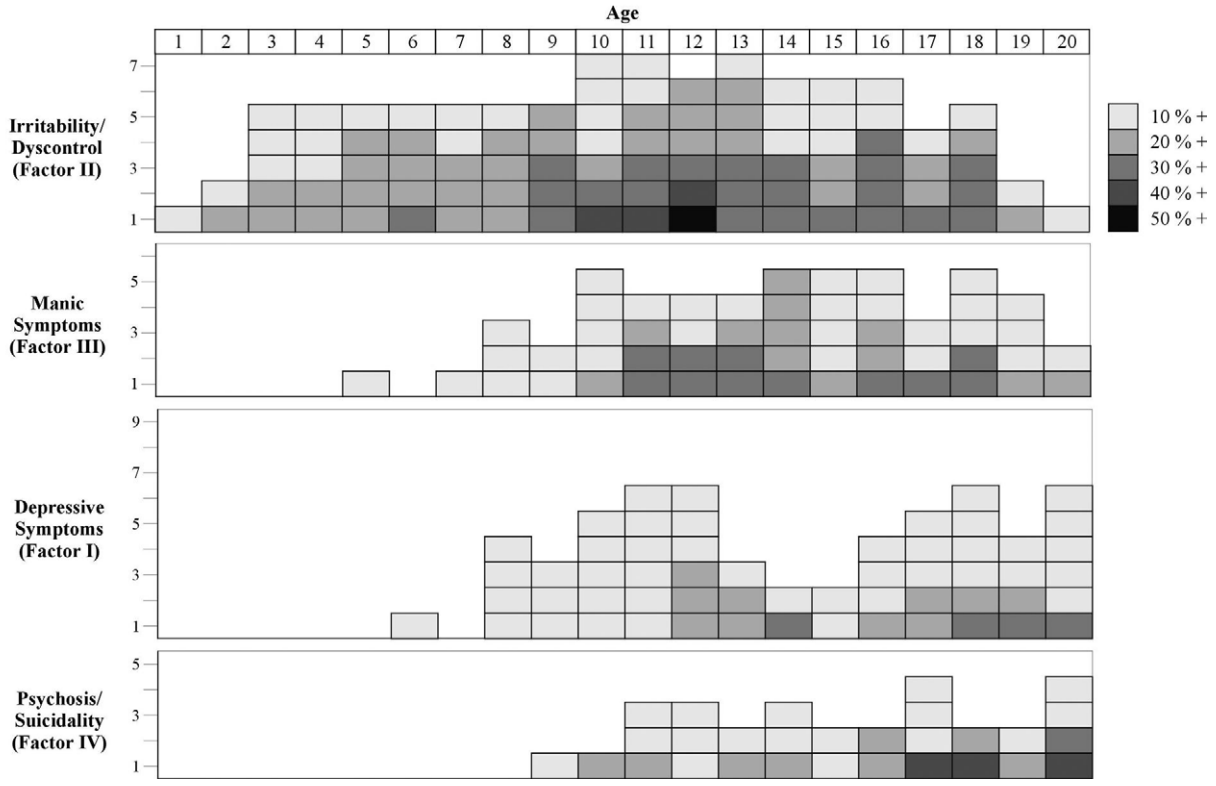

Fig. 1. Age at which bipolar group's incidence is higher (10–50%) than comparison groups.

we preliminarily matched the presence of symptoms reported by the parents to those listed in the DSM-IV, the vast majority of the community diagnoses were internally validated. Further, the method of recruiting volunteers was purposefully selective and not representative of the general population. The current study recruited volunteers through a newsletter on bipolar illness and a clinic specializing in the treatment of that illness, and accordingly, 44.9% of the bipolar children had a parent diagnosed with bipolar illness. This could have distorted illness severity or presentation compared with a more representative sample, although an examination of symptoms in those with and without a parent with bipolar illness did not reveal major differences.

Another limitation of the current study is that the non-bipolar psychiatrically diagnosed comparison group was comprised of children with a variety of disorders (i.e., unipolar disorder, ADHD, Tourette's syndrome, etc.) and, therefore, we were unable to directly compare the presentation of bipolar children to any single disorder. Because childhood bipolar disorder is highly comorbid with ADHD (Biederman et al., 1996; Geller et al., 1998b, 2000; Hechtman and Greenfield, 1997; Weller et al., 1995; Sachs et al., 2000) or conduct disorder (Weller et al., 1995), it will be important for future studies to follow the different development courses of each disorder separately. Moreover, recent observations suggest there are distinctly different types of presentations of childhood onset bipolar disorder, including those with more classical BP-I and II characteristics emerging from a healthy baseline (Biederman et al., 2000) versus those with a long BP-NOS prodrome, and the illness trajectories of these presentations should be distinguished.

On the positive side, these retrospective yearly ratings were a first look at bipolar illness symptom evolution from a consistent parental observer, who would likely continue to have the same rating biases

over each year. They thus provide realistic descriptive data that may be of assistance in designing more rigorous prospective studies. These subsequent studies, however, will have the liabilities of requiring a decade or more for completion, and additionally the difficulty of choosing the appropriate high-risk or identified patient population. Considering the difficulties and complexities of a better-controlled prospective study, these preliminary data are unique and therefore worthy of dissemination to see if they can be replicated and verified using other methods.

4.2. Principle components: time course of differentiation

The principal component analysis (PCA) enabled the classification of 27 of the 37 symptoms that were included in the survey into four components. Among these, Component II showed the earliest ability to discriminate the bipolar children from the other groups. This irritability/dyscontrol factor was comprised of seven symptoms including temper tantrums, poor frustration tolerance, impulsivity, increased aggression, decreased attention span, hyperactivity, and irritability. In this survey population the bipolar group had a 10% or greater incidence of one of the symptoms in this factor by age one, and five of the seven symptoms by age three. Although these symptoms are not sufficient to make the diagnosis of bipolar illness and are not typically regarded as classic bipolar symptoms, it appears that this irritability/dyscontrol factor is associated with later clusters of more classic manic and depressive symptoms sufficient to lead to a diagnosis of bipolar illness in the community.

Much of the past literature suggests that childhood bipolar disorder is characterized by predominantly irritable and dysphoric mood (Bowring and Kovacs, 1992; Varanka et al., 1988; Geller et al., 1994, 1998b; Carlson, 1983; Carlson et al., 1998; Weinberg and Brumback, 1992), with ultra-rapid and ultradian cycling (Geller et al., 1995, 1998a,b, 2000, 2002a; Findling and Calabrese, 2000), of sufficient severity and impairment to merit a diagnosis of BP-NOS (Biederman et al., 2000). It is interesting that Component II contains three symptoms that are commonly associated with ADHD: hyperactivity, impulsivity, and decreased attention span. This finding and the high comorbidity of ADHD with formally diagnosed bipolar illness in children and adolescents (Biederman et al., 1996, 1998, 2000; Chang et al., 2000; Wozniak et al., 1995) suggest further for the ambiguity in the early presentations of the two conditions. The irritability/dyscontrol component (II) support and extend the previous literature by identifying them as a coherent cluster of symptoms, and potentially, the earliest precursors to classic manic and depressive clusters seen in adults and some adolescents.

The depression component (I) was made up of nine typical depressive symptoms. Although eight of the nine symptoms are part of the DSM-IV criteria for a major depressive episode, this cluster did not begin to distinguish the bipolar group from the others until between the ages of 8 and 12 (Fig. 1). Carlson (1983) reported a similar developmental trend, noting that children ages 9–12 years with bipolar disorder experienced classic depressive symptoms, whereas the children younger than age nine did not.

All the symptoms in the mania component (III) (racing thoughts, extended mood elevation, brief mood elevation, pressured speech, grandiosity), except for bizarre behavior, are included in the DSM-IV criteria for manic/hypomanic episodes. This factor, like the depression factor, also did not begin to differentiate the bipolar children from the other groups until the ages of 7–12 (Fig. 1).

Component IV included symptoms of psychosis and suicidality, which also distinguished bipolar children from the other groups at a much later age (9–12) than the irritability/dyscontrol cluster. In late childhood and into early adolescence, bipolar children were more likely to show extreme behavior such as expressing inappropriate sexual behavior or acting on suicidal impulses.

5. Conclusions

Given the numerous caveats enumerated above, these retrospective parental survey data, nonetheless, allow for a preliminary look at the longitudinal evolution of symptoms later recognized and labeled clinically as bipolar disorder. To the extent that these parental views are confirmed in formal prospective studies, they suggest a transition from symptom

clusters reflecting the irritability/dyscontrol component (II) to the more classic adult symptoms reflected in the mania (III), depression (I), and psychosis/suicidality (IV) factors, respectively. As the sequential transition occurs, children with a bipolar diagnosis begin to be differentiated from those without such a diagnosis.

Since a prospective study of this possible evolution in symptom presentation would take 10–12 years to complete (and require very large numbers of subjects without the use of a high risk sample), these retrospective longitudinal views by parents at least provide an initial series of rudimentary findings that can help provide a framework for more systematic studies using other methods and approaches in the future. The possible differentiation of sequentially unfolding symptom clusters in at least a subgroup of those with prepubertal onset bipolar illness, is consistent with the emerging cross-sectional literature, and should help in the early consideration of what symptom clusters might ultimately herald the onset of bipolar illness.

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