

## Issue Focus: Child and Adolescent Bipolar Illness

### Clinical Trials Update

Investigators from the five Stanley Foundation Bipolar Network sites met in Pittsburgh on Wednesday, June 16, 1999, just prior to the Third International Conference on Bipolar Disorder. The meeting was highly successful from a number of perspectives:

#### Early Intervention Initiative Update

New data from the Early Intervention Initiative (E.I.I.) were presented, identifying five symptoms—grandiosity, suicidality, rapid thoughts, irritability, and hyperactivity—that may strongly predict the onset of childhood and adolescent bipolar illness. Early identification of symptoms that cause moderate to severe mood dysfunction should help facilitate the design and implementation of treatment interventions. The E.I.I.'s purpose is to ultimately be able to intervene early in the development of mood disorder symptoms that cause dysfunction in children, especially in children at a very high risk. The Network has already determined from survey data that parents greatly favor early intervention for their children with affective symptoms that cause dysfunction, even before a formal diagnosis has been established.

The topic of early intervention was the theme of an NIMH-sponsored meeting (see "Meeting Highlights," page 3) as well as the subject of a major symposium chaired by Dr. Richard Wyatt at the National Alliance for the Mentally Ill convention in Chicago, with Dr. Robert Post from the Bethesda Network site also participating in that symposium. Stanley Foundation-supported work will also be highlighted at the annual meeting of the American Academy of Child and Adolescent Psychiatry in Chicago this October. There will be three presentations from the Network (Dr. Robert Post, Ms. Gabriele Leverich, Ms. Emily Fergus) and two from the U.S. Stanley Centers—by Dr. Robert Findling (Case Western Reserve University) and Dr. Robert Kowatch (University of Texas Southwestern Medical Center). The Stanley Foundation is playing an important role in helping to clarify some of the complex issues

involved in the early recognition and treatment of bipolar illness in childhood and adolescence. The continued nurturing of this E.I.I. collaborative effort between the Network sites and the Stanley Centers will be a major focus of the Network in the future. This effort stems from the recognized need to better help parents and their children with bipolar illness, as well as the unique mission of the Network to study bipolar illness longitudinally and intervene as early as possible to prevent serious consequences.

#### Informed Consent

All Network investigators participated in an active discussion of how best to conduct clinical research studies in the current research environment wherein some public concerns have been expressed about the adequacy of the informed consent process, and about the fairness of clinical trial designs using placebo substitution. The meeting participants agreed that forming an advisory committee for the Network composed of patients and advocacy group members might be particularly helpful in addressing any potential concerns about informed consent issues in the Network. This action would supplement and extend the efforts of local Investigational Review Boards (IRBs) and other review panels already federally mandated. The Network investigators have been extremely sensitive to this issue from

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## Clinical Trials Update

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the beginning in providing an ongoing and longitudinal approach to the illness (rather than acute trials only), and have purposely designed most clinical trials to be comparisons of two active agents rather than placebo-controlled clinical trials. Although a placebo is used in the omega-3 fatty acids study, the active and placebo capsules are randomized as augmentation to existing treatment, thus not putting the patient at an increased risk because of absence of treatment. In addition, all patients are offered an additional eight months of add-on active treatment with omega-3 fatty acids in an open trial after the end of the first four-month randomized, double-blind phase.

### Bipolar Network News

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The BNN is published four times a year by an international group of investigators who work with patients with bipolar disorder to better understand the long-term course and treatment of bipolar disorder. The goal of the Network is to help develop new and more effective treatment.

We welcome any comments or suggestions you may have. For communication or to be placed on the mailing list, please contact us at:

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### Clinical Case Series Data

- Data from the first 54 patients to undergo an open augmentation treatment with the newly-approved anticonvulsant topiramate (Topamax<sup>®</sup>) have been submitted for publication. As noted in the last issue of the *BNN*, preliminary evidence of topiramate's efficacy in mania and in cycling was suggested in this open add-on case series, but there was little evidence of improvement in the treatment of acute depression. Topiramate has the positive side effect of weight loss, making it a potentially important treatment adjunct or option when so many of the other major psychotropic drugs are associated with weight gain for many patients.

- Our Network experience in 22 patients exposed to tiagabine (Gabatril<sup>®</sup>), a newer anticonvulsant, has been mixed. Although several patients showed a good response to tiagabine (but not to many other agents), two instances of seizures were observed. All Network investigators and our European colleagues (Drs. Walden and Grunze) agreed that the initial series should be published with an important cautionary note about the occurrence of seizures.

- Dr. Susan McElroy's paper reporting high rates of psychiatric illness comorbidity in patients with bipolar disorder will be resubmitted to the *American Journal of Psychiatry* for final review after completion of some requested reliability studies. As noted in the last issue

of the *BNN*, all 22 of the raters in the Network have been tested and found to be highly reliable on the Structured Clinical Interview for DSM-IV (SCID) Axis I disorders (intraclass correlation coefficient = 0.93).

- Network recruitment continues to be highly successful, exceeding expectations; 533 patients are now involved in longitudinal follow-up. These individuals are treated openly with drugs of interest that are widely used in the community or in randomized protocols already available for patients who become symptomatic. Patients are now enrolled in the omega-3 fatty acid protocol at the Cincinnati site; protocol approvals have been granted or are pending at the other Network sites.

- Professors Jörg Walden and Heinz Grunze from the separately funded Stanley Foundation European Centers Program joined us at this meeting and have adopted most of the methodology of the Network, and have already enrolled patients in the naturalistic follow-up study (NFS), two patients in the AD-1 protocol in Munich, and four patients in the NFS in Freiberg. We hope that other European Centers will join us as well. Drs. Alan Young and Ian Ferrier of Newcastle-upon-Tyne are also interested in adopting the methodology and participating in some of the clinical trials of the Bipolar Network. ■

### CORRECTION:

Last issue, the incorrect address was given for patients wishing to receive a free pocket NIMH-LCM calendar to systematically track their moods and medications. The correct address is: Lydia Lewis, Executive Director, National DMDA, 730 N. Franklin Street, Suite 501, Chicago, IL 60610-3526. We apologize for this error.

### DISCLAIMER:

Although the editors of the BNN have made every effort to report accurate information, much of the work detailed here is in summary or prepublication form, and therefore cannot be taken as verified data. The BNN can thus assume no liability for errors of fact, omission, or lack of balance. Patients should consult with their physicians, and physicians with the published literature, before making any treatment decisions based on information given in this issue or in any issue of the BNN.

## Meeting Highlights

### Early recognition and treatment of schizophrenia and bipolar disorder in children and adolescents

NIMH Research Workshop  
May 10–11, 1999, Bethesda, Maryland

**NIMH**  
National Institute  
of Mental Health

RESEARCH WORKSHOP

The NIMH Research Workshop on schizophrenia and bipolar disorder in children and adolescents was convened to address the questions: 1) How early can the symptoms of bipolar disorder and schizophrenia be recognized; and 2) what is the risk-to-benefit ratio of treating children and adolescents with prodromal (i.e., early) symptoms.

Considerable agreement about the methods and interventions for treating prodromal symptoms of schizophrenia was evident, and ample progress in the design and conduct of these studies in schizophrenia was equally apparent. In contrast, the controversies that have plagued the diagnosis of full-blown manic-depressive illness in children and adults have had a significant impact on the consideration of early intervention in children, even in those at high risk because of severe prodromal symptoms. Much of this contrast appeared to emanate from the more chronic and predictable worsening course of prodromal symptoms in schizophrenia, compared with the more labile and chaotic course in manic-depressive and mixed presentations that characterize bipolar illness. As noted in previous issues of the *BNN*, such controversies, even in the literature concerning adult patients, have led to a two-decade long lack of study funding in adult bipolar illness compared with the other major psychiatric illnesses, which is only now just beginning to be addressed.

#### Part I: Early Intervention in Prodromal Schizophrenia

**Dr. Patrick McGorry**, of the University of Melbourne, spoke on **approaches to early treatment**. He noted that half of the time, schizophrenia begins before age 16, and therefore warrants significant intervention efforts. Dr. McGorry focused his early intervention efforts in an overall youth health services program in a catchment area of 800,000 individuals. He found that if patients met criteria for group II prodromal symptoms consistent with attenuated forms of the illness (reaching criteria for psychosis for one week), 40% of these individuals would show full-blown schizophrenic psychoses after one year and two-thirds by year two. These data indicated that even the first week of disabling symptoms put these children at very high risk, despite the provision of extensive psychosocial services and interventions. Neither neuropsychological testing nor small hippocampal size discriminated between those who would and would not develop full-blown schizophrenic psychosis. In fact, those with smaller hippocampal volumes appeared to be relatively protected against developing a full-blown psychosis.

Dr. McGorry suggested that these early states be labeled *precursor states* to indicate the at-risk nature of these early presentations, but not be called *prodromes*, which has a more inevitable connotation. His group offered treatment of 1–2 mg/day of risperidone (Risperdal®) and a cognitive therapy treatment package for those with these precursor states.

They found that 36% of 25 individuals in the unmedicated group developed a full-blown psychosis diagnosis compared with only 9.5% of the 21 individuals receiving treatment. Interestingly, in those who were fully compliant with treatment, no patient progressed to a full-blown diagnosis. This study represented just a small sample, because only 60 individuals per year came to their Personal Assessment and Crisis Evaluation (PACE) Center as opposed to an expected 250 new cases per year from this catchment area.

**Editor's Note:** These initial data appear highly promising, with an apparently reasonable ratio of treatment need versus inconvenience (risks and side effects) burden of intervening in these individuals who might otherwise develop a full-blown diagnostic syndrome. Whether treatment might also benefit the individuals who are not going to develop the full-blown syndrome but are still at risk for other disorders short of schizophrenia, such as schizotypal disorders and others associated with considerable morbidity and even potential mortality, remains to be assessed as well.

**Dr. Barbara Cornblatt**, from Long Island Jewish Medical Center, described her work at the **RAPP Clinic, an intervention program for patients in the prodromal phase of schizophrenia**. RAPP stands for “Recognition and Prevention of Psychiatric Problems,” and treats children at high risk, i.e., siblings

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## Meeting Highlights: Early Intervention - Schizophrenia

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of patients with schizophrenia and those at various stages of syndrome evolution. These stages of syndrome evolution are: 1) very early and nonspecific symptoms; 2) attenuated symptoms; 3) symptoms with psychotic features; 4) full-blown episodes reaching criteria for psychosis NOS (not otherwise specified); and 5) full-blown schizophrenia. In the first stage, children have decreased function, depression, social isolation, strange behavior, and a major decline in school and social functioning. Children in this category are offered support groups and social skills training, whereas those in the second and third stages are offered atypical neuroleptics in addition to the treatments offered in stage one. Of those patients treated with olanzapine (Zyprexa®), 67% improved, 27% showed no change, and 6% showed worsening or progression of their illness. In those administered risperidone (who were more ill at onset of treatment than the olanzapine group), 46% improved, 27% showed no change, and 27% worsened or progressed to a diagnosis of psychosis NOS.

Twenty-two percent of the children showed a 15 pound weight gain on olanzapine as did 9% on risperidone, with an additional 11% and 9%, respectively, showing less substantial but notable degrees of weight gain. Olanzapine was somewhat more sedating than risperidone, and risperidone was associated with motor side effects in 18% of the children.

**Editor's Note:** These data, although preliminary, give insight into the cost-to-benefit ratio of early intervention, suggesting that it may be helpful in the majority of such individuals, even in the short-term, with the additional possibility (yet unproven) that longer-term administration of neuroleptics prevents the onset of full-blown schizophrenic syndromes in otherwise highly predisposed people. At the same time, the data indi-

cate that even with the use of atypical neuroleptics, a small number of unwanted and unpleasant side effects may still be involved. Ziprasidone (Zeldox®), which is not yet Food and Drug Administration approved, based on European studies may not have the same proclivity for weight gain as the other atypical antipsychotics.

**Dr. Linmarie Sikich**, of the University of North Carolina, along with **Dr. Jeffrey Lieberman**, studied a cohort of children with heterogeneous psychotic presentations (one-half with affective disorders), **comparing the efficacy of haloperidol (Haldol®), olanzapine, and risperidone**. Half of the children on haloperidol experienced severe extrapyramidal (motor) symptoms whereas, in the risperidone group, 10% had severe symptoms and 60% had mild to moderate symptoms. Sixty-five percent showed mild to moderate parkinsonian side effects with olanzapine. All of these side effects occurred in the context of a 50–70% decrease in psychosis scores at 20 weeks of treatment; all three medications were approximately equal in efficacy. Children gained approximately 0.4 pounds per week on haloperidol, 1.8 pounds per week on risperidone, and 1.7 pounds per week on olanzapine. After 8 weeks, children had gained an average of 4 pounds on haloperidol and 12 pounds on risperidone, and after 16 weeks, 30 pounds on olanzapine.

**Dr. Jeffrey Lieberman** of the University of North Carolina and **Dr. John Kane** of Long Island Jewish Medical Center both noted the great importance of the work in prodromal schizophrenia, particularly given the research literature indicating that the longer the duration of untreated illness, the poorer the outcome in the schizophrenic syndromes, as recently summarized by many investigators, including Wyatt and Henter (1998; *J Psychiatr Res* 32: 169–177). In adults, the data indicate that with each succes-

sive episode of relapse, individuals with schizophrenia may be increasingly treatment-refractory, as evidenced by the neuroleptic response time and other indices.

Dr. Kane raised the issue of considering early intervention with safer but unproven agents, such as high potency benzodiazepines or antioxidants, which have some rational basis; antioxidants could help prevent the postulated loss of brain substance as evidenced by a number of studies using various imaging techniques.

**Dr. Laura Lee Hall**, of the National Alliance for the Mentally Ill (NAMI), offered a **NAMI and family perspective**, noting that even the possibility of preventive treatment in the schizophrenia syndromes is met with a new sense of excitement, along with some regret that these possibilities were not available for many children who have already suffered a severe deteriorating course of schizophrenia. She also indicated that the most frequent calls that NAMI now receives are from parents frantic for further information on how to negotiate for their bipolar children the difficulties of finding an appropriate physician and knowing how to intervene. One hundred fifty phone calls on the issue of treatment of children with bipolar illness were recently received in a short period of time.

**Editor's Note:** It would appear that the field of psychiatry should place a moratorium on the controversy surrounding diagnostic thresholds for bipolar illness and temporarily agree to call these syndromes bipolar-like rather than bipolar *per se*. The one area that child psychiatrists in the field agree on is that these bipolar-like children are suffering greatly and are highly dysfunctional, whatever their ultimate diagnostic labels. In this area, experience and empirical data on treatment efficacy should be favored over theoretical perspectives and historical biases.

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## Meeting Highlights: Early Intervention - Bipolar Illness

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### Part II: Early Intervention in Prodromal Bipolar Illness

**Dr. Gabrielle Carlson**, of the State University of New York (SUNY)-Stony Brook, addressed **early detection of bipolar illness in adolescents** by reviewing her data on 191 6–12 year olds referred for outpatient evaluation between 1968 and 1973 for hyperkinetic (excessive muscular activity) disorders and other evidence of minimal cerebral dysfunction. One hundred fifty four of these children were followed-up through ages 21 to 23; only six had confirmed manic diagnoses. Hyperactivity, impulsivity, and negative affect were prominent in these individuals.

**Editor’s Note:** These data confirm the view that the vast majority of children presenting with hyperkinetic and attentional disorders consistent with a diagnosis of attention-deficit hyperactivity disorder (ADHD) do not develop bipolar disorder. At the same time, it is widely agreed that the majority of children who have bipolar disorder also meet criteria for concurrent ADHD and often require treatment for this syndrome, but only after their mood disorder has been stabilized is ADHD treatment likely to be effective.

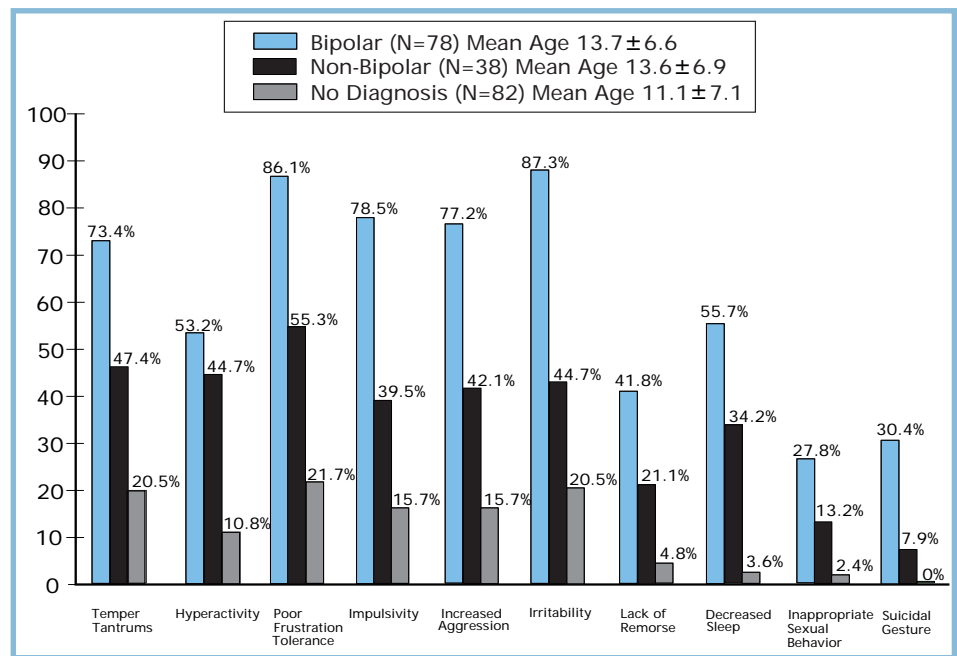
In Dr. Carlson’s study, the 6 children who later became manic had a high degree of comorbidity including depression, anxiety, panic disorder, alcohol and substance abuse, antisocial behavior, increased numbers of hospitalizations, decreased school performance, and decreased GAS (overall function) scores. These data are consistent with the high degrees of comorbidity reported in adult bipolar disorder (Regier et al., 1990, *JAMA* 264: 2511–2518; Kessler et al., 1997, *Arch Gen Psychiatry* 54: 313–321) as well as in our own Network (Suppes et al., 1999, *J Affect Disord*, in press).

**Editor’s note:** Perhaps the extremely high level of comorbidity in child, adolescent, and adult presentations of bipo-

lar disorder can be used as a diagnostic aid for arriving at an appropriate diagnosis, rather than as a diagnostic confound in search of the pure bipolar presentation, which may only be present in a small minority of patients.

from the controversial diagnostic issues toward approaches based on target symptoms and their treatment.

**Dr. Robert Post**, from the National Institute of Mental Health and the Stanley Foundation Bipolar Network,



**Incidence of selected symptoms in childhood bipolar illness; from Fergus et al. 1999 (see below)**

**Dr. Elizabeth Weller**, of the University of Pennsylvania, spoke on **early detection of bipolar illness in children**, reviewing data from 152 children (average age of ten years) who had an average age of onset of bipolar illness of approximately six years, with bipolar symptoms lasting seven to ten days.

In discussing both presentations on early detection, **Dr. Neal Ryan**, from the University of Pittsburgh, spoke of the **importance of early, open, uncontrolled treatment data** that would be critical in designing subsequent studies with enough children to achieve statistical significance. He also spoke of the importance of dimensional rather than categorical approaches and of moving away

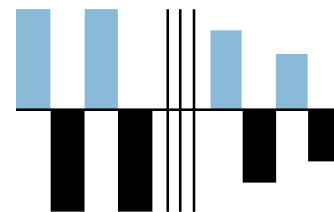
presented a talk on **early intervention in children with a very high risk for bipolar illness—a Stanley Foundation initiative**. This talk—summarizing a poster presented by Emily Fergus at the 1999 American Psychiatric Association meeting—indicated that a group of five symptoms highly predict a diagnosis of bipolar disorder. This finding is based on a retrospective survey of parents on the earliest symptoms associated with moderate to severe dysfunction in 78 children with a diagnosis of bipolar illness, 38 children with a non-bipolar diagnosis (such as unipolar illness or ADHD), and 82 children with no psychiatric illness. The average age of the children at the

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## Life Chart Highlight

### Nimodipine treatment of an adolescent with ultradian cycling bipolar affective illness\*

Pablo A. Davanzo, MD, Natalie Krah, MD,  
Jillian Kleiner, MD, and James McCracken, MD



In preschool, the patient illustrated in the life chart (p. 7) was described as aggressive and cruel to animals. He was also noted to have difficulties learning to read and was diagnosed as dyslexic (figure 1). At the age of six he was diagnosed with attention deficit hyperactivity disorder (ADHD) and treated with methylphenidate (Ritalin®) for a period of nine months (figure 1, right), followed by dextroamphetamine (Adderall®, Dexedrine®) for a period of 14 months (figure 2, left). On stimulants he continued to experience difficulty concentrating and developed noticeable “rebound”, rapid speech, and occasional stomach ache.

In January 1991, at age nine, he was diagnosed with chronic fatigue syndrome by his pediatrician and treated for symptoms of depression a year later with fluoxetine (Prozac®) 20 mg daily for a period of two weeks. After ten days on fluoxetine, the patient became acutely manic, requiring his first inpatient psychiatric admission in October 1992, at the age of ten (figure 2). At that time he presented with severe agitation and dyscontrol and was diagnosed with bipolar disorder and ADHD. After three weeks, he was discharged on lithium and clonidine (Catapres®). In March 1993, at the age of ten years, seven months, he had a second manic episode. He was treated with adjunctive neuroleptics as an outpatient for approximately eight

months, in addition to lithium and clonidine in adjusted doses. During this episode, he suffered from intermittent periods of depression (i.e., lack of energy, wanting to watch TV all day), anhedonia, melancholia, and lack of appetite, lasting two to three months and remitting spontaneously. He was hospitalized for a second time in November 1993 at age 11, with the diagnosis of bipolar I disorder, most recent episode manic, with psychotic features, and rapid cycling. This (his third) manic episode manifested with severe irritability, cruelty to animals, impulsivity (i.e., crossing the street without looking) and grandiosity (i.e., nothing can happen to me), hypersexuality (i.e., increased masturbation), suicidal ideation, and abnormal perceptions (i.e., reports of seeing a monster in his room).

Daily behaviors charted by staff showed an alternating pattern of lethargy, introversion, and depressed mood in the mornings, followed by hypertalkativeness, poor impulse control, agitation and irritability, and suicidality at bedtime, almost on a daily basis. Carbamazepine (Tegretol®) was started and titrated to a level of 8 µg/dL. Decreased suicidal ideation, irritability, and overall mood swings were documented after two weeks. In addition to medication, the patient received weekly individual psychotherapy and parent training.

Four months later, in March of 1994, despite compliance with lithium and carbamazepine, he was readmitted to the hospital due to a relapse. He appeared manic and reported depressed mood with

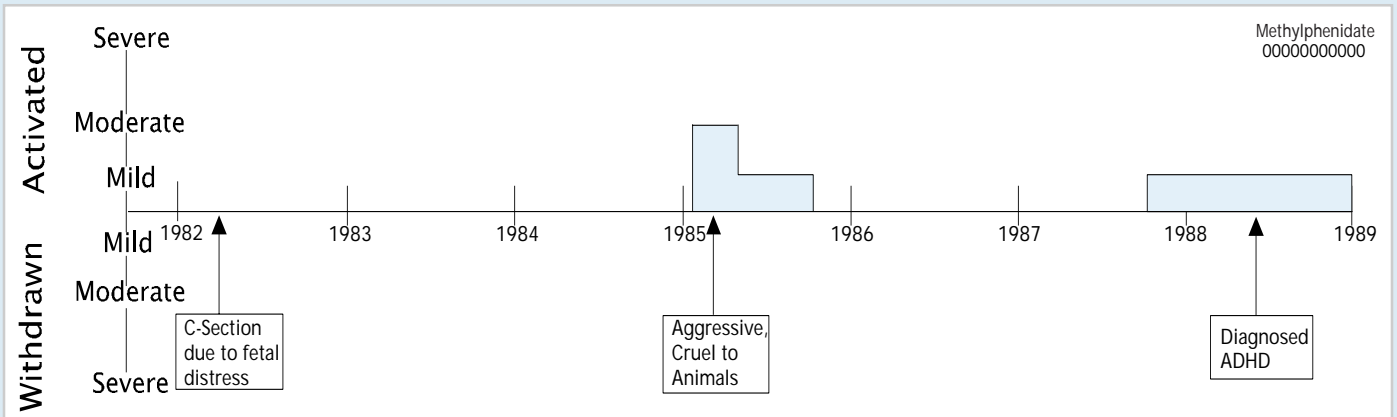
suicidal ideation, as well as command and visual hallucinations. Carbamazepine was switched to divalproex sodium (Depakote®), and a therapeutic level of 93 µg/dL was achieved after ten days. By the third week of treatment he became less pressured in speech, more redirectable, and less hyperactive and irritable. He voiced no suicidal ideation and was discharged on lithium carbonate, divalproex sodium, levothyroxine (T<sub>4</sub>), and clonidine.

The patient remained in remission for approximately two months, but was soon readmitted to the hospital for a fourth time in a manic psychotic state. His lithium level was 0.8 mM and his valproate level was 124 µg/dL. Standard chemistry laboratory was normal. The lithium dosage was increased, and chlorpromazine (Thorazine®) was added, resulting in partial resolution of symptoms. He was discharged on chlorpromazine, divalproex sodium, levothyroxine, lithium, and clonidine. On this regimen he gained weight and developed an intention tremor in both hands. He was reported to have low energy and difficulty walking.

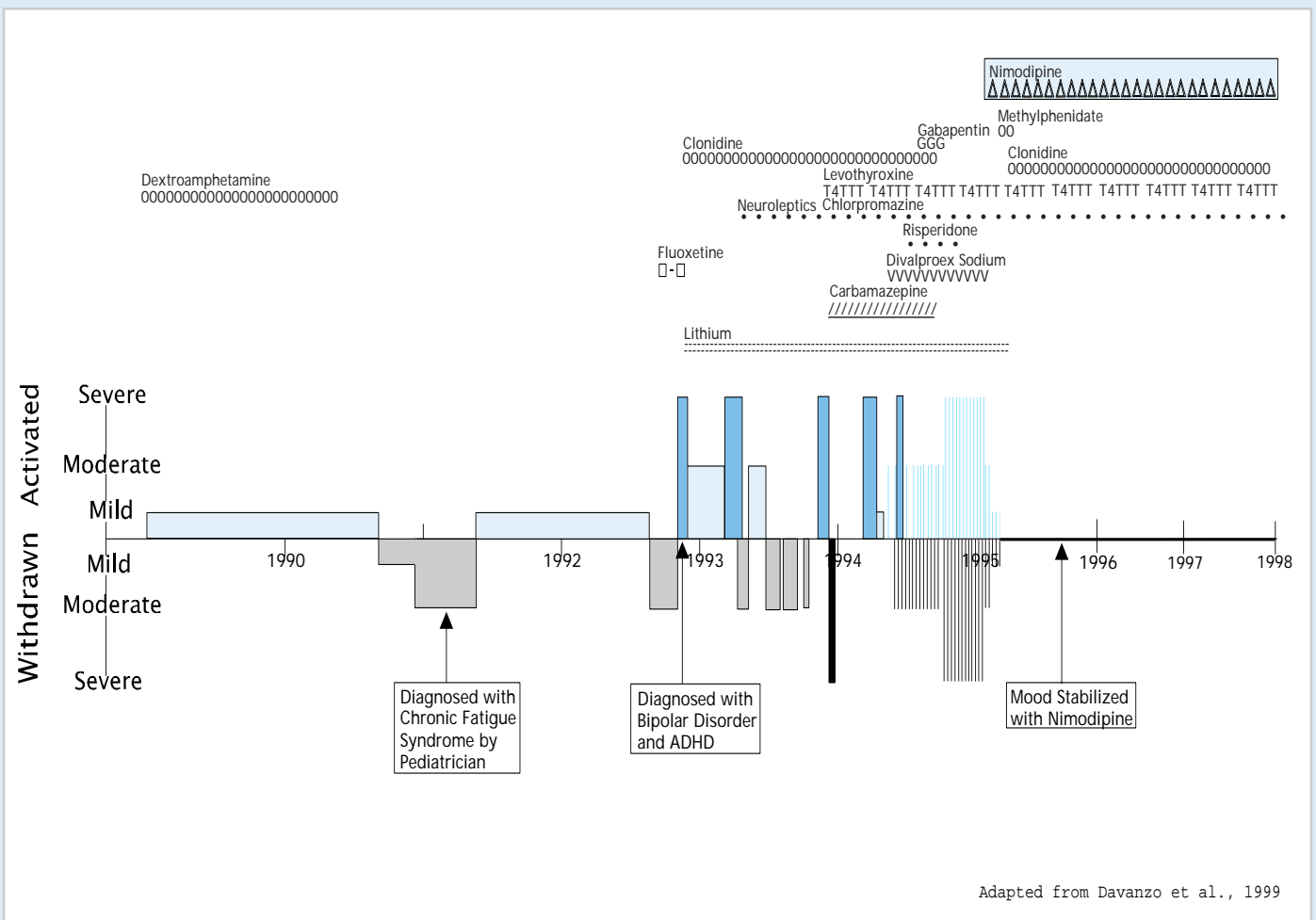
One month later he was noted to be “more creative, fearful and hyperactive,” and had hit a peer in school. The patient was unable to tolerate an increase in levothyroxine and chlorpromazine or clonazepam (Klonopin®) due to the intolerable side effects of tachycardia, heat intolerance, and sweating. He also failed trials of risperidone (Risperdal®) and gabapentin (Neurontin®) due to side effects (figure 2, right).

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**Figure 1:** Life chart showing poor response to stimulants for a presumptive diagnosis of ADHD.



**Figure 2:** Life chart showing fluoxetine-related switch into mania; inadequate response to lithium, plus adjunctive neuroleptics, carbamazepine, divalproex sodium, gabapentin, levothyroxine, and clonidine; excellent response to the dihydropyridine calcium channel blocker nimodipine.

## Life Chart Highlight

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### Nimodipine Trial

The patient was admitted in a manic state, intermittently depressed and agitated. Daily behaviors charted by staff revealed a chaotic pattern of introversion, depressed mood, and suicidality interspersed with episodes of hypertalkativeness, hypomania, poor impulse control, agitation, and severe irritability. These shifts occurred within 24-hour periods and therefore were considered to satisfy criteria for an ultradian cycling type of bipolar affective illness (Kramlinger & Post, 1996, *Br J Psychiatry* 168: 314–323).

After written informed parental consent, nimodipine (Nimotop®) was started at 30 mg at bedtime. The drug was titrated up to 60 mg orally three times daily over a period of 12 days, with daily monitoring of blood pressure and heart rate. The patient entered the trial taking lithium 450 mg twice daily, levothyroxine 200 µg/day, and chlorpromazine 25 mg twice daily. These medications were held constant, except for lithium, which was decreased by half the dose on day 10, and discontinued on day 13. By day three, the patient showed de-

creased severity of depression, although he continued to experience repeated, rapid, and clinically significant changes of mood. Nimodipine was increased to 30 mg three times daily on day four. On day six, although still manic, the patient slept well for the first time in months, followed by two days of hypersomnia and sedation. On day nine the patient's mood stabilized. His nimodipine dosage was 30 mg twice daily and 60 mg at bedtime. He reported "feeling better than ever before in his life." He appeared calmed and participated appropriately in ward activities. On days nine through 12 he was generally euthymic. Several days later, an attempt was made to taper levothyroxine, which resulted in increased hyperactivity. This was attributed to comorbid ADHD and methylphenidate was initiated. By discharge on day 18, the patient's mood remained stable, with no evidence of cycling for nine days. He was discharged on the following medications: nimodipine 60 mg three times daily, levothyroxine 200 µg every morning, methylphenidate 10 mg twice daily, and chlorpromazine 25 mg twice daily. One

month after discharge clonidine was substituted for methylphenidate due to the development of persistent motor tics on methylphenidate.

The patient has remained in remission for three years and has not required hospitalization since 1995 (figure 2, far right). He remains compliant with medication treatment and denies significant side effects. In the spring of 1998 his nimodipine dosage was reduced from 180 mg/day to 150 mg/day; however, he developed signs of hypomania, prompting a return to the original dose.

This patient illustrates a response to the L-type calcium channel blocker nimodipine in combination with T<sub>4</sub>, methylphenidate, and chlorpromazine when many other mood stabilizer regimens had failed. Illness exacerbation with fluoxetine (1992) and lack of adequate response to stimulants until after the mood was stabilized are not unusual. Other dihydropyridine calcium channel blockers such as isradipine (Dynacirc®) and amlodipine (Norvasc®) also appear effective with amlodipine the easiest to use because of its long half-life. ■

### Meeting Highlights: Early Intervention - Bipolar Illness

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time of the survey was approximately 13 years. As illustrated in the figure on page 5, there was a high incidence of a variety of symptoms in children diagnosed with bipolar disorder compared with non-bipolar diagnosed children and children without any diagnosis. Most of these symptoms would fall in the activated symptoms category rather than in the withdrawn or depressed spectrum (such as suicidal gestures).

A statistical analysis (logistic regression) indicated that the symptoms of grandiosity, suicidality, rapid thoughts, irritability, and hyperactivity best pre-

dicted a bipolar diagnosis, with any combination of three of the five symptoms yielding an 80% or greater likelihood of a bipolar diagnosis. There was only a 9% false positive rate, indicating that if one used these symptoms to decide to intervene with a medication, only 9% of the children in the sample would be unlikely to have a childhood diagnosis of bipolar disorder (and thus potentially treated unnecessarily). The presence of this symptom profile in a population of high-risk children (by virtue of a two-parent family history for affective disorder, with at least one parent diagnosed with bipolar

disorder), would appear to justify an early intervention study (with valproate [Depakote®] or another mood stabilizer) to determine if these early symptoms could be ameliorated, and whether the progression to full-blown bipolar illness could be prevented. Lithium or other treatment could be added on an open basis if children did not respond adequately in the initial randomized phase.

A parental survey that many *BNN* readers participated in also suggested that parents were very supportive of

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## Meeting Highlights: Early Intervention - Bipolar Illness

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such attempts at early intervention, and more than 90% felt that long-term medication interventions at or before diagnosis were appropriate in children at high or very high risk for developing bipolar disorder. Many investigators at the workshop did not feel that an intended Bipolar Network long-term study was warranted yet, suggesting instead that the acute efficacy of valproate and/or lithium be demonstrated on these early symptomatic presentations prior to the ultimate design of a long-term prevention study. Workshop participants felt that the proposed early use of rescue medicine with lithium, although further assuring parents that their children could rapidly move to an active treatment regardless of whether their child was randomized to the valproate or placebo arm of the study, would at the same time confound the interpretation of the preventive component of the study.

The Bipolar Network has thus redesigned the early intervention study (described in previous *BNNs*) to initially focus on an acute treatment phase in children at very high risk, with a naturalistic follow-up phase thereafter. Thus, for the many families who have already volunteered to participate in the early intervention initiative for children at very high risk, an acute study will still be available. The Network hopes to initiate such a study in six months to one year after all of the scientific, institutional, and ethical review approvals are received.

**Dr. Vivian Kafantaris**, of Long Island Jewish Medical Center, discussed the **effectiveness and safety of early treatment in bipolar illness**, reporting that only 27 (26%) of 103 children tolerated discontinuation of antipsychotic medicines used with lithium monotherapy at one month, and few tolerated the withdrawal of lithium therapy itself once a manic syndrome was treated. Overall lithium response was quite good

in 23 (77%) of 30 children not previously exposed to medications, whereas it was much less substantial in 17 (35%) of 48 patients with prior medication histories. In subsequent analyses, prior antidepressant therapy was specifically associated with this differential outcome; however, outcome was not related to mixed or dysphoric mania, as had been noted in multiple studies in adults. In those children with prior antidepressant exposure, only 11 (33%) of 33 responded to lithium, whereas 29 (64%) of 46 responded in the group not previously exposed to antidepressants.

**Editor's note:** These data are very similar to those of Kukopulos et al. (1980; *Pharmakopsychiatr Neuropsychopharmakol* 13: 156–167) indicating that concurrent treatment with antidepressants in adults with bipolar illness not only may be associated with cycle acceleration and conversion to a continuously cycling form of the illness, but also may be associated with a less robust response to lithium. Given Dr. Maria Kovacs' data that prepubertal children presenting with severe depression have a 30% risk of displaying mania following the institution of antidepressant treatment, these data from Dr. Kafantaris raise an additional caution concerning the use of antidepressants in children at high risk for bipolar illness.

**Dr. Joseph Biederman**, of the Harvard Medical School, in the context of a presentation on the **relevance of comorbidity**, reviewed his data on a cohort of bipolar children that met formal diagnostic criteria for bipolar illness. Almost all of the children presented with mixed symptoms and with continuous and ultra-rapid cycling, whereas only seven of the 43 showed a clear episodic course more characteristic of the adult illness. The mean age of the children in his sample was seven, with a number of children showing this mixed bipolar pic-

ture at ages three and four. Seventeen percent presented with euphoria, 92% with irritability, 97% with distractibility, 97% with increases in activity and poor judgment, 66% with inordinate crying, 63% with flight of ideas, 54% with grandiosity, and 29% with decreased sleep. As suggested previously, nearly all patients met criteria for ADHD, 93% reached criteria for oppositional defiant disorder, and 40% for conduct disorder. Dr. Biederman found that these children responded almost exclusively to mood stabilizers and antipsychotics, with negligible response to tricyclic antidepressants, serotonin selective re-uptake inhibitors, and stimulants (in the absence of prior mood stabilization). Also striking was the intractability of these illnesses, with only 17% of the children remitting at six months, 30% at one year, and 65% at two years.

**Editor's note:** Given these data, it is easy to see why parents of children with presumptive bipolar illness are calling NAMI in crisis to find appropriate health care providers and treatments for their children. This illness does not respond to treatments that are likely to be used (i.e., tricyclic antidepressants, serotonin selective reuptake inhibitors, and stimulants) and is relatively slow to remit, even with appropriate treatment. Once the illness does remit, 28% show recurrences within one month and 42% within two months, further suggesting the crucial importance of long-term prophylaxis once remission is achieved.

**Dr. Robert Kowatch**, from the University of Texas Southwestern Medical Center (and a recipient of a Stanley Foundation grant for his work on early intervention), **reported results from the first 42 children** with bipolar I (n = 20) or bipolar II (n = 22) illness who were in a manic episode, **randomized to ei-**

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## Preliminary Suggestions for Parents Seeking Treatment for their Children with Bipolar-like Illnesses

The diagnostic controversies involved in the presentation of childhood bipolar illness and the disagreements about diagnostic thresholds make it particularly important for parents to have a rough set of guidelines from which they may begin to pursue treatment options. Dr. Robert Kowatch and associates at the Stanley Center in Dallas are in the process of writing a book for parents of bipolar children and for professionals most likely to be intimately involved in the treatment of these children. However, this book and its details will not be available for at least another year. The excellent book by D. Papolos and J. Papolos (*The Bipolar Child*) is also not yet available (December 1999, Broadway Books). Therefore, members of the Early Intervention Initiative (E.I.I.) have decided to make a series of preliminary suggestions and recommendations based on the minimal evidence available to date in the field. We acknowledge that these are only the roughest guidelines and should rapidly be supplanted by those more empirically based as further studies are completed and new information is gained from the various NIMH, Stanley Foundation, and other research initiatives.

It should also be stated from the outset that these are “consensus” views from a group of individual investigators, each of whom agrees with the general principles as stated, but many of whom would have some differences when approaching different patients in their own clinical practices. In addition, they do not represent the views of many others in the field who would advise more conservative approaches while awaiting a more systematic database upon which to build such recommendations. Therefore, they do not represent NIMH guidelines nor Stanley Foundation guidelines, but are only the initial set of working suggestions from our E.I.I. work group. These individuals include: Drs. Kiki Chang (Stanford); Robert Kowatch (Dallas); John Zajecka (Chicago); Cesar Soutullo, Melissa DelBello, and Susan McElroy (Cincinnati); Robert Findling (Cleveland); Robert Post, Andrew Speer, and Ms. Gabriele Leverich (Bethesda); and Willem Nolen and Catrien Reichart (Utrecht, the Netherlands).

You should be open to the possibility that your child does or does not have bipolar illness, but as in adults, childhood bipolar illness is often associated with other coexisting (comorbid) diagnoses.

- I. **Don't get discouraged.**
- II. No matter how severe, frustrating, or apparently willful your child's behavior appears, try to view it as part of the **symptoms of bipolar illness and out of the child's volitional control.**
- III. **Chart the course** of your child's mood swings on a daily basis, preferably in a systematic graphic format. One format of a systematic “Kiddie-Life Chart” is available from the Stanley Foundation Bipolar Treatment Outcome Network (5430 Grosvenor Lane, Suite 200, Bethesda MD 20814; [800] 518-SFBN). This or a related longitudinal assessment tool will be essential from several perspectives:
  - it will be extremely helpful in arriving at the appropriate **diagnosis**;
  - it will track the symptomatic presentation of the illness which will help engender more **effective treatment efforts from professionals**; and
  - it will help you and clinicians **develop optimal treatment approaches.**
- IV. **Initiate treatment with mood stabilizers rather than antidepressants or stimulants.** As noted on page 11, Dr. Kowatch found in an open randomized study that **lithium, carbamazepine (Tegretol®), and valproate (Depakote®)** are all effective in approximately 40–50% of children with childhood onset bipolar mania. Because these drugs are accepted and effective mood stabilizers in adult illness, they likely have long-term efficacy in preventing both manic and depressive episodes in children and adolescents as well (based on indirect inferences from the modicum of acute antimanic efficacy data in this age group). The details of the side-effects profiles and potential range of efficacy of these well accepted mood stabilizers are readily available and discussed in detail elsewhere (see Table, p. 12, for overview). Antidepressants and stimulants may exacerbate or destabilize the illness if used without a mood stabilizer first.

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- V.** If one mood stabilizer is not effective, **a second mood stabilizer** may be tried as an alternative or may be added to the regimen. If this is not effective, a revision of the mood stabilizer regimen should be considered or a third drug added.
- VI.** Many of the other drugs currently being evaluated as **potential mood stabilizers** are similar to carbamazepine in that they are Food and Drug Administration-approved for use as anticonvulsants in patients with epilepsy, but not mood disorders. Use of these alternative drugs should generally be explored after the options of lithium, carbamazepine, or valproate have been tried.

**a)** Among the newer anticonvulsants, **gabapentin** (Neurontin®) has an excellent side effects and safety profile in adults and children, but its efficacy in adult mood disorders remains controversial and formal studies in pediatric populations of patients with mood dysregulation remain to be performed. Nonetheless, there are anecdotal reports that it may, at times, have dramatic effects on anxiety and depressed mood when used as an adjunctive agent in younger individuals. Although in our larger NIMH study of six weeks of monotherapy (Frye et al., 1999) gabapentin did not have a better overall response rate than placebo, those who did have a good to excellent response were younger adults with shorter durations of illness. There are, however, isolated reports that gabapentin can exacerbate behavioral dyscontrol in some individuals, particularly in those with preexisting brain damage.

**b)** Another newly approved anticonvulsant, **lamotrigine** (Lamictal®), showed an overall 52% response rate in monotherapy in adults, which was significantly greater than either gabapentin (26%) or placebo (22%) in patients with treatment-refractory affective disorders (most of whom

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## Meeting Highlights: Early Intervention - Bipolar Illness

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**ther carbamazepine (Tegretol®), lithium, or valproate** and followed in an open trial. Using Clinical Global Impressions (CGI) criteria or the Mania Rating Scale (MRS), respectively, the response rate to carbamazepine was 31% or 38%, the response rate to lithium was 38% or 31%, and the response rate to valproate was 40% or 53%. In the “completer” analysis on the 32 subjects who received five weeks of treatment, the response rates were 44% for carbamazepine, 45% for lithium, and 50% for valproate.

**Editor’s note:** On the positive side, lithium, carbamazepine, and valproate all appear to be equally effective for intervention in childhood and adolescent acute manic presentations.

However children, like adults, appear to often require combination therapy, and most of the patients in Dr. Kowatch’s study required several mood stabilizers in combination, as well as the later addition of a psychomotor stimulant for residual ADHD symptoms, before achieving adequate remission. These data are consistent with those of Dr. Robert Findling from the Stanley Center at Case Western Reserve University, who found much better responses to the combination of lithium and valproate in children than he did to either in monotherapy.

Although most would agree that Dr. Kowatch’s study would be enhanced with a placebo phase, there are nonetheless practical consequences

and important implications of this study. The study was randomized from the beginning, and therefore probably reflects the ultimate response rate, meaning the differences in efficacy among these three agents (lithium, carbamazepine, and valproate) are not likely to eventually emerge as large. Given its open rather than double-blind design, the relatively low response rates are more likely underestimates rather than overestimates of the degree of efficacy that would result from blind studies. These data also suggest a probable continuum of efficacy with adult mania, because considerable evidence shows that each of these three compounds is effective in adult bipolar illness. ■

Preliminary Clinical Impressions of Comparative Clinical and Side-Effects Profiles of Lithium,  
Nimodipine, and the Putative Mood-Stabilizing Anticonvulsants in Adults

	Lithium (0.5-1.2 mEq/L)	Carbamazepine (4-12 µg/mL)	Valproate (50-120 µg/mL)	Nimodipine	(Lamotrigine) <sup>A</sup>	Gabapentin	Topiramate
<b>Clinical Profiles</b>							
● <i>Acute Episodes</i>							
Mania (M)	++	++	++	+	(±)	—	(±)
Dysphoric mania	+	(++)	++	(+)	?	—	(±)
Depression (D)	+	+	±	(+)	++	(±)	(±)
● <i>Prophylaxis</i>							
Mania	++	++	++	(+)	(+)	(±)	(±)
Depression	+	+	+	(+)	+	(+)	(±)
Rapid cycling	+	+	++	(+)	(+)	(±)	(+)
Continuous cycling	+	+	+	+	?	?	(+)
● <i>Seizures</i>							
Generalized (and complex partial)	—	++	++	±	++	++	++
Absence	—	—	++	?	++	?	?
● <i>Paroxysmal pain syndromes</i>							
Migraine	+	±	++	+	?	(±)	?
<b>Side-Effects Profiles</b>							
White blood cell count	↑↑ <sup>§</sup>	↓↓	(↓)	—	—	—	—
Diabetes insipidus	↑↑ <sup>§</sup>	↓	—	—	—	—	—
Thyroid hormones: T <sub>3</sub> , T <sub>4</sub>	↓↓	↓↓	↓	—	?	(↑)?	?
Thyroid stimulating hormone	↑↑ <sup>§</sup>	—	?	—	—	—	?
Serum calcium	↑	↓	?	?	?	?	—
Weight	↑↑	(↑)	↑↑	—	↓	↑	↓↓
Tremor	↑↑	—	↑↑	—	↑	↓, ↑	(↑)
Memory disturbances	↑	↑	↑	↓	(↑)	↑	↑↑
Diarrhea, gastro-intestinal distress	↑↑	↑	↑↑	(↓)	—	(↑)	(↑)
Teratogenesis	(↑)	↑	↑↑	—	?	?	?
Psoriasis	↑	—	—	—	—	—	—
Rash	↑	↑↑	(↑)	(↑)	↑↑ <sup>§</sup>	(↑)	?
Alopecia	(↑)	—	↑	—	—	—	—
Agranulocytosis, aplastic anemia	—	(↑)	—	—	—	—	—
Thrombocytopenia	—	(↑)	↑	—	—	—	—
Hepatitis	—	↑	↑	—	?	—	(↑)?
Hyponatremia, water intoxication	—	↑	—	—	—	—	—
Dizziness, ataxia, diplopia	↑	↑↑	↑	(↑)	↑	↑	↑

**Clinical Efficacy:** — = none; ± = equivocal; + = effective; ++ = very effective; ( ) = weak or questionable data; ? = unknown; — — = exacerbation

**Side Effects:** ↑ = increase; ↓ = decrease; ( ) = inconsistent or rare; — = absent

<sup>A</sup> Lamotrigine rash is common in approximately 10% of patients; severe, life-threatening rash occurs in about 1 out of every 100 children and is thus not recommended for children under the age of 16.

<sup>§</sup> Effect of lithium predominates over that of carbamazepine when used in combination.

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were bipolar) (Frye et al., 1999). These results were similar to a recently published double-blind trial of the significant benefits of either 50 or 200 mg/day of lamotrigine monotherapy compared with placebo in bipolar depression (Calabrese et al., 1999, *J Clin Psychiatry* 60: 79–88). Another recent unpublished study presented at the 1999 American Psychiatric Association meeting also showed superiority of lamotrigine over placebo and equal efficacy with the tricyclic antidepressant desipramine in unipolar depression (Londborg et al., 1999). However, lamotrigine is associated with an approximately 5–8% risk of rash, with about 1 in 300 of these rashes in adults progressing to a severe and potentially life-threatening rash requiring hospitalization (Stevens-Johnson Syndrome, or toxic epidermal necrolysis). It appears that the risk for this uncommon but severe medical complication is increased with rapid dose increases, a combination of lamotrigine with valproate, a history of rashes on other psychotropic and anticonvulsant treatments, **and a younger age**. The incidence of severe rash in children is about 1 in 100. Thus, **lamotrigine is not recommended by the FDA for anyone younger than 16 years of age**. In all individuals, a very slow dose increase is strongly recommended by the pharmaceutical company and clinicians. The recommended dosage is one 25 mg pill/day for two weeks and then two pills/day for two weeks, with 25 mg increments per week thereafter. One-half this rate of dose titration is recommended in patients on concurrent valproate treatment (because valproate doubles lamotrigine levels). Conversely, a faster rate of increase is possible with carbamazepine (because carbamazepine halves the levels of lamotrigine).

c) Another newly approved add-on treatment for refractory epilepsy is **topiramate** (Topamax®). Two open studies with topiramate have been performed, one in the Bipolar Treatment Outcome Network (McElroy et al., 1999). Both of these open, add-on studies and the study of Marcotte (1998; *J Affect Disord* 50: 245–251) suggest potential antimanic and mood stabilizing effects of this agent with a moderate degree of dose-related weight loss. Acute antidepressant effects were not observed (McElroy et al., 1999). This potential for weight loss can be a positive side effect of topiramate, and contrasts with the currently available atypical neuroleptics and, to some extent, lithium and valproate, and some of the unimodal antidepressants (which can cause weight gain). This side-effect may give topiramate, even with unproven efficacy in affective illness in either adults or children, added advantages for the patient with drug-related weight gain. Adverse side effects of topiramate also include a 1% incidence of kidney stones because it is a carbonic anhydrase inhibitor. The kidney stones occur predominately in men and are made up of calcium deposits which respond readily to sonication treatment (lithotripsy) in an emergency room setting. Another potential side effect of this agent in some 5–10% of patients is speech or word-finding difficulties which may occur more often in patients on prior complex medication regimens and in those in whom topiramate is added rapidly and used in high doses. Thus, an ultraconservative regimen for this agent is to start with one 25 mg pill/day and increase the dose by one pill on a weekly basis to avoid this side effect.

d) Another unproven but promising class of agents for adult bipolar illness are the dihydropyridine L-type calcium channel blockers which are used medically for high blood pressure, arrhythmias, subarachnoid hemorrhage, and migraine. These agents include **nimodipine** (Nimotop®), **isradipine** (DynaCirc®), and **amlodipine** (Norvasc®). Small double-blind, controlled case series have suggested efficacy of nimodipine and isradipine, but several patients responsive to these agents did not respond to the more widely used drug verapamil (Calan®, Isoptin®), which is not a dihydropyridine (Pazzaglia et al., 1993, *Psychiatry Res* 49: 257–272; Pazzaglia et al., 1998, *J Clin Psychopharmacol* 18: 404–413). Case vignettes suggest similar positive results compared with nimodipine in some individuals with the easier to use and

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longer-acting agent amlodipine. Amlodipine has a longer half-life than either nimodipine or isradipine and is suitable for single nighttime or twice-daily dosing. Davanzo et al. (1999, see page 6) have reported an excellent response to nimodipine in an adolescent bipolar patient, and this whole class of agents (which may have a more benign side-effects profile compared with lithium) deserves further investigation and controlled trials in children and adolescents with bipolar-like syndromes.

**e)** The role of **omega-3 fatty acids** is also beginning to be studied in adults with bipolar illness. As reported in the last issue of the *BNN*, Stoll et al. (1999; *Arch Gen Psychiatry* 56: 407–412) reported that omega-3 fatty acids (9 grams/day) were superior to an olive oil placebo in stabilizing mood when used as an add-on treatment. Recurrent bipolar depressions were particularly reduced. Further clinical trials in large numbers of adult subjects are exploring this promising approach, which has few serious side effects. Data on efficacy and side effects are not yet available in children.

**VII.** Additional augmentation of the mood stabilizer treatment regimen can be targeted to residual symptoms with one of the following options:

**a) If ADHD symptoms remain after optimal mood stabilization has been achieved,** augmentation with a psychomotor stimulant may then be considered, i.e., methylphenidate (Ritalin®), amphetamine (Dexedrine®, Adderal®), or pemoline (Cylert®).

**b) If persistent depressive elements of the syndrome remain particularly severe,** one might consider augmentation of the mood stabilizers with the antidepressant bupropion (Wellbutrin®). In addition to the promise of antidepressant effects, bupropion might also target concurrent ADHD symptoms, because one study reported bupropion and methylphenidate showed equal efficacy on ADHD symptoms in children without comorbid depression (Barrickman et al., 1995; *J Am Acad Child Adolesc Psychiatry* 34: 649–657).

The utility of adding one of the serotonin-selective reuptake inhibitors (SSRIs), such as fluoxetine (Prozac®), paroxetine (Paxil®), sertraline (Zoloft®), fluvoxamine (Luvox®) and citalopram (Celexa®), or the serotonin-norepinephrine reuptake inhibitor venlafaxine (Effexor®) also require further examination. Anecdotal data of Dr. Biederman et al. (see page 9) suggest that the antidepressants without an adjunctive mood stabilizer are not particularly effective in childhood or adolescent bipolar illness, and tricyclic antidepressants should be avoided because of reduced safety in overdose and questionable efficacy compared with the newer antidepressants. The SSRIs can be useful for comorbid anxiety, panic, and obsessive-compulsive symptoms.

Thyroid potentiation of an antidepressant or mood stabilizing regimen is often considered in adults in light of positive effects of T<sub>3</sub> (Cytomel®, 25–37.5 µg/day) in studies independent of whether or not there are abnormalities in thyroid function; no efficacy data exist in children, however.

**c) If residual manic or psychotic symptoms remain** after otherwise partial efficacy with one or more mood stabilizers in combination, one could consider augmenting with one of the newer atypical neuroleptics that does not require weekly blood monitoring, as opposed to clozapine (Clozaril®), which does require intensive (weekly) monitoring. These drugs, which include risperidone (Risperdal®), olanzapine (Zyprexa®), and quetiapine (Seroquel®) may not be quite as benign in children and adolescents as originally conceptualized in adults because substantial degrees of weight gain and a moderate amount of extrapyramidal motor side effects such as

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parkinsonism or akathisia can occur. It is hoped that the soon-to-be-released atypical neuroleptic ziprasidone (Zeldox®) will be better tolerated, because it is not associated with weight gain.

- VIII. We suggest a focused **search for a compatible doctor** who is willing to be sympathetic, but yet inventive and aggressive in his or her treatment approaches, and willing to listen to you and the nature of your child's responses to treatment or initial lack thereof. This doctor could be an adult psychiatrist specializing in psychopharmacology if a so-inclined child psychiatrist cannot be easily located. As with adult onset bipolar illness, where talk therapy alone does not appear to be a sufficient treatment, individual or family treatment may be helpful in early onset bipolar illness but most of the time medications are required as well. As with any medical illness, you should feel free to obtain a second opinion.
- IX. If you as a parent have unipolar or bipolar illness, consider making use of **your own treatment team** for advice, suggestions, and support about your child's treatment, and let your child's doctor know which medications have been particularly helpful for you.
- X. If you have a child with bipolar illness, request **regular child or family sessions** with a knowledgeable therapist. Any managed health care system should recognize that this treatment is very much in their as well as your long-term best interest, because helping to prevent major difficulties, hospitalizations, etc. will ultimately save money in the long-term. Insist that therapy, in addition to psychopharmacologic intervention, is authorized by your insurance company.
- XI. Finding a **support group**, with the help of advocacy groups such as the National Depressive and Manic Depressive Association or the National Alliance for the Mentally Ill, may be helpful as well. Some support groups are specifically directed at the problems of children with bipolar illness, and The Child and Adolescent Bipolar Foundation is launching an interactive website at [www.cabf.org](http://www.cabf.org). They can also be reached via their e-mail address: [cabf@bpso.org](mailto:cabf@bpso.org), or you can write to them for further information or to add your name to their mailing list at: The Child and Adolescent Bipolar Foundation, 1187 Wilmette Ave, #331, Wilmette, IL 60091.
- XII. You may want to consider some approaches to managing your child during difficult times as suggested by Dr. Ross Greene at Massachusetts General Hospital in his book *The Explosive Child* (1998, pp. 133–173). He proposes a framework in the form of three "Baskets" into which your child's behaviors can be placed during times of conflict between parent and child. **Basket A**, the "**Safety Basket**" would contain a very few behaviors that are not negotiable because they relate to issues of unsafe behaviors, i.e., behaviors that could be harmful to your child, other people, animals, or property. For Basket A you are the authority figure who makes the decision about the safety of behaviors. "**Basket B**" could be called the "**Compromise Basket**" into which behaviors fall that are a "high priority" but over which you do not want to induce a "meltdown" between yourself and your child. Basket B provides the opportunity for communication, negotiation, and compromise between yourself and your child. This may be a very difficult and slowly developing process, however. "**Basket C**" could be seen as the "**Reduction of Frustration Basket**" where most behaviors, once considered a high priority, are placed because they have been downgraded by you as of lesser importance and something that could be put aside, at least for now. Placing as many things as possible initially in this basket recognizes that your child may not have good control over his or her irritability, impulsivity, and frustration tolerance and avoiding as many unnecessary confrontations (that may lead to meltdowns) as possible is desirable. ■

## **Bipolar Network News**

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### **CHANGE SERVICE REQUESTED**

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**Nimodipine Treatment of a Bipolar Adolescent**  
**Suggestions for Parents with Bipolar Children**

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