Volume 3 Issue 2
July 1997

A Stanley Foundation Bipolar Network Publication

Bipolar Network News

Clinical Trials Update: A Focus on Early Onset

This issue of the *BNN* focuses almost exclusively on issues pertinent to childhood- and adolescent-onset bipolar illness. There is increasing recognition of early presentations of bipolar illness in children and adults, often with considerable family, social, and educational disability. Whereas several decades ago the existence of bipolar illness in preadolescent children was considered a rarity or an anomaly, it is now increasingly recognized, with the additional observation that some patients can have rapid-cycling presentations in their first several years of life. Over the past several years, the NIMH has acknowledged this dilemma and has held several conferences on the problems of early presentation, diagnosis, and treatment of this syndrome. A summary of the latest meeting is presented in the Meeting Highlights section of this *BNN*.

As an offshoot of the Stanley Foundation Bipolar Treatment Outcome Network for adults, we decided to approach some of the issues of early onset bipolar illness with a concerted Early Intervention Initiative (E.I.I.). A subcommittee of concerned investigators, including Drs. Robert Kowatch of Dallas, Willem Nolen and Catrien Reichart of Utrecht, Robert Findling of Case-Western Reserve, and Robert Post and Gabriele Leverich, LCSW, of the NIMH, met on several occasions to discuss a core instrument rating and assessment package that might be adopted by interested investigators to insure a common set of descriptive measures (in addition to each center's typical or more focused and specialized instruments). The recommendations of the subcommittee were then brought back to the entire Network for approval, as well as to a wider circle of colleagues sharing these common interests.

The core instrument packet includes 1) the Kiddie LCM (K-LCM™); 2) the K-SADS; 3) the Young Mania Rating Scale (YMRS); 4) the Inventory of Depressive Symptomatology (IDS); and 5) the Clinical Global Impressions Scale-Bipolar Version (CGI-BP) as noted below.

The Kiddie LCM (K-LCM™) is a prospective longitudinal daily rating by parents of children's mood and behavior and associated functional impact. It also has a retrospective version based on monthly rating domains. The rationale for the development of this measure, including the need for longitudinal assessment and continuity with the adult LCM, is described in more detail throughout this *BNN* issue.

The Kiddie SADS was chosen over the Kiddie SCID because it is more detailed, sensitive, and DSM-IV compatible. For more intense cross-sectional evaluation of manic and depressive symptoms, the Young Mania Rating Scale (YMRS) and the Inventory of Depressive Symptomatology (IDS) were chosen with the acknowledgment that both were largely inadequate for children, but had the advantage of continuity with the same scales used in the adult Network. The IDS has the asset of having both a clinical- and self-rated version. The measurements would at least allow systematic development of more appropriate childhood rating measures in comparison with these core measures.

The fifth measure is the Clinical Global Impressions Scale as revised for use with bipolar illness (CGI-BP). Again, it was acknowledged that this scale, while imperfect, at least provided a means of assessing severity and treatment-related improvement in manic and depressive domains reflecting clinically relevant degrees of change (i.e., A.- Excellent/Very Much Improved; B.- Moderate/Much Improved; C.- Mild/Slight improvement; D.- No change; E.- Slightly worse, etc.).

(Continued on page 2)

(Continued from page 1)

This core assessment package is available to clinicians and investigators interested in using all or parts of it for clinical investigations and comparisons with other instruments. Please call 1-800-518-SFBN (7326) or write: Stanley Foundation Bipolar Network, Early Intervention Initiative (E.I.I.), 5430 Grosvenor Lane, Suite 200, Bethesda, MD, 20814.

Another element of the E.I.I. was an attempt to circumvent the hurdle of questioning the utility of early intervention in mood disorders in children based on the uncertainty of their diagnosis and clinical course. After consulting many experts in the field, the Network decided to preselect children of families in which both parents had affective illness (one bipolar) to begin a focus on early intervention, if not primary prophylaxis. This was done because there is a very high risk of mood disorders in these children, and in these circumstances, parents would be more likely to desire effective treatment for their children. To this end, we designed a survey of parental attitudes about the ethics of early intervention and will be using this survey to develop a systematic and controlled clinical trial of very early intervention in the illness (likely at first symptoms) rather than at a much later time when children have already reached full diagnostic thresholds.

Parents in families with bipolar illness on one or both sides are encouraged to participate in this survey to help us better understand and study the earliest presentations of the illness. In addition to this planned Early Intervention study, several randomized, controlled clinical trials are already in existence, funded by a separate Stanley Foundation grants program in Dallas, the Stanley Center program at Case-Western Reserve University, or the Stanley Network site in Utrecht, as supplemented by a major grant from the Government of The Netherlands.

Editors-in-Chief:
Robert M. Post, MD
Gabriele S. Leverich, LCSW

Managing Editor:
Thomya L. Hogan

For communication or to be placed on the mailing list, please contact:
Bipolar Network News
c/o Stanley Foundation
Bipolar Network
5430 Grosvenor Lane
Suite 200
Bethesda, MD 20814
Telephone: (800) 518-SFBN (7326)
Fax: (301) 571-0768

Internet address:
stanley@sparky.nimh.nih.gov

Stanley HomePage:
chief@sparky.nimh.nih.gov

The Dallas study involves randomized, open treatment with lithium, carbamazepine, or valproate for six months, with nonresponders crossing over to the second drug and then the two drugs in combination. Dr. Kowatch, who is heading this study, has already recruited several other collaborative groups to participate in the study in order to acquire a larger database more rapidly and to make more systematic recommendations for the field. Children ages six through 18 who meet full diagnostic criteria for bipolar illness are eligible for this study in Dallas, as well as at several collaborating sites.

At the Network's Utrecht site, children ages 12 to 20 with full syndromal diagnoses but inadequate treatment response will be randomized to the addition of valproate versus placebo to their current treatment regimen.

Children over the age of 18 who are subsyndromal, but at high risk because of bipolar illness in one parent, will also be eligible for a randomized comparison of valproate plus aggressive psycho-educational treatment, versus placebo and psycho-educational treatment, in order to assess the relative acute and long-term benefits of early intervention at the Network Center in Cleveland.

We are very appreciative of the generous contributions of Ted and Vada Stanley of the Stanley Foundation, who have provided the variety of funding mechanisms to enable the Early Intervention Initiative and its wider consortium of concerned investigators to proceed with a core instrument package and this series of initial controlled clinical trials. These and other efforts described in the Meeting Highlights section should rapidly bring new data to bear on crucial treatment decisions for children and adolescents with mood disorders.

Questionnaire on Early Intervention in Childhood Bipolar Illness

The Stanley Network/Early Intervention Initiative (E.I.I.) is looking for families with a mood disorder on one or both sides (with at least one parent bipolar) to fill out a questionnaire about their children and the ethics of early intervention. This information will not only help us identify the symptoms and behaviors associated with bipolar disorder in children and adolescents, but will also help us design early intervention protocols for this population.

If you are interested in filling out the questionnaire, please call (301) 496-6827 or 1-800-518-SFBN (7326); e-mail stanley@sparky.nimh.nih.gov; or write to: The Stanley Foundation Bipolar Network, 5430 Grosvenor Lane, Suite 200, Bethesda, MD 20814.

Life Chart Highlights

The Kiddie LCM (K-LCM™)

In the first issue of the *BNN*, we outlined the importance of careful documentation and graphic depiction of the course of bipolar illness in adults. We thought that this approach was so important that we made it a routine section of the *BNN*, publishing a life chart in each issue to illustrate a specific problem in the illness or an important approach to treatment intervention.

Over the past several years, we have been increasingly convinced of the utility of this method, as have many other clinical investigators in the field. Dr. Charles Nemeroff, Chairman of the Department of Psychiatry at Emory University, has made life-charting a part of each psychiatry resident's workup of a patient, attaching the life chart to the front of each patient's clinical record, so that an immediate perspective about course of illness and prior treatment responsivity can be gleaned. Patients equally have found the process useful, enabling them and their physicians to better titrate and manage different medications and ascertain optimal therapeutic outcomes.

Recognizing the utility of the adult version of the life chart, we have developed a related method for documenting course of illness in young children. Faced with the diagnostic conundrums described in the Meeting Highlights Section, we thought that such an effort was of great importance. Obviously, one of the diagnostic dilemmas in many illnesses (even including acquired immune deficiency syndrome [AIDS]), is to decide when the threshold for illness has been reached or exceeded. The diagnosis of childhood onset bipolar illness has similarly been plagued with issues as to whether the same diagnostic criteria present in adults need to be reached in children. Moreover, it is equally apparent that the early presentations of bipolar illness can be extremely diverse and pleomorphic, not necessarily displaying discrete periods of classic mania or depression lasting several weeks or more.

Thus, as in the adult version of the NIMH-LCM™ in which symptom-driven dysfunction is the main illness severity indicator, we thought it was important not to prejudice the overall observations of illness severity with diagnostic and syndromal preconceptions but rather to map mild, low and high moderate, and severe dysfunction (parallel to the adult LCM) in children. We therefore decided not to limit the rating to just manic and depressive symptoms charted above and below baseline, but to more leniently allow the recording on the K-LCM™ of any kind of activated or inhibited behavior in children that was associated with dysfunction. In this fashion, tantrums, aggression, and the like could be graphed above the line, in addition to more classical manic symptoms of grandiosity, hyperactivity, and hypersexuality. Similarly, all types of inhibited, anxious, withdrawn behavior observed in children could be charted below the normal mood baseline to the extent that the behaviors interfered with functioning, even if they did not meet full diagnostic criteria for a depressive episode.

Similar to the adult version, the degree of symptom-driven dysfunction is characterized as mild, low and high moderate, or severe for either the activated or the inhibited-withdrawn behaviors. Mild dysfunction would relate to behavior and mood distinctly different from normal but with little or no functional impact or incapacitation. In contrast, low and high moderate dysfunction would relate to some and much difficulty, respectively, in the child's usual family, social, or academic roles with the ability to continue in these roles, but with notable problems and difficulty. Severe would relate essentially to incapacitation, with the child being unable to leave his room, function in school, and requiring intensive intervention or hospitalization.

As in the case of the adult version, two types of the Kiddie LCM are available — one for **r**etrospective assessment of these different kinds of activated or inhibited behaviors assessed on a **monthly** basis (K-LCM™-r), and a **p**rospective version on which the parent can rate the child on a much more detailed **daily** basis (the K-LCM™-p). We have included a sample version of the Kiddie LCMs (on pages 14-15) that can be copied and utilized on a longitudinal basis in the assessment of children and adolescents with either clear cut diagnoses of bipolar illness or in instances in which there is some doubt.

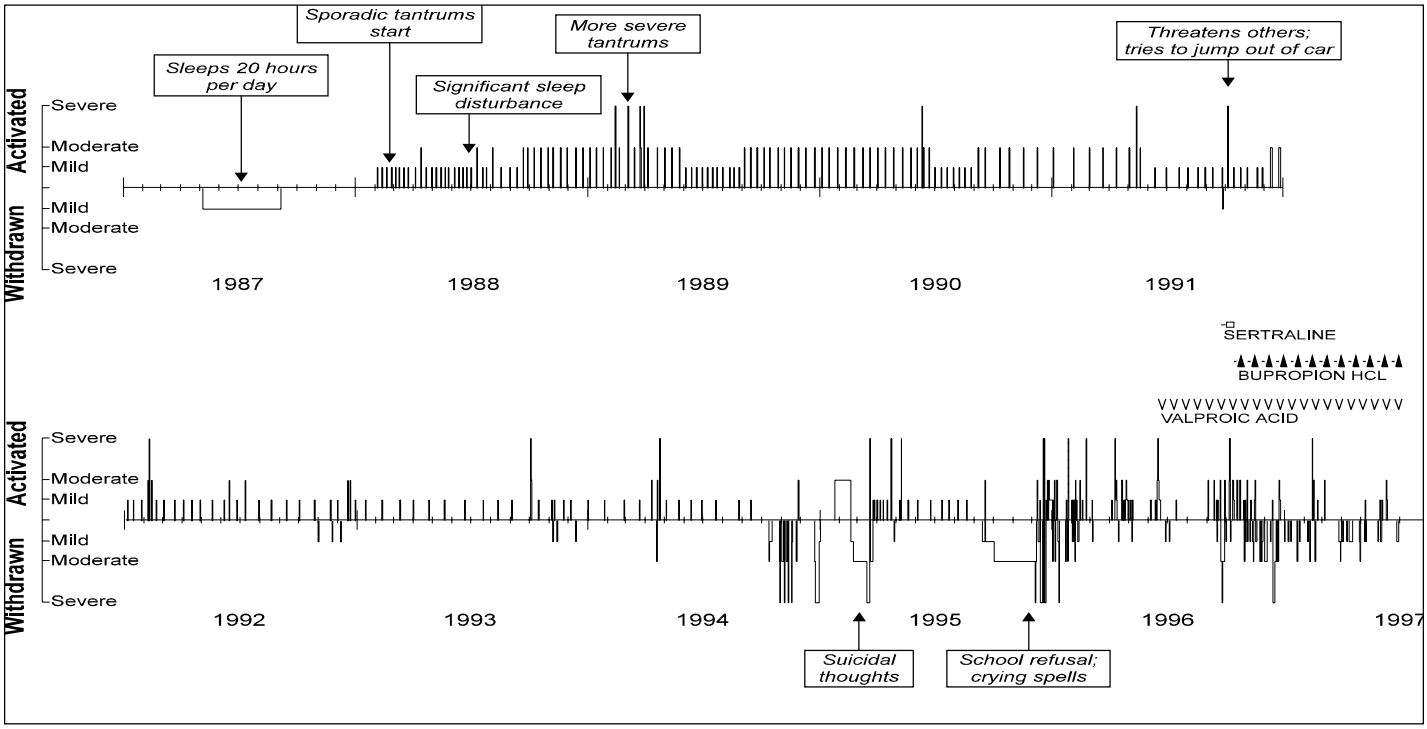
This rating instrument is being utilized by the group of investigators involved in the Early Intervention Initiative and has been adopted by other working groups as the core (longitudinal) rating instrument in addition to the Kiddie SADS (for diagnostics), the Young (mania), the IDS (depression), and the Clinical Global Impressions scale for bipolar illness (CGI-BP). Among all of these instruments, the Kiddie-LCM specifically speaks to the longer-term perspective in an illness

(Continued on page 4)

(Continued from page 3)

that is characterized by marked fluctuations and waxing and waning of symptoms. As such, we hope that it will also be an important tool for accurately assessing the impact of treatment and facilitating the development of new and early treatment interventions for child and adolescent onset bipolar illness.

Kiddie Life Chart (K-LCM™) of a Ten Year Old with Affective Dysfunction from the First Year of Life



This graphic depiction of the course and evolution of a child's activated and withdrawn behaviors is derived from extensive typewritten notes of the patient's mother. Additionally, several lengthy telephone interviews with the mother were used to further clarify and evaluate the observed behaviors and their impact on her child's ability to continue to interact and function at home, with friends, at school, and in after-school activities. Furthermore, the mother related that there was a history of mood disorders in the families of both parents for two or more generations.

As an infant, her child slept most of the time for the first three months and was very hard to awaken even to be nursed. When awake she was generally "smiley". At five months she developed very disturbed sleep with multiple awakenings attributed to ear infections but this also seemed to herald future difficulties with sleep.

Sporadic tantrums began to emerge when she was nine months old, and she seemed to crave constant interaction with her mother. In her second and third year her tantrums increased in severity and frequency and were, at times, accompanied by unusually aggressive behaviors toward her mother, who also observed that her daughter was remarkably fearless on the playground when using the equipment or going down slides.

After her third birthday, her tantrums decreased in frequency and she seemed overall somewhat better. However, in October 1991 (age 4 1/2) she had an extraordinarily severe tantrum, tried to jump out of the car, fiercely attacked her mother, and wished her dead. Kindergarten and first grade were much better years for her, and her mother thought that her child had outgrown her previous difficult and troubling behaviors .

Another severe tantrum occurred in October 1993 accompanied by suicidal thoughts and homicidal threats toward others. The child had thoughts of her own death in November 1993 and the fall of 1994 marked the

(Continued on page 5)

(Continued from page 4)

reemergence of more extreme dysfunction with tantrums more severe and frequent than before and now with distinct depressive behaviors, suicidal thoughts, great sadness with crying spells, school refusal, as well as extreme irritability and angry, threatening outbursts toward others. In-between times she could be cheerful, cooperative, friendly, very creative and playful with many expressions of love and affection for her mother and others. The summer of 1995, as summers before, was a calmer and better time only to be followed by a return in the fall of the previous episodic symptom patterns.

In 1996 the child was diagnosed as bipolar by Dr. William Bradbury, of Chicago, and in June, the mood stabilizer valproate (Depakote®) was instituted starting with 125 mg and eventually titrated to 1250 mg/day. This helped ameliorate the most severe tantrums which were now reduced to "short, angry outbursts". In September 1996 a brief trial of sertraline (Zoloft®) for continuing depressive symptoms brought too much sedation in the morning and too much activation in the evening. After tapering sertraline, bupropion (Wellbutrin®- now at 300 mg/day) was started in October and remains in the current regimen together with valproate (1000 mg/day) as of July 1997.

Although much improved, the remaining symptoms of her bipolar illness still cause some difficulties in functioning and, at this time, consideration is given to the addition of a second, novel putative mood stabilizing agent, gabapentin (Neurontin®).

As noted in the Clinical Trials Update of this *BNN*, Dr. Robert Kowatch in Dallas is heading a randomized, comparative trial of valproate, carbamazepine, and lithium, and hopes to not only assess relative efficacy on different target symptoms, but also to help establish predictors of response so that a child such as the one illustrated here can be more rapidly matched to the optimal therapeutic regimen. Until such data are forthcoming, a series of sequential clinical trials would appear most promising. Child psychiatrists have observed that many patients with severe mood dysregulation such as manifested here respond dramatically to appropriate therapies that lead to the normalization of many of the dysfunctional behaviors charted. We look forward to the rapid achievement of this positive outcome so that all of the wonderful traits discussed by the patient's mother in her article (on this page) can come to the fore and the proclivity for mood disorder becomes a minimal factor in this child's life.

Such a dramatic outcome is described in an article in *Good Housekeeping* (November 1996) about an adolescent with equally severe mood dysregulation, prominently involving anxiety and depression almost from the time of birth, whose symptoms were almost completely alleviated with appropriate pharmacological combination therapy.

Parenting a Bipolar Child: A Mother's Thoughts

by Martha H.

The light spring rain falling upon my garden reminds me that it's been a year since Rose's baffling tantrums, mood swings and annual winter sadness were finally given a name: bipolar disorder, a diagnosis made by Dr. William Bradbury of Chicago around her ninth birthday. It's been a year of reading textbooks and medical journals, grappling with how this news impacts our family, and reaching out to other parents of similar "wild angels" for advice and support.

The chart of my daughter's moods (in the Life Chart Highlights section) does not begin to convey the unique and wonderful person she is. Where can I note the lovely altar she made for her room? Where to indicate the delight she expressed with her new canopy bed, a curtained lair designed to soothe the onset of her fire-breathing moods? Where to record the eagerness with which she anticipates the weekly visits of Michael, a baby she adores, or the patience she displays while helping teach karate to disabled kids? Such a chart is useful in detecting and diagnosing symptom patterns and tracking medication response, but we must never forget that our kids are unique individuals with feelings, interests, and talents of their own.

Our challenge as parents, once we have processed the inevitable feelings of shock and grief upon diagnosis, is to seize these years as a window of opportunity in which to educate our kids in methods of self-awareness, self-control, and self-expression. One of the easiest, yet most important, contributions we can make in our collaboration with treatment professionals is to observe and record our child's moods, sleep habits, outbursts, troublesome encounters with others, and other behaviors of concern. A few notes made at the end of each day can capture valuable facts soon lost to memory. These notes are of immense value prior to diagnosis in discerning patterns, and later in deciding which medications to prescribe.

(Continued on page 6)

(Continued from page 5)

Eventually, our children will be encouraged to do this monitoring themselves. Until then, attending to this task on a regular basis is something we can do when, at times, it seems there is nothing else we *can* do.

To help our kids with self-control, beyond the essential medications, might be training in the martial arts, yoga, neurofeedback or meditation, with teachers who understand the special challenges faced by bipolar kids. All of the arts — writing, music, painting and drawing, ceramics and sculpture, dance — as well as sports offer means for expressing the passions and channeling the incredible energy that, at times, floods a bipolar child's whole being. It is essential to find flexible teachers; Rose's piano teacher, for example, gauges the length of her lesson each week by Rose's energy level that day. The lessons run anywhere from l5 minutes to over an hour.

Crucial coping strategies at our house and in the families I've met include a sense of humor, a tolerance for eccentricity, flexibility, and support from other parents. We call our angelic-looking little girl with the blonde hair and big brown eyes "Mountain Goat," for her facility at scaling the kitchen cupboards, and send her to a summer camp that offers climbing lessons where she can safely indulge her need for risk-taking. We have accepted that we must be prepared to leave any situation that Rose finds overwhelming, and don't mind cooking artichokes for breakfast at times. In a parent support group, we discover that all of our kids have, at one time or another, attempted to jump out of a moving car; we are not surprised to find that they share a deep affinity with animals, and an innate spirituality. Our kids often blame us for their rages, emotional hijackings in which their hair-trigger limbic systems perceive even the gentlest parental guidance as nuclear attack and react accordingly. So we dub ourselves honorary lifetime members of the Mean Moms Club, but when the dust has settled take our kids on our laps and point out the difference between thoughts, feelings, and actions, and teach ways they can make choices about those things.

"Parenting Rose must be really interesting," a friend said recently. It certainly is. Yet, many days I wonder how I'll survive the roller-coaster mood swings, the creativity utilized in devising yet another scheme to test my patience (the latest: photocopying our Siamese cat), and an intensity that can exhaust several adults in a day. It is heartbreaking to witness one's young child trash her room in a rage, then threaten to kill herself, sobbing, "Why do I have to cry all the time?" And to find her older sister silently weeping on the kitchen steps, after listening through her bedroom wall to my hour-long struggle to restrain Rose during a wall-kicking, ear-splitting tantrum.

In my stronger moments, I regard the challenge of parenting Rose as a gift; she blesses me with plenty of Zen-like practice at staying present and in the moment. Her days of irritability that begin with a barrage of angry words and end with slammed doors are sometimes endured only with help of the deep breathing techniques I learned for childbirth. Her sunny moods, longer and more frequent since she began taking Depakote® and Wellbutrin®, are welcome oases of calm affection. On one of those precious days, she might wrap her arms around my neck and say, "I'm glad you're my mom, even though I don't always think so." Those days, I am grateful for all the things she's taught me about patience, and love, and how much we take for granted in life. *[**Editor's Note:** Martha H. can be reached at 104107.2557@Compuserve.com]*

Information Requested in a Questionnaire for Clear Lithium Non-Responders/Responders

Lithium Non-Responders: The Stanley Foundation Bipolar Network is conducting a questionnaire study to identify the characteristics of bipolar illness that are associated with either an excellent response to lithium (well for five or more years) or a poor response to lithium. Appropriate participants for the poor response group are those who have not had a good long-term response to an adequate trial of lithium (at least six weeks, with good medication compliance, at therapeutic blood levels) for preventing manic and depressive recurrences. If you have had such an unsuccessful experience with lithium in the past and would be willing to complete a questionnaire about your bipolar illness, please call 1-800-518-SFBN or Nancy Palmer at (301) 496-6827, E-mail: stanley@sparky.nimh.nih.gov, or write to: NIMH/ BPB; Bldg. 10 - Rm. 3N212; 10 Center Drive, MSC 1272; Bethesda, MD 20892-1272.

Lithium Responders: Many thanks to all who have responded to the recruitment for the "lithium-well" study (i.e., an excellent, sustained response to lithium for five or more years) and have filled out the bipolar illness questionnaire. We continue to recruit for this study as well. Please use the above address and/or phone number to contact us so that the questionnaire can be mailed to you. The response up to this point has been wonderful and we truly enjoy collaborating with all of you in this important project.

Meeting Update

Highlights of NIMH Workshop on Prepubertal Bipolar Disorder Bethesda, March 10-11, 1997

This conference, organized by Editha Notelman, Ph.D., NIMH, and Gabrielle Carlson, M.D., SUNY at Stony Brook, was the second NIMH workshop on child and adolescent bipolar illness (the first occurred in 1995). Ironically, the meeting was supported by the NIH Office of Rare Diseases but a number of investigators indicated that childhood and adolescent bipolar illness is not that rare, and may, in fact, be growing more common. Both meetings, however, were called to better deal with some of the clinical and research issues involved with diagnostic assessment, treatment, and long-term follow up of early-onset (child and adolescent) bipolar disorder.

A number of major themes and areas of consensus emerged from this meeting and will be published in a peer-reviewed journal some time next year. However, an overview may be particularly helpful to parents of bipolar children, or to parents with bipolar illness who question whether their children's behavioral symptoms represent initial phases of bipolar illness. These become crucial questions since, in the absence of good treatment, there is some evidence that childhood onset bipolar illness can have severe manifestations and outcomes.

Drs. Carlson and Dennis Cantwell, UCLA, started the meeting describing some of the symptoms of bipolar disorder and diagnostic conundrums that the symptoms present. Particularly in childhood, bipolar illness may not only appear with a great deal of emotional lability, but also with a variety of other co-morbid disorders including attention deficit hyperactivity disorder (ADHD), oppositional defiance disorder (ODD), and conduct disorder (CD). Epidemiological samples reveal that childhood and adolescent mania occurs in six percent of the population. By DSM-III criteria it occurs in as many as 7.3% of the population, and in DSM-III-R, in which a distinct period of mania is not required, more than 10% of children have manic symptomatology. They reported that the peak age of onset of illness is 15-20 and that 50% of patients had abused drugs and alcohol. They indicated, as did others at the meeting, that early-onset bipolar illness is a very high risk factor for subsequent drug abuse rather than vice-versa. Dr. Cantwell presented data showing childhood depression has a high incidence of suicide attempts (22 of 102 patients) and this may be an underestimate (as another 11 of these patients made serious suicide attempts of which the parents were not aware). He described some of the florid manic and psychotic symptomatology these patients displayed and stated that, "Hypersexuality [in a child] in the absence of a history of sexual abuse is almost always attributable to mania."

Dr. Pamela Cole, Pennsylvania State University, reviewed data on the development of normal and pathological emotion regulation. The data indicated that while most children had modulated affect, the subgroup with unexpressive affect showed decreased electrodermal and heart rate changes to external stresses, while those with expressive and anger-dysregulated responses had increased electrodermal and heart rate responses.

Dr. Michael Potegal, University of Wisconsin, followed with a description of some of the detailed characteristics of temper tantrums that appear in high incidence in children with affective disorders, with some evidence that the tantrums become longer as one moves from 1.5 years of age to 2.5 years of age, although they were still brief. In contrast, tantrums associated with whining and crying lasted much longer.

*[**Editor's Note:** While the management of anger attacks is controversial, Dr. Arnold Meyersburg has proposed the "holding technique" for young children with temper tantrums in which they are held on an adult's lap with the child's back toward the parent and the child's arms crossed in front of them. The child is held by the parent so that he cannot strike out towards himself or the adult. The child will initially attempt to escalate and resist by kicking, screaming, and/or crying, but if the adult holds on long enough, the tantrum eventually ends, usually in some one-half to three-quarters of an hour. If this holding technique is repeated during the next tantrum, it lasts for a shorter period of time, and by the third session, the tantrum may only last a matter of minutes. Thereafter, the child may begin to approach the parent or care giver for holding and comforting and cease displaying tantrums altogether.]*

Dr. Hagop Akiskal, University of California, San Diego, presented data on the psychiatric diagnosis of children with

(Continued on page 8)

(Continued from page 7)

bipolar parents and behavioral disorders. Surprisingly, none of these 68 children was initially diagnosed with an affective disorder or bipolar disorder and yet, on three-year follow up, 27% of these individuals displayed affective diagnoses (with dysthymia in four, major depression in six, cyclothymic bipolar II disorder in 11, and mania in four). These data, published in 1993, highlight the problem that mania in children is often misdiagnosed and is therefore improperly treated.

This issue becomes all the more crucial in relationship to Dr. Melvin McInnis' presentation of the work from Dr. Raymond DePaulo's laboratory at Johns Hopkins University reporting a ten-year earlier age of onset of bipolar illness in affected children compared with their bipolar parent. For bipolar I disorder, this earlier age of onset could be as great as 20 years. These data are convergent with the secular trends or "cohort effects" observed by Gershon and colleagues, 1987, and Lasch and colleagues, 1990, in which each successive generation of individuals born since WWI appears to have a higher incidence and earlier age of onset of both unipolar and bipolar affective illness.

This cohort effect may or may not be related to the phenomenon of genetic anticipation, now observed in a number of genetic disorders such as Huntington's chorea, which are associated with a transgeneration expansion of a DNA nucleotide triple repeat sequence (i.e., the repeat of a three base pair sequence which codes for a single amino acid). In the Huntington's chorea gene on the short arm of chromosome 4, if there are less than 36 triple repeats, one does not get the illness. However, with increasing numbers of triple repeats over 40, there is an increased vulnerability for the disorder as well as earlier onset with greater severity. If one has 60-80 triple repeats, onset of Huntington's chorea occurs in childhood. A parent having 45 repeats may transmit many more to their offspring. Whether this type of anticipation effect occurs in bipolar illness (in other genes) is currently unknown, but it is being explored. Nonetheless, one of the take-home messages of this conference is that whereas childhood depression and mania were not readily recognized some two decades ago, there is now increasing recognition of the severity of childhood and adolescent presentations of these disorders, whether or not it is based on a genetic anticipation phenomenon.

Dr. Barbara Geller, Washington University, reviewed data on 42 bipolar children with a mean age of 9.1 years. She noted a very high incidence of co-morbid conduct disorder (anxiety disorder-50%, ODD-83.3%, ADHD-85.5%) with the ADHD diagnoses occurring three to four years earlier than the full bipolar diagnoses. Elated mood, grandiosity, daredevil actions, increased sexuality, and racing thoughts, appeared particularly prominent in these children. Laughing fits were sometimes an early manifestation of this disorder. Eighty-three percent of her patients had mixed manias with substantial amounts of co-occurring depression, and patients often changed from laughing to crying within an instant. She emphasized that, in children, chronic mood dysregulation may be more characteristic than the clear episodic form typically presented by adults.

Dr. Joseph Biederman's data from Massachusetts General Hospital paralleled those of Dr. Geller. Virtually all of his manic children (mean age of seven) met criteria for ADHD (ADD-90% and conduct disorder-40%). A high incidence of anxiety disorders was also observed. He, too, found that the early-onset presentation of co-morbidity with attention deficit hyperactivity (ADH) was a high risk factor for substance abuse in adolescence, which occurred in 40% of the subjects.

*[**Editor's Note:** Since bipolar disorder is the psychiatric illness most associated with multiple co-morbid conditions, the diagnosis of bipolar disorder in childhood should trigger not only appropriate treatment efforts for the mood disorder itself, but diagnosed bipolar children should be entered into appropriate substance abuse prevention programs. Substance abuse can have additional impact on gene expression and brain function and would only further complicate an already difficult to treat illness.]*

Dr. Biederman also noted that children with mania had an increased amount of physical trauma in the family (perhaps precipitated in part by their own manic behavior), and that this behavior was subsequently followed by an increased incidence of depression. In his retrospective chart reviews, Dr. Biederman found that mood stabilizer treatment of childhood mania was associated with significant improvement, while other treatment approaches were not effective and **tricyclic antidepressants made the syndrome worse**. He also noted that, with effective

(Continued on page 9)

(Continued from page 8)

treatment of the manic syndrome, many individuals had residual ADHD which required additional treatment with a stimulant in combination with a mood stabilizer (i.e., lithium, carbamazepine, or valproate).

These data suggest that patients diagnosed with bipolar disorder are likely to be in need of treatment of their bipolar disorder first with a mood stabilizer which will, in many instances, also result in the clearing of the concomitant ADHD-like symptoms. If this does not occur, the symptoms can then be separately treated with additional medication after a mood stabilizer is used.

*[**Editor's Note:** Since bupropion (Wellbutrin®) has recently been reported to be as effective as methylphenidate (Ritalin®) in ADHD, Dr. Akiskal, Dr. Robert Post, and several others wondered whether it might not be more appropriate to use this agent, which might have the benefit of treating not only the ADHD, but also the potential for treating breakthrough depression of bipolar disorder, especially in families with children at high risk, i.e., where there is a positive family history of bipolar illness.]*

This suggestion remains for direct experimental verification in appropriate controlled clinical trials. Nonetheless, it would appear prudent for families, in which bipolar illness is present on one or both sides, to raise a serious question regarding initial use of the psychomotor stimulants. Much indirect evidence suggests the benefits of a clinical trial of mood-stabilizer and other non-psychomotor-stimulant approaches to ADHD prior to the use of psychomotor stimulants. Further caution is warranted in this regard since stimulant abuse is a high risk factor in adolescent bipolar disorder, and alternative modes of treatment that do not place the patient at increased risk for potential use and abuse of stimulants would appear indicated.

Dr. Stan Kutcher of Dalhousie University in Halifax, Canada, presented further evidence on the increased incidence of a positive family history of psychiatric illness in families of individuals with adolescent mania. For example, first-degree relatives of patients with adolescent mania had a 30% incidence of major depressive disorder (versus 5% in the normal controls), 15% bipolar disorder (versus zero in the normal controls), and 34% anxiety disorder (versus 10% in the normal controls). These data are parallel to those of UCLA's Dr. Michael Strober (discussed later) and suggest that childhood and adolescent bipolar illness typically occurs in a background of high genetic loading.

Dr. Kutcher emphasized the excellent premorbid functioning of his patients with adolescent bipolar I illness until the year before onset of their illness. In contrast, those with a bipolar II picture of adolescent mania showed a considerably higher degree of (pre-diagnosis) psychopathology and functional impairment in school in the many years prior to illness onset.

*[**Editor's Note:** Thus, it would appear that these adolescents with bipolar II illness are similar to patients with childhood onsets described earlier by Dr. Geller, who have much turmoil and major problems with many co-morbid syndromes, many years prior to diagnosis.]*

Dr. Kutcher also reported on a study indicating that children of parents who were lithium non-responders were much more likely to have psychiatric diagnoses and more chronic problems with their illness than those whose parents were lithium responders (Duffey et al., unpublished data). These preliminary observations are consistent with others suggesting that lithium-responsive illness may run within families, and that such a history may help in the choice of treatment in the offspring (a proposition that remains to be directly tested). These data also suggest the possible importance of other mood-stabilizing anticonvulsant agents in the treatment of lithium non-responsive families.

In data very like that of Dr. Kutcher, Dr. Strober of UCLA reported that bipolar illness ran in the families of children and adolescents diagnosed bipolar as a direct proportion to age of onset of the illness of the child. That is, those with adult onset mania had first-degree relatives (parents and siblings) with bipolar illness in only 4% of the family members; with adolescent onset-12%; and those with prepubertal onset had 30% incidence of bipolar illness in first-degree relatives, further supporting the concept of higher genetic vulnerability in the early onset forms of bipolar illness. Dr. Strober distinguished between those with an earlier history of ADHD and a variety of "externalizing" disorders, such as conduct disorder and oppositional defiant disorder. These latter patients had a very slow onset of response to lithium. In the mixed manic presentations, valproate was as effective as lithium in acute treatment of an episode (using historical controls). Valproate appeared to be a better long-term treatment in those with prepubertal, co-morbid, externalizing disorders.

(Continued on page 10)

(Continued from page 9)

As is clear from the brief overview of the meeting on early onset bipolar illness, there is much uncertainty as to the diagnostic thresholds and implications for treatment and clinical response. Many of these issues will hopefully be remedied by more treatment-oriented and early intervention studies in the near future. It is apparent that NIMH wishes to make this an important part of their clinical and research portfolio, as indicated by the presence of NIMH Director Dr. Steven Hyman at the morning session on the second day of the meeting. However, until this effort is translated into new findings, many parents with seriously disturbed children are at somewhat of a loss as to how to proceed with optimal treatment approaches. Many experts in the field agree that parents of children with bipolar illness are usually ahead of pediatricians and adult psychiatrists not only in recognizing bipolar illness symptoms, but also in asking for early and effective pharmacological intervention.

Until systematic protocols are developed and controlled data garnered, interpreted, and published in the literature, we recommend that families in which both parents have affective illness begin to chart the behavior of their children on the K-LCM™ (or Kiddie life chart), a version of the NIMH-LCM™, to facilitate early assessment and intervention with appropriate treatments when warranted. Such life-charting would also serve as an excellent template for assessing the efficacy of intervention which needs to proceed on a careful sequential clinical trials basis (using approaches found to be effective in adults) in the absence of other, more predictive, approaches to childhood pharmacotherapeutics.

With such a careful documentation of prior course of illness, one would be able to make a good assessment of the type of impact that lithium, or some of the other mood stabilizer treatments (such as carbamazepine and valproate) are making and the need for other or adjunctive treatment approaches. While there was some disagreement at the meeting about the precise diagnosis and appropriate diagnostic instruments and cut-off thresholds, all agreed that patients with bipolar-like presentation in childhood and adolescence were often severely impacted by their disorder, resulting in marked dysfunction in the usual social and educational roles of the individual children themselves and causing much distress in others in the family, school, and community because of their often extreme (sometimes dangerous) and uncontrolled behaviors.

*[**Editor's Note:** In light of this consensus, it would appear prudent for parents to consult with physicians who are willing to pursue appropriate systematic attempts at therapeutics with both pharmacologic and focused psychotherapeutic outcomes, rather than believe that childhood and adolescent mania is a rarity, diagnostic mistake, or misnomer and that it will go away by itself. There was general agreement among most participants that an appropriate place to start would be with medications known to be effective in adults with bipolar illness in order to assess their relative efficacy in such childhood and adolescent syndromes, and to then explore other agents that might be uniquely effective in the childhood and adolescent presentations because of either a different illness process, the relative developmental immaturity of the neurotransmitter systems in children, or some combination of the two.*

In this regard, models from other medical illnesses might be highly revealing. For example, childhood-onset diabetes mellitus usually requires insulin replacement, while the adult onset variety can often be treated with a variety of oral hypoglycemic agents. While none of us presumes that such a dramatic differential approach to the pharmacotherapeutics of the affective illnesses exists in children compared with adults, it is nonetheless possible that some substantial differences will exist and will have to be appropriately uncovered.

The central nervous system is dramatically programming and re-programming itself throughout development and this may relate to pharmacological responsiveness. For example, animal studies indicate that the $GABA_B$ agonist baclofen is a potent anticonvulsant in very young animals, and that this ceases to be the case in adults. Whether there would be similar differential pharmacological responses as a function of age of onset of the affective disorders remains to be more systematically assessed. The preliminary data in the field already suggest that effective antidepressants for adults with depression are not as effective in adolescent-onset depression (when compared to placebo). However, in this instance, it is unclear to what extent this is attributable to the high placebo responsiveness in adolescent depression as opposed to the relative inefficacy of the antidepressants themselves.

(Continued on page 11)

(Continued from page 10)

Concern about stigma and the potential long-term impact of psychotropic drugs has often delayed institution of long-term prophylaxis, even in adult bipolar illness. This latter issue is raised to a new level in children, with added concerns about the potential impact of drug treatment on their development and the developing nervous system. However, this very much needs to be weighed against the potential devastating impact of bipolar illness with its inherent numerous other incapacitating co-morbidities. Many of these children are unable to perform adequately in school or within the community, and family relationships are equally precarious despite best attempts by parents and other professionals interested in their treatment. The cost of illness-related loss of adequate educational and social input in children with unipolar and bipolar presentations must also be factored into the treatment equation. Moreover, the high risk for suicide, and the rapidly growing incidence of completed suicides in children and adolescents also speak to the need for early intervention. In the face of such painful and potentially lethal consequences, it would appear clinically inappropriate not to proceed with the best attempts at clinical and pharmacologic intervention based on data in adults, even in the relative absence of well-informed randomized clinical trials data in children.

This approach has been adopted in most other serious medical disorders of childhood such as rheumatoid arthritis, malignancy, and seizure disorders. Particularly in light of the evidence that prior numbers of untreated seizures conveys a relatively poor prognosis in epilepsy, one needs to raise the question of whether similar late treatment interventions in childhood-onset bipolar illness and its multiple variants and concomitants does not also prejudice outcome in a negative direction, even above and beyond the pain and suffering incurred. As in the epilepsies, there is some preliminary evidence in the affective disorders that increasing numbers of episodes prior to treatment may carry a negative prognosis for lithium response or to the time and incidence of rehospitalization for major unipolar and bipolar depression.

While one of the arguments against early intervention in the general population is the ambiguity about which patients will have benign and self-correcting clinical courses, more active and aggressive intervention would be prudent in situations where one or both parents have bipolar illness. That is, the family history suggests an added vulnerability factor in addition to the already manifested early behaviors, perhaps compelling the need for early intervention. Such risk factors in adults are already weighed to favor early preventive and primary preventive approaches in other areas of medicine, such as in cardiology for the prevention of heart attacks and increased intensity of screening in breast cancer.

We wish to further check directly with parents with bipolar illness and others in the treatment community their feelings about the ethics of early intervention and attempts at primary prevention. When the risks of bipolar illness are high (i.e., when both parents have affective illness and one is bipolar), the risk:benefit ratio for early intervention may weigh more heavily in favor of earlier treatment, even with the presence of symptoms that do not yet meet the arbitrary threshold for a formal diagnosis. Those wishing to fill out a questionnaire on the relative merits of early intervention versus watchful waiting, so that this information will help us in the design and development of new treatment protocols, are asked to write: The Stanley Foundation Bipolar Network, c/o Early Intervention Initiative, 5430 Grosvenor Lane, Suite 200, Bethesda, MD 20814 or call 1-800-518-SFBN requesting the mailing of this Early Intervention Initiative (E.I.I.) questionnaire.

Parents who want the best outcomes for their children may be willing to assess the risk:benefit ratio for early intervention differently from academics and physicians who are taught the appropriate and conservative principles for intervening with only FDA-approved agents for a given indication, and then only after a wealth of controlled clinical trial literature has been accumulated. It is equally apparent that even with a dramatic increase in these types of pharmacological intervention studies in adults and some data on treatment of early-onset bipolar illness, many of these issues will have to be decided by parents and their physicians in the relative absence of the desired intensive systematic database.

It is to this end that we suggest the potential utility of careful mapping of the longitudinal course of illness by parents of children with severe behavioral problems so that they can participate and, at times, lead in the informed consent process and assessment of risk:benefit ratios of aggressive interventions (at least with agents

(Continued on page 12)

(Continued from page 11)

already proven effective for the adult variety of the illness).

It is in this spirit that the NIMH-Stanley Foundation consortium has tried to speed up the process of systematic data acquisition to better inform parents and physicians of the optimal choices, and why we have chosen to air these issues in the BNN, in many instances in advance of the formal, peer-reviewed publication of the material at the conference. Nonetheless, abstracts and presentations are often the material of press releases and public discussion prior to formal publication. We begin these discussions so that parents can be as adequately informed as possible when taking highly individualized treatment decisions to their appropriate treating clinicians and physicians. Given the potential severity of impact of this illness on one's life, it would appear that discussion of such diagnostic and treatment implications and their potential stigma would, in most instances, outweigh the likely harm of not addressing the needs of a seriously ill individual.]

References

1. Geller B and Luby J (1997). Child and adolescent bipolar disorder: a review of the past 10 years. *J Am Acad Child Adolesc Psychiatry* 36(9):1168-1176.

2. Strober M, Morrell W, Burroughs J, Lampert C, Danforth H, Freeman R (1988). A family study of bipolar I disorder in adolescence. Early onset of symptoms linked to increased familial loading and lithium resistance. *J Affect Disord* 15(3):255-268.

3. Strober M, Morrell W, Lampert C, Burroughs J (1990). Relapse following discontinuation of lithium maintenance therapy in adolescents with bipolar I illness: a naturalistic study. *Am J Psychiatry* 147(4):457-461.

Around the Network

As noted in previous editions of the *BNN*, the Stanley Foundation Treatment Outcome Bipolar Network consists of five core sites located in Los Angeles (Dr. Lori Altshuler), Dallas (Drs. John Rush and Trisha Suppes), Cincinnati (Drs. Sue McElroy and Paul Keck), Bethesda, MD (Drs. Robert Post, Kirk Denicoff, Mark Frye, and Gabriele Leverich, LCSW), and Utrecht, The Netherlands (Drs. Willem Nolen and Ralph Kupka), and an affiliated site in Minneapolis (Dr. Joseph Westermeyer). The Network administrative and data coordinating site is headed by Stephanie Reardon at the Stanley Headquarters on Grosvenor Lane in Bethesda.

In addition, E. Fuller Torrey and Ted and Vada Stanley of the Stanley Foundation have generously funded seven centers specializing in new directions in bipolar research. These include:

- A center in Stanford (CA), headed by Dr. Terence A. Ketter, that has a special focus on the relationship of brain imaging to treatment response;

- A center in Chicago, headed by Drs. Jan Fawcett and John Zajecka, investigating novel bipolar algorithms and examining the optimal parametrics and acute and long-term efficacy of repeated transcranial magnetic stimulation (rTMS) of the brain in bipolar patients;

- A center at Johns Hopkins in Baltimore (MD), headed by Dr. Raymond DePaulo, focusing on the genetics of bipolar illness, as well as a special initiative on brain imaging in association with Godfrey Pearlson;

- A center in Pittsburgh, under the leadership of Drs. David Kupfer and Ellen Frank, which is developing a large registry of bipolar patients in that locale and proceeding with randomized clinical trials of new potential interventions;

- A center in Boston at McLean Hospital, headed by Drs. Steven M. Mirin and Bruce M. Cohen and associates, focusing on new brain imaging techniques, including traditional functional brain imaging with positron emission tomography (PET) utilizing deoxyglucose and O^{15} water, as well as newer techniques of functional MRI and magnetic resonance spectroscopy;

- A center at the NIMH in Bethesda, which focuses on development of new treatment modalities with the anticonvulsant mood stabilizers and rTMS, as well as being the home base for the six-site bipolar Network; and

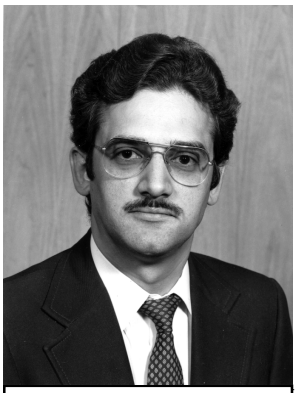
- A center at Case-Western Reserve University headed by Joseph Calabrese, M.D. and Robert Findling, M.D., focusing on childhood and adolescent onset of bipolar illness and the development of early treatment interventions. ***(Editor's Note:*** *In keeping with the overall*

(Continued on page 13)

theme of this issue of the BNN on childhood and adolescent presentations of bipolar illness, we highlight this group in the current issue and then will review the other centers in subsequent volumes).

Case-Western Reserve University Center: Drs. Joseph Calabrese and Robert Findling

Joseph R. Calabrese graduated summa cum laude with a Bachelors of Science from Xavier University, was trained in medicine at Ohio State University School of Medicine, and graduated from a psychiatry residency at the Cleveland Clinic Foundation. He then took a clinical fellowship at the NIMH before taking up his current position as Director, Mood Disorders Program at Case-Western Reserve University. In this role Dr. Calabrese has conducted pioneering studies in rapid cycling bipolar illness, not only helping to delineate valproate's acute and long-term efficacy in this difficult patient population, but also describing some of the characteristics of the illness associated with good clinical responsivity. He was awarded the Young Investigators Research Prize of the NDMDA in 1991 for this work.



Joseph R. Calabrese, M.D.

In a parallel fashion, Dr. Calabrese has now conducted the first major open study of the new anticonvulsant lamotrigine (Lamictal®) in treatment-refractory bipolar patients. His careful clinical observations and systematic ratings have helped document impressive early findings with this drug in both manic and depressive phases of the illness and have propelled the field to an extensive series of controlled investigations that will hopefully lead to the drug's receiving approval for use in bipolar illness. Dr. Calabrese, with his considerable energy and expertise, will be working with Dr. Findling to perform some of the breakthrough studies on child and adolescent bipolar illness and establish early intervention with randomized trials of valproate compared with placebo.

Robert Lawrence Findling received his Bachelors of Arts from Johns Hopkins University and his M.D. from the Medical College of Virginia. He then took his residency at Mt. Sinai Hospital in New York where he completed the Triple Board Joint Training Program (in pediatrics, psychiatry, and child psychiatry). He has been at Case-Western Reserve University as Assistant professor of Psychiatry, Pediatrics, and Adolescent Health for the past five years. Both Drs. Findling and Calabrese early on recognized the importance of identification and aggressive intervention in the early presentations of bipolar illness. This was particularly apparent in many of the children of parents studied and treated in Dr. Calabrese's inpatient and outpatient studies.

Robert L. Findling, M.D.

Together they began treating early onset bipolar illness with pharmacological and psychotherapeutic interventions, recognizing the seriousness of this illness and the need to treat it in a fashion parallel to other serious medical illnesses of childhood, including diabetes, epilepsy, arthritis, and a variety of malignancies. The wealth of clinical experience they bring to this task will now be invaluable in designing and conducting systematic clinical trials to better document the relative efficacies of different treatment interventions in the childhood presentations of the illness.

These investigators have already used the adult life chart method (NIMH-LCM™) to map the onset and course of early presentations of the illness. This systematic longitudinal approach should ultimately provide an invaluable database for better diagnosis and intervention in the illness. The Stanley Foundation family and the larger group of patients and their families suffering from bipolar illness are indeed fortunate to have two such dedicated and creative investigators taking the lead in this important area of clinical work and research at the Stanley center at Case-Western Reserve University.

Patient Recruitment for NIMH Studies

NIMH is seeking unipolar and bipolar depressed patients who need inpatient hospitalization and would like to participate in a study comparing the efficacy of gabapentin (Neurontin®) vs. lamotrigine (Lamictal®) vs. placebo. NIMH is also recruiting depressed patients for an inpatient or outpatient study comparing the efficacy of different frequencies of repeated transcranial magnetic stimulation (rTMS). Please call (301) 496-6827 or write to: NIMH/BPB, Bldg. 10, Room 3N212, 10 Center Drive MSC 1272, Bethesda, MD 20892-1272 for information on this or any other study.

K-LCM™/R: The Child Life Chart Method - Parents RETROSPECTIVE Ratings

Patient Name or ID# _____ Patient Initials ☐☐☐ (F M L) Clinician Initials ☐☐☐ (F M L) Date Completed ☐☐/☐☐/☐☐

Please Check√ **ALL BEHAVIORS AND SYMPTOMS*** Observed in Your Child During This **THREE- YEAR Period**:

ACTIVATED Behaviors Might Include:

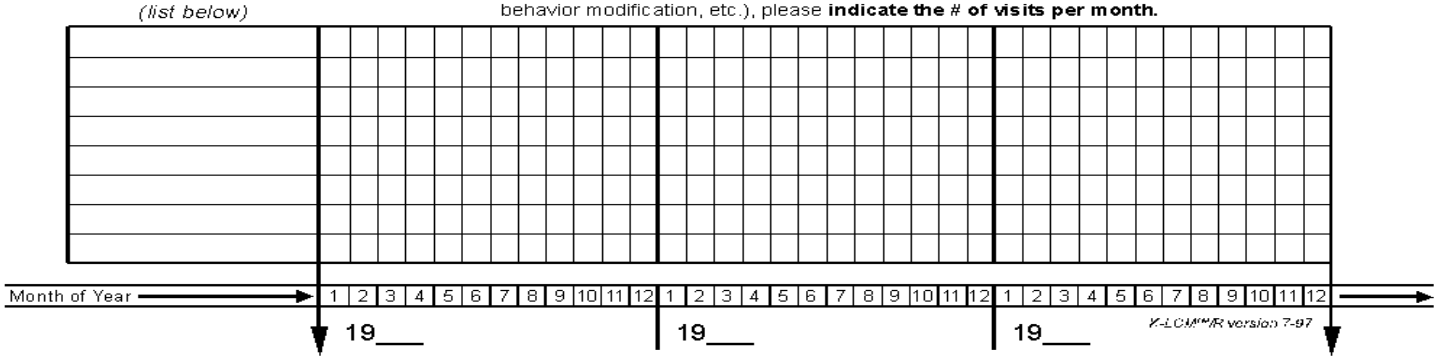
YEAR (Below) 1	2	3		YEAR (Below) 1	2	3	
___	___	___	1 Impulsivity	___	___	___	13 Stealing
___	___	___	2 Irritability	___	___	___	14 Disregard for authority
___	___	___	3 Temper tantrums	___	___	___	15 Fighting
___	___	___	4 Sleeps less than usual	___	___	___	16 Destruction of property
___	___	___	5 Hyperactivity	___	___	___	17 Excessive risk taking
___	___	___	6 Increased aggression	___	___	___	18 Trouble with the law
___	___	___	7 Skips school	___	___	___	19 Lack of remorse
___	___	___	8 Decreased attention span	___	___	___	20 Frequent lying
___	___	___	9 Inappropriate sexual behavior	___	___	___	21 Racing thoughts
___	___	___	10 Unusually happy and enthusiastic	___	___	___	22 Bizarre behavior
___	___	___	11 Excessively talkative	___	___	___	23 Other: _____
___	___	___	12 Unreasonably and excessively self-confident	___	___	___	24 Other: _____

WITHDRAWN Behaviors Might Include:

YEAR (Below) 1	2	3		YEAR (Below) 1	2	3	
___	___	___	25 Periods of sadness	___	___	___	35 Suicidal gesture
___	___	___	26 Low self-esteem/sense of worthlessness	___	___	___	36 Serious suicide attempt
___	___	___	27 More withdrawn than usual	___	___	___	37 Physical complaints
___	___	___	28 Cries more easily than usual	___	___	___	38 Sleeps more than usual
___	___	___	29 Unusually clingy & dependent	___	___	___	39 Obsessive thoughts
___	___	___	30 Less active & energetic than usual	___	___	___	40 Night terrors
___	___	___	31 Excessive guilt	___	___	___	41 Does not talk or respond
___	___	___	32 More anxious (tense/worried) than usual	___	___	___	42 Paranoid thinking
___	___	___	33 Change in appetite	___	___	___	43 Hearing voices
___	___	___	34 Suicidal thinking	___	___	___	44 Other: _____
				___	___	___	45 Other: _____
				___	___	___	46 Other: _____

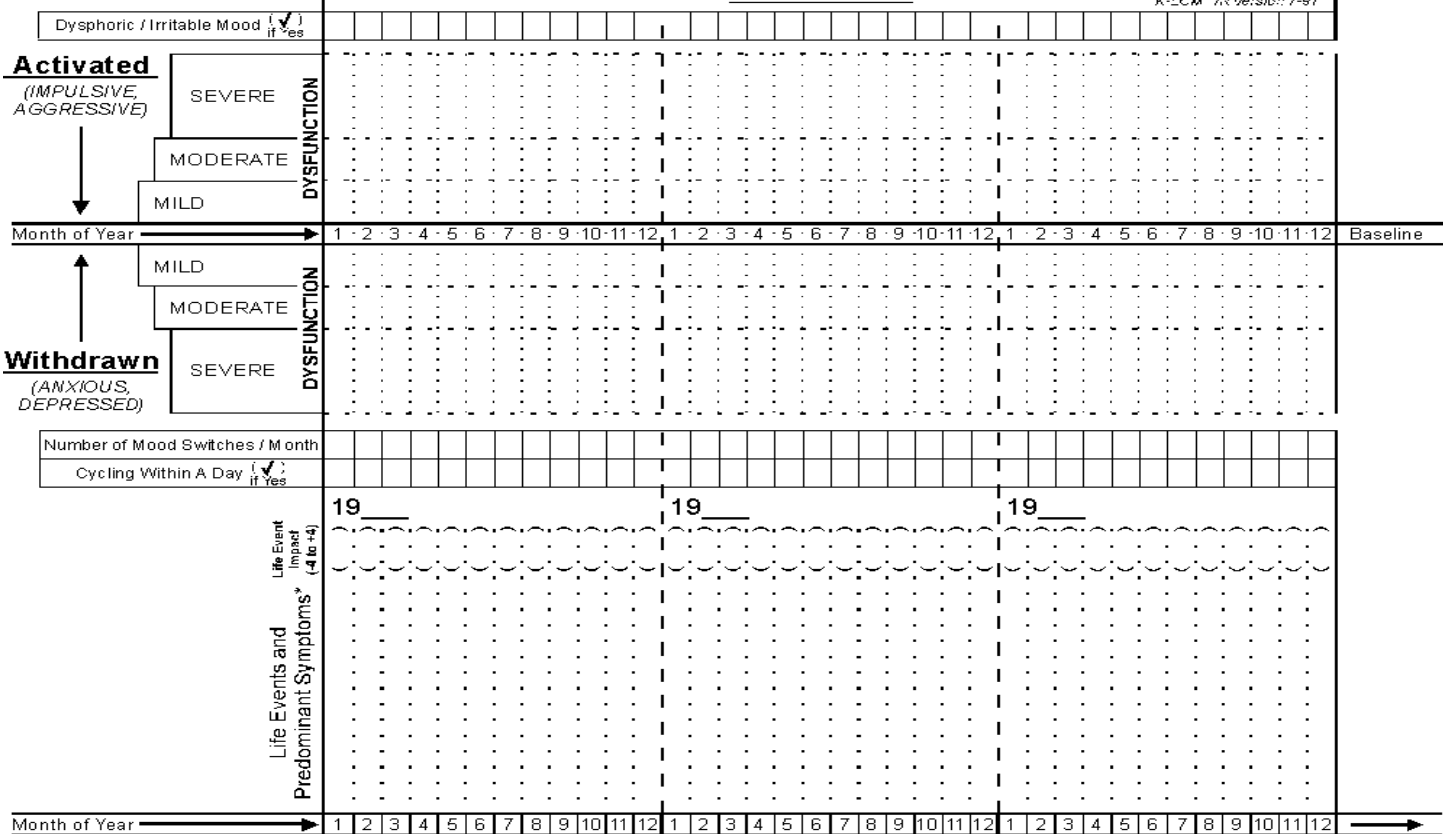
Interventions or Treatments *(list below)*

For each **MEDICATION**, please enter (by month) the **maximal dose per day taken** by the child. For **OTHER TREATMENT INTERVENTIONS** (e.g., psychotherapy, behavior modification, etc.), please **indicate the # of visits per month.**



Please rate the degree of dysfunction caused by either ACTIVATED or WITHDRAWN behaviors above and below the midline.

K-LCM™/R version 7-97



K-LCM™/P: The Child Life Chart Method - *Parent Daily* PROSPECTIVE Ratings

Patient Name or ID# _____ Patient Initials ___ ___ ___ (F M L) Month _____ Year _____

Protocol Code _____ Clinician Initials ___ ___ ___ (F M L) Blinded Rating? ☐No ☐Yes ☐N/A

Please Check √ **ALL BEHAVIORS AND SYMPTOMS*** Observed in Your Child **THIS MONTH:**

ACTIVATED				*WITHDRAWN*			
___ 1	Impulsivity	___ 13	Stealing	___ 25	Periods of sadness	___ 35	Suicidal gesture
___ 2	Irritability	___ 14	Disregard for authority	___ 26	Low self-esteem / sense of worthlessness	___ 36	Serious suicide attempt
___ 3	Temper tantrums	___ 15	Fighting	___ 27	More withdrawn than usual	___ 37	Physical complaints
___ 4	Sleeps less than usual	___ 16	Destruction of property	___ 28	Cries more easily than usual	___ 38	Sleeps more than usual
___ 5	Hyperactivity	___ 17	Excessive risk taking	___ 29	Unusually clingy and dependent	___ 39	Obsessive thoughts
___ 6	Increased aggression	___ 18	Trouble with the law	___ 30	Less active and energetic than usual	___ 40	Night terrors
___ 7	Skips school	___ 19	Lack of remorse	___ 31	Excessive guilt	___ 41	Does not talk or respond
___ 8	Decreased attention span	___ 20	Frequent lying	___ 32	More anxious (tense/worried) than usual	___ 42	Paranoid thinking
___ 9	Inappropriate sexual behavior	___ 21	Racing thoughts	___ 33	Change in appetite	___ 43	Hearing voices
___ 10	Unusually happy and enthusiastic	___ 22	Bizarre behavior	___ 34	Suicidal thinking	___ 44	Other: _____
___ 11	Excessively talkative	___ 23	Other: _____			___ 45	Other: _____
___ 12	Unreasonably and excessively self-confident	___ 24	Other: _____				

Interventions or Treatments *(list below)*

For each MEDICATION, please enter the **total dose taken** per day.
For OTHER TREATMENT INTERVENTIONS (e.g., psychotherapy, behavior modification, etc.), please **check the days the treatment was received.**

Days of Month 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31

K-LCM™/P version 7-97

Please rate the degree of dysfunction caused by either ACTIVATED or WITHDRAWN behaviors above and below the midline.

K-LCM™/P version 7-97

Psychosis (✓ if Yes)

Hours of Sleep

RATE DEGREE of Dysfunction:

Activated *(IMPULSIVE, AGGRESSIVE)*

SEVERE
HIGH MODERATE
LOW MODERATE
MILD
DYSFUNCTION

SEVERE
HIGH MOD
LOW MOD
MILD
DYSFUNCTION

Days of Month 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 Baseline

MILD
LOW MODERATE
HIGH MODERATE
SEVERE
DYSFUNCTION

Withdrawn *(ANXIOUS, DEPRESSED)*

MILD
LOW MOD
HIGH MOD
SEVERE
DYSFUNCTION

Number of Switches/Day

Life Events and Predominant Symptoms* Life Event Impact (-4 to +4)

Days of Month 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31

Bipolar Network News

Stanley Foundation Bipolar Network
A Program of the NAMI Research Institute
5430 Grosvenor Lane
Suite 200
Bethesda, Maryland 20814

Inside This Issue

A Focus on Early Onset Bipolar Illness
Life Chart Highlights
Around the Network: The Cleveland Site