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Barbara Geller Washington University School of Medicine

Rebecca Tillman Washington University School of Medicine

Kristine Bolhofner Washington University School of Medicine

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Proposed Definitions of Bipolar I Disorder Episodes and Daily Rapid Cycling Phenomena in Preschoolers, School-Aged Children, Adolescents, and Adults

Barbara Geller, M.D., Rebecca Tillman, M.S., and Kristine Bolhofner, B.S.

ABSTRACT

Objective: Recent data from several large studies of pediatric bipolar I disorder reported baseline (current) episode duration ranging from less than a month to ≥ 1 year. These data may reflect actual sample differences, but the absence of uniformly applied definitions of episode duration, number of lifetime episodes and daily rapid cycling patterns during episodes may also account for these differences.

Method: Proposals for definitions of episode and cycling phenomena were based upon data from the Washington University in St. Louis Kiddie Schedule for Affective Disorders and Schizophrenia (WASH-U-KSADS).

Result: Episode would be used for the interval between onset and offset of full DSM-IV criteria for bipolar I disorder. Cycling would be used only to describe daily (ultradian) switching of mood states that occurs during an episode.

Conclusion: Historically, in the adult bipolar literature the words "episode" and "cycle" were used interchangeably. "Rapid cycling," in this earlier literature, actually referred to multiple episodes per year. To avoid confusing episodes with daily cycling, the proposal is to use "episode" for the duration of DSM-IV criteria, to use "cycling" for daily switching phenomena during an episode, and to replace the historical term "rapid cycling" with "multiple episodes per year." These clarifications will be especially important for phenomenological research on preschool populations.

OUR UNIT PREVIOUSLY communicated about the need for uniformly applied definitions of episode and cycling to provide comparability of data across studies (Tillman and Geller, 2003). But, recent data from several large studies (see Table 1) demonstrate the need for further clarification. Three studies reported base-

line (current) episode duration (Geller et al., 2004; Birmaher et al., 2006; TEAM Study, unpublished data) of at least one year. By contrast, Wagner et al. (2006) reported 17.1 ± 18.9 episodes per year; implying that the mean episode duration was less than one month. Because the Wagner et al. (2006) study reported

Washington University School of Medicine, Department of Psychiatry, St. Louis, Missouri. Supported by NIMH grants R01 MH-53063 and U01 MH-64846 to Dr. Geller.

Geller et al. $86 10.8 \pm 2.7$	$Age \neq SD$	Prospective	Recruitment	SADS Series tool	Blinded & controlled assessment	Current episode duration	% First episode	N lifetime episodes	% Subjects with daily cycling
(2004)	± 2.7	yes	consecutive new case	WASH-U ^b	Yes	79.2 ± 66.7 weeks	81.4	1.2 ± 0.4	9.77
Biederman et al. 197 8.4 (SD N/A) (2005)	(N/A)	оп	consecutive referrals	Е	No	N/A	N/A	N/A	N/A
Birmaher et al. 152 13.2 ± 3.0 (2006)	+ 3.0	partly	convenience	P/L ^d	No	median 52.0 weeks	N/A	N/A	N/A ^f
Wagner et al. 115 Range 7–18 yr (2006)	7–18 yr	по	convenience	P/L	No	N/A	N/A	17.1 ± 18.9°	N/A
TEAM ^a study $283 10.1 \pm 2.7$ (still recruiting)	± 2.7	по	convenience	WASH-U	No	4.8 ± 2.5 years	90.8	1.1 ± 0.3	98.9

ł Лŀ ì OL D -Ē IN ĥ í e Ċ TABLE 1

^cKSADS-E = Kiddie Schedule for Affective Disorders and Schizophrenia—Epidemiologic Version (Orvaschel and Puig-Antich, 1987). ^dKSADS-P/L = Kiddie Schedule for Affective Disorders and Schizophrenia—Present and Lifetime Version (Kaufman et al., 1997).

^eNumber of episodes within past year in active drug group. ^fThese investigators reported 82.3% with mood lability, which may be measuring the same concept as daily cycling (Axelson et al., 2006). NA = not applicable.

 17.1 ± 18.9 episodes per year, the mean duration of the current episode must have been far less than the minimum of one year found in the three other studies in Table 1. Two studies reported a mean lifetime number of episodes of 1.1–1.2, and in these studies 81.4%–90.8% of subjects were in their first episode (Geller et al., 2004; TEAM Study, unpublished data). These striking differences in number of lifetime episodes and in current episode duration between studies strongly support the need for definitions of episode and daily cycling that will provide comparable data across studies. It is possible that the apparent differences between Wagner et al. (2006) and the other studies in Table 1 are definitional rather than phenomenological.

This issue of daily cycling, i.e., mood switching during a single day for every day of the episode, is especially cogent to the preschool population. One of the most challenging aspects of assessing preschool children for psychopathology is the oftentimes protean nature of the symptoms (Luby et al., 2007). Preschool manic symptoms noted in Luby et al. (2007) were typical of mania but occurred for multiple brief periods daily for years, similar to descriptions in older children.

Another problem extant for all ages, but more so for preschoolers, is what constitutes pathological, impairing mood states. For depressed moods, this is relatively more straightforward, because *any* sustained sadness or anhedonia is considered abnormal. For example, there would be little disagreement that the anhedonic preschoolers reported by Luby et al. (2004) are impaired, as all children are expected to play. By contrast, Geller et al. (2002) have published on the counterintuitive conception that children can be psychopathologically too happy or too grandiose. And this would be even more so for preschoolers who are not yet "burdened" with school regulations or homework (Luby and Belden, 2006).

These observations on the pattern of manic symptoms in preschool children are highly similar to those reported for children aged 7 and older. In subjects aged 7 and older (Geller et al., 2004) and in those aged 6 and older (TEAM Study, unpublished data), daily mood switching during an episode was the most common presentation in studies that used the WASH-U-KSADS tool, which documents onset and offset of each current and lifetime episode (see Table 1). This tool also asks about the presence and number of daily cycles, and mood state during the daily cycle (Geller et al., 2001).

A problem has been how to define and document these daily phenomena so that comparable data across studies can be obtained. Authors studying both pediatric and adult samples have used the phrase "rapid cycling" in diverse contexts. Historically in the adult bipolar literature, "rapid cycling" was defined as four or more episodes per year (see Table 2). Thus, rapid cycling was defined as equivalent to multiple episodes per year, i.e., one episode equaled one cycle, as depicted in Table 2.

Episode duration in the Geller et al. (2004) and Birmaher et al. (2006) studies in Table 2 was defined using the Frank et al. (1991) criteria, which were developed for adults. These criteria were that recovery was defined as 8 consecutive weeks without meeting DSM-IV criteria for mania or hypomania, remission was defined as 2–7 weeks without meeting DSM-IV criteria for mania or hypomania, and relapse after recovery was defined as 2 consecutive weeks of meeting DSM-IV criteria for mania or hypomania with clinically significant impairment. Thus, investigators across the age span have used similar definitions of remission, recovery, and relapse.

 TABLE 2.
 PROBLEM WITH THE HISTORICAL DEFINITIONS OF RAPID

 Cycling in the Adult Bipolar I Disorder Literature

Problem: This definition did not account for daily cycling during episodes.

Proposal: "Rapid cycling" be used only for daily switching phenomena that occur during an episode.

Historically: The words "episodes" and "cycling" were used interchangeably so that ≥ 4 episodes/year = rapid cycling.

Phenomenon	Definition
episode	onset to offset of full DSM-IV criteria for bipolar I disorder ^b
ultra-rapid cycling ^a	mood switches every few days during an episode
ultradian cycling ^a	mood switches multiple times daily during an episode

 TABLE 3.
 PROPOSED DEFINITIONS OF EPISODES AND CYCLING PHENOMENA

^aThese terms are from Kramlinger and Post (1996).

^bEpisodes are defined using Frank et al. (1991) criteria.

One important question is whether these daily rapid cycling definitions would pertain to adults with bipolar I disorder (BP-I). To examine this issue, data on daily cycling were collected in a blindly rated, controlled study of psychopathology of parents of BP-I probands who had BP-I themselves (Geller et al., 2006). Among these parents, 40.3% had daily cycling (Geller et al., unpublished data).

Uniform definitions of episode and cycling would help to clarify developmental, age-specific manifestations of mania. Therefore (see

TABLE 4.	Examples of Episode Duration and Daily (Ultradian) Cycling in
	PRESCHOOLERS, SCHOOL-AGE CHILDREN, AND ADULTS

Note that most children are in their first episode at baseline. Therefore, there may be a history of onset of DSM-IV bipolar I disorder but not of offset.

Example 1: Preschooler

A 6-year-old had an onset of DSM-IV symptoms of bipolar I disorder one year ago. During this year, there was a mean of 4 cycles per day. Cycles were from mania to euthymia. Child would be said to be in a current episode (and first episode) of bipolar I disorder symptoms that has a duration of one year, and the episode is characterized by daily cycling.

Example 2: School-Aged Child

An 8-year-old had an onset of DSM-IV bipolar I disorder two years ago. During these two years, there was a mean of 3 cycles per day. Cycles were from mania to depression or mania to euthymia. Child would be said to be in a current episode (and first episode) of bipolar I disorder with a duration of two years, and the episode is characterized by daily cycling.

Example 3: Adult

A 25-year-old patient had a history of two prior episodes of DSM-IV bipolar I disorder. One of these episodes was mania with a duration of three months and was without daily cycling. The second of these prior episodes was MDD for four weeks without daily cycling, immediately followed by two weeks of mania, also without daily cycling. This second episode, therefore, had a duration of six weeks characterized by four weeks of MDD and two weeks of mania, and without daily cycling. The current DSM-IV manic episode began 1 week ago and is without daily cycling.

Example 4: Adult

A 35-year-old patient had a history of onset of DSM-IV bipolar I disorder at age 16 characterized by 2–3 daily cycles from mania to depression or mania to euthymia and without a DSM-IV bipolar I disorder free period of at least eight weeks.^a Thus, this adult had a current (and first) episode of bipolar I disorder with a duration of 19 years (no intervening euthymic period of at least eight weeks), characterized by daily (ultradian) cycling.

^aThe definition of separate episodes defined by eight week intervals of not meeting full DSM-IV criteria is used by multiple authors (Findling et al., 2001; Frank et al., 1991; Geller et al., 2004).

MDD = major depressive disorder.

Table 3), the proposal is as follows. A definition of episode that best fits the data is that episode refer to the onset and offset of full DSM-IV bipolar I disorder. Cycling would be used only to describe daily (ultradian) switching of mood states that occurs during an episode. Examples of the use of these definitions of episode and of cycling appear in Table 4. These examples also include how depressive states are incorporated into episode and cycling definitions.

For these definitions to have clinical utility, clinicians will need to ask parents and, separately, children whether they have daily cycles. If they say yes, then the number of cycles per day and the character of the cycles (elated, depressed, etc.) needs to be documented.

In summary, historically the words "episode" and "cycle" were used interchangeably. "Rapid cycling," in this historical schema, actually referred to multiple episodes per year. To avoid confusing episodes with daily cycling, the proposal is to use "episode" only for the duration of DSM-IV criteria, to use "cycling" only for daily phenomena during an episode, and to replace the historical term "rapid cycling" with "multiple episodes per year."

TREATMENT OF EARLY AGE MANIA (TEAM)

The Treatment of Early Age Mania (TEAM) study (NCT00057681) is conducted with the participation of the following sites: Washington University in St. Louis, St. Louis (coordinating site): Barbara Geller, M.D., Rebecca Tillman, M.S., Kristine Bolhofner, B.S., Betsy Zimerman, M.A., Jeanne Frazier, B.S.N., Linda Beringer, R.N., Nancy Strauss, B.S.N., Patricia Kaufmann, M.S.N., Jan Lautenschlager, B.S.; Children's National Medical Center, Washington D.C.: Paramjit Joshi, M.D., Adelaide Robb, M.D., Jay A. Salpekar, M.D., Nasima Nusrat, M.D.; Johns Hopkins Medical Institutions, Baltimore: John Walkup, M.D., Mark Riddle, M.D., Elizabeth Kastelic, M.D., Shannon Barnett, M.D., Shauna Reinblatt, M.D., Maria Rodowski, M.D., Jessica Foster, B.A., Andrea Galatis, B.S., Maureen Masarik, M.S., Samuel Walford, M.A.; University of Pittsburgh, Pittsburgh: David Axelson, M.D., Boris Birmaher, M.D., Neal Ryan, M.D., Annette Baughman, B.S.N., Leah Giovengo, B.A., Susan Wassick, R.N., Jennifer Fretwell, B.A., Christine Hoover, M.S.N.; University of Texas, Southwestern, Dallas: Graham Emslie, M.D.; University of Texas Medical Branch, Galveston: Karen Dineen Wagner, M.D., Ph.D., Melissa Martinez, M.D., Aileen Oandasan, M.D.; Washington University in St. Louis, St. Louis: Joan Luby, M.D., Samantha Blankenship, M.S.W., Mary Nail, M.A., Molly McGrath, L.C.S.W.; National Institute of Mental Health, Bethesda, MD: Benedetto Vitiello, M.D. (scientific collaborator), Joanne B. Severe, M.S. (operations staff). Please note that there are two separate sites at Washington University in St. Louis.

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AUTHOR DISCLOSURE

The authors have no conflicts of interest to disclose.

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Address reprint requests to: Barbara Geller, M.D. Department of Psychiatry Washington University 660 South Euclid Avenue St. Louis, MO 63110

E-mail: gellerb@medicine.wustl.edu