

THE RATIONALE FOR COMBINING INTERPERSONAL AND SOCIAL RHYTHM THERAPY (IPRST) AND PHARMACOTHERAPY FOR THE TREATMENT OF BIPOLAR DISORDERS

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Abstract

Interpersonal and social rhythm therapy (IPSRT) is an individual psychotherapy for patients with bipolar disorder. IPSRT focuses on stabilizing patients' social and circadian rhythms, given that bipolar disorder symptoms might be exacerbated or triggered by circadian rhythm and sleep-wake cycle abnormalities. From a theoretical point of view, the notion of a psychosocial intervention in bipolar disorders derives from the bio-medical approach: on one hand, symptoms of bipolar disorder almost inevitably disrupt interpersonal relationships and social functioning at different levels; on the other hand, psychosocial factors such as stressful life events, lack of social support, familial expressed emotion usually influence the illness course and reduce treatment response. When administered in concert with pharmacotherapy, IPSRT may shorten time to remission of bipolar depression, may prolong time to relapse, reduce severity of episodes, and improve the adherence to medication regimens. This article focuses on the rationale for combining IPSRT and pharmacotherapy for patients with bipolar disorders, and summarizes the evidence for their efficacy.

Key Words: interpersonal, bipolar, combined treatment, bio-psychosocial, rhythmicity

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Introduction

Treatment guidelines for bipolar disorders continue to evolve. Research and clinical management of bipolar disorder have two aims: to provide the most symptom relief to patients suffering from a (hypo)manic, mixed or depressive episode, as rapidly as possible; and to implement long-term treatment strategies, in order to minimize risk of relapse, recurrence, and persisting symptoms and dysfunction. Several longitudinal studies have reported that patients with bipolar disorder spend more than 40 to 50% of their lives in a symptomatic condition (Gitlin et al. 1995, Judd et al. 2002). Rates of relapses and recurrences remain high, despite new forms of treatment. Recurrences range from 40 to 75% in the first 2 years of treatment, even when patients regularly take pharmacotherapy (Gitlin et al. 1995, Miklowitz 2008).

Thus the combination of pharmacotherapy and psychosocial intervention has been proposed as a pragmatic strategy. Combining treatments has the

rationale of potentiating and augmenting the symptomatic benefits of pharmacotherapy with the *'necessary behavioral, and lifestyle changes'* fundamental to a lifetime perspective. Nonetheless, only a few investigations of patients with bipolar disorders have compared combined to single treatments. Evidence that combined treatment has superior efficacy has not alleviated concerns about the costs of routinely providing combined treatment to patients with bipolar disorder. Identifying specific subgroups of patients who may significantly benefit from a potentially more expensive approach remains under investigation. Meanwhile, *'providing combined treatment to everyone seeking care would likely overwhelm the capacities of existing health services'* (Jindal and Thase 2003).

From a theoretical point of view, the notion of a psychosocial intervention in bipolar disorders derives from the bio-medical approach. The clinical manifestations of bipolar disorders are affective, cognitive, neurovegetative and behavioral; as a consequence, symptoms almost inevitably disrupt interpersonal relationships and social functioning at

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different levels. On the other hand, psychosocial factors such as stressful life events (Johnson and Roberts 1995, Hlastala and Frank 2000), lack of social support (Johnson et al. 2000), controversial familial expressed emotion (Miklowitz et al. 1988) may trigger, exacerbate or influence the course and reduce treatment response. In fact, while biological factors play the strongest role in the pathophysiology of bipolar disorders, the timing of individual episodes is strongly related to environmental, psychological and psychosocial factors, reinforcing the rationale for psychosocial treatments (Frank 2005).

At present, a large proportion of mental health professionals believe that patients with bipolar disorders need a more comprehensive approach. Psychological intervention is not only of primary importance to establishing a strong therapeutic alliance during the initial phase of treatment, but is also an additional benefit for those patients who continue to have interpersonal difficulties and poor social skills, despite their response to pharmacological treatment. The level and intensity of this support may range from basic psycho-educational intervention, in the context of a psychiatric clinical management, to group psychoeducation, familial interventions and finally to specific individual psychotherapies.

Recently, Miklowitz (2008) suggested that integrated chronic care models, similar to those established for other severe chronic disorders such as schizophrenia, could be more efficacious and cost-effective than non-combined approaches. This assumption reflects the spectrum of bipolar disorders: at one extreme, patients experiencing a single manic episode with minimal interference on family, social and work functioning; at the opposite extreme, patients with a severe bipolar disorder with mood incongruent psychotic features or with a rapid cycling course or with comorbid Axis-I and II disorders, all correlates of poor response to pharmacological treatment. According to this approach, patients with a more severe clinical course require a combined intervention from a multi-profession staff based on flexible treatment algorithms. These treatment algorithms should consider a number of clinical variables such as current levels of severity, the presence of suicidal ideation, early onset of the illness, type of cycle, persistence of low levels of insight, psychotic features, and the occurrence of psychiatric and medical comorbidity.

The improved characterization of multiple factors influencing the course of bipolar disorder (mainly the presence of stressful life events, family conflict, circadian-biological instability, treatment non-compliance) have led to the investigation of other therapeutic interventions, such as interpersonal and social rhythm therapy (IPSRT) (Frank et al. 2005), cognitive-behavioral therapy (Zaretsky et al. 1999, Scott et al. 2001, Lam et al. 2003), family-focused treatment (Miklowitz et al. 2003), and group psycho-educational treatment (Colom et al. 2003). A number of studies have demonstrated that these interventions result in a significant reduction of relapse rates, efficacy in lowering the impact of symptomatology and subjective improvement in social functioning and quality of life (Scott and Colom 2005, Miklowitz 2008).

The aims of this paper are: to review the theoretical basis of the interpersonal and social rhythm therapy (IPSRT), an adaptation for bipolar disorder of interpersonal psychotherapy for depression (IPT) (Klerman et al. 1984), to summarize the major findings of its application and to describe an adapted form of IPSRT recently developed for adolescents with BD (IPSRT-A).

The Theoretical Basis of IPSRT

Although the most important and empirically supported theories of the etiology of BD are those related to genetic vulnerability and neurotransmitters, neuropeptides and/or neuroendocrine dysregulation, it is now generally accepted that environmental, psychological and psychosocial factors play a role in the timing of individual episodes, particularly manic episodes (see Goodwin and Jamison 2007, for a review).

In the '80s, several efforts were devoted to combining knowledge on the biological aspects of mood disorders with evidence of the role of life stressors and lack of social support. More recently, several studies have provided empirical support for this hypothesis, exploring how sleep disturbances (Wehr et al. 1987, Wehr 1989, Harvey 2008), stressful life events (Johnson and Roberts 1995, Hlastala & Frank 2000, Hlastala et al. 2000, Dienes et al. 2006), lack of social support (Johnson et al. 1999, Johnson et al. 2000) and social routine disruption (Malkoff-Schwartz et al. 1998, Malkoff-Schwartz et al. 2000) can trigger the onset or the relapse/recurrence of bipolar disorder.

In particular, Dienes et al. (2006) suggested, in line with the kindling hypothesis, that severe early precipitating events may activate biological vulnerability, determine an earlier onset of BD and induce an higher rate of recurrences or relapses. Kendler et al. (2000) analyzing the course of illness in twins affected by unipolar depression, concluded that the influence of life events is more important at the beginning of the disorder. Moreover, a number of studies have documented the existence of a relationship between psychosocial stressors and changes in biological rhythms (Ehlers et al. 1988, Ehlers et al. 1993); on the other hand alterations in biological rhythms (sleep routine, appetite, energy and alertness rhythms) can cause significant psychosocial stress and disability (Wehr et al. 1987, Wehr 1989, Harvey 2008).

Sleep abnormalities, observed in both depression and mania, may be placed in the broader context of the pervasive circadian disturbances hypothesized in bipolar disorders. Circadian rhythm researchers have defined the exogenous environmental factors that set the 'master circadian clock' *zeitgebers* or 'time givers' (Aschoff 1981): physical *zeitgebers* (e.g.: light, temperature, humidity, electromagnetic fields), environmental (e.g.: food availability) and social *zeitgebers* (e.g.: work, marriage, etc). The most important physical *zeitgeber* is the day-night cycle. However, especially in industrialized societies, habits within the family routine, meal-times, work patterns, TV watching or night addiction to Internet significantly influence circadian rhythms. The main hypothesis is that when

these patterns undergo sudden alterations, circadian rhythms may be upset and in susceptible individuals, ultimately in manifestation of affective episodes.

IPSRT (Frank et al. 2005, Frank 2005) is a manual-based psychotherapy focused on the instability model of BD postulated by Goodwin and Jamison (1990, 2007) and the Social Zeitgeber theory of mood disorders (Ehlers et al. 1988, Ehlers et al. 1993) (**Figure 1**).

As Hlastala and Frank (2006) hypothesized, *‘these two models suggest that at least one aspect of the biological diathesis for BD is a vulnerability of the circadian system and an increased susceptibility of neurotransmitter systems to dysregulation.’*

Based on these concepts, IPSRT works on five different levels: 1) the link between mood and life events, 2) the importance of maintaining regular daily rhythms as elucidated by the Social Rhythm Metric (SRM) (Frank et al. 1994), a 17-item self-report form that requires patients to record daily activities (see Figure 2 for a simpler, five item version of the SRM used in the Systematic Treatment Enhancement Program for Bipolar Disorder Study [STEP-BD]; Sachs et al. 2003), 3) the identification and management of potential precipitants of rhythm dysregulation, with special attention to interpersonal triggers, 4) the facilitation of mourning the lost healthy self, and 5) the identification and management of affective symptoms.

The patient is helped to better understand the relationship between stressful life events and mood swings; moreover, he/she is encouraged to deal with interpersonal problems and manage the affective symptoms in order to reduce their severity and negative influence. Lastly, clinicians help patients to express their feelings about having a severe lifetime illness and to overcome the loss of their “healthy self” and to accept the impact of the disorder on their lives.

Structure of IPSRT

IPSRT is divided into four phases: a) initial phase, b) intermediate phase, c) preventative phase, d) termination.

During the initial phase the clinician follows both a medical approach, with the collection of a detailed history of the illness, and an interpersonal approach, utilizing the ‘interpersonal inventory.’ The rationale is to identify as early as possible an interpersonal problem area related to the onset of the most recent illness episode or to a partial response to psycho-pharmacological treatment. Moreover, the clinician educates the patient about the main characteristics of bipolar disorder and introduces the patient to the systematic use of the SRM. Treatment can be started with weekly

Figure 1. Scheme for Social Zeitgeber Theory

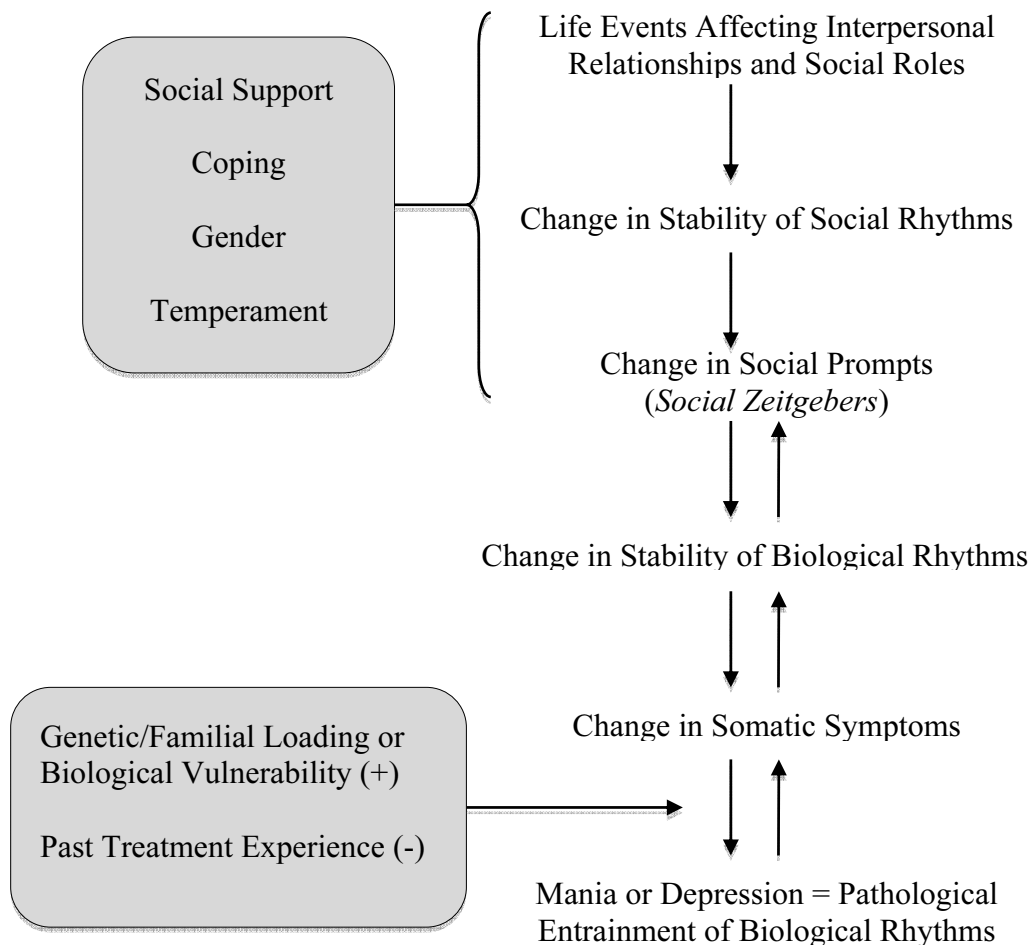


Table 1. *Structure and tasks of IPSRT*

A. Initial phase (weekly sessions from few weeks to several months)	
1) History of the illness	<ul style="list-style-type: none"> • To collect psychiatric and medical history • To explore the relationships between interpersonal and social rhythm alterations and the onset of symptoms • To pay attention to other important rhythm alterations (menstrual cycle, seasonality, regular pattern of cyclicality) that may influence mood, using psychosocial and pharmacological strategies in order to prevent or delay future mood dysregulations
2) Interpersonal inventory	<ul style="list-style-type: none"> • Review of significant relationships in the patient's life, starting from the present and focusing on the current episode
3) Identification of patient's main interpersonal problem area	<ul style="list-style-type: none"> • Grief • Loss of 'Healthy Self' • Role Transitions • Role Disputes • Interpersonal Deficit
4) Psychoeducation	
5) Social Rhythm Metric (SRM)	
B. Intermediate phase (weekly sessions over several months)	
1) To develop strategies to manage affective symptoms	
2) To stabilize daily rhythms	<ul style="list-style-type: none"> • Reviewing of 'free running' SRMs to find particularly unstable rhythms • Identifying specific SRM targets • Recognizing sources of rhythm disruption (zeitstörers) • Finding the right balance between stability and spontaneity • Managing changes in social routines
3) To resolve the selected interpersonal problem area	
C. Preventive phase (monthly sessions over 2 or more years)	
1) To consolidate treatment gains	
2) To increase patient's confidence in his/her capacity to apply IPSRT techniques outside the sessions	
D. Termination phase (monthly sessions over 4 to 6 months)	
1) To review gains during treatment	
2) To offer encouragement about patient's ability to exercise new skills independently from the therapist	

45-minute sessions while the patient is currently experiencing a full-blown depressive episode, when he/she has a sub-syndromal depressive condition, or when he/she is euthymic. The duration of the initial phase may vary from several weeks to several months, depending mainly on the severity of the patient's current symptoms. Special attention is devoted to the detailed inquiry for evidence of alterations or disruptions in the patient's daily routines and interpersonal interactions that might have preceded the development of symptoms, or the occurrence of a new episode of illness. For example, it is well-known how manic or mixed episodes are frequently preceded by a social rhythm disrupting event, especially when it is able to influence and modify the quality and quantity of sleep (Malkoff-Schwartz et al. 1998). These historic details will help the therapist to understand the patient's patterns of illness and aid in identifying potential triggers tailored specifically for *'that'* patient. Moreover, following the same principles of *'classic'* IPT, the therapist conducts

a review of the significant others in the patient's life, namely the *'interpersonal inventory.'* The therapist asks about the patient's life circumstances and requests a description of the important people in his or her life, starting from the present and then focusing on the past. The interpersonal inventory starts in the initial phase of treatment, but continues throughout the whole therapy. Patients with bipolar disorder usually have a *'complicated life,'* and new people may have different roles or may become *'significant'* for the patient in a short amount of time. It is crucial for the clinician and for the patient to remain focused on the quality of the relationships, with a systematic description of the most satisfying or unsatisfying aspect of every relationship. Moreover, the unmet expectations of others and the aspects of relationships that the patient would like to change are explored. A bifocal attitude should be maintained by the clinician: perturbations in relationships may be the consequence of a transitory exacerbation of mood dysregulations; conversely,

Figure 2. *Social Rhythm Metric-II-Five-item Adult Version (SRM II-5)***Directions:**

- Write the **ideal** target time you would **like** to do these daily activities.
- Record the **time** you actually did the activity each day.
- Record the **people** involved in the activity: 0 = Alone; 1 = Others present; 2 = Others actively involved; 3 = Others very stimulating

Date (week of): _____

Activity	Target Time	Sunday		Monday		Tuesday		Wednesday		Thursday		Friday		Saturday	
		Time	People	Time	People	Time	People	Time	People	Time	People	Time	People	Time	People
1. Out of bed															
2. First contact with other person															
3. Start work/school/ Volunteer/family care															
4. Have dinner															
5. Go to bed															
Rate MOOD each day from -5 to +5 - 5 = very depressed +5 = very elated															

interpersonal issues may trigger or exacerbate mood symptoms. Understanding this bi-directional relationship between interpersonal difficulties and affective symptoms should help the therapist toward identifying the appropriate treatment focus for the intermediate phase of therapy. The selection of the interpersonal problem area usually depends on deciding which of the IPSRT problem areas is most closely linked to the onset of the patient's current (or most recent) episode of illness. The therapist presents the chosen problem area to the patient in easily understandable, non-pejorative terms. The therapist and the patient discuss and sometimes reformulate the problem area until they reach an agreement on the focus of the interpersonal part of the therapy.

Finally, the initial phase of treatment includes several psycho-educational issues, such as information about bipolar symptoms, prescribed medications, medication side effects and the administration of the SRM.

During this phase the first part of the session is dedicated to the review of the SRMs filled out during the week to highlight the possible role of social and circadian rhythm disruptions in precipitating a new episode.

This self-report form (**Figure 2**, SRM-II-5 item) assesses patients' daily activities (e.g., time out of bed, first contact with another person, meal-times, bedtime), if the patient was alone or with others during each of these activities and how stimulating (i.e., quiet vs. interactive) these others were. The patient also rates his/her mood every day. After becoming familiar with the forms, patients spend 5 to 15 minutes per day completing the SRM.

The intermediate phase of treatment is conducted weekly over several months. Take-home points of this phase are: the development of strategies for the management of affective symptoms, the stabilization of daily rhythms and the management of the selected interpersonal problem areas with specific strategies and techniques.

Regardless of the choice of the problem area, the clinician helps the patient when '*he/she is missing the highs*'. In fact the mood stabilization obtained with pharmacotherapy is often associated with a subjective feeling of loss of spontaneity, and is frequently related to reduced treatment compliance.

The therapist helps the patient to become fully aware of specific strategies dedicated to the management of affective symptoms, through the stabilization of daily rhythms and the resolution of problematic interpersonal areas. A behavioral approach usually facilitates the management of the activities related to circadian rhythm irregularities. In this phase it is important to systematically assess the severity of circadian rhythm instability through a detailed review of the first 3 or 4 weeks of 'free-running' SRMs. A special effort is dedicated to determining whether the social rhythm instability is a prodromal symptom of recurrence/relapse, or whether it simply derives from a lifestyle choice. Frequently, rhythm disruption is a consequence of a complicated lifestyle, partially deriving from dysfunctional strategies that the patient has learned or acquired, in the effort to manage long-lasting mood instability. For example, patients with

bipolar disorders often seek over-stimulation, or tend to consider as normal being lethargic during the first part of the day, and extremely active during the second part. As a consequence, circadian rhythm integrity is disrupted. At some point in the treatment, most patients with bipolar disorder tend to question the need for protecting the integrity of their 'peculiar' social rhythms. They perceive a regular lifestyle as 'boring', unappealing and not consistent with their expectations. If this is the case, the therapist has to stress the importance of stabilizing social rhythms, as a way to reduce the occurrence and the severity of mood symptoms. He or she focuses on patient's daily rhythms and environmental stressors that may induce or influence a circadian rhythm dysregulation, with the aim to promote significant lifestyle changes.

Therapist and patient interactively discuss possible strategies for regulating rhythms and interpersonal stimulation. These strategies encompass short term (i.e., adhering to a 7 AM wake-up time for 7 consecutive days), intermediate (i.e., sustaining a regular sleep-wake cycle for a month), and long-term (i.e., finding regular employment) objectives.

A significant part of the effort is devoted to the prevention both of the '*highs*' and of the extreme inactivity consequent to depressive mood or to interpersonal deficits. Inactivity contributes to isolation and depressive symptoms in the same way that excessive interpersonal stimulation may precipitate an hypo/manic state.

Moreover, it is well known that circadian rhythms and interpersonal stimulation vary during the year, and the therapist should consider the seasonality of the disorder.

Some patients, for instance, may benefit from a busier schedule of activities during the winter months, when they typically tend toward depression, and curtail the amount of activities during the summer months when the risk for mania is higher.

Every significant change in routine has to be managed, discussed and optimized in order to help the patient to modify daily activities.

During the preventative phase of treatment, session frequency decreases to monthly. This phase of IPSRT lasts 2 or more years and pursues, as a main objective, the prevention of future mood episodes and the optimization of functioning during the inter-episodic periods. It is crucial to encourage the patient to maintain long-lasting regular social rhythms and to manage interpersonal problems as they arise, considering that interpersonal foci may change during time, and may be different from the initial ones. The preventative phase of treatment often requires occasional additional crisis sessions to address either a symptom exacerbation or an interpersonal dilemma.

The termination phase of treatment is mainly focused on reviewing treatment successes (as well as potential vulnerabilities still present) and on helping the patient to identify strategies for future management of interpersonal difficulties or symptom recurrences. This phase is often complicated and may require over four to six monthly sessions. Thus, it is crucial to encourage the patient to exercise the acquired skills independently from the therapist, and to highlight the improvement in terms of better quality of interpersonal

relationships and long-lasting stability of social rhythms.

Brief Description of Interpersonal Problem Areas

Contextually to rhythm stabilization, the therapist should identify one or more interpersonal problem area. IPSRT problem areas are basically the same as those of classic IPT, namely: 1) grief; 2) interpersonal disputes; 3) role transition; 4) interpersonal deficit plus a fifth focus: the lost '*healthy self*'. IPSRT adapts the traditional IPT strategies to the specific needs of patients with a bipolar disorder. The interpersonal foci, techniques and strategies are described in detail in E. Frank's manual (Frank 2005).

As in IPT, *grief or complicated bereavement* refers to symptoms deriving from incomplete mourning or unresolved feelings about the death of an important person in the patient's life. These symptoms exceed in duration and intensity the characteristic of the normal mourning process.

The *interpersonal dispute problem area* is chosen as the IPSRT focus when the onset of the most recent mood episode is related to any close relationship in which there are nonreciprocal expectations. It is a frequent focus in IPSRT, considering that patients with bipolar disorder often have a tumultuous interpersonal style, in which signs, symptoms, or personality traits are mixed together and contribute to interpersonal disputes. Conversely, the interpersonal disputes may continuously over-stimulate the patient and precipitate or exacerbate mood symptoms.

The *role transition* in IPSRT is considered when difficulties and symptoms are raised by major life role changes. On one hand, patients with bipolar disorder are sensitive to a wide number of potential stressors, including new employment, unemployment, matriculation, graduation, retirement, marriage, divorce, or pregnancy and delivery; on the other hand, the profoundly disruptive nature of bipolar disorder may cause significant interpersonal upheaval in a patient's life. The therapist should be especially sensitive to these issues and probe for the status of important relationships pre- and post-episode.

Patients with early-onset, long-lasting or rapid cycling bipolar disorder frequently experience a long-standing condition of impoverished or contentious social relationships. According to the IPSRT approach they develop *interpersonal deficits*. This focus is of primary importance when social withdrawal, or extreme mood fluctuations contribute to multiple failed relationships, recurrent patterns of conflict with coworkers, or constricted social networks.

Grief for the Lost 'Healthy Self': This problem area was developed specifically for patients who suffer from bipolar disorder. Because of the often catastrophic nature of bipolar episodes, many of these individuals divide their life into two parts: before the onset of the disorder and after its onset. This problem area is chosen when a patient grieves for the abilities, the potentialities and the interpersonal role he/she had lost with the onset of the bipolar disorder (the '*former self*') and has difficulties on adapting to the demands of living with a chronic illness.

Data Supporting the Efficacy of IPSRT

To date, IPSRT has been studied in two clinical trials in adults: the Maintenance Therapies in Bipolar Disorder Study (MTBD) (Frank et al. 2005), and the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) (Sachs et al. 2003).

The MTBD is a large randomized controlled trial (Frank et al. 2005) in which 175 bipolar I patients were randomly assigned to one of four psychosocial treatment strategies combined with a manual-driven pharmacotherapy protocol: 1) acute and maintenance IPSRT (IPSRT/IPSRT), 2) acute and maintenance Intensive Clinical Management (ICM) (ICM/ICM), 3) acute IPSRT followed by maintenance ICM (IPSRT/ICM), 4) acute ICM followed by maintenance IPSRT (ICM/IPSRT). ICM represents the 'control' intervention and was designed as a nonspecific but active psychosocial treatment based on 10 elements: education about BD, education about pharmacotherapy of BD, detailed description of symptoms, exhaustive inquiry about somatic symptoms and/or medication side effects, medical and behavioral management of side effects/somatic symptoms, education about sleep hygiene, discussion of strategies to manage early warning signs of recurrent episodes, use of rescue medication when indicated, empathic listening and nonspecific support, and availability of a 24-hr on-call service.

Patients entered in the study during the acute illness phase. In case of a new affective episode during the preventative maintenance phase, patients remained in their randomly assigned psychosocial treatment and were treated pharmacologically according to the polarity of the new episode. Frequency of visits was weekly in the preliminary phase. In the preventative phase, patients who remained clinically remitted were seen biweekly for the first 3 months and then monthly for an additional 21 months. Patients who received IPSRT showed significantly higher stability of daily social routines and sleep/wake cycles during acute treatment than patients treated with ICM, suggesting that IPSRT could be efficacious in regularizing the daily life styles of patients with BD who are recovering from a major episode. The acute phase of IPSRT was associated with an increase in SRM scores. During the maintenance phase, higher SRM scores were significantly associated with a longer survival time, suggesting that increased regularity of daily routines is a mediator of the effects of acute phase IPSRT on likelihood of recurrence. However, no significant differences between acute IPSRT and ICM were found on time to remission. After controlling for covariates that were significantly associated with survival time without a new episode but were not well distributed between the two conditions (marital status, index episode polarity, anxiety disorder and medical burden), the study indicated that patients who were assigned to IPSRT during the acute treatment phase survived significantly longer without a new affective episode during the 2-year maintenance phase of the study ($z = -2.58$, $p = 0.01$). In a recently published paper based on the same trial, Frank and colleagues (Frank et al. 2008) demonstrated that IPSRT was associated with significantly more rapid improvement in occupational functioning over the course of the approximately 2.5

year study ($F=4.08$, $df=1.111$, $p=0.046$).

More recently, a large multicenter study on the effectiveness of 4 different psychosocial interventions in conjunction with pharmacotherapy was conducted in fifteen clinics affiliated with the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) (Miklowitz et al. 2007a). Participants were 293 patients with bipolar I or II depression who already entered a 26-week double-blind placebo-controlled study in which remission rates with a mood stabilizer plus placebo vs a mood stabilizer plus a standard antidepressant (paroxetine or bupropion) were compared. The psychopharmacological treatment was combined with 3 different psychosocial treatments: IPSRT, FFT, and CBT, for a 9 month period (up to 30 sessions). Psychosocial treatments were compared to the Collaborative Care (CC) (three sessions of psycho-educational intervention conducted over 6 weeks). The hypotheses were that compared with CC, adjunctive intensive psychosocial intervention would hasten time to recovery from bipolar depression and increase the likelihood of remaining well for 12 months and that the 3 intensive interventions (FFT, IPSRT, and CBT) differed in their impact on depressive symptoms.

The rate of recovery from depression at the end of the study was 58.7% and the median \pm SD time to recovery was 122 ± 79 days. As hypothesized, cumulative 1-year recovery rate was in favor of psychosocial treatments: 105/163 (64.4%) versus 67/130 (51.5%) of CC group ($P=.01$), with a shorter median time to recovery (113 ± 78.2 days in the intensive psychotherapy group vs 146 ± 80.0 days in the CC group).

Furthermore, patients in the intensive treatment were 1.58 times more likely to be well in any given study month than patients in the CC group ($P=.003$). Nonetheless, no differences were found in the efficacy of promoting and maintaining recovery among the three intensive psychosocial treatments. This result was probably due to the relatively small sample size for each psychotherapy.

In another analysis based on this data-set, (Miklowitz et al. 2007b) patients in intensive treatments had a better functional outcome regarding quality in relationships and life satisfaction levels. Patients following intensive psychotherapies attended less than half (mean 14.3) of the 30 scheduled sessions. Psychotherapies affected relationship functioning but not vocational functioning, and only 54% had family members available to be involved in FFT (Miklowitz 2008).

These results support the rationale of combining psychosocial intervention and pharmacotherapy for patients with BD.

Adapting IPSRT to the Treatment of Adolescents with BD

Adolescence is traditionally considered a critical period of development from puberty onwards. The influence of socio-cultural factors such as further education have drawn out this normative and biological transition phase in which psychological, social and biological role changes occur more frequently than in

other stages of life with the exception of infancy (Holmbeck et al. 2000). For these reasons adolescence represents a high-risk period for onset of mood disorders. Sexual maturity together with rapid somatic changes give rise to a profound modification of the self-representation and determine changes in the structure of relationships with parents and peers and romantic partners. The contrast between needs of individuation/differentiation from the familial environment and affiliation/sharing experiences with peers may lead to significant disputes with parents and to ambivalent feelings and behaviors. Adolescents usually present a more severe and recurrent form of BD, high risk of suicide and greater functional impairment (Lewinsohn et al. 1995, Birmaher et al. 2006).

To date, there are few preliminary findings suggesting the utility of psychosocial interventions for adolescents with BD (Fristad et al. 2003, Miklowitz et al. 2004, Miklowitz et al. 2008).

An adapted form of IPSRT was recently developed for adolescents with BD (IPSRT A), starting from the adapted form of IPT for depressed adolescents (IPT-A; Mufson et al. 2004).

It is widely accepted that one of the most fundamental domains in adolescence specifically regards changes in expectations and social roles (Steinberg and Morris 2001, Weisz and Hawley 2002, Dahl 2004). IPT A focuses on specific problematic interpersonal areas that can influence mood in adolescents: interpersonal events, interpersonal skills (Marx and Schulze 1991, Stader and Hokason 1998, Hammen 1999) and current interpersonal issues such as the drive for independence from parents, development of romantic relationships and management of peer pressure. Adolescents with BD exhibit significantly more interpersonal problems compared to depressed adolescents (Lewinsohn et al. 1995). For this reason, "*the interpersonal interventions of IPSRT-A are not only developmentally relevant but disorder relevant*" (Hlastala and Frank 2006).

The adaptation of each interpersonal area in IPSRT A is briefly discussed below.

Grief in adolescents. Several differences can be observed between adult and adolescent grieving: feelings are similar but briefer and tend to recur throughout adolescence (Christ 2000, Christ et al. 2002). Reaction to bereavement may change depending on age: for example, complicated grief in early adolescents (12-14 years) is characterized by anhedonia, school refusal, substance abuse, precocious sexual behaviors, shifting to a more delinquent group of friends or persistent physical symptoms without an underlying cause (Christ et al. 2002).

Among adolescent patients with BD, grief is considered the primary interpersonal problem area in two cases: in the presence of an abnormal grief reaction or during a normal bereavement period to promote a successful grieving process. The therapist helps the patient to cope with the real loss, reviewing positive and negative aspects in the relationship with the deceased and to consider other relationships that can provide support, companionship, or guidance (Mufson et al. 2004). As with adults, another important issue is to help the adolescent keep his or her social rhythms stable, particularly regarding family routines after the

death of a parent or sibling who lived at home (Hlastala and Frank 2006).

Interpersonal disputes in adolescents. A normal adolescence is characterized by a wide range of interpersonal relationships, at different levels of intimacy, that play an important role in the development of social competency, motor performance and cognitive abilities (Hartup 1996). This notwithstanding, disputes with parents or friends can contribute to the pathogenesis of depressive episodes (Vernberg 1990, Lewinsohn et al. 1994, Aseltine et al. 1994). In addition, Geller and colleagues (2000) found that patients with prepubertal onset BD had significantly greater impairment than youth ADHD in child-parent and child-peer interactions. These disputes are associated with non compliance and increased distress among family members .

Typically, in the presence of nonreciprocal expectations with parents the therapist chooses the area of interpersonal disputes. In these cases, parents are involved in the therapy for a psychoeducational intervention and for the development of a management plan.

Role transitions in adolescents. Adolescence is a prototypical example of a series of normative role transitions spanning from puberty to the assumption of adult role. These role transitions coincide with the multiple biological changes of puberty and often cause a complicated and at times extremely stressful period (Hlastala and Frank 2006). While the majority of adolescents go through this period without any significant problems (Arnett 1999), this is not the case for adolescents with BD. In fact, unexpected negative events (e.g.: illness, changes in social status or family structure) or even expected positive life changes (e.g.: starting college, graduation, onset of a desired romantic relationship) can increase the risk of onset and/or exacerbations of affective symptomatology. Apparently positive life events, implying a loss of familiarity with current life stage, can constitute a psychological stress and trigger episodes of mania or depression (Mufson et al. 2004). Affective symptoms, vice versa, can interfere with coping abilities. Role transition is considered as the primary problem area if there is evidence that onset/exacerbation of depression or mania is concomitant with a social role changing event. Strategies and aims are the same as with adults with the exception of the involvement of parents. Mufson and colleagues (2004) underline the need to help parents to understand their child's role transition, as well as to cope with feelings elicited by the transition. In addition, since events like parental divorce and issues relating to single parenting are highly prevalent in adolescents with mood disorders, the authors introduced in IPT-A a specific focus tailored to changes within the family structure.

Interpersonal deficits in adolescents. Adolescence is characterized by developmental change within the social domain (Weisz and Hawley 2002). Adolescents have to learn strategies to steer a course through an often turbulent social world. The onset of a severe mental illness before or during adolescence obviously interferes with a regular acquisition of interpersonal skills. Geller et al. (2000), found that prepubertal children with bipolar disorder were

significantly impaired in parental/peer social interaction and social skills when compared with patients with ADHD and youth controls.

Even if 'interpersonal deficits' has been chosen as the problem area of the patient, the therapist usually begins by focusing on current interpersonal disputes and problems (often with parents). Following improvement in this area, the focus then shifts in an attempt to transfer or generalize the interpersonal skills acquired to other significant relationships. This process is achieved through reviewing past and current relationships, including the relationship with the therapist. In the mean time the therapist tries to point out strengths and skills obtained to encourage the patient (Mufson et al. 2004).

Sleep and the modified version of SRM-II-5 (SRM-A). Sleep deprivation among today's adolescents is widely acknowledged in the literature. Carskadon (2002) observed that changes in circadian rhythms tending towards a more 'nocturnal' behavior are frequent in adolescents. The urge for independence may stimulate adolescents to stay up after the rest of the family has gone to bed. Advances in technology, that permit 24-hour communication via internet or phone, act as an additional stimulus, delaying bedtimes still further, and consequently contributing increasingly to a build-up of lack of sleep as the week goes on. Carskadon and Mancuso (1988) noted how circadian irregularity may be affected by swift changes from the sleep/wake schedules of school nights to those of weekends or holidays. Emotional, behavioral and cognitive functioning in healthy adolescents are negatively influenced by this upheaval in sleep/wake patterns (Wolfson and Carskadon 1998) and there is evidence suggesting that subsequent build-up of sleep debt and disruption of social routine have potentially devastating effects on bipolar adolescents.

The SRM-A is an 8 item adapted version of the SRM-II-5 (Monk et al. 2002) (Figure 3) aimed to assess social rhythms in adolescents. With respect to the adult version, the SRM-A included three adjunctive items: healthy adolescent behaviors like exercise, homework and extracurricular activity (SRM-A). Starting from the analysis of the SRM-A, the therapist and the patient establish an ideal amount of time to spend on different activities. Of crucial importance is to help the patient to understand the usefulness of reducing changes in weekend sleep patterns. An acceptable proposal is one night of 1 or 2 hours later bedtime to be compensated for with no more than 2 hours later wake time. Dahl et al. (2004) reported that an earlier return to weekend normal sleep patterns may lead to less disruption of circadian rhythms and fewer problems going back to the weekly school routine. The same principle applies to shifts in rhythms at the beginning and end of the school year. Starting the therapy well before school ends could help to structure the adolescent's schedules during the holiday break.

While most teenagers accept that disruption of sleep affects mood, comprehending the rationale behind stabilizing sleep rhythms, others are unwilling or forget to complete the SRM-A. In these cases it is advisable to concentrate more on the interpersonal interventions and go back to the SRM-A when the adolescent is more

Figure 3. *Social Rhythm Metric Adolescent Version (SRM-A)*

Date (week of): _____

Actual Time

Activity	Target Time	Mon	Tues	Wed	Thurs	Fri	Sat	Sun
1. Out of bed								
2. First contact (in person or by phone) with another person								
3. Start school or main activity of the day								
4. Physical exercise								
5. Have dinner								
6. Homework								
7. Other activity: _____ _____								
8. Go to bed								
Rate your mood (-5 to +5)								

motivated. It may be useful to provide counsel on when/where to complete the questionnaires and even include parental involvement.

Family involvement. Engaging parents' support can significantly influence the treatment of adolescents although the degree of their involvement is strictly related to factors such as the cognitive and social development of the adolescent and the chosen interpersonal focus. Providing information about BD to parents could encourage collective collaboration. Moreover, disputes pertaining specifically to the family have a greater chance of being resolved if parents are involved. Furthermore, since young people may not easily recall details of onset/offset of mood episodes, any precipitating life events, precedent interpersonal functioning and medication taken, it may be very useful to enlist parents' help in taking the history.

Concluding Remarks

Interpersonal and social rhythm therapy appears to be a promising intervention for individuals with bipolar disorder. The initial trials suggested that the ideal time for intervention with this form of treatment is while the patient is acutely ill. Even if this intervention was not associated with more rapid remission than an intensive clinical management approach, it did lead to better long-term outcome. In contrast, the STEP-BD study of bipolar depression, using a much less intensive control condition, did suggest a value to the acute intervention in terms of both the proportion remitting and time to remission. New studies of IPSRT are being directed at establishing its efficacy in adolescents and in trying to determine whether there is a subpopulation of individuals with bipolar II disorder who can be effectively treated with IPSRT monotherapy. A small pilot study is also testing the feasibility of IPSRT as a preventative treatment for adolescents who are not yet ill, but are at high risk for the development of bipolar disorder by virtue of having a first degree relative with the illness. Equally important will be efforts to extend this treatment to the elderly and efforts to connect efficacy in all age groups to specific biomarkers.

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