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Social and Familial Factors in the Course of Bipolar Disorder: Basic Processes and Relevant Interventions

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Abstract

This article reviews the role of social factors, notably life events and family relationships, in the course of bipolar illness in adults and youth. We also discuss psychological variables that help explain the vulnerability of bipolar patients to social environments, including personality factors (e.g., neuroticism), reward sensitivity, and difficulty with the accurate perception of facial emotions. Bipolar patients are highly sensitive to reward, and excessive goal pursuit after goal-attainment events may be one pathway to mania. Negative life events predict depressive symptoms, as do levels of familial expressed emotion. Psychosocial interventions can speed recoveries from episodes and delay recurrences over 1–2 year intervals. Future research should examine the nature of vulnerability/stress interactions at different phases of development, and the role of psychosocial interventions in altering these processes.

Keywords

risk factors; personality; expressed emotion; life events; reward sensitivity; psychosocial treatment

Bipolar disorder (BD) affects about 2%–4% of the US population in its various syndromal and subsyndromal forms (Merikangas et al., 2007). It is a highly recurrent, costly, and impairing illness leading to high rates of disability, comorbidity, medical problems, and suicide attempts or completions. The illness has broad-ranging effects on functioning during and between episodes, including impaired work performance, family distress, relationship dysfunction, and low life satisfaction (Goldberg, Harrow, & Grossman, 1995). Social impairments characterize bipolar youth as well, even during the remitted phases (Goldstein, Miklowitz, & Mullen, 2006). Functional impairment can be the direct result of symptoms, but impairment also increases the speed of recurrence (Gitlin, Swendsen, Heller, & Hammen, 1995; Weinstock & Miller, 2008).

The course of BD can be understood from a lifespan/developmental psychopathology perspective. Episodes of the illness result from a complex interplay between genes, neurobiology, stress, and psychological vulnerabilities at various points in development (Miklowitz & Cicchetti, 2006). Findings from twin, family, and adoption studies make a compelling case for genetic transmission in the onset of the disorder (Smoller & Finn, 2003). Functional and structural changes in the brain – notably cortico-limbic circuitry - distinguish BD from other disorders (Mayberg, Keightley, Mahurin, & Brannan, 2004). However,

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interpersonal variables play risk or protective roles in the onset and course of the disorder. Childhood adversity (i.e., sexual or physical abuse, neglect), life events, and high familial expressed emotion and discord appear to evoke or at least exacerbate certain preexisting vulnerabilities, resulting in more debilitating courses of illness for some patients (Leverich et al., 2002; Miklowitz & Johnson, 2006).

Although pharmacotherapy is the first-line treatment for stabilizing episodes of bipolar disorder, psychosocial treatments that accompany pharmacotherapy and address stress variables, cognitive, interpersonal, or emotional vulnerabilities, and their interactions will be more effective in preventing recurrences and enhancing functioning than pharmacotherapy alone. There is now considerable evidence that psychosocial interventions are effective adjuncts to pharmacotherapy in illness stabilization and maintenance (Miklowitz, in press).

In this article, we review evidence for the role of social variables - notably life events and family discord – in the longitudinal course of BD. We also examine several key personality or psychological variables (neuroticism, positive affectivity, reward sensitivity, and deficits in sensitivity to facial displays of emotions) that may influence the vulnerability of patients to social and family problems, or help explain their associations with illness outcomes. Then, we briefly review randomized controlled trials indicating that psychosocial interventions are effective adjuncts to pharmacotherapy in improving symptomatic and interpersonal functioning in BD. A final section offers recommendations for future research and clinical practice.

In describing this literature, we consider an important methodological and conceptual issue. Current symptoms exacerbate social and psychological impairments. Depressive symptoms may increase the reactivity of patients to social concerns, and subjective reports of the social environment may become more negative. Likewise, manic symptoms can positively distort patients' perceptions of the quality of their family or social supports. The best longitudinal studies, then, examine whether a given psychological variable predicts increases in symptoms over time after controlling for baseline symptoms. Hence, we focus our review on prospective research, and make clear when current symptoms have been statistically controlled in examining predictor/outcome relationships. Where such evidence is not available, we describe cross-sectional research on social variables during periods of illness remission, to clarify directions for future prospective research.

PERSONALITY AND TEMPERAMENT

Researchers have focused on both personality (trait-like individual differences) and temperament (putatively genetic components of personality traits) in the study of BD. Much of the research has focused on neuroticism, defined as excessive frequency and intensity of negative mood states. Other research has focused on tendencies towards positive mood states, including pride, joy, and subsyndromal states of elevation.

Cross-Sectional Studies

BD patients are often co-diagnosed with personality disorders, although the prevalence rates dissipate markedly as symptoms remit. When patients are systematically evaluated in remission, overall rates of axis II comorbidity are approximately 30% (George, Miklowitz, Richards, Simoneau, & Taylor, 2003; Colom et al., 2000). Cluster B personality disorders are particularly common among persons with BD, and are associated with histories of emotional and physical abuse or neglect (Garno, Goldberg, Ramirez, & Ritzler, 2005; Mantere et al., 2006).

Beyond the studies of personality disorders, people with bipolar disorder report higher global positive affect in their everyday lives than do those without the disorder, whether measured using the NEO Personality Inventory (Bagby et al., 1996), the Temperament Evaluation of Memphis, Pisa, Paris and San Diego-autoquestionnaire version (TEMPS-A) cyclothymia scale (Akiskal et al., 2005, 2006), or repeated daily ratings on scales such as the Positive Affect and Negative Affect Scales (Hofmann & Meyer, 2006; Lovejoy & Steuerwald, 1995). Undergraduates at risk for hypomania (as measured with the Hypomanic Personality Scale; Eckblad & Chapman, 1986) endorse particularly high levels of dispositional pride and joy, but do not tend to show elevations of more prosocial positive emotions, such as love and compassion (Gruber & Johnson, in press).

In contrast, cross-sectional findings have been inconsistent about whether people with remitted bipolar disorder demonstrate elevations in neuroticism compared to the general population (Klein, Durbin, & Shankman, in press). In major depressive disorder (MDD), neuroticism is particularly related to the severity of depressive symptoms, and appears to have genetic overlap with depression (Kendler, Gatz, Gardner, & Pederson, 2006). Two studies found that Neuroticism is related to the severity of depressive symptoms among persons with BD (Hecht, van Calker, Berger, & von Zerssen, 1998) or persons with undiagnosed bipolar symptoms (Murray, Goldstone, & Cunningham, 2007).

Given that a diagnosis of bipolar II disorder requires recurrent depressive episodes (and bipolar I disorder does not), and the relatively higher rates of depressive symptoms in bipolar II than bipolar I disorder (Judd et al., 2003), one might expect elevated neuroticism and other traits related to negative affectivity in bipolar II disorder. Using the TEMPS-A, Akiskal et al., 2006 assessed 413 persons with bipolar I, bipolar II, and major depressive disorder (MDD) who were recovered from affective episodes. Compared to persons diagnosed with bipolar I disorder, persons diagnosed with bipolar II disorder described themselves as more labile in mood, sensitive and brooding than did those with bipolar I disorder. People with bipolar II disorder also endorsed some traits that were separable from negative affectivity, such as being highly energetic and assertive, at levels that were higher than those with MDD or bipolar I disorder. This research provides cross-sectional evidence that interepisode temperamental variables can be informative during periods of recovery in distinguishing between different forms of mood disorders.

Despite the potential pragmatic value of such findings, cross-sectional research on personality and mood disorders has been heavily criticized. As noted by Klein et al. (in press), personality and mood disorder can be linked through several different mechanisms: “(1) personality and mood disorders have common causes; (2) personality is a precursor of mood disorders; (3) personality predisposes to developing mood disorders; (4) personality has pathoplastic effects on mood disorders; (5) personality features are state-dependent concomitants of mood disorder episodes; and (6) personality features are complications (or scars) of mood disorders.” Even subsyndromal symptoms, which are quite common in bipolar disorder, may complicate interpretation of personality scores. For example, current symptoms of depression artificially elevate neuroticism scores (Klein et al., in press).

Prospective Studies

Personality profiles can help predict the course of symptoms in BD. Among BD persons with a comorbid personality disorder, the course of the mood disorder is worse (Colom et al., 2000; Barbato & Hafner, 1998; Dunayevich et al., 2000; Garno et al., 2005).

Research has focused on predicting future manic versus depressive symptoms from personality profiles. Two small studies of bipolar I participants suggest that neuroticism predicts increases in bipolar depression after controlling for baseline depression levels (Heerlein, Richter,

Gonzalez, & Santander, 1998; Lozano & Johnson, 2001). These findings are comparable to findings in the unipolar literature (Gunderson, Triebwasser, Phillips, & Sullivan, 1999).

Regarding prediction of mania, scales such as the Hypomanic Personality Scale, the TEMPS-A, or the General Behavior Inventory (Depue, Kleinman, Davis, Hutchinson, & Krauss, 1985), each of which cover subsyndromal fluctuations in positive mood symptoms, are associated with the onset of bipolar spectrum disorders among previously undiagnosed persons (Klein, Dickstein, Taylor, & Harding, 1989; Kochman et al., 2005; Kwapil et al., 2000; but see also the non-replication by Reichart et al., 2005). Trait positive affectivity, as measured using the Tridimensional Personality Questionnaire, has been found to predict a more severe course of mania over a 6-month period among people already hospitalized for BD (Strakowski, Stoll, Tohen, Faedda, & Goodwin, 1993). Hence, baseline levels of positive affectivity may be important to consider as predictors of the course of manic symptoms.

In sum, assessing temperamental and personality variables may help clinicians to distinguish between bipolar I, II, and MDD among patients in remission; to identify patients at highest risk for depression; and to identify which patients (notably, those with high positive affectivity or comorbid personality disorders) are at greater risk for more severe manic symptoms over time. Individual differences in temperament or affectivity may also shape the types of life events and interpersonal relationships experienced by persons with BD. For example, patients with premorbid cyclothymic temperaments (Akiskal et al., 2000) may be more prone to relationship failures or work impairment after the onset of the disorder than those without these temperaments. Thus, personality variables may inform us as to which patients with bipolar disorder are at highest risk for developing manic or depressive symptoms in different interpersonal contexts.

LIFE EVENTS

Three types of life events have been studied in relation to bipolar disorder: *negative*, *social-rhythm disrupting*, and *goal-attainment*. Here, we focus on those studies that used life event interviews and rating systems to measure independent life events (events not caused by the person's behavior). In considering life event findings, we note emergent literatures on variables that might increase vulnerability to these specific forms of stressors.

Negative Life Events

Given the above-cited evidence concerning neuroticism and the course of bipolar depression, it would make sense that negative life events would be related to the course of depressive (versus manic) symptoms. Here, we limit our discussion to those studies that have used interview-based measures of severe and negative independent events (e.g., a life-threatening illness in a family member), such as the Life Events and Difficulties Scale (LEDS; Brown & Harris, 1978). Two out of three cross-sectional studies found that negative life events were more common in the months before a bipolar depressive episode than during control intervals (Malkoff-Schwartz et al., 1998; Hunt, Bruce-Jones, & Silverstone, 1992). One cross-sectional study failed to find an increase in negative life events in the three months before a depressive episode (McPherson, Herbison, & Romans, 1993).

Several longitudinal studies have shown robust predictive power for life events. Severe independent negative events were associated with a four-fold increase in the risk of relapse in one study of 61 persons with bipolar I disorder (Ellicott, Hammen, Gitlin, Brown, & Jamison, 1990), and a three-fold increase in the time until recovery in another study of 67 persons with bipolar I disorder (Johnson & Miller, 1997). Negative life events were particularly associated with the recurrence of depressive symptoms among college students at risk for BD who had negative cognitive styles (Alloy, Reilly-Harrington, Fresco, Whitehouse, & Zechmeister,

1999; Reilly-Harrington, Alloy, Fresco, & Whitehouse, 1999). Finally, negative life events were associated with the onset of depressive disorders among 140 offspring of parents with BD followed over 5 years (Hillegers et al., 2004).

Chronic interpersonal stress, as opposed to discrete life events, may also be important in the course of bipolar depression among younger age groups. Among adolescents with bipolar I and II disorder, those with more chronic, ongoing stress in family and romantic relationships experienced more sustained depressive symptoms over time (Kim, Miklowitz, Biuckians, & Mullen, 2007). Other forms of stress did not appear tied to depressive symptoms in this study.

In contrast to the robust findings for depression, six studies indicate that severe independent negative events are equally common before and after manic episodes among bipolar I patients (for review, see Johnson, 2005a). Similarly, five longitudinal studies have indicated that negative life events do not directly predict increases in manic symptoms (Johnson, 2005a). Summing across longitudinal studies, then, negative life events have effects on the course of bipolar depression, but have little direct effect on mania. Most of the studies did not separately examine bipolar II patients. It is possible that bipolar II patients are more likely to experience depression following a negative life event than bipolar I patients, especially if they are also high in neuroticism (Akiskal et al., 2006).

The nature and strength of vulnerability/stress interactions may change at different phases of the development and progression of the illness. The stress sensitization model suggests that, as the illness becomes more and more recurrent, less stress is needed to provoke episodes (Hammen & Gitlin, 1997; Post & Leverich, 2006). In contrast, one study concluded that life events become *less* powerful in precipitating mood episodes over time among children at risk for BD (Hillegers et al., 2004). Longitudinal studies on whether and how stress reactivity changes over time in BD would help to resolve current ambiguities regarding the predictions of “kindling” models (Post & Leverich, 2006).

Life Events that Disrupt Social Rhythms

Harvey (this issue) has reviewed the growing evidence that bipolar disorder is related to poor regulation of sleep and circadian rhythms. This dysregulation might be one mechanism through which life events influence symptoms. More specifically, Wehr, Sack, & Rosenthal (1987) hypothesized that sleep disruption might trigger manic symptoms. Naturalistic studies find that manic symptoms follow sleep loss (Leibenluft, Albert, Rosenthal, & Wehr, 1996). Congruently, carefully controlled experimental studies indicate that more than 10% of patients with bipolar depression develop hypomanic or manic symptoms after sleep deprivation is induced (Colombo, Benedetti, Barbini, Campori, & Smeraldi, 1999). Effects of sleep deprivation appear similar in bipolar I and bipolar II disorder. Case studies suggest that increasing sleep duration may help prevent symptoms of bipolar disorder (Wehr et al., 1998).

Ehlers, Frank, & Kupfer (1988) extended findings on sleep disruption to consider the role of a broader range of schedule disruptions and their effects on symptoms. They argue that social events and routines influence daily schedules and their regularity, and therefore influence underlying biological circadian rhythms. In two retrospective studies, people with bipolar I disorder reported more schedule-disrupting life events (i.e., events that disrupt meals, daily routines, and sleep) before manic than depressive onsets (Malkoff-Schwartz et al., 1998, 2000). Because depressive episodes lasted much longer than manic episodes, patients were asked to recall events from much further back in regard to depression as compared to mania. Hence, there is a need for prospective research to confirm this pattern of findings.

Goal-Attainment Life Events

A growing body of research has focused on sensitivity to cues of reward (Johnson, 2005b). Much of this work stems from observations that mania may be tied to brain regions involved in regulating responses to reward cues. BD appears to be associated with elevated activity of the basal ganglia and ventral tegmental area, regions that are intricately involved in reward sensitivity (Depue et al., 1985). Basal ganglia activity appears particularly elevated during periods of mania (Blumberg et al., 2000). Consistent with the hypersensitivity of these dopaminergic pathways, people with remitted BD show atypically large behavioral responses to amphetamine, which increases levels of dopamine (Anand et al., 2000). Hence, reward pathways may be overly sensitive in BD.

When confronted with an incentive stimulus, dopaminergic pathways are thought to trigger positive affect, approach motivation (e.g., a feeling of desire), and approach behavior. As this system is activated, "system outputs" serve to increase the probability of incentive acquisition. The outputs of this system, including increased effort, energy, and focus on goal pursuit closely mirror the symptoms of mania (Depue et al., 1985).

People with remitted BD and those vulnerable to BD report that they experience more excitement and enthusiasm in the context of opportunities to earn rewards and pursue goals than do people without BD (Meyer, Johnson, & Winters, 2001; Salavert et al., 2007; Alloy et al., 2006; Gruber & Johnson, in press; Meyer, Johnson, & Carver, 1999). In laboratory-based behavioral tasks, persons at risk for bipolar disorder and euthymic persons with BD are more sensitive to positive stimuli (Hayden et al., 2008; Sutton & Johnson, 2002). Reward sensitivity also predicted increases in manic symptoms over a one-year follow-up among 59 participants with bipolar I disorder (Meyer et al., 2001) as well as among at–risk college students (Alloy et al., 2008; Meyer & Hofmann, 2005).

At first glance, this increased reward sensitivity might only seem to predict euphoria and elation symptoms, rather than the irritability characteristic of many manic episodes and most mixed and rapid cycling states. However, rage and irritability are often the natural outcomes of valuing a goal and having it thwarted. Indeed, recent research suggests that people with bipolar disorder and those at risk for bipolar disorder demonstrate greater psychophysiological reactivity to goal-thwarting (Harmon-Jones et al., 2002; Harmon-Jones et al., 2008).

Reward Sensitivity and Reactivity to Life Events

Using the LEDS, Johnson and colleagues (2000) found that life events involving goal attainment predicted increased manic symptoms over a two-month follow-up among 43 persons diagnosed with bipolar I disorder, even after controlling for baseline symptoms. A more recent study of 125 persons with bipolar I disorder who completed an average of 27 months of follow-up replicated this result (Johnson et al., 2008), as did a study of college students with bipolar II and cyclothymic conditions (Nusslock, Abramson, Harmon-Jones, Alloy, & Hogan, 2007).

Research on cognitive processes helps explain why manic symptoms emerge after goal attainment (Johnson, 2005b). Notably, persons with BD demonstrate greater increases in confidence after small success experiences, even after controlling for current symptoms (Eisner, Johnson, & Carver, 2008). Greater confidence appears to lead to more intense pursuit of goals, which then predict increases in manic symptoms (Johnson, Ruggero, & Carver, 2005; Lozano & Johnson, 2001). Thus, the reward sensitivity of persons with bipolar disorder results in more sensitivity to life events that involve success, as manifested in unusual elevations in confidence and goal engagement. These processes might form one pathway into mania.

IMPAIRMENT IN FAMILY RELATIONSHIPS

Low social support predicts higher levels of depression over time among persons with BD (Johnson, Lundstrom, Aberg-Wistedt, & Mathe, 2003; Johnson, Winett, Meyer, Greenhouse, & Miller, 1999). Given the centrality of marital and family functioning to social support, we focus on those core relationships here, with an emphasis on how BD influences these relationships, and in turn how these relationships influence the depressive course of the disorder. As was the case for personality attributes, concurrent symptoms explain some of variance in family functioning within BD, suggesting the importance of studying family processes during periods of remission.

Expressed Emotion (EE)

EE is an index of the degree to which caregiving relatives (parents or spouses) express critical, hostile, or emotionally overinvolved or overprotective attitudes toward the patient when interviewed during or shortly after an acute episode. Typically, EE is assessed from the 1 to 1 and ½ hr Camberwell Family Interview, which has the best reliability and validity among EE measures (Hooley & Parker, 2006). Several longitudinal studies have found that bipolar I patients who are associated with high-EE spouses or parents have higher rates of relapse over 9-month periods than patients associated with low-EE, less critical or normally involved relatives, even after baseline symptoms have been covaried (Miklowitz, Goldstein, Nuechterlein, Snyder, & Mintz, 1988; Miklowitz et al., 2000; O'Connell, Mayo, Flatow, Cuthbertson, & O'Brien, 1991; Priebe, Wildgrube, & Muller-Oerlinghausen, 1989; Yan, Hammen, Cohen, Daley, & Henry, 2004).

Two studies have found that the EE/outcome relationship is stronger for depressive than manic relapses or symptom states among bipolar I patients (Kim & Miklowitz, 2004; Yan et al., 2004). Although it did not measure EE, one 5-year study found that self-reported family impairment was more closely associated with depressive relapse than manic relapse (Gitlin et al., 1995). Likewise, Townsend, Demeter, Youngstrom, Drotar, & Findling (2007) found that poor family problem-solving (as revealed by a questionnaire measure) predicted depressive but not manic symptoms over 8 weeks among youth with bipolar I or II disorder. Possibly, depression in bipolar disorder is exacerbated by familial criticism or other dimensions of family impairment; family support (i.e., effective communication and problem-solving) may in turn offer protection against depressive symptoms or relapses (Simoneau, Miklowitz, Richards, Saleem, & George, 1999).

Several studies have examined the correlates of EE within families of BD patients. During a post-episode period of stabilization, high-EE parents and spouses of bipolar I patients are more likely to attribute negative events involving the patient to personal and controllable factors than low-EE parents and spouses (Wendel, Miklowitz, Richards, & George, 2000), an association also found among families of patients with MDD and schizophrenia (Hooley & Gotlib, 2000). Second, high-EE couples and families are characterized by highly conflictual, bidirectional patterns of negative interaction which escalate and become more personal as they progress. Low-EE families, in contrast, are able to interrupt these escalations after a short number of exchanges (Simoneau, Miklowitz, & Saleem, 1998).

One longitudinal study found that negativity within family interactions is correlated with relapses of the disorder and ongoing social impairments (Miklowitz et al., 1988). Rosenfarb et al. (2001) found that, among bipolar I adults who relapsed during a 9-month prospective period, there was a strong correlation between unusual thought content in patients and harsh criticisms from parents during a family interaction task conducted at the beginning of the period. The association was nonsignificant among patients who did not relapse during the prospective interval.

Finally, a cross-sectional examination of 44 adolescents offered clues as to how EE attitudes might emerge in the parents of BD I or II offspring (Coville, Miklowitz, Taylor, & Low, 2008). Parents of girls were more likely to be high in EE-criticism than parents of boys, but only when the child had an adolescent onset of mood disorder. Girls were more likely to have depression at the time of the EE assessment than boys. Parents of boys were more critical when the child had a preadolescent onset (often first diagnosed as ADHD). Thus, parents may become critical of younger boys whose first symptoms consist of externalizing or aggressive behavior. In contrast, parents may react negatively to the irritability, withdrawal, or anergia of depressed girls once they enter adolescence and press for more autonomy.

Although social and familial relationships tend to improve as patients improve, impaired family interactional processes associated with high-EE attitudes (for example, negatively escalating patterns of conflict or criticism) are still observed when the patient is fully or partially remitted (Miklowitz et al., 1988; Simoneau et al., 1998). Thus, family discord during a post-episode stabilization period may be one of many factors – in conjunction with genetic, biological, and cognitive vulnerabilities - that contributes to earlier depressive recurrences of BD. Future studies should examine the personality or temperamental attributes of bipolar patients that contribute to high-EE attitudes or negative patterns of family interaction.

Family Factors in Childhood-Onset Bipolar Disorder

The family has a risk or protective role early in the course of the disorder, depending on when BD is diagnosed, whether the parents themselves have mood disorders, how conflicts are resolved, and whether the family is intact. One study found that adolescent BD patients who were undergoing family treatment and medication had more persistent mood symptoms over 2 years up if their parents were high-EE than low-EE (Miklowitz, Biuckians, & Richards, 2006). Low maternal warmth – based on the self-reports of children and their mothers - was associated with a shorter time to recurrence in a 4-year follow-up of pediatric and early adolescent BD patients (Geller, Tillman, Craney, & Bolhofner, 2004).

Mother/child relationships in childhood-onset bipolar disorder are characterized by less warmth, greater tension, greater conflict, and more hostility than mother/child relationships in healthy control or ADHD children (Schenkel, West, Harral, Patel, & Pavuluri, 2008; Geller et al., 2000). When pediatric BD is accompanied by ADHD or other externalizing disorders, families have greater conflict, lower cohesion scores, and greater use of “power assertion” in parenting strategies (Schenkel et al., 2008; Esposito-Smythers et al., 2006). Frequent behavioral outbursts in the child in the absence of well-defined episodes increases the chance that parents attribute the child’s problems to personality or willful opposition, which may increase criticism (Schenkel et al., 2008).

The high levels of conflict and low levels of cohesion characteristic of families with a bipolar offspring can sometimes be attributed to BD in the parents. In a sample of 36 families of 56 high-risk children, all of which contained at least one bipolar parent, Chang, Blaser, Ketter, & Steiner (2001) found lower levels of cohesion and organization and higher levels of conflict than population norms. In this study, family impairment appeared to be more a function of the parent’s diagnoses than of the parents’ reactions to their child’s psychopathology. A second study of 24 families with a bipolar parent found lower levels of cohesion and expressiveness relative to 27 families of healthy controls, although family environment scores did not predict whether the offspring had BD or not (Romero, Delbello, Soutullo, Stanford, & Strakowski, 2005).

In a large-scale (N = 272) cross-sectional study of families in which one parent had a mood disorder, Du Rocher Schudlich, Youngstrom, Calabrese, & Findling (2008) found a direct relationship between parental diagnoses and child diagnoses. When the child had BD, the

association between parental and child diagnoses was mediated by whether parents reported high levels of family conflict. Thus, parental diagnoses and family impairment may jointly contribute to child functioning.

It is difficult to assemble a sample of remitted bipolar youth given its characteristic pattern of frequent cycling, lengthy episodes, and severe interepisode symptoms (Birmaher et al., 2006). Thus, most of these studies were not able to disentangle the behavior of parents or other family members from the concurrent symptom states of children. Further, most studies do not make clear distinctions between depression and mania symptoms given their frequent co-occurrence in younger-onset patients. Interestingly, the single randomized trial of an adjunctive psychosocial intervention for bipolar adolescents found that family intervention had greater effects on bipolar depression than mania over 2 years (Miklowitz et al., in press).

FACIAL EMOTION PROCESSING

The high levels of conflict and low levels of cohesion observed within families of bipolar patients raises the question of whether patients have impaired perceptions of the motives, emotional states, or intentions of their family members, and in turn, whether these misperceptions affect their response choices. The accurate perception of facial emotions is believed to be key to social competence and conflict resolution, since one must code subtle changes in another's emotions in order to respond effectively (Rich et al., 2008). A series of studies has suggested that bipolar adults show impairments in the processing of facial emotions, although the nature and specificity of these deficits vary from study to study (Addington & Addington, 1998; Bozikas, Tonia, Fokas, Karavatos, & Kosmidis, 2006; Getz, Shear, & Strakowski, 2003). Few studies have attended to concurrent mood state in measuring facial affect recognition deficits. In one study, deficits in the recognition of negative facial affect were extremely pronounced during manic episodes and dissipated during remission (Lembke & Ketter, 2002).

Bipolar youth make more errors on facial emotion recognition tasks than healthy controls or youth with MDD or ADHD. These errors occur across a variety of facial emotions and types of tasks (Brotman et al., 2008; McClure et al., 2005; Rich et al., 2006; Rich et al., 2008; Guyer et al., 2007). Similar to children who have experienced trauma or abuse (e.g., Pollak & Tolley-Schell, 2003), children with BD are especially likely to misclassify neutral facial expressions as hostile and threatening, even though they do not rate angry faces as more angry than healthy children do (Rich et al., 2006).

Rich et al. (2008) compared "narrow spectrum" (i.e., bipolar I or II with elation or grandiosity) bipolar youth, youth with severe mood dysregulation (chronic irritability and hyperarousal), and healthy control participants on an experimental task involving rating gradations of facial emotions (happiness, surprise, fear, sadness, anger, and disgust). The task required that participants indicate when they were certain of the emotion being expressed as the faces "morphed" from neutral to full expressions of emotion. Regardless of the emotion purveyed on the facial stimuli, BD youth who were in a hypomanic or mixed state required more intense facial expressions before they were able to accurately identify the emotion. The euthymic bipolar youth also required more intense facial stimuli than the healthy controls, but only for faces that expressed disgust or happiness. Interestingly, the youth with severe mood dysregulation also showed emotion recognition deficits. Impaired face emotion labeling predicted the degree to which the bipolar youth showed social reciprocity skill deficits – the capacity to process social information and enact responses that fit the situation.

Progress has been made in clarifying the neural circuitry underlying facial affect labeling. Using functional magnetic resonance imaging, Rich et al. (2006) found that a subcortical limbic circuit was activated among bipolar youth during a face labeling task (judging facial emotions

versus estimating nose width). When rating facial hostility, the BD youth had greater activation in the left amygdala, nucleus accumbens, putamen, and ventral prefrontal cortex; and when rating their fear of the face, greater activation in the left amygdala and bilateral accumbens, than age- and gender-matched controls.

Thus, most studies have found that BD youth misinterpret emotional faces, misidentify threat in neutral faces, and, when they accurately identify an emotion, require more intense displays of the emotion than are typical in real-life social situations. The literature is not consistent, however. One study found that undergraduates at risk for mania were *more* sensitive to positive facial expressions after small successes than controls (Trevisani et al., in press). Furthermore, facial emotion recognition deficits do not appear to be specific to pediatric BD; for example, they appear in children with post-traumatic stress disorder. No study to date has demonstrated that emotion labeling deficits predict the onset of BD among genetically at-risk youth, an important focus of future research.

A key area for future research is the overlap between emotion recognition deficits and family discord or EE. Theoretically, the degree to which bipolar youth have trouble labeling the emotions (or are biased toward the perception of negative emotions) of their parents may correlate with whether parents express highly critical attitudes toward the youth, or whether dyadic conflicts routinely escalate into “point-counterpoint” struggles (Simoneau et al., 1998). When both the parent and child suffer from BD, emotion labeling deficits may become bidirectional. It is not clear whether pediatric BD patients have difficulty reading the emotions of their parents– the emotion labeling tasks typically use standard stimuli rather than faces of adults known to the child, raising questions about the ecological validity of these measures. Videotape feedback studies, in which parents and children are asked to identify each others’ emotions following a direct interaction task could test these hypotheses, and also serve as an intervention strategy for teaching family members to correctly read each others’ more subtle emotional reactions.

Finally, studies of facial emotion processing need to examine more systematically the influence of current symptoms and prior interpersonal history (i.e., the degree to which individual patients have experienced conflict in their family or peer relationships) on facial affect recognition scores. Possibly, emotion recognition deficits may serve as mediators in the complex network of associations between prior relationship functioning, current symptoms, and future relationship functioning in BD.

PSYCHOSOCIAL INTERVENTION AS A MEANS OF ENHANCING INTERPERSONAL FUNCTIONING

Randomized Trials

There is now considerable evidence that the course of bipolar disorder is enhanced by combining pharmacotherapy with structured psychosocial interventions. There are 18 randomized trials which support the effectiveness of family, group, interpersonal, and cognitive-behavioral approaches to relapse prevention and episode stabilization over 1–2 year intervals (for reviews, see Miklowitz & Johnson, 2006; Miklowitz, in press). The common element in these approaches is psychoeducation – a didactic, information-sharing approach to coping with the disorder. Most of the approaches also involve problem-solving, encouraging adherence with medications, and teaching patients to recognize and intervene early with prodromal signs of relapse.

The existing approaches are more varied in the degree to which they address the social, familial, or work impairments characteristic of BD. CBT uses cognitive restructuring to help patients evaluate and restructure their core assumptions about relationships (Lam, Hayward, Watkins,

Wright, & Sham, 2005). Interpersonal and social rhythm therapy (Frank, 2005) uses social problem-solving, clarification, and interpretation to help patients to grasp the ways in which their mood states affect relationships, and how their relationships affect their mood fluctuations. Family-focused therapy (Miklowitz, 2008) uses communication and problem-solving skills training to enhance functioning within the family unit and the broader social milieu. Group psychoeducation focuses on skills for managing the disorder and functioning after an episode (Colom et al., 2003; Bauer et al., 2006).

The comparative effects of different forms of psychotherapy were examined in a large-scale randomized trial conducted across 15 sites, known as the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD; Miklowitz, Otto, Frank, Reilly-Harrington, Wisniewski et al., 2007; Miklowitz, Otto, Frank, Reilly-Harrington, Kogan et al., 2007). STEP-BD examined 293 bipolar I and II patients who began in an episode of bipolar depression. Patients were randomly assigned to up to 30 sessions of CBT, interpersonal and social rhythm therapy, family-focused therapy, or a 3-session psychosocial control called collaborative care. Over 1 year, patients who received one of the three intensive therapies had higher rates of recovery and more rapid recoveries from depression (median 169 days) than patients in CC (median 279 days), and were 1.58 times more likely to be well in any given month of the 1-year study than patients in collaborative care. Moreover, patients in intensive therapy showed better overall functioning, relationship functioning, and life satisfaction scores over 9 months than those in collaborative care, even after concurrent levels of depression were statistically controlled.

In contrast to relationship functioning, vocational functioning in BD patients is more difficult to enhance through psychosocial interventions. A substantial proportion of bipolar patients have impairments in neuropsychological functioning even when clinically stable (Murphy et al., 1999; Schretlen et al., 2007). Possibly, cognitive remediation programs such as those used for the treatment of schizophrenia (McGurk, Twalmey, Sitzer, McHugo, & Mueser, 2007) may be helpful in enhancing vocational functioning for BD patients after a mood episode.

Psychosocial Interventions and Personality Attributes

A few studies have examined whether personality attributes moderate the impact of adjunctive psychotherapy on BD. Lam Wright, & Sham (2005) found that a sense of “hyperpositive self” among BD patients – dynamism, persuasiveness, and productiveness – was associated with a poorer response to CBT. These attributes may map on to high risk behaviors such as medication nonadherence, expansive goal-setting, or impulsive risk taking, but may be especially difficult to change using standard cognitive restructuring techniques.

A small open trial examined the impact of interpersonal and social rhythm therapy on bipolar I patients who had comorbid borderline personality disorder (Swartz, Pilkonis, Frank, Proietti, & Scott, 2005). Only 25% (3/12) of the comorbid BD patients stabilized within a 2-year time frame when treated with IPSRT, whereas 74% (43/58) of the BD patients without borderline personality disorder stabilized. Patients with comorbid presentations also required more adjunctive antipsychotic medications and were more likely to drop out of treatment. One study found that structured group psychoeducation could be administered successfully to bipolar patients with comorbid axis II disorders (Colom et al., 2004). Thus, dysfunctional personality traits may moderate the effectiveness of manual-based psychosocial interventions. Nonetheless, structured interventions can be adapted to the needs of these more complicated patients.

Future studies should examine psychosocial treatments that incorporate strategies found to be effective in the treatment of patients with axis II disorders. Notably, dialectical behavior therapy has been found to be more effective than treatment as usual (Linehan et al., 2006) in

the treatment of suicidal behaviors among borderline personality disorder patients. An open trial combining family-focused therapy with dialectical behavior therapy for adolescents with bipolar disorder observed pre- to post-treatment improvements in suicidality, nonsuicidal self-injurious behavior, emotional dysregulation, and depressive symptoms (Goldstein, Axelson, Birmaher, & Brent, 2007).

SUMMARY AND FUTURE DIRECTIONS

This review concludes that personality, temperament, life stress, and family discord are important influences on the course of BD, alone and in interaction with each other. Patients with comorbid personality disorders are more treatment-refractory and generally have poorer outcomes of their bipolar disorder. Temperamental attributes that are related to subsyndromal manic symptoms, such as hyperthymia, cyclothymia, and positive affectivity predict the onset of more severe manic symptoms. BD patients are highly sensitive to reward, and excessive goal pursuit after goal-attainment life events may be one pathway to mania. Negative life events and neuroticism are more closely associated with depressive recurrences than manic recurrences. High levels of intrafamilial criticism and other dimensions of family functioning (e.g., low cohesion, low warmth, or ineffective problem-solving) are most consistently associated with depressive symptoms and recurrences.

This summary relies on a small number of prospective studies, and there is a need for replication of most of the findings. Beyond this, few studies have directly tested multivariate vulnerability/stress models of episode onset and occurrence, so this is a fertile area for future research. For example, goal-attainment life events may be especially potent in predicting mania when patients have heightened reward sensitivity, but calming, low-intensity, and supportive marital or family interactions may help protect against manic symptoms during those moments. Patients from families with high-EE attitudes may be especially relapse-prone when they show emotion labeling deficits, but these risk factors may be especially potent when the patient has had early experiences of adversity. Studies that take a developmental perspective, examining the interactions of risk and protective processes at different phases of the life cycle, are likely to be more informative than cross-sectional studies, especially given that mood cycling patterns are a “moving target” in this disorder.

The course of BD is characterized by a multifinality of outcomes, which can include recovery, remission, relapse, recurrence, ongoing symptoms, or psychosocial impairments (Frank et al., 1991; Martinez-Arán et al., 2008). It is rare for psychosocial studies to distinguish recovery from remission (i.e., lengthy versus brief asymptomatic periods) or recurrence from relapse (i.e., periods of symptom exacerbation that follow lengthy periods of recovery versus those that follow briefer periods of remission). These distinctions could help determine whether psychosocial predictors (or moderators of treatment outcome) are equally relevant to the short-term and long-term course of the disorder.

Adjunctive psychotherapy is a vital part of the effort to stabilize episodes of bipolar depression, prevent recurrences, and enhance functioning. This observation is beginning to be reflected in practice guidelines (e.g., Yatham et al., 2005; Goodwin & the Consensus Group of the British Association for Psychopharmacology, 2003). A major limitation of the existing psychosocial approaches, however, is their inaccessibility to most community clinicians. Future research should examine the most cost-effective methods for training clinicians and monitoring their adherence in practice settings.

The mechanisms by which psychosocial treatments operate – through altering patients’ cognitive biases, enhancing the protective effects of the family, teaching interpersonal effectiveness or emotional self-regulation skills, or simply increasing patients’ adherence to

medications – need to be clarified in randomized trials. Future trials should also attempt to identify the subgroups of patients who respond best to each form of treatment (for example, those who present with primarily depressive versus primarily manic illness courses, or those with bipolar I versus II disorder), as a means of further refining practice guidelines for different presentations of BD. Finally, the role of psychosocial stressors in accelerating the onset of BD among genetically at-risk children, and the role of psychosocial interventions in delaying or staving off the first onset of the disorder, are important areas for the next generation of research.

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