2010

Social Cognition and Cognitive Flexibility in Bipolar Disorder

Erin Tone
Georgia State University, etone@gsu.edu

Recommended Citation
McClure-Tone, E. B. (2010). Social Cognition and Cognitive Flexibility in Bipolar Disorder. In D. Miklowitz & D. Cicchetti (Eds.), *Understanding Bipolar Disorder: A Developmental Psychopathology Perspective* (pp. 331-369). New York: Guilford.

From *Understanding Bipolar Disorder: A Developmental Psychopathology Perspective.*
Edited by David J. Miklowitz and Dante Cicchetti.

CHAPTER 11

Social Cognition and Cognitive Flexibility in Bipolar Disorder

Erin B. McClure-Tone

A rapidly growing literature examines the impact of bipolar disorder (BD) on social cognition, or patterns of thought about interpersonal interaction, and social behavior. Considerable evidence indicates that acquisition and implementation of an array of social cognitive and behavioral skills are disrupted in the context of this psychiatric illness. Furthermore, numerous studies link the social deficits evident in BD with atypical development in brain regions implicated in social and emotional processing. Elucidating the social disruptions evident across the life span in individuals with BD, how these disruptions relate to specific behavioral deficits or endophenotypes, and their underlying neural mechanisms may help inform our understanding not only of psychopathological processes but also of typical social development at the behavioral and neural levels. Additionally, clarification of social deficits and strengths associated with BD, as well as their neural underpinnings, may facilitate the development of effective and explicitly targeted interventions.

Several factors, however, complicate the description and evaluation of social functioning, its component processes, and their typical or atypical development in the context of BD. First and foremost, researchers and clinicians have in recent years classified a diversity of conditions as representative of the BD spectrum, particularly among children and adolescents (Geller et al., 2003; Leibenluft, Charney, Towbin, Bhangoo, & Pine, 2003; Soutullo et al., 2005; Staton, Volness, & Beatty, 2008; Youngstrom, Birmaher, & Findling, 2008). Whether or not symptoms such as grandiosity or elation need to be present in youth and how best to define these symptoms in youth of different ages remain controversial (Staton et al., 2008), as do the boundaries between attention-deficit/hyperactivity disorder

(ADHD) and the BD spectrum (Galanter & Leibenluft, 2008). Furthermore, some researchers have developed criteria for distinguishing strictly diagnosed BD from related conditions; Leibenluft, Charney, and colleagues (2003), for example, make a distinction between narrow and broad phenotypes for mania in pediatric BD. According to this system, individuals with the narrow phenotype meet full *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV; American Psychiatric Association, 1994) diagnostic criteria for hypomania or mania; those with a related, but broader, phenotype that they term severe mood dysregulation (SMD) exhibit severe irritability and hyperarousal, but do not show the hallmark symptoms of elation or grandiosity (Leibenluft, Charney, et al., 2003). Finally, the role of irritability in BD has been extensively debated (Biederman, Klein, Pine, & Klein, 1998; Leibenluft, Blair, Charney, & Pine, 2003; Leibenluft, Cohen, Gorrindo, Brook, & Pine, 2006). This issue has been complicated to resolve, in part because irritability is normatively common, particularly during some developmental periods, and also frequently reported as characteristic of youth with a range of psychopathology (Leibenluft, Blair, et al., 2003). Thus, not surprisingly, different research groups over the past decade have used varied inclusion criteria to identify participants with pediatric BD, rendering direct comparisons of results across studies difficult. Because of the importance of clarity around fundamental issues of diagnosis and categorization, this chapter will note instances where criteria used to identify youth with BD vary from those listed in the DSM (American Psychiatric Association, 1994).

Second, it remains unclear whether social impairments associated with BD are state dependent (i.e., present only during mood episodes) or reflective of enduring trait-like characteristics that influence cognition and behavior even when individuals are asymptomatic. Commendably, many studies now clearly describe participants' mood states and medications at the time of research participation, and a growing body of research compares medicated and unmedicated and/or euthymic and symptomatic subgroups. Almost no research, however, has looked at whether patterns of social cognition and behavior differ *within* individuals when they are euthymic versus symptomatic or medicated versus unmedicated. This gap in the literature reflects the complexity of conducting such studies. Although within-subject research is of great interest, it is difficult to carry out. Thus, little is known about whether patterns of performance on research tasks reflect stable or transient deficits or strengths within individuals.

Third, the impact of acute BD symptoms and more stable illness-related deficits on social cognition and behavior is likely to vary across development, given differing social demands and expectations that individuals face at different ages. Mood-related behaviors or intensity levels that are considered typical at one developmental stage (e.g., need-related crying among infants, irritability in mid-adolescence) may be considered atypical at other points (Leibenluft et al., 2006; St. James-Roberts & Plewis, 1996). Thus, the developmental context of the affected individual, both at the time of study participation and at illness onset, should ideally be taken into account in evaluating the roles that symp-

GOALS OF THIS CHAPTER

- Within a developmental psychopathology context, review the literature regarding affective cue processing, flexible response generation and inhibition, and management of affective states in BD across the life span.
- Identify similarities and differences in social functioning between individuals with and without BD.
- Highlight study, participant, and task characteristics that complicate the interpretation of findings.

toms, illness-related deficits, and risk-related deficits play in social success or impairment. Onset before adolescence, for example, may interfere with the successful mastery of basic social cognitive skills (e.g., facial expression decoding or response inhibition) that form the basis of later emerging, more complex skills. In contrast, later onset of illness may result in a markedly different pattern of spared and impaired functions.

The following review of select aspects of social cognitive and behavioral development as they relate to BD is written with an effort to take these complicating factors into account. This review briefly summarizes primary social milestones and their emergence during typical development as well as what we know about their neural underpinnings. It then shifts focus to the literature regarding social functioning in individuals with BD across development and, finally, examines behavioral and neural research regarding component social cognitive and behavioral processes in affected individuals and those who are genetically at risk for BD. There is a particular focus on affective cue processing, flexible response generation and inhibition, and management of affective states that are likely to interfere with effective implementation of these skills.

Typical Social Cognitive Development

Across development, social success depends on the ability to navigate complex, frequently shifting interpersonal and environmental demands. This navigation requires the integration of multiple discrete skills, including accurately perceiving and interpreting social cues, responding flexibly and appropriately to those cues, and regulating one's own emotional reactions throughout (Crick & Dodge, 1994). In typical development, these skills emerge gradually from infancy through adulthood, evolving as the individual negotiates increasingly complex social interactions. In the first years of life, infants learn to use adult cues as reference points, laying a foundation of core social cognitive skills, including joint attention and the capacity for progressively more sophisticated dyadic and triadic interactions with people and objects (Carpenter, Nagell, & Tomasello, 1998). During the

preschool years, as their verbal and nonverbal language skills develop, children build on this social cognitive base to become increasingly adept at discriminating among and interpreting social and emotional cues such as facial expressions (McClure, 2000); theorizing about others' states of mind (Milligan, Astington, & Dack, 2007; Wellman, Lopez-Duran, LaBounty, & Hamilton, 2008); and selecting or inhibiting behavioral responses in accordance with situational demands (Lagattuta, 2005).

In the middle childhood period, between approximately 7 and 11 years of age, as peer relationships become increasingly important and focused on mutual trust and assistance (Sullivan, 1953), social cognitive skills refine and expand. Children develop more complex mechanisms for managing their emotions and behaviors in stressful situations (Kliewer, Fearnow, & Miller, 1996), conform more tightly to social rules for displaying emotion (Jones, Abbey, & Cumberland, 1998), become more sophisticated in their understanding of others' mental states (Schwanenflugel, Fabricius, & Alexander, 1994), and learn to implement more flexibly a broad array of tools for and approaches to social problem solving (Crick & Dodge, 1994). These skills continue to develop through adolescence and into adulthood, with successful mastery increasingly important for both personal and occupational success (Fullerton & Ursano, 1994; Reisman, 1985).

Neural Underpinnings of Social Cognitive Development

The acquisition of social cognitive and behavioral skills, a process that begins early in development, appears to depend, at least in part, on the healthy maturation of a core set of interconnected neural structures (Blakemore, 2008; Nelson, Leibenluft, McClure, & Pine, 2005; Paterson, Heim, Friedman, Choudhury, & Benasich, 2006). These brain regions, which undergo structural and functional changes from infancy through adulthood (Giedd, 2004; Gogtay et al., 2004; Sowell, Trauner, Gamst, & Jernigan, 2002), constitute what Nelson and colleagues (2005) have termed the social information processing network (SIPN). This network consists of three reciprocally interactive primary "nodes": the detection node, the affective node, and the cognitive-regulatory node.

The detection node includes the superior temporal sulcus, fusiform face area, and inferior temporal and occipital cortices, all structures that play key roles in the detection and decoding of socially salient environmental features. Available data, which include findings from electrophysiological studies demonstrating distinct neural responses to various classes of social stimuli in human infants, suggest that functional aspects of this node mature as early as the first years of life (Halit, Csibra, Volein, & Johnson, 2004; Halit, de Haan, & Johnson, 2003; Johnson et al., 2005).

The affective node, which comprises regions engaged by reward or punishment cues (e.g., amygdala and ventral striatum), evaluates the emotional significance of salient stimuli and participates in the coordination of appropriate

behavioral responses. Available data in nonhuman species suggest that structures within this node contribute to social cognition and behavior in meaningful ways as early as the neonatal period (Bauman, Lavenex, Mason, Capitanio, & Amaral, 2004; Goursaud & Bachevalier, 2007). They continue to evolve across development, undergoing relatively abrupt functional and structural changes during the surge of gonadal hormones that accompanies puberty (Giedd, Castellanos, Rajapakse, Vaituzis, & Rapoport, 1997; Nelson et al., 2005).

The cognitive-regulatory node encompasses several regions within the frontal cortices. Structures within this node, which appear to continue developing well into adolescence and early adulthood (Gogtay et al., 2004), participate in theory-of-mind processes (e.g., attributing mental states to others), inhibition of prepotent responses, and generation of goal-directed behavior (Nelson et al., 2005). Evidence from animal studies indicates that projections between the cognitive-regulatory and affective/detection nodes are consistent with reciprocal feedback loops, such that activity in one node influences or modifies activity in others (Barbas, 2007). Thus, atypical functioning in one node is likely to affect functioning in other nodes, even those that might, in artificial isolation, operate in typical ways.

Interestingly, the different developmental courses for structures in the detection, affective, and cognitive-regulatory nodes might relate to the emergence of dysfunctional behavior patterns at different developmental stages. Many investigators have speculated, for example, about the degree to which adolescent impulsivity and risk taking stem from emotional influences and other processes mediated by the affective node, in the context of limited inhibition or other regulatory influences mediated by the cognitive-regulatory node (Nelson et al., 2005). Such behavioral tendencies may reflect operation of the mature affective node in concert with the immature cognitive-regulatory node. Similarly, atypical development within the early-maturing detection node could have a cascade of effects on functioning in associated brain regions that mature later. It is critical that research articulate more clearly the developmental course of BD at neural as well as phenomenological and functional levels; underlying neural mechanisms may be critically important in determining both concurrent and delayed functional outcomes. Such research needs to focus not only on youth who have been diagnosed with BD but also those at risk, who may show atypical patterns of neural development in the absence of active symptoms.

Studies of Social Functioning in Individuals with Bipolar Disorder

Social Functioning in Adults with Bipolar Disorder

Social functioning is commonly impaired in adults with BD, which presents obstacles to personal and occupational success during both symptomatic and euthymic periods (Fagiolini et al., 2005; Pope, Dudley, & Scott, 2007; Simon, Bauer, Lud-

man, Operskalski, & Unutzer, 2007). Indeed, one literature review found that between 30 and 60% of affected adults showed detectable social and occupational impairment during and even after long periods of remission (MacQueen, Young, & Joffe, 2001). Social impairment in adults with BD has typically been measured using self-report scales and has focused on the broad presence or absence of difficulty forming and maintaining close relationships or participating in social leisure activities. A small body of research has examined more specific social skills as well. In one study of adults diagnosed with BD, for example, euthymic individuals generated fewer solutions during a hypothetical social and moral problem-solving task than healthy controls. Furthermore, the more mood episodes experienced by individuals with BD, the less effective their generated solutions were likely to be, by both self- and observer rating (Scott, Stanton, Garland, & Ferrier, 2000).

In adults, social functioning difficulties appear to be pronounced in the presence of active manic or depressive symptoms and, more generally, vary depending on current affective state. For example, hypomania has been particularly strongly associated with elevated friction in relationships (Morriss et al., 2007). Mood states that can be associated with both mania and depression, such as anger, also have the potential to disrupt adult social functioning. For example, adults with BD reported more bursts of sudden, intense, situationally inappropriate anger during depressive episodes than did adults with unipolar depressive disorders (Perlis et al., 2004). Such expressions of unpredictable, inappropriate negative affect are likely to impede effective social interaction under many circumstances (Rydell, Thorell, & Bohlin, 2007; Tamir, Mitchell, & Gross, 2008).

Social Functioning in Youth with Bipolar Disorder

Findings regarding social functioning among youth diagnosed with BD are less consistent than those in the adult literature. This reflects several factors: first, the heterogeneity of conditions labeled as BD among children and adolescents; second, the differing social demands that youth face at different ages; third, variability in study designs, which include retrospective, cross-sectional, and longitudinal approaches; and fourth, the need to obtain reports regarding social behavior from multiple sources, such as parents and their affected children. Although data from both sources are valuable, parent reports need to be evaluated carefully because parent mood symptoms/disorders, which are likely to be common given the familial nature of BD, may influence parents' perceptions of and interactions with their children (Brotman et al., 2007; De Los Reyes & Kazdin, 2006; Edvardsen et al., 2008). In light of this caveat, some research has found that youth with BD have impaired relationships with family members and peers. Most of this research has focused on older children and adolescents (Geller et al., 2000; Robertson, Kutcher, Bird, & Grasswick, 2001; Schenkel, West, Harral, Patel, & Pavuluri, 2008); published research that characterizes patterns of social behavior in preschool and early elementary–age children with BD spectrum disorders or symptoms is notably lacking.

A few studies focused on middle childhood through late adolescence have yielded evidence of elevated conflict between individuals with BD and their parents, regardless of the child's current mood state (Table 11.1). In one of the first studies of psychosocial functioning in pediatric BD, Geller and colleagues found that affected youth (some of whom also had comorbid ADHD) and their mothers reported less maternal–child warmth, more maternal–child and paternal–child tension, and more problematic peer relationships than did both ADHD and nonpsychiatric control groups (Geller et al., 2000). Further research on this sample, which the authors followed longitudinally for 2 years, yielded evidence of additional differences in social behavior among groups. By parent report, youth with BD were less cooperative than both youth with ADHD and controls. Furthermore, compared with controls, members of the BD and ADHD groups were more novelty seeking, more reward dependent, and less persistent or self-directed. Youth with BD described themselves as less persistent and self-directed as well as more novelty seeking than controls but did not differ in self-report from peers with ADHD (Tillman et al., 2003).

Schenkel, West, and colleagues (2008) replicated and extended Geller and colleagues' findings regarding family interaction patterns by asking mothers to evaluate their relationships with their 8- to 17-year-old (mean, 11.27 years) children with or without BD. In this study, mothers of healthy controls (n = 30) reported feeling more warmly toward and having better relationships and less conflict with their children than did mothers of medicated, euthymic BD youth (n = 30). Mothers with younger children with BD, as well as those whose children had earlier symptom onset, reported the most conflictual relationships with their offspring (Schenkel, West, et al., 2008). Notably, the presence of both mother and father mood disorder diagnoses predicted significantly lower maternal ratings of warm and intimate relationships with their children, underscoring the importance of taking parent, as well as child, mental health into account when evaluating social and relational characteristics of youth with BD.

A few studies have examined self-perceived social and family functioning in adolescents with BD, yielding findings similar to those obtained from affected adults. In research focused on family interaction, for example, older adolescents (18–19 years old) with bipolar I disorder who were mildly symptomatic but not in depressive or manic episodes reported significantly more problems with their parents than did peers with unipolar major depressive disorder (MDD) or community controls. For all groups, however, problematic interactions between adolescents and parents were minor and infrequent. Youth with BD, relative to controls, reported less positive relationships with siblings and described their families as less cohesive (Robertson et al., 2001).

A study focused more explicitly on individual social coping skills also yielded findings consistent with those from adult-focused research. Specifically, 13- to 17-year-old adolescents with postpubertal-onset BD (n = 24) reported more external loci of control and greater difficulties regulating emotion in anger-provoking situations than healthy comparison youth (n = 39). Participants with BD also

TABLE 11.1. Summary of Studies of Social Functioning in Bipolar Disorder from Childhood through Adulthood

Study	BD group (*n*)	Mood state at time of study	Mean age, years (*SD*)	Comparison group (*n*)	Mean age, years (*SD*)	Method	Findings
Child/adolescent cross-sectional studies							
Geller et al. (2000)	BDI: 93	Manic	10.9 (2.7)	ADHD: 81 HC: 94	9.7 (2.0) 11.1 (2.6)	Mother report	Mother–child warmth: BD < ADHD, HC Parent–child tension: BD > ADHD, HC Peer relationship quality: BD < ADHD, HC
Tillman et al. (2003)	BDI: 101	Not reported	~12.8[a]	ADHD: 68 HC: 94	~11.6[a] ~13.1[a]	Mother report	Cooperativeness (mother): BD < ADHD, HC
						Self-report	Persistence/self-direction (mother): BD < HC Persistence/self-direction (self): BD < HC Novelty seeking (mother/self): BD < HC Reward dependence (mother): BD < HC
Schenkel, West, et al. (2008)	BD: 30	Euthymic	11.6 (2.7)	HC: 30	10.9 (2.7)	Mother report	Mother–child warmth: BD < HC Mother–child conflict: BD > HC

Robertson et al. (2001)	BDI: 44	Euthymic	19.9 (2.9)	UD: 30 HC: 45	18.5 (2.8) 18.2 (1.6)	Self-report	Parent relationship quality: BD < UD, HC Sibling relationship quality: BD < UD, HC Family cohesion: BD < UD, HC
Rucklidge (2006)	BDI/II/NOS: 24	Not reported	13–17[b]	HC: 39	13–17[b]	Self-report	External locus of control: BD > HC Anger regulation: BD < HC Effective coping: BD < HC
Retrospective studies							
Kutcher et al. (1998)	BDI: 28	Euthymic	13–19 years at time of first mood episode	—	—	Retrospective parent report re premorbid functioning, school records	Peer relations: rated "excellent" in 30%, "as expected" in 60%, "problematic" in 10%
Cannon et al. (1997)	BD: 28	n/a	32 (9.3) 23.4 (5.4) at first hospital admission	SZ: 70 HC: 100	26.8 (6.7) 23.3 (5.7) at first hospital admission 27.5 (7.1)	Retrospective maternal report re premorbid functioning	Social adjustment: HC > BD > SZ

(cont.)

TABLE 11.1. *(cont.)*

Study	BD group (*n*)	Mood state at time of study	Mean age, years (*SD*)	Comparison Group (*n*)	Mean age, years (*SD*)	Method	Findings
High-risk studies							
Reichart et al. (2007)	High risk (parent with BD): 11–17 years old, 102; 18–26 years old, 106	n/a	11–17 years, 18–26 years (means not reported)	Low risk (no parent with BD): 11–17 years old, 1,122; 18–26 years old, 1,175	11–17 years, 18–26 years (means not reported)	Parent, teacher, and child report	11–17 years: no differences 18–26 years: adaptive functioning, family relationships: high risk < low risk
Petti et al. (2004)	High risk (parent with BD): 23 (9 had an affective disorder diagnosis)	n/a	7–16 years (mean age by risk group not reported)	Low risk (no parent with BD): 27 (three had an affective disorder diagnosis)	7–16 years (mean age by risk group not reported)	Parent and self-report	Social dysfunction associated with child diagnosis but not with risk group status
Anderson & Hammen (1993)	High risk (parent with BD): 18		13.7 (2.8)	High risk (parent with MDD): 22 Low risk (no parent disorder): 38	12.4 (2.6) 11.7 (2.3)	Mother and teacher report	Social functioning: high MDD risk < high BD risk, low risk

Adult cross-sectional studies							
Fagiolini et al. (2005)	BDI/II/NOS: 103	Euthymic	42.6 (11.2)	—	—	Self-report	General functional and social impairment relative to normative data
Pope et al. (2007)	BDI/II: 77	Euthymic, mildly depressed, hypomanic	42.1 (11.1)	—	—	Self-report	Moderately impaired interpersonal functioning
Scott et al. (2000)	BDI: 41	Euthymic	44.7 (10.5)	HC: 20	42 (14.6)	Self- and observer ratings on Means Ends Problem-Solving Scale	Number of solutions generated: BD < HC
Morriss et al. (2007)	BDI/II: 253	Euthymic (*n* = 171) MDD (*n* = 60) Hypomanic (*n* = 22)	41.2 (10.9)	—	—	Interviewer rating (Social Adjustment Scale)	Full sample: moderately impaired social functioning Social performance: H, MDD < E Interpersonal behavior: H, MDD < E Interpersonal friction: H > MDD, H > E
Perlis et al. (2004)	BDI/II: 29	Depressed	42.9 (11.9)	MDD: 50	38.2 (13.8)	Self-report (Anger Attacks Questionnaire)	Anger attacks: BD > MDD

Note. BD, bipolar disorder (BDI, bipolar disorder type I; BDII, bipolar disorder type II; BD NOS, bipolar disorder not otherwise specified); ADHD, attention-deficit/hyperactivity disorder; HC, healthy control; UD, unipolar depression; MDD, major depressive disorder; SZ, schizophrenia; E, euthymia.

[a]Tillman et al. (2003) gathered 2-year follow-up data on the sample recruited for Geller et al. (2000). Ages at follow-up were not reported (ages at baseline were), so ages presented are estimates based on the baseline data.

[b]Means and standard deviations were not reported.

endorsed less effective coping strategies than control participants; for example, in coping with difficult situations, they described themselves as less capable, more likely to reduce tension using maladaptive methods (e.g., screaming, substance use, taking frustration out on others), and more likely to blame themselves for their problems. Furthermore, adolescents with BD perceived themselves as less solution focused than controls (Rucklidge, 2006).

Social Impairment in Bipolar Disorder: Marker of Illness or Vulnerability to Illness?

The studies described previously provide important snapshots of perceived social functioning in youth with BD, from both their own and their parents' perspectives. They are limited, however, on several fronts, leaving many questions open. First, they provide limited insight into the timing of social impairments in pediatric BD. Are such deficits "episode indicators" evident during active periods of illness but not remission (Nuechterlein & Dawson, 1984)? Alternatively, do they constitute "mediating vulnerability indicators" or chronic characteristics of affected youth, which become particularly severe during episodes? Given findings regarding state-related cognitive deficits in adults with active or remitted BD (Bozikas et al., 2005; Iacono, Peloquin, Lumry, Valentine, & Tuason, 1982; Liu et al., 2002), this question merits closer examination.

One approach is to examine functioning before illness onset in youth who eventually develop BD, either retrospectively in affected populations or prospectively in high-risk groups. The first studies to take this approach examined school records or asked parents to evaluate retrospectively whether affected children had displayed social impairment before their symptoms became evident. Kutcher, Robertson, and Bird (1998) found that parent recollections and school records regarding a sample of individuals with adolescent-onset BD (mean age at first depressive episode, 15.8 years; mean age at first manic episode, 16.7 years) yielded little evidence of premorbid social impairment. Indeed, their data indicated that 90% of the sample had average to excellent peer relationships before illness onset (Kutcher et al., 1998). In a second retrospective study, mothers of older adolescents and adults with BD, schizophrenia, or no impairment (aged 16–50 years) were asked to evaluate childhood and adolescent social functioning in their offspring. In contrast to Kutcher and colleagues' findings, individuals who had developed BD were rated as less socially adept during youth than controls, although impairment was less severe and long standing in the BD group than in those who later developed schizophrenia (Cannon et al., 1997).

These findings must be interpreted cautiously because of their retrospective nature. First, awareness of their children's diagnoses and, later, diagnosis-associated behaviors may have biased parents' recollections of earlier behavior either positively or negatively. Second, because no data were provided regarding family history of psychopathology in either study, it is unclear whether and how current or past symptoms in the maternal reporters influenced their descrip-

tions of their children. Such confounds are difficult to avoid in retrospective studies, although use of additional sources, such as the school records that Kutcher and colleagues (1998) reviewed, mitigates the potential impact of parent biases. Therefore, researchers have shifted to studies focused on current behavior or, when possible, prospective longitudinal designs, typically targeting the offspring of adults with BD.

Using cross-sectional data from a longitudinal study, researchers compared social functioning between high- and low-risk youth in both younger (11–18 years) and older (18–26 years) age ranges (Reichart et al., 2007). Participants in the high-risk group each had a parent with BD; low-risk peers were drawn from large samples of the Dutch general population. Within both age ranges, the two risk groups differed minimally on well-normed, standardized parent-, teacher-, and child-report measures of social functioning, but adaptive functioning and family relationships were poorer in older high-risk participants than in their low-risk peers, particularly those who had been diagnosed with a lifetime mood or other disorder. Findings from this study are complicated by the fact that over half of the high-risk sample had been diagnosed with either a mood disorder or another psychiatric illness by the end of the study. Thus, current symptoms at the time of evaluation may have affected their social behavior independently of familial risk.

Petti and colleagues (2004) used a within-family design to contrast an array of psychosocial variables between 7- to 16-year-old offspring with parents who either did (n = 23) or did not (n = 27) have BD. Of the youth with affected parents, nine had affective disorders of their own; three of the offspring of nonaffected parents received affective disorder diagnoses. Children with affective disorders, regardless of parent diagnosis, reported receiving more social support in the form of positive regard from classmates, teachers, and parents than did healthy youth. Neither child nor parent diagnostic status differentiated participants with regard to perceptions of family closeness, although parents of diagnosed children reported more disciplinary issues than parents of healthy children (Petti et al., 2004).

Although several prospective longitudinal studies of offspring at risk for BD have been conducted or are underway (Alloy, Abramson, Walshaw, Keyser, & Gerstein, 2006; Anderson & Hammen, 1993; Hillegers et al., 2004), surprisingly few have published data regarding social functioning in their participants. In one such study, Anderson and Hammen (1993) followed four groups of 8- to 16-year-old children (offspring of unipolar depressed, bipolar, medically ill, and psychiatrically typical women; n = 96) for 2 years. During the course of the study, mothers evaluated the social competence, academic performance, and behavior problems of their children at 6-month intervals. Teachers also completed standard measures, whenever possible, regarding each child's behavior and social functioning at school. Results yielded little evidence of social or behavioral impairment among children of mothers with BD, who differed minimally from the children of control mothers. In contrast, children of mothers with unipolar depression

showed chronically and significantly poorer social functioning on all measures compared with the other three groups, including the offspring of BD (Anderson & Hammen, 1993). This finding could reflect a number of factors, including differences between mothers with unipolar depression and BD in symptom severity or chronicity, treatment history (e.g., mothers with BD may have received treatment earlier or more consistently than those with unipolar depression), or social support. Furthermore, although the researchers gathered data regarding child diagnoses, these data were not presented in the Anderson and Hammen study; it is thus difficult to evaluate the impact, if any, of active child symptoms on social functioning.

Social Functioning in Bipolar Disorder: Summary and Future Directions

Taken together, these findings suggest that once children have begun to exhibit BD symptoms, they are likely to lag behind their peers in terms of social functioning regardless of whether they are observed in an active mood episode. The research base with regard to this example of equifinality is strikingly incomplete, and further study is clearly warranted, with attention to several factors. First, although researchers have begun to conduct prospective, longitudinal studies focused on outcomes in children who are at risk for BD or show early symptoms of the disorder, few characterize social functioning in these youth across different developmental phases.

Second, almost no research has targeted participants in infancy or early childhood and followed their development through adolescence or adulthood. Indeed, most prospective studies focused on pediatric BD or risk for BD have enrolled participants in middle childhood or early adolescence and followed them for 2 to 5 years (Anderson & Hammen, 1993; Geller et al., 2002; Hillegers et al., 2004). Research over longer periods of time is expensive and difficult to conduct but absolutely essential to answer questions about the onset of social deficits associated with BD. Notably, several groups have prospective studies underway that are aimed at identifying and following young children with mood symptoms and/or family histories of BD.

Third, as noted earlier, extant studies differ according to whether they take into account child and parent symptoms and medication status at the time of data collection and the impact of these variables on reports regarding child behavior and functioning. Given the risk that current mood state may bias responses, future research, in keeping with recent trends in work on pediatric BD, must evaluate the impact of mood on reports regarding social behavior. More routine inclusion of reports from nonfamilial sources (teachers, peers, research observers) would not only provide useful information regarding potential biases in parent or child reporters but would also help clarify how social functioning in affected or at-risk youth varies across different settings (e.g., school, home).

Fourth, even if social functioning is typically healthy before the onset of BD, trajectories of social functioning may, in keeping with the concept of multifinal-

ity, vary across youth who become symptomatic at different ages, who express the disorder in different ways (e.g., rapid cycling, predominantly depressed, predominantly manic), who have varying comorbid diagnoses, or who experience different levels of environmental support or adversity. For example, symptoms that manifest early may, in keeping with the "scar hypothesis" (Lewinsohn, Steinmetz, Larson, & Franklin, 1981), affect children in enduring ways that influence their later social functioning. Children whose symptoms cycle more unpredictably or rapidly may elicit different responses from those in their environments (e.g., increased frustration) than do children whose symptoms appear in the context of circumscribed episodes, leading the two groups to develop different styles of interpersonal interaction and different types of social strengths and weaknesses. No research has examined individual difference variables such as sex and age in relation to psychosocial outcomes in BD.

Environmental factors that may serve as protective or risk factors and thus diminish or amplify the social consequences of BD also merit attention. In particular, what do families, teachers, peers, and others in the environment do that helps some children avoid negative social outcomes or that increases risk for such outcomes in others? Additionally, where do youth with BD resemble typical peers? Findings from at least one study, for example, suggest that adolescents with BD show social *performance* deficits by their own and their parents' reports. Specifically, adolescents with BD rate themselves as more inappropriately assertive, impulsive, jealous, withdrawn, and overconfident than do healthy controls, and their parents rate them as more likely to behave inappropriately in social situations. However, they do not differ from healthy controls in their social *knowledge* (Goldstein, Miklowitz, & Mullen, 2006). Notably, social skills evaluations in this study took place when participants' BD symptoms were well controlled, decreasing the possibility of mood/state-related biases in self-ratings.

Finally, there is a need to elucidate the specific deficits that underlie social dysfunction in BD. Difficulties in encoding facial emotions, for example, may be more likely than global patterns of social behavior or cognition to represent stable endophenotypes (enduring vulnerability characteristics) of the disorder. By isolating component skills, in addition to global patterns of social success or failure, research may facilitate the development of targeted prevention or intervention approaches that will decrease the effects of BD on social development and functioning. In the next sections, research on specific social deficits associated with BD, as well as their neural correlates, is reviewed.

Specific Social Deficits Associated with Bipolar Disorder

Clinicians and researchers have long recognized that individuals with BD show not only evidence of general social dysfunction but also broad symptomatic patterns (e.g., irritability, impulsivity, withdrawal) that are likely to interfere with relationships. Only recently has research begun to characterize more precisely

the nature of behavioral and social cognitive deficits associated with the disorder. Studies over the past several years have compared individuals with and without BD on a wide array of social and social cognitive variables that reflect multiple social information processing stages, such as those that Crick and Dodge (1994) described in a seminal theoretical report (Crick & Dodge, 1994). In keeping with Crick and Dodge's model, the present chapter focuses specifically on work regarding the accurate perception and interpretation of social cues, the formulation of flexible and appropriate responses to those cues, and the regulation of emotional reactions in individuals, predominantly youth, with and without BD.

Perception and Interpretation of Social Cues

Several studies in recent years have targeted the recognition and interpretation of social cues as potentially deficient skills in individuals with BD. Much of this research has found that BD is associated with deficits in the labeling of emotional facial expressions, in samples of both adults (Getz, Shear, & Strakowski, 2003; Lembke & Ketter, 2002) and children (Guyer et al., 2007; McClure, Pope, Hoberman, Pine, & Leibenluft, 2003; McClure et al., 2005; Rich, Grimley, et al., 2008; Schenkel, Pavuluri, Herbener, Harral, & Sweeney, 2007), although specific patterns of performance vary across studies. Studies have focused predominantly on adults or adolescents; relatively little is known about facial expression processing in younger children with BD or individuals who are at risk for the disorder. Furthermore, whether documented deficits are trait based or state based (i.e., related to current mood state) remains unclear, although some studies have made efforts to address this issue. A growing body of evidence indicates that at least some aspects of facial expression processing are impaired regardless of current mood.

In the most comprehensive study to date of youth with different psychological disorders, Guyer and colleagues (2007) compared performance on a facial emotion labeling task among adolescents (mean ages by group ranged from approximately 12–15 years) with BD (n = 42), severe mood dysregulation (SMD; n = 39) (Leibenluft, Charney, et al., 2003), anxiety or MDD (n = 44), ADHD/conduct disorder (n = 35), and controls (n = 92). Consistent with earlier, smaller studies (e.g., McClure et al., 2003, 2005), results indicated expression labeling deficits across an array of facial emotions (happy, sad, angry, fearful) in the BD and SMD groups relative to controls and other clinical groups. Errors did not differ based on the ages of the face stimuli or the emotions (happy, sad, angry, or fearful) displayed; however, the authors note that power limitations may have obscured such specific group differences (Guyer et al., 2007). Interpretation of study findings is complicated by the facts that current mood state (euthymic, manic, depressed) varied within the BD group, and that many participants within the BD and SMD groups were medicated at the time of evaluation, unlike members of the other groups. Post hoc analyses, however, comparing euthymic participants with BD (n = 25) and control (n = 92) groups indicated comparable deficits to those seen in the combined euthymic/symptomatic BD group. Indeed, McClure and colleagues

(2005) obtained similar results in a smaller sample. Furthermore, unmedicated BD/SMD youth differed from controls in their overall task performance, with consistently lower scores.

Whereas Guyer and colleagues (2007) examined skill at classifying emotions into discrete categories, Rich, Grimley, and colleagues (2008) evaluated capacity to correctly identify facial expressions presented at gradually increasing emotional intensity in adolescents with narrow-phenotype BD, SMD, and no diagnosis. Each stimulus began as a neutral face and was morphed gradually into an emotional (happy, surprised, sad, angry, fearful, disgusted) face; participants pressed a button as soon as they believed they had accurately identified the depicted expression. Regardless of the emotion presented, youth with BD and SMD required more intensity to be apparent before they responded at all; they also correctly identified disgusted, surprised, happy, and fearful faces at later points than did controls.

Another recent study focused more explicitly on associations between facial expression processing deficits and both medication and current mood state in youth with DSM-IV BD (Schenkel et al., 2007). This study compared performance on two facial expression processing tasks in young adolescents (mean age, 11–12 years) who were either healthy (n = 28), diagnosed with BD and euthymic (n = 29), or diagnosed with BD and acutely symptomatic (n = 29). On the first task, which required participants to identify which of two faces displayed a single emotion more intensely, only symptomatic youth with BD performed more poorly than controls. On the second task, which involved rating emotional expressions along a 7-point continuum ranging from *very happy* to *neutral* to *very sad*, both euthymic and symptomatic youth with BD underestimated the intensity of emotional faces compared with healthy controls. Results suggest that some emotion processing impairments may be associated with acute symptomatology, whereas other kinds of impairment may constitute trait or risk markers.

Consistent with the possibility that impairment in particular aspects of emotion processing may be related to risk for BD, Brotman and colleagues (2008) found that 4- to 18-year-olds without BD diagnoses but with an affected parent or sibling performed more poorly than controls on a facial expression labeling task. Their peers diagnosed with BD also performed more poorly than controls (Brotman et al., 2008).

Thus, on tasks that involve different kinds of facial expression processing (e.g., discrimination, labeling, evaluation of intensity), children and adolescents with BD appear to show fairly consistent deficits, some of which are apparent regardless of current mood state (e.g., expression labeling and intensity rating) and thus may represent endophenotypes for the disorder and others of which relate more specifically to the presence of active symptoms (e.g., discrimination between expressions that differ subtly in intensity). More research is needed to delineate the impact that such facial expression processing deficits have on day-to-day social behavior; the first study to examine this question in youth with BD indicates that they may correlate meaningfully with impaired social reciprocity skills (Rich, Grimley, et al., 2008). In notable contrast, in this study, facial expres-

PERCEPTION AND INTERPRETATION OF SOCIAL CUES

- Both adults and youth with BD, as well as youth at risk for BD, perform more poorly than controls on facial expression recognition tasks.
- Although some deficits appear consistent across euthymic and manic/depressed mood states (e.g., facial expression labeling), others appear to emerge only during mood episodes (e.g., discrimination among subtly differing expressions).
- Deficits in processing more complex social cues, such as those associated with inferences regarding others' mental states, are also evident in adolescents and adults with BD.

sion processing deficits correlated significantly with family dysfunction in youth with SMD, but not with BD, which suggests that the effects of emotion processing deficits may vary markedly depending on the nature and severity of a child's dysfunction.

At least two studies on perception of social cues in individuals with BD focused more broadly on performance on theory-of-mind or social inference tasks. Like most of the research on facial expression processing in BD, this body of work has been limited to studies of adolescents and adults (Kerr, Dunbar, & Bentall, 2003; Schenkel, Marlow-O'Connor, Moss, Sweeney, & Pavuluri, 2008), with little to no attention yet to preadolescent children or asymptomatic individuals at risk for BD. This small literature suggests that BD may be associated not only with deficits in basic emotion processing but also with impairment in more complex social cognitive domains. Schenkel, Marlow-O'Connor, and colleagues (2008) examined performance on two theory-of-mind tasks, one designed to measure ability to infer others' intents and the other developed to tap false-belief understanding in emotional contexts. Adolescents with BD who showed at least two hallmark symptoms (elation, irritability, grandiosity; $n = 26$) performed significantly more poorly than healthy controls ($n = 20$) on both tasks (Schenkel, Marlow-O'Connor, et al., 2008). Findings were comparable to those obtained in studies of adults with BD, in which symptomatic individuals (Kerr et al., 2003) and, in some studies, euthymic patients with BD (Bora et al., 2005; Pollak & Tolley-Schell, 2003) showed theory-of-mind deficits.

Formulation of Appropriate Responses to Social Cues

Surprisingly little research has examined whether BD is associated with aberrant responses in social situations, particularly early in development. Such a pattern of deficits seems plausible, given the evidence that affected individuals appear to misread or misinterpret others' cues and thus may generate responses that are incongruent or inappropriate. Towbin, Pradella, Gorrindo, Pine, and Leibenluft (2005) compared patterns of social behavior among 8- to 18-year-old youth with

BD, SMD, or major depression and/or anxiety disorders using a series of parent-report measures developed to identify children with characteristics of pervasive developmental disorders (e.g., autism, Asperger) and describe their social functioning. Results indicated marked social interaction deficits in the BD and SMD groups compared with the MDD/anxiety group. Furthermore, when scores were compared with normative data, 62% of youth with bipolar type I disorder, 67% of youth with bipolar type II disorder, and 72% of youth with SMD scored in the autism spectrum range on at least one measure (Towbin et al., 2005). Although these findings are striking, they also raise questions about the discriminant validity of the instruments. In a recent follow-up to this study, Pine, Guyer, Goldwin, Towbin, and Leibenluft (2008) administered the same three measures to a larger sample of youth with BD, SMD, MDD, an anxiety disorder, or no diagnosis. Consistent with their earlier findings, scores on all three measures were higher in participants with mood disorders (BD, SMD, MDD) than in those with anxiety disorders or no diagnosis, reflecting more impairment in social reciprocity and language as well as elevated levels of behavioral rigidity and stereotypy in the mood-disordered groups.

The measures that Towbin and colleagues (2005) and Pine and colleagues (2008) administered tapped a broad array of expressive language and interpersonal interaction skills as rated by parents. Although informative about general social behavior as observed by adults who interact frequently with the child, global scores from these measures provide limited information about specific response formulation skills that might be impaired in youth with BD. As a first step toward addressing this question, McClure and colleagues (2005) administered to adolescents with BD (n = 40) and healthy controls (n = 22) a more focused measure of pragmatic language skill or the ability to use language effectively to achieve social goals. Comparison of BD and control groups showed that even when global oral expression skill was covaried, the BD group obtained lower scores on the pragmatic language measure, as well as on measures of facial expression labeling, than controls (McClure et al., 2005).

FORMULATION OF RESPONSES TO SOCIAL CUES

- Limited research has examined patterns of response to social stimuli in individuals with BD.
- There is some evidence that youth with BD and other mood disturbances perform atypically on measures of social reciprocity and language and show elevated levels of behavioral rigidity and stereotypy.
- Pragmatic language deficits have also been observed in youth with BD.
- Questions remain, however, regarding specificity of these deficits to BD, associations with mood state, and associations with medication status.

Further research is clearly needed examining social communication skills, at both macro- and microlevels, in individuals with BD across development. The small number of existing studies provides suggestive evidence that impairment in these domains may be associated with the disorder. However, these studies provide little information about whether and how mood state, age, or medication status may relate to patterns of spared and impaired function. Further research exploring links between social perceptual deficits in domains such as facial expression processing and social communication deficits would also be informative.

Regulation of Behavioral and Emotional Reactions

Social situations require not only that individuals generate appropriate responses, but also that they implement these responses in ways that are consistent with continually changing environmental demands. Such cognitive and behavioral flexibility (Cools, Clark, & Robbins, 2004) must further be combined with effective regulation of one's own emotional reactions to an unfolding interaction, which may not proceed in expected ways and may provoke frustration or anger. A number of studies have examined cognitive flexibility and emotional regulation in individuals with BD. Research on adults consistently suggests the presence of at least subtle and enduring deficits regardless of mood state (Fleck et al., 2003; Martínez-Arán et al., 2004; Mur, Portella, Martínez-Arán, Pifarré, & Vieta, 2007).

In adolescent samples, researchers have typically examined cognitive flexibility outside of social contexts, using neuropsychological tasks designed to measure aspects of executive functioning, such as the ability to shift attention between the perceptual features of complex stimuli in response to contingency cues. Such tasks include the classic Trails B measure (Lezak, 2004) and Wisconsin Card Sorting Test (WCST; Heaton, Chelune, Talley, Kay, & Curtiss, 1993), as well as the intra-extra dimensional (IED) shift task (Robbins et al., 1998). The IED shift task, which incorporates simple and compound reversal trials of varying difficulty, was originally designed as an analogue to the WCST for use with nonhuman primates but has been adapted for use with humans as well. Additionally, the change task, which measures the ability to inhibit a prepotent response and substitute an alternate one, provides another approach to examining response flexibility (Logan, Schachar, & Tannock, 1997). This task has the advantage that difficulty can be adjusted with a tracking algorithm to ensure that subjects execute correct responses approximately 50% of the time on trials requiring response substitution.

Dickstein, Nelson, and colleagues (2007) administered the IED shift task and the change task to youth with BD (n = 50; mean age, 13.1 years) and SMD (n = 44; mean age, 12.2 years) and to controls (n = 43; mean age, 13.6 years). On the IED shift task, adolescents with BD were impaired on simple reversal learning trials compared with control and SMD groups. Furthermore, on the change task, the BD group members were also impaired on change trials that involved substituting novel responses for prepotent responses relative to adolescents with SMD. These

deficits appeared to be independent of current mood state, comorbid anxiety, and comorbid ADHD and could, according to the authors, reflect impaired capacity to adapt to altered stimulus–reward associations. Participants with SMD only showed impaired performance relative to controls on compound reversal trials, which the authors speculated may represent deficits in selective attention (Dickstein, Nelson, et al., 2007).

Meyer and colleagues (2004) conducted a prospective study of cognitive flexibility in offspring of mothers with mood disorders (unipolar or bipolar) or no history of psychiatric illness. Offspring, who had been administered the WCST and Trails B during adolescence, were grouped according to their own diagnoses in young adulthood and compared with regard to their performance on both measures. Of the offspring of mothers with mood disorders who had developed BD themselves by their late teens or 20s, 67% showed impairment on the WCST, making perseverative errors and generating fewer conceptual-level responses. Impairment rates were much lower among offspring who remained free of psychopathology (17%) or who developed major depression (19%). The presence of this impaired pattern of performance before the onset of BD symptoms is consistent with the possibility that cognitive flexibility deficits represent a risk marker for the disorder (Meyer et al., 2004). Additional data, however, indicate that the associations between cognitive inflexibility and risk for BD are more complex. In a subsequent study of the same sample, Meyer and colleagues (2006) found that WCST performance mediated associations between maternal negativity when their offspring were toddlers and the later development of BD in their children. This pattern of findings suggests a dynamic pattern of interactions among genetic risk, parent behavior, child cognition, and child outcome and points to the need for further longitudinal work that examines reciprocal influences among these and other relevant variables.

One recent study of youth with BD focused on emotion regulation in response to changing contingencies, in addition to regulation of cognitive and behavioral responses to such environmental demands (Rich et al., 2007). Children and adolescents (ages 7–17 years) with BD (most were euthymic; four had hypomania or mixed hypomania; 88.6% were medicated), SMD (all were euthymic, 9.5% were medicated), or no diagnosis completed the Affective Posner Task, which assesses attention under a variety of emotional circumstances and contingencies. In the first (nonemotional) condition, participants received verbal feedback about their accuracy and speed on an attentional measure; in the second condition, they won or lost money based on their performance on the same task; and in the third (frustration) condition, they won or lost money based on a rigged algorithm that caused them to lose money on most trials on which they performed accurately as well as those on which they made errors or responded too slowly. Groups showed significant differences in self-reported arousal during the frustration condition, with the patient groups reporting more arousal than controls. In the two conditions that linked speed and accuracy to monetary gain or loss, the patient groups also responded more quickly than controls when they lost money. The similarities

REGULATION OF BEHAVIORAL AND EMOTIONAL REACTIONS

- Adults and adolescents with BD show deficits on measures of cognitive flexibility.
- Some prospective longitudinal research suggests that cognitive flexibility deficits may be a risk marker for BD.
- Youth with BD and other mood pathology show heightened emotional reactions to frustration relative to healthy peers.

in response between the BD and SMD groups suggest that heightened emotional reactions to frustration may be broadly associated with mood pathology rather than specifically linked to BD. Further research that includes additional clinical samples, such as youth with pervasive developmental disorder or schizophrenia, would help clarify this issue.

Neural Correlates of Social Cognitive Deficits in Bipolar Disorder

Recent models of BD conceptualize the condition in terms of dysfunction in two primary neural systems that, as described in Nelson and colleagues' (2005) SIPN framework, are thought to mediate mood regulation/emotion processing and cognitive control functions (Phillips & Vieta, 2007). Indeed, considerable evidence suggests that individuals with BD across the life span show atypically elevated activity in a system that encompasses the amygdala and subcortical structures, combined with abnormally decreased activity in a prefrontal cortical neural system that subserves control processes such as cognitive flexibility (Bearden, Hoffman, & Cannon, 2001; Phillips & Vieta, 2007). The next section presents a review of the literature regarding these two systems as they relate to BD across development, with a focus on studies that have examined neural correlates of social cue perception, specifically facial expression processing, and cognitive or response flexibility.

Neural Differences Associated with Facial Expression Processing in Bipolar Disorder

Given the evidence that impaired processing of social cues such as facial expressions may represent an endophenotype for BD, as well as the importance of accurate and efficient perception and interpretation of such cues for successful social interaction, it is not surprising that a growing body of research has examined neural correlates of this skill in BD. In adults, several studies comparing neural activation during different facial expression processing tasks among healthy controls, actively manic patients with BD (Altshuler et al., 2005), and individuals

with medication-stabilized BD in varying current mood states (Yurgelun-Todd et al., 2000) have yielded a fairly consistent pattern of increased activation in the amygdala and other subcortical regions and decreased prefrontal activation in participants with BD.

Findings have varied across studies, possibly reflecting differences in tasks, facial expressions displayed, and participant characteristics, including clinical state. One study, for example, indicated elevated activity in subcortical structures and prefrontal regions in euthymic and depressed patients with BD relative to both controls and patients with MDD during passive viewing of emotional faces (Lawrence et al., 2004), and another study demonstrated decreased amygdala and subgenual cingulate cortex and increased posterior cingulate cortex and posterior insula activation in manic patients with BD when they rated the intensity of sad faces (Lennox, Jacob, Calder, Lupson, & Bullmore, 2004). Indeed, findings from one study that compared manic BD, depressed BD, and control groups during both implicit and explicit recognition of facial expressions suggest that, although atypical activation is present regardless of mood state in BD, it varies in pattern depending on the task and stimulus used (Chen et al., 2006). Few data are available regarding neural responses to facial expressions in euthymic adults with BD. One study found more hippocampal activation rather than amygdala activation to fearful faces in euthymic adults with BD versus controls (Malhi et al., 2007).

Thus, in adults with BD, the literature points to a pattern of atypical subcortical, typically amygdala or hippocampal, activation in combination with atypical prefrontal activation, with differences across studies and participant mood states in the structures that show hyper- or hypoactivation. More recent research has focused on interactions among different neural systems during facial expression viewing tasks. In manic adults with BD, the ventrolateral prefrontal cortex shows reduced regulation of the amygdala during expression labeling (Foland et al., 2008). Findings from several recent studies suggest that these functional neural anomalies may be ameliorated by medication: Patterns of activation in response to facial expressions during a recognition task changed after treatment with lamotrigine so that patterns among patients with BD more closely resembled those in healthy controls (Haldane et al., 2008; Jogia, Haldane, Cobb, Kumari, & Frangou, 2008). Blumberg and colleagues (2005) obtained similar findings following treatment with varied medications in a sample of 17 adults with BD. A recent review of the literature on medication effects on functional neuroimaging findings in BD, however, suggests that it may be premature to draw conclusions on this front (Phillips, Travis, Fagiolini, & Kupfer, 2008).

Studies examining neural correlates of facial expression processing in youth with BD have focused primarily on older children and adolescents. Neuroimaging studies of younger children are rare, particularly in clinical populations that are likely to find the imaging context stressful and have difficulty lying still in the magnetic resonance imaging (MRI) scanner for long periods of time. Furthermore, although several studies include at least some participants as young as 7 to 8 years, few samples have yet been large enough to permit examination of age or

pubertal status effects. As in the adult literature, sample composition has varied across studies in terms of current mood state, and tasks and target facial expressions have also differed from study to study, rendering direct comparisons of findings difficult. Broadly, however, results have resembled those obtained in research on adults, with atypical activity to emotional faces apparent in subcortical limbic regions and in prefrontal structures.

One study compared patterns of neural activation during passive viewing of emotionally expressive (happy, angry, neutral) faces between euthymic, unmedicated adolescents with BD (mean age, 14.3 years) and healthy comparison participants (mean age, 14.9 years). Relative to the comparison group, adolescents with BD showed decreased activation to angry and happy faces in orbitofrontal and dorsolateral prefrontal regions as well as in the occipital visual cortex. In response to happy faces alone, the BD group showed decreased medial prefrontal activation and greater activation in the right amygdala and bilateral pregenual anterior cingulate cortex (Pavuluri, O'Connor, Harral, & Sweeney, 2007). Another study required participants to rate different characteristics of emotional faces that they then had to identify during a surprise recognition task (Dickstein, Rich, et al., 2007). In this study, adolescents with BD (mean age, 14.2 years) who were either euthymic, depressed, or hypomanic showed increased neural activation relative to controls (mean age, 14.7 years) in the striatum and anterior cingulate cortex in response to happy faces that they recognized later during a memory task and in the orbitofrontal cortex in response to successfully encoded angry faces.

Interestingly, neutral as well as emotional faces appear to elicit differential responses from youth with BD (Rich et al., 2006). In a mixed sample of euthymic, depressed, and hypomanic adolescents with BD, Rich and colleagues (2006) found evidence of greater activation in patients, compared with controls, in the left amygdala, accumbens, putamen, and ventral prefrontal cortex when rating the hostility conveyed by neutral faces. Furthermore, when participants rated their own fear of neutral faces, the BD group showed greater activation in the left amygdala and bilateral accumbens. Participants with BD appeared to perceive the faces more negatively than did controls; they rated neutral faces as more hostile and reported more fear when viewing them. Taken together with Rich, Grimley, and colleagues' (2008) finding that youth with BD were slower than healthy controls to identify emotions depicted on faces as they morphed from neutral to intensely emotional, these results could suggest that, although youth with BD may be biased to perceive ambiguous cues as negative, they have difficulty making finer discriminations among the negative emotions that the cue might convey. Alternatively, this set of findings could indicate that youth with BD are overly sensitive to negative facial expressions across the board.

As in the adult literature, research has started moving away from examination of activation in specific structures in isolation and toward a focus on patterns of connectivity or interaction among brain regions. In one such study, Rich, Fromm, and colleagues (2008) examined functional connectivity between the left amygdala and other neural structures during a task that directed attention toward

emotional and nonemotional aspects of expressive faces in adolescents with BD and controls. Results, which resembled Foland and colleagues' (2008) findings in adults, indicated less functional connectivity between the left amygdala and the right posterior/precuneus region, as well as the right fusiform/parahippocampal gyri, in youth with BD than in controls (Rich, Fromm, et al., 2008).

Findings from research that used emotionally valenced pictures (scenes rather than faces) as stimuli (Eaton et al., 2008) provide preliminary evidence that treatment may alter these patterns of activation in adolescents, as it appears to do in adults. In this study, a small sample (n = 8) of adolescents with BD who were currently in depressive episodes were treated with lamotrigine for 8 weeks, and patterns of neural activation in response to positive and negative pictures before and after treatment were compared. Results indicated that amygdala activation in response to negative images declined from pre- to posttreatment scans in association with clinical improvement. As the authors point out, replication in a controlled sample is needed to evaluate whether other factors, such as habituation, might have influenced changes in activation patterns; however, this study provides an important first step toward more precisely characterizing the effects of successful treatment.

Taken together, the adult and adolescent literatures on neural correlates of facial expression processing in BD provide compelling evidence that subcortical, primarily limbic, and prefrontal systems interact atypically in response to social cues such as expressive faces in the context of the disorder. Although few studies have compared participants across mood states, findings suggest that atypical patterns of activation are present in the context of euthymia as well as mania and depression, but that euthymia achieved via successful treatment may dampen the effects of the disorder. Further research is needed that replicates existing studies in samples of participants in different developmental stages (e.g., comparisons of adults and adolescents with BD) and mood states (e.g., comparisons of manic vs. euthymic participants or within-participant longitudinal research with scans obtained during different mood episodes). Additionally, consistent use of stan-

NEURAL CORRELATES OF FACIAL EXPRESSION PROCESSING

- Both adults and youth with BD show atypical activity to emotional faces in subcortical limbic regions and in prefrontal structures.
- Atypical patterns of activation are present in euthymic as well as manic and depressed individuals.
- Euthymia achieved through successful treatment has been linked to normalization of activation patterns to emotional faces.
- Direct comparisons of activation patterns between individuals with BD in different age groups and mood states as well as standard task procedures across studies are needed to clarify the literature.

dard tasks may help clarify the literature. The diverse array of facial expression processing tasks used in neuroimaging research makes it more difficult to elicit subtly different patterns of neural response than would comparable stimuli.

Neural Differences Associated with Cognitive Flexibility and Related Functions in Bipolar Disorder

The literature on neural correlates of cognitive flexibility and related functions in BD, such as response inhibition and regulation, is less explicitly socioemotional in focus than the facial expressing processing literature. However, in at least a few studies of adults and adolescents, researchers have used tasks that combine cognitive and emotional demands and thus tap underlying skills comparable to those required by effective social interactions. Like studies regarding facial expression processing, research on cognitive flexibility and response inhibition in the context of BD consistently points to the presence of atypical activation in prefrontal and subcortical networks that include limbic and striatal structures, although patterns of anomaly differ among the samples under study.

Studies of cognitive flexibility and response inhibition in adults with BD have typically used modifications of the classic Stroop and go/no-go tasks, which require selective attention, inhibition of prepotent responses, and substitution of alternate responses that demand more effort to generate. In samples of adults with BD who were euthymic (Kronhaus et al., 2006; Lagopoulos & Malhi, 2007; Malhi, Lagopoulos, Sachdev, Ivanovski, & Shnier, 2005) or in varied mood states (Roth et al., 2006; Yurgelun-Todd et al., 2000), activation during emotional and nonemotional variants of the Stroop task differed significantly from that observed in healthy controls. Specifically, across most studies, researchers found evidence of decreased prefrontal activation in patients compared with controls, regardless of the task variant used. The precise location of reduced prefrontal activation varied from study to study; however, findings of attenuated activity in ventral and medial prefrontal regions emerged with some consistency. Notably, one study found evidence of increased dorsolateral prefrontal activation, combined with decreased anterior cingulate activity, in adults with BD versus controls (Yurgelun-Todd et al., 2000), and two studies that focused on depressed adults with BD found no differences from controls in frontal regions during a Stroop measure (Marchand, Lee, Thatcher, Jensen, et al., 2007; Marchand, Lee, Thatcher, Thatcher, et al., 2007). Thus, the literature in adults is not entirely consistent. Task variations, as well as sample differences, may have influenced study outcomes, underscoring the need for consistent use of tasks across studies.

In research that has used go/no-go tasks, findings have varied depending on participants' mood states. In a study of neural activity during emotional versus nonemotional go/no-go tasks, euthymic adults with BD showed increased activation in the orbitofrontal cortex, temporal regions, insula, and both anterior and posterior cingulate cortices relative to healthy controls (Wessa et al., 2007). In contrast, Altshuler and colleagues (2005) found evidence of decreased right orb-

itofrontal cortex, hippocampus, and left cingulate cortex activation in actively manic adults with BD during a nonemotional go/no-go variant. Differences in both tasks and conditions used to construct contrasts, as well as sample differences, probably influenced study findings, which again highlights the need for replication using identical tasks in different samples and task variants in samples that differ according to mood state. Furthermore, explicit incorporation of emotional versus nonemotional stimuli into go/no-go tasks elicits different patterns of neural engagement (Shafritz, Collins, & Blumberg, 2006), which underscores the need for caution in directly comparing findings across studies that use different measures.

In adolescents, research using Stroop tasks has also yielded evidence of atypical neural activation. Patterns of activation difference, however, have been only partially consistent with those observed in most studies of adults. In one study, Blumberg and colleagues (2003) replicated adult findings of increased ventral prefrontal cortical activation in samples of depressed and euthymic adolescents with BD during a Stroop color-naming task; manic participants with BD, in contrast, showed attenuated activation in this region (Blumberg, Leung, et al., 2003). In a second study, the same research group found increased putamen and thalamus activation in adolescents with BD relative to controls during a Stroop color-naming task but no evidence of group differences in prefrontal activation (Blumberg, Martin, et al., 2003). Given that prefrontal regions continue to develop during adolescence and into early adulthood (Gogtay et al., 2004), these findings, in conjunction with those in adults, raise questions about whether developmental factors may influence patterns of atypical neural development in the context of BD.

A series of neuroimaging studies has used the stop signal task, a go/no-go task variant that permits separate examination of successful and unsuccessful response inhibitions and substitutions, to compare neural activation between adolescents with BD and healthy controls (Leibenluft et al., 2007; Nelson et al., 2007). Nelson and colleagues (2007) focused on trials tapping response flexibility, or the successful substitution of an effortful response for a prepotent response. They found that, in the context of comparable task performance, participants with BD showed more activation in the dorsolateral prefrontal cortex and primary motor cortex than did matched controls. In the Leibenluft and colleagues (2007) study, analyses focused instead on failure to correctly inhibit responses and yielded evidence of attenuated striatal and right ventral prefrontal cortex activation in BD patients compared with controls. Taken together, these findings suggest that dysfunction in frontostriatal circuits disrupts regulation of cognitive and motor responses in BD during adolescence.

Little functional neuroimaging research in adolescents with BD has incorporated socioemotional components into cognitive and behavioral flexibility measures. In their 2007 study, however, during which they administered the Affective Posner Task to adolescents with BD, adolescents with SMD, and healthy controls, Rich and colleagues gathered data regarding event-related potentials (ERPs) along

NEURAL CORRELATES OF COGNITIVE FLEXIBILITY

- Results indicate dysfunction of frontostriatal regions in the pathophysiology of BD across development.
- Frontostriatal circuitry may be involved in cognitive, affective, and motor responses: response inhibition, flexibility, planning, or modulating emotions when making choices.
- These pathophysiological findings are not unique to BD but have also been observed in ADHD or obsessive–compulsive disorder.
- Findings are not exclusive to BD, but studies are limited by use of different procedures, lack of control over mood states, and sampling differences.

with the behavioral data discussed earlier. ERP activation patterns differed significantly between youth with BD and members of the other two groups in the frustration condition, with the BD group showing decreases in parietal P3 amplitude. The authors interpreted this finding as suggestive of attentional deficits in the context of frustration in the participants with BD (Rich et al., 2007).

Taken together, the adolescent and adult literatures regarding neural correlates of cognitive flexibility and response inhibition in BD implicate dysfunction in frontostriatal regions in the pathophysiology of the disorder across development. As Blumberg and colleagues (2004) have asserted, however, the manifestations of this dysfunction may vary depending on the timing of disorder onset because of variability in the maturation rates of different structures within frontostriatal circuits. Thus, disorder onset during early adolescence may affect neural activity and behavior differently than does disorder onset in early adulthood (Blumberg et al., 2004).

Notably, comparable findings of atypical activation during cognitive flexibility and response inhibition tasks have been obtained in studies focused on varied clinical groups, such as individuals with ADHD (Smith, Taylor, Brammer, Toone, & Rubia, 2006) and obsessive–compulsive disorder (Gu et al., 2008). This suggests that frontostriatal anomalies may be markers associated broadly with psychopathology rather than with specific disorders. Research comparing patterns of activation between different clinical groups during cognitive flexibility and response inhibition tasks would help to clarify this issue.

Summary, Conclusions, and Further Questions

The preponderance of evidence is consistent with the presence of neurally mediated social cognitive deficits associated with BD. These deficits appear consistently in affected individuals regardless of whether their symptoms emerge early or later in development. Atypical patterns of emotional cue (particularly facial expres-

sion) processing, which have been identified fairly consistently in both euthymic individuals with BD and those at risk for the disorder, are of great interest as potential endophenotypes mediated by functional anomalies in frontolimbic neural circuits. Similarly, cognitive and behavioral inflexibility in social and nonsocial contexts holds promise as a risk-related marker, although more research is needed on this topic in at-risk and euthymic samples. Focus on such discrete and specific aspects of social cognition and behavior is likely to be more fruitful for researchers than examination of broader measures of social function, particularly if the aim is to identify correlates of risk rather than active symptoms. It may also enhance development of specific interventions that target these dysfunctions.

A number of questions remain to be answered if we are to understand and address the functional impact of BD on social behavior and cognition. First, most published research, particularly with regard to neural mechanisms, still focuses on actively ill participants (either those who are currently in mood episodes or remission from such episodes) rather than those at risk for BD. Studies that test the same individuals with BD in different mood states, although difficult to conduct, are critically important for the elucidation of risk and prodromal markers that might inform prevention and early treatment efforts. Numerous research groups are working to fill this gap.

In a groundbreaking study of neural markers of risk, Gogtay and colleagues (2007) gathered longitudinal data regarding brain structure in youth who were undiagnosed but were suspected to have childhood onset schizophrenia. All 32 participants, who underwent repeated structural MRI scans over a 4- to 8-year period, showed diffuse impairment in multiple domains, including emotional and attentional dysregulation at study onset. In a subsample (n = 9) who developed manic episodes in the course of the study, the authors examined patterns of neural change. Results indicated subtle differences from controls, including bilateral decreases in anterior cingulate regions and increases in left temporal structures over time in the youth who developed mania, as well as the nonmanic but impaired participants, who met DSM-IV criteria for psychosis not otherwise specified and ADHD as well as other comorbid disorders (Gogtay et al., 2007). Such research, with a focus on functional and structural changes over time in high-risk youth, is critical if we are to clarify the antecedents of BD and identify markers of risk.

Given the mixed findings regarding broad patterns of social function before illness onset, premorbid neural markers have the potential to be more reliable early indicators of risk for BD. The specificity of such neural markers, however, remains in question: Gogtay and colleagues (2007) obtained similar atypical findings both in youth who developed mania and in those who did not, which could indicate that neural anomalies are generic markers of risk for later impairment.

Second, consistency among researchers in their definitions of BD, particularly pediatric BD, is needed. Although experts in the field increasingly recognize that children and adolescents can show episodic patterns of mood dysfunction that parallel those documented in adults, studies vary in the breadth of their inclusion criteria and the symptoms that they identify as cardinal. Until there is

consensus about a clear, empirically validated phenotype or set of phenotypes for the disorder across development, investigators should articulate the precise criteria according to which participants were identified as having BD. Given the many variations in manifestations of mood dysregulation, particularly among youth (e.g., rapid cycling, predominantly irritable), it is important that research participants be as carefully characterized as possible so that the same diagnostic label is not applied to individuals with related, but diverse, conditions. One framework that has proved useful is Leibenluft, Charney, and colleagues' (2003) distinction between narrow-phenotype BD and severe mood dysregulation, which resembles BD but does not follow the episodic pattern observed in adults. Similarly, Geller and colleagues have defined an ultrarapid cycling phenotype in youth that merits continued study (Tillman & Geller, 2007). Careful attention to different expressions of bipolar spectrum conditions will only advance the field and facilitate the effective treatment of and provision of social support for affected individuals.

Third, it will be important to consider the impact of development on the socioemotional impact of BD. Mixed findings regarding the interpersonal correlates and consequences of actively symptomatic and remitted BD, particularly among youth, may reflect at least in part the different effects that the disorder may have at different ages or during different developmental periods. Symptoms that emerge in early childhood are likely to disrupt different social learning processes compared with those that do not emerge until adolescence or later. Furthermore, the varying social demands that individuals face at different ages as well as the varying amounts of control that they have over their social environments (e.g., whereas children are required to attend school, older adolescents and adults can opt to avoid structured social settings) are likely to interact with BD manifestations to influence the impact of the disorder. Consideration of such developmental differences will be useful as researchers continue to elucidate the social cognitive and behavioral effects of BD across development.

A fourth question that relates closely to the third revolves around the interaction of neural and environmental factors to influence social outcomes in youth and adults with BD. In particular, are there family or community characteristics that might ameliorate or prevent negative outcomes or, conversely, promote them? Not surprisingly, given the difficulty of recruiting sizable samples of youth with or at risk for BD, only recently has research begun to target interactions of environmental and neural factors as predictors of social and functional outcomes, particularly at different points in development. Such work will be critically important not only for the development of preventive approaches (Chang, Howe, Gallelli, & Miklowitz, 2006) but also for the refinement and targeting of existing pharmacological (DelBello & Kowatch, 2006) and empirically based psychosocial treatments (Miklowitz & Otto, 2007). Research regarding outcomes associated with various combinations of neural vulnerabilities and environmental stressors may be especially helpful for clinicians and community support agencies as they

develop and implement preventive and remedial measures aimed at helping families and schools support affected or high-risk youth.

In particular, multisystemic interventions designed to promote resilience, such as those that have been successfully implemented to treat aggressive or conduct-disordered youth (Bierman et al., 2004; Henggeler, Schoenwald, Borduin, Rowland, & Cunningham, 1998) may be able to make effective use of research that integrates environmental and biological perspectives. Multisystemic interventions are family- and community-based approaches to treatment that target factors in the social ecology (family, peers, school, neighborhood, and community) that contribute to problem behavior (Henggeler et al., 1998). Not only do they treat psychological problems as multiply determined and maintained, but they also have demonstrated at least modest long-term success at changing patterns of social behavior and cognition in both peer (Bierman et al., 2004) and family contexts (Curtis, Ronan, & Borduin, 2004). Comparable intervention at multiple levels (pharmacological, psychotherapeutic, family, school, community) in youth with BD, particularly if implemented early in the course of the disorder, might help affected individuals compensate for or remediate the socioemotional problems that commonly accompany their psychiatric symptoms.

Acknowledgments

I would like to thank the editors and Dr. Ellen Leibenluft for helpful feedback on earlier versions of this chapter.

References

Alloy, L. B., Abramson, L. Y., Walshaw, P. D., Keyser, J., & Gerstein, R. K. (2006). A cognitive vulnerability-stress perspective on bipolar spectrum disorders in a normative adolescent brain, cognitive, and emotional development context. *Development and Psychopathology*, *18*(4), 1055–1103.

Altshuler, L. L., Bookheimer, S., Proenza, M. A., Townsend, J., Sabb, F., Firestine, A., et al. (2005). Increased amygdala activation during mania: A functional magnetic resonance imaging study. *American Journal of Psychiatry*, *162*(6), 1211–1213.

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.

Anderson, C. A., & Hammen, C. L. (1993). Psychosocial outcomes of children of unipolar depressed, bipolar, medically ill, and normal women: A longitudinal study. *Journal of Consulting and Clinical Psychology*, *61*(3), 448–454.

Barbas, H. (2007). Flow of information for emotions through temporal and orbitofrontal pathways. *Journal of Anatomy*, *211*(2), 237–249.

Bauman, M. D., Lavenex, P., Mason, W. A., Capitanio, J. P., & Amaral, D. G. (2004). The development of mother–infant interactions after neonatal amygdala lesions in rhesus monkeys. *Journal of Neuroscience*, *24*(3), 711–721.

Bearden, C. E., Hoffman, K. M., & Cannon, T. D. (2001). The neuropsychology and neuro-

anatomy of bipolar affective disorder: A critical review. *Bipolar Disorders*, *3*(3), 106–150; discussion 151–103.

Biederman, J., Klein, R. G., Pine, D. S., & Klein, D. F. (1998). Resolved: Mania is mistaken for ADHD in prepubertal children. *Journal of the American Academy of Child and Adolescent Psychiatry*, *37*, 1091–1096; discussion, 1096–1099.

Bierman, K. L., Coie, J. D., Dodge, K. A., Foster, E. M., Greenberg, M. T., Lochman, J. E., et al. (2004). The effects of the fast track program on serious problem outcomes at the end of elementary school. *Journal of Clinical Child and Adolescent Psychology*, *33*(4), 650–661.

Blakemore, S.-J. (2008). Development of the social brain during adolescence. *Quarterly Journal of Experimental Psychology*, *61*(1), 40–49.

Blumberg, H., Donegan, N., Sanislow, C., Collins, S., Lacadie, C., Skudlarski, P., et al. (2005). Preliminary evidence for medication effects on functional abnormalities in the amygdala and anterior cingulate in bipolar disorder. *Psychopharmacology*, *183*(3), 308–313.

Blumberg, H. P., Kaufman, J., Martin, A., Charney, D. S., Krystal, J. H., & Peterson, B. S. (2004). Significance of adolescent neurodevelopment for the neural circuitry of bipolar disorder. *Annals of the New York Academy of Sciences*, *1021*(1), 376–383.

Blumberg, H. P., Leung, H.-C., Skudlarski, P., Lacadie, C. M., Fredericks, C. A., Harris, B. C., et al. (2003). A functional magnetic resonance imaging study of bipolar disorder: State- and trait-related dysfunction in ventral prefrontal cortices. *Archives of General Psychiatry*, *60*(6), 601–609.

Blumberg, H. P., Martin, A., Kaufman, J., Leung, H.-C., Skudlarski, P., Lacadie, C., et al. (2003). Frontostriatal abnormalities in adolescents with bipolar disorder: Preliminary observations from functional MRI. *American Journal of Psychiatry*, *160*(7), 1345–1347.

Bora, E., Vahip, S., Gonul, A. S., Akdeniz, F., Alkan, M., Ogut, M., et al. (2005). Evidence for theory of mind deficits in euthymic patients with bipolar disorder. *Acta Psychiatrica Scandinavica*, *112*(2), 110–116.

Bozikas, V. P., Andreou, C., Giannakou, M., Tonia, T., Anezoulaki, D., Karavatos, A., et al. (2005). Deficits in sustained attention in schizophrenia but not in bipolar disorder. *Schizophrenia Research*, *78*(2–3), 225–233.

Brotman, M. A., Guyer, A. E., Lawson, E. S., Horsey, S. E., Rich, B. A., Dickstein, D. P., et al. (2008). Facial emotion labeling deficits in children and adolescents at risk for bipolar disorder. *American Journal of Psychiatry*, *165*(3), 385–389.

Brotman, M. A., Kassem, L., Reising, M. M., Guyer, A. E., Dickstein, D. P., Rich, B. A., et al. (2007). Parental diagnoses in youth with narrow phenotype bipolar disorder or severe mood dysregulation. *American Journal of Psychiatry*, *164*(8), 1238–1241.

Cannon, M., Jones, P., Gilvarry, C., Rifkin, L., McKenzie, K., Foerster, A., et al. (1997). Premorbid social functioning in schizophrenia and bipolar disorder: Similarities and differences. *American Journal of Psychiatry*, *154*(11), 1544–1550.

Carpenter, M., Nagell, K., & Tomasello, M. (1998). Social cognition, joint attention, and communicative competence from 9 to 15 months of age. *Monographs of the Society for Research in Child Development*, *63*(4), 1–143.

Chang, K., Howe, M., Gallelli, K. I. M., & Miklowitz, D. (2006). Prevention of pediatric bipolar disorder: Integration of neurobiological and psychosocial processes. *Annals of the New York Academy of Sciences*, *1094*(1), 235–247.

Chen, C.-H., Lennox, B., Jacob, R., Calder, A., Lupson, V., Bisbrown-Chippendale, R., et al. (2006). Explicit and implicit facial affect recognition in manic and depressed states of bipolar disorder: A functional magnetic resonance imaging study. *Biological Psychiatry*, *59*(1), 31–39.

Cools, R., Clark, L., & Robbins, T. W. (2004). Differential responses in human striatum and

prefrontal cortex to changes in object and rule relevance. *Journal of Neuroscience*, *24*(5), 1129–1135.

Crick, N. R., & Dodge, K. A. (1994). A review and reformulation of social information-processing mechanisms in children's social adjustment. *Psychological Bulletin*, *115*(1), 74–101.

Curtis, N. M., Ronan, K. R., & Borduin, C. M. (2004). Multisystemic treatment: A meta-analysis of outcome studies. *Journal of Family Psychology*, *18*(3), 411–419.

De Los Reyes, A., & Kazdin, A. E. (2006). Informant discrepancies in assessing child dysfunction relate to dysfunction within mother–child interactions. *Journal of Child and Family Studies*, *15*(5), 645–663.

DelBello, M. P., & Kowatch, R. A. (2006). Pharmacological interventions for bipolar youth: Developmental considerations. *Development and Psychopathology*, *18*, 1231–1246.

Dickstein, D. P., Nelson, E. E., McClure, E. B., Grimley, M. E., Knopf, L., Brotman, M. A., et al. (2007). Cognitive flexibility in phenotypes of pediatric bipolar disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *46*(3), 341–355.

Dickstein, D. P., Rich, B. A., Roberson-Nay, R., Berghorst, L., Vinton, D., Pine, D. S., et al. (2007). Neural activation during encoding of emotional faces in pediatric bipolar disorder. *Bipolar Disorders*, *9*(7), 679–692.

Eaton, W. W., Shao, H., Nestadt, G., Lee, B. H., Bienvenu, O. J., & Zandi, P. (2008). Population-based study of first onset and chronicity in major depressive disorder. *Archives of General Psychiatry*, *65*(5), 513–520.

Edvardsen, J., Torgersen, S., Roysamb, E., Lygren, S., Skre, I., Onstad, S., et al. (2008). Heritability of bipolar spectrum disorders. Unity or heterogeneity? *Journal of Affective Disorders*, *106*(3), 229–240.

Fagiolini, A., Kupfer, D. J., Masalehdan, A., Scott, J. A., Houck, P. R., & Frank, E. (2005). Functional impairment in the remission phase of bipolar disorder. *Bipolar Disorders*, *7*(3), 281–285.

Fleck, D. E., Shear, P. K., Zimmerman, M. E., Getz, G. E., Corey, K. B., Jak, A., et al. (2003). Verbal memory in mania: Effects of clinical state and task requirements. *Bipolar Disorders*, *5*(5), 375–380.

Foland, L. C., Altshuler, L. L., Bookheimer, S. Y., Eisenberger, N., Townsend, J., & Thompson, P. M. (2008). Evidence for deficient modulation of amygdala response by prefrontal cortex in bipolar mania. *Psychiatry Research: Neuroimaging*, *162*(1), 27–37.

Fullerton, C. S., & Ursano, R. J. (1994). Preadolescent peer friendships: A critical contribution to adult social relatedness? *Journal of Youth and Adolescence*, *23*(1), 43–63.

Galanter, C. A., & Leibenluft, E. (2008). Frontiers between attention deficit hyperactivity disorder and bipolar disorder. *Child and Adolescent Psychiatric Clinics of North America*, *17*(2), 325–346.

Geller, B., Bolhofner, K., Craney, J. L., Williams, M., DelBello, M. P., & Gundersen, K. (2000). Psychosocial functioning in a prepubertal and early adolescent bipolar disorder phenotype. *Journal of the American Academy of Child and Adolescent Psychiatry*, *39*(12), 1543–1548.

Geller, B., Craney, J. L., Bolhofner, K., DelBello, M. P., Axelson, D., Luby, J., et al. (2003). Phenomenology and longitudinal course of children with a prepubertal and early adolescent bipolar disorder phenotype. In B. Geller & M. P. DelBello (Eds.), *Bipolar disorder in childhood and early adolescence* (pp. 25–50). New York: Guilford Press.

Geller, B., Craney, J. L., Bolhofner, K., Nickelsburg, M. J., Williams, M., & Zimerman, B. (2002). Two-year prospective follow-up of children with a prepubertal and early adolescent bipolar disorder phenotype. *American Journal of Psychiatry*, *159*(6), 927–933.

Getz, G. E., Shear, P. K., & Strakowski, S. M. (2003). Facial affect recognition deficits in bipolar disorder. *Journal of the International Neuropsychological Society*, *9*(4), 623–632.

Giedd, J. N. (2004). Structural magnetic resonance imaging of the adolescent brain. *Annals of the New York Academy of Sciences*, *1021*(1), 77–85.

Giedd, J. N., Castellanos, F. X., Rajapakse, J. C., Vaituzis, A. C., & Rapoport, J. L. (1997). Sexual dimorphism of the developing human brain. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *21*(8), 1185–1201.

Gogtay, N., Giedd, J. N., Lusk, L., Hayashi, K. M., Greenstein, D., Vaituzis, A. C., et al. (2004). Dynamic mapping of human cortical development during childhood through early adulthood. *Proceedings of the National Academy of Sciences USA*, *101*(21), 8174–8179.

Gogtay, N., Ordonez, A., Herman, D. H., Hayashi, K. M., Greenstein, D., Vaituzis, C., et al. (2007). Dynamic mapping of cortical development before and after the onset of pediatric bipolar illness. *Journal of Child Psychology and Psychiatry*, *48*(9), 852–862.

Goldstein, T. R., Miklowitz, D. J., & Mullen, K. L. (2006). Social skills knowledge and performance among adolescents with bipolar disorder. *Bipolar Disorders*, *8*(4), 350–361.

Goursaud, A.-P. S., & Bachevalier, J. (2007). Social attachment in juvenile monkeys with neonatal lesion of the hippocampus, amygdala and orbital frontal cortex. *Behavioural Brain Research*, *176*(1), 75–93.

Gu, B.-M., Park, J.-Y., Kang, D.-H., Lee, S. J., Yoo, S. Y., Jo, H. J., et al. (2008). Neural correlates of cognitive inflexibility during task-switching in obsessive–compulsive disorder. *Brain*, *131*(1), 155–164.

Guyer, A. E., McClure, E. B., Adler, A. D., Brotman, M. A., Rich, B. A., Kimes, A. S., et al. (2007). Specificity of facial expression labeling deficits in childhood psychopathology. *Journal of Child Psychology and Psychiatry*, *48*(9), 863–871.

Haldane, M., Jogia, J., Cobb, A., Kozuch, E., Kumari, V., & Frangou, S. (2008). Changes in brain activation during working memory and facial recognition tasks in patients with bipolar disorder with lamotrigine monotherapy. *European Neuropsychopharmacology*, *18*(1), 48–54.

Halit, H., Csibra, G., Volein, A., & Johnson, M. H. (2004). Face-sensitive cortical processing in early infancy. *Journal of Child Psychology and Psychiatry*, *45*(7), 1228–1234.

Halit, H., de Haan, M., & Johnson, M. H. (2003). Cortical specialisation for face processing: Face-sensitive event-related potential components in 3- and 12-month-old infants. *NeuroImage*, *19*(3), 1180–1193.

Heaton, R. K., Chelune, G. J., Talley, J., Kay, K. K., & Curtiss, G. (1993). *Wisconsin Card Sorting Test manual*. Odessa, FL: Psychological Assessment Resources.

Henggeler, S. W., Schoenwald, S. K., Borduin, C. M., Rowland, M. D., & Cunningham, P. B. (1998). *Multisystemic treatment of antisocial behavior in children and adolescents*. New York: Guilford Press.

Hillegers, M. H. J., Burger, H., Wals, M., Reichart, C. G., Verhulst, F. C., Nolen, W. A., et al. (2004). Impact of stressful life events, familial loading and their interaction on the onset of mood disorders: Study in a high-risk cohort of adolescent offspring of parents with bipolar disorder. *British Journal of Psychiatry*, *185*(2), 97–101.

Iacono, W. G., Peloquin, L. J., Lumry, A. E., Valentine, R. H., & Tuason, V. B. (1982). Eye tracking in patients with unipolar and bipolar affective disorders in remission. *Journal of Abnormal Psychology*, *91*(1), 35–44.

Jogia, J., Haldane, M., Cobb, A., Kumari, V., & Frangou, S. (2008). Pilot investigation of the changes in cortical activation during facial affect recognition with lamotrigine monotherapy in bipolar disorder. *British Journal of Psychiatry*, *192*(3), 197–201.

Johnson, M. H., Griffin, R., Csibra, G., Halit, H., Farroni, de Haan, M., et al. (2005). The

emergence of the social brain network: Evidence from typical and atypical development. *Development and Psychopathology*, *17*(3), 599–619.

Jones, D. C., Abbey, B. B., & Cumberland, A. (1998). The development of display rule knowledge: Linkages with family expressiveness and social competence. *Child Development*, *69*(4), 1209–1222.

Kerr, N., Dunbar, R. I. M., & Bentall, R. P. (2003). Theory of mind deficits in bipolar affective disorder. *Journal of Affective Disorders*, *73*(3), 253–259.

Kliewer, W., Fearnow, M. D., & Miller, P. A. (1996). Coping socialization in middle childhood: Tests of maternal and paternal influences. *Child Development*, *67*(5), 2339–2357.

Kronhaus, D. M., Lawrence, N. S., Williams, A. M., Frangou, S., Brammer, M. J., Williams, S. C. R., et al. (2006). Stroop performance in bipolar disorder: Further evidence for abnormalities in the ventral prefrontal cortex. *Bipolar Disorders*, *8*(1), 28–39.

Kutcher, S., Robertson, H. A., & Bird, D. (1998). Premorbid functioning in adolescent onset bipolar I disorder: A preliminary report from an ongoing study. *Journal of Affective Disorders*, *51*(2), 137–144.

Lagattuta, K. H. (2005). When you shouldn't do what you want to do: Young children's understanding of desires, rules, and emotions. *Child Development*, *76*(3), 713–733.

Lagopoulos, J., & Malhi, G. S. (2007). A functional magnetic resonance imaging study of emotional Stroop in euthymic bipolar disorder. *NeuroReport*, *18*(15), 1583–1587.

Lawrence, N. S., Williams, A. M., Surguladze, S., Giampietro, V., Brammer, M. J., Andrew, C., et al. (2004). Subcortical and ventral prefrontal cortical neural responses to facial expressions distinguish patients with bipolar disorder and major depression. *Biological Psychiatry*, *55*(6), 578–587.

Leibenluft, E., Blair, R. J., Charney, D. S., & Pine, D. S. (2003). Irritability in pediatric mania and other childhood psychopathology. *Annals of the New York Academy of Sciences*, *1008*, 201–218.

Leibenluft, E., Charney, D. S., Towbin, K. E., Bhangoo, R. K., & Pine, D. S. (2003). Defining clinical phenotypes of juvenile mania. *American Journal of Psychiatry*, *160*(3), 430–437.

Leibenluft, E., Cohen, P., Gorrindo, T., Brook, J. S., & Pine, D. S. (2006). Chronic versus episodic irritability in youth: A community-based, longitudinal study of clinical and diagnostic associations. *Journal of Child and Adolescent Psychopharmacology*, *16*(4), 456–466.

Leibenluft, E., Rich, B. A., Vinton, D. T., Nelson, E. E., Fromm, S. J., Berghorst, L. H., et al. (2007). Neural circuitry engaged during unsuccessful motor inhibition in pediatric bipolar disorder. *American Journal of Psychiatry*, *164*(1), 52–60.

Lembke, A., & Ketter, T. A. (2002). Impaired recognition of facial emotion in mania. *American Journal of Psychiatry*, *159*(2), 302–304.

Lennox, B. R., Jacob, R., Calder, A. J., Lupson, V., & Bullmore, E. T. (2004). Behavioural and neurocognitive responses to sad facial affect are attenuated in patients with mania. *Psychological Medicine*, *34*(5), 795–802.

Lewinsohn, P. M., Steinmetz, J. L., Larson, D. W., & Franklin, J. (1981). Depression-related cognitions: Antecedent or consequence? *Journal of Abnormal Psychology*, *90*, 213–219.

Lezak, M. D. (2004). *Neuropsychological assessment* (4th ed.). New York: Oxford University Press.

Liu, S. K., Chiu, C.-H., Chang, C.-J., Hwang, T.-J., Hwu, H.-G., & Chen, W. J. (2002). Deficits in sustained attention in schizophrenia and affective disorders: Stable versus state-dependent markers. *American Journal of Psychiatry*, *159*(6), 975–982.

Logan, G. D., Schachar, R. J., & Tannock, R. (1997). Impulsivity and inhibitory control. *Psychological Science*, *8*(1), 60–64.

MacQueen, G. M., Young, L. T., & Joffe, R. T. (2001). A review of psychosocial outcome in patients with bipolar disorder. *Acta Psychiatrica Scandinavica*, *103*(3), 163–170.

Malhi, G. S., Lagopoulos, J., Sachdev, P. S., Ivanovski, B., & Shnier, R. (2005). An emotional Stroop functional MRI study of euthymic bipolar disorder. *Bipolar Disorders*, *7*(Suppl. 5), 58–69.

Malhi, G. S., Lagopoulos, J., Sachdev, P. S., Ivanovski, B., Shnier, R., & Ketter, T. (2007). Is a lack of disgust something to fear? A functional magnetic resonance imaging facial emotion recognition study in euthymic bipolar disorder patients. *Bipolar Disorders*, *9*(4), 345–357.

Marchand, W. R., Lee, J. N., Thatcher, G. W., Jensen, C., Stewart, D., Dilda, V., et al. (2007). A functional MRI study of a paced motor activation task to evaluate frontal-subcortical circuit function in bipolar depression. *Psychiatry Research: Neuroimaging*, *155*(3), 221–230.

Marchand, W. R., Lee, J. N., Thatcher, J., Thatcher, G. W., Jensen, C., & Starr, J. (2007). A preliminary longitudinal fMRI study of frontal-subcortical circuits in bipolar disorder using a paced motor activation paradigm. *Journal of Affective Disorders*, *103*(1–3), 237–241.

Martínez-Arán, A., Vieta, E., Reinares, M., Colom, F., Torrent, C., Sánchez-Moreno, J., et al. (2004). Cognitive function across manic or hypomanic, depressed, and euthymic states in bipolar disorder. *American Journal of Psychiatry*, *161*(2), 262–270.

McClure, E. B. (2000). A meta-analytic review of sex differences in facial expression processing and their development in infants, children, and adolescents. *Psychological Bulletin*, *126*(3), 424–453.

McClure, E. B., Pope, K., Hoberman, A. J., Pine, D. S., & Leibenluft, E. (2003). Facial expression recognition in adolescents with mood and anxiety disorders. *American Journal of Psychiatry*, *160*(6), 1172–1174.

McClure, E. B., Treland, J. E., Snow, J., Schmajuk, M., Dickstein, D. P., Towbin, K. E., et al. (2005). Deficits in social cognition and response flexibility in pediatric bipolar disorder. *American Journal of Psychiatry*, *162*(9), 1644–1651.

Meyer, S. E., Carlson, G. A., Wiggs, E. A., Martinez, P. E., Ronsaville, D. S., Klimes-Dougan, B., et al. (2004). A prospective study of the association among impaired executive functioning, childhood attentional problems, and the development of bipolar disorder. *Development and Psychopathology*, *16*(2), 461–476.

Meyer, S. E., Carlson, G. A., Wiggs, E. A., Ronsaville, D. S., Martinez, P. E., Klimes-Dougan, B., et al. (2006). A prospective high-risk study of the association among maternal negativity, apparent frontal lobe dysfunction, and the development of bipolar disorder. *Development and Psychopathology*, *18*(2), 573–589.

Miklowitz, D. J., & Otto, M. W. (2007). Psychosocial interventions for bipolar disorder: A review of literature and introduction of the systematic treatment enhancement program. *Psychopharmacology Bulletin*, *40*(4), 116–131.

Milligan, K., Astington, J. W., & Dack, L. A. (2007). Language and theory of mind: Meta-analysis of the relation between language ability and false-belief understanding. *Child Development*, *78*(2), 622–646.

Morriss, R., Scott, J., Paykel, E., Bentall, R., Hayhurst, H., & Johnson, T. (2007). Social adjustment based on reported behaviour in bipolar affective disorder. *Bipolar Disorders*, *9*(1–2), 53–62.

Mur, M., Portella, M. J., Martínez-Arán, A., Pifarré, J., & Vieta, E. (2007). Persistent neuropsychological deficit in euthymic bipolar patients: Executive function as a core deficit. *Journal of Clinical Psychiatry*, *68*(7), 1078–1086.

Nelson, E. E., Leibenluft, E., McClure, E. B., & Pine, D. S. (2005). The social re-orientation of adolescence: A neuroscience perspective on the process and its relation to psychopathology. *Psychological Medicine, 35*(2), 163–174.

Nelson, E. E., Vinton, D. T., Berghorst, L., Towbin, K. E., Hommer, R. E., Dickstein, D. P., et al. (2007). Brain systems underlying response flexibility in healthy and bipolar adolescents: An event-related fMRI study. *Bipolar Disorders*, *9*(8), 810–819.

Nuechterlein, K. H., & Dawson, M. E. (1984). A heuristic vulnerability/stress model of schizophrenic episodes. *Schizophrenia Bulletin*, *10*(2), 300–312.

Paterson, S. J., Heim, S., Friedman, J. T., Choudhury, N., & Benasich, A. A. (2006). Development of structure and function in the infant brain: Implications for cognition, language and social behaviour. *Neuroscience and Biobehavioral Reviews, 30*(8), 1087–1105.

Pavuluri, M. N., O'Connor, M. M., Harral, E., & Sweeney, J. A. (2007). Affective neural circuitry during facial emotion processing in pediatric bipolar disorder. *Biological Psychiatry*, *62*(2), 158–167.

Perlis, R. H., Smoller, J. W., Fava, M., Rosenbaum, J. F., Nierenberg, A. A., & Sachs, G. S. (2004). The prevalence and clinical correlates of anger attacks during depressive episodes in bipolar disorder. *Journal of Affective Disorders*, *79*(1–3), 291–295.

Petti, T., Reich, W., Todd, R. D., Joshi, P., Galvin, M., Reich, T., et al. (2004). Psychosocial variables in children and teens of extended families identified through bipolar affective disorder probands. *Bipolar Disorders*, *6*(2), 106–114.

Phillips, M. L., Travis, M. J., Fagiolini, A., & Kupfer, D. J. (2008). Medication effects in neuroimaging studies of bipolar disorder. *American Journal of Psychiatry*, *165*(3), 313–320.

Phillips, M. L., & Vieta, E. (2007). Identifying functional neuroimaging biomarkers of bipolar disorder: Toward DSM-V. *Schizophrenia Bulletin*, *33*(4), 893–904.

Pine, D. S., Guyer, A. E., Goldwin, M., Towbin, K. A., & Leibenluft, E. (2008). Autism spectrum disorder scale scores in pediatric mood and anxiety disorders. *Journal of the American Academy of Child and Adolescent Psychiatry*, *47*(6), 652–661.

Pollak, S. D., & Tolley-Schell, S. A. (2003). Selective attention to facial emotion in physically abused children. *Journal of Abnormal Psychology*, *112*(3), 323–338.

Pope, M., Dudley, R., & Scott, J. (2007). Determinants of social functioning in bipolar disorder. *Bipolar Disorders*, *9*(1), 38–44.

Reichart, C. G., van der Ende, J., Wals, M., Hillegers, M. H. J., Nolen, W. A., Ormel, J., et al. (2007). Social functioning of bipolar offspring. *Journal of Affective Disorders*, *98*(3), 207–213.

Reisman, J. M. (1985). Friendship and its implications for mental health or social competence. *Journal of Early Adolescence*, *5*(3), 383–391.

Rich, B. A., Fromm, S. J., Berghorst, L. H., Dickstein, D. P., Brotman, M. A., Pine, D. S., et al. (2008). Neural connectivity in children with bipolar disorder: Impairment in the face emotion processing circuit. *Journal of Child Psychology and Psychiatry*, *49*(1), 88–96.

Rich, B. A., Grimley, M. E., Schmajuk, M., Blair, K. S., Blair, R. J., & Leibenluft, E. (2008). Face emotion labeling deficits in children with bipolar disorder and severe mood dysregulation. *Development and Psychopathology*, *20*(2), 529–546.

Rich, B. A., Schmajuk, M., Perez-Edgar, K. E., Fox, N. A., Pine, D. S., & Leibenluft, E. (2007). Different psychophysiological and behavioral responses elicited by frustration in pediatric bipolar disorder and severe mood dysregulation. *American Journal of Psychiatry*, *164*(2), 309–317.

Rich, B. A., Vinton, D. T., Roberson-Nay, R., Hommer, R. E., Berghorst, L. H., McClure, E. B., et al. (2006). Limbic hyperactivation during processing of neutral facial expressions in children with bipolar disorder. *Proceedings of the National Academy of Sciences USA*, *103*(23), 8900–8905.

Robbins, T. W., James, M., Owen, A. M., Sahakian, B. J., Lawrence, A. D., McInnes, L., et al. (1998). A study of performance on tests from the CANTAB battery sensitive to frontal lobe dysfunction in a large sample of normal volunteers: Implications for theories of

executive functioning and cognitive aging. *Journal of the International Neuropsychological Society*, *4*(5), 474–490.

Robertson, H. A., Kutcher, S. P., Bird, D., & Grasswick, L. (2001). Impact of early onset bipolar disorder on family functioning: Adolescents' perceptions of family dynamics, communication, and problems. *Journal of Affective Disorders*, *66*(1), 25–37.

Roth, R. M., Koven, N. S., Randolph, J. J., Flashman, L. A., Pixley, H. S., Ricketts, S. M., et al. (2006). Functional magnetic resonance imaging of executive control in bipolar disorder. *NeuroReport*, *17*(11), 1085–1089.

Rucklidge, J. J. (2006). Psychosocial functioning of adolescents with and without paediatric bipolar disorder. *Journal of Affective Disorders*, *91*(2), 181–188.

Rydell, A.-M., Thorell, L. B., & Bohlin, G. (2007). Emotion regulation in relation to social functioning: An investigation of child self-reports. *European Journal of Developmental Psychology*, *4*(3), 293–313.

Schenkel, L. S., Marlow-O'Connor, M., Moss, M., Sweeney, J. A., & Pavuluri, M. N. (2008). Theory of mind and social inference in children and adolescents with bipolar disorder. *Psychological Medicine*, *38*, 791–800.

Schenkel, L. S., Pavuluri, M. N., Herbener, E. S., Harral, E. M., & Sweeney, J. A. (2007). Facial emotion processing in acutely ill and euthymic patients with pediatric bipolar disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *46*(8), 1070–1079.

Schenkel, L. S., West, A. E., Harral, E. M., Patel, N. B., & Pavuluri, M. N. (2008). Parent–child interactions in pediatric bipolar disorder. *Journal of Clinical Psychology*, *64*(4), 422–437.

Schwanenflugel, P. J., Fabricius, W. V., & Alexander, J. (1994). Developing theories of mind: Understanding concepts and relations between mental activities. *Child Development*, *65*(6), 1546–1563.

Scott, J., Stanton, B., Garland, A., & Ferrier, I. N. (2000). Cognitive vulnerability in patients with bipolar disorder. *Psychological Medicine*, *30*(2), 467–472.

Shafritz, K. M., Collins, S. H., & Blumberg, H. P. (2006). The interaction of emotional and cognitive neural systems in emotionally guided response inhibition. *NeuroImage*, *31*(1), 468–475.

Simon, G. E., Bauer, M. S., Ludman, E. J., Operskalski, B. H., & Unutzer, J. (2007). Mood symptoms, functional impairment, and disability in people with bipolar disorder: Specific effects of mania and depression. *Journal of Clinical Psychiatry*, *68*(8), 1237–1245.

Smith, A. B., Taylor, E., Brammer, M., Toone, B., & Rubia, K. (2006). Task-specific hypoactivation in prefrontal and temporoparietal brain regions during motor inhibition and task switching in medication-naive children and adolescents with attention deficit hyperactivity disorder. *American Journal of Psychiatry*, *163*(6), 1044–1051.

Soutullo, C. A., Chang, K. D., Díez-Suárez, A., Figueroa-Quintana, A., Escamilla-Canales, I., Rapado-Castro, M., et al. (2005). Bipolar disorder in children and adolescents: International perspective on epidemiology and phenomenology. *Bipolar Disorders*, *7*(6), 497–506.

Sowell, E. R., Trauner, D. A., Gamst, A., & Jernigan, T. L. (2002). Development of cortical and subcortical brain structures in childhood and adolescence: A structural MRI study. *Developmental Medicine and Child Neurology*, *44*(1), 4–16.

St. James-Roberts, I., & Plewis, I. (1996). Individual differences, daily fluctuations, and developmental changes in amounts of infant waking, fussing, crying, feeding, and sleeping. *Child Development*, *67*(5), 2527–2540.

Staton, D., Volness, L. J., & Beatty, W. W. (2008). Diagnosis and classification of pediatric bipolar disorder. *Journal of Affective Disorders*, *105*(1), 205–212.

Sullivan, H. S. (1953). *The interpersonal theory of psychiatry*. New York: Norton.

Tamir, M., Mitchell, C., & Gross, J. J. (2008). Hedonic and instrumental motives in anger regulation. *Psychological Science*, *19*(4), 324–328.

Tillman, R., & Geller, B. (2007). Diagnostic characteristics of child bipolar I disorder: Does the "treatment of early age mania (team)" sample generalize? *Journal of Clinical Psychiatry*, *68*(2), 307–314.

Tillman, R., Geller, B., Craney, J. L., Bolhofner, K., Williams, M., Zimerman, B., et al. (2003). Temperament and character factors in a prepubertal and early adolescent bipolar disorder phenotype compared to attention deficit hyperactive and normal controls. *Journal of Child and Adolescent Psychopharmacology*, *13*(4), 531–543.

Towbin, K. E., Pradella, A., Gorrindo, T., Pine, D. S., & Leibenluft, E. (2005). Autism spectrum traits in children with mood and anxiety disorders. *Journal of Child and Adolescent Psychopharmacology*, *15*(3), 452–464.

Wellman, H. M., Lopez-Duran, S., LaBounty, J., & Hamilton, B. (2008). Infant attention to intentional action predicts preschool theory of mind. *Developmental Psychology*, *44*(2), 618–623.

Wessa, M., Houenou, J., Paillere-Martinot, M.-L., Berthoz, S., Artiges, E., Leboyer, M., et al. (2007). Fronto-striatal overactivation in euthymic bipolar patients during an emotional go/nogo task. *American Journal of Psychiatry*, *164*(4), 638–646.

Youngstrom, E. A., Birmaher, B., & Findling, R. L. (2008). Pediatric bipolar disorder: Validity, phenomenology, and recommendations for diagnosis. *Bipolar Disorders*, *10*, 194–214.

Yurgelun-Todd, D. A., Gruber, S. A., Kanayama, G., Killgore, W. D., Baird, A. A., & Young, A. D. (2000). fMRI during affect discrimination in bipolar affective disorder. *Bipolar Disorders*, *2*(3, Pt. 2), 237–248.