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Social neuroscience of child and adolescent depression

Anita Miller

Department of Psychology, Skidmore College, USA

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Abstract

The social neuroscience of child and adolescent depression is inherently multidisciplinary. Depressive disorders beginning early in life can have serious developmental and functional consequences. Psychopathology research has described depression's defining clinical and contextual features, and intervention research has characterized its response to treatment and prevention programs. Neuroendocrine, electrophysiological, and neuroimaging studies have identified core neurobiological aspects of early-onset mood disorders. These areas are reviewed using a developmental social neuroscience perspective for integrating disparate observations. The paper introduces a dynamic adaptive systems framework, and it discusses hedonic capacity, stress sensitivity, ruminative self-focus, and attentional impairments as fundamental components of mood disorders.

Keywords: Mood disorders; Major depression; Risk factors; Developmental systems; Psychological adaptation

1. Introduction

Neuroscience focuses on the intricate details of nervous system anatomy and physiology. Social development largely concerns how youngsters interpret contextual experiences, such as emotional events and interactions. Developmental social neuroscience integrates the elaborate details of neurobiology with the multifaceted context of childhood experiences. This multidisciplinary perspective can be particularly fruitful for understanding the early development of emotions and emotional disorders (Allen & Badcock, 2003; Cacioppo, 2002; Dahl, 2004; Davidson et al., 2002; Gunnar, 2003; Harmon-Jones & Devine, 2003; Nelson et al., 2002; Ochsner, 2004; Schmidt & Schulkin, 2000). The current paper focuses specifically on the social neuroscience of depressive disorders beginning during childhood or adolescence.

A growing scientific literature addresses the functional neurobiology of early-onset depressive disorders. Using neuroendocrine, electrophysiological, and neuroimaging assessments, investigators seek neurobiological correlates of depressive disorders, with the ultimate goal of disentangling the causes and consequences of the initial onset of affective illness. However, biological observations from isolated studies can be difficult to interpret, and findings across studies often vary. This paper argues that neurobiological studies of child and adolescent depression can benefit from a multidisciplinary research perspective that integrates not only principles of social neuroscience but also empirical findings from the clinical research literature. In particular, developmental psychopathology research has described the clinical and contextual features of early-onset depression, and intervention studies have characterized responses to prevention and treatment programs. After introducing the basic nosology of early-onset depression, this paper reviews relevant psychopathology, intervention, and neurobiological research. Although space constraints limit detailed methodological discussions of individual studies, the review emphasizes replicated empirical findings and notes fundamental research design principles. The paper then introduces a developmental social neuroscience perspective about early-onset depression. The central goal is to organize the fundamental features of depression in a

E-mail address: amiller@skidmore.edu

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manner that generates testable alternative hypotheses about relations among psychopathology, intervention, and neurobiology within a developmental framework.

2. Nosology of child and adolescent depression

From a psychiatric diagnostic perspective, depressive disorders include a heterogeneous group of conditions, most of which have been recognized in children and adolescents since the late 1970s (see Cicchetti & Toth, 1998; Kovacs, 1997a). Before the late 1970s, sadness in youngsters was often assumed to be a transient emotional response to difficult circumstances that differed fundamentally from the syndrome of major depressive disorder in adulthood. Research in this area shifted fundamentally with the development and use of semi-structured interviews (Chambers et al., 1985; Hien et al., 1998; Sherrill & Kovacs, 2000) and the application of operational diagnostic criteria for depression in youths, as specified in the third and subsequent revisions of the Diagnostic and Statistical Manual of the Mental Disorders (DSM-III, DSM-IIIR, DSM-IV; APA, 1980, 1987, 1994). The current paper focuses specifically on studies that used such standardized diagnostic criteria for defining depression in youngsters.

The criteria for major depressive disorder in youths have remained essentially unchanged from the DSM-III through DSM-IV. Major depression is defined by a combination of protracted dysphoria, anhedonia, or irritability along with a cluster of other symptoms including dysregulated sleep (e.g., insomnia, hypersomnia, fatigue), eating (e.g., appetite change, weight loss, failure to make expected weight gains), motor behavior (e.g., psychomotor retardation, agitation, or restlessness), thought (e.g., distractibility, indecisiveness, hopelessness), and self-esteem (e.g., feelings of worthlessness or guilt and suicidal ideation). To be diagnosed with major depression, a youth must have at least five such co-occurring symptoms for at least two weeks (APA, 1994). Dysthymic disorder is a symptomatically less severe but temporally more protracted form of depression. The criteria have changed significantly from DSM-III to DSM-IV. DSM-IV criteria require that depressed mood and two or more associated symptoms last for at least one year in youths, along with personal distress or functional impairment.

Depression can also present as a subthreshold, subsyndromal, or subclinical condition. In other words, the individual may experience dysphoric moods and associated symptoms (e.g., negative self-esteem, pessimism) that are more severe and numerous than the norm in his or her reference groups. Elevated symptom states often are identified with rating scales or questionnaires rather than semi-structured clinical interviews. Subsyndromal or mild depressive symptoms have been shown to increase risk for later major depressive episodes and functional impairment (Gotlib, Lewinsohn, & Seeley, 1995; Lewinsohn, Roberts, Seeley, & Rohde, 1994; Lewinsohn, Rohde, & Seeley, 1998; Williams, Anderson, McGee, & Silva, 1990).

Most epidemiological data about rates of depression in youngsters pertain to major depressive disorder. Risk of major depression increases almost exponentially across development. According to epidemiological studies involving more than 2500 youngsters, approximately 2% of young children, roughly 4% of young adolescents, and at least 16% of older adolescents suffer from major depression each year (Anderson, Williams, McGee, & Silva, 1987; Feehan, McGee, Raja, & Williams, 1994; Harrington, Fudge, Rutter, Pickles, & Hill, 1990; Kessler & Walters, 1998; McGee et al., 1990; Newman et al., 1996; Weissman et al., 1996). These findings mean that about 1 in 50 young children, 1 in 25 young adolescents, and almost 1 in 6 older adolescents are depressed each year. During childhood, rates are higher in boys than girls, but during adolescence and after puberty, prevalence rates for girls become approximately twice those for boys (i.e., a 2:1 female-to-male ratio; Kessler, McGonagle, Swartz, Blazer, & Nelson, 1993; Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993). The U.S. lifetime occurrence of a depressive disorder between ages 15 and 24 years is 21% among females and 11% among males (Blazer, Kessler, McGonagle, & Swartz, 1994; Kessler et al., 1994).

3. Developmental psychopathology

Developmental psychopathology research has identified the defining clinical and contextual features of early-onset depression. Although the specific context of particular studies contributes variability to empirical observations, growing consensus exists about the basic descriptive and epidemiological features of depressive disorders in youngsters. In particular, systematic empirical studies have characterized the longitudinal course of major depressive disorder and common patterns of comorbid psychopathology. The functional concomitants and developmental consequences have also been documented. Furthermore, much is known about the familial and psychological context in which depression develops in youngsters. In addition, studies are beginning to identify specific genetic and experiential risk factors, but basic questions remain about the details in this area. In general, several core patterns of convergence and divergence of depressive presentations across the lifespan are beginning to emerge, underscoring the need for researchers and clinicians to account for the unique developmental aspects of depressive disorders beginning early in life (Birmaher et al., 2004; Kaufman, Martin, King, & Charney, 2001; Yorbik, Birmaer, Axelson, Williamson, & Ryan, 2004).

3.1. Longitudinal course

In longitudinal clinical studies of youngsters age 7–17 years, operationally defined major depressive episodes have a median duration of 7–9 months from onset to recovery (Kovacs, Finberg, Crouse-Novack, Paulauskas, & Finkel-

stein, 1984a; Kovacs, 1997b; McCauley et al., 1993). Most such youths recover in less than a year, but up to 20% have episodes lasting longer than 18 months, suggesting that a sizable minority have a more protracted clinical course. Likewise, youngsters with dysthymic disorder have a lengthy clinical course, with a median episode length of approximately four years and typical age at onset about three years earlier than major depression (Kovacs, 1996). Although almost 80% of youngsters with dysthymic disorder go on to develop major depression, very few youngsters who initially present with major depression develop dysthymia later (Kovacs, Akiskal, Gatsonis, & Parrone, 1994).

From another perspective, almost 100% of depressed youngsters with a diagnosed depressive disorder ultimately get better. Among clinically referred youngsters, the cumulative proportion of recovery from a major depressive episode is 70–80% after one year and 86–98% after two years (Kovacs, 1996, 1997a, 1997b; McCauley et al., 1993). Yet, many become depressed again after symptomatic recovery. In one longitudinal nosological study, almost 40% of youths with major depression had a recurrent episode within two years (Kovacs et al., 1984b). Across longer time intervals of 7–18 years, recurrence rates of 40–70% are documented in 6- to 18-year-old clinical samples of depressed youths ($n = 417$; Harrington et al., 1990; Hughes et al., 1990; Kovacs et al., 1994; McCauley et al., 1993; Weissman, Warner, Wickramaratne, Moreau, & Olfson, 1997). In these studies, risk of recurrent depression exceeds risk for other disorders.

In addition, youngsters with a diagnosis of major depression are more likely than nondepressed youngsters to become depressed in the future (Kovacs et al., 1984b; Lewinsohn, Rohde, Seeley, Klein, & Gotlib, 2000), and dysthymic disorder or minor depression is often a precursor of major depressive disorder and functional impairments (Kovacs et al., 1994; Lewinsohn, Rohde, Seeley, & Hops, 1991). Dysthymia typically occurs at an earlier age than major depression, and over 80% of dysthymic children later develop major depression (Kovacs, 1996). When followed into adulthood, approximately half of depressed adolescents from community samples have major depression in adulthood (Lewinsohn et al., 1998), and about half of depressed young adults had their first episode as a child or adolescent (Newman et al., 1996).

In summary, systematic nosologic studies using standardized diagnostic criteria document that mood disorders that begin between ages 7 and 18 years are episodic, but often chronic, underscoring the fact that outcomes likely change over time. This observation establishes a strong rationale for the value of longitudinal evaluations in both research and clinical settings. Particular attention is needed for those depressed youngsters with incomplete recovery, relapse episodes, or recurrent episodes, as well as those who develop other disorders over time. Too many studies within emerging interdisciplinary areas such as social neuroscience fail to account for fundamental variability from well-established clinical features of depressive disorders. In order for interdisciplinary clinical neuroscience studies to yield replicable effects, the research must be anchored with rigorous standards for current and lifetime clinical diagnoses.

3.2. Comorbid psychopathology

A striking and widely replicated characteristic of clinic-referred youngsters with major depression is that more than 90% of them also have other forms of psychopathology during their index episode, which complicates clinical diagnosis and treatment as well as research protocols (Angold & Costello, 1993; Kovacs, Gatsonis, Paulauskas, & Richards, 1989; Kovacs, Paulauskas, Gatsonis, & Richards, 1988; Mitchell, McCauley, Burke, & Moss, 1988; Puig-Antich, 1982; Rao et al., 1995; Ryan et al., 1987; Shain, King, Naylor, & Alessi, 1991). For example, dysthymic disorder co-occurs with major depression at rates of 13–40% ($n = 391$), and anxiety disorders are present in 23–51% of depressed youths ($n = 208$). Behavior disorders (i.e., conduct, oppositional, attention deficit disorders) occur in about one-fourth of depressed youngsters. As they get older, depressed youths are at increased risk for alcohol and drug abuse (Hughes & Preskorn, 1989; Hughes et al., 1990) as well as suicide (Brent, Baugher, Bridge, Chen, & Chiappetta, 1999). Approximately 70% of behavior and substance abuse problems that occur concomitantly with an initial episode of prepubertal-onset major depression remit with the depression, but a second episode is often preceded by disrupted behavior (Puig-Antich, 1982). Such uncoupling is particularly common in boys. In girls, comorbid disorders tend to co-occur with depressive episodes (Kovacs, Obrosky, & Sherrill, 2003).

Longitudinal follow-up studies have shown that a sizeable minority of pediatric clinical populations with major depression develop manic episodes and have a chronic bipolar variant of mood disorder. In bipolar disorder, depressive episodes are intermixed or alternate with manic symptoms, including extreme patterns of elevated, expansive, or irritable mood along with related symptoms such as hyperactivity, pressured speech, racing thoughts, inflated self-esteem, decreased sleep, distractibility, and impulsivity (APA, 1994). Reported rates of "switch" from unipolar to bipolar mood disorder in youngsters have generally been from 10 to 20%, but conversion rates above 30% have also been found in some clinical populations (Geller, Zimerman, Williams, Bolhofner, & Craney, 2001a; Kovacs & Pollock, 1995; Strober, Lampert, Schmidt, & Morrell, 1993). Variable findings may reflect difficulties with obtaining reliable retrospective reports and diagnoses of complex and changing symptoms over long time periods. In addition, community samples may have lower base rates of bipolar disorder than child psychiatric populations (Lewinsohn, Klein, & Seeley, 1995, 2000). Such observations underscore the need for social neuroscience studies of early-onset depression to document comorbid internalizing and externalizing disorders as well as manic episodes.

3.3. Functional concomitants

The functional problems that characterize depressed youngsters suggest that the disorder can interfere with developmental milestones. For example, interpersonal problems and academic declines are common, along with delays in social, emotional, and cognitive development (Geller, Zimerman, Williams, Bolhofner, & Craney, 2001b; Kovacs & Goldston, 1991; Kovacs & Devlin, 1998; Puig-Antich et al., 1985a, 1985b). Interpersonal dysfunction is often characterized by low self-esteem, spending considerable time alone, and eliciting overt negative reactions from peers and adults (e.g., Altmann & Gotlib, 1988; Kovacs & Lohr, 1995; Messer & Gross, 1995). Intellectual problems are frequently marked by attentional difficulties that interfere with other cognitive tasks on standardized intelligence and neuropsychological tests (e.g., Brumback & Weinberg, 1990). In addition, negative outcomes of severe depression often include substance use (Rao et al., 1995), suicide attempts (Harrington et al., 1990, 1994; Kovacs, Goldston, & Gatsonis, 1993), and employment incapacity (Harrington et al., 1990). Such factors affect a youngsters' clinical prognosis, particularly with protracted depression and marked developmental delays, and they can confound depression effects in psychological and biological studies of early-onset depression. Researchers should document and control for such possible confounds.

3.4. Familial context

Family studies show that early-onset depression should be considered in relation to the history of depression in the larger family unit (Sheeber, Hops, & Davis, 2001). In studies of children with major depression, familial rates of mood disorders range from 35 to 70% in first-degree relatives and 10–25% in second-degree relatives (Kovacs, Devlin, Pollock, Richards, & Mukerji, 1997; Mitchell, McCauley, Burke, Calderon, & Schloredt, 1989; Neuman, Geller, Rice, & Todd, 1997; Puig-Antich et al., 1989; Todd, Neuman, Geller, Fox, & Hickok, 1993). Familial aggregation can be lower in adolescent-onset than childhood-onset depression, but rates for both groups exceed those of the controls (Klein, Lewinsohn, Seeley, & Rohde, 2001; Williamson et al., 1995). When the entire family was the unit of analysis in a longitudinal study of clinic-referred cases, 94% of depressed children with onset prior to age 15 years had affected pedigrees, with a 5:1 odds ratio of risk relative to controls (Kovacs et al., 1997). Substance abuse and conduct disorder/antisocial personality disorder are also common in family pedigrees with early-onset depression, particularly in male relatives (Rush et al., 1995). Such research suggests that familial psychopathology may account for significant variance among samples of depressed youngsters.

A positive family history of depression and discord increases risk for childhood-onset depression. Epidemiology studies have established that parental depression predicts offspring depression. In particular, children of depressed parents are 3 times more likely than non-psychiatric controls to develop major depressive disorder, with lifetime risk up to 45% (Downey & Coyne, 1990; Fendrich, Warner, & Weissman, 1990; Hammen, 1991; Jensen, Bloedau, Degroot, & Ussery, 1990; Kaminski & Garber, 2002; Orvaschel, Walsh-Allis, & Ye, 1988). In addition, family history appears essential for predicting recurrence. In one prospective study of depressed youngsters, those who developed recurrent depression during young adulthood also had a positive parental history of depression (Wickramaratne, Warner, & Weissman, 2000). In other words, depressed youngsters whose parents were never depressed did not differ from a healthy comparison group in their risk for major depression during adulthood. The study also documented that family history predicts recurrent depression more strongly when depression begins during childhood than during adolescence (Wickramaratne, Greenwald, & Weissman, 2000). Thus, young adults at highest risk for developing depression are those who have a family history of depression along with a personal history of depression beginning very early in life. Prospective studies of depressed youths with a high family loading support this notion (Williamson, Birmaher, Axelson, Ryan, & Dahl, 2004).

3.4.1. Genetic studies

Genetic research also provides evidence for familial risk factors. Twin studies have documented heritability estimates that are twice as high for childhood-onset depression (79%; Thapar & McGuffin, 1994) than adult depression (30–46%; Jardine, Martin, & Henderson, 1984; Kendler, Heath, Martin, & Lindon, 1986). In addition, multi-generational studies identify patterns of increasingly severe and earlier age of onset across successive generations in families with recurrent unipolar depression (Engström et al., 1995; Ohara, Suzuki, Ushimi, Yoshida, & Ohara, 1998) or bipolar disorder (McInnis et al., 1993; Nylander, Engström, Chotai, Wahlström, & Adolfsson, 1994). This phenomenon, called "genetic anticipation", often occurs in highly heritable disorders and has been associated with large trinucleotide repeats in molecular genetic studies (e.g., Vincent et al., 2000). However, limited cases of large trinucleotide repeats appear to exist in groups with childhood-onset depression (Vincent, Kovacs, Krol, Barr, & Kennedy, 1999). Segregation analyses suggest a recessive major effect with significant parental effects (Marazita et al., 1997). Some association studies of genetic variants, such as cyclic AMP responsive element binding protein (CREB1), have reported conflicting results (Burcescu et al., 2005; Zubenko et al., 2002, 2003).

Replicated molecular genetic effects related to early-onset mood disorders have been observed on chromosome 11p14, related to brain derived neurotrophic factor (BDNF; Strauss et al., 2004, 2005; see also, Schumacher et al., 2005). BDNF is a nerve growth factor involved in

regulating cellular development, neuronal survival, synaptic plasticity, and stress resistance (Thoenen, 1995). Growing evidence implicates BDNF-dependent processes in the pathophysiology of depressive disorders and the therapeutic action of antidepressant treatments (Duman, 2002). However, functional outcomes of BDNF-dependent processes can be complex and paradoxical, with documented age-related changes and sexual dimorphisms (Bland et al., 2005; Mattson, Maudsley, & Martin, 2004; Scharfman & MacLusky, 2005; Tsai, 2005). Such observations suggest the intriguing hypothesis that neurobiological factors in early-onset mood disorders may be characterized not by static focal deficits but rather by variations in dynamic developmental brain mechanisms that are shaped by environmental inputs.

3.4.2. Psychosocial studies

In psychosocial studies of familial risk factors, one of the most consistent findings is that family discord predicts negative outcomes in high-risk offspring of depressed parents (Beardslee, Versage, & Gladstone, 1998; Hammen, 1991; Orvaschel et al., 1988; Puig-Antich et al., 1985a, 1985b). Psychosocially, depressed parents tend to be withdrawn and fatigued or else irritable and critical (Cohn, Matias, Tronick, Donnell, & Lyons-Ruth, 1986; Field, Healy, Goldstein, & Guthertz, 1990). The extent to which such parental behaviors predict later child outcomes depends both on the severity of parental depression (Campbell, Cohn, & Meyers, 1995) as well as the child's problem history and developmental stage (Chess & Thomas, 1984; Wickramaratne & Weissman, 1998). During infancy, high-risk cohorts show less visual and vocal reciprocity with severely withdrawn-unresponsive caregivers, and they often display distress with intrusive-hostile caregivers (Cohn et al., 1986; Murray, Kempton, Woolgar, & Hooper, 1993; Shaw & Vondra, 1995; Zlochower & Cohn, 1996). During preschool years, depressed parent–child interactions tend to be brief and interrupted (Jameson, Gelfand, Kulcsar, & Teti, 1997), and discipline problems may increase out-of-control or aggressive behaviors (Zahn-Waxler, Iannotti, Cummings, & Denham, 1990). Parents may struggle to teach effective coping strategies to their school-aged children (Garber & Dodge, 1991; Gottman, 1997; Hillsman & Garber, 1995), and children may mirror their parents' tearfulness and pessimism (Graham & Easterbrooks, 2000). During adolescence, high-risk family relationships tend to be marked by conflict, control, rejection, and guilt (Garber, Keiley, & Martin, 2002; Goldstein, 1995; Schwartz, Dorer, Beardslee, Lavori, & Keller, 1990; Sheeber & Sorensen, 1998). During teen years, family discord and emotional patterns predict the onset of depressive episodes in high-risk youngsters (Garber, Martin, & Keiley, 1999). Such observations suggest a developmental progression of early emotion discord and dysregulation, culminating in depressive disorders in some high-risk youngsters. The empirically supported principle of dynamic developmental trajectories creates a particularly strong rationale for multidisciplinary, longitudinal studies. Cross-sectional studies of isolated component processes often cannot capture this inherent feature of early-onset mood disorders.

3.5. Psychological context

Empirical studies have demonstrated that during a depressive episode, youngsters have characteristic patterns of affect, behavior, cognition, and interpersonal style. Methodologies differ across studies, but replicated effects suggest convergent patterns that establish basic principles for a multi-disciplinary conceptualization of early-onset depression. For example, a number of studies support the notion that depressed teens have difficulties with emotion regulation strategies and behaviors such as support seeking, cognitive reappraisal, and affect change (Garber, Braafladt, & Weiss, 1995), and they are also likely to sustain their negative emotions longer than non-depressed teens (Sheeber, Allen, Davis, & Sorensen, 2000). Socially, hostility is common in boys, whereas conflict avoidance is common in girls (Davis, Sheeber, Hops, & Tildesley, 2000; Garber et al., 1995). In addition, depressed youngsters often selectively attend to negative emotions and events, and they frequently expect aversive outcomes to continue in the future (McCauley, Mitchell, Burke, & Moss, 1988; Kendall, Stark, & Adam, 1990).

Emotion regulatory problems are further supported by reports that many depressed youngsters are self-focused and ruminative about their feelings and shortcomings, and such self-focus tends to disrupt active task engagement and environmental exploration (Nolen-Hoeksema, 1991). Depressed youths commonly give low ratings of their academic and social competence, which may or may not reflect actual performance (Cole, Jacquez, & Maschman, 2001). When asked about the causes of negative events, depressed youngsters frequently make attributions that are self-blaming and catastrophic (Curry & Craighead, 1990; Gladstone, Kaslow, Seeley, & Lewinsohn, 1997; Kaslow, Rehm, Pollack, & Siegel, 1998; Nolen-Hoeksema, Girgus, & Seligman, 1986). Given that negative or biased cognitive patterns appear to escalate dysphoric mood and maintain depressive symptoms over time (Harrington & Vostanis, 1995), it is not surprising that depressed youths report greater daily sadness, fear, anger, and irritability than their peers (Altmann & Gotlib, 1988; Larson, Raffaelli, Richards, Ham, & Jewell, 1990; Quiggle, Garber, Panak, & Dodge, 1992). They appear to perseverate in a prolonged pattern of negative emotions in that they tend to continue or repeat dysfunctional emotional behaviors even after the cessation of emotionally provocative events.

Prior to the initial onset of an affective disorder, stress and regulatory factors increase risk of developing depression. Research links such life events primarily to the onset of an initial major depressive episode early in life (Lewinsohn, Allen, Seeley, & Gotlib, 1999). For example, serious illness or injury with functional impairment is a risk factor

for an initial depressive episode in youngsters (Lewinsohn, Seeley, Hibbard, Rohde, & Sack, 1996). In addition, relationship loss is documented as a prospective risk factor for the first onset, but not recurrent episodes, of major depressive disorder (Monroe, Rohde, Seeley, & Lewinsohn, 1999). Witnessing family violence also predicts major depressive episodes (Daley, Hammen, & Rao, 2000). High risk for depression and suicide exists following physical or sexual abuse, with an eight-fold increase relative to controls (Brent et al., 1998, 1999; Brown, Cohn, Johnson, & Smailes, 1999; Kaplan et al., 1998; Kaufman, 1991; Kazdin, Moser, Colbus, & Bell, 1985; Roosa, Reinholtz, & Angelini, 1999). Such stressful life events may lead to prolonged emotional arousal that a youngster cannot control or regulate, which over time can become maladaptive and develop into an emotional disorder.

Although most youngsters are able to regulate their emotional arousal to stressful events with cognitive, behavioral, or social strategies, some are unable to adapt effectively. Existing data suggest that those who fail to regulate their arousal adaptively and develop depression may have a lower threshold for dealing with stress. In particular, longitudinal data from over 1500 community adolescents suggest that among those who experience stressful life events, depression occurs primarily in those who display highly dysfunctional cognitive-emotional patterns (Lewinsohn, Joiner, & Rohde, 2001). Other studies show that when youngsters become depressed, their cognitive patterns deteriorate and remain dysfunctional even after their depression subsides, putting them at risk for future episodes of depression (Nolen-Hoeksema, Girgus, & Seligman, 1992). In community samples, dysphoric mood and dysfunctional thinking styles are more highly correlated among adolescents with a previous history of depression than among adolescents without a depression history, and dysfunctional thinking is a stronger predictor of recurrent depression than the first episode (Lewinsohn et al., 1999; Nolen-Hoeksema et al., 1986, 1992). Findings support different interactions between stress and regulatory patterns in first onset depression relative to recurrent depression. Once youngsters develop dysregulated cognitive patterns, they may have reduced thresholds for high emotional arousal and depressive symptoms. Taken together, convergent evidence demonstrates that dysregulated or maladaptive affect is a core aspect of depression. Furthermore, problems with emotion adaptation appear to precede the onset of the disorder, and such difficulties increase risk for protracted symptoms and functional impairments necessary for a clinical diagnosis.

4. Intervention

Intervention research has identified empirically supported prevention and treatment programs for early-onset depression. Empirically supported interventions are those with beneficial effects shown in two or more independent, randomized clinical trials for a particular population (American Psychological Association Task Force, 1995; Chambless & Hollon, 1998; Hollon et al., 2002; Kazdin & Weisz, 1998). The current literature includes few meta-analyses, but a number of published empirical studies using standardized diagnostic criteria have systematically evaluated interventions for early-onset depression. Such systematic, controlled studies exemplify core findings and issues relevant for a broader multi-disciplinary discussion.

4.1. Prevention

In recent years, tools and incentives have become available for systematically evaluating primary prevention programs for depression (Brent, 2004; Harrington & Clark, 1998; Rutter, 1995). Primary prevention interventions typically target risk factors for depressive disorders, in a similar way that lung cancer prevention targets smoking behaviors. The current review focuses on primary prevention programs that specifically address depression in youngsters. The major empirically evaluated primary prevention programs include educational, cognitive-behavioral, family-focused, and combined cognitive-behavioral-interpersonal approaches.

Early studies documented that lecturing to large, unselected groups of youngsters about depression prevention had minimal effects on symptom reduction, depression knowledge, treatment attitudes, and treatment seeking (Clarke, Hawkins, Murphy, & Sheeber, 1993). However, benefits have been observed with more focused and intensive selective prevention programs, targeting only youngsters with elevated depressive symptoms. For example, Clarke and his colleagues adapted the program content from Lewinsohn and Clarke's Coping with Depression Course for Adolescents (CWD-A), a cognitive-behavioral program used in treatment outcome research (see Clarke, 1999; Clarke & Lewinsohn, 1989; Lewinsohn, Clarke, & Hoberman, 1989). The 15-session, small-group prevention program teaches youngsters skills for identifying and challenging negative or biased thoughts that may lead to depression (i.e., mood monitoring, social skills, activity scheduling, relaxation, constructive thinking, communication techniques, problem solving, and maintenance strategies). Randomized clinical trials with high-risk adolescents showed significant benefits of prevention by substantially reducing cases of major depression and dysthymia during the follow-up period (Clarke et al., 1995, 2001).

A second research group also tested a 12-week cognitive-behavioral depression prevention program in school-aged youngsters, called the "Penn Resiliency Program", based on the helplessness model of depression (Freres, Gillham, Reivich, & Shatte, 2002; Seligman, Reivich, Jaycox, & Gillham, 1995). The model draws analogies between depression in humans and passivity in lab animals in uncontrollable, aversive situations (see Peterson, Maier, & Seligman, 1993). Human helplessness is predicted by explanatory styles, or habitual "optimistic" or

"pessimistic" causal explanations of aversive events. Key features of explanatory style are the degree of personalization (i.e., internal vs. external), permanence (i.e., stable vs. unstable), and pervasiveness (i.e., global vs. specific). The program promotes optimistic explanatory style, personal control, and mastery experiences using cognitive-behavioral techniques and social skills training. Controlled outcome studies showed that the prevention program reduced self-reported depressive symptoms, and follow-up studies documented continued depressive symptom reduction, improved classroom behavior, and more optimistic explanatory styles (Gillham & Reivich, 1999; Gillham, Reivich, Jaycox, & Seligman, 1995; Jaycox, Reivich, Gillham, & Seligman, 1994; Seligman et al., 1995).

Using a family-focused approach, Beardslee and his associates developed a 6- to 10-session program for high-risk youths with a depressed parent (Beardslee, Gladstone, Wright, & Cooper, 2003; Gladstone & Beardslee, 2000). Based on their work on resilience and self-understanding, the researchers designed the intervention to enhance understanding of depression in families and to decrease the impact of risk factors in youths (Beardslee, 1989; Beardslee & Poderefsky, 1988). Controlled studies documented that the intervention was associated with high parental satisfaction, overall symptom changes, improved communication, and interpersonal understanding (Beardslee et al., 1997a, 1997b). Follow-up studies documented sustained positive behavior and attitude changes. Change was related to a process that demystified depression, modulated shame and guilt, and increased self-awareness (Beardslee et al., 1998). A healthy family dialog promoted resilience among children (Focht & Beardslee, 1996).

Additional studies have combined cognitive-behavioral and interpersonal approaches in depression prevention. For example, Shochet and associates (2001) developed and evaluated a school-based program with an unselected group of 260 youngsters in Australia. Their active intervention program emphasized rapport and included both cognitive-behavioral and family-interpersonal techniques (e.g., calming skills, cognitive patterns, problem solving, support networks, family interactions). The investigators documented a high recruitment rate, low attrition rate, and satisfactory protocol adherence. The program resulted in reduced depressive symptoms in the 20% of adolescents with elevated symptomatology, whereas, clinical depression increased markedly in a control group that did not participate in the program. Beneficial effects were sustained at the 10-month follow-up assessment.

In general, research shows that promising depression prevention programs: (1) build specific cognitive and behavioral skills as protective factors, (2) help children and families improve emotional awareness and regulation, and (3) improve relationships of children and parents (Surgeon General, 2001). Large-group universal prevention strategies can have potentially harmful effects (Harrington & Clark, 1998). Small-group programs that actively relate skill-building to personal experience appear more effective than large-group lecture programs.

4.2. Treatment

Controlled treatment trials with acutely depressed children and adolescents who meet diagnostic criteria for major depression or dysthymia mainly focus on brief psychological or pharmacological interventions (see Birmaher et al., 1996a, Birmaher, Ryan, Williamson, Brent, & Kaufman, 1996b; Birmaher, Brent, & Benson, 1998; Harrington, Whittaker, & Shoebridge, 1998; Hughes et al., 1999; Kovacs & Sherrill, 2001; Martin, Kaufman, & Charney, 2000). The following review summarizes published randomized clinical trials with youngsters between ages 6 to 18 years who met operational diagnostic criteria for major depression or dysthymic disorder based on the DSMIII, DSMIII-R, or DSMIV or who were diagnosed with Research Diagnostic Criteria (RDC) for major, intermittent, or minor depressive disorder. Diagnoses were determined through standardized, structured, or semi-structured psychiatric interviews. Meaningful comparisons across study studies were complicated by differences in design and outcome measures. To address this, summary statistics reported here were computed by noting the number of participants who entered each clinical trial and the number of youngsters who remitted from depression at the end of the acute treatment phase. By considering all eligible participants for computing response rates, the summary reflects an intent-to-treat approach described by Pocock (1983). General comparisons were then made within and across major pharmacological and psychological treatment modalities and trends were identified for further discussion.

4.2.1. Psychological treatments

Various versions of cognitive-behavioral therapy have been the most widely studied type of non-somatic intervention for depressed youths (Harrington et al., 1998; Hibbs & Jensen, 1996; Kovacs & Sherrill, 2001). Cognitive-behavioral treatments, which represent adaptations from interventions originally designed for adults, generally seek to help youths identify and modify negative thoughts, dysfunctional beliefs, and pessimistic attributions as well as to build more adaptive behavioral, communication, and problem solving repertoires. Randomized clinical trials with standardized outcome measures for acute depression compared cognitive-behavioral therapy with control interventions, including family therapy, non-directive supportive therapy, and waiting lists (see Brent et al., 1997; Harrington et al., 1998; Lewinsohn, Clarke, Hops, & Andrews, 1990; Lewinsohn, Clarke, Rohde, Hops, & Seeley, 1996; Vostanis, Feehan, Grattan, & Bickerton, 1996; Wood, Harrington, & Moore, 1996). In general, half to three-fourths of depressed youngsters remitted from depression with cognitive-behavioral therapy, a somewhat lower percentage remitted with nondirective supportive

therapy, and 5–50% remitted on waiting lists. A high recovery rate of 75% has also been reported for interpersonal therapy (Mufson, Weissman, Moreau, & Garfinkel, 1999).

4.2.2. Medication treatments

Pharmacological treatments for depression target chemical dysfunction in the nervous system, and medication use for depressed youngsters has increased markedly during the past decade (Ryan, 2003a, 2003b; Surgeon General, 1999). Some of the earliest empirical studies focused on tricyclic antidepressants, which primarily affect norepinephrine and serotonin systems (see Birmaher et al., 1998, amitriptyline; Boulos et al., 1991, desipramine; Geller, Cooper, McCombs, Graham, & Wells, 1989, 1990, nortriptyline; Hughes et al., 1990, imipramine; Klein et al., 1998, desipramine; Kutcher et al., 1994, desipramine; Kye et al., 1996, amitriptyline; Puig-Antich et al., 1987, imipramine). Individual studies as well as a meta-analysis reported no significant outcome differences between youngsters assigned to tricyclic treatment or a placebo medication (Hazell, O'Connell, Heathcote, Robertson, & Henry, 1995). In general, such studies show minimal efficacy for tricyclics, and they document risk for cardiotoxicity in pediatric populations (Gutgesell, Atkins, & Barst, 1999; Werry, Biederman, Thisted, Greenhill, & Ryan, 1995).

Additional pharmacologic research has focused on the serotonin reuptake inhibitors (SRIs), given their improved safety profile relative to the tricyclics. Published reports have focused primarily on fluoxetine (i.e., Prozac), paroxetine (i.e., Paxil), or sertraline (i.e., Zoloft). In randomized controlled studies, over half of depressed youngsters treated with fluoxetine were rated "much" or "very much improved" on the Clinical Global Impression Scale, and approximately one-third remitted from depression (Emslie et al., 1997). When given paroxetine, almost two-thirds of depressed youngsters remitted from their depression, with slightly better clinical outcomes than depressed youngsters in the placebo control condition (Keller et al., 2001). In addition, almost 70% of youngsters with major depressive disorder who were given sertraline showed substantial decreases in depressive symptoms in pooled multicenter, randomized, double-blind, placebo-controlled trials (Wagner et al., 2003). Response rates above 70% have been observed with combined fluoxetine and cognitive-behavioral therapy in adolescents with major depressive disorder (March et al., 2004). Collective evidence underscores the need to balance risk-benefit ratios for SRI use in youngsters, and a meta-analysis of both published and unpublished data indicates that only fluoxetine has a favorable risk-benefit profile among medications for treating depressed youngsters (Whittington et al., 2004).

Taken together, research shows that two-thirds to three-fourths of depressed youngsters show symptomatic improvement with acute treatment. However, not all treatments are equally effective. The most consistently replicated benefits occur when youngsters learn various cognitive and behavioral techniques for coping with their depression, and such effects show continuity with established cognitive-behavioral depression prevention programs. In addition, when medications are needed, treatment benefits improve with combined SRI and psychotherapy. Serious side effects have been clearly documented with the tricyclic antidepressants. Evidence that tricyclic treatment is not effective for depressed youngsters contrasts with positive effects for adults. These findings underscore the limitations of generalizing results from treatment studies with depressed adults to children and adolescents (Kaufman et al., 2001). Depressed children and adolescents need interventions optimized for their unique needs (Coyle et al., 2003; Shonkoff, 2000, 2003).

5. Neurobiology

Neurobiological studies with depressed children and adolescents have primarily used neuroendocrine, electrophysiological, and neuroimaging techniques. Such measures have been assessed during resting baseline and challenge conditions. In addition, researchers have used cross-sectional research designs to identify neurobiological correlates of the acute disorder, and they have developed longitudinal research designs to study factors that precede illness onset and predict risk status over time. Such studies are not without methodological limitations, but convergent patterns across studies allude to important principles that can inform both applied clinical work and ongoing basic research. Perhaps most fundamentally, such studies suggest that multiple neurobiological factors contribute to one's capacity for adaptive emotional responses, which become dysfunctional in depressive illness.

5.1. Neuroendocrinology

Neuroendocrine studies have documented neurochemical dysregulation in depressed youngsters, which changes across development. Although depressed adults show marked abnormalities in 24-h baseline cortisol patterns (Gold, Goodwin, & Chorousos, 1988a, 1988b; Post, 1992), studies with prepubertal depressed children suggest that such children do not tend to display such stress hormone dysregulation (Feder et al., 2004; Puig-Antich, 1986a, 1986b; Puig-Antich et al., 1989). Resting cortisol dysregulation in depression appears to emerge after puberty, specifically in the evening hours and during sleep disturbance (Dahl et al., 1991; Dahl et al., 1992; Kupfer, 1993). Such replicated observations establish that abnormal 24-h baseline cortisol patterns may be a consequence, rather than a cause, of depressive disorder.

A longitudinal study of depressed adolescents followed into adulthood showed a relation between significant pre-sleep cortisol elevations and later suicide attempts (Mathew et al., 2003). Researchers observed that depressed adolescents often have reduced growth hormone before sleep onset, and those who are suicidal tend to display rapid increases after sleep onset (Coplan et al., 2000). Disrupted

sleep processes during a depressive episode may increase subsequent biological and psychological dysregulation (Dahl, 1998; Dahl et al., 1996; Steiger & Holsboer, 1997a, 1997b). Thus, even though sleep-related cortisol changes may be a consequence of a depressive disorder, such processes contribute fundamentally to ongoing and escalating problems with regulating stress responses.

In addition to the baseline cortisol studies, a number of neuroendocrine challenge studies have been conducted. In general, pubertal status affects girls' and boys' responses differently. Healthy girls show increasing CRH-related cortisol responses with pubertal development, but boys have similar total responses across pubertal stages (Stroud, Papandonatos, Williamson, & Dahl, 2004). Prepubertal girls, but not boys, with depressive disorders display augmented prolactin responses to serotonin-related drug challenges relative to healthy comparison participants (Ryan et al., 1992). Some effects are present in both girls and boys. In particular, prepubertal depressed girls and boys who are given serotonin-related drug challenges produce blunted cortisol responses (Ryan et al., 1992) as well as blunted pituitary growth hormone responses (Ryan et al., 1994). Such cortisol and growth hormone responses to serotonin-related challenges have also been observed in non-depressed high-risk children with a strong family loading for severe depression (Birmaher et al., 1997). In addition, blunted growth hormone responses after insulin-induced hypoglycemia exist both after remission in depressed youngsters (Ryan et al., 1994) and prior to an initial episode in high-risk children with a family history of severe depression (Birmaher et al., 2000; Dahl et al., 2000). Such longitudinal evidence suggests that dysregulated growth hormone patterns may have a causal role in depression, particularly among some youths with a family history of mood disorder.

5.2. Electroencephalography

Baseline physiological studies of electroencephalographic (EEG) alpha suppression have been conduced with multiple populations. Adolescents with major depressive disorder tend to have decreased left frontal and right parietal brain electrical activity, two of the brain areas that are implicated in emotional expression and perception, respectively (Kentgen et al., 2000; Tomarken & Keener-Miller, 1998). However, parietal asymmetry was reduced in the presence of comorbid anxiety (Kentgen et al., 2000). In high-risk youngsters of depressed mothers, investigators have documented left hypoactivation and atypical frontal brain electrical activity relative to low-risk children (Dawson, Frey, Panagiotides, & Osterling, 1997a, 1997b, 1999a, 1999b; Field, Fox, Pickens, & Nawrocki, 1995; Tomarken & Keener-Miller, 1998; Tomarken, Dichter, Garber, & Simien, 2004). In a study of young adults with a history of familial childhood-onset depression, investigators found that frontal EEG alpha asymmetry differed between men and women and varied in relation to longitudinal clinical course (Miller et al., 2002). Women showed greater alpha power at all sites than men, and young women with childhood-onset depression had greater right frontal alpha suppression while men with childhood depression had greater left frontal alpha suppression. Participants with a bipolar spectrum course had the most extreme patterns of frontal EEG asymmetry. This study illustrates the principle that clinical variability accounts for important variance in electroencephalographic studies of familial, early-onset depression.

EEG sleep measures have shown considerable variability with regard to group differences between depressed youngsters and control participants. Such measures are influenced substantially by age and gender (Armitage et al., 2000), and depression-related effects appear to interact with medication effects and longitudinal clinical course. Armitage, Emslie, and Rintelmann (1997) observed that fluoxetine (Prozac) treatment in depressed children and adolescents increases subjective sleep disturbance, light Stage 1 sleep, number of arousals, myoclonic activity, and rapid eye movement (REM) density. However, REM latency was largely unaffected. In a longitudinal follow-up study, EEG sleep measures differed among depressed adolescents with a unipolar or bipolar course (Rao et al., 2002). A unipolar course was associated with reduced REM latency, higher REM density, and increased early REM sleep. A bipolar course was related to more Stage 1 sleep and less Stage 4 sleep. In a study assessing the temporal coherence of EEG rhythms during sleep (Armitage et al., 2000), both depressed children and adolescents had lower intrahemispheric coherence than healthy controls, suggesting a disruption in basic brain arousal and organization. In addition, coherence between the two cerebral hemispheres was reduced among depressed adolescents (but not children), with the lowest interhemispheric coherence observed among depressed adolescent girls.

5.3. Neuroimaging

Neuroimaging studies have also been done with depressed adolescents. Such studies are marked by small sample sizes and inconsistent findings. One set of studies has focused on frontal cortex abnormalities. For example, Steingard et al. (1996) reported reduced frontal lobe volumes in depressed adolescents, and later documented smaller frontal white matter volumes, but larger frontal gray matter volumes, in depressed adolescents compared to healthy controls (Steingard et al., 2002, 2000). Nolan et al. (2002) studied psychotropically-naive 9- to 17-year-old youngsters with major depressive disorder and found that frontal volumes differed among those with or without a family history of affective illness. Those adolescents with familial depression had left frontal volumes that were 6% smaller than healthy comparison participants, but adolescents with non-familial major depressive disorder had left frontal volumes that were 11% larger than the comparison group. Such findings underscore the basic principle that the

familial patterns are essential for understanding the nature of early-onset depression.

Another set of studies focused specifically on medial prefrontal areas. For example, Botteron and her associates (2002) reported volume reductions specifically in the left orbitofrontal cortex (i.e., medial subgenual cingulate) in depressed adolescents. The left subgenual cortex of the depressed adolescents was on average 19% smaller than control participants. This work extends prior findings that adults with familial-pure unipolar or bipolar depression have abnormal left medial frontal glucose metabolism, structural volume reduction, and glial cell reduction. Such effects may possibly reflect developmental abnormalities in medial frontal and related areas that modulate autonomic and neuroendocrine stress responses and reward sensitivity (Drevets, 2000; Rajkowska et al., 1999). Questions remain about why some investigators have been unable to replicate subgenual cortex volumetric effects in independent samples (e.g., Sanches et al., 2005).

Another set of studies has focused on the amygdala, hippocampus, striatum, and temporal cortex using both structural and functional neuroimaging. In these studies, depression-related effects appear to be moderated by the presence of anxious and/or manic symptoms. For example, MacMillan et al. (2003) found that medication-free children and adolescents with major depressive disorder had 14% larger left and 11% larger right amygdala-hippocampal volume ratios than comparison participants. However, such volume differences were directly related to the severity of anxiety symptoms, but not depressive symptoms nor illness duration. Rosso et al. (2005) reported reduced bilateral amygdala volumes in pediatric major depression, but effects were unrelated to symptom severity. Thomas et al. (2001) used functional magnetic resonance imaging with an emotional face task to study children and adolescents with major depressive disorder, generalized anxiety or panic disorder, or no psychiatric history. Youths with anxiety disorders showed an exaggerated amygdala response to fearful faces relative to comparison participants, whereas youths with major depression showed a blunted amygdala response to the faces. The magnitude of the amygdala's signal change between fearful and neutral faces was positively correlated with the anxious symptom severity.

In a study of adolescents with bipolar disorder and healthy controls, investigators documented reduced left total superior temporal gyrus volumes in the bipolar group, and the effect was related to differences in bilateral white matter volume (Chen et al., 2004a). Researchers also showed that amygdala volume was positively correlated with age among adolescents with bipolar disorder but negatively correlated with age among healthy comparison participants (Chen et al., 2004b). Dickstein et al. (2005) examined children with bipolar disorder and documented reduced gray matter volume in the left dorsolateral prefrontal cortex, accumbens, and amygdala. Focusing specifically on subcortical temporal structures, Blumberg et al. (2003a) reported a significant 15.6% amygdala volume reduction and a marginal 5.3% hippocampal volume reduction in adolescents and young adults with bipolar disorder relative to healthy control participants. However, such volume effects appeared unrelated to bipolar illness duration, mood state, rapid cycling, medication, or substance dependence. These researchers also assessed adolescents with bipolar disorder or no psychiatric history using event-related functional magnetic resonance imaging during a color-naming Stroop task (Blumberg et al., 2003b). Relative to healthy adolescents, those with bipolar disorder had greater left striatal and thalamic activity as well as an absence of age-related prefrontal activity. Within the bipolar group, signal increases in the ventral striatum correlated positively with depressive symptoms. The results suggest developmental dysfunction in subcortical fronto-striatal brain regions in adolescents with bipolar disorder (Blumberg et al., 2004).

5.4. Summary of neurobiological research

Neuroendocrine, electrophysiological, and neuroimaging research suggests that child and adolescent depression emerges from dysfunction in neural systems involved in emotion. Neurobiological factors change during the course of development (DeBellis et al., 2001), and developmentally-influenced neurobiological factors appear to contribute to one's capacities for adaptive emotional responses. The limited available evidence to date suggests that emotion-related neurobiological processes that change with development may become impaired during depressive disorders. Longitudinal developmental studies that account for familial and clinical variability allude to this possibility, and cross-sectional studies that fail to account for developmental changes, gender differences, and family history have produced inconsistent results.

As reviewed above, currently depressed prepubertal children, previously depressed children, and non-depressed high-risk children show blunted cortisol and growth hormone responses to serotonin-related drug challenge or insulin-induced hypoglycemia. Neuroendocrine findings underscore the importance of basic biological rhythms involved in sleep, eating, and stress sensitivity. Differences between depressed and non-depressed youngsters have been identified in the structure and function of cortical, limbic, and striatal brain areas. Much remains to be learned about how observed human brain activity relates to particular functional components of mood disorders, but basic research with laboratory animals suggests that the prefrontal cortex and related cortical-limbic-striatal circuits regulate emotional functions such as neuroendocrine stress responses, autonomic reactivity, and reward sensitivity (Ongur & Price, 2000).

An important direction for future neurobiological research is to translate findings across different levels of analysis. For example, as stated above, early-onset mood disorders have been associated with BDNF gene polymorphisms, blunted peripheral cortisol and growth hormone

responses, as well as prefrontal and cortical-limbic-striatal brain circuit changes. Future inquiries should identify relations among such molecular, chemical, and functional neurobiological processes and address questions about gender and developmental influences. In addition, much remains to be learned about how such processes relate to the complex treatment responses and clinical presentations of depressed youngsters. As such interactions become understood, the science will increasingly inform better matching between symptoms and treatments. Yet, the compelling challenge of matching symptoms and treatments is complicated by emerging data. Neurobiological factors in early-onset mood disorders may fundamentally involve variations in dynamic developmental brain mechanisms that are formed through interactions with the environment. Rather than correcting focal deficits, the key challenge may be finding ways to intervene in dynamic biological processes that are inherently shaped by the environment.

6. A social neuroscience perspective

Translational research aims to integrate our understanding of interventions, neurobiology, psychopathology, and normal development. Such efforts depend fundamentally on both basic and clinical science. The scientific literature about child and adolescent depression provides a substantial empirical foundation for beginning to develop an integrative research framework that has implications for both typical and atypical development.

In this context, developmental social neuroscience offers a useful perspective. The goal is neither to reduce child and adolescent depression to isolated neurobiological measures nor to give broad generalizations with metaphorical terminology. Rather, this dynamic system perspective seeks to understand developmental variations in specific brain processes that are shaped by environmental inputs. The framework embraces the multi-disciplinary goal of programmatically developing, testing, and refining theories of early-onset depression that bring together the elaborate details of neuroscience with the multifaceted context of early emotional experience. Important tasks at hand are (1) to characterize core features of emotional processes and disorders, (2) to differentiate component processes of complex emotional function and dysfunction, (3) to identify relations among such component processes and their contextual influences, and (4) to elaborate the developmental changes inherent in the early emergence of depressive disorders. Such tasks serve the goal of identifying the mechanisms of how the initial-onset of depression occurs in different individuals and how it can be prevented.

Analyzing component parts of typical and atypical emotional processes must proceed in concert with a vision for a unified gestalt, and so another important scientific challenge is developing a heuristic for generating hypotheses about etiology and guiding interventions for early-onset mood disorders. Growing evidence suggests that emotional adaptation should be at the core of such a heuristic (Shelton, 2000). Emotional adaptation is a fundamental process that enables the brain to receive and integrate environmental and somatic information and to guide appropriate responses over time. It can be examined at multiple levels of analysis. For example, cellular mechanisms contribute to emotional adaptation, synaptic plasticity, and depressive disorders (Duman, 2002; Shelton, 2000; Tsai, 2005). Emotional adaptation is also essential to research about brain reward circuits (Leibenluft, Charney, & Pine, 2003; Ongur & Price, 2000) and neuroendocrine systems (Romeo, 2005; Sisk & Foster, 2004). In addition, emotional regulatory processes are being examined across physiological, behavioral, cognitive, and social domains (Calkins & Fox, 2002). An emotional adaptation heuristic serves the goal of seeking convergent, replicable observations made from different viewpoints and with different methodologies.

6.1. A dynamic adaptive systems framework

The central guiding hypothesis of the dynamic adaptive systems framework is that mood disorders reflect core deficits in emotional adaptation, and facilitating emotional adaptation provides a pathway to resilience. This framework begins by juxtaposing two fundamental principles from the adult depression literature. First, Charney and his colleagues (2002) emphasize parsing mood disorders into core features that are clinically meaningful and quantitatively assessable. Second, Shelton (2000) uses emotional adaptation as an explanatory heuristic for investigating the mechanisms of risk for depression and response to treatment. These perspectives exemplify ways to investigate complex interacting systems that change dynamically over time. They provide a structure for integrating observations reviewed in this paper and for generating multiple working hypotheses for studying early-onset depression and emotional resilience (Chamberlin, 1965).

Studying nosology teaches us that depressive disorders comprise disparate symptoms, with disturbance of mood, sleep, eating, motor behavior, thought, and self-esteem (Charney et al., 2002). The symptoms collectively indicate a coherent syndrome. However, they do not occur in the same distribution in every depressed person. In addition, early-onset depression is marked by inherent patterns of overlap among symptoms of other internalizing and externalizing disorders. In order to examine the core components, dimensions, and categorical boundaries of depression, several investigators have conducted factor analytic studies of mood-related symptoms in children (Lahey et al., 2004) and adults (Brown, DeNardo, Lehman, & Campbell, 2001; Gullion & Rush, 1998; Korszun et al., 2004; Nelson & Charney, 1981). The general factor structure emerging from such work informs investigations of how diverse psychological, biological, and clinical observations may converge and diverge.

6.1.1. Hedonic capacity

One of the most consistent observations among factor analytic studies of depression is that substantial unique variance in symptomatology is accounted for by a decreased hedonic capacity factor, characterized by items such as sad mood, anhedonia, loss of interest, lack of pleasure and enjoyment, decreased energy, fatigability, daytime sleepiness, psychomotor retardation, and walking or talking slower. As Hasler, Drevets, Manji, and Charney (2004) have noted, anhedonia has trait-like characteristics (Farmer et al., 2003). In addition, it is relatively specific to the depressive syndrome (Fawcett, Clark, Scheftner, & Gibbons, 1983; Loas, Boyer, & Legrand, 1999), often prodromal to major depression (Dryman & Eaton, 1991), and relatively stable over time (Oquendo et al., 2004).

A hedonic capacity construct has biological significance due to relations with brain reward systems and adaptive processes. Variations in reward sensitivity have been linked to the prefrontal cortex and related brain circuits (Kringelbach & Rolls, 2004; Rolls, 2004; Price, Carmichael, & Drevets, 1996) as well as dopaminergic and serotonergic neuromodulation in such brain circuits (Miner, Schroeter, Blakely, & Sesack, 2000; Sasaki-Adams & Kelley, 2001; Tremblay, Naranjo, Cardenas, Herrmann, & Busto, 2002). In addition, both neurotransmitters and neurotrophic factors mediate long-term alterations of the brain reward system and enable adaptive emotional responses (Nestler, Barrot, & Self, 2001, 2002). A large body of basic research has examined the brain reward system at multiple levels of analysis.

The current adaptive systems framework suggests that early-onset depression may be characterized by deficits in hedonic capacity and dysregulation of the brain reward system. This hypothesis would be supported by neurobiological evidence that youngsters with early-onset mood disorders have prefrontal and limbic abnormalities marked by disrupted brain development. This hypothesis also relates to molecular genetic evidence implicating neurotrophin gene variants in childhood-onset mood disorders. Such genetic polymorphisms may fundamentally alter brain development and adaptive processes. In addition, the mechanisms of reward-related prefrontal neurotransmitter and neurotrophic processes have implications for understanding the efficacy of antidepressant drugs and how such processes may change during development. Furthermore, promoting healthy mastery and reward-related behaviors, such as regular aerobic exercise, may be an important component of treating and preventing depression.

6.1.2. Stress sensitivity

A second fundamental component of depressive symptomatology is increased stress sensitivity, marked by dysfunction following major life events, sympathetic arousal, somatic anxiety, gastrointestinal symptoms, headaches, agitation, and irritability. Stress sensitivity also can be related to dysregulated sleep and eating. Debate exists about potential overlaps in stress-related symptoms among depressive and anxiety disorders. Data are converging and suggest that depression shares considerable variance with generalized anxiety disorder but less with other anxiety disorders such as phobias (Lahey et al., 2004). Notably, the stress-related component of depressive symptoms may be influenced by age and gender. For example, a factor analytic study of symptoms reported by third graders, their parents, and their teachers supported a single dimension of anxiety and depression, but separate anxiety and depression dimensions emerged when the children reached the sixth grade (Cole, Truglio, & Peeke, 1997). Such evidence raises the possibility that stress-related depressive symptoms may change in critical ways with pubertal development.

Considerable basic research has examined stress sensitivity in relation to neuroendocrine and autonomic systems. In addition, basic studies reveal the exquisite details of neuroendocrine processes involved in puberty (Sisk & Foster, 2004). Pubertal hormones fundamentally influence not only male and female genitalia. Hormonal changes also alter hypothalamic and related brain areas that regulate the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system. When people experience prolonged and elevated stress, they may develop dysregulated biological and psychological feedback mechanisms. The cycle may reduce thresholds for triggering autonomic arousal and depressive symptoms.

The current adaptive systems framework suggests that early-onset depression may be characterized by increased stress sensitivity and dysregulated HPA and autonomic responses. Early aspects of this dynamic process may include blunted growth hormone responses that influence developmental processes. Cortisol and other stress-hormone dysregulation may come later in response to prolonged distress. In addition, gender differences may be a fundamental aspect of such processes. Previous studies document that males and females differ in the exposure rates and depressogenic effects of stressful life events (Kendler, Thornton, & Prescott, 2001). Likewise, aforementioned biological studies of stress and 24-h cortisol levels have revealed puberty- and gender-related effects, including the finding that post-pubertal females generally show greater neuroendocrine stress responses than men (Young, 1998) and that women and men display greater cortisol responses to social rejection and achievement challenges, respectively (Stroud, Salovey, & Epel, 2002). Findings in this area are important for pharmacologic and cognitive-behavioral interventions (see Jacobs, 2001; Sherrill & Kovacs, 2004). In addition, studies have implications for novel approaches for regulating stress such as social bonding and massage (see Field, 2002; Frank, Swartz, & Kupfer, 2000).

6.1.3. Ruminative self-focus

Third, factor analytic studies of depressive symptoms emphasize a ruminative self-focus factor, characterized by items such as negative emotional bias, self-dislike, worthlessness, self-criticism, self-blame, guilt, sense of failure,

feeling punished, and interpersonal rejection sensitivity. Limited evidence exists for the stability and heritability of negative rumination, except that suicidal rumination and recurrent thoughts of death appear to be a specific characteristic of familial major depressive disorder (Kendler, Gardner, & Prescott, 1999). Further studies are needed to investigate whether persistent ruminations about death, self-destruction, and self-injury mark a particularly serious form of familial mood disorders with high risks for acting on such thoughts. Questions also remain about the extent to which suicidal rumination is categorically distinct from or exists on a continuum with other aforementioned ruminative symptoms.

The current adaptive systems framework suggests that early-onset depression may be characterized by ruminative self-focus. Such patterns may emerge with growing capacities for abstract thought during typical development, and self-destructive ruminations may be particularly severe among youngsters with a family history of mood disorders. Psychological science and neuroscience studies of ruminative self-focus have much to offer a multidisciplinary social neuroscience research program (Tomarken & Keener-Miller, 1998). A guiding hypothesis is that depressed adolescents may perseverate in a prolonged pattern of negative emotions. They may continue or repeat dysfunctional emotional behaviors even after the cessation of emotionally provocative events, and they may display emotionally-impaired decision making. Notably, perseverative and maladaptive emotional behaviors characterize laboratory animals with experimentally induced prefrontal cortex lesions (Jacobsen, 1935; Nauta, 1971). The prefrontal cortex and related areas appear fundamental to both emotional dysfunction and adaptive resilience. Critical work remains with linking basic neuroscience observations about prefrontal and related brain circuits to the developmental emotional trajectory of depressed youngsters.

Ruminative self-focus has psychological and clinical relevance, because it is related to both cognitive-behavioral and interpersonal formulations of depressive disorder and intervention strategies. Highly elaborate intervention techniques are available for addressing maladaptive ruminative patterns. Developing healthy appraisal and attribution skills for examining beliefs and interpretations provides a powerful way to cope with stress. Factor analytic studies of child psychopathology may offer ways to extend such work (Lahey et al., 2004). Among children, rumination-related items loading on the depression factor were characterized by isolation and anger (e.g., wanting to be alone, anger at other people or things, and social hostility), and an independent factor represented social anxiety and fear (e.g., nervous in front of people, embarrassed, shy, lacking self-confidence, not feeling good looking or smart, and worried about mistakes). These observations clearly distinguish patterns related to anger and fear, and they allude to a potential developmental progression of social and egocentric cognitions, such that ruminative content may change as children develop greater self-other awareness and emotional affordances. If so, such developmental processes for learning to navigate one's relationships with the environment and other people could be targeted to promote emotional resilience across the lifespan.

6.1.4. Attentional impairments

Fourth, factor analytic studies of depressive symptoms have addressed general cognitive problems such as inattention, distractibility, and trouble concentrating. However, such studies generally have not identified a discrete depression-related factor. In a study of child psychopathology, an inattention factor emerged separately from hyperactivity/oppositional behavior, depression, conduct problems, and anxiety (Lahey et al., 2004). In general, difficulties with attention and concentration are included in DSM-IV diagnostic criteria for a major depressive episode, but such impairments are not specific for depression and tend not to be stable over the course of depressive illness (Oquendo et al., 2004).

The current adaptive systems framework hypothesizes that attention-related symptoms are common during depressive and manic episodes, but that they may not reflect a specific, stable, causal mechanism of unipolar or bipolar depression. Despite the weak explanatory power of attention-related processes, such cognitive issues may be an essential part of treatment and prevention programs aimed at facilitating healthy development. For example, intervention and remediation focused on attention, learning, and memory may be an essential treatment component for youngsters with depression and other psychopathology in order to alleviate some of the consequences of the disorder, particularly when disorders are protracted or recurrent. Functional concomitants that can create confounds for etiologic studies may be among the most essential factors to address in general intervention programs to improve people's lives. This notion may be especially important for depressed youngsters with comorbid attention deficit disorder or learning disabilities. In addition, suffering with depression during childhood or adolescence can interfere with achieving developmental milestones. Caring for such youngsters involves recognizing such potential delays and nurturing their optimal development.

7. Closing remarks

In summary, the current paper reviewed a growing scientific literature about the psychopathology, intervention, and neurobiology of child and adolescent depression. A developmental social neuroscience perspective provides a theme for integrating disparate findings and spawning testable hypotheses about the relations among symptom presentation, biopsychosocial processes, and clinical interventions. An emerging principle is that early-onset depression may be related to developmental variations in neurobiological processes that are shaped by environmental inputs.

A dynamic adaptive systems framework is based on the guiding hypothesis that mood disorders may reflect core deficits in emotional adaptation. Emotional adaptation is a fundamental process that enables the brain to receive and integrate environmental and somatic information and to guide appropriate responses over time, and the construct can be examined from multiple levels of analysis. The adaptive systems framework addresses how the symptoms of depressive phenomenology can be parsed into empirically-derived terms of hedonic capacity, stress sensitivity, ruminative self-focus, and attentional impairments. Such components are clinically meaningful and quantitatively assessable and can be related to basic adaptive neurobiological, psychological, and developmental processes that are relevant to etiology and intervention. The dynamic adaptive systems framework suggests continuity between typical and atypical developmental processes, and it can be applied to study processes involved in depressive disorders as well as pathways to emotional resilience.

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