

CHAPTER 2

Depression

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It is estimated that 16% of the general population experiences clinically significant depression in a given 12-month period (Kessler, Tat Chiu, Demler, & Walters, 2005). In addition to the impact on affected individuals and their families, depressive disorders place a burden of almost \$50 billion per year on the American economy, accounting for over 20% of costs for all mental illness (Stewart, Ricci, Chee, Hahn, & Morganstein, 2003). Compared to other physical and mental disorders, depression is the leading cause of disability worldwide according to the World Health Organization (James et al., 2018). Given the substantial personal and societal costs of this disorder, efforts to identify vulnerability factors and effective interventions for depression are particularly important.

Our goal in this chapter is to present basic psychopathology research in depression and to discuss the treatment implications of these findings. Though all depressive disorders share similar features (Gotlib & LeMoult, 2014), there are some important differences between diagnostic categories that are not covered in this chapter. Instead, we focus here on depressive symptoms in general and major depressive disorder (MDD) in particular. We first describe the phenomenology of depression, including its associated clinical features and course. We then discuss the etiology of depression and focus in particular on novel empirical findings. After each section, we address the clinical implications of the findings. This is a timely and important task because, even though effective depression treatments exist, these interventions have undergone few changes in the past decades, and rates of recurrence of depression are still high even after successful treatment.

Cognitive-behavioral therapy (CBT), for example, is currently one of the most empirically supported and effective treatments for this emotional disorder. It is fascinating to see, however, that CBT for depression has undergone few changes in the last 50 years. This is surprising given the impressive increase in depression research in recent years, which has led to important improvements in models of depression, including cognitive models, regarding the risk for the onset and maintenance of this disorder. This is not by any means unique to CBT; Joiner and Timmons (2009) note that proponents of interpersonal psychotherapy (IPT) have yet to incorporate several basic findings from interpersonal research. Indeed, the majority of treatment-outcome research on IPT has used existing IPT protocols (Markowitz & Weissman, 2012).

PHENOMENOLOGY

As described earlier, we first review the phenomenology of depression. Toward this goal, we describe the clinical symptoms, associated clinical features, prevalence, course and outcome, and common comorbid conditions. We then discuss the clinical implications of these findings.

Typical Symptoms

Depression is typified by low mood and/or loss of interest or pleasure in daily activities. People with MDD also experience cognitive, affective, and somatic difficulties, such as weight/appetite disturbance, sleep disturbance, psychomotor agitation/retardation, fatigue, feelings of worthlessness or guilt, and difficulty concentrating. Thoughts of suicide or death are also present in MDD at rates higher than those in the general population (as reviewed by Klonsky, Saffer, & Bryan, 2018).

The diagnostic criteria place much emphasis on vegetative or somatic symptoms of depression, but it is important to note that these symptoms are not specific to depression and are observed in many disorders, such as generalized anxiety disorder (GAD). There is evidence, however, to support the view that these symptoms are important to diagnosis but may not be central to the disorder. Mitchell, Goodwin, Johnson, and Hirschfeld (2008) found that somatic symptoms, when present, have high rule-in value for diagnosis but do not provide adequate classification on their own. Instead, according to these authors, mood and emotional symptoms are most clinically useful for making accurate diagnoses. This suggests that somatic symptoms play a role in depression but may not be central to the disorder in all cases. That being said, somatic symptoms do have prognostic significance; they are associated with more severe depression and predict greater depressive symptoms 6 months and 2 years later (Hung, Liu, Wang, Juang, & Yang, 2010).

However, what seems to particularly define depression across heterogeneous presentations is that it is a disorder of mood or affect. As a consequence, many newer etiological models of depression emphasize difficulties in emotion regulation as a central feature of the disorder (LeMoult & Gotlib, 2019; Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). Thus, we discuss emotion regulation in more detail in the etiology section of this chapter.

Associated Clinical Features

Depression is associated with several common clinical features not included in the diagnostic criteria. Anger or hostility is often a characteristic of depression (e.g., Painuly, Grover, Gupta, & Mattoo, 2011). Importantly, it seems that irritability is correlated with higher severity of depression (Perlis et al., 2005) and that it represents an additional risk factor within this population rather than a subtype of irritable depression. Others have also found that anger distinguished those with a history of a suicide attempt from those without one (Jandl, Steyer, & Kaschka, 2010; Perlis et al., 2005). Moreover, anger also appears to characterize depressed individuals' relationships with others, including friends, strangers, therapists, and spouses (Coyne, Burchill, & Stiles, 1991; Joiner, 2002). It is notable in this context that irritability is listed in the DSM as a symptom of depression in children and adolescents, but not in adults.

Interpersonal problems associated with depression are not restricted to hostility. Depressed individuals show social skills deficits and tend to seek both excessive reassurance and negative feedback from others. These aversive interpersonal behaviors can lead to frustration in close others and eventually, to rejection. Moreover, evidence from longitudinal studies indicates that excessive reassurance seeking and negative feedback seeking are robust risk factors for depression (Evraire & Dozois, 2011; Joiner & Timmons, 2009). Considering such interpersonal difficulties, it is not surprising that depression has been associated with elevated levels of marital dissatisfaction and discord, which appear to be both causes and consequences of depression (Davila, Stroud, & Starr, 2009; Joiner & Timmons, 2009).

The most serious associated feature of MDD is the increased risk for suicide. While death by suicide is rare, the consequences are dire. Depressive disorders are among the psychiatric disorders associated with the highest risk for suicide (as also reviewed by Bryan & Klonsky, Chapter 15, this volume). The likelihood of attempting suicide increases with depression severity, and acute and intense negative mood tends to precede attempts (Berman, 2009). Recent research has identified risk factors associated with suicidal ideation and attempts (Klonsky et al., 2018). Klonsky and May's (2015) three-step theory of suicide posits that the transition from suicide ideation to attempt occurs in three steps. In Step 1, the combination of pain (often psychological pain) and hopelessness leads to suicidal ideation. In Step 2, ideation escalates if pain exceeds level of connectedness with others, with valued roles, or with a sense of meaning and purpose. In Step 3, this can escalate to a suicide attempt if the individual has the capacity to attempt suicide. This includes dispositional capacity (e.g., high pain threshold, low fear of death), acquired capacity (habituation to pain, fear, or death through exposure to life events involving these themes), and practical capacity (knowledge and access to lethal means). Importantly, psychological pain, hopelessness, and low connectedness are all common features of depression.

Individuals with depression also display significant distress and/or impairment across domains of functioning. For example, depression is associated with sexual dysfunction, as well as relationship or marital problems (see Sbarra, Manvelian, Salinger, & Whisman, Chapter 12, and Pukall & Bergeron, Chapter 13, this volume). It is also frequently noted that occupational difficulties, including unemployment, absenteeism, and reduced work performance, are common in depression and are associated with greater symptom severity (e.g., Birnbaum et al., 2010).

Medical conditions are frequently comorbid with MDD. While there does not seem to be a consensus regarding whether (or which) medical conditions predict the occurrence of depressive episodes, numerous prospective studies have shown that depression increases the likelihood of physical illness (e.g., Salaycik et al., 2007). While depression may lead to physical illness as a result of engagement in maladaptive health behaviors (e.g., sedentary lifestyle, poor nutrition), there is also strong evidence that depression is associated with higher levels of systemic inflammation. Over time, high levels of inflammation may not only promote depressive symptoms but also result in the physical diseases commonly comorbid with depression (e.g., arthritis, cardiovascular disease, cancer; Slavich & Irwin, 2014). When a medical condition co-occurs with depression, the course of the medical condition is often longer, and the condition may complicate treatments for depression (Carney & Freedland, 2017; Freedland & Carney, 2009). Given its effects on physical health, it follows that depression also impacts all-cause mortality rates, particularly among older individuals. Evidence suggests that the mortality rate for people over age 55 increases three to four times with depression, and that mortality is substantially higher among individuals with depression during the first year living in a nursing home (American Psychiatric Association, 2013).

It should also be noted that cognitive factors are closely associated with depression. As described in the section on etiology, some cognitive content and processes have been identified as risk factors for depression (e.g., biased information processing), whereas others (e.g., negative automatic thoughts) appear as features or symptoms of current depression episodes.

Epidemiology

Depression is highly prevalent, with lifetime prevalence rates varying between 10 and 21% (Hasin, Sarvet, & Meyers, 2018). The 12-month and lifetime prevalence rate is between 13 and 26% for women, and between 7 and 15% for men (Hasin et al., 2018). Prevalence rates differ considerably by age group, with higher prevalence rates in individuals ages 18–64 years compared to individuals 65 years or older (Hasin et al., 2018). Interestingly, there has been a steady increase in prevalence rates of depression since World War II (Kessler et al., 2003). Although there are some discrepancies, most studies indicate that prevalence rates differ among people who identify as White, Asian, Native American, Hispanic, and Black (e.g., Hasin et al., 2018). For example, Hasin and colleagues (2018) reported higher prevalence rates in individuals who identify as White or Native American compared to individuals who identify as Asian, Hispanic, or Black in the United States. Higher rates of depression are also found among people living in poverty or who have less education (Kessler et al., 2003). Furthermore, the manifestation of depression symptoms can vary across cultures and ethnic groups. For instance, somatic complaints are more common in some non-Western populations, highlighting how culture can dramatically influence how clients present their complaints (American Psychiatric Association, 2013).

Another key finding is that women are 1.5 to 3 times as likely as men to experience depressive episodes (American Psychiatric Association, 2013). The gender difference in rates of depression begins to present around age 13 (Hankin et al., 1998), and the likelihood of developing depression is twofold for females compared to males by age 15 (Cyranowski, Frank, Young, & Shear, 2000). This gender gap may be

influenced by pubertal maturation differences between females and males, and the hormonal changes that occur during this time (e.g., changes in gonadal hormones; Cyranowski et al., 2000). However, the biological changes during puberty are not solely responsible for depression onset, as they interact with an increase in negative life events that occur during this developmental period (Cyranowski et al., 2000). A critical explanation for gender differences in the prevalence of depression is that differences in emotion regulation make females more prone than males to respond to major life events with depressive episodes (Jose & Brown, 2008; Nolen-Hoeksema et al., 2008). We return to this explanation later in the chapter when we discuss etiological models of the disorder.

Course

The first onset of a major depressive episode can occur at any age, with data from prospective studies suggesting that the first onset of depression typically occurs during adolescence (Kim-Cohen et al., 2003). An earlier age of onset is associated with greater impairment across several domains (e.g., social and occupational functioning, quality of life, suicide attempts, recurrence; e.g., Zisook et al., 2007). Importantly, individuals who develop depression frequently report a history of depressive symptoms even before their first episode. Put another way, subclinical forms of depression are very common and may predict the onset of clinical episodes of the disorder (Jeuring, Huisman, Comijs, Stek, & Beekman, 2016).

Moreover, depression can be both a chronic and recurrent disorder. The typical time to recovery from a depressive episode ranges from 3 to 6 months; however, a proportion of individuals continue to meet criteria for a depressive episode a year after initial diagnosis (Whiteford et al., 2013). In a recent study, approximately 37.6% of a depressed sample experienced a subsequent depressive episode within 4 years of remission (Scholten et al., 2016). Research shows that the probability of onset of another episode of depression increases by 16% with every episode a person experiences (Solomon et al., 2000).

Even though initial success rates of treatment are high, relapse rates also remain high; thus, there is considerable room to improve treatment effectiveness (Steinert, Hofmann, Kruse, & Leichsenring, 2014). For example, whereas Hollon, Stewart, and Strunk (2006) reported less than a 5% relapse rate 6 months after CBT for most anxiety disorders, they reported an almost 20% relapse rate 6 months after discontinuing cognitive therapy for depression. This is despite the fact that booster sessions were included in the depression, but not in the anxiety, treatment protocol. Furthermore, relapse rates may be worse for individuals who do not fully benefit from treatment. In a study of inpatients with depression, Conradi, Ormel, and de Jonge (2011) found that residual symptoms during remission were highly prevalent. Indeed, approximately one-third of patients reported residual symptoms during remission, and these symptoms enhanced risk for short-term relapse, poor social functioning, and poor health outcomes (Kennedy & Foy, 2005).

Comorbidity

Comorbidity among psychiatric disorders has received increasing attention in both clinical research and practice. The presence of comorbidity is now frequently

accepted as the rule rather than the exception. Moreover, the presence of comorbidity has important implications for the course, prognosis, and treatment of depression.

Results from the National Comorbidity Survey Replication indicate that 45% of individuals with psychopathology meet criteria for more than one disorder (Kessler et al., 2005). Of those with MDD, the percentage of people with comorbidity increases to 76%. There are particularly high correlations among MDD, GAD, social anxiety disorder (SAD), and agoraphobia. Within an outpatient sample with depression, for example, anxiety disorders (particularly SAD at 29.3% and GAD at 20.8%) were the most common comorbid disorders (Rush et al., 2005). Additionally, posttraumatic stress disorder (PTSD) and depression are commonly comorbid, with approximately 52% of individuals with PTSD presenting with comorbid MDD (Ikin, Creamer, Sim, & McKenzie, 2010; Rytwinski, Scur, Feeny, & Youngstrom, 2013). Individuals in the military and those who have experienced interpersonal trauma show higher rates of comorbid MDD and PTSD compared to the general population and survivors of natural disasters (Rytwinski et al., 2013). Concordance estimates are also high between lifetime MDD and substance-related disorders (Hasin, Goodwin, Stinson, & Grant, 2005). Finally, personality disorders, especially borderline personality disorder, are also highly associated with depression (Lenzenweger, Lane, Loranger, & Kessler, 2007).

The onset, frequency, and duration of depressive episodes are influenced by the presence of comorbid psychiatric disorders. For example, comorbidity of depression and anxiety disorders is associated with earlier onset and longer depressive episodes compared to the presence of depression alone (Penninx et al., 2011). Interestingly, symptoms of depression are also a risk factor for developing symptoms of anxiety, suggesting a bidirectional association between anxiety and depression (Jacobson & Newman, 2017). There is also a bidirectional association between PTSD and MDD; however, PTSD typically precedes depression (see Stander, Thomsen, & Highfill-McRoy, 2014, for a review). Similarly, the majority of longitudinal epidemiological data indicate strong evidence for a bidirectional association between depression and substance use. Heavier alcohol use and more frequent drug use during periods of childhood, adolescence, or early adulthood predicts the development of MDD (Brook, Brook, Zhang, Cohen, & Whiteman, 2002). Other studies have suggested that MDD might also be a precursor to substance use disorders (Armstrong & Costello, 2002; Rao & Chen, 2008). Regardless of temporal sequencing, the presence of substance use disorders is associated with more prolonged and recurrent depressive episodes.

When comorbidity is present, it is strongly related to the severity of symptom presentation. Comorbidity of depression and anxiety, in particular, has been associated with more severe complaints, increased behavioral avoidance, greater impairment in social and occupational functioning, higher risk of suicide, and higher utilization of mental health services (as reviewed in Belzer & Schneier, 2004). Of the anxiety disorders, the presence of depression with comorbid SAD or GAD is associated with particularly poor outcomes. Comorbidity of SAD and MDD is generally associated with increased risk for suicidality and alcohol dependence (Belzer & Schneier, 2004). Furthermore, data from an epidemiological study indicate that the presence of depression and comorbid GAD is highly disabling, over and above that of depression alone (Hunt, Slade, & Andrews, 2004). Those with comorbid PTSD and depression report reduced life satisfaction, diminished quality of life, and higher symptom severity compared to those presenting with either disorder alone (Ikin et

al., 2010). The co-occurrence of addictive disorders and depression is also associated with greater impairment, including more severe substance-related problems, increased frequency of behavioral problems, and more severe impairment in family, school, and legal domains (see Rao & Chen, 2008, for a review).

The co-occurrence of depression and other psychiatric disorders has been explained by a variety of factors, including cognitive biases, biological dysregulation, and coping strategies. Depressed individuals with a comorbid anxiety disorder show different attention and memory biases than do those without comorbidity (Dannowski et al., 2006), as detailed in the section on etiology. Biased processing of negative information may place some individuals at risk for both depression and anxiety disorders. In addition, some anxiety disorders (e.g., SAD or agoraphobia) may lead to decreased social support, which increases risk for the onset of a depressive episode following stress. Researchers posit that the bidirectional association between PTSD and MDD is due to shared vulnerability factors (genetics, family environment) that increase the likelihood of the onset of both disorders (Stander et al., 2014). Depression is also associated with impaired executive functioning (Chakrabarty, Hadjipavlou, & Lam, 2016), which may preclude the ability to effectively manage trauma-related cognitions and may worsen prognosis of PTSD (Olf, Polak, Witteveen, & Denys, 2014). Other research has documented that increased risk for substance use disorders in depressed individuals might be partially accounted for by increased activation in the hypothalamus–pituitary–adrenal (HPA) axis (Rao, Hammen, & Poland, 2009). Substance use may also be an attempt to improve mood, particularly for individuals who do not use more adaptive emotion regulation strategies.

Clinical Implications

Research findings on the phenomenology of depression have various clinical implications that are relevant to therapists, irrespective of their theoretical orientation. To begin with, while psychopathology research indicates that low mood and diminished pleasure are the most characteristic features of this disorder, it also suggests that the presence of somatic symptoms, including changes in sleep, appetite, and psychomotor changes, is indicative of more severe and chronic depression. Because these symptoms do not always receive as much emphasis in the psychotherapy literature as psychological symptoms (e.g., feelings of worthlessness, guilt), vegetative or somatic features of depression may not always be on the therapist's "radar" despite their prognostic relevance. Therapists should assess these somatic symptoms when forming a case conceptualization and evaluating their clients' progress. The presence of somatic symptoms may inform the need for a greater number of sessions focused on interventions that target somatic symptoms and disengagement. For example, a cognitive-behavioral therapist may work through a more graduated hierarchy of activity scheduling as part of behavioral activation when working with a patient with vegetative symptoms to ensure that goals are realistic, achievable, and reinforcing. Across all forms of psychotherapy, therapists should assist patients who have difficulty with sleep or low energy with establishing a routine and may need to provide psychoeducation on sleep hygiene.

It is also important for therapists to remember that even though anger is not part of the diagnostic criteria, it is likely to be present and to manifest in the therapeutic relationship with a depressed client. Since the psychotherapeutic setting can be

viewed as a “microcosm” (Goldfried & Davison, 1976) of the client’s ways of reacting with others, we can predict from basic research that some depressed clients will feel frustration toward treatment and therapists. Such frustration may lead to, and be exacerbated by, negative responses (at times referred to as “countertransference reactions”) that have been observed across various theoretical orientations (Castonguay & Hill, 2017). When such interactions emerge, clinical judgment is needed to discern how much of this is a manifestation of the client’s disorder and how much is a reflection of an alliance rupture (e.g., due to a lack of fit between the client’s needs and the treatment implemented by the therapist, or the result of empathic failures on the part of the clinician).

Irrespective of the causes of the client’s anger or hostile transactions, process-oriented discussions about maladaptive interpersonal behaviors may be instrumental to meaningful therapeutic change. Potential growth opportunities include increasing the client’s awareness of the reactions the therapist and others have to the client’s verbal and nonverbal communication style, as well as providing a model of how to recognize and discuss one’s own negative emotions and their contributions to the dynamics of relationships (which scholars such as Safran & Segal, 1990, have referred to as “meta-communication”). As we discuss later in this chapter, other interpersonal issues related to the onset and maintenance of depression may merit being a foci of treatment.

When treating depressed clients, therapists must closely assess and monitor clients’ risk for suicide. Several factors have been associated with suicide attempts and deaths, such as comorbid substance abuse and older age. In addition, specific symptoms and comorbid diagnoses are highly associated with suicide in depressed individuals, including anxiety, panic attacks, anhedonia, alcohol use, difficulty concentrating, and global insomnia (Klonsky, May, & Saffer, 2016). These should be carefully assessed before and during treatment with depressed clients. Furthermore, given findings from the three-step theory of suicide (Klonsky & May, 2015), pain (including psychological pain), hopelessness, and connectedness also need to be monitored and treated. Capacity to attempt suicide should be assessed, including dispositional (e.g., high pain tolerance, low fear of death), acquired (e.g., history of physical abuse, nonsuicidal self-injury, combat training) and practical (knowledge, expertise, and access to lethal means) contributors.

Therapists also need to assess nonsymptomatic aspects of client functioning, such as work performance and satisfaction, sexual functioning, health problems, and health behaviors. Treatments that target affect may lead to a decrease in depressive symptoms, but they may not directly or immediately impact these other dimensions, which can have critical effects on a person’s quality of life. Unless these domains are addressed by specific therapeutic interventions or referral to other services, the scope of the therapist’s interventions may be limited. While clients may experience better mood at the end of short-term therapy, they may have a recurrence of depression if they continue to be confronted with serious occupational and health difficulties—as suggested by basic research on stressors associated with the onset of depressive episodes.

In line with increasing the specificity of psychological treatments for depression, clinicians would be wise to familiarize themselves with cultural differences in the manifestation and report of depressive symptoms. This has clear implications for the possibility of over- or underdiagnosing individuals due to cultural insensitivity, and

could also have important impacts on treatment process, fit, and ultimately, effectiveness. For instance, establishing a shared understanding of the causes of somatic symptoms may be key in building a therapeutic alliance, and could provide a focus for monitoring treatment progress.

Basic psychopathology research also suggests that clinicians would be well advised to ask when clients experienced their first depressive episode, as well as to assess for other disorders frequently associated with depression (e.g., anxiety, substance abuse, and personality disorders) to inform treatment planning. As mentioned earlier, both early onset of depression and comorbidity have been linked with greater impairment. Because depressed clients with higher levels of impairment have also been shown to require longer-term therapy to achieve significant symptom reduction (as reviewed by Beutler, Blatt, Alimohamed, Levy, & Angtuago, 2006), an a priori limited number of sessions, which is frequently mandated in clinical trials and managed care settings, may not be sufficient for these clients. Comorbidities may also need to be addressed as part of treatment and, based on the case conceptualization, may need to be included in the treatment plan. Newer transdiagnostic therapies, such as the unified protocol for emotional disorders (Barlow et al., 2010) and group transdiagnostic CBT (tCBT; Norton, 2012), are designed to simultaneously treat multiple and comorbid disorders, and these should be considered when selecting interventions and planning treatment. Transdiagnostic empirically supported treatment (EST) provides an evidence-based framework for effectively targeting common mechanisms underlying multiple disorders, and represents a promising advance in psychotherapy research.

Careful assessment of the idiographic course of the disorder for a particular client is also informative for treatment planning. Basic research demonstrates that people experience a number of symptoms before suffering from a full episode of depression, and that having such an episode is a strong predictor of future recurrences. Subthreshold levels of depression should therefore be an important target of prevention and intervention efforts. Furthermore, considering the strong relationship between the number of previous episodes and the likelihood of future episodes, clinicians should assess their clients' past episodes of major depression. Since repeated episodes may indicate extreme vulnerability, therapists should expect that stronger (more intense, longer) doses of treatment might be necessary to foster restoration and/or consolidation of adaptive ways of functioning than the amount of therapy typically delivered in current EST for depression. Irrespective of the length and intensity of the treatment required, data also suggest that treatment should continue until symptoms fully abate; failure to do so may predict relapse.

Given that a substantial number of untreated individuals with depression do not experience remission from their symptoms for a year or longer, treatment should not be delayed with the hope that depression will go away by itself (i.e., spontaneous recovery). This recommendation for treatment can and should be made strongly by therapists, government agencies, and managed health care organizations because several psychological (and pharmacological; see Nathan & Gorman, 2021) treatments have received empirical support for their efficacy. In a review, Fолlette and Greenberg (2006) categorized three treatments as "well established" (behavior therapy, cognitive therapy, and IPT); two as "probably efficacious" (short-term psychodynamic therapy, process-experiential therapy); and one (mindfulness therapy) as "experimental," based on promising initial results. The evidence supporting the effectiveness of

these different treatment orientations for depression means that it may be clinically unsound for clinicians not to use ESTs, at least as first lines of intervention.

Follette and Greenberg (2006) also derived six principles of change from treatment manuals of empirically supported psychological therapies that could guide evidence-based practice for depression: (1) challenging cognition and behavior; (2) increasing positive reinforcements and decreasing negative reinforcements (for avoidant and depressotypic behavior) in the client's life; (3) improving the client's interpersonal functioning; (4) improving marital, family, and social environment; (5) fostering emotional awareness, acceptance, and regulation; and (6) providing a treatment that is both structured and focused. These therapeutic strategies cut across several ESTs and may be incorporated into most forms of psychological treatments. Moreover, these principles are precise enough to guide the focus of clinicians' interventions without being restricted to a narrow and orientation-specific set of prescribed procedures (see Castonguay & Beutler, 2006). There are, for example, many techniques (e.g., interpretation, cognitive restructuring) that therapists can use to challenge client appraisals or views of self and others, all with similar aims (Goldfried, 1980). In addition, principles of change can help therapists to increase their repertoire of interventions and individually optimize treatment if their treatment protocol does not sufficiently target factors believed to cause or maintain depression for that particular client. For example, in addition to using effective techniques to address "internal" or intrapersonal issues (e.g., exploring a client's emotions or challenging distorted cognitions), experiential, psychodynamic, and cognitive-oriented therapists should also assess and, if necessary, address interactional issues that are frequently associated with depression, such as social isolation, interpersonal skills deficits, and dysfunctional marital or familial relationships. Detailed descriptions of how these and other empirically derived principles of change are implemented in routine treatment of depression (both with or without comorbid substance abuse or personality disorder) by experienced therapists of different theoretical orientations have been recently presented (Castonguay, Constantino, & Beutler, 2019).

As mentioned earlier, however, not all depressed clients benefit from therapy, and many who do benefit fail to retain their therapeutic gains after the completion of treatment. There is much room for improvement in our interventions for this debilitating and costly disorder. While it is unlikely that devising new forms of therapy is the best strategy to improve treatment outcomes, a more fruitful strategy may be to build on and improve already established and supported treatments. This could be done by modifying existing therapies based on the findings of psychotherapy process research. As an example, promising evidence suggests that integrating interpersonal and humanistic interventions aimed at repairing alliance ruptures (which are robustly linked to worse outcomes in depression treatment) may improve the efficacy of cognitive therapy for depression (Castonguay et al., 2004; Constantino et al., 2008; Safran & Muran, 2000). Other researchers have found that therapists are more effective when they promote their client's autonomy by encouraging them to set therapeutic goals and make decisions (Zuroff, Koestner, Moskowitz, McBride, & Bagby, 2012).

As most clinicians are already aware, depression is one of the most common problems encountered in clinical practice. Interestingly, and perhaps alarmingly, research has shown that the prevalence of depression may be increasing (Hidaka, 2012). According to Seligman (1989), this increase points to social/environmental

determinants of depression. Contrasting a 10-fold increase in prevalence observed in the general population with the rate of depression in some “nonmodern” cultures (e.g., Amish), he argued that contemporary society’s emphasis on individualism rather than on the common good plays a causal role in depression. It may be that the lack of commitment to common goals has reduced opportunities for group activities and a sense of belongingness that buffer against depression when one is confronted with personal difficulties or failures. An overinvolvement in activities aimed at increasing individualistic accomplishments, wealth, and comfort might make it more difficult to ask others for help when we are experiencing major difficulties. With this in mind, and irrespective of their orientation, clinicians are encouraged to help clients renew or create meaningful relationships. They should teach clients skills to be appropriately vulnerable, and they should encourage clients to become involved in purposeful and pleasurable activities with others. These clinical recommendations focused on improving clients’ interpersonal functioning, as well as improving the marital, family, and social environment, emerge from the basic research described earlier and are consistent with the principles of change derived from ESTs. Such a convergence of findings across different domains of research may not be a surprise considering the core aspects of human functioning to which they appear to be linked. As argued by MacLean (1985), communication and attachment are two of the evolutionary developments that differentiate humans, and all mammals, from reptiles. Denying or not attending to such ways of being forces ourselves and our clients to fight a losing evolutionary battle!

Helping clients to be more engaged interpersonally, however, may be more difficult with some people than with others. Individual preferences and cultural norms vary in terms of agency and communion needs and tendencies. As described by Bonanno and Castonguay (1994), when conducting therapy with agency-oriented people, it might be best to initially focus on intrapersonal or individualistic issues, so that the tasks and goals of therapy may be more synchronized with individuals’ typical ways of coping with life difficulties. With the development of a stronger therapeutic alliance, however, we may begin to focus more on what are likely to be deficits in the interpersonal functioning of these individuals.

ETIOLOGY

As we mentioned earlier in this chapter, the extent of the empirical literature on the determinants of depression prevents us from providing a comprehensive review of vulnerability factors for this disorder. Among the most obvious omissions in the following subsections are basic findings related to some biological models (e.g., neurochemical abnormalities, genetic disposition) and learning (e.g., operant and vicarious conditioning) that have been associated with depression (for reviews, see Burke, Davis, Otte, & Mohr, 2005; Johnson, Joormann, LeMoult, & Miller, 2009; Sullivan, Neale, & Kendler, 2000). These well-established vulnerability factors have provided a foundation for some of the currently supported psychological and pharmacological treatments. Our goal, however, is to focus primarily on recent basic findings and etiology research that have not yet been sufficiently incorporated in our current treatments.

Cognitive Theories

Cognitive models of depression posit that depressed individuals exhibit cognitive biases in all aspects of information processing, including memory, attention, and interpretation (Mathews & MacLeod, 2005). These cognitive biases may increase risk for the onset and maintenance of depressive episodes. Although empirical results for some of these biases are mixed, others have been consistently associated with depression and may have important treatment implications.

Memory

Overall, there is strong evidence for biased memory in depression (Mathews & MacLeod, 2005). In fact, better recall of negative relative to positive information represents one of the most robust cognitive findings associated with major depression. Memory biases are found most consistently in free recall and explicit memory tasks. For example, when attempting to recall details of past events or recently viewed words, individuals with depression are more likely than nondepressed controls to recall negative or unpleasant information.

Additional evidence that individual differences in memory play an important role in depression comes from research on overgeneral memory (Williams et al., 2007). These studies show that depressed participants respond to positive and negative cues with memories that summarize a category of similar events. For example, when asked to describe a specific positive memory, nondepressed controls provide specific details of a past event (e.g., “the day my family went to Lake Michigan”); however, individuals with depression tend to recall a more general period in time (e.g., fifth grade). Importantly, this research has demonstrated that overgeneral memories are associated with poor problem solving, difficulty imagining specific future events, and delayed recovery from episodes of depression. Moreover, overgeneral memories remain stable outside of episodes of the disorder and have been shown to predict later onset of depressive episodes following life events.

Attention

Researchers have also investigated whether depressed individuals display biases in attention, which refers to the tendency to visually attend to negative versus positive information in the environment (see LeMoult & Gotlib, 2019, for a review). Although evidence for attentional biases in depression has been mixed, there are specific circumstances when depressed individuals do display attentional biases, and understanding these circumstances can offer treatment-relevant insights. For example, whereas depressed and nondepressed individuals do not differ in their attention to negative information presented for short durations, depressed individuals spend *more* time attending to negative information that has captured their attention. These findings suggest that depressed individuals do not automatically orient their attention toward negative information in the environment, but once such information becomes the focus of their attention, they have greater difficulty disengaging from it. Notably, difficulty disengaging attention from negative stimuli has important implications, such as predicting greater reactivity to stress (Sanchez, Vazquez, Marker,

LeMoult, & Joormann, 2013) and a worse course of depression symptoms over time (Disner, Shumake, & Beevers, 2017).

Interpretation

Results also have been mixed regarding whether depression is characterized by an interpretation bias (Lawson, MacLeod, & Hammond, 2002). Recent evidence, however, suggests that those with depression typically make negative interpretations of ambiguous information, and that symptom severity correlates with the magnitude of their negative interpretation bias (see LeMoult & Gotlib, 2019, for a review). In a meta-analysis, Everaert, Podina, and Koster (2017) found that negative interpretation biases are stronger for self-referential stimuli (i.e., referencing personal experience) than for non-self-referential stimuli. Other research indicates that healthy control participants show a positive cognitive bias that does not appear in participants with depression. Thus, whereas healthy controls have a positive interpretation bias, individuals with depression may have a more “realistic” view of the world (McKendree-Smith & Scogin, 2000).

Cognitive Control

Recent cognitive theories posit that the aforementioned depressogenic biases in attention and memory are due in large part to biases in cognitive control (Joormann, 2010). Indeed, depression is associated with difficulty in multiple aspects of cognitive control, including difficulty inhibiting negative information from entering working memory, difficulty shifting away from negative information held in working memory, and difficulty disengaging from negative material in working memory (LeMoult & Gotlib, 2019). Consequently, depressed individuals exhibit sustained processing and increased elaboration of negative content, often observed as biases in attention and memory (described earlier) or as rumination (described in more detail later in this chapter). Because the experience of negative mood states and negative life events is associated with the activation of mood-congruent cognitions in working memory, the ability to control the contents of working memory may be critical in differentiating people who recover easily after experiencing negative affect from those who initiate a vicious cycle of increasingly negative ruminative thinking and deepening sad mood.

Summary

Overall, the literature points to several cognitive biases that may have important treatment implications in depression. For example, as described earlier, depressed individuals have difficulty disengaging from negative stimuli once it enters into their awareness (e.g., Joormann & Gotlib, 2007), and this may lead to the increased elaboration of negative information and the negative memory biases frequently observed in depression (Mathews & MacLeod, 2005). In addition, overgeneral memory in response to negative cues is thought to contribute to negative mood states and is considered a risk factor for the development of depression (e.g., Rawal & Rice, 2012). Moreover, evidence suggests that deficits in cognitive control might underlie

the attention and memory biases observed in depression. Such deficits might also contribute to increased elaboration of negative information and rumination (Joormann, 2010), which are key contributors to prolonged negative affect. As such, training individuals to control the contents of working memory could interrupt the cognitive mechanisms that contribute to depressive episodes.

Emotion Regulation in Depression

Depression has been referred to as a disorder of emotion regulation (ER; Gross & Muñoz, 1995; Joormann & D'Avanzato, 2010). Sustained negative affect and persistent reduction in positive affect are the hallmark features of a diagnosis of a major depressive episode. How can we explain why some people respond to minor stressors with increasingly negative affect that can devolve into a full-blown depressive episode, while others seem never to become depressed, even when they face major adversity? Individual differences in ER, the important ability to regulate affective states, may provide an answer to these questions (Bonanno, 2005). Specifically, depression-vulnerable and nonvulnerable people do not differ in their initial response to a negative life event. Both groups experience sadness and respond with the activation of mood-congruent cognitions and increased accessibility of mood-congruent memories. Depression-vulnerable and nonvulnerable people do differ, however, in their ability to recover from this initial response (Teasdale, 1988). This suggests that we need to examine factors that impair or support this recovery.

The construct of ER, which evolved from the more general concept of coping, involves the use of behavioral and cognitive strategies to influence the duration, intensity, and experience of affect (Thompson, 1994). Emotions are regulated for a variety of reasons, such as to enhance desirable feelings, maintain social norms, and foster interpersonal relationships (Fischer, Manstead, Evers, Timmers, & Valk, 2004). Theories of depression emphasize that increased risk for MDD stems from the use of strategies that fail to down-regulate negative emotions after their initial onset (e.g., LeMoult & Gotlib, 2019; Nolen-Hoeksema et al., 2008), which leads to prolonged negative affect (John & Gross, 2004). In response to distress, the use of less effective ER strategies (e.g., rumination, suppression) has been associated with multiple psychological disorders, including depression (Kring & Werner, 2004), whereas effective ER strategies (e.g., reappraisal, emotional disclosure) are typically characteristic of healthy psychological functioning and mood (Gross, 1998; Nils & Rimé, 2012). In fact, studies indicate that less frequent use of effective ER strategies such as reappraisal is not only characteristic of those with depression, but it also predicts an increase in depressive symptoms (Dryman & Heimberg, 2018). These findings support the claim that more frequent use of certain maladaptive strategies (e.g., emotion suppression, rumination, and catastrophizing) and less frequent use of other, more adaptive strategies (e.g., reappraisal, self-disclosure) are related to depression (e.g., Garnefski & Kraaij, 2006; Kahn & Garrison, 2009).

An emerging line of research has focused on ER *flexibility*, the ability to flexibly use ER strategies to meet situational demands (Aldao, Sheppes, & Gross, 2015). This research deemphasizes the uniform effectiveness of ER strategies (described earlier) and instead argues that ER strategies are adaptive when they fit the context and facilitate goal pursuit (Aldao et al., 2015; Bonanno & Burton, 2013). For instance,

although reputed to be uniformly effective, reappraisal is less effective at regulating emotions elicited by stressors that are controllable by the individual. In this instance, engaging with and solving the problem itself is more effective (Bonanno & Burton, 2013). Indeed, research indicates that higher ER flexibility is associated with reduced symptoms of psychopathology (Aldao et al., 2015).

In addition, studies suggest that impaired ER not only characterizes currently depressed people but also may be observed after recovery. For example, Ehring, Fischer, Schnülle, Bösterling, and Tuschen-Caffier (2008) found that remitted depressed participants had greater difficulty regulating their negative emotions and more frequently used rumination and catastrophizing compared to control participants. Within the depression literature, rumination and distraction have received the most attention; however, emerging evidence also points to the important role of suppression and reappraisal.

Rumination

Rumination is a process of responding to distress by repetitively and passively focusing on symptoms of low mood and the potential causes or consequences of these symptoms. It is differentiated from negative automatic thoughts because it is a *style* of thinking rather than being characterized solely by negative thought *content* (Nolen-Hoeksema et al., 2008). This ER strategy is a particularly salient risk factor for depression because it exacerbates and prolongs depressed mood (see review by Nolen-Hoeksema et al., 2008). Empirical evidence has shown that rumination predicts the onset of major depressive episodes and higher levels of depressive symptoms, and that it mediates the gender difference in depressive symptoms (for a review, see Nolen-Hoeksema et al., 2008). Many studies that experimentally tested the effects of rumination show that induced rumination leads to sustained negative mood, increased negative cognitions, increased overgeneral autobiographical memory, and decreased problem solving in depressed participants (e.g., Nolen-Hoeksema et al., 2008).

Distraction

In contrast to rumination, “distraction” involves engaging in positive or neutral activities in order to divert one’s thoughts from symptoms of distress and depression (Lyubomirsky, Caldwell, & Nolen-Hoeksema, 1998). For example, one may lower the level of subjective emotion experienced by focusing on thoughts unrelated to the situation (e.g., planning a supermarket shopping list). It is important to differentiate attentional distraction, which involves shifting visual or auditory attention away from emotion-producing stimuli, as discussed earlier, from cognitive distraction described here, which involves shifting one’s thoughts away from the emotion or emotion-producing stimuli. Researchers have reported that dysphoric, clinically depressed, and recovered depressed people can use cognitive distraction to repair an induced negative mood state (Joormann & Siemer, 2004; Joormann, Siemer, & Gotlib, 2007). Indeed, distraction has been associated with adaptive outcomes such as faster physiological recovery from stress (Vickers & Vogeltanz-Holm, 2003), decreased depressed mood (Kuehner, Huffziger, & Liebsch, 2009), and shorter duration of

depressive symptoms (Nolen-Hoeksema, Morrow, & Fredrickson, 1993). However, depressed participants are less likely to use distraction even though they state that it could help them alleviate their negative affect (Lyubomirsky & Nolen-Hoeksema, 1993). Importantly, while distraction may be adaptive for limited periods, persistent distraction is an ineffective long-term ER strategy because it hinders effective problem solving (Campbell-Sills & Barlow, 2007; Kross, Ayduk, & Mischel, 2005).

Suppression

Suppression comprises both thought suppression and expressive suppression. Whereas thought suppression involves attempting not to think of an emotion-provoking event or stimuli, expressive suppression involves inhibiting the outward expression of an emotional experience, including facial, postural, and verbal cues. Ironically, research has shown that thought suppression can lead to increases in the accessibility and frequency of the thought the individual is attempting to suppress (Kircanski, Craske, & Bjork, 2008), which in turn increases their emotional response (e.g., Campbell-Sills, Barlow, Brown, & Hofmann, 2006). Several studies suggest that depressed and recovered depressed people are more likely than control participants to use thought suppression, and that the use of this ER strategy may play an important role in the onset and maintenance of depression (Wenzlaff, Rude, Taylor, Stultz, & Sweatt, 2001). Kahn and Garrison (2009) documented that depression is associated with not only more suppression but also less emotional self-disclosure (Kahn & Garrison, 2009), a technique that has far-reaching benefits. Indeed, self-disclosure can free up cognitive resources, can buffer against the effects of stress, has long-term health benefits, and can serve as an emotionally therapeutic experience (Pennebaker, 1997a, 1997b).

Although studies reveal that participants can successfully engage in expressive suppression when instructed, participants also show greater physiological activation when doing so. This suggests that expressive suppression is an effortful means of regulating emotion (Gross, 1998). Expressive suppression has also been found to be ineffective at regulating negative feelings, and several studies indicate that it decreases the experience of positive, but not negative, emotions (e.g., Gross & John, 2003; Nezlek & Kuppens, 2008). Moreover, the habitual use of this strategy is associated with lower well-being and greater symptoms of depression (Haga, Kraft, & Corby, 2009; LeMoult & Gotlib, 2019). Even outside the laboratory, greater use of expressive suppression has been linked to lower social support, lower social satisfaction, and decreased closeness to others (Srivastava, Tamir, McGonigal, John, & Gross, 2009).

Reappraisal

Reappraisal has increasingly become a focus within the depression literature. This construct refers to the process of changing the way one thinks about a situation to alter its emotional impact (John & Gross, 2004). Some people may reappraise a situation by changing their point of view (i.e., taking a third-person rather than a first-person perspective), whereas others change their interpretation of the situation (i.e., viewing a difficult task as a challenge rather than as a threat; Ray et al., 2005).

Habitual use of this strategy has been associated with adaptive changes in emotions, cognitions, and physiological arousal. For example, reappraisal has been linked to increased well-being, fewer depressive symptoms, increased inhibition of negative material, greater positive autobiographical recall, more adaptive physiological reactivity to distress, and better interpersonal functioning (Gross & John, 2003; LeMoult & Gotlib, 2019). Compared to other ER strategies, such as expressive suppression, reappraisal is associated with the experience of more positive affect and less negative affect (Gross & John, 2003).

Neuroendocrinology

Stressful life events and other psychosocial stressors are robustly associated with the onset, severity, and course of MDD (see review in Hammen, 2005). Dysfunctions in the neuroendocrine system might partially explain the link between stress and depression, making “neuroendocrinology”—the study of interactions between the endocrine and the nervous system—increasingly important (LeMoult, 2020). A central component of the neuroendocrine system is the HPA axis, which is essential in regulating the hormone cortisol. Cortisol affects many aspects of the body, including metabolism, immune function, and the brain. In addition to being released in response to stressors, it is released spontaneously throughout the day and shows patterns of diurnal variation. Diurnal cortisol production is influenced both by sleep–wake cycles and by affective state (Dedovic & Ngiam, 2015).

Given that functioning of the HPA system is so integrally related to the human stress response, it is not surprising that atypical patterns of both diurnal HPA functioning and acute HPA stress reactivity have been documented in various psychiatric disorders, including depression (e.g., Porter & Gallagher, 2006). Investigating neuroendocrine response in these disorders is important because it might represent a crucial link to the neurobiological research we describe later. For example, the hippocampus and the prefrontal cortex (PFC) are the brain regions with the highest density of glucocorticoid receptors. Chronic exposure to stressful events that result in persistent and increased cortisol secretion might lead to neurotoxicity in these areas (Sapolsky, 2000). Chronic cortisol secretion may also disrupt functioning in regions of the brain that are responsible for regulating emotion (e.g., the PFC and the amygdala), which, in turn, can interfere with the ability to cope effectively with subsequent stressors.

Differences in basal HPA activity and diurnal cortisol fluctuations have been found in individuals with MDD compared to their healthy control counterparts. Specifically, compared to healthy control participants, individuals with depression tend to show an exaggerated cortisol awakening response (CAR) and elevated cortisol levels throughout the day (see reviews by Burke et al., 2005; Dedovic & Ngiam, 2015; Pariante & Lightman, 2008). In a meta-analysis, Burke and colleagues (2005) reported that depressed individuals exhibit less cortisol reactivity in response to stress and slower cortisol recovery poststress compared to nondepressed individuals. They also reported that the higher the cortisol levels at baseline, the less cortisol produced after the stressor. Whereas some researchers have reported that HPA axis abnormalities in depressed individuals are state-dependent and ameliorate with clinical remission (e.g., Ribeiro, Tandon, Grunhaus, & Greden, 1993), more recent research has

documented dysregulated HPA-axis function in those with a history of depression (LeMoult, Chen, Foland-Ross, Burley, & Gotlib, 2015; Lok et al., 2012). Those remitted individuals who continue to show abnormal cortisol profiles during periods of remission also have a higher rate of relapse (e.g., Aubry et al., 2007; Zobel et al., 2001).

Importantly, elevated evening cortisol levels have been found in depressed adolescents compared to nondepressed adolescents, and elevations in evening cortisol levels within the sample of depressed adolescents predicted a recurrent course of the disorder at a 7-year follow-up assessment (Mathew et al., 2003; Rao et al., 1996). In addition, numerous studies have indicated elevated cortisol secretion in response to acute stressors in depressed children (e.g., Luby et al., 2003; Watamura, Donzella, Alwin, & Gunnar, 2003). Elevated levels of cortisol have also been found in healthy youth at risk for depression based on a maternal history of the disorder (LeMoult, Chen, et al., 2015), and in turn, elevated cortisol has been shown to predict the first onset of depression in these youth (LeMoult, Ordaz, Kircanski, Singh, & Gotlib, 2015).

Neuroimaging

Brain areas and neural circuits associated with the generation and regulation of emotional states have received increasing attention in research on affective disorders (see Davidson, Pizzagalli, & Nitschke, 2002, for a review). Theorists have posited that emotional behavior is linked to the functioning of two neural systems, a ventral system and a dorsal system. The ventral system involves brain regions that are important for identifying the emotional significance of a stimulus and producing affect; the dorsal system is important for executive function and cognitive control, including selective attention, planning, and effortful regulation of affective states. Adaptive emotional behavior is posited to depend on the integrity and balanced interaction of these systems (Ochsner & Gross, 2005).

Although the ventral system includes many different brain structures, the vast majority of mood disorders research on this system focuses on the amygdala and the subgenual anterior cingulate cortex (ACC). The dorsal region that has received the most attention is the PFC, with a particular focus on the dorsolateral PFC (DLPFC), and some focus on the ventromedial PFC (VMPFC; e.g., Gotlib et al., 2010). Although we focus on these brain regions, it is worth noting that they interact with many different divisions of the ACC, the PFC, and other brain regions in important ways that have repercussions for understanding emotion. The amygdala has been shown to play a prominent role in emotionally mediated attention, in assigning emotional significance to stimuli, and in memory of emotionally significant events. The subgenual ACC appears to mediate the subjective experience of emotion and emotional reaction to stimuli, particularly in guiding reward-seeking behavior (Pizzagalli et al., 2004). The DLPFC appears to be involved in the regulation of emotion (Drevets, 2000). For example, it appears to diminish amygdala activity in response to an emotional challenge (Siegle, Steinhauer, Thase, Stenger, & Carter, 2002).

Depression is associated with dysregulated neural functioning, particularly with a hyperactive ventral system (more specifically, the amygdala and subgenual ACC) and a hypoactive dorsal system (DLPFC; see Mayberg, 2002), as well as deficits in areas associated primarily with the processing of rewarding stimuli (Davidson et al., 2002). For example, compared to controls, depressed individuals exhibit greater activity in the amygdala (e.g., Siegle, Thompson, Carter, Steinhauer, & Thase,

2007) and subgenual ACC in response to emotional stimuli (e.g., Gotlib et al., 2005). Depression is also associated with diminished top-down activation in areas of the brain responsible for regulating emotion (i.e., DLPFC; see Gotlib et al., 2010, for a review), which exacerbates excess bottom-up activation in the ventral system.

A concern, though, is that much of this research examines participants during episodes of MDD, when group differences in activation could reflect a state-dependent feature of depression rather than an etiological risk factor. To disentangle epiphenomena from causal mechanisms, studies examining at-risk and unaffected family members are particularly important. Although more extensive research is needed, preliminary studies indicate that compared to healthy controls, youth at risk for depression display increased activation of the ventral system (Gotlib & Hamilton, 2008) and decreased activation of the dorsal region (e.g., Joormann, Cooney, Henry, & Gotlib, 2012). These findings suggest that amygdala response to emotional stimuli in depression is not just a state marker, but rather a preexisting vulnerability factor that could precipitate disorder onset.

Given that anhedonia is a cardinal symptom of depression and that aberrant reward responsivity is therefore important for understanding MDD (Kasch, Rottenberg, Arnow, & Gotlib, 2002), researchers have also begun to attend to areas implicated in the anticipation and response to reward. These include the ventral striatum and the nucleus accumbens (e.g., Knutson, Fong, Adams, Varner, & Hommer, 2001), which are regulated by the PFC (e.g., Phillips, Drevets, Rauch, & Lane, 2003). Along these lines, researchers have found that depressed individuals exhibit reduced activation in the nucleus accumbens relative to controls (Pizzagalli et al., 2004). Moreover, deep brain stimulation of the accumbens and the ventral capsule/ventral striatum has been shown to significantly reduce symptoms of anhedonia in those with depression (Malone et al., 2009).

Interpersonal and Developmental Contributions

Interpersonal factors have been associated with the onset, maintenance, and recurrence of depression across different phases of development. Early risk factors for depression include several manifestations of inadequate parenting, childhood maltreatment, and interpersonal life stress (Humphreys et al., 2020; LeMoult et al., 2020). Caregiver deficits that are risk factors for later depression in children (both in youth and adulthood) include various types of neglect, such as inattentiveness, withdrawal, understimulation, emotional unresponsiveness, lax enforcement, inconsistent reinforcement, and low frequency of positive reinforcement. Experiences of severe neglect and deprivation are particularly common when children are reared in institutions such as orphanages (Gunnar, Van Dulmen, & International Adoption Project Team, 2007). Other forms of early life interpersonal stress and childhood maltreatment may involve aggression toward the child, such as overt hostility, intrusiveness, and antipathy, as well as emotional overinvolvement, overstimulation, exposure to maladaptive interpersonal behavior and affect, and physical and sexual abuse. Insecure parent-child attachment and parental conflict have also been identified as early vulnerability factors for developing depression. Similarly, losing a parent, particularly to suicide or an accident, and having a depressed parent are robust predictors of depressive disorders (Davila et al., 2009; Goodman & Brand, 2009; Hammen, 2009).

A number of these early risk factors frequently co-occur and act in tandem to cause later depression. Impaired parenting, for example, has been found to mediate the relationship between parental depression and child psychological difficulties (Goodman & Brand, 2009; Hammen, 2009). Furthermore, children who are exposed to greater cumulative adverse events experience more negative outcomes in adolescence (Appleyard, Egeland, van Dulmen, & Sroufe, 2005). It should also be noted that children's vulnerabilities or problems (biological, cognitive, affective, and behavioral) may contribute to parenting difficulties, for instance, by prompting criticism from parents (see Goodman & Brand, 2009; Hammen, 2009). Regardless of whether their impact is direct or indirect, early interpersonal adversities and maltreatment likely contribute to the development of difficulties (e.g., deficits in emotion regulation and interpersonal skills, social-cognitive biases, insecure attachments, dysfunctional attributions, and poor ability to respond to stress) that make children vulnerable to later depression (Goodman & Brand, 2009; Jopling, Tracy, & LeMoult, 2020; Rnic et al., 2018).

In addition to childhood adverse experiences, major stressful events across the lifespan have also been associated with depression. As reviewed by Monroe, Slavich, and Georgiades (2009), most of the major events that have been linked with the onset of depression are interpersonal, such as humiliation, social defeat, rejection, social exclusion, ostracism, and loss. Among the evidence reported by Monroe and colleagues on the role of social-environmental factors is the finding that depressed individuals who experience major stress before the onset of depression have more severe symptoms than depressed people who were not confronted with such stressors (Monroe, Harkness, Simons, & Thase, 2001; Tennant, 2002). Research also suggests that stressful events occurring during a depressive episode may interfere with recovery (Mazure, 1998). Although interpersonal stressors are most closely associated with an onset of depression, other noninterpersonal events, such as occupational failure or job loss, also predict the disorder. Though findings are somewhat inconsistent, evidence indicates that some individuals may be particularly vulnerable to noninterpersonal stressors due to personality or cognitive styles related to placing a strong emphasis on achievement and autonomy (e.g., Mazure, Bruce, Maciejewski, & Jacobs, 2000).

Stressful events occurring in adulthood may also be an important mechanism for the intergenerational transmission of depression. For instance, studies suggest that parental stressful life events may mediate the relationship between parental depression and psychological problems experienced by their children. For example, the chronically stressful conditions in which depressed individuals live can increase the prevalence of depression in offspring (Hammen, 2009).

Romantic difficulties are frequently experienced interpersonal risk factors for depression in adulthood. When romantic relationships are supportive, they can be protective against depression. However, depression is also associated with challenges in romantic relationships, including a lack of support from one's spouse, couples' difficulties with solving problems, lower relationship satisfaction, and dissolution in romantic or marital relationships (Davila et al., 2009). Importantly, the association between depression and romantic problems is bidirectional. Negative events or chronic stressors in close relationships (e.g., conflict, tension, or loss) place individuals at risk for depression. In turn, depressed individuals are more likely to

contribute to negative dynamics and events in their relationships (Davila et al., 2009), often via maladaptive interpersonal behaviors.

Other research supports the role of specific interpersonal behaviors/styles as risk factors for the onset and maintenance of depression. These include excessive reassurance seeking, interpersonal dependency, and an insecure attachment style in adulthood (Joiner & Meltalsky, 2001; Joiner & Timmons, 2009; Roberts, Gotlib, & Kasel, 1996), all of which result in negative interpersonal life events, including conflict and rejection by others. Depression is also associated with *negative* feedback seeking, a concept linked to the social-psychological concept of self-verification (Swann, 1983). Numerous studies have demonstrated that depressed individuals prefer to be with (and/or give more credibility to) people who react negatively to them compared to people who provide them with positive feedback (e.g., Giesler, Josephs, & Swann, 1996; Swann, Wenzlaff, Krull, & Pelham, 1992). The inferred mechanism is that the desire for safety in having one's self-concept confirmed (even when it is negative) is stronger than the disconfirming (but positive) impact that enhancement feedback can have. However, as noted earlier, depressed individuals also tend to excessively seek reassurance from others. Evraire and Dozois (2011) posit that this discrepancy in the types of feedback depressed individuals attempt to elicit is explained by a desire for *global* enhancement, attained through reassurance seeking, and verification of *specific* attributes, pursued via negative feedback seeking.

As can be evidenced in several of the previous examples, depression-prone individuals have characteristics and engage in behaviors that increase their exposure to stressors—particularly interpersonal stressors—that in turn further increase depression risk. This process is referred to as “stress generation” (Hammen, 2006), and it is a key mechanism through which the cycle of stress and depression intensifies over time.

Clinical Implications

Several clinical recommendations can be derived from the vulnerability factors we have described. As previously mentioned, cognitive and affective factors involved in the onset and maintenance of depression are closely interconnected. Interestingly, research investigating both cognitive biases and ER strategies suggests that depressed individuals become stuck in maladaptive patterns of automatic reactions. Studies on attention, interpretation, and memory indicate that depressed individuals have difficulty disengaging from negative information. Similarly, ER studies show that depressed individuals inflexibly use strategies that prevent them from recovering from the initial response of sadness and its related mood-congruent thoughts and memories. If these factors do play a causal role in the onset and maintenance of depression, therapeutic interventions that can directly modify them may be particularly promising.

Cognitive Biases

Interestingly, experimental studies suggest that it might be possible to modify depressed mood by modifying the cognitive biases posited to underlie it. Initial studies demonstrated that training depressed people to disengage their attention

from negative material improves mood and reduces reactivity to stressful events (as reviewed by Hertel & Mathews, 2011). Positive attentional biases can also be trained (Wadlinger & Isaacowitz, 2008). Moreover, positive attentional bias training reduces attention to negative images during a stress induction (Wadlinger & Isaacowitz, 2008), and reduces self-reported and cortisol responses to stress (Dandeneau, Baldwin, Baccus, Sakellaropoulo, & Pruessner, 2007). These findings provide an exciting example of the way modifying cognitive biases may remediate dysfunctions in the neuroendocrine system, and they are consistent with theoretical models of depression positing a bidirectional association between cognitive and biological dysregulation (LeMoult, 2020).

Encouraging results have also been documented for interpretation bias training (see Hallion & Ruscio, 2011). Researchers have found that adults and youth can be trained to positively interpret ambiguous information (Holmes, Lang, & Shah, 2009; LeMoult et al., 2018), and that doing so attenuates depressed mood and responses to stress (Hallion & Ruscio, 2011). For example, Holmes and colleagues (2009) demonstrated that training positive biases helped to alleviate a subsequently induced negative mood state. These results suggest that changes in interpretation biases can lead to changes in emotional responding.

Other training studies have targeted the negative memory biases often found in depression (LeMoult & Gotlib, 2019). Overall, findings suggest that it is possible to alter the negative and overgeneral memory biases associated with depression. In positive memory enhancement training (PMET), for example, depressed participants were asked to recall a happy memory in a way that facilitated vivid recall of the moment-to-moment details (Arditte Hall, De Raedt, Timpano, & Joormann, 2018). Arditte Hall and colleagues (2018) found that PMET enhanced the specificity of depressed participants' positive memories and facilitated mood repair following a sad mood induction. Memory specificity training (MEST) has also been used to combat memory biases in depression. In MEST, participants are trained to recall specific details of their autobiographical memories. One focus of MEST is on making negative memories more specific; this is done to make negative memory less overgeneral (e.g., "I'm a failure") and specific memory (e.g., "I did not receive the promotion at work"; Raes, Williams, & Hermans, 2009). Both PMET and MEST training are associated with multiple benefits, including more specific positive memories, fewer intrusive negative memories, improved emotion regulation, and positive changes in mood state (Arditte Hall et al., 2018; Lang, Moulds, & Holmes, 2009; Raes et al., 2009; Watkins, Baeyens, & Read, 2009).

Researchers have also started to investigate the possibility of training cognitive control in depression and of examining the effects of this training on emotion regulation. Joormann, Hertel, LeMoult, and Gotlib (2009), for example, showed that depressed participants can be trained to forget negative material when provided with a strategy for how to keep irrelevant material out of working memory. These training paradigms typically ask participants to practice removing irrelevant negative material from working memory and replacing it with relevant positive or neutral materials for later recall. Brief interventions that target increasing cognitive control in severely depressed outpatients have, in turn, led to significant decreases in both depressive symptoms and rumination (Siegle, Thompson, et al., 2007). Moreover, Jopling, Gotlib, and LeMoult (2020) documented that depressed participants who

completed cognitive control training also exhibited more adaptive neuroendocrine and physiological responses to stress compared to depressed participants who received sham training.

Thus, taken together, findings suggest that cognitive biases can be modified in relatively few training sessions using easily implemented designs. Modifying cognitive biases has, in turn, been linked to short-term improvements in mood and stress reactivity, which highlights the interconnection between cognitive and psychobiological responses to stress (LeMoult, 2020) and suggests that such training might play an important role in treatment. Future research is needed to extend these investigations to a clinical population, and to examine the persistence of cognitive changes and mood states over longer durations of time.

ER Strategies

Consistent with some of the studies on cognitive biases, researchers interested in ER have found that ruminating about negative thoughts, feelings, and events is linked with depression. In contrast, research findings suggest that reappraisal is an effective strategy to shift individuals' affect from negative to positive. These findings highlight a clear convergence between basic psychopathology research and applied psychotherapy research. One of the best examples of this convergence is a new therapy focused on reducing engagement in maladaptive emotion regulation strategies. Rumination-focused CBT for depression (Watkins, 2018) is an EST centered around helping clients to shift from ruminative thinking to more action-oriented, concrete, specific, and experientially focused thoughts and behaviors.

As mentioned earlier, helping clients to change their cognitive appraisals has been identified as a key principle of change underlying psychological treatments that work for depression. Similarly, the basic finding that emotional disclosure has a positive effect on mood and functioning, as opposed to the negative impact of emotion suppression, is also consistent with another principle of change identified earlier (i.e., improving awareness, acceptance, and regulation of emotions). Interestingly, however, while therapists from different theoretical orientations have consistently recognized the importance of changing clients' views of self and others, and employ a range of techniques to do so (e.g., reformulation, or cognitive restructuring), an explicit focus on the experience and processing of emotion is emphasized to a greater and lesser extent across ESTs. Brief psychodynamic, process-experiential and interpersonal therapies, exposure-based CBT, and newer emotion-focused CBT (e.g., Unified Protocol for Emotional Disorders; Barlow et al., 2010) tend to place the greatest emphasis on emotional processing in session. Moreover, emotional activation has been linked with treatment outcome across a variety of theoretical orientations (Peluso & Freund, 2018). Not surprisingly, this has been the case in experiential and humanistic therapies, such as emotion-focused therapy (EFT; Greenberg & Watson, 2006), which specifically and explicitly focus on the processing and transformation of emotion (see Elliott, Watson, Greenberg, Timulak, & Freire, 2013). However, emotional deepening has also been associated with treatment outcome in traditional CBT (e.g., Castonguay, Goldfried, Wisner, Raue, & Hayes, 1996; Watson & Bedard, 2006), an important finding given that cognitive behavioral therapists tend to try to control or reduce emotions—at least compared to psychodynamic therapy (Blagys &

Hilsenroth, 2000). Thus, both basic and psychotherapy research appear to suggest that therapists might foster clients' improvement by facilitating emotional disclosure and expression, irrespective of their preferred theoretical orientation.

While basic research findings on reappraisal and suppression are consistent with principles of change derived from psychotherapy research, this is not the case for distraction. Distraction has received only limited attention in EST treatments for depression despite evidence from basic research that it is an effective ER strategy that is less effortful, and therefore more accessible, to those who are severely depressed. One exception is dialectical behavioral therapy (Linehan, 1993), a CBT that includes a module on distress tolerance skills, in which clients are taught to use strategies to self-soothe and distract themselves during crises. Clinicians and scholars of different orientations are encouraged to complement their clinical repertoires with interventions that use distraction to help depressed clients to disengage, at appropriate times and places and for limited periods, from rumination and negative emotions. For example, one of the authors of this chapter (L. G. C.) has learned that blasting Beethoven's Ninth Symphony in response to pervasive and recurrent ruminations late at night is not incompatible with (and may actually be a powerful adjunct to) verbally oriented forms of therapy. In other words, although there are times to explore emotions and examine maladaptive cognitions, there are also times when individuals would benefit from taking their minds away from them, for example, at bedtime or when they need to be present and engaged in other interpersonal or occupational activities.

Stress

Research conducted within both biological and psychological domains of psychopathology has demonstrated that stressful life events have an impact on the onset and maintenance of depression. A central implication of such findings is that therapists who are working with depressed clients should be prepared to use interventions to help clients decrease their levels of stress and to deal more effectively with the stressors they encounter in their lives.

Most CBTs for depression include teaching relaxation, coping, and problem-solving skills to help patients manage ongoing stressors (see Follette & Greenberg, 2006). Of note, exposure-based cognitive therapy (EBCT)—a newer CBT for depression—makes stress management a primary focus in an attempt to build on and increase the efficacy of current ESTs for depression (see Hayes, Feldman, Beevers, Laurenceau, & Cardaciotto, 2007). The exposure-based phase of this therapy involves activating and emotionally processing key experiences and feelings of worthlessness, hopelessness, and defectiveness that drive individuals' depression. However, depressed individuals who seek treatment frequently experience high levels of distress and depletion of resources, and their depressive symptoms and attempts to cope with stressors can generate even more stress. These problems may make processing core beliefs challenging and counterproductive. Therefore, the initial stage of this treatment aims to increase resources that build resilience, motivation, and stability in preparation for exposure. This initial stabilization phase involves emotion regulation and mindfulness meditation techniques to help clients recognize and reduce avoidance and rumination, behavioral activation exercises, problem solving,

and strategies for increasing the health and regularity of sleep, eating, and exercise patterns. The purpose of this first phase of therapy is to teach stress management skills and to reduce maladaptive processes, including avoidance, rumination, and stress generating behaviors that maintain depression. These skills are thought to be critical both to prepare for deeper emotional and cognitive change and to prevent relapse.

Importantly, there is no reason to assume that the addition of these stress-regulating strategies should be restricted to CBT-based interventions. They are not likely to interfere with flexible and competent use of traditional interventions prescribed in any EST-based treatment for depression, and they may help individuals to better cope with stressors they encounter.

Interpersonal Factors

Research on interpersonal vulnerability for depression underscores the influence of adverse interpersonal relationships, especially early caregiving relationships, in the pathogenesis of depression. As such, more adaptive relational patterns may be core to achievement of successful therapy. Alexander and French (1946) posited that clients improve in psychodynamic therapy not because they acquire insights about previously unconscious conflicts, but because therapy provides them with a corrective emotional experience. Therapeutic change takes place, more precisely, when the therapist reacts to the client in a way that disconfirms the client's negative expectations of others that the client derived from the relationship with their parents or other early attachment figures. While the construct of corrective experience emerged from the psychodynamic literature, it is now recognized as a core mechanism of change that cuts across different orientations (Castonguay & Hill, 2012).

There can be no doubt that the relational stance embraced in all ESTs for depression (including CBT; see Castonguay, Youn, Xiao, & McAleavey, 2018) sharply contrasts with the neglect (e.g., inattentiveness, withdrawal, emotional unresponsiveness) and abuse (e.g., overt hostility, antipathy) that have been experienced by some depressed individuals. Interacting with clients in an attentive, warm, engaged, empathic, accepting, affirming, autonomy-granting, calm, structured, and consistent way (as promoted in the writing of leading clinicians of different orientations; e.g., Carl Rogers, Lorna Benjamin, Marsha Linehan, and Marvin Goldfried), is likely to differ from the way many depressed people have been treated. This new way of being treated violates the client's expectations that they will be treated poorly by a person with whom they have shared personal information and have been emotionally vulnerable, one whom they may view as an authority figure, and with whom they have developed an attachment, not unlike that with a parent. As described elsewhere (see Hill et al., 2012), this disconfirmation of expectations may facilitate the reduction of symptoms, change the view of self and others, and allow the client to test out, practice, and integrate more adaptive interpersonal patterns.

In contrast, interacting in a hostile and dismissive way might reenact old aversive interpersonal patterns and prevent change. This is consistent with a number of applied psychotherapy studies. For example, fine-grained analyses of therapist-client transactions indicated that poorer outcomes were associated with therapists using "blaming" or complex communications (i.e., seemingly "supportive" statements that

also convey hostility or criticism; Henry, Schacht, & Strupp, 1986). In a subsequent study, Henry, Schacht, and Strupp (1990) found that therapists exercised more disaffiliative interpersonal behaviors (e.g., belittling and blaming, ignoring and neglecting) with clients who had a poor outcome, as defined by no change in how they treated themselves, compared to those clients who had a good outcome. For those with a good outcome, therapists displayed an almost complete absence of such negative interpersonal processes. These authors also found a significant positive correlation between the frequency of therapist statements marked by disaffiliative control and hostility and the frequency of patient utterances marked by self-criticism and self-blame. Altogether, these findings suggest that the contrast between the early experiences of many depressed clients and the experience of a supportive relationship with a therapist may mediate (at least in part) the positive link between the working alliance and outcome across different forms of therapy.

In addition to underscoring the importance of adopting an interpersonally warm and involved attitude, research findings indicate that clients may benefit from exploring early relationship events, including traumas, and their ramifications relative to clients' relationships with others during their life. This is at the core of at least two ESTs: process-experiential (i.e., emotion-focused) and short-term psychodynamic therapies. Consistent with the emotion-focused model, the resolution of unfinished business with significant others has been linked with therapeutic change (Elliott et al., 2013). In line with psychodynamic theory, process research indicates that the therapist's accurate interpretation of core relationships in the client's life is linked with positive outcomes (Crits-Christoph & Connolly Gibbons, 2002). Interestingly, a focus on past relationships and the pattern of interactions they might have influenced may also be beneficial in other forms of treatment. For example, while process studies indicate that CBT focuses less on developmental and interpersonal issues than does psychodynamic therapy (see Blagys & Hilsenroth, 2000), other investigations suggest that it might be helpful when CBT therapists do focus on these issues. For example, Hayes, Castonguay, and Goldfried (1996) found that the degree to which CBT therapists focused on attachment with early caregivers predicted therapeutic outcomes at the end of treatment and relapse rates 2 years after therapy. In addition, a study by Jones and Pulos (1993) suggests that CBT therapists may improve treatment outcomes by eliciting and processing memories of interpersonal experiences using the following psychodynamic techniques: linking patients' feelings or perceptions to situations or behavior of the past; discussing memories or reconstructions of childhood; drawing connections between the therapeutic relationship and other relationships; and identifying recurrent themes in patients' experience or conduct.

These findings suggest that generating emotional memories in therapy for depression might be helpful, a finding that will not surprise practitioners of CBT for PTSD, exposure-based methods for depression, and psychodynamic therapies. However, given the presence of memory biases and ruminative tendencies in depression, the timing of interventions that elicit emotional memories need to be considered carefully in the context of the therapeutic relationship and the client's current functioning, resources, and ability to regulate their emotions. Moreover, these interventions are not necessary in all cases, and therapists should use their skills in case conceptualization and progress monitoring to determine whether and when these techniques are indicated.

In addition to the developmental influence of interpersonal events and relationships, basic findings also point to the importance of addressing current interpersonal issues. Phenomenological research on interpersonal irritability and marital discord provides support for some of the specific principles of change underlying ESTs for depression, in particular IPT. Moreover, research on interpersonal factors that are involved in the etiology of depression can inform more specific treatment targets. When working with depressed clients, therapists should inquire about and, if necessary, work to help change clients' tendency to seek excessive reassurance and verification of their negative view of self, as well as other aversive behaviors that generate interpersonal stress and subsequent depression. As discussed by Joiner and Timmons (2009), such foci of interventions are not explicit components of current IPT. While they are consistent with principles of change underlying behavior therapy (i.e., "decreasing reinforcement for depressive and avoidant behavior"; Folllette & Greenberg, 2006, p. 94), full recognition of these issues may further improve the efficacy of traditional CBT for depression. For example, Hayes and colleagues (1996) found that relative to interpersonal issues, cognitive therapists tend to focus more on changing patients' cognitions about others than on direct interpersonal change. While the latter was linked with positive outcomes, the former was predictive of worse outcomes. Thus, attempting to foster concrete behavioral change in the interpersonal domain may be an important recommendation across many forms of therapy.

CONCLUSION

A great deal of research has been conducted on the psychopathology of depression. Studies investigating its phenomenology have revealed the preponderance, severity, recurrence, chronicity, and debilitating nature of this disorder. This descriptive research highlights several issues that therapists should assess and address when treating individuals with depression. Many of these issues are not frequently emphasized in the psychotherapy literature, including treatment implications of somatic symptoms, anger, poor health and occupational functioning, and timing of disorder onset.

Basic research on the etiology of depression has also identified several vulnerability factors involved in the onset and maintenance of this disorder. Some of these vulnerability factors are consistent with the principles of change that underlie currently validated psychological treatments for depression. However, other vulnerability factors have clinical implications that need to be more explicitly examined as ways to further improve evidence-based psychotherapy.

Basic research also conveys that the etiology of depression is not restricted to one set of causal or maintaining variables. Depression is likely to have multiple determinants. In addition, these determinants are interconnected (e.g., LeMoult, 2020), thereby creating complex networks of moderating and mediating influences on client's functioning. Accordingly, rather than restrict their understanding of depression within the confines of a single theory, clinicians are likely to increase their effectiveness by assessing an array of potentially underlying variables (biological, developmental, emotional, cognitive, behavioral, interpersonal). When forming a case conceptualization, clinicians are also encouraged to determine which of these

variables are likely to play primary roles for that specific client, and should therefore be core targets of their treatment.

In addition to targeting primary determinants of depression, the therapist's case formulation and treatment plan should take into account how these determinants interact with each other to interfere with the client's optimal level of functioning. While eclectic or prescriptive approaches to treating depression are likely to be effective (e.g., using social skills techniques with clients whose depression appears to be primarily related to their negative impact on others; using cognitive interventions when a highly functioning individual holds unreasonable standards), therapists should also develop integrative frameworks that assimilate different dimensions of functioning into broad and cohesive models (e.g., Gotlib & Hammen, 1992). Moreover, consistent with both prescriptive and integrative approaches, it is important to keep in mind that improvement in one domain of functioning is likely to have a positive impact on other domains. Adopting a more affiliative way of relating to others not only helps a client to find more fulfillment in relationships but is also likely to have an impact on their views of self. Therefore, therapists should assess multiple effects of interventions as part of ongoing outcome monitoring and in refining the treatment plan as therapy progresses. However, it is also important for the therapist to consider that a set of interventions may not have an impact on all potential determinants of depression; thus, they should broadly assess a client's functioning before terminating therapy, even if substantial changes have been achieved in one core dimension of functioning.

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