An integrative developmental psychopathology approach to depression

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Abstract

This chapter aims to describe an integrative developmental psychopathology approach to the conceptualization and treatment of depression. Based on evolutionary and developmental psychopathology approaches, we discuss empirical findings concerning three biobehavioral systems that are central in depression: stress or emotion regulation, reward, and mentalizing or social cognition. We discuss interrelated disturbances in each of these biobehavioral systems and how they typically lead to developmental cascades involved in depression. We focus on the impact of these interacting impairments on normative developmental tasks that rely on capacities associated with each of the three biobehavioral systems. We highlight the importance of adolescence and early adulthood, as these developmental phases involve the need to establish a new balance between relatedness and agency/autonomy, capacities that rely heavily on the stress-regulation, reward, and mentalizing systems. We also discuss how this approach sheds a new light on the high comorbidity between depression and other psychiatric and (functional) somatic disorders. Finally, we consider the implications of these views for prevention and intervention approaches.

Introduction

Depression is one of the most common and most prevalent mental health problems, and ranks among the leading causes of disability, morbidity, and mortality (Collins et al., 2011). Depression is best conceptualized as dimensional, ranging from subclinical to mild to severe and persisting mood problems. The distinction between normal variations in mood and depression as a clinical condition that warrants treatment is therefore to some extent arbitrary and influenced by sociohistorical factors (Jackson, 1986). Yet, even subclinical mood problems are responsible for considerable suffering, and the highly recurrent nature of depression in a sizeable proportion of individuals is associated with large personal and socioeconomic costs.

A wide variety of effective pharmacological and psychosocial interventions for depression have been developed and empirically evaluated. A recent review included more than 500 clinical trials examining the effects of antidepressants and more than 600 trials investigating the effects of psychotherapy for depression, with little evidence for superiority of any bona fide treatment for depression (Cuijpers, Stringaris, & Wolpert, 2020). A recent meta-analysis including 385 comparisons of 15 different types of psychotherapy reached a similar conclusion, reporting little or no differences in the effects of these treatments (Cuijpers, Karyotaki, de Wit, & Ebert, 2020).

Depression is a relatively common and highly prevalent condition. Studies suggest that 3–8% of children and adolescents meet criteria for clinical depression (Birmaher, Ryan, Williamson, Brent, & Kaufman, 1996; Costello, Erkanli, & Angold, 2006). Lifetime estimates of prevalence range between 15% and 20% (Birmaher et al., 1996; Demyttenaere et al., 2004). In childhood, depression is equally prevalent in boys and girls, but from age 14 women are twice as likely as men to be diagnosed with depression (see Angold, Erkanli, Silberg, Eaves, & Costello, 2002; Birmaher et al., 2007). Hence, a developmental view is necessary but surprisingly lacking in many extant theories of depression. Moreover, there is still a lack of integration between biological and psychosocial approaches to depression.

This chapter presents an integrative developmental psychopathology approach to depression building on other integrative efforts (Auerbach, Admon, & Pizzagalli, 2014; Davey, Yücel, & Allen, 2008; Gilbert, 2006; Luyten & Fonagy, 2018;

Pizzagalli, 2014). It focuses on the developmental emergence of depression. Three biobehavioral systems that are centrally involved in depression throughout the life span are discussed: the *stress*, *reward*, and *mentalizing* systems (Luyten & Fonagy, 2018). We integrate findings concerning disruptions in these three systems in depression within a broad developmental psychopathology perspective, focusing on disruptions in both the content of cognitive-affective schemas or internal working models of self and others on the one hand, and mentalizing or metacognitive capacities on the other hand (Luyten, Blatt, & Fonagy, 2013).

In brief, the need to adapt to ever-changing environments, and the growing complexity of human communication, exchange, and collaboration, fostered the development and coordinated action of (a) the stress/threat system, involved in responses to threat and distress, (b) the reward system, which produces feelings of reward particularly related to experiences involving attachment relationships (e.g., infant–caregiver, caregiver–infant, pair-bonding, and other attachment relationships and experiences of agency and autonomy); and (c) the mentalizing or social cognition system, as the capacity to understand oneself and others in terms of intentional mental states (e.g., feelings, desires, wishes, attitudes, and values) is essential for humans to be able to establish fundamentally positive relationships with others that also reinforce their feelings of agency and autonomy (Luyten, 2017; Luyten & Fonagy, 2018).

From this perspective, depression is not in itself maladaptive or pathological. Depressive states of mind can be seen as attempts to minimize or end distress associated with separation and loss (Davey et al., 2008; Gilbert, 2006; Panksepp & Watt, 2011). However, excessive and/or age-inappropriate stress, particularly in combination with biological vulnerability, may lead to a vicious cycle characterized by impairments in reward sensitivity, which results in attachment and agency/autonomy becoming less rewarding, and in the capacity for mentalizing or social cognition (Figure 1), hindering the effective negotiation of normative developmental tasks and further increasing the risk for depression and associated conditions.

Hence, from a developmental perspective, the risk for depression typically increases during developmental transitions (e.g., from childhood to adolescence, from adolescence to early adulthood, and from adulthood to old age), when the individual faces challenges that rely on the stress, reward, and mentalizing systems. For example, adolescence involves the establishment of new and more complex

relationships, as well as a sense of agency and autonomy: both of these tasks rely heavily on the three biobehavioral systems, which may explain the increased prevalence of depression during adolescence (Figure 2), particularly in those that are at greater risk because of biological and/or environmental factors. With the onset of old age, issues of autonomy and relatedness are challenged once again, as the aging individual is increasingly confronted with the loss of physical and mental capacities and loved ones (Van Assche et al., 2013). In what follows, we discuss research findings concerning the role of these three biobehavioral systems in depression.

The stress system

The role of stress in explaining vulnerability to depression is fairly well established. First, there is good evidence to suggest that early adversity plays a key role in vulnerability to depression (Auerbach et al., 2014; McCrory, De Brito, & Viding, 2012; O'Brien & Sher, 2013). Estimates of the population attributable fractions –that is, the proportion of psychiatric disorders and suicide that could be explained by early adversity – range from 20% (Afifi et al., 2008) to 80% (Dube et al., 2001), with the vast bulk of the explained variance being related to depression, in particular chronic depression (Negele, Kaufhold, Kallenbach, & Leuzinger-Bohleber, 2015). For many individuals with chronic depression, trauma is deeply ingrained in their experience of themselves and others, and experiences of (perceived) rejection, criticism, or abandonment are re-traumatizing (Luyten, Campbell, & Fonagy, 2020; Luyten & Fonagy, 2014). The effects of early adversity on the onset of depression remain stable across the lifespan, even when controlling for the onset of previous episodes, suggesting that there are strong ‘programming’ effects of the stress response, which are reviewed in more detail below (McLaughlin et al., 2010). These findings may also explain why chronic depression is so difficult to treat (Rost, Luyten, Fearon, & Fonagy, 2019). Not surprisingly, longer-term treatments have been shown to be more effective for individuals with chronic depression (Leichsenring et al., 2016; Rost et al., 2019).

Second, there is also good evidence for the role of later-life stress in depression. Both major and minor life stressors, as well as chronic stress, have been causally related to the onset of depression, either alone or in interaction with personality features (e.g., neuroticism and self-critical perfectionism) and genetic

factors (Kendler & Gardner, 2014; Kendler, Kuhn, & Prescott, 2004; Luyten, Blatt, Van Houdenhove, & Corveleyn, 2006). Mechanisms underlying the relationship between early and later-life stress involved both increased stress sensitivity and the active generation of stress (Auerbach et al., 2014; Blatt, 2004; Hammen, 2005; Kendler et al., 2004; Luyten et al., 2006; Shahar, 2006). Indeed, individuals who are vulnerable to depression unwittingly and unconsciously tend to generate their own stressful environment, typically involving self-fulfilling prophecies (Luyten & Fonagy, 2018); for instance, highly dependent individuals who constantly fear rejection and abandonment tend to become emotionally demanding and clinging in interpersonal relationships, leading to the others in their relationships becoming frustrated and angry, thus increasing the risk that they will be abandoned and rejected by those others. Similarly, highly perfectionistic individuals, who typically fear criticism and failure, tend to become competitive and demanding in their relationships, leading to criticism from others, which confirms their underlying conviction that they are unlovable.

Research suggests that these interpersonal dynamics play a greater role in the transition to adulthood than in other developmental phases (Auerbach et al., 2014). Indeed, in adolescence, peers play an increasingly important role at the same time as issues of autonomy and achievement take center stage (see Figure 2); this may in part explain the increase in prevalence of depression during adolescence, particularly in girls (Auerbach et al., 2014). Within Western societies at least, women tend to place greater emphasis on relatedness and attachment (for a review, see Blatt, 2008), which may make them more vulnerable to internalizing disorders, including depression (Kendler & Gardner, 2014).

From a neurobiological perspective, the stress system is one of the most extensively studied and best-circumscribed systems. It involves the amygdala and hippocampus, the anterior cingulate cortex, orbitofrontal cortex, and medial prefrontal cortex (MPFC) (McEwen, 2007; Pervanidou & Chrousos, 2012). These neural structures underpin the human capacity for *allostasis*, the capacity to continuously adapt to changing circumstances (McEwen, 2007), and serve the fight/flight/freeze response when the individual is faced with acute stress (Gunnar & Quevedo, 2007; McEwen, 2007; Pervanidou & Chrousos, 2012). This response involves the hypothalamic–pituitary–adrenal (HPA) axis, the autonomic nervous system, the metabolic system, the gut, the kidneys, and the immune system. Each of

these systems has relatively distinct biomediators (e.g., cortisol, sympathetic and parasympathetic transmitters, metabolic hormones, and cytokines). The effects of stress on these systems explains why stress-related disorders such as depression are highly comorbid with somatic disorders (e.g., cardiac disorders, diabetes) and functional somatic disorders (e.g. chronic pain and fatigue) (Afari et al., 2014; Anda et al., 2006).

Meta-analyses have suggested that depression is typically associated with HPA axis hyperactivity in adolescents (Lopez-Duran, Kovacs, & George, 2009) and in adults (Zorn et al., 2017). However, findings in this area have not always been consistent, and short-term hyperactivity of the HPA axis seems to be largely due to chronic stress/early adversity. In the longer term, a switch from HPA hyperactivity to hypoactivity seems to be typical because of the wear and tear on physiological systems (Miller, Chen, & Zhou, 2007). In addition, HPA axis hypoactivity may delineate atypical depression and/or be more typical of depression in women (Zorn et al., 2017); this observation may also explain the high comorbidity and overlap between depression and functional somatic syndromes (Luyten, De Meulemeester, & Fonagy, 2019).

Animal studies have yielded some of the strongest findings on programming of the stress system associated with (early) stress. Early development in particular seems to be characterized by high sensitivity to programming effects, which may last until early adulthood in humans (Heim & Binder, 2012; Lupien, McEwen, Gunnar, & Heim, 2009). Of particular importance are findings that neural structures involved in the stress system undergo structural changes and functional reorganization in adolescence, at a time when the stress system is particularly challenged by increasing demands for autonomy and relatedness. Indeed, adolescence has been shown to be characterized by a marked increase in HPA axis reactivity to stress (Casey, Getz, & Galvan, 2008), particularly in response to social rejection (Masten et al., 2009; Sebastian, Viding, Williams, & Blakemore, 2010; Sebastian et al., 2011). Sleeping problems and problems related to disturbances of the circadian rhythm (Tsuno, Besset, & Ritchie, 2005) also seem to be related to increased stress sensitivity associated with depression.

Genetic factors are also important when considering the role of stress in depression, particularly as heritability estimates of depression are estimated to be around 30–40% in adults (Middeldorp et al., 2010; Sullivan, Neale, & Kendler, 2000).

Studies in this context have focused on gene–environment correlations and interactions in depression, although there is still mixed evidence at best from studies in humans given the many methodological problems of studies in this area (Auerbach et al., 2014; Bleys, Luyten, Soenens, & Claes, 2018; Dick et al., 2015), and the fact that the vast majority of studies in this domain have been conducted in samples of people of Western descent (Krause et al., 2016; Leighton, Botto, Silva, Jiménez, & Luyten, 2017). Similarly, while findings of research on epigenetic effects (i.e., the effects of environmental factors on gene expression) in animals have been quite consistent, more research concerning their potential role in depression in humans is needed (Cecil, Zhang, & Nolte, 2020).

The Reward System

Phenomenologically, depression can to a large extent be described as a reward depletion disorder: the depressed person feels that everything is hopeless and meaningless, and that nothing brings joy, pleasure, or satisfaction. Various theories suggest that two key areas of reward are central in depression: *social/attachment relationships* and *agency/autonomy* (see Figure 2) (Beck, 2009; Blatt, 2008; Dawood, Dowgwillo, Wu, & Pincus, 2018; Gilbert, 2006; McFarquhar, Luyten, & Fonagy, 2018; Ryan, Deci, & Vansteenkiste, 2016).

Most research in this area has focused on issues of reward associated with attachment relationships (Feldman, 2017; Insel & Young, 2001; Panksepp & Watt, 2011; Rutherford, Williams, Moy, Mayes, & Johns, 2011; Swain, Lorberbaum, Kose, & Strathearn, 2007), although there has been increasing interest in the role of impairments in agency/autonomy in relation to the reward system, particularly from the perspective of self-determination theory (Murayama, Matsumoto, Izuma, & Matsumoto, 2010; Ryan et al., 2016; Vandenkerckhove et al., 2020).

From a neurobiological perspective, the reward system involves mesolimbic and mesocortical pathways. Mesolimbic pathways include the ventral tegmental area, with projections to the ventral striatal regions (and the nucleus accumbens in particular), the hippocampus and amygdala. Mesocortical pathways involve projections to the prefrontal cortex and the anterior cingulate cortex (Pizzagalli, 2014; Russo & Nestler, 2013; Spear, 2000). Dopamine, oxytocin, opioids, and cannabinoids are the key biological mediators of the reward system, reflecting the fact that there is a close relationship between depression and substance use

disorders, as both disorders involve the same biological mediators (Hsu et al., 2015; Panksepp & Watt, 2011; Spear, 2000). From this perspective, substance abuse can be be seen as an attempt to deal with feelings of depression and despair.

The reward system plays a central role in the development of the stress system and its regulation throughout the life span (Feldman, 2017; Hostinar, Sullivan, & Gunnar, 2014; Strathearn, 2011; Swain et al., 2014). Secure attachment experiences serve to buffer the effects of stress. In early development, secure attachment has been shown to be key in fostering adaptive hypoactivity of the HPA axis (Gunnar & Quevedo, 2007). Insecure attachment experiences, by contrast, lead to impairments in the reward system and, as a result, dysfunction of the HPA axis (Auerbach et al., 2014; Pizzagalli, 2014; Strathearn, 2011).

These effects have been particularly demonstrated by research on the hormones oxytocin and vasopressin. Oxytocin fosters affiliative behavior in individuals who are faced with distress, albeit only in relation to in-group members and for those who are securely attached. In such circumstances, opportunities for the distressed individual to effectively co-regulate stress with others are optimized. These effects have their roots in early development, and thus tend to generalize to other attachment relationships. Mothers with high serum levels of oxytocin, for example, tend to make more affectionate contact with their infants, and are more likely to follow their infant's gaze with an affectionate touch (Apter-Levi, Zagoory-Sharon, & Feldman, 2014; Kim, Fonagy, Koos, Dorsett, & Strathearn, 2014). Oxytocin has also been shown to have direct anxiolytic and anti-stress effects via down-regulation of the HPA system (Feldman, Vengrober, & Ebstein, 2014). Importantly, oxytocin also fosters mentalizing and trust in others, which leads to the effective down-regulation of stress (Bartz, Zaki, Bolger, & Ochsner, 2011; Neumann, 2008).

However, the down-regulatory effects of oxytocin are limited to close relationships, (i.e., parent–infant and partner relationships) and in-group members. By contrast, the experimental administration of oxytocin has been shown to lead to decreases in trust and cooperation in relation to out-group members (Bartz et al., 2011). In addition, individuals with an insecure attachment history, not only have lower basal levels of oxytocin, but also show increased distrust of others and an increased cortisol response to stress following oxytocin administration (Bartz et al.,

2011). The effects of oxytocin thus seem to be fundamentally mediated by the context and factors related to the individual.

Consistent with these findings from biological studies, behavioral studies have consistently reported robust associations between vulnerability for depression and impairments in reward associated with both relatedness and autonomy. Most research in this area has focused on impairments in agency/autonomy expressed as, for instance, high levels of self-criticism or self-critical perfectionism – a pernicious combination of high personal standards and high levels of self-criticism. As a result, self-critical individuals have great difficulty experiencing a sense of joy or accomplishment, as they always fall short of the standards they set for themselves. Features of self-critical perfectionism have been empirically associated with increased vulnerability for depression. Self-critical/perfectionistic individuals have also shown a poor response to treatment across a number of therapeutic modalities, although they may respond better to longer-term treatments (Blatt, Zuroff, Hawley, & Auerbach, 2010; Rost et al., 2019; Shahar, 2015).

Various theoretical approaches have focused on the association between vulnerability for depression and impairments in reward associated with affiliation, as expressed in high levels of dependency (Blatt, 2008), sociotropy (Beck, 2009), and insecure attachment (Agerup, Lydersen, Wallander, & Sund, 2015; Grunebaum et al., 2010; Lee & Hankin, 2009). For instance, a meta-analysis of 55 samples (N = 4,386) in which attachment was measured with the Adult Attachment Interview (George, Kaplan, & Main, 1985) reported that insecure individuals had higher levels of depression compared with secure-autonomous individuals (d = 0.21, 95% CI [0.08, 0.33]) (Dagan, Facompre, & Bernard, 2018). This effect was particularly pronounced in insecure-preoccupied individuals (d = 0.48, 95% CI [0.30, 0.65]), whereas it was small for insecure-dismissing individuals (d = 0.09, 95% CI [–0.03, 0.22]). The difference between insecure-preoccupied and insecure-dismissing individuals should be interpreted with caution, as dismissive attachment has been associated with the denial and underreporting of distress (Mikulincer & Shaver, 2007). Adults with unresolved attachment showed higher levels of depression than those with organized attachment (d = 0.29, 95% CI [0.13, 0.44]). Similarly, a comprehensive meta-analysis in children and adolescents, including 643 effect sizes based on 123 independent samples, found an overall effect of r = .31 between insecure attachment to primary caregivers and depression (Spruit et al., 2020).

Importantly, there is good evidence from prospective multi-wave studies showing that attachment anxiety and avoidance are both associated with increases in depressive symptoms over time (Khan, Fraley, Young, & Hankin, 2019), suggesting a causal role for attachment experiences in vulnerability for depression. Moreover, longitudinal studies have shown that insecure working models of self and others mediate the relationship between early adversity and later vulnerability for depression through their negative effects on affect regulation, stress responsivity, and impairments in social problem-solving skills (Bifulco et al., 2006; Brown, Harris, & Craig, 2019; Styron & Janoff-Bulman, 1997; Widom, Czaja, Kozakowski, & Chauhan, 2018).

There is some evidence that dismissive attachment is associated with greater vulnerability for a hostile/aggressive subtype of depression (MacGregor et al., 2014), while attachment disorganization, characterized by the use of both attachment hyperactivating and deactivating strategies, may be typical of individuals with marked borderline level functioning, expressed in more severe depression and marked feelings of emptiness, anger, shame, and identity diffusion (Lecompte, Moss, Cyr, & Pascuzzo, 2014; Luyten & Fonagy, 2014).

From an evolutionary perspective, insecure attachment strategies appear to reflect different strategies to deal with the (perceived) unavailability, unresponsivity, or intrusiveness of attachment figures (Ein-Dor, Mikulincer, Doron, & Shaver, 2010). Hence, these responses are, at least in the short term, adaptive. However, in the long term they typically seem to lead to considerable intrapersonal and interpersonal costs. This functional-adaptive perspective on depression contrasts markedly with a disease model that considers depression as a static end-state.

How can the relationship between reward and depression be understood at a more subjective, phenomenological level, including its many embodied manifestations? This leads us back to the ground-breaking work of pioneering researchers on the association between depression and loss, namely Rene Spitz (1945), John Bowlby (1973), Harry Harlow (1958), Joseph Sandler and Walter Joffe (1965), and Anna Freud (1963). They were among the first to systematically describe the often detrimental consequences of early loss of an attachment figure, and their descriptions were to become the foundation for current understanding of the relationship between mourning and depression.

Loss of a loved object by separation or death – and, by extension, the loss of any ideal or wished-for state – leads to massive activation of the attachment system (Mikulincer & Shaver, 2007). However, with the loss of the object (or wished-for state), a source of reward has disappeared from the individual's life. The object exists only at the representational level, and is particularly difficult for those with mentalizing impairments to hold on to, as they typically experience difficulties representing mental states (a more detailed discussion of the role of mentalizing impairments in depression is provided in the next section). However, as depressed mood impairs mentalizing, a vicious cycle is set in motion, and the individual increasingly finds him/herself in a state of despair and loneliness, which is accompanied by psychological and embodied manifestations of that despair and loneliness. Typical human responses to loss, as first described by Spitz and Bowlby, entail protest (e.g., anger, aggression) and/or denial of the loss, followed by resignation, which is typically only partial. A painful psychobiological, embodied response is involved in the loss of an attachment figure, marked by acute distress lasting from minutes to hours (evident as, for example, crying, agitation, or sighing). As well as this acute distress, more chronic features, typically lasting for a period of weeks to months (e.g., social withdrawal, cognitive problems, eating problems, sleep disturbances), are characteristic of loss (Hofer, 1984).

Particularly during the acute distress associated with loss, the individual is constantly reminded of their lost loved one, who provided an important regulatory function – that is, as an important source of reward. Now the lost object exists only at the representational level, and is thus physically missed, but at the same time the individual is constantly reminded of the lost object by environmental cues. The ensuing activation of the attachment system may be so strong that it leads to delusional experiences (e.g., denial that the lost person has gone, the conviction that they will return, or feeling the presence of the lost person). This is probably one of the main reasons why depressed states typically tend to last for weeks to months, as the relinquishing of the lost object/ is usually a slow and gradual process, which takes longer with loved attachment figures who were more important to the individual. As Freud noted in his seminal paper *Mourning and Melancholia* (Freud, 1915), memories of the lost person/object are activated during the mourning process one by one, as if the individual needs to revisit all the memories associated with the lost object before he/she can move on. Hence, depressed states of mind and the

tendency to cling on to the lost object, which is impossible to replace, are understandable responses to loss. As Freud commented to one of his friends who lost his son to an illness: “We know that the acute sorrow we feel after such a loss will run its course, but also that we will remain inconsolable, and will never find a substitute. No matter what may come to take its place, even should it fill that place completely, it yet remains something else. And that is how it should be. It is the only way of perpetuating a love that we do not want to abandon” (Freud, 1961). As is now well known, the above-described basic psychobiological response to loss may be complicated by various defense mechanisms, such as anger (i.e., protest, in an attempt to relieve the pain associated with loss), survivor guilt (particularly when the attachment relationship with the lost object was characterized by high levels of ambivalence), and/or shame.

This model of loss of an attachment figure can be generalized to the loss of a wished-for state more generally. Just as a lost person may provide an important regulatory function for the individual, so can a wished-for state, and the loss of this wished-for state can lead to a similarly painful psychobiological response marked by increased distress and reward deficiency. Consider, for example, the depressed adolescent sitting on the school bus on his way home, contemplating a life very different from his current one; or the nurse who has just heard that she has been fired, dreading telling her husband, fearing losing her friends at work, and worrying about whether she will find a new job any time soon.

Again, adolescence may be a pivotal stage in the emergence of vulnerability to depression. The reorganization of the reward system in adolescence, combined with changing sociocultural expectations, makes it even more difficult for adolescents to deal with experiences of (perceived) loss. Adolescents are faced with challenges both in peer and romantic relationships (as is also expressed in increased rejection sensitivity during this stage of life) and in terms of increasing demands for achievement (as is reflected in increased sensitivity to failure). Perhaps not surprisingly, therefore, adolescence is characterized by a “reward deficiency syndrome” (Spear, 2007). Compensatory behaviors such as risk-taking, self-harm, or substance abuse may be used to ward off feelings of depression, explaining in part the high comorbidity with externalizing disorders observed in adolescents with depression (Davey et al., 2008; Spear, 2000). Reward deficiency in adolescence may also explain the high levels of novelty- and sensation-seeking behavior typical

of this developmental phase; these behaviors serve to foster autonomy and enable the formation of romantic relationships. Yet, as adolescents increasingly have the ability to realize that things that they perceive as rewarding (e.g., love, status) are temporally distant and can be truly achieved only in the distant future, they may experience alternating feelings of excitement and depression (Davey et al., 2008).

The Mentalizing System

Mentalizing is largely species-specific human capacity that enables complex forms of communication and collaboration. It also greatly facilitates self-awareness and self-consciousness, including the capacity to envision oneself in the future. Yet, this capacity for increased self-awareness and self-consciousness also has a flipside (Luyten, Fonagy, Lemma, & Target, 2012). Self-awareness and self-consciousness also enable self-conscious emotions such as shame and guilt. Whilst these emotions serve important adaptive interpersonal functions, when too intense or chronic, they lead to depression. Furthermore, self-consciousness also implies the awareness that one may not be able to achieve one's goals and desires (related to either autonomy or relatedness or both), leading to feelings of despair and depression (Luyten et al., 2012). We have already discussed how this latter process may be even more important in certain developmental stages and transitions (such as adolescence, mid-life and old age). The fact that neural circuits involved in mentalizing undergo major structural and functional changes in both adolescence and old age, may help to explain the increased risk for depression associated with these developmental stages (Cusi, Nazarov, Holshausen, MacQueen, & McKinnon, 2012; Drevets, Price, & Furey, 2008; Kerestes, Davey, Stephanou, Whittle, & Harrison, 2014). Moreover, age-specific changes typically further challenge mentalizing capacities. For example in adolescence, the emergence of sexuality and new forms of aggression typically challenge mentalizing capacities eve further. Adolescents are often unable to make sense of these changes, leading either to excessive mentalizing (so-called pretend mode functioning or hypermentalizing) or to the avoidance of mentalizing (hypomentalizing, typically expressed in psychic equivalence mode functioning: "I feel worthless, so I am worthless, and everything is worthless"). In a teleological mode of functioning, adolescents often try to deal with such unmentalized experiences by trying to evacuate them through acting out (e.g., self-harm, substance abuse, reckless behavior). Likewise, in old age, the loss of physical

capacities and loved ones, may lead to extreme feelings of despair in psychic equivalence mode (“Everything is lost”) or extensive rumination about lost opportunities in the past in pretend mode functioning (“if only I had made other choices in life”).

Studies suggest that depression in individuals who predominantly use attachment hyperactivating strategies in response to stress, results in part from a failure to reappraise and regulate negative affect, suggestive of problems with controlled mentalizing, leading to a predominance of automatic, affect-driven mentalizing. Attachment deactivating strategies, by contrast, appear to results in an excessive downregulation of reward circuitry in combination with hyperactivation in the MPFC and ventral anterior cingulate cortex, suggesting a pattern of cognitive overcontrol and overregulation (Luyten & Fonagy, 2015; Vrticka & Vuilleumier, 2012).

Mentalizing impairments in depression have been extensively documented, ranging from impaired facial emotion recognition and Theory of Mind to more complex mentalizing capacities involved in human interactions (Billeke, Boardman, & Doraiswamy, 2013; Bistricky, Ingram, & Atchley, 2011; Kerestes et al., 2014; Weightman, Air, & Baune, 2014). Moreover, these impairments have been shown to be related to the severity and duration of depressive episodes, to prospectively predict relapse in major depression and to persist in euthymic patients, suggesting that such impairments often remain present as latent vulnerability (Bistricky et al., 2011; Schreiter, Pijnenborg, & Aan Het Rot, 2013; Weightman et al., 2014).

Conclusions

This chapter outlines a developmental psychopathology approach to depression across the life span. Basically, we suggest that depression results from a disruption – due to biological or environmental factors, or a combination of both – of the balanced functioning of three key biobehavioral systems involved in stress and arousal regulation, reward, and social cognition or mentalizing. As each developmental transition in life typically entails a biological reorganization of these three biobehavioral systems, and new environmental demands challenge the balanced functioning of these systems, life transitions and other events that challenge the functioning of the three systems (e.g., loss of a loved one, unemployment, migration) is likely to increase the risk for depression.

From the perspective of prevention and intervention strategies, a transdiagnostic and transtheoretical approach is needed. The biobehavioral systems involved in depression are also involved in many if not all other psychological disorders (e.g. anxiety disorder, post-traumatic stress disorder, anorexia, antisocial personality disorder, and borderline personality disorder) and are a central focus of many pharmacotherapeutic and psychosocial treatments. This view is also consistent with the developmental psychopathology principles of *equifinality* and *multifinality* (Cicchetti & Rogosch, 1996) – that is, that different etiological factors (e.g., childhood trauma) are involved in developmental pathways toward depression (equifinality), and etiological factors that are implicated in depression may also be involved in the etiology of other psychological disorders (multifinality).

The efficacy of treatments may be improved by a greater and more consistent focus on each of the biobehavioral systems involved in depression. For instance, several antidepressant medications primarily target the stress system, while psychological treatments often primarily focus on the social cognition/mentalizing system. Moreover, a stronger focus on the developmental roots of dysregulations among the biobehavioral systems in depression may similarly increase the effectiveness of treatments for depression. There is increasing consensus that most psychological disorders, including depression, have their roots in development, and that this reflects a broader underlying general vulnerability for psychopathology (Caspi et al., 2014). Research on this general psychopathology factor, or “p” factor, suggests that treatments (with the exception of those for the mildest psychological problems) should thus focus on this broader underlying vulnerability.

Consistent with the assumptions expressed in this chapter, we suggest that both biological and environmental factors may constrain individuals’ capacity to adapt to their ever-changing environment, leading to disruptions in the balance between the stress, reward, and mentalizing systems. This view may also explain why distorted mood and symptoms of depression are implicated in most psychological conditions. We hope that this chapter will contributes not only to a greater developmental focus in research on depression, but also to the development and empirical evaluation of broad transdiagnostic and transtheoretical psychosocial interventions that focus on the underlying biobehavioral systems implicated in depression and associated conditions.

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Figure 1. The role of Stress, Reward and Mentalizing Systems in Depression (adapted from Luyten, P., & Fonagy, P. (2018). The stress-reward-mentalizing model of depression: An integrative developmental cascade approach to child and adolescent depressive disorder based on the Research Domain Criteria (RDoC) approach. Clinical Psychology Review, 64, 87-98. doi: 10.1016/j.cpr.2017.09.008)

Figure 2. Developmental challenges in adolescence and vulnerability for depression (adapted from Luyten, P., & Fonagy, P. (2018). The stress-reward-mentalizing model of depression: An integrative developmental cascade approach to child and adolescent depressive disorder based on the Research Domain Criteria (RDoC) approach. Clinical Psychology Review, 64, 87-98. doi: 10.1016/j.cpr.2017.09.008)