The phenomena we deal with do not belong only to psychology; they have also an organic and biological aspect, and accordingly in the course of our efforts at building up psychoanalysis we have also made important biological discoveries and have not been able to avoid framing new biological hypotheses.

—Sigmund Freud, *An Outline of Psychoanalysis*

Decades before writing *An Outline of Psychoanalysis*, Freud’s *Project for a Scientific Psychology* attempted to define the unconscious in neurological terms. Due to the technological restraints of the time, Freud was forced to abandon the *Project* and turn his focus to investigating the unconscious though dream analysis (Roffman & Gerber, 2008). In modern times, biological discoveries continue to inform and support hypotheses about the development and amelioration of psychological distress. The body of research identifying biological support for the cognitive theory of depression may serve as an exemplar for furthering the study and practice of psychoanalysis.

**SIMILARITIES BETWEEN COGNITIVE THEORY AND PSYCHOANALYSIS**

The cognitive theory and psychoanalytic approaches are concerned with similar phenomena. Both approaches involve exploration of content that is private, nonmaterial, and nonspatial (Beck, 2004). The individual’s introspective report of physically
intangible phenomena provides the basis for intervention in both cognitive theory and psychoanalytic approaches. Likewise, changes in an individual’s symptoms, level of distress, and/or functioning are theorized to result from changes in this private content.

In addition, both cognitive theory and psychoanalytic approaches are concerned with the importance assigned to the meaning of events. Both acknowledge that meanings enhance the richness of our experiences as well as contribute to our personal and interpersonal problems. Both approaches suggest that meaning exists at several levels and is arranged hierarchically. Cognitive theory and classical psychoanalytic theory differ in the degree to which the deeper—and more crucial—levels are accessible. In cognitive theory, the deeper cognitive levels are generally not explicit (Alford & Beck, 1997) but may be made conscious through skillful questioning. In psychoanalysis, the aversive meanings are presumed to be ego-alien and thus are sealed off by repression or other defense mechanisms. In cognitive theory, conscious meaning may be derived from basic beliefs embedded in cognitive structures (known as schemas). Thus, a person may become very upset by a presumed slight (‘She is putting me down’) because the interaction activates a lower-level belief (e.g., ‘I am undesirable’). At the lowest level the beliefs are overly general, abstract, and dysfunctional. In severe psychopathology (e.g., clinical depression), the absolute negative beliefs are preemptive, persistent, and conscious (Beck, 1967). In the psychoanalytic approach, the explanation for the individual’s distress might be that it results from an intolerable repressed meaning or an ego-alien emotion/drive, such as unconscious rage.

In addition to similarities in their content, both cognitive theory and psychoanalysis postulate dual systems of cognitive processing. The basic cognitive processes in cognitive theory and psychoanalysis have been labeled primal process and primary process, respectively (Beck, 1999). These automatic and resource-sparing processes are presumed to account for emotions and urges. The secondary processing in both theories is reflective and resource demanding, and is designed to correct or inhibit primary processes. Improved functioning, as described by psychoanalysis,
results from the resolution of conflict between primary and secondary processes. Improved functioning from a cognitive theory perspective is due to addressing dysfunctional patterns of primary and/or secondary processing. The underlying similarities between cognitive theory and psychoanalysis suggest that the methods by which biological underpinnings of the cognitive model of depression have been identified may be similarly valuable for identifying biological correlates of psychoanalytic theory.

COGNITIVE MODEL OF DEPRESSION

The prototype cognitive model of depression was based on observations of depressed patients in psychotherapy. The model was based on a developmental perspective that presupposed a constitutional vulnerability that sensitized the patient to negative experiences. It was proposed that later aversive experiences analogous to those in childhood would precipitate symptoms of depression. Early research by our group indicated that severely depressed patients who had lost a parent in childhood and subsequently experienced a significant loss (breakup of relationship, divorce, or bereavement) would experience depression (Beck, Sethi, & Tuthill, 1963). We theorized that the earlier experience of severe loss biased the child’s view of subsequent negative experiences, leading to the formation of a negative memory schema. When this schema was activated by a significant loss later in life, it formed a systematic negative bias toward the patient’s view of experiences and expectancies referred to as the negative cognitive triad (Beck, 1967). Thus the patient was very critical of the self, and considered the past filled with failures and the future as hopeless. In addition to distorting the patient’s interpretations, the systematic negative bias was found to impair other cognitive processes such as attention and memory, whereby the depressed patient would selectively attend to and recall negative information. Ultimately, the systematic negative bias produces a feedback loop that initiates and maintains an episode of depression (see Figure 1).

The original cognitive model of depression could account for many of the symptoms of depression, such as loss of interest,
loss of motivation, withdrawal, and in many cases suicidal tendencies; however, two important pieces of the model were missing. The model could not account for the fact that only a subset of individuals who had traumatic childhood experiences followed by later trauma actually developed depression. Also the model did not account for “sickness behaviors” such as fatigue, loss of appetite, sleep disturbances, and loss of libido. Recent biologically based depression research has helped fill the gaps in the cognitive model, and efforts to synthesize research across disciplines have yielded a more comprehensive understanding of depression and its treatment (Disner, Beevers, Haigh, & Beck, 2011).

The following section will outline the biological underpinnings of the cognitive model of depression (see Figure 2 for a graphical representation). In addition, we will discuss how gaps in the cognitive model have been filled by recent research, specifically genetic studies and investigations of the inflammatory response in depression.
Dual Processing

Several lines of research suggest that cognitive biases in depression are related to maladaptive biological “bottom-up processes” that are analogous to primal process in cognitive theory. Bottom-up processes are patterns of activation starting in subcortical brain regions that are lower along the cognitive hierarchy and are associated with quick, low-level, affective analyses of stim-
uli. Brain regions associated with bottom-up processing include the amygdala, thalamus, nucleus accumbens (NA), hippocampus, caudate, putamen, and the anterior cingulate cortex (ACC). In contrast, “top-down” processes, which are analogous to secondary processing in cognitive theory, refer to higher-level cognitive processes, such as cognitive appraisal, that draw upon stored knowledge. Brain regions associated with top-down processing include the prefrontal cortex (PFC) medial PFC (MPFC), ventral lateral PFC (VLPFC), dorsal lateral PFC (DLPFC), rostral ACC, and the superior parietal cortex.

Bottom-up processes proceed sequentially to connected cortical areas higher up and are generally perpetuated by attenuated cognitive control. In this sense, top-down processes associated with regions higher on the cognitive hierarchy fail to effectively regulate activity in those lower regions; for a detailed review see Disner, Beevers, Haigh, and Beck (2011). Broadly stated, growing research suggests that the cognitive model of depression can be understood biologically as the failure of top-down cortical processes to dampen overactive bottom-up limbic processes (Disner et al., 2011; Mayberg, 1997, 2003; Phillips, Drevets, Rauch, & Lane, 2003a, 2003b).

Negative Self-referential Schemas

The cognitive model presupposes that negative self-referential schematic activation sets in motion the negative cognitive bias characteristic of depression, and there is preliminary evidence for the biological underpinnings of depressogenic schemas. Research has shown that when depressed individuals complete negative self-referential tasks (e.g., judging whether a trait adjective is representative of oneself), performance is associated with increased activation in the amygdala, ACC and MPFC, and with depression severity (Craik et al.,1999; Fossati et al., 2003; Gusnard, Akbudak, Shulman, & Raichle, 2001; Kelley et al.,, 2002). The amygdala is implicated in emotionality and emotional processing, while the MPFC is a region thought to be related to internal representation of the self. The ACC serves two roles: The ventral ACC influences whether incoming stimuli is labeled with emotional valence, and
the rostral ACC influences the extent to which the stimuli is labeled as self-referential. Hyperactivation of the amygdala, ACC, and MPFC likely facilitates and maintains a person’s negative self-referential thoughts (Disner et al., 2011). Another line of research has established a link between serotonin, pessimism (a specific self-referential schema), and depression by demonstrating that depressed participants who endorsed marked pessimism evidenced decreased serotonin expression (Meyer, 2007; Meyer et al., 2003). In summary, self-referential schemas are related to activity in the amygdala, which detects emotion (bottom-up processing); in the intermediate ACC regions involved in coding emotional stimuli; and in the MPFC, a top-down region involved in self-referential thought. Finally, alteration in serotonin expression is associated with the presence of dysfunctional attitudes or schemas.

Negatively Biased Attention for Emotional Stimuli

The cognitive model predicts that activated depressogenic schemas lead to information processing biases in attention. As such, depressed individuals selectively attend to (Gotlib, Krasnoperova, Yue, & Joormann, 2004) and have difficulty disengaging from negative stimuli (Hasler, Drevets, Manji, & Charney, 2004). The inability to disengage from negative stimuli is thought to exacerbate symptoms of dysphoria and perpetuate the positive feedback loop of depressive symptoms. Research suggests that impaired attentional disengagement from negative stimuli is associated with decreased activity in the right VLPFC, DLPFC, and right superior parietal cortex for depressed individuals compared to healthy controls (Beevers, Clasen, Stice, & Schnyer, 2010). One factor that may contribute to inability to disengage is deficient inhibition or the impaired ability to inhibit attention for negative stimuli. Inhibitory processing in healthy individuals is associated with the rostral ACC. Depressed individuals show greater activation in the rostral ACC when successfully inhibiting attention to negative stimuli as compared to controls (Elliott, Rubinsztein, Sahakian, & Dolan, 2002; Eugene, Joorman, Cooney, Atlas, & Gotlib, 2010; Mitterschiffthaler et al. 2008). These lines of re-
search suggest that negatively biased attention and inhibitory deficits are associated with cortical regions associated with top-down processing (VLPFC, DLPFC, and right superior parietal cortex, rostral ACC).

**Negatively Biased Processing of Emotional Stimuli**

A central element of the cognitive model is the putative role of negatively biased processing of internal and external emotional stimuli. Several lines of research have identified neural regions associated with negatively biased processing of emotional stimuli. Research has found that when depressed individuals process negative stimuli, they demonstrate more intense (by up to seventy percent) and longer lasting (up to three times as long) amygdala reactivity than healthy controls, even when an emotional task is immediately followed by a nonemotional task (Drevets, 2001; Siegle, Steinhauer, Thase, Stenger, & Carter, 2002). Genetic factors have been implicated in the biased processing of negative stimuli. For example, recent research has shown that hyperactivity of the amygdala in the short 5-HTTLPR variant carriers is associated with increased sensitivity to negative stimuli (Munafò, Brown, & Hariri, 2008).

Research on biased processing of positive stimuli has revealed a bias against attending to positive stimuli as reflected by difficulty maintaining activation of the reward circuitry (Heller et al., 2009). Research has found decreased activity in the NA and PFC among depressed subjects asked to consciously maintain or enhance positive emotion, which suggests an impaired capacity to maintain positive affect through top-down control.

In addition to providing evidence for positive and negative emotional processing biases, research has revealed that these biases can be identified at various levels of awareness. In particular, a recent study investigated amygdala response to sad, happy, and neutral faces presented below the level of conscious awareness in medicated participants with major depressive disorder (MDD) and healthy controls (Suslow et al., 2010). Depressed participants exhibited potentiated right amygdala reactivity to masked negative stimuli along with a reduced responsiveness to masked posi-
tive stimuli compared to healthy controls (Suslow et al., 2010). The work by Suslow and colleagues (2010) was replicated and findings were extended to unmedicated depressed and remitted depressed participants (Victor, Furey, Fromm, Ohman, & Drevets, 2010). In addition, Victor and colleagues (2010) included a longitudinal component and reexamined cognitive processing biases following eight weeks of antidepressant treatment. Results showed that both the currently and remitted depressed participants had greater amygdala activity than healthy controls when processing masked sad versus happy faces. The healthy control group demonstrated the reverse pattern for happy and neutral faces. Following antidepressant treatment for the MDD group, results showed that the negative bias resolved and a positive bias developed (Victor et. al., 2010). These data suggest that cognitive processing biases are evident at an automatic or early processing level.

A related line of research examining the neuropharmacological action of antidepressants has provided biological support for the primary role of cognitive processing biases in the cognitive theory of depression. For example, a recent study found differential responses to a cognitive processing task following the single administration of an antidepressant or placebo among unmedicated depressed participants and healthy controls (Harmer et al., 2009). The medicated depressed participants demonstrated increased recognition of positive facial expressions, increased processing speed for positive self-relevant personality traits and increased memory for positive information compared to healthy volunteers receiving placebo (Harmer et al., 2009). In another study, participants being treated with either a selective serotonin reuptake inhibitor (SSRI) antidepressant or a noradrenaline reuptake inhibitor (NaRI) antidepressant were examined in the context of a facial recognition task (Tranter et al., 2009). Results showed that increased recognition of happy faces after two weeks of antidepressant use preceded changes in emotions and other symptoms. These results suggest that antidepressant drug use may influence cognitive processing before changes in mood and symptoms are reported, which is compatible with cognitive theories of depression (Harmer et al., 2009).
In sum, research examining the biological underpinnings of biased emotional processing has implicated both bottom-up (increased amygdala activity, hypoactive NA) and top-down (DLPFC and PFC hypoactivity) processes. Research also has revealed that processing biases exist below the level of awareness and can be resolved following antidepressant treatment. Finally, research demonstrating that antidepressant administration leads to changes in positive cognitive processing prior to changes in emotion and other depressive symptoms has provided support for primacy of cognitive processing in depression.

**Biased Memory for Negative Stimuli**

An important component of the cognitive model of depression is biased memory or the extent to which negative stimuli are encoded and recalled. Research has identified brain regions implicated in biased memory in depressed individuals. In particular, the amygdala facilitates encoding and retrieval of emotional stimuli in healthy individuals by influencing activity in the hippocampus and in the caudate and putamen regions (Adolphs, Cahill, Schul, & Babinsky, 1997). In depressed participants, hyperactivity in the amygdala has been associated with enhanced encoding and recall for negative as compared to positive stimuli (Hamilton & Gotlib, 2008). The amygdala also has been implicated in biased memory through bottom-up influence (Hamilton, & Gotlib, 2008). Another line of research examining recall of happy and sad events has found a differential association with the MPFC, a region associated with abstract representations of reward (Elliott, Friston, & Dolan, 2000; Knutson, Fong, Adams, Varner, & Hommer, 2001). Finally, compared to healthy controls, depressed participants exhibit hyperactivity in the MPFC during recall of self-relevant happy events and hypoactivity during recall of self-relevant negative events (Keedwell, Andrew, Williams, Brammer, & Phillips, 2005). In sum, both bottom up (increased amygdala) and top-down processing (alterations in MPFC activity) have been associated with biases in encoding and recall of events.

While the cognitive model has been successful in accounting for the mood component of depression, the model has struggled
to account for two important aspects of depression. First, only a subset of individuals who initially experience a stressor and presumably develop depressogenic schemas actually go on to develop depression after experiencing a stressor that activates latent schema. Second, the model does not account for “sickness behaviors” such as fatigue, loss of appetite, sleep disturbances, and loss of libido. These gaps in the model have been filled by recent research, specifically genetic research and investigations of the inflammatory response in depression.

**Cognitive Vulnerability to Depression**

Whether someone who experiences a negative life event goes on to develop depression as the result of activated depressogenic schemas may be due in part to specific biological factors. A number of genetic variants have been associated with the likelihood of developing depression. The most widely researched genetic variance has been the 5-HTTLPR short allele (or serotonin transporter gene variation), which was found to interact with life experiences to produce depression (Caspi et al., 2003; Karg, Burmeister, Shedden, & Sen, 2010).

**Sickness Behaviors in Depression**

A body of immunological research developed over the past thirty years has provided a key to understanding the origin of fatigue, loss of appetite, sleep disturbance, and loss of libido in depression. It is now well-established that elevated levels of inflammatory cytokines have been associated with these physiological and behavioral symptoms, termed “sickness behaviors” (Kent, Bluthé, Kelley, & Dantzer, 1992). Moreover, the current body of research on inflammatory cytokines supports the cognitive model’s proposition that the onset of depressive symptoms, including sickness behaviors, is catalyzed by an aversive event experienced by a vulnerable individual. Specifically, psychosocial stress such as one might experience following an aversive event has been shown to activate the inflammatory response (Miller, Maletic, & Raison,
Individuals’ responses to social rejection appear to be particularly illustrative. Life events associated with rejection confer significantly greater risk for depression than other life events (Kendler, Hettema, Butera, Gardner, & Prescott, 2003), and rejection also precipitates an immune response and subsequent depressive symptoms (Slavich, O’Donovan, Epel, & Kemeny, 2010). In the first study of its kind, Slavich and his colleagues demonstrated not only that healthy individuals who completed a socially threatening task in the laboratory demonstrated increased levels of inflammatory activity, which is consistent with previous research (see Dickerson, Kemeny, Aziz, Kim, & Fahey, 2004), but also that greater increases in inflammatory activity were associated with greater activation of neural regions implicated in the processing of rejection-related negative affect (Slavich, Way, Eisenberger, & Taylor, 2010). Subsequently, Slavich and his colleagues proposed that differences in individuals’ neural processing of social rejection may influence the extent to which they demonstrate an inflammatory response and “sickness behaviors” following rejection (Slavich, O’Donovan, et al., 2010).

Also consistent with the cognitive model, certain psychological, physiological, and social factors appear to render some individuals particularly vulnerable to depressive symptoms associated with cytokine activity. For example, Capuron and her colleagues (Capuron et al., 2002; Capuron, Ravaud, Miller, & Dantzer, 2004) reported that baseline levels of sadness predicted the severity of depressive symptoms following one month of cytokine treatment for cancer. Physiological factors that appear to impact susceptibility to cytokine-induced depressed mood include sleep disturbance and increased responsiveness of the HPA system (Capuron et al., 2004). Social factors including socioeconomic status (SES) and social support also appear to increase vulnerability to sickness behaviors. Yirmiya et al. (2000) reported that low SES conferred vulnerability to more severe depressed mood, poor concentration, and social problems in response to acute infection and the accompanying elevated levels of pro-inflammatory cytokines, and Capuron et al. (2004) found that low social support predicted greater severity of depressed mood following cytokine treatment.
These findings appear consistent with the cognitive model of depression, in that specific psychological, physiological, and social factors may confer vulnerability to depression via immune system pathways.

Although much of the research on inflammatory cytokines and depression supports a unidirectional relationship (i.e., that cytokines induce sickness behaviors in depression), the relation between cytokines and depression may turn out to be more complex than a unidirectional hypothesis suggests. In a recent study, Thornton and her colleagues (Thornton, Andersen, Schuler, & Carson, 2009) found that cancer patients who demonstrated improvement in depressive symptoms following psychological intervention exhibited reductions in inflammatory markers and that these reductions appeared to be mediated by change in depressive symptoms. Further research examining the mechanisms by which psychological interventions impact the relation of inflammatory activation and depressive symptoms is warranted and may provide additional support for the cognitive model of depression.

In sum, significant advances have been made in terms of identifying the biological correlates of the cognitive model of depression (see Table 1 for an overview). Furthermore, biologically based discoveries have helped to inform and refine our understanding of the cognitive model of depression. It follows that research has also focused on identifying the biological correlates of cognitive therapy for depression. The following section will review the biological correlates of cognitive therapy and associated mechanisms.

**BIOLOGICAL CORRELATES OF COGNITIVE THERAPY FOR DEPRESSION**

Kandel (1998) proposed, “Insofar as psychotherapy or counseling is effective and produces long term changes in behavior, it presumably does so through learning, by producing changes in gene expression that alter the strength of synaptic connections and structural changes that alter the anatomical pattern of interconnections between nerve cells of the brain” (p. 460). This principle is evident in the substantial body of research that identifies bio-
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*Note.* ACC, anterior cingulate cortex; MPFC, medial prefrontal cortex; VLPFC, ventral lateral prefrontal cortex; DLPFC, dorsal lateral prefrontal cortex; 5-HTTLPR, serotonin-transporter-linked polymorphic region; NA, nucleus accumbens; PFC, prefrontal cortex; ADM, antidepressant medication.

<sup>a</sup>Craik et al., 1999; Fossati et al., 2003; Gusnard et al., 2001; Kelley et al., 2002.  
<sup>b</sup>Meyer, 2007; Meyer et al., 2003.  
<sup>c</sup>Beevers et al., 2010.  
<sup>d</sup>Elliott et al., 2002; Eugene et al., 2010; Mitterschiffthaler et al., 2008.  
<sup>e</sup>Drevets, 2001; Siegle et al., 2002.  
<sup>f</sup>Munafò et al., 2008.  
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<sup>j</sup>Harmer et al., 2009.  
<sup>k</sup>Tranter et al., 2009.  
<sup>l</sup>Hamilton & Gotlib, 2008.  
<sup>m</sup>Keedwell et al., 2005.
logical correlates of change in cognitive therapy, consistent with Kandel’s call for an intellectual framework that synthesizes modern psychiatry with modern biology.

Cognitive therapy is an active, time-limited, structured approach used to treat a variety of mental disorders including depression (Beck, Rush, Shaw, & Emery, 1979). Cognitive therapy for depression involves a variety of cognitive and behavioral strategies to help the client critically examine the accuracy and helpfulness of negatively biased beliefs about the self, world, and future. Successful cognitive therapy is associated with a reduction in schema-based information-processing biases.

Relatively recent advances in neuroimaging techniques have allowed researchers to examine the neural mediators of change in cognitive therapy (for a review see Etkin, Pittenger, Polan, & Kandel, 2005; Frewen, Dozois, & Lanius, 2008; Linden, 2006; Porto et al., 2009). In response to this growing line of research, Clark and Beck (2010) expanded Beck’s cognitive formulation of depression and anxiety to include neural mediational processes of cognitive therapy. Briefly stated, this expanded model suggests that depression and anxiety are related to impaired reflective cognitive controls (i.e., top-down processes) that fail to inhibit reflexive, automatic cognitive processes (i.e., bottom-up processes; Clark & Beck, 2010). The expanded model suggests that top-down and bottom-up processes can be represented on a neural level and are sensitive to cognitive therapy. As previously described, bottom-up processes appear to be associated with limbic processes while top-down processes are associated with activity in cortical regions (Clark & Beck, 2010).

In a seminal study investigating the neural responses to cognitive therapy, Goldapple and colleagues showed that the neural pattern of change associated with recovery from depression with cognitive therapy is consistent with top-down mechanisms theorized to mediate cognitive theory response (Goldapple et al., 2004). Further, in a follow-up study, Kennedy and colleagues (2007) found that response to cognitive therapy was related to cortical-limbic connectivity.

Several studies have examined neural activity following cognitive therapy by examining group differences in emotional pro-
cessing tasks (Costafreda, Khanna, Mourao-Miranda, & Fu, 2009; Fu et al., 2008; Ritchey, Dolcos, Eddington, Strauman, & Cabeza, 2011; Siegle, Carter, & Thase, 2006). Insofar as the main goal of cognitive therapy is to alter the way individuals process emotion-relevant stimuli, imaging studies that record neural activity in the context of an affective or cognitive task are likely to uncover important neural indicators of cognitive therapy–related change. In one such study, Siegle and colleagues (2006) examined whether pretreatment neural response to emotional stimuli predicted response to cognitive therapy. The results suggested that cognitive-behavioral therapy CBT is most useful to those who demonstrate increased limbic activity and who cannot engage regulatory structures associated with cortical regions (Siegle et al., 2006). In a related study, Fu and colleagues (2008) examined CBT influences on neural activity during an implicit facial affect processing task. Following CBT, decreased bias toward sad faces in depressed patients was associated with normalization of bottom-up processing. Changes in cortical regions commonly impaired in depression increased following CBT and were predictive of treatment response with CBT (Fu et al., 2008). The finding that neural activity in cortical regions was predictive of successful response to CBT was replicated in a recent prospective study (Costafreda et al., 2009). In another study, Ritchey and colleagues (2011) examined neural activity associated with an emotional processing task in depressed patients before and after CBT. The results suggested that hypoactivation of cortical regions and hyper-responsivity of the limbic structures change in the direction of normalization after CBT. These findings are consistent with the view that cognitive therapy treatment response is mediated by its impact on neural regions associated with higher-order cognitive processes.

The studies reviewed here suggest that the neural correlates of depression are responsive to cognitive therapy and may predict treatment outcome. While the pattern of interactions is not fully understood, there is convincing preliminary evidence that cognitive therapy may be effective in increasing inhibitory executive control, which in turn interrupts or dampens automatic limbic reactions characteristic of depression.

In addition to evidence suggesting that cognitive therapy,
as a complete treatment modality, is associated with important changes in neural activity, recent research also supports the mechanisms of change proposed by the cognitive model. For example, a preliminary fMRI study examined the neural correlates of cognitive reappraisal, the emotion-regulation strategy of purposefully changing thinking about situations to produce a change in affect (Cristea et al., 2011). Cognitive reappraisal is similar to the cognitive therapy approach to cognitive restructuring, in which the individual is encouraged to consider a distressing cognition from alternative perspectives in order to develop a more accurate, adaptive view. Results showed that cognitive reappraisal was associated with areas involved in higher cognitive functions (DLPFC), theory of mind (temporal pole, TP) and self-mentalizing (posterior cingulate cortex, PCC). In addition, amygdala activity was reduced during practice of cognitive reappraisal, which the authors speculated might represent a possible neurobiological correlate of down-regulation of negative emotions.

Another mechanism of change similar to cognitive restructuring is self-distancing, a type of reflection in which the perspective of a distanced observer is adopted (Ayduk & Kross, 2010; Kross, Davidson, Weber, & Ochsner, 2009). Ayduk & Kross (2010) examined the neural and physiological correlates of self-distancing and reported a relation between higher levels of spontaneous self-distancing and decreased peripheral autonomic nervous system activity during recall of a distressing event, suggesting that a self-distancing perspective is associated with a more adaptive profile of physiological response to stress. This is particularly revealing in light of findings that rumination, which is quite distinct from the cognitive restructuring approach used in cognitive therapy, is associated with delayed physiological recovery from stress (Gerin, Davidson, Christenfeld, Goyal, & Schwartz, 2006). Kross and colleagues (2009) also reported that individuals who used a self-distanced perspective when reflecting on a distressing event demonstrated less activity in the subgenual anterior cingulate cortex (sgACC), MPFC, and right VLPFC than individuals who adopted a self-immersed perspective, in which they were instructed to reflect on the feelings experienced in response to the event.
The self-distancing strategy was also associated with a significantly less self-reported negative affect than the self-immersed stance.

IMPLICATIONS FOR RESEARCH ON THE PSYCHOANALYTIC PERSPECTIVE

The preceding sections described how the cognitive model of depression has been supported and refined by biological research. The cognitive model has not only served to guide interpretation of biological data, but new biological advances also have helped to expand the cognitive model. It is now possible to consider how depression-related phenomena can be represented both cognitively and in biological terms. The integration of biological and psychological research to enhance the cognitive model of depression may provide a useful model for psychoanalytically oriented researchers seeking to define the psychoanalytic model in biological terms.

Biological findings similar to those presented here also have been cited as support for psychodynamic theory and therapy (e.g., Roffman & Gerber, 2008; Shedler, 2010). This observation suggests that psychoanalytically oriented researchers are adopting an approach similar to that initially taken by cognitively oriented researchers, namely, using their theoretical orientation to guide interpretation of the existing biological data. The extent to which future biological research will provide distinct support for, and enhancement of, psychoanalytic constructs will depend on the extent to which the psychoanalytic constructs measured in relation to biological correlates are clearly and uniquely operationalized.

The strongest support for the psychoanalytic perspective would result from such operationalization at two levels: at the level of construct definition and at the level of measurement. At the first level, it will be important that researchers focus on psychological constructs that are uniquely linked to psychoanalytic theory (such as the Unconscious) rather than constructs (such as unconscious processing) that are part and parcel of cognitive psychology. Similarly, constructs such as therapeutic alliance, which have been described in the literature as distinct to psychodynamic theory/therapy (Blagys & Hilsenroth, 2000), are now
considered inherent to most psychotherapeutic modalities. As such, it will be critical for researchers to carefully isolate constructs that distinguish psychoanalytic theory from other explanations for psychological distress or impairment. At the second level, the psychoanalytic constructs being measured in relation to biological correlates must, themselves, be defined in measurable terms. For example, as described in greater detail by Roffman and Gerber (2008), a behavioral method used by Susan Andersen and her colleagues (e.g., Andersen, Glassman, Chen, & Cole, 1995; Berk & Andersen, 2000) to measure transference has yielded promising findings and is now being employed in neuroimaging studies. The success of Andersen and her colleagues in employing a behavioral method to measure the transference construct provides a model for researchers interested in similarly operationalizing other key constructs of psychoanalytic theory. Clear operationalization of constructs unique to psychoanalytic therapy will be a necessary step toward identifying the type of biological support for psychoanalytic theory that exists for cognitive therapy.

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