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Implications for Reward Processing in Differential Responses to Loss: Impacts on Attachment Hierarchy Reorganization

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Abstract

When an attachment relationship is severed, so is homeostatic maintenance, leading to dysregulation of multiple physiological systems. Expanding upon Sbarra and Hazan's original model, we suggest that the degree to which an individual's physiological systems remain dysregulated depends on the state of one's attachment hierarchy—namely, whether an individual continues to seek a lost partner for support as their primary attachment figure. To recover from the loss of a romantic partner, an individual's attachment hierarchy must be reorganized. Our model proposes that an individual will go through a series of physiological changes before their attachment hierarchy is reorganized, which can either help or hinder their recovery. We consider the role of reward processing, including endogenous opioids, in this recovery process. Along the way, we identify mechanisms for continued dysregulation of biological systems among those who take longer to recover from a loss.

Keywords

attachment hierarchy; social loss; separation distress; opioids; reward

Forming and maintaining strong social connections with others is a fundamental human need (Baumeister & Leary, 1995). In adulthood, spouses or long-term romantic partners typically serve as primary attachment figures and play a critical role in physiological homeostasis. Accordingly, when these attachment relationships are severed, so is homeostatic maintenance, leading to dysregulation of physiological systems. Sbarra and Hazan (2008) proposed that successful loss recovery is contingent on adopting a self-regulatory strategy that attenuates the dysregulating effects of the attachment disruption.

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Expanding upon Sbarra and Hazan's (2008) original model, we suggest that the degree to which an individual's physiological systems remain dysregulated depends on the state of one's attachment hierarchy—namely, whether an individual continues to seek their lost partner for support as their main attachment figure. To recover from the loss, an individual's attachment hierarchy must be reorganized such that, over time, they can direct their attachment-related needs toward a new primary attachment figure (Hazan & Zeifman, 1994; Mikulincer & Shaver, 2008). We propose a model suggesting that an individual will go through a series of physiological changes before their attachment hierarchy is reorganized, which can either help or hinder their recovery. We identify mechanisms for continued dysregulation of biological systems among those who take longer to recover from a loss and discuss implications of this model when interpreting existing data and facilitating future investigations. Importantly, we propose that reward processes may facilitate the motivation for continuing to seek a lost partner absent from the top of the attachment hierarchy. Furthermore, differences in reward processing may distinguish differential recovery trajectories. For example, our model has novel implications for differentiating complicated grief (CG) from depression, as discussed later in this article.

Sbarra and Hazan's (2008) model outlined how multiple biological systems are regulated by close relationships (i.e., "co-regulation"), dysregulated by separation and loss, and potentially re-regulated through recovery efforts. Their article emphasized the nature and function of *intact* attachment bonds. Thus, we will keep our current discussion of intact attachment bonds brief; our aim in discussing co-regulation is to foreshadow the type of dysregulation that occurs when a romantic attachment is severed. In contrast, the current article places the most emphasis on dysregulation due to loss, and recovery efforts thereafter. We add to Sbarra and Hazan's model by highlighting the empirical research over the past decade, which implicates specific neurobiological systems (e.g., PANIC/GRIEF and SEEKING systems; Panksepp & Watt, 2011) involved in separation distress, as well as reward and approach behaviors, as instrumental in forming responses to loss. Furthermore, we propose that Sbarra and Hazan's model may be better informed through an understanding of how reward processes influence attachment hierarchy reorganization.

The implication of specific neurobiological systems in social loss is not new. Over the last two decades, social neuroscientists have investigated the shared neural substrates of social and physical pain. MacDonald and Leary's (2005) seminal article, which utilized a large amount of work from the animal model literature by Jaak Panksepp and others (e.g., Herman & Panksepp, 1978; Nelson & Panksepp, 1998), promoted enormous interest in the social and physical pain overlap. Since then, researchers identified areas of the human brain (e.g., anterior cingulate cortex [ACC] and anterior insula [AI]; see Eisenberger, 2015, for a review¹), which coincide with the anatomy first identified by Panksepp and his colleagues (e.g., Herman & Panksepp, 1978; Nelson & Panksepp, 1998), suggesting these early animal models of attachment may have some utility. In response to MacDonald and Leary's seminal article, Panksepp (2005) noted that MacDonald and Leary did not prioritize "the most

¹There is currently debate on the selectivity of brain regions (e.g., dorsal anterior cingulate cortex) that have shown some social/physical pain overlap as being selective markers of pain exclusively (see Lieberman, Burns, Torre, & Eisenberger, 2016; Wager et al., 2016).

important emotional system,” in their social pain theory arguments—the separation-distress/PANIC system (later referred to as the PANIC/GRIEF system; Panksepp & Watt, 2011). Since then, Panksepp’s work has been missing in most theoretical discussions of attachment and loss. We intend to reintegrate some of the early work on the neurobiological underpinnings of attachment and responses to loss to prompt new discussions and empirical investigations. In doing so, worth noting is the ongoing debate among neuroscientists regarding locationist versus constructionist approaches to understanding the brain basis of emotion. In the current article, we theorize using Panksepp’s locationist perspective because his experiments of maternal deprivation directly modeled attachment-related behaviors. Importantly, however, we acknowledge the possibility that the PANIC/GRIEF and SEEKING systems (Panksepp & Watt, 2011) may not be operating as discrete and modular circuits, as inter-region and inter-network interactions that commonly underlie a range of discrete emotion categories are currently being elucidated (Lindquist, Wager, Kober, Bliss-Moreau, & Barrett, 2012). Thus, we hope researchers from a more constructionist approach will build from the parsimonious model presented here to further elucidate how different systems in our model may be operating.

With rare exceptions (e.g., Fagundes, 2012; Hazan & Zeifman, 1999; Trinke & Bartholomew, 1997), the adult attachment literature has focused on the individual differences of attachment anxiety and avoidance. Although we will address individual differences in attachment orientations, we will focus on “normative” attachment processes. We will consider how attachment hierarchies are formed, maintained, and—especially—reorganized after the loss of an attachment figure, which may correspond to physiological dysregulation occurring “under the skin” (Miller, Chen, & Cole, 2009).

We will focus primarily on losing an established romantic partner (e.g., a spouse) by death for the following reasons: (a) established romantic partners typically serve as primary attachment figures in adulthood, (b) opioids are thought to be most active in the maintenance of established relationships, compared with newly formed relationships² (Inagaki, 2018), and (c) there is an existing theoretical framework for understanding attachment and bereavement compared with other types of relationship dissolution. However, we will discuss implications for adjustment after relationship dissolution (e.g., breakups and divorce).

Overview of the Proposed Model

Throughout the lifespan, people selectively orient attachment-related functions toward one primary attachment figure, as well as a number of other secondary attachment figures; the attachment figures are organized hierarchically (Bowlby, 1969/1982; Trinke & Bartholomew, 1997). Individuals’ attachment hierarchies reorganize across the lifespan as new social circumstances arise. In adulthood, spouses or long-term romantic partners

²The current theoretical perspective held by those conducting social pharmacological manipulations of opioids is that opioids are most active in the maintenance of *established* relationships (Inagaki, 2018; Inagaki, Hazlett, & Andreescu, 2019). Thus, this article focuses on the loss of established romantic relationships, where a feeling of opioid withdrawal likely influences differential responses to the loss of romantic partners. Oxytocin is also involved in the reinforcement of romantic pair bonds (e.g., during sexual behaviors; Carter & Altemus, 1997). However, oxytocin appears to be most relevant to rein-forcing romantic bonds in the early stages of romantic relationships (Machin & Dunbar, 2011).

typically serve as primary attachment figures and play a critical role in physiological homeostasis, thereby reciprocally providing a feeling of felt security, and contributing to the control of body temperature, sleep-wake cycles, and general physiological functioning (Polan & Hofer, 1999). When a person's romantic partner (who served as a primary attachment figure) dies, an "empty" space is created at the top of the surviving partner's attachment hierarchy. Accordingly, there is no one available to whom the surviving partner can effectively direct his or her attachment-related needs. In turn, this also disrupts homeostatic maintenance, leading to dysregulated physiological systems.

As depicted in our conceptual model (see Figure 1), we propose that people will go through a series of stages (sometimes overlapping) before their attachment hierarchy reorganizes, which will ultimately facilitate a return to homeostasis (i.e., recovery). The first is *disorganization*, which refers to the dysregulation of homeostatic mechanisms (e.g., body temperature, sleep, cardiovascular functioning; Hofer, 1978) that occurs immediately after the attachment bond is severed. Importantly, the disorganization phase includes an endogenous opioid withdrawal, brought on by the cessation of endogenous opioid release when a previously conditioned, and thereby expected, reward is no longer available once the partner is gone. The opioid withdrawal is fast acting and may precede the dysregulation of other physiological systems. In addition to the loss of coregulatory reward processes, the recently severed attachment bond promotes activation of the sympathetic branch of the autonomic nervous system (ANS), which characterizes the *protest* phase (Sbarra & Hazan, 2008). When the ANS response proves unable to resolve the threat of lost coregulatory resources, the body initiates a second stage of the stress response involving the hypothalamic pituitary adrenal (HPA) axis and glucocorticoid response to attempt to regain homeostasis (Selye, 1956). The "protest" phase, which is analogous to that conceptualized by Bowlby (1973), and then later by Weiss (1988), is characterized by enduring preoccupation with the missing person, psychological disorientation, and distress, similar to the response seen among infants separated from a caregiver.

Separation from a romantic partner by death prompts anxiety and searching behaviors as the individual attempts to reestablish a social connection with the deceased (Weiss, 1988). These behaviors coincide with activation of the neurocircuitry responsible for approach behaviors (i.e., what Panksepp referred to as the "SEEKING" system), as well as separation distress (i.e., stemming from the "PANIC/GRIEF" system), which will be reviewed later in the article. Ultimately, the protest phase aims to reunite the individual with their lost partner. If reuniting is not successful, despair arises (Hofer, 1978).

It is a natural progression then that the *despair* phase is made up of the consequences of sympathetic-adrenal-medullary (SAM)/HPA activation (e.g., inflammation, depression, sickness behaviors). As part of the HPA cascade, corticotropin-releasing factor is synthesized by the hypothalamus and leads to cytokine production (Black, 2002; Hennessy, Deak, Schiml-Webb, 2001; Larson & Dunn, 2001). Cytokines can help fight infection or heal injuries; pro-inflammatory cytokines can also induce sickness behaviors (e.g., fever, increased sleep, reduced activity), that in the short term, serve an evolutionarily adaptive purpose to conserve energy for healing (Dantzer, 2001). Sickness behaviors and observed behavioral reactions to loss overlap (e.g., social withdrawal, depressed mood, disturbed

sleep; Maier & Watkins, 1998), which indicates a functional value of these symptoms in aiding the body's return to homeostasis. In our model, this is reflected in the despair phase, where we no longer expect an activation of SEEKING neurocircuitry; the surviving partner is no longer motivated by the reward of the lost partner, which manifests in social withdrawal and avoidance behaviors.

We surmise that an adaptive response to a lost partner no longer being available, would be to give up on seeking the lost partner, after having experienced the negative effects of the lost partner's inaccessibility. According to our model, if the surviving partner can redirect their attachment-related behaviors to someone else, and reorganize their attachment hierarchy, their organized stress response will reflect an adaptive pattern that should help them return to homeostasis (i.e., recovery). If the surviving partner continues to expect or perhaps experience rewarding contact (even if imagined) with the lost attachment figure, they are likely to continue seeking the partner, which will inevitably lead to let down and a continuation of grief. In essence, these individuals may get stuck in an oscillation between the *protest* and *despair* phases, causing prolonged HPA activation. Chronic over-activation of the neuroendocrine system inhibits cellular immunity and leads to a pro-inflammatory state as a result of glucocorticoid resistance (Bremner & Vermetten, 2001; Miller, Cohen, & Ritchey, 2002). Thus, physiological reactions to loss can be thought of in terms of an acute phase that can evolve into a full-blown organized stress response that promotes immune dysregulation (Miller & Raison, 2016). We hypothesize that the degree to which an individual's physiological systems remain dysregulated depends on the state of one's attachment hierarchy—namely, whether an individual continues to seek their lost partner for support as their main attachment figure, rather than reorienting their attachment-related behaviors to someone else, thereby reorganizing their attachment hierarchy, and regaining homeostasis.

This conceptualization of loss is both broadly interesting and utilitarian in that it applies to different types of social loss, and the loss of different types of attachment figures. While we think the proposed model may apply best to romantic relationship partners, this model is likely to apply to the loss of any *primary* attachment figure in adulthood—thus, any relationship partner whose absence elicits separation distress. In a study of adult attachment hierarchies (Trinke & Bartholomew, 1997), researchers found that adults with romantic partners ranked their romantic partners most highly as attachment figures, followed by mother, father, sibling, and best friend. Thus, for those without romantic partners, the proposed model may apply to losing another attachment figure they consider primary.

Before the Loss: The Behavioral Conditioning of Rewards in Adult Romantic Relationships

Adult attachment relationships serve many different functions that promote survival: *proximity maintenance*, *separation distress*, *safe haven*, and *secure base* (Fraley & Shaver, 2000; Hazan, Gur-Yaish, & Campa, 2004). *Proximity maintenance* occurs when individuals seek the proximity of their attachment figure, gain reward from being nearby, and exhibit *separation distress* when away from their attachment figure. Individuals use attachment

figures as a *safe haven* by seeking them for support when distressed. Finally, attachment figures serve as a *secure base*, from which individuals can confidently explore their environment, and provide a core sense of emotional security (Feeney & Thrush, 2010; Hazan et al., 2004). Maintaining attachments and their related functions provides a sense of safety and security. For example, when an attachment figure is nearby and accessible, individuals experience “felt security” (Mikulincer & Shaver, 2008), or a sense of safety in the world which manifests in greater sociability and exploration of their environment. In contrast, when separated from the attachment figure, individuals exhibit “protest” behaviors such as calling, crying, or searching to seek proximity to the attachment figure once again. It should be emphasized that separation distress is unique to attachment relationships; separation distress is the strongest indicator that an attachment relationship exists (Bowlby, 1980; Fraley & Shaver, 1999; Hazan et al., 2004; Weiss, 2001).

Across the lifespan, from infancy to adulthood, attachment relationships regulate physiological processes (Hofer, 1978). In adulthood, each partner aids in maintaining the physiological homeostasis of the other, thereby reciprocally providing a feeling of felt security (Sbarra & Hazan, 2008; Shear & Shair, 2005). Thus, romantic partners not serve only as a “safe haven” and a “secure base” but also contribute to the control of body temperature, sleep-wake cycles, and general physiological functioning (Polan & Hofer, 1999). Consequently, interactions with relationship partners shape an individual’s physiology, and this becomes especially evident when the partners are separated. For example, even naturally occurring temporary separations (e.g., 4- to 7-day travel-related separations) between cohabiting romantic partners can elicit physiological changes among both partners (Diamond, Hicks, & Otter-Henderson, 2008).

One of the key components in the formation of attachment bonds is behavioral conditioning, in the form of both negative and positive reinforcement (Sbarra & Hazan, 2008). Bowlby (1969/1982) first referred to this process as “exposure learning,” where over time, individuals begin to associate their primary attachment figure with certain positive experiences. For example, a primary attachment figure consistently providing comfort (i.e., positive reinforcement), and alleviating distress (i.e., negative reinforcement), reinforces proximity maintenance behaviors, which encourage the individual to continue seeking support from this source in the future. Researchers have even suggested that the capacity to experience affiliative reward is necessary for any individual to acquire and maintain attachments; without affiliative reward, normative attachment is not possible (Depue & Morrone-Strupinsky, 2005). Sexual behavior also activates and conditions physiological attachment systems, namely the opioid system, which helps to maintain attachment relationships with romantic partners (Hazan & Zeifman, 1994; Panksepp, Herman, Conner, Bishop, & Scott, 1978). The opioid system plays an important role in providing the physiological basis for felt security, making attachment relationships pleasurable and distress-reducing.

After the Loss, but Before Hierarchy Reorganization: Theoretical Extensions of Disorganization, Protest, and Despair Phases

The Disorganization Phase

Opioids are only one component of a complex biological system that helps an individual maintain homeostasis. The disorganization phase of the proposed model emerges from the loss of coregulatory reward and is marked with a withdrawal reaction, resulting in the free running of biological and psychological systems under homeostatic control (Sbarra & Hazan, 2008). Out of all of these biological systems, the opioid system has been most popular among recent empirical investigations in humans, since the publication of Sbarra and Hazan (2008). Thus, we review the latest evidence for opioid involvement in the behavioral conditioning of rewards within social relationships, as these data apply to our theoretical discussion of the loss of those rewards after losing a spouse.

Affiliative reward, in the form of positive reinforcement, dominates the early stages of attachment formation with romantic partners, as pleasure becomes associated with the partner. Using functional magnetic resonance imaging (fMRI), researchers observed activation of several reward-processing regions in the brain (e.g., caudate head, nucleus accumbens, lateral orbitofrontal cortex, amygdala, and dorsolateral prefrontal cortex) among participants who viewed pictures of their romantic partner, while being administered a painful stimulus, suggesting that viewing an image of a romantic partner stimulates the endorphin-based reward system, which leads to a reduction in the experience of pain (Younger, Aron, Parke, Chatterjee, & Mackey, 2010). We can infer that participants were rewarded (i.e., the opioid system was activated) when prompted with a visual cue of their partner, which may have provided negative reinforcement (i.e., the removal or lessening of a negative stimulus) in the form of reduced pain perception.

Extensive animal research has demonstrated an association between endogenous opioid release and affiliative behavior. Furthermore, inhibiting opioids increases feelings of social disconnection and motivates reaffiliative behavior (see Loseth, Ellingsen, & Leknes, 2014, for a recent review). More recently, researchers have assessed the translation of earlier animal models to human social connection, using pharmacological methods. Thus, the rationale follows that if opioids also contribute to feelings of human social connection, then using a drug to block opioids should decrease the feelings humans usually experience when bonding with others, compared with placebo conditions where opioids are not altered (Inagaki, 2018). Indeed, naltrexone (i.e., an opioid antagonist) compared with placebo, reduced feelings of warmth and affection in response to watching an affiliative film among women with high levels of trait affiliation (Depue & Morrongiello, 2005). More recently, researchers induced either a neutral emotional state or “warmth-liking” (associated with feelings of affection and acceptance in social contexts) in women after taking naltrexone or placebo. Participants in the warmth-liking condition who also took the placebo reported more warmth-liking compared with those in the warmth-liking condition who took naltrexone; thus, blocking opioids reversed the effects of the warmth-liking induction (Schweiger, Stemmler, Burgdorf, & Wacker, 2013). Interestingly, naltrexone also reduced feelings of social connection that, in the past, have been successfully induced by having

participants hold a warm object (Inagaki, Irwin, & Eisenberger, 2015). However, these studies assessed responses to socially distant strangers or used broad social analogies in their paradigms, which do not directly map on to the early animal models that tested opioid involvement in affiliative interactions with close social contacts. Fortunately, researchers recently began to rectify this issue (Inagaki, Ray, Irwin, Way, & Eisenberger, 2016). For example, naltrexone reduced feelings of social connection compared with placebo when researchers induced social connection by asking participants to read personal notes from their close friends and family members (significant others, parents, siblings, grand-parents, friends). Furthermore, naltrexone reduced feelings of daily social connection, when measured using daily reports over 4 days, suggesting opioids are likely involved in the maintenance and continuation of human social bonds with close others (Inagaki et al., 2016). Most recently, researchers found naltrexone reduced ventral striatum and middle-insula activity to social and physical warmth, therefore disrupting experiences of social connection (Inagaki, Hazlett, & Andreescu, 2019). Importantly, the effect of naltrexone was specific to close others, as naltrexone did not alter neural responses to strangers (Inagaki et al., 2019). Taken together, there is little doubt the opioid system plays a role in the maintenance of close relationships. An equally important aspect of the opioid system's role in social relationships is the impact of opioid (i.e., reward) withdrawal after losing a romantic partner.

The Brain Opioid Theory of Social Attachment (BOTSA; built from what was earlier known as the brain opioid hypothesis of attachment; Panksepp et al., 1978) posits that μ -opioids underlie the pleasure humans experience when socially connected with others, particularly those with whom individuals have formed an attachment bond (Panksepp et al., 1978).³ People who develop a dependence on a romantic relationship, as well as individuals who develop a physical dependence on exogenous opioids (i.e., originating outside the body; not naturally occurring) such as morphine, experience three stages in the development of the chemical relationship (with either a person or drug). The first stage is euphoria followed by addiction (Machin & Dunbar, 2011). The brain ensures repetition of important life-sustaining activities by associating those activities with reward. Whenever this reward circuit is activated, it motivates individuals to seek rewarding behavior, again and again, creating an addiction of sorts. The second stage involves tolerance and habituation. In human relationships, this manifests during the period of the relationship in which individuals shift from attraction to attachment (Liebowitz, 1983). Finally, the third stage involves an intense phase of withdrawal if the object of dependence is removed. Separation from an attachment figure prompts abrupt cessation of opioid release, which is thought to contribute to the pain humans experience in response to separation (Panksepp & Watt, 2011). In a positron emission tomography (PET) study (Zubieta et al., 2003), women exhibited decreased μ -opioid-mediated neurotransmission when recalling the death of a loved one, the breakup of a romantic relationship, or an interpersonal problem with someone close to them, indicating that μ -opioid-related activity is involved in responding to the loss of connections to significant others. In the case of social relationships, withdrawal symptoms may manifest in

³. We discuss the Brain Opioid Theory of Social Attachment (BOTSA), as it is directly related to opioids, but it should be noted that more recent partner addiction hypotheses (i.e., Burkett & Young, 2012) integrate the latest neurochemical data to elaborate on the original theory and extend beyond merely opioids.

behaviors associated with distress or depression (Liebowitz, 1983). In the proposed model, these behavioral manifestations appear at the beginning of the *protest* phase.

The Protest Phase

In the last decade, a group of affective neuroscientists sought to identify the neurobiological regions of the attachment system (e.g., Panksepp & Watt, 2011). Here, we extend Sbarra and Hazan's (2008) model by integrating two key neurobiological systems: PANIC/GRIEF and SEEKING (Panksepp & Watt, 2011).

Panksepp and Watt (2011) identified seven genetically provided general emotional systems: SEEKING (responsible for approach behaviors), RAGE, FEAR, sexual LUST, maternal CARE, separation-distress PANIC/GRIEF, and joyful PLAY⁴ (Panksepp & Watt, 2011) with each neural system name corresponding to a specific set of emotional brain circuitry (see Watt & Panksepp, 2009, for an in-depth review). Particularly relevant to the proposed model are the PANIC/GRIEF and SEEKING emotional systems. The PANIC/GRIEF circuitry begins in the midbrain central gray regions (i.e., periaqueductal gray [PAG]), and continues through medial diencephalic structures, particularly the dorsomedial thalamus, and ends in the basal forebrain nuclei, and anterior cingulate forebrain regions. Declining opioid levels located in these brain regions are partially responsible for separation-distress signals (e.g., calls of protest; Watt & Panksepp, 2009). Thus, from an affective neuroscience perspective, the distress produced by social loss is a product of continuous overactivity of the separation-distress system (Bowlby, 1980; Heim & Nemeroff, 1999), analogous to hyperactivation of the attachment system. The arousal of the PANIC/GRIEF system is an index of social attachment, such that if there is no attachment, then there is no separation distress. Thus, the evidence collected from research in affective neuroscience adds credence to earlier ideas of separation distress as a required feature of attachment relationships (Bowlby, 1980; Fraley & Shaver, 1999; Hazan et al., 2004; Weiss, 2001).

Of equal importance to the proposed model is the SEEKING system, which is responsible for reward learning and approach behaviors (Alcaro & Panksepp, 2011). The mesolimbic dopaminergic (ML-DA) system, which plays a central role in motivated behaviors, reward, and cognition, activates a SEEKING state, that broadly evolved to induce organisms to search for life-supporting stimuli (Alcaro, Huber, & Panksepp, 2007). The ML-DA mammalian system connects midbrain and forebrain nuclei, serving as a "neurochemical bridge" through which SEEKING patterns of brain activation are transformed through learning into larger and more complex patterns. This SEEKING network is innervated by ML-DA projections that originate in the ventral tegmental area (VTA) and diffuse to large portions of the anterior limbic brain (Alcaro & Panksepp, 2011). Many of the neural structures that make up the SEEKING network promote exploration/approach and incentive and reward behaviors, when stimulated in animal models (see Alcaro & Panksepp, 2011, for a review of the neuroarchitecture). Thus, the SEEKING system influences attention, the salience of incentives, associative learning, and anticipatory predictions (i.e., expectations).

⁴Each neural system name is capitalized to distinguish each as a genetically provided neural system distinct from words we commonly understand as, for example, "panic" or "grief" (Watt & Panksepp, 2009). Whether these are truly distinct modular systems is still under debate (e.g., Lindquist et al., 2012).

Despair Phase

Recall that activation of the HPA axis and pro-inflammatory processes (e.g., cytokines) may perpetuate “despair” or depression (Hennessy et al., 2001). According to affective neuroscientists, this transition to despair could be due to a diminished SEEKING urge (Panksepp & Watt, 2011). If protest fails to facilitate reconnection with the lost attachment figure, a behavioral “shutdown” occurs (with symptoms that present as depression; Panksepp & Watt, 2011), which protects against the consequences of prolonged PANIC/GRIEF—referring back to what Bowlby (1980) originally described as evolutionarily adaptive, given that prolonged vocalizations in response to separation could attract predators. This protective shutdown of the neurocircuitry associated with distress vocalizations is associated with somewhat of a decrease in the activation of PANIC/GRIEF circuitry (Panksepp & Watt, 2011). Then, SEEKING activity subdues the distress vocalizations of protest. The individual typically exhibits a “giving up” response, which may manifest in continued psychological pain from separation combined with an inability to seek rewards (Panksepp & Watt, 2011). Although it is not fully clear what reduces these seeking urges, dynorphins are one possible mechanism. These brain opioids mediate a distinct type of negative affect caused by social loss and reduce the responsivity of the brain reward SEEKING system (McLaughlin, Li, Valdez, Chavkin, & Chavkin, 2006). Panksepp and Watt (2011) also propose that individuals may differ in their degree of SEEKING system shutdown. Important for the current discussion, the anticipation of reward is thought to be intrinsically related to the operation of the SEEKING system (Alcaro & Panksepp, 2011).

It appears that different types of separation responses may depend on the interplay between the PANIC/GRIEF and SEEKING system; this recent work corresponds to Sbarra and Hazan’s (2008) model. The PANIC/GRIEF and SEEKING neuro-affective circuitry can thus be integrated into the loss literature (e.g., Hofer, 1978; Sbarra & Hazan, 2008) in the following way: the “depression” related to social loss is ultimately related to (a) sustained overactivity of the separation-distress PANIC/GRIEF system, which can lead to Hofer’s idea of “despair,” and (b) the “despair” phase that follows an acute PANIC/GRIEF response is characterized by low activity of the SEEKING system. As described above, this sequence can be adaptive and aid in recovery in some circumstances. However, if prolonged HPA axis activation occurs due to cyclic activation of the SEEKING and PANIC/GRIEF systems, a full-blown organized stress response that dysregulates immune function will likely follow. For example, recent marital separation and greater “attachment” to an ex-husband predicted worse psychological symptoms and poorer immune function among women who separated or divorced from their spouse (Kiecolt-Glaser et al., 1987). Similarly, the death of a partner dysregulates autonomic and immune systems (Fagundes et al., 2018; Hall & Irwin, 2001; Schultze-Florey et al., 2012). In addition, many symptoms of grief have established relationships with inflammatory processes related to the stress response (Fagundes et al., 2018; Maier & Watkins, 1998).

Three Patterns of Physiological Activation in Response to Loss

The proposed model suggests three overarching patterns of responses to the loss of a romantic partner (see Figure 2). Pattern A refers to the normative grief pattern, and while still painful, the most ideal and perhaps adaptive recovery pattern to social loss. This pattern

involves physiological dysregulation (including a withdrawal of endogenous opioids), which transitions into a more organized stress response coupled with activation of both the PANIC/GRIEF and SEEKING systems. The separation-distress response reflects PANIC/GRIEF activation, and the seeking of the lost attachment figure reflects SEEKING activation. It is important to note, however, that the seeking of the lost attachment figure *early* in the loss recovery process is considered normative, as this reflects the naturally occurring “protest” phase both Bowlby (1980) and Hofer (1978) proposed. Over time, as the individual comes to terms with the fact that their partner is not coming back, they shift from protest to a period of despair that is brief, and ultimately adaptive in assisting in the return to homeostasis.

Pattern B reflects a “depression” pathway, which can vary greatly depending on many factors including whether individuals were already depressed before the loss. Similar to the normative pathway (Pattern A), once into the despair phase, these individuals experience minimal activation of the SEEKING system, reflected in a loss of motivation and expectation for rewards, which inhibits the continuation of seeking the lost partner for support. People who follow this depression pathway may continue to experience depression after the loss if the despair phase becomes prolonged. Specifically, depressive symptoms (e.g., sickness behaviors, pain, disturbed sleep), and negative health behaviors (e.g., poor diet and lifestyle factors) may act as mediating pathways that can lead to further inflammation, which in turn, fuels depression (see Kiecolt-Glaser, Derry, & Fagundes, 2015 for a review). The inflammation–depression cycle becomes difficult to break, and may develop into the treatment-resistant depression characteristic of that connected to pro-inflammatory origins (e.g., Raison et al., 2013). The surviving partner may never return fully to homeostasis unless they can reorganize their attachment hierarchy. A cycle of inflammation and depressed mood, mediated by reductions in reward-related neural responses (Eisenberger et al., 2010), may keep them from returning to homeostasis. Reorganization of the attachment hierarchy requires social affiliation with other attachment figures, and in some cases, the formation of new relationships; depressed people are unlikely to feel motivated to facilitate the social interactions demanded of them to effectively reorganize their hierarchy. Lowered activity in brain reward centers may also manifest in blunted positive affect among depressed people (see Forbes & Dahl, 2005, for a discussion of the role of diminished positive affect in depression). This will become more important in our discussion of the differences between depression and complications in the grieving process.

Pattern C refers to an individual who experiences the initial normative dysregulation, enhanced PANIC/GRIEF and SEEKING, but is unable to inhibit the desire to seek their primary attachment figure, and therefore, is unable to reorganize. The desire to continue seeking their partner may be reflected in enhanced activation of the SEEKING system among these individuals. Furthermore, this prolonged period of protest followed by despair keeps them in a cycle of elevated HPA axis activation. If a surviving partner’s SEEKING system continues to be activated, they may get stuck in a cycle of reward-seeking from an attachment figure that is no longer available for attachment-related functions. Furthermore, they continue to experience enhanced activation of their PANIC/GRIEF neurocircuitry, facilitating a recurring state of separation distress when, inevitably, they find that their

attachment figure is no longer available. This cycle keeps them from reorganizing their attachment hierarchy and returning to physiological homeostasis (i.e., recovery).

Looking Forward: An Empirical Agenda for the Study of Loss and Recovery

Much of the available evidence in support of co-regulated attachment and the neurobiological underpinnings of the attachment system derives from animal studies. Complications in the grieving process likely have multiple etiologies, some of which are not discussed in this review (e.g., cognitive variables, Boelen, Stroebe, Schut, & Zijerveld, 2006; making meaning of the loss, Currier, Holland, & Neimeyer, 2006; caregiving factors, Schulz, Boerner, Shear, Zhang, & Gitlin, 2006; relationship-contingent self-esteem, Knee, Canevello, Bush, & Cook, 2008). We acknowledge that our proposed model remains incomplete until further research fills in the gaps. However, there is utility to the model in its current form; specifically, the proposed model can help us interpret existing data about social loss, expand how we conceptualize loss and recovery, and change how we study responses to loss. In this section, we discuss seven questions emerging from this analysis, all of which we hope will facilitate new empirical investigations and debate.

Can Researchers Use the Proposed Model to Identify Grief Trajectories That are Normative Versus Problematic?

The three proposed patterns should be investigated further using longitudinal observational study designs with individuals experiencing loss. This would be particularly helpful to identify when normative loss trajectories deviate to becoming more problematic. Specifically, when possible, it is imperative that future empirical investigations employ preloss measures to better elucidate the physiological and psychological changes that occur during the disorganization phase. Also, one weakness of our proposed model is that it is unknown how much time it takes to move from one phase to another in the model. The timing of each phase likely depends on many factors including when the individual can start reorganizing their attachment hierarchy and reach out to other figures for support. Longitudinal studies of responses to a loss in different contexts are needed to understand how time corresponds to different response phases after a social loss. Finally, the obvious next steps to better understanding how and when the PANIC/GRIEF and SEEKING systems affect loss outcomes include assessing the different pathways proposed in this model. Much of the existing human neurological evidence reviewed in this article was collected with the use of fMRI techniques. However, PET is more sensitive than fMRI to changes in slowly firing neural circuits, where globally acting neuromodulators like endogenous opioids can best be captured (Panksepp, 2005). Thus, researchers should utilize PET to map trajectories of affective arousal specific to loss in human brains, over time.

Can the Proposed Model Contribute to Our Understanding of Existing Models of Loss?

The proposed model may also inform the interpretation of existing data. For example, Bonanno, Wortman, and Nesse (2004) established five unique trajectories of depressive symptoms throughout bereavement, using data collected from a large sample ($N = 1,532$) at multiple timepoints: before the loss of a spouse, 6 months post-loss, and 18 months post-loss. They refer to a “chronic depression” trajectory as high levels of depressive symptoms

before the loss, slightly higher levels at 6 months post-loss, and then a return to high “baseline” levels 18 months after the loss. “Depressive improved” referred to those exhibiting high levels of depression pre-loss, with significant improvement of symptoms post-loss, much lower than their originally high baseline levels (Bonanno et al., 2004). These possible depression trajectories are reflected in Pattern B in our proposed model (Figure 2); importantly, Pattern B captures the range of variability in depression—particularly, pre-loss—which could greatly influence the pattern of depressive symptoms over time.

Improvement in depression from pre- to post-loss may reflect an already initiated reorganization of the attachment hierarchy, as may be the case when an individual loses an attachment figure, but there is some warning of the impending loss (e.g., “living bereavement,” when a spouse has a progressive chronic illness, such as dementia). Importantly, Bonanno et al.’s (2004) depressive symptom trajectories also included a “chronic grief” group which closely matches the depiction of Pattern C in Figure 2. Likewise, they identify a “common grief” group, who exhibit low depression before the loss, higher depression 6 months post-loss (but still lower than chronic depression and chronic grief), and returning close to baseline after the loss. Last, a “resilience” trajectory includes those with low levels of depression pre- and post-loss, with minimal change throughout the bereavement period. These final two trajectories map onto Pattern A in Figure 2. What is particularly elegant about Bonanno et al.’s (2004) model is the differentiation of individuals who experience forms of depression from those who experience forms of grief, even when depressive symptoms are the outcome of interest. Importantly, both our model and Bonanno et al.’s (2004) data illustrate differences between depression and grief.

Can the Proposed Model Elucidate Differences Between Depression Versus Prolonged or Complicated Grief?

The continued activation of the SEEKING system (i.e., neurocircuitry involved in reward and approach behaviors) may reflect why individuals with complications in the grieving process (e.g., “Prolonged Grief”) can experience positive affect, while depressed people cannot. It is natural to experience acute grief, or intense emotional pain, early in the bereavement period. The emotional pain brought on by the loss of a spouse is seen as an inevitable but adaptive response (Bowlby, 1980). Fortunately, for most people, grief symptoms dissipate over time following the first 6 months after the loss (Utz, Caserta, & Lund, 2012). In the first 6 months after the loss of a spouse, between 30% and 50% of adults’ depressive symptoms qualify for classification of “major depressive disorder.” This number drops to around 20% after 6 months. If these symptoms continue to meet a certain clinical threshold after the 6-month mark, bereaved individuals may be characterized as having Complicated Grief (CG), a condition involving a persistent yearning/longing for the deceased, which may be associated with intense sorrow and frequent crying, or preoccupation with the deceased, difficulty accepting the loss, and a number of distressing symptoms (*Diagnostic and Statistical Manual of Mental Disorders*, 5th ed.; *DSM-5*; American Psychiatric Association, 2013). Over the past decade, there has been an ongoing debate about whether or not the *DSM-5* should include CG; the debate centers on what should be considered a “normal” grief trajectory. The current consensus is that CG can be best understood as an unusually severe and prolonged form of acute grief (Shear & Shair,

2005), which includes a stress response as well as a separation response. This fits into our current model (Figure 2) with Pattern C modeling such a trajectory.

An fMRI study revealed differential activation of brain parts responsible for reward processing (i.e., the nucleus accumbens, part of the SEEKING circuitry) among those with and without CG when viewing cues of the deceased (O'Connor et al., 2008). Individuals with CG showed reward-related activity, while those without CG did not, suggesting that reminders of the deceased may still activate neural rewards for those with CG, a maladaptive response that may reinforce the pattern of intense yearning and longing for the deceased, characteristic of CG; this is consistent with previous research suggesting that social attachments may activate reward pathways and have addiction-like properties (Insel, 2003). Furthermore, for people with CG, the addictive properties of past close relationships may still be active after the relationship partner has passed on.

CG is empirically and conceptually understood as distinct from depression (Prigerson et al., 1995). It is still unclear whether CG shares the same biological pathways (i.e., inflammatory) as persistent depression (Miller et al., 2009; Schultze-Florey et al., 2012). Although we do see enhanced inflammation among bereaved individuals with higher grief severity compared with those with lower grief severity about 3 months after the loss (Fagundes et al., 2019), it is unknown whether this effect persists beyond this point. Furthermore, individuals with CG can experience positive affect, whereas those with depression cannot. In addition, individuals can be depressed before losing a partner, whereas grief is brought on by the loss of the partner, and would be alleviated by the return of the lost attachment figure, whereas depression likely would not. Importantly, the reward system may not function in the same way among those with CG and those who are depressed. Indeed, depression is characterized by decreases in SEEKING-related drives (Panksepp & Watt, 2011). In contrast, CG appears to be related to an increase in SEEKING-related drives. Furthermore, in addition to positive affective states, approach motivation can also be associated with negative affective states, such as anger, a symptom of CG (Harmon-Jones, 2003).

Do People Need to Reorganize Their Attachment Hierarchy to Adjust to Loss?

Continued desires to direct attachment needs to a lost partner suggests that the bereaved spouse has not effectively reorganized his or her attachment hierarchy. Attachment theory suggests that continued desires to direct attachment needs to those who are not available should interfere with adjustment, although no prior research has directly tested this link in relation to CG. A straightforward way to begin to answer questions related to attachment hierarchy reorganization would be to begin to measure attachment hierarchies in the context of social loss.

Our model may also have interesting applications to the idea of “continuing bonds” (CBs) during bereavement. CBs can be defined as an ongoing connection between the bereaved and the deceased that is maintained over time (Klass, Silverman, & Nickman, 1996), and has recently regained interest in the bereavement literature (e.g., Root & Exline, 2014). Some expressions of CBs may simply represent attempts to gain felt security again, and the degree to which these expressions are adaptive may depend on when they are expressed (e.g., the

protest phase vs. the despair phase; see Field, Gao, & Paderna, 2005, for a discussion). CB expression during the protest phase, considered the normative period of “searching” for the deceased, may be adaptive (Bowlby, 1980). In contrast, at 6 months after the loss, CB expressions linked to an inability to relinquish the goal of reestablishing proximity (e.g., excessive use of the deceased possessions for comfort) are associated with more severe grief symptoms and distress (Field, Nichols, Holen, & Horowitz, 1999). Empirical literature suggests that the role of CBs in bereavement is complex; whether maintaining a connection with a deceased loved one is adaptive appears to depend on whether a bereaved individual can gain feelings of comfort and support from their CB with the deceased (Field & Filanosky, 2009). Future research is needed to identify just how the reward system may be involved in individuals’ utilization of CBs, and how CBs may help or hinder the reorganization process.

How Might Attachment Orientations Moderate Responses to Loss?

Given that the purpose of the attachment system is to regulate feelings of felt security (synonymous with physiological homeostasis), individuals may implement anxious and avoidant responses in an attempt to maintain homeostasis. The two orthogonal dimensions of attachment insecurity, anxiety and avoidance, describe how individuals regularly monitor and perceive their experiences in close relationships (Bartholomew & Horowitz, 1991; Fraley & Shaver, 2000). Attachment anxiety is characterized by fears of abandonment and a heightened response to attachment-related threats. Attachment avoidance is characterized by attempts to inhibit a heightened emotional response to threats to attachment-figure availability. Bowlby (1980) originally proposed that those high in attachment anxiety and/or avoidance would be more prone to poor loss adjustment. Since then, many grief studies indicate that higher levels of attachment anxiety are associated with more grief symptoms (Field & Sundin, 2001; Fraley & Bonnano, 2004; Meier, Carr, Currier, & Neimeyer, 2013; Van Doorn, Kasl, Beery, Selby Jacobs, & Prigerson, 1998; Waskowic & Chartier, 2003; Wayment & Vierthaler, 2002; Wijngaards-de Meij et al., 2007). Those high in attachment anxiety are, by definition, more likely to seek and respond to loss by “clinging.” According to Stroebe, Schut, and Stroebe’s (2005) dual process model, those high in attachment anxiety are more likely to become fixated on the loss compared with those who are low on attachment anxiety. In turn, this may result in prolonged grief symptoms. It is possible that prolonged grief symptoms reflect greater activation of the SEEKING system, which is characteristic of those who are high in attachment anxiety. Further empirical evidence is needed in this area of inquiry.

The role of attachment avoidance in response to bereavement remains less clear (Bonanno, Keltner, Holen, & Horowitz, 1995; Fraley & Shaver, 1999). The lack of consistent findings for attachment avoidance may be partially due to individual differences in avoidant individuals’ expectations of interpersonal relationship reward. In a recent series of studies, those high in attachment avoidance expected less social connection when there was the potential for intimacy compared with those low in attachment avoidance (Spielmann, Maxwell, MacDonald, & Baratta, 2013). Lower expectations for reward may protect against the vulnerability of lost reward (i.e., a lost primary attachment figure). Also, these

individuals may be less likely to continue seeking their lost partner during the grieving process, which may protect them from complications in the grieving process.

The strategies highly avoidant individuals employ may be highly effective in the context of bereavement for those who have the self-regulatory strength to effectively utilize these strategies but not for those who are unable to utilize these strategies. The association between attachment avoidance and poor loss adjustment appears to depend on an individual's respiratory sinus arrhythmia (RSA; a physiological index of self-regulation; Fagundes, Diamond, & Allen, 2012; Sbarra & Borelli, 2013). There are now multiple studies demonstrating that the association between attachment avoidance and poor loss adjustment is positive for those who have low RSA (indicating less self-regulatory strength), but negative for those who have high RSA (indicating greater regulatory strength). Thus, it is possible that an avoidantly attached individual's ability to resist reward (i.e., high regulatory strength) may prevent an individual from continuing to seek a lost attachment figure, which in turn, facilitates adjustment (Ingjaldsson, Laberg, & Thayer, 2003).

Does Genetic Risk Affect Responses to Loss?

Individuals with certain genetic polymorphisms may be more prone to maladaptive patterns of SEEKING. For instance, possessing the G variant of the *OPRM1* gene (i.e., the *A118G* allele) is related to an increase in social affiliation as well as a neurobiological reward (Troisi et al., 2011; Way, Taylor, & Eisenberger, 2009). Genetic variations should be considered as possible factors influencing the recovery trajectory after a social loss. However, the current evidence linking the *OPRM1* gene to social loss may not directly translate to bereavement-related outcomes, as the majority of previous studies involved manipulations of overt social rejection, which may reflect the introduction of a negative stimulus, rather than withdrawal of a reward. In addition, many of these studies investigated a single gene (e.g., *MAO-A*, Kersting et al., 2007), which has limitations compared to the genome-wide association (GWAS) approach. In addition, there has been increased interest in combining multiple genetic markers into a single score for predicting disease risk. These polygenetic risk scores are proving to have more predictive power than individual single nucleotide polymorphisms (SNPs) alone (e.g., Dudbridge, 2013). Researchers interested in genetic risk as a possible moderator of responses to loss may be more successful in designing future studies to investigate polygenetic risk scores rather than looking for significant relationships between social loss variables and single SNPs.

Can the Proposed Model Be Applied to Relationship Dissolution More Broadly?

In addition to the death of an established romantic partner, many facets of the proposed model may also apply to relationship dissolution. For parsimony, we will refer to situations in which relationships end because one or both relationship partners choose to leave the relationship (for reasons other than death) as "relationship dissolution"; this includes divorce and "break-up" scenarios.

In the context of relationship dissolution, the former partner is available for attachment-related behaviors in a way that is impossible for a deceased partner. Thus, there is an opportunity for relationship partners to continue to directly seek each other for attachment-

related functions. Doing so, however, is typically thought to be maladaptive, given that any kind of contact or sexual relationship will likely maintain the attachment. Such maladaptive patterns may reflect attempts to satisfy unmet needs for social reward (Spielmann, MacDonald, & Tackett, 2012). Physical intimacy provides the strongest and fastest conditioning of physiological rewards, and oxytocin released during sexual behavior may reinforce social bonds between partners (Carter & Altemus, 1997). However, recent empirical findings suggest that pursuing and engaging in sex with an ex-partner may not be associated with breakup recovery after all (Spielmann, Joel, & Impett, 2018). People who still desired to utilize their ex-partner as an attachment figure 1 month after a breakup reported less improved emotional adjustment compared with individuals who exhibited less desire (Fagundes, 2012). People who did not choose to terminate their relationship reported less emotional adjustment immediately after the breakup, and this association was mediated by their greater desire to utilize their ex-partner as an attachment figure (Fagundes, 2012). Future research should elucidate which relationship characteristics (e.g., duration of the relationship, former relationship status: “casual” vs. “serious” dating partner) may determine whether seeking an ex-partner affects recovery.

Attachment orientations may also influence adjustment after relationship dissolution. Those who recently experienced the dissolution of a romantic relationship and were high in attachment anxiety exhibited lower levels of initial emotional adjustment compared with those low in attachment anxiety (Fagundes, 2012). In contrast, avoidance was not associated with post-breakup emotional adjustment. Furthermore, people who reported high levels of rumination about the breakup reported worse initial emotional adjustment compared with people who reported low levels of rumination about the breakup, particularly if they were high in attachment anxiety (Fagundes, 2012). These findings are in line with our current model which proposes that continued seeking of the lost attachment figure may be maladaptive for adjustment after the loss. Future research should investigate whether these differences can be partially accounted for by individual differences in expectation of rewards, particularly among individuals high in attachment anxiety and avoidance.

The person who terminates a romantic relationship likely starts to reorganize their attachment hierarchy before the relationship ends. Thus, by the time of the breakup, these people may have already started redirecting attachment-related needs away from their ex-partner. This is not likely to be the case for the other partner (the one being “broken up with”), which may be one reason why such people typically exhibit more distress immediately after a breakup and more prolonged distress (Sbarra & Emery, 2005). Based on the very limited empirical data in this area, it appears as though a continued desire for the lost relationship partner may still be important; desired attachment was associated with emotional adjustment after a breakup even after controlling for attachment orientations and terminator status (i.e., whether the individual decided to end the relationship; Fagundes, 2012).

In contrast, having no choice in terminating the relationship (i.e., getting “dumped”) involves not only the withdrawal of a reward but also the introduction of a negative stimulus—relational devaluation or rejection. If a relationship partner has ended the relationship, there is an inherent relational evaluation component that suggests he or she did not regard

their relationship as valuable, important, or close (Leary, 1999). This type of social evaluation is likely to signal social threat detection mechanisms, and elicit “social pain,” the emotional response to a loss, or potential loss of a social connection (MacDonald & Leary, 2005). Thus, when it comes to responses to social loss in the form of rejection by established relationship partners, the loss may be experienced as both a withdrawal of a reward as well as a punishment. Carefully designed studies involving multiple neuro-affective pathways should be conducted to test this possibility.

Conclusion

When an attachment relationship is severed, so is homeostatic maintenance, promoting dysregulation of multiple physiological systems. Sbarra and Hazan (2008) proposed that successful recovery is contingent on adopting a self-regulatory strategy that attenuates the dysregulating effects of the attachment disruption. Expanding upon Sbarra and Hazan’s original model, we suggested that the degree to which an individual’s physiological systems remain dysregulated depends on the state of one’s attachment hierarchy—namely, whether an individual continues to seek a lost partner for support as their main attachment figure. Our model proposes that an individual will go through a series of physiological changes before their attachment hierarchy can be reorganized, which can either help or hinder their recovery. These physiological changes may be influenced by the neurobiology responsible for approach behaviors (i.e., what Panksepp referred to as the “SEEKING” system), as well as separation distress (i.e., stemming from the “PANIC/GRIEF” system), potentially resulting in different patterns of loss outcomes over time. We also considered the role of reward processing, including endogenous opioids, in this recovery process. This model may have implications for interpretation of existing data and facilitation of future investigations.

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Figure 1. Overview of the proposed model.

Note. To recover from the loss of a romantic partner, an individual's attachment hierarchy must be reorganized. Our model proposes that an individual will go through a series of physiological phases (i.e., disorganization, protest, despair) before their attachment hierarchy can be reorganized, which can either help or hinder their recovery. SAM = sympathetic-adrenal-medullary; HPA = hypothalamic pituitary adrenal.

Figure 2. Depiction of three patterns of physiological activation over time after losing a spouse.

Note. Pattern A reflects normative loss recovery, Pattern B reflects a typical depression trajectory in response to loss, with the greatest amount of variability (indicated by the thin dotted line) because of individual differences in depression before the loss of a partner. Pattern C reflects a response to loss complicated by enhanced seeking of the lost partner for rewards, perpetuating a problematic cycle of recurring grief responses. Response phases: *disorganization*, *protest*, and *despair* are listed in the order in which we expect they are most typically experienced. However, these phases likely overlap to some degree, and individuals may oscillate between *protest* and *despair* if they continue seeking their lost partner for attachment-related functions. ANS = autonomic nervous system; SAM = sympathetic-adrenal-medullary; HPA = hypothalamic pituitary adrenal.