

BEREAVEMENT AND THE BRAIN: INVITATION TO A CONVERSATION BETWEEN BEREAVEMENT RESEARCHERS AND NEUROSCIENTISTS

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A recent development by neuroscience is neuroimaging, a method of looking into the “black box” of the brain while people are feeling, doing, and thinking in real time. The first fMRI study of bereavement has recently been published, and the present article summarizes it in non-specialist language, focusing on its theoretical and clinical applications. In an attempt to bridge the gap between bereavement researchers and neuroscientists, the author discusses how these two fields could assist each other in forwarding both fields. Three current debates in the field of bereavement research are outlined, including (a) adaptation in the normal grief process, (b) complicated grief vs. resilience, and (c) meaning-making vs. return-to-baseline models of bereavement. The potential contribution of neuroscientific data to these debates is discussed in several hypothetical examples. These examples stimulate thinking about the reciprocity between 2 questions: What can bereavement teach us about the brain? and What can the brain tell us about bereavement? This article is designed to provide enough background for investigators who are primarily concerned with the brain and those primarily concerned with bereavement to open a dialogue between both of these fields.

The field of psychology, and the field of bereavement research, stands on the brink of a new era. The brain is a nexus between the input of an understanding that a loved one has died and the output of emotion, behavior, and thought. A recent development by neuroscience is neuroimaging, one method to look into the “black box” of the brain while people are feeling, doing, and thinking in real time in a way that has not been possible previously. “In the past few years, there has been an increase in the use of neuropsychological

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populations and functional neuroimaging techniques to more directly connect social and emotional functions with neurocognitive systems and to test new and enduring hypotheses about the nature of social cognition” (Ochsner & Lieberman, 2001, p. 718).

This article is an attempt to bridge the divide in psychology between those who have a background in physiological methodologies and those who have a background in clinical, social, and cognitive theory. This article will provide some background for both fields, and thereby create an invitation to a conversation between bereavement researchers and neuroscientists. It will provide some thought-provoking questions to entice bereavement researchers to think about neuroscience, or the implication of their theories for physiology. Similarly, this article attempts to demonstrate for neuroscientists how bereavement theory is crucial to neuroimaging.

Bereavement researchers and clinicians may have distinct questions and be interested in different aspects of the bereavement–brain connection. While not focusing primarily on the answers to questions that are current in bereavement research, instead it will highlight the debates, and perhaps contribute to how a physiological understanding may help refine the questions.

An fMRI Study of Bereavement

Arguably, the most important new research technology added to the study of socioemotional phenomena is fMRI, which allows researchers to identify the location of task-related brain activity to within a few millimeters in both cortical and subcortical brain structures. . . [fMRI] provide measures of activity in specific areas of the brain that are correlated with the performance of specific tasks, the experience of certain states, or membership in a particular group . . . Experiments using PET and fMRI typically compare brain activation in two different psychological states (e.g., happy vs. sad), during the performance of two different kinds of tasks (e.g., remembering as opposed to passively viewing words) or for members of two different groups (e.g., depressed vs. nondepressed). (Ochsner & Lieberman, 2001, p. 718)

As a hallmark of this new era of bereavement and the brain, the first fMRI study of bereavement was published in the *American Journal of Psychiatry* (Gündel et al., 2003). The present article will summarize the research and orient the reader to its main conclusions. As much as possible, it will “translate” the research into

non-specialist language, and focus on the theoretical and clinical applications of this research.

Participants in the study included eight volunteers who had experienced the death of a first-degree relative in the past year (a group average of 6 months). These included the death of both parents and spouses. All participants were female, right-handed, and native English speakers. Exclusion criteria included Axis I psychiatric disorders (including current depression) and medical disorders. Participants were interviewed regarding the circumstances surrounding the death of their loved one 24 to 72 hours prior to scanning.

Participants provided a photograph of their deceased loved one, in which the loved one was the only figure in the photo. These photos were matched with control photos. Because our brains are constantly active, doing all sorts of tasks, it is necessary in fMRI to use a subtraction paradigm. In this case, the task design subtracted the brain activity resulting from viewing pictures and words in a non-emotional state from the brain activity in the grief state. Therefore, photos of the deceased were matched for gender, age, and environment with the photos of a stranger (control photos). Fifteen key words that had an autobiographical connotation to the death of the loved one were taken from their interview (e.g., collapse, funeral, loss). These 15 keywords were then matched for part of speech, number of letters, and frequency of usage in the English language with 15 neutral words (e.g., announce, ceiling, list).

These photos and words were put together as composites (see Figure 1 for an example). The grief-eliciting paradigm included four conditions. These included picture–word composites of the following: (a) deceased + grief word, (b) stranger + grief word, (c) deceased + neutral word, and (d) stranger + neutral word. Each condition consisted of 15 picture–word composites, with 60 composites total. The composites were presented by scanning them into a computer program and presenting them via goggles worn during the neuroimaging. The goggle surface was blank between composites. The composites were presented continuously and in random order, comparable to a slide show.

Participants' skin conductance responses to each slide were measured and the participants rated their subjective grief in response to each slide on a 1–10 scale. The results of these two measures increased the validity that grief had been elicited. In both

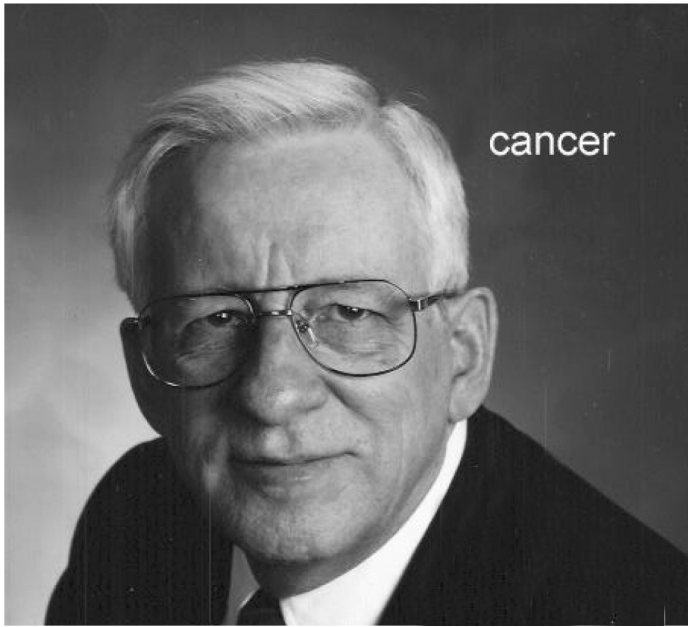


FIGURE 1 A graphical example of a picture-word composite slide for the grief-elicitation paradigm. Note: This example is only one slide, whereas the whole presentation is 60 slides.

the self-report measure of grief and the skin conductance responses, the grief factor (deceased + grief word) was significantly greater than the neutral factor (stranger + neutral word) in analysis of variance (ANOVA) analyses at the $p < .0001$ and $p < .05$ levels, respectively.

Results of the fMRI Study of Bereavement

Supported by studies of deficits due to brain damage, studies of brain stimulation and neuroanatomical tracing studies, current understanding suggests that particular brain functions are localized to specific brain areas (Nolte, 1999). These functions include cognition, emotion, perception, memory, motor, autonomic, and endocrine regulation, among others. However, even the simplest of tasks (e.g., looking at a picture) requires many small component brain functions and consequently many areas are activated across the brain in distributed networks, which helps to explain why

many brain areas are activated in neuroimaging studies. Thus, while neuroimaging results in localized brain regions, most researchers place these in the context that these regions are a part of a large, connectionist network (for a review, see Page, 2000). In this study, the task included bereaved participants looking at a picture of their deceased relative (or a stranger) with a caption from their narrative of the death event (or a neutral word). The functions in this grief response included affect processing, mentalizing, episodic memory retrieval, processing of familiar faces, visual imagery, autonomic regulation, and the modulation and coordination of these functions.

The resulting maps of the brain show colored areas representing statistically significant levels of activation. There are several steps to determine the statistical significance. First, the areas are present at a certain level of significance after the subtraction of the control task activation. Second, the areas are called 'clusters,' and they represent the likelihood that one millimeter square area (or voxel) is active while controlling statistically for multiple comparisons across all the other possible activations in the brain. Finally, the clusters are at least 10 voxels wide, meaning that 10 voxels had to meet the above criteria and that all were contiguous. Investigators can set the level of significance.

Three brain regions were activated by the picture (brain activity in response to the deceased minus the stranger) and the words (brain activity in response to the grief-related word minus the neutral word): the posterior cingulate cortex, medial/superior frontal cortex, and cerebellum. The pictures also resulted in distinct activity in the cuneus, superior lingual cortex, insula, dorsal anterior cingulate cortex, inferior temporal cortex, and fusiform gyrus. The words also resulted in distinct activity in the precuneus, precentral cortex, midbrain, and cerebellar vermis.

Given that the fMRI results in a network of many areas, this article will highlight the functions of just a few of the areas that resulted from the grief-eliciting paradigm. First, an area that was strongly activated was the posterior cingulate cortex. This is an area that is activated during autobiographical memories (Maddock et al., 2001), and it is likely that those memories were being recalled during viewing. In fact, neuronal damage in this area is associated with the loss of memory for personal events, such as in Alzheimer's disease (Reiman et al., 1996). In addition to memory,

this area is activated by emotionally salient stimuli. In studies of panic disorder, this area is activated by threat-related words (Maddock et al., 2003). In contrast, several studies have found lower activity in this area in depression, instead of higher activity as in the present study (Mayberg et al., 1999). This may contribute to a hypothesis that normal grief shares more similarities with (separation) anxiety than depression. In summary, the posterior cingulate cortex was activated during the grief elicitation, most likely due to its role in the interaction between memory and emotion.

Neuroimaging has contributed data that grief demands attentional resources directed inward toward the body. This is reflected in phrases such as “a broken heart” or “pangs of grief.” The painful nature of social loss appears to have a somatic component. The above study demonstrated that another set of areas were activated, the anterior cingulate cortex (ACC) and the insula. The anterior cingulate cortex is thought to play an important role in attention (Posner & Driver, 1992). The insula contains a topographical map of the body and is specialized in processing visceromotor information (Augustine, 1996). These areas are often activated together, perhaps in the role of attention to the bodily state (Craig, 2003). In reflecting on how the participants felt as they viewed the pictures, attention to their bodily state seems likely. It is also interesting to note that in a later study of social exclusion, where participants in the scanner believed that they were being excluded from a game by other participants, these same two areas were also activated (Eisenberger et al., 2003). The painful nature of social loss, through death or exclusion, seems to require attentional resources and has a somatic component. Many bereaved individuals remark on the somatic symptoms they experience (Bonanno et al., 1995), and perhaps future research will explore whether this has a neural basis.

Two additional studies are similar in their neuroimaging tasks. Studies of maternal and romantic love (Bartels & Zeki, 2000, 2004) used pictures of their own children or current romantic partner as compared to another known child or a non-romantic friend, and a stranger. These studies also found activation in the ACC and insula, supporting the idea that they play a role in social and emotive processing. Finally, another relevant study investigated the feeling of grief after the break-up of a romantic relationship (Najib et al., 2004). Although the task was different in this case (participants

were instructed to think about their partner vs. another known person without pictures or words), many of the brain regions activated were the same. For example, posterior cingulate activity was present in both. Areas also found in both studies included activity in the cerebellum, pons, cuneus, superior lingual gyrus, precuneus, and fusiform gyrus.

The convergence of several studies into the neuroimaging of attachment relationships is interesting in light of a long history of theorizing regarding the physiological basis of attachment. Bowlby (1980) viewed grief as an expression of the “attachment behavioral system,” evoked to discourage prolonged separation of an individual from a primary attachment figure. Initially used to describe the behavior of children, more recent empirical work has suggested that the effects of disrupted attachment in childhood continues into adulthood and contributes to grief reactions (Silverman et al., 2001).

There are several limitations to the original bereavement neuroimaging study described here. First, the small sample size requires replication and validation of the results. Second, there was not a condition that used a picture of a person known to the participant that was not deceased. This means that brain activation could be attributed to recognition of familiar people rather than necessarily evoked by recognition of the deceased (i.e., grief). However, studies that have investigated familiarity (Maddock et al., 2001) have not shown activity in the anterior cingulate or cerebellum in contrast to the described bereavement study. As these are known to be areas that contribute to emotional processing and modulation, these areas may represent a functional correlate of the intense feeling of grief beyond mere familiarity with the person. Third, some of the words used to elicit grief (i.e., collapse) could be conflated with words that would elicit threat. However, because the words were drawn directly from the narrative of the participant, these do represent an aspect of the death event for the individual, which may include some feelings of threat or anxiety. Future studies could place these words in separate conditions so as to evaluate whether they activate different brain regions.

Applications of Neuroscience to Bereavement Research

The next three sections will outline three current debates in the bereavement literature. These debates arise in part because different

theoretical models of the bereavement process produce different hypotheses (Bonanno & Kaltman, 1999; Stroebe et al., 2001). Neuroscience is one tool, among others, that we can use to test these hypotheses and contribute data to these debates. Beyond the pure scientific value of contributing to these debates, there are clinical applications of this neuroscientific perspective. The application to clinicians will be discussed through the rest of the article.

Adaptation in the Normal Grief Process

One debate currently discussed in the bereavement literature is how adaptation occurs in the normal grief process. Understanding the normal process of bereavement is very important and should not be lost as more attention is focused on complicated grief (Stroebe et al., 2001). Understanding complicated grief will be aided by understanding the phenomena of normal grief. Nonetheless, it is vital to distinguish these two groups, as the field seems to be converging on the realization that they are distinct (Hartz, 1986; Horowitz et al., 1997; Jacobs, 1993; Prigerson & Jacobs, 2001; Rando, 1993).

The data from the above fMRI study was a snapshot of what normal bereaved individuals look like at one point in time. However, the idea of adaptation, or the idea of a bereavement process, necessarily requires more than one point in time. The question arises, where in the bereavement process were these individuals who were scanned? That information was not documented in the prior study and consequently is an important topic for future research. One method of studying the change in brain activity through the bereavement process would be to scan individuals several times (e.g., two or more) during their adaptation. If the task in the scanner was the same for each scan, the brain activity could be compared and any changes in brain activity determined.

One might ask, what is the value in knowing how brain activity changes across the bereavement process? Some hypotheses as to what changes may occur, and the theoretical importance of these changes, may be a helpful thought experiment. For example, in the very earliest period of bereavement, one might see amygdala activity that is not seen later in the process. The amygdala is known to be active when there is a fear response by the individual to a stimulus in the environment (among other roles

the amygdala plays; LeDoux, 1996). It is also known to operate largely outside of conscious awareness. This is because the neural pathway from the eyes to the amygdala is much faster than from the eyes to areas known to be involved in conscious processing. If it were the case that amygdala activity was present in early bereavement and not in later bereavement, this might suggest that the initial emotional reaction to learning that a loved one has died may operate outside of conscious awareness. Although the individual may be consciously aware of the knowledge that the death has occurred, many of the environmental triggers for the individual's emotional grief response may not be consciously perceived. This may be particularly true if the environmental cues about the death are fear-producing for the individual. For example, the individual may have a strong experience of restlessness without conscious recognition that it is an avoidance response to environmental reminders of the loss. The above fMRI study did not find amygdala activity, but the average time since the death event was 6 months, and this may be too late to elicit amygdala activity in response to pictures of the deceased.

Having done this thought experiment we can discuss a complication in studying the normal grief process. Many bereavement researchers have proposed stage or phase models of bereavement (Bowlby, 1980; Parkes & Weiss, 1983; Zisook, 1987). What is the best way to characterize where a person is in the normal bereavement process? Should we categorize research participants according to stages of adaptation, such as shock, expression, and recovery (Zisook, 1987)? Or is there an incremental adaptation across time, and therefore is using time since death as a continuous variable the most valid way to investigate the process?

Neuroimaging (in addition to other studies) may contribute data to this debate. One method would be to analyze the imaging results categorically according to the participants' bereavement stage, and then analyze the same data by the time since death. Different results from the two analyses may show us that different processes can be seen across the stages that fit with different theoretical understandings of bereavement. Using the above hypothetical example, perhaps amygdala activity operating outside of consciousness is only activated in those participants who are in the shock stage. Clinically, we know that the length of time individuals are in this stage of shock varies widely across individuals

(Clayton, 1990). Thus, individuals may not be able to consciously process their grief until this amygdala activity decreases. This observation would support one theory (stage models) and not support the other (chronological adaptation). As a single piece of data, this would not prove or disprove the theories, but would advance our understanding of grief phenomena. This purely hypothetical experiment and results demonstrate one advantage of neuroimaging applications to bereavement research.

Our neuroscientific knowledge of which areas of brain activity are available to conscious processing (very broadly speaking, cortical areas) and which are not available to conscious processing (very broadly speaking, subcortical areas) may also help with another debate in the current literature regarding the normal process of adaptation in bereavement. Some have observed that bereaved individuals need to do “grief work” in order to adapt successfully (Worden, 2002). Others have provided some empirical data that “grief work” as originally conceptualized may not be necessary (for a review of this debate, see Bonnano et al., 2002, and Wortman & Silver, 1989).

It is possible that correlates of the phenomena of grief work could be observed through brain imaging. One possibility (while clearly oversimplified) is that the emotional and cognitive processes correlated with grief work might be subconscious. In this case, one might imagine that there are subcortical changes that occur, such that across time subcortical structures are less active in response to environmental cues of the deceased. It may be the case that some individuals have a pattern of brain activity that shows both subcortical and cortical activations, and thereby includes conscious emotional and cognitive processing. Other individuals, who might adapt equally well, may not have this subcortical and cortical (and conscious) processing. Thus, neuroscientific evidence could hypothetically show that there is a process of “grief work” in the change across time in subcortical brain activation, but that it may not need to be conscious in all individuals in order for them to adapt successfully.

Complicated Grief vs. Resilience

Another important and current debate in the field of bereavement research is whether complicated grief should be included as a

separate clinical disorder in the DSM-V. Prominent bereavement researchers argue in favor of diagnostic status for complicated grief (Hartz, 1986; Horowitz et al., 1997; Jacobs, 1993; Prigerson & Jacobs, 2001; Rando, 1993). Stroebe et al., (2001) review of the literature suggests that complicated grief has been consistently documented, even if somewhat different criteria have been used. A growing literature demonstrates the distinction between complicated and normal grief and its relationship to other disorders, such as depression and PTSD (Boelen et al., 2003; Latham & Prigerson, 2004; Lichtenthal et al., 2004; Prigerson & Jacobs, 2001; Silverman et al., 2000; Swarte et al., 2003).

Neuroimaging can provide one kind of validity for this distinction, by assessing whether there are discriminant physiological substrates of normal and complicated grief. This comparison could be done by scanning those who are diagnosed with complicated grief by a clinician with a standardized interview (Prigerson & Jacobs, 2001) with those who do not meet these criteria. These two groups can be presented with the same set of grief-eliciting stimuli. These stimuli may include playing a recording of the narrative that the participant has previously provided through earphones, or presenting photos of the deceased on a screen in the scanner. These grief-eliciting stimuli would need to be matched with neutral stimuli, such as the recording of a neutral event told by the participant, or pictures of a stranger. The resulting brain activation patterns could be compared between the two groups. Different areas of activation would provide some data that those with complicated grief tend to process the same grief-eliciting stimuli differently in the brain than those who do not meet criteria for complicated grief.

Secondly, neuroimaging can contribute data to how complicated grief is related to other psychiatric disorders. Neuroimaging has been done in conditions of depression and anxiety (including PTSD), and replicable findings have emerged. For example, the dorsolateral part of an area called the prefrontal cortex in depressed individuals frequently shows decreased activation (Drevets & Wayne, 1998). The dorsal part of the anterior cingulate cortex (ACC) also often shows decreased activation in depressed individuals (Beauregard et al., 1998; Mayberg et al., 1994). Interestingly these areas often show increased activity following treatment (prefrontal cortex: Kennedy et al., 2001; ACC: Buchsbaum et al., 1997, and Mayberg et al., 2000). These are just two areas that are

probably a part of a large network that underlies depressive symptoms (Davidson et al., 2002). To the degree that complicated grief shows decreased activation in these two areas, depressive symptoms and symptoms of complicated grief may have similar neural mechanisms.

Post-traumatic stress disorder (PTSD) is also associated with replicable findings in brain activity. Some tasks in the scanner are designed to examine the processing style of a particular group, such as those with PTSD who are hypervigilant to environmental cues. One way that has been used to measure this processing style is to measure the reaction to visual cues (e.g., such as fearful faces) that are presented too fast to be consciously recognized, and then quickly following them with a different visual picture that “masks” what was previously seen. In those with PTSD, in contrast to control participants, the amygdala showed much higher levels of activity to this task (Rauch et al., 2000). Because we know that the amygdala responds to fear-related cues, and operates below the level of consciousness, it is interesting that those with PTSD who are hypervigilant have greater responses in this area. A similar study could be done in bereaved versus control participants. The processing of environmental cues is relevant clinically in bereavement as well, as many bereaved individuals experience intrusive thoughts related to the deceased that may be cued subconsciously by the environment (Horowitz et al., 1997). Greater amygdala activity to these subliminally presented visual cues in participants with complicated grief might suggest that one aspect of complicated grief is similar to PTSD.

Another region of the brain that is consistently activated in PTSD is the posterior cingulate cortex (PCC; Bremner et al., 1999). To the degree that those with complicated grief show increased activation in this area, symptoms of PTSD and symptoms of complicated grief may have similar neural mechanisms. The clinical finding that exposure therapy has been useful for complicated grief (Shear et al., 2001) when other therapies are not very effective (Jordan & Neimeyer, 2003) would dovetail nicely if a similarity in brain activity between PTSD and complicated grief were found. Neuroimaging can add data to existing clinical and bereavement research regarding the similarities and differences in physiological substrates between complicated grief, depression, and PTSD.

Meaning-Making vs. Return-to-Baseline Models of Bereavement

Our traditional understanding is that bereavement is a psychological injury, and, like a physical injury, individuals will return to baseline functioning following a period of time. An alternative theory is based on a learning model, suggesting that those who experience the death of a loved one may gain knowledge that allows them to function differently than they had prior to the death (see O'Connor, 2002, for a review). This has come to be known as stress-related growth (see Park et al., 1996, for a review). Many researchers interested in positive emotion have focused on the idea that the resolution of negative emotion may or may not co-occur with positive emotion.

One way to design a neuroimaging study for stress-related growth is to scan currently bereaved individuals who have experienced multiple deaths versus those who have not previously experienced a death. A hypothetical result is less global brain activity in those with multiple death experiences or higher stress-related growth, as the participant may not need as many resources to process the current death. This could be contrasted with the return-to-baseline hypothesis, which might predict that those with resolved grief would not process the death-related stimuli differently than those who had not yet experienced a death.

Significant losses pose a threat to the autobiographical narrative of the individual, as well as the social construction of the individual's new identity (Neimeyer, 2005). The manner in which meaning of the loss is constructed allows the event to be accommodated into the individual's narrative. This process of accommodation is based upon a learning model of bereavement, whereby the individual reconstructs the narrative of his or her life following the disorganization caused by the death event. Another way to investigate a learning model of bereavement would be to use the Stress-Related Growth Scale (SRG; Park et al., 1996). Among a bereaved sample, those who score high on the scale could be compared with those who score low on the scale. Neuroimaging findings might include brain regions (e.g., lateral prefrontal cortex) that are known to be important to cognitive flexibility or emotional regulation (Ochsner et al., 2004; van Veen & Carter, in press).

Conclusion

Bereavement researchers bring to any collaboration a unique ability to invent tasks that bereaved individuals could perform in the scanner, and to understand different bereavement subgroups. Bereavement researchers are most familiar with the phenomena of grief. Bereavement researchers are equipped with the theories that allow us to parse grief into meaningful categories. Neuroscience must be careful in testing psychological theories not to downplay subjective mental experience in favor of externally observable brain metabolic processes. Bereavement researchers are more familiar with the first-person, experiential phenomena than neuroscientists.

Therefore bereavement researchers can contribute ideas about what tasks would elicit grief reactions (of different types) in the scanner, or which are the relevant groups to test. Neuroscientists who are not as familiar with the phenomena of grief would not create the same tasks, or choose the same participant groups, and thus the data that they produce without input of bereavement researchers may not be helpful in advancing and testing the theories that will move the bereavement field forward. By the same token, bereavement researchers may not have the background in neuroscience to interpret the results in light of current knowledge of brain functioning. It is my hope that this article will provide a starting point for these conversations.

What the brain can tell us about bereavement will undoubtedly improve our ability to identify the grief process, treat the complications, and generalize about loss. Brain function may clarify many aspects of bereavement. Exploring how functional neuroimaging and physiology could be used to investigate bereavement and attempting to design research studies using neuroscience refines the concepts and questions in bereavement research.

In addition, neuroscience would be improved with the addition of bereavement research. Bereavement research, as demonstrated here, suggests when, how and with whom to do neuroimaging research. Many decades of bereavement research have demonstrated that those with a complicated grief process are different than those with a resilient grief process. Therefore, it is vital for neuroscience to question how these two groups may differ physiologically. Bereavement research has also shown us that both the

length of time since a death and the stage of the grief process are important variables. Neuroscience must account for these descriptive variables when investigating bereaved individuals, and also tackle how these two measurements of the bereavement process affect neural function. Clinicians have developed a wealth of methods to access the core issues or “hot” emotions in bereaved clients. These techniques may be applied to the scanner to make the tasks done during neuroimaging more valid.

The reciprocity between investigators who are primarily concerned with the brain and those primarily concerned with bereavement may open up a dialogue benefiting both. It is extremely rare that one investigator can be broadly and deeply knowledgeable in many areas, especially areas as diverse as bereavement research and neuroscience. It is important for these researchers to be very deeply knowledgeable in their own area, and yet be willing and able to engage in conversations with other investigators. It is a collaborative team of investigators that engages in conversation with each other that will allow the neuroscience of bereavement to move forward.

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