The Neuroscience of Empathy, Compassion, and Self-Compassion

Edited by **Larry Stevens and C. Chad Woodruff**

CHAPTER

8

Can We Change Our Mind About Caring for Others? The Neuroscience of Systematic Compassion Training

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INTRODUCTION AND SCOPE OF THE REVIEW

The emerging field of applied contemplative science (Desbordes & Negi, 2013; Farb, 2014; Giorgino, 2015; Wallace, 2007, 2012) is in large measure concerned with empirically investigating how specific mental states and traits can be made stronger, more consistent, and resilient. In this chapter, we present a review of the scientific literature on the changes in brain activation associated with systematic training in compassion, including the seminal work of Richard Davidson and colleagues on the neurobiological correlates of long-term systematic compassion training in highly experienced contemplative practitioners. We also review the programs of research conducted at Stanford and Emory Universities, both of which have developed and evaluated the efficacy of their manualized and secularized compassion training programs. Additionally, we describe the work of Tania Singer and her colleagues at the Max Planck Institute as well as the new intervention (PEACE) developed at Northern Arizona University.

Finally, we also provide an integrative summary of the current neuroscientific findings on systematic compassion training. The summary and synthesis of these complex findings is presented in a series of figures, including two particularly detailed brain maps, which allow for the graphic condensation of current research findings in a clear and compelling way while simultaneously maintaining a respect for the complexity

The Neuroscience of Empathy, Compassion, and Self-Compassion. http://dx.doi.org/10.1016/B978-0-12-809837-0.00008-8

of these outcomes. These brain maps graphically capture the principal findings of our review—that research outcomes investigating compassion training consistently show correlations with activity in a matrix of brain areas that extend from the frontal/prefrontal area posteriorly to the temporoparietal junction (TPJ) and that incorporate multiple cortical (e.g., dorsolateral prefrontal cortex (dlPFC), inferior frontal gyrus (IFG), medial orbital frontal cortex (mOFC), temporal gyrus, superior temporal sulcus (STS), and TPJ), embedded (e.g., insula and amygdala [Amyg]), subcortical (e.g., nucleus accumbens [NAcc], striatum, and ventral tegmental area [VTA]), and midline (e.g., medial anterior cingulate cortex [mACC], pregenualanterior cingulate cortex [pACC], and dorsomedial prefrontal cortex [dmPFC]) structures in a pattern that is visible in both EEG and fMRI studies.

Questions to Consider

Evaluation of compassion training efficacy must consider the questions below, offered here as a heuristic framework for this compelling and rapidly burgeoning body of research. They are very similar to the types of questions that have very effectively guided the multi-decade research on psychotherapy processes and outcomes. At this stage in the development of research on compassion training, many of the following questions remain unanswered:

- Can systematic compassion training reliably result in specific neurobiological changes?
- Is it reasonable to assume that these neurobiological changes reliably associate with predictable changes in cognition, emotion, behavior, and/or perception?
- To what degree might these neurobiological and/or psychological changes be influenced by the specific technique employed, by the length and intensity of the practice (i.e., the "dosage" of the training), by specific characteristics of individuals undertaking compassion training (e.g., devoted long-term Buddhist practitioners as compared to novices with no particular interest in Buddhism, religion, or spirituality), and/or by the experience and skillfulness of the compassion training teacher?
- Is it reasonable to assume that any neurobiological and/or psychological changes are the direct result of the putative "active ingredients" (e.g., the cultivation of self-compassion) of the compassion training technique? Or, might the neurobiological correlates/sequelae be the result of more general "non-specific" factors such as belief in the efficacy of the technique, general learning, and/or changes in attentional focus?

- Are there distinct neurobiological sequelae/correlates of specific components of training (e.g., does training in empathy vs. training in compassion have different effects)?
- Of what specific practical/clinical/training value is there to knowing the neurobiological correlates/sequelae to compassion training and/or the specific and putatively unique components of compassion training?

Answers to these questions ideally can be addressed through a "transdisciplinary study of contemplative practices" (Dunne, 2016). Development of the CBCT and CCT models of secular compassion training provide excellent vehicles for such an approach. The training manuals for each of these programs were developed and written by geshes. A *geshe* holds a doctoral degree in Tibetan Buddhism and requires approximately 20 years to complete. There is a great deal of complexity involved in understanding the very significant differences in compassion training techniques and how these differences might affect the psychological and/or neurobiological (as well as spiritual) outcomes. Each of these programs of research also integrates varied levels of neuroscience expertise. Similarly, the research conducted by Richard Davidson as well as Tania Singer and collaborators has been done in conjunction with experts in contemplative practice as well as those with neuroscience expertise. In preparing this chapter, we have attempted to emulate this approach by bringing together a neuroscience teacher and researcher (Ahern), a clinical psychologist with approximately 20 years of intensive study and practice of a range of contemplative techniques (Pruzinsky), and an advanced student in Behavioral Neuroscience who has conducted research in this area as well (Calderon).

Compassion Training Techniques Reviewed

Table 8.1 provides an overview of the compassion training techniques discussed in this chapter. To more clearly address the question "Does compassion training reliably result in psychological and/or neurobiological changes?" it is essential to understand distinctions among the training programs. The table encapsulates many of the key similarities and differences among contemporary compassion training strategies.

For example, the highly experienced meditators described in the papers by Lutz et al. (2004, 2008, 2009) and Weng et al. (2013) utilized a form of compassion training that is embedded in the Tibetan Buddhist tradition. For many, if not most, highly experienced meditators, the religious/spiritual context is central to the compassion training process and directly influences the motivation to devote tens of thousands of hours to compassion meditation practice. In contrast, CBCT and CCT

TABLE 8.1 Compassion Meditation Techniques

Type of Training	Origins and Development of the Technique	Training Protocol Brief Description	Standard Amount of Training ("Dose")	Representative Publications
Highly Experienced Meditators (HEMs)	For HEMs, training is highly individualized and part of an ongoing teacher–student relationship. HEMs are committed to the tradition and also subscribe to Tibetan Buddhist worldview and values	HEMs trained by highly accomplished teachers including training in 'wisdom-based' practices (e.g., a deeply practiced form of mindfulness) intended to reduce the probability of being personally distressed by negative emotions associated with compassion training (see Lutz et al., 2008a, b)	Highly intensive training ranging from 10,000–50,000 h of meditative experience in the context of long-term study and/or meditation retreat contexts	Lutz et al. (2004, 2008 a,b, 2009 a,b); Weng et al. (2013)
Cognitively-Based Compassion Training (CBCT)	Developed at Emory University by Geshe Negi Lobsang and colleagues based on the Tibetan Buddhist Lojong (Mind Training) tradition	CBCT is taught in a sequence of 6 weeks addressing specific components which are described in Pace et al. (2009)	6 weeks of training, twice weekly for 1 h with at-home meditation practice	Mascaro et al. (2012, 2013, 2016); Pace et al. (2009, 2010, 2013); Reddy et al. (2013)
Compassion Cultivation Training (CCT)	Developed at Stanford University by Geshe Thupten Jinpa based on the Tibetan Buddhist Lojong (Mind Training) tradition	CCT is taught in a sequence of 8 weeks addressing specific components described in Jazaieri et al. (2013)	8 weeks of training, once weekly 2 h class with daily compassion-focused meditation practice	Jazaieri et al. (2013, 2014, 2015); Chapin et al. (2014)
Project for Empathy and Compassion Education (PEACE)	Developed by Lisa Doskocil at Northern Arizona University in order to engender compassion for others and for oneself, particularly for use in the public school system	PEACE is presented over 6 weeks in which participants are taught compassion, empathy, and self-compassion through lectures and guided practices	Participants meet once a week for 2 h for 6 weeks with daily homework	This is a new compassion training program implemented and tested over a 5-year period with outcome data collected but not yet published

are completely secularized, despite having been directly derived from the same *Lojong* (Mind Training) tradition of Tibetan Buddhism, and these protocols have been developed for individuals with no background and/or interest in Tibetan Buddhist epistemology, cosmology, ontology, or psychology.

COMPASSION TRAINING PROGRAMS

Cognitively-Based Compassion Training (CBCT)

CBCT was created by Geshe Lobsang Tenzin Negi and colleagues at Emory University. The CBCT definition of compassion includes five separate and distinct components: (1) *cognitive* (recognizing suffering in oneself or another); (2) *affective* (a sense of concern or affection for the other); (3) *aspirational or motivational* (the wish to relieve the suffering of the other); (4) *attentional* (the degree of immersion and focus); and (5) *behavioral* (the compassionate response; an action that stems from compassion) (Dodson-Lavelle, Ozawa-de Silva, Negi, & Raison, 2015). As noted above, while CBCT is based on the Lojong (Mind Training) tradition of Tibetan Buddhism, it is entirely secular in its presentation.

The initial studies of CBCT focused on whether or not CBCT would improve psychosocial functioning among adolescents in foster care (Reddy et al., 2013). These researchers found that CBCT, despite the lack of significant between-groups differences, was helpful to some of the adolescents in this pilot study. For instance, CBCT practice sessions were correlated with reduced C-reactive protein (an immune marker associated with stress) (Pace et al., 2013). In addition, CBCT has also been found to decrease loneliness and depression when compared to a control condition (Mascaro, Kelley, Darcher, Negi, Worthman, Miller, & Raison, 2016).

Pace et al. (2009, 2010) observed significant correlations between amount of meditation practice and immune and behavioral responses to psychosocial stress for adults who engaged in CBCT but not for normal controls. The study showed that compassion meditation is an effective method to learn how to cope with social stress and the individuals who practiced this specific type of meditation had lower cortisol levels.

Compassion Cultivation Training (CCT)

Geshe Thupten Jinpa, in collaboration with researchers at Stanford University and the Center for Compassion and Altruism Research and Education (CCARE), has created a compassion intervention program called CCT. Similar to CBCT, CCT is a manualized and secularized approach to compassion training that derives from the Tibetan Buddhist

Lojong (Mind Training) tradition. CCT follows a structured protocol that consists of a 2-h introductory orientation, 9 (once-weekly) 2-h classes, and daily compassion-focused meditation practice. Each class includes: (1) pedagogical instruction with active group discussion, (2) a guided group meditation, (3) interactive practical exercises related to the specific step of the week, and (4) exercises designed to prime feelings of openheartedness or connection to others, either through reading poetry or through reflecting on inspiring stories (Jazaieri et al., 2013).

The first published study evaluating the efficacy of CCT in a randomized-control trial found that compassion training led to increases in compassion felt for others, compassion offered from others, and compassion for the self, and that the amount of meditation practice was related to increased compassion for others (i.e., a dose–response effect) (Jazaieri et al., 2013). Another paper by Jazaieri et al. (2014), using the same sample as the 2013 study, reported increases in mindfulness and well-being in addition to improvements in mood (e.g., worry) and emotional suppression. Experienced meditators had significantly better outcomes than inexperienced meditators on measures of worry and emotional suppression (Jazaieri et al., 2014). Furthermore, a third clinical study also found that individuals had a reduction in pain severity and anger and increased pain acceptance after participating in CCT (Chapin et al., 2014).

Project for Empathy and Compassion Education (PEACE)

In 2012, a new compassion training program called "Project for Empathy and Compassion Education (PEACE)" was developed by Lisa Doskocil at Northern Arizona University. The goal of PEACE is to create educational opportunities for communities to learn about compassion and empathy and to intentionally foster and strengthen compassionate interactions in our daily lives, particularly in the public schools. PEACE is a 6-week course on compassion during which participants meet for training once-a-week for 2 h where they attend lectures and discussions on compassion, empathy, and positive psychology. Toward the end of each session, the instructor leads guided compassion-related practices (30–60 min) which vary from week to week. These activities include yoga, compassionate role-playing, Metta meditation, mindfulness meditation, and compassionate communicating. Outside of class, participants complete a community volunteer assignment and weekly homework tasks, including readings from the scholarly literature on compassion and empathy as well as applying meditation and behavioral practices to one's life (e.g., Tonglen meditation, Vipassana meditation, exploring Non-Violent Communication, doing one positive thing for oneself each day, and engaging in one mindful daily routine). Psychosocial and neuroscience investigations of the effects of PEACE are underway and are anticipated to be published over the coming year.

Highly Experienced Meditators

Highly experienced meditators represent a unique research cohort for neuroscience investigations as they offer quasi-experimental longitudinal investigations of the effects of long-term meditation practice, sometimes relative to no-treatment or brief-practice controls. From a contemplative science perspective, the kinds of meditation that these highly experienced meditators engage in require: (1) highly focused attention; (2) sustained over long periods of time; (3) the steady deepening of concentration over time; (4) mindful development of metacognitive awareness; and (5) an acute awareness of the suffering of all living beings. These meditation techniques also often involve quite elaborate visualization practices, further adding to the complexity of the cognitive processing which is occurring. Convenience samples of such long-term meditators have been made available through the benevolence and scientific interest of His Holiness, The Dalai Lama, as well as through unique community samples. Results of those studies are reviewed below.

THE NEUROSCIENCE OF SYSTEMATIC COMPASSION TRAINING

Highly Experienced Meditators Exhibit Distinct Patterns of Brain Activity

In a 128-channel EEG investigation, Lutz et al. (2004) found that highly trained Buddhist monks (with 10,000–50,000 h of meditation practice) were able to induce synchronized, high frequency and relatively high-amplitude gamma band oscillations (25–42 Hz) during meditation. These differences were most pronounced in the frontal and parietal/temporal lobe regions of the brain (Fig. 8.1). Gamma activity has been shown to be associated with hyperfocused attention and "neural binding", that is, the rapid integration of information across multiple sensory domains (Opitz, 2010). Historically, gamma wave band oscillations have often been overlooked due to their similarity to high-frequency muscle activity. However, their presentation in the Lutz et al., study following careful editing and control of muscle artifacts in these seasoned meditators, suggests hyperattention during the integration of complex, multisensory information, perhaps similar to an elevated information processing state.

While Lutz and colleagues' EEG studies revealed distinct gamma activity in medial and lateral frontoparietal electrodes for expert meditators

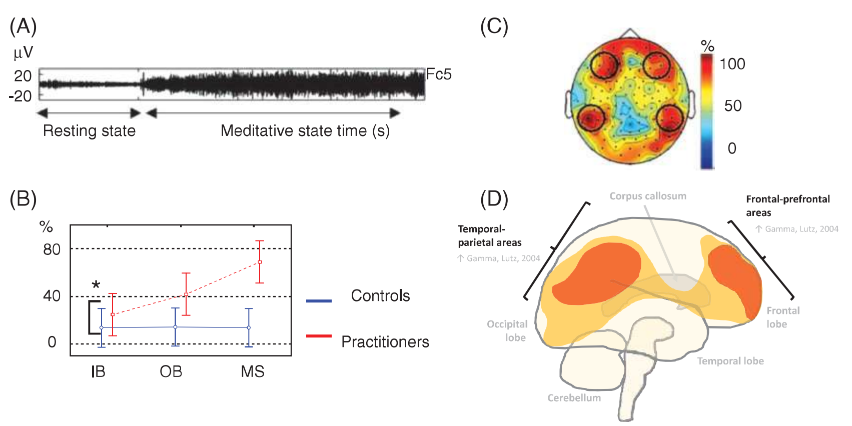

FIGURE 8.1 Adapted from Lutz et al. (2004): (A) depicts the change in EEG brain wave activity of a meditator who has had over 10,000 h of compassion meditation training as he moves from a rest state to a meditative state. The fast, higher-amplitude brain waves are Gamma oscillations. (B) Illustrates that highly experienced meditation practitioners have greater Gamma wave activity at baseline (IB), but they also significantly increase their Gamma activity as they move into a meditative state, whereas novice (Control) meditators do not. (C) With the nose pointing toward the top of the page, this figure shows the approximate locations of the EEG electrodes and areas that showed high levels of Gamma activity in experienced practitioners. (D) This is a graphic depiction of the lateral perspective of the right hemisphere with Red and Orange areas representing the high Gamma wave activity. Note that frontal and temporal-parietal areas show the greatest increase in Gamma wave activity.

(Lutz, Greischar, Rawlings, Ricard, & Davidson, 2004), they did not look for activation of more specific brain areas. In 2010, Engstrom and Soderfelt used fMRI to investigate the neural correlates of compassion meditation in a single experienced meditator and found activity in left medial prefrontal cortex (mPFC) extending to the anterior cingulate gyrus (ACC) (Engström & Söderfeldt, 2010).

Additional studies have added to the constellation of brain areas related to expert meditation and meditation training. For example, one investigation used fMRI to examine how experienced meditators react to emotional stimuli while meditating (Lutz, Brefczynski-Lewis, Johnstone, & Davidson, 2008a). The stimuli were emotionally valenced sounds of human vocalizations, such as a woman screaming or a baby crying. The results showed that experienced meditators exhibited higher Amyg, right TPJ, and right posterior STS (pSTS) activation compared to novices. Furthermore, experts had greater activation in the insula in response to negative sounds than to positive or neutral sounds in comparison to novice meditators. The implication of these outcomes was that, when compared to novice meditators, experts experience more empathy, and empathic arousal, when observing or hearing suffering. The same research group also examined which fMRI-measured brain activity changes were also associated with heart rate (Lutz et al., 2009 a,b). Under compassion meditation conditions, expert meditators exhibited increased heart rates compared to novice meditators and showed increased activity in the Insula and ACC. These outcomes are somewhat paradoxical to the notion that expert meditators would show lower heart rates, decreased activation of midline structures, and less empathic distress when exposed to suffering. However, the authors suggest that, unlike novice meditators, experts have attained through training unique regulatory capabilities (e.g., cultivating equanimity) to allow a deeper experiencing of compassion without undue personal or empathic distress.

In summary, examining the responses of highly experienced meditators reveals several important neuroscientific findings. Prefrontal cortex (PFC) and TPJ cortical regions appear to show enhanced EEG gamma binding activity and increased fMRI blood oxygen-level dependent (BOLD) responses in expert meditators compared to novice meditators when both are engaged in compassion meditation, particularly in response to distressing stimuli (Lutz, Greischar, Perlman, & Davidson, 2009a). fMRI studies have also revealed that a number of midline (e.g., ACC), embedded (e.g., Insula), and subcortical structures (e.g., Amyg) are also activated differentially by experts and novices, and that some of this activity (Insula and ACC) is closely coupled to changes in peripheral state (e.g., heart rate) in response to compassion-inducing stimuli. See Fig. 8.2.

Brief Compassion Training and Neurobiology

Given that the neuroscientific study of meditation is in its infancy, relatively few studies have assessed how experimental manipulation of compassion meditation can alter brain activity. Further, current studies rarely compare different types of training. Taken together, however, the extant literature does reveal a putative network of brain areas and electrophysiological changes affected by compassion training. The use of EEG and fMRI to study expert meditators described above has revealed important changes in the brain wave activity of PFC and TPJ regions as well as increased fMRI BOLD signals in pSTS, ACC, Insula, and Amyg when engaged in compassion meditation in response to distressing stimuli when compared to novices. Many of these same areas have shown altered activity in a number of subsequent studies of much less experienced meditators.

For example, two studies (Desbordes et al., 2012; Mascaro et al., 2013) found that compassion training in novices can apparently induce changes in some of these previously identified brain areas. In the Desbordes et al. (2012) study, participants randomly assigned to Mindful Attention Training (MAT) after 8 weeks of training exhibited significantly decreased Amyg BOLD activity in response to emotional images, even though

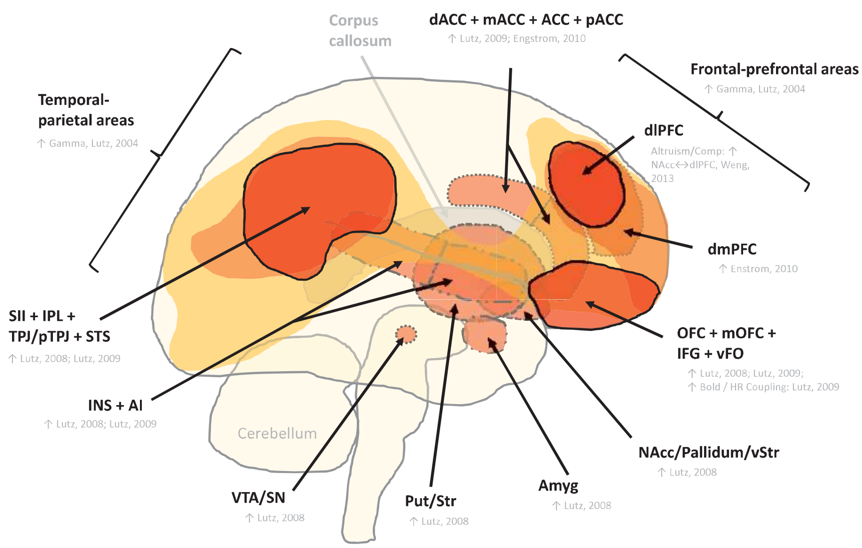

FIGURE 8.2 A graphic depiction/brain map illustrating the approximate location of increased EEG gamma activity in expert practitioners of compassion meditation (*red* and *orange* shading with no lines; compare to Fig. 1D), as well as specific brain areas that show increases in fMRI BOLD signals in expert meditators when compared to baseline or novice trainees. Note the overlap in peak Gamma activity and several cortical (—) areas. Embedded (— · · —), subcortical (– – –), and midline cortical (······) structures also showed increases in fMRI BOLD activity in experts, and the dlPFC and NAcc showed greater coupling (↔). Some changes in brain activity occurred bilaterally, but the most prominent changes occurred in right hemisphere, which are illustrated above. Each area is accompanied by articles that investigated changes in brain activity: First author and year. ***Abbreviations:*** *ACC*, anterior cingulate cortex; *AI*, anterior insula; *mACC*, medial anterior cingulate cortex; *Amyg*, amygdala; *dACC*, dorsal ACC; *dlPFC*, dorsolateral prefrontal cortex; *dmPFC*, dorsomedial PFC; *IFG*, inferior frontal cortex; *IPL*, inferior parietal lobule; *INS*, Insula; *mOFC*, medial orbitofrontal cortex; *NAcc*, nucleus accumbens; *OFC*, orbitofrontal cortex; *pACC*, pregenual ACC; *pSTS*, posterior superior temporal sulcus; *pTPJ*, posterior temporal parietal junction; *SII*, postcentral somatosensory gyrus (Brodman 40); *SN*, substantia nigra; *TPJ*, temporal parietal junction; *VFO*, ventral frontal operculum; *VTA*, ventral tegmental area.

participants were in a non-meditative rest state during the MRI procedure. This decrease was not observed in either the control group or the group engaged in CBCT training. Interestingly, these researchers also saw a trend toward increased Amyg activation in the CBCT group, suggesting that this CBCT tended to increase Amyg activity in response to distressing images. There was also a trend toward a relationship between these Amyg increases and general affective state (i.e., depression score). However, the sample size was small and not gender matched. Therefore, these apparent CBCT-related changes must be interpreted very cautiously.

Similarly, the second study also used fMRI but in this study they assessed how CBCT might alter both empathic accuracy and BOLD signals.

This study too had a small sample size with gender imbalances (N = 21; CBCT = 7 females, 6 males; Control group = 2 females, 6 males), still the results indicated that CBCT could enhance empathic accuracy as well as alter brain function. In particular, CBCT training significantly increased IFG, STS, dmPFC, and anterior paracingulate cortex activity, and these changes correlated with empathic accuracy (Mascaro, Riling, Negi, & Raison, 2013).

There are also data suggesting that the dlPFC, right inferior parietal cortex (IPC), and the NAcc are affected by compassion-related meditation training. Since compassion training encourages meditators to take the perspective of the sufferer, Weng et al. (2013) hypothesized that compassion training would result in increased altruistic behavior along with changes in brain activity. Using a money-distribution game, participants witnessed one player providing an unfair distribution of money to another player. The participant then had a chance to correct the apparent wrong by contributing a sum that had to be matched by the first player. The more money the participant gave, the higher the altruism score. The group that received compassion training was then compared with a control group that had undergone reappraisal training. Not only did the compassion group redistribute more money (greater altruistic behavior) than the reappraisal group but also the compassion-trained participants exhibited greater fMRI BOLD activity in the right IPC and right dlPFC. Moreover, the degree of signal change was significantly correlated with the level of altruistic redistribution.

Two other findings from this study are important to note. First, the authors reported greater "coupling" between the right dlPFC and NAcc. That is, as the activity of one region increased there was a corresponding increase in the other. The degree of coupling was also associated with altruistic behavior. In short, Weng et al. (2013) observed that compassion training appeared to influence an interconnected network of brain areas simultaneously rather than independently.

Second, the reappraisal training altered the BOLD signals and dlPFC-NAcc coupling in the opposite way. Instead of a positive correlation between brain activity and redistribution behavior, there was a negative correlation. This finding suggests that, while the same brain areas might be affected by cognitive/meditative engagement, the type of training significantly influenced the direction of change.

Compassion training seems to induce greater levels of positive affect and approach behavior. Klimecki et al. (2013) investigated the affective and neurobiological consequences of short-term compassion training. Based on the nature of the training and prior research, they predicted that they would see increased activation in the anterior insula and mACC in comparison to baseline and that by empathizing more with individuals in distressing situations, pain network activity would be enhanced, especially in response to high distress stimuli. Given the focus on compassion, they also predicted that brain areas associated with approach, affiliation, and positive affect would show greater activation (Klimecki, Leiberg, Lamm, & Singer, 2013). These researchers found that short-term compassion training induced increased activity in the mOFC, VTA/SN (ventral tegmental/substantia nigra area, both major sources of dopamine), putamen, and pallidum. Interestingly, the most pronounced changes occurred in the right hemisphere, consistent with the above-cited research, where the increases for the novice trainees paralleled those of expert meditators engaging in compassion (Klimecki et al., 2013).

The goals of empathy and compassion training are similar in some ways but distinct in others. Despite their similarity as social emotions, they tend to activate different, and in some important ways, opposing affective and cognitive process. Specifically, empathy training increases empathic concern, perspective taking, and a sharing in the emotions of another (Singer & Lamm, 2009). However, when witnessing another's suffering, participants can experience empathic (personal) distress, marked by negative affect, avoidance behavior, and burnout, particularly if there is insufficient differentiation between the self and the other (Klimecki et al., 2014). Compassion training, on the other hand, involves a sensitivity to the suffering of another but not necessarily a sharing of their emotional experience. Individuals who undergo compassion training may exhibit greater empathy and negative affect, but compassion is also accompanied by positive affect in the anticipation of the alleviation of suffering, as well as approach and helping behaviors (Klimecki, Leiberg, Ricard, & Singer, 2014). This difference between empathy and compassion suggested to Klimecki, Singer, and colleagues that perhaps these different types of training could lead to different patterns of brain activity.

By directly comparing empathy training with compassion training, Klimecki et al. (2014) aimed to tease apart which patterns of brain activity were associated with which type of training. Such distinct patterns of neurological activation might help explain the affective and behavioral outcomes associated with each type of training. On the neural level, short-term empathy training increased fMRI BOLD signals in the Insula (specifically, AI) and Cingulate Cortex (specifically, medial ACC) compared to compassion training and a control group (i.e., participants who received memory training). They also found increased activity in the temporal gyrus, dlPFC, operculum, and parts of basal ganglia (posterior putamen and head of the caudate). Klimecki et al. (2014) noted that this constellation of structures comprises the pain matrix, which becomes activated when experiencing pain or witnessing other people in pain. The increased activity of the dlPFC and middle temporal gyrus may be related to distress management, as both regions are important for emotion and pain regulation. Compassion training, however, resulted in increased fMRI BOLD activity in the mOFC, pregenual ACC (pACC), and striatum, including the ventral striatum-NAcc. As Klimecki et al. noted, these areas have consistently been linked to positive affect, reward, and pleasure, as might be expected to occur from compassion training (Klimecki et al., 2013, 2014). Given that, when compared directly to empathy training, compassion training resulted in less activation of the mACC and Insula and more activation of the mOFC, pACC, and NAcc, the results suggest that different types of meditation training have distinct effects on how the brain responds to distressing stimuli.

Overlapping but Distinct Systems

The survey of how empathy and compassion training relate to brain activity above suggests a number of important conclusions. First, as discussed at the beginning of this chapter, studying experts who have over 10,000 h of compassion training is a valuable approach for identifying brain systems that might show different activity after training (e.g., Lutz et al., 2004). Given the inherently correlational nature of those studies and the inability to test a specific kind of compassion training as an intervention limits the conclusions we can draw. Nonetheless, the painstaking efforts to conduct these studies with Tibetan monks are indeed laudatory and clearly have advanced the field.

Second, to effectively compare different types of meditation treatments, it is essential that they be compared within the same experimental framework—same training duration, similar training protocols, same measurement techniques, etc. Without such an approach, researchers will continue to see what has been described above, overlapping but not directly comparable measures of brain activation. In the absence of direct comparisons, it will be difficult to identify whether the differences are due to the type of training or simply to an artifact of experimental design.

Understanding these caveats leads us to the third conclusion: many brain areas seem to be affected by training, but identification of specific effects can be daunting. Fig. 8.3 provides an image that is based on the current cutting edge of empathy and compassion training research discussed in this chapter. By no means is it exhaustive, but we believe that it illustrates the pattern of empirical findings related to research on the neuroscience of compassion training. This current mapping suggests a sequence of brain areas that extends from the frontal/prefrontal area posteriorly to the temporo-parietal junction and incorporates multiple cortical (e.g., dlPFC, IFG, mOFC, temporal gyrus, STS, and TPJ), embedded (e.g., Insula and Amyg), subcortical (e.g., NAcc, Striatum, and VTA), and midline (e.g., mACC, pACC, and dmPFC) structures in a pattern that is represented by both EEG and fMRI studies.

The complexity of this system can be reduced to some degree by grouping brain areas based on the networks, affective states, and behaviors to

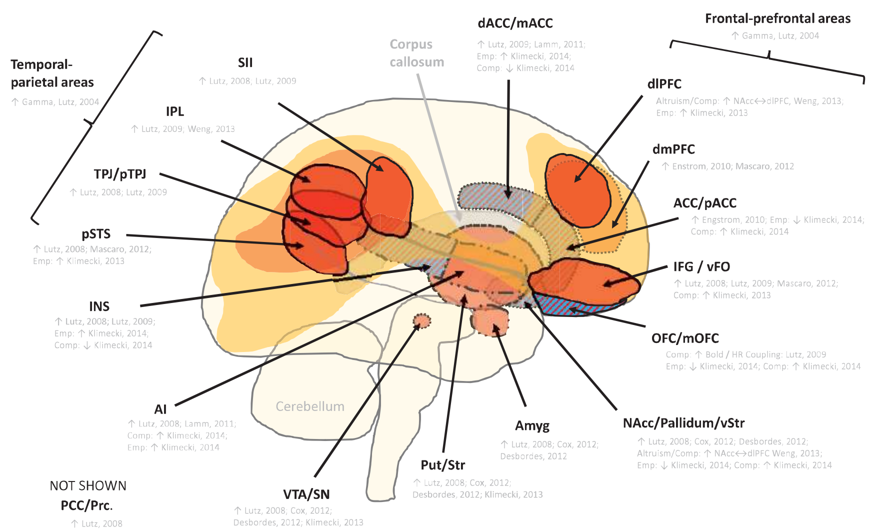

FIGURE 8.3 This graphic depiction adds more detail than presented in Figs. 1D and 2, and provides a more comprehensive map of all of the empathy and compassion findings detailed in this chapter. The graphic clearly demonstrates that there is substantial overlap between studies of the relationship between empathy/compassion meditation and changes in brain activity. There are cortical (—), embedded (— · · —), subcortical (– – –), and midline cortical (······) structures. Most regions show increases in brain activity (↑), some showed decreases (↓), and two areas showed greater coupling/connectivity (↔), depending on whether the study was assessing empathy (Emp) or compassion (Comp) training. Areas illustrated in Blue/Red hashing show increased activation (*Red*) in response to one training regime and less activation (*Blue*) under a different training protocol. Abbreviations: *ACC*, anterior cingulate cortex; *AI*, anterior insula; *mACC*, medial anterior cingulate cortex; *Amyg*, amygdala; *dACC*, dorsal ACC; *dlPFC*, dorsolateral prefrontal cortex; *dmPFC*, dorsomedial PFC; *IFG*, inferior frontal cortex; *IPL*, inferior parietal lobule; *INS*, Insula; *mOFC*, medial orbitofrontal cortex; *NAcc*, nucleus accumbens; *OFC*, orbitofrontal cortex; *pACC*, pregenual ACC; *pSTS*, posterior superior temporal sulcus; *pTPJ*, posterior temporal parietal junction; *SII*, postcentral somatosensory gyrus (Brodman 40); *Put*, putamen; *SN*, substantia nigra; *Str*, striatum; *TPJ*, temporal parietal junction; *VFO*, ventral frontal operculum; *vStr*, ventral striatum; *VTA*, ventral tegmental area.

which they typically contribute. For example, the Insula and mACC are part of the network that underlies pain perception and management, while mOFC, pACC, VTA, and NAcc are part of the network that regulates reward, pleasure, and positive affect. Likewise, the dmPFC and TPJ have been associated with mentalizing or thinking about the mental states of others, also called Theory of Mind (ToM: see Chapter 3 for a more comprehensive presentation of ToM) (Mascaro, Rilling, Negi, & Raison, 2013; Weng et al., 2013).

Such anatomical and functional linkages are essential for making sense of how different types of training might differentially influence brain activity and in turn alter affect, cognition, and behavior. The linkages also provide a basis for future hypotheses or for making predictions about how the training "treatments" that are being developed might enhance one type of brain pattern or another. Klimecki (2015) and Mascaro, Darcher, Negi, and Raison (2015) have both reviewed the distinct patterns of brain activity associated with empathy versus compassion training with Klimecki proposing that the type of training in which participants engage shapes the functioning of two antagonistic systems. Empathy training tips the balance toward one system, while compassion training tips the balance in favor of the antagonistic system. It is proposed that these changes underlie the measured differences in emotional state and behavioral responses. Fig. 8.4A and B illustrate these findings.

DIRECTIONS FOR FUTURE RESEARCH

As impressive as many of the studies we have reviewed are, they are also a good reminder that we are only beginning to probe the questions outlined at the start of the chapter. To outline our view of what to explore next, it is worth looking at a few of the limitations of the current literature. These will provide a foundation for the future studies we propose in the second section.

Understanding the Current Limitations

Techniques like EEG and fMRI are remarkable investigative tools. Moreover, given the overlap between so many studies, it is reasonable to currently conclude that meditation, empathy, compassion, and other cognitive and affective changes really are associated with changes in brain activity. But we must also be appropriately cautious. For example, fMRI requires sophisticated technology, corrections for artifacts (e.g., motion, individual differences in brain morphology, slice acquisition asynchrony, etc.), and the correct choice of statistical methods, any of which has the potential to introduce errors or unknown biases into the data. For example, a recent report by Eklund and colleagues indicated that approximately one in 10 published fMRI studies may be flawed due to processing errors, particularly spatial autocorrelation functions (Eklund, Nichols, & Knutsson, 2016). Thus, we recommend being cautious about taking the results of any single study as irrefutable evidence for a particular outcome.

Additionally, fMRI is an indirect measure of brain activity, recording BOLD blood flow responses associated with an experience. While reflecting metabolic demands of neurons and, by inference, increased activation, fMRI does not directly measure neuronal activity. The same concern can be levied at single-photon emission computed tomography and positron-emission tomography studies. Interestingly, although not yet generating high-resolution neuroimages of neural tissue, EEG is actually a more direct and temporally precise measurement of the activation of large neural networks. With the development of improved cortical and subcortical current source density (CSD) algorithms directly associated with surface EEG potentials, particularly with denser arrays, EEG has the potential to offer more direct measures of electrocortical activity (compared to relatively indirect hemodynamic measures) as well as reliable and valid localization methods.

There is also the concept of neuroplasticity to consider. Such physical brain changes in response to experience comprise some of the most exciting discoveries of contemporary neuroscience. These changes occur throughout life, have been demonstrated at molecular, neuronal, circuit, system, and whole-brain levels, and seem to be the basis of most, if not all, learning and behavioral change (Sweatt, 2016). Though not discussed here, in the compassion literature, as in much neuroscience research, there are many references to neural plasticity. It is important to note, however, that not a single study in this review directly measured neural alterations; such changes are inferred from blood flow or electrocortical modifications. This inference is well-considered in that changes in level of activity following training are likely due to changes in strength of neural connections (e.g., Hebb's Rule, Long-Term Potentiation, Long-Term Depression, etc.; see Sweatt, 2016 for a review). Notwithstanding the challenges in directly measuring in human studies specific alterations in neural networks associated with interventions, it is hoped that technological advances on the horizon will someday allow such measures in a nonintrusive manner.

It is also important to point out that even for studies in which there was an experimental manipulation (e.g., empathy training vs. compassion training vs. memory training; e.g., Klimecki et al., 2014), the relationship between brain measures (e.g., mOFC activity) and the cognitive and affective states are only correlational. None of the studies have shown directly that artificially inducing increased activity in the mOFC, pACC, and ventral striatum, while simultaneously decreasing the activity of the left and right insula and anterior medial cingulate cortex will induce a state of compassion that is accompanied by positive affect and decreased negative affect. A correlational relationship has been shown which suggests that this effect might be possible, but the causal relationship between distinct profiles of brain activity and distinct cognitive and affective states has not been directly demonstrated, as concerns empathy and compassion research. Advancements in transcranial magnetic stimulation (TMS) and deep brain stimulation (de Weijer et al., 2014; Kahan et al., 2014) may soon allow us to perform the types of experiments we propose below to make causal inferences, but as yet, they have not been conducted.

Finally, it is important to note that all of the studies referenced above have limitations with regard to external validity (e.g., the generalizability of the findings). As Davidson's group notes in multiple papers: "novices and experts differ in many respects other than simply the extent of meditative training (such as culture of origin and first language)," as well as belief systems, teachers and their expertise, an assumed prerequisite training of highly experienced meditators (HEMS), etc. (Lutz, Brefczynski-Lewis, Johnstone, & Davidson, 2008a). In addition to culture of origin and first language differences between novices and HEMS, there may also be self-selecting biases when recruiting study participants. Some may self-select for meditative training. Cautions with regard to such volunteer biases are important for consideration in future research (Demir, Haynes, Orthel-Clark, & Ozen, 2016).

Equally important is the fact that several early experimental training studies utilized groups that were not gender matched (i.e., different ratios of males and females in the training vs. control groups [Desbordes et al., 2012; Mascaro et al., 2013]) or studied only female participants (Klimecki et al., 2013, 2014). In practice, recruiting sufficiently large groups of both genders is a challenge and focusing on only one (e.g., females who are more empathetic) enhances homogeneity and provides greater control. However, many of the expert studies, which were based on predominantly male experts, also make generalizing across genders more difficult. Future research needs to address these imbalances in order to clarify our understanding of brain function as it pertains to empathy and compassion (Sacher, Neumann, Okon-Singer, Gotowiec, & Villringer, 2013).

Future Studies

As research advances on compassion training, the field could benefit by focusing on three directions, by conducting studies that are more: (1) descriptive; (2) experimental; as well as (3) deeply collaborative.

Descriptive: Being more descriptive here suggests that researchers compare and contrast different types of training (e.g., CBCT, CCT, PEACE). Specific questions that can be addressed include: Is one type of compassion training more effective than another? Is there a sequence of training components (e.g., the specific components of CBCT, CCT, PEACE) that is more efficacious (e.g., the CBCT training program emphasizes cultivation of equanimity as foundational to compassion training, whereas CCT places somewhat less emphasis on this particular component)? Is there a way to match the specific type of training to the specific individual characteristics (e.g., some individuals might benefit from practicing self-compassion earlier in the training, whereas others may not)?

An increase in the overall specificity in describing the neurobiological effects of compassion training would also be helpful. For example, utilizing more fine-grained analyses of EEG data (e.g., using CSD) as well as comparing, contrasting, and combining EEG assessment with fMRI data could help describe cortical and subcortical brain activation differences between training regimens and during segmented time periods to establish if there are specific changes from baseline measures. Additionally, it would be informative to increase the amount and type of neurophenomenological forms of assessment conducted. If we could make only one suggestion for future research on compassion training, it would be to further develop and to refine a range of phenomenological/qualitative/first-person methodologies (Englander & Folkesson, 2014; Lutz, Slagter, Dunne, & Davidson, 2008b; Lutz & Thompson, 2003; Petitmengin, 2006) in order to link subjective and objective EEG (van Lutterveld et al., 2016) and fMRI data (Garrison et al., 2013). Such an approach could potentially provide unique information regarding how to enhance the efficacy of the training. For example, when some individuals engage in cultivating gratitude and/or self-compassion in the context of compassion training, if not applied correctly, participants can be harshly judgmental of themselves which can be quite a negative subjective experience that may not be captured by current psychometric measures. Additionally, being able to "map" this type of experience onto the neurobiological assessment may help to clarify the neuroimaging conducted thus far.

Experimental: A compelling experimental question is whether there is a "critical period" of development during which one can potentially maximize the efficacy of compassion training. For example, in terms of adult developmental outcomes, would it be more beneficial to provide developmentally appropriate forms of compassion training for young adolescents when compared with older adolescents? Since adolescent brains are more "plastic," it is reasonable to posit that compassion training may have more positive psychosocial and neurobiological effects if started earlier in life. The PEACE program described earlier was developed expressly for this purpose and we await publication of neuroscience outcomes to clarify the differential developmental effects suggested above.

A potentially illuminating experimental approach to enhancing compassion could include using targeted noninvasive stimulation techniques such as TMS (e.g., de Weijer et al., 2014) and Transcranial Direct Current Stimulation (e.g., Zheng, Alsop, & Schlaug, 2011) to selectively activate or deactivate specific brain areas in the compassion/empathy networks. Such strategies could evaluate whether these interventions directly cause a change in the *experience* of compassion/empathy feelings, cognitions, or behaviors and perhaps, even more intriguing, could determine if such interventions bring about neurobiological changes that have putatively arisen from compassion training. Ideally, since fMRI data show the importance of multiple brain areas (networks) changing activity together rather than individually, it would be exciting to extend such a study further to directly manipulate multiple areas simultaneously. In short, could one electromagnetically induce the effects noted in Fig. 8.4A versus B without the need for systematic compassion training?

Deeply Collaborative: To make valid, reliable, and practical progress toward the goal of maximizing the efficacy of compassion training, we believe that researchers involved in this work must have expertise in three separate and distinct disciplines: neuroscience, contemplative practice, and clinical psychology. It is rare that any single individual will have true expertise in two of these three areas and exceptionally rare for any single individual to be expert in all three areas. Therefore, it is imperative when using neuroscience data to evaluate the efficacy of compassion training that an expert perspective from these three disciplines be included in order to maximize our understanding and cultivation of the benefits of such training and to prevent the occurrence of any potential psychological distress that might occur as a result of intensive compassion training (i.e., *primum non nocere*).

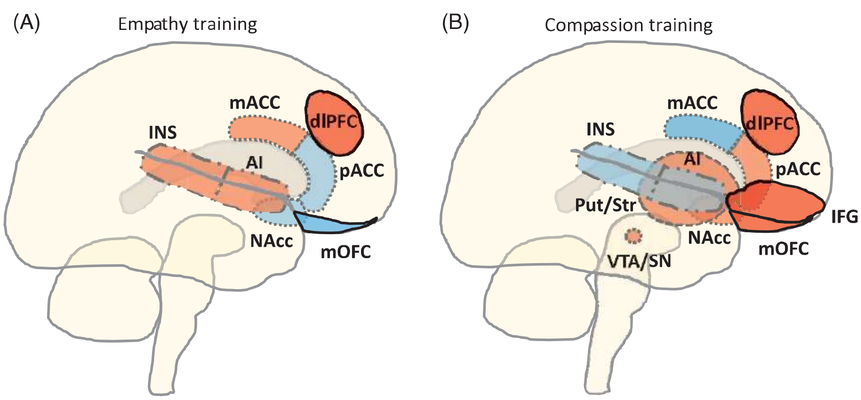

FIGURE 8.4 Distinct brain activity patterns post-empathy training (A) and post-compassion training (B) (Klimecki et al., 2013, 2014). There are cortical (—), embedded (— · · —), subcortical (– – –), and midline cortical (······) structures. In response to each type of training, areas colored *Red* represent increases in activation when the participant is confronted with distressing video clips, whereas areas colored *Blue* represent less or decreased activation in response to the same stimuli. Klimecki et al. (2014) have noted that empathy training (A) increases activation of a pain relevant network, while compassion training (B) increases the activity of pleasure and reward areas associated with approach behavior. Abbreviations: *ACC*, anterior cingulate cortex; *AI*, anterior insula; *mACC*, medial anterior cingulate cortex; *Amyg*, amygdala; *dACC*, dorsal ACC; *dlPFC*, dorsolateral prefrontal cortex; *dmPFC*, dorsomedial PFC; *IFG*, inferior frontal gyrus; *IPL*, inferior parietal lobule; *INS*, insula; *mOFC*, medial orbitofrontal cortex; *NAcc*, nucleus accumbens; *OFC*, orbitofrontal cortex; *pACC*, pregenual ACC; *pSTS*, posterior superior temporal sulcus; *pTPJ*, posterior temporal parietal junction; *SII*, postcentral somatosensory gyrus (Brodman 40); *SN*, substantia nigra; *TPJ*, temporal parietal junction; *VFO*, ventral frontal operculum; *VTA*, ventral tegmental area.

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