From: Zerbo, E., Schecter, A., Desai, S., & Levounis, P. (Eds.). (2016). *Becoming Mindful: Integrating Mindfulness into Your Psychiatric Practice* (pp. 9–24). Washington, DC: American Psychiatric Association Press.

Allostasis, Plasticity, and Integration: The Neuroscience of Mindfulness

Joseph Loizzo, M.D., Ph.D.
Weill Cornell Center for Integrative Medicine
Nalanda Institute for Contemplative Science

> *"Mental activities, such as purposely paying attention to the present moment, actually stimulate the brain to become active in specific ways that then promote the growth of integrative regions. These neuroplastic changes...help us see the link between mindful awareness and the creation of well-being."*
>
> —Daniel Siegel, The Mindful Brain

The growing role of mindfulness in psychiatry dates to the beginnings of meditation research. As soon as Benson (Beary & Benson, 1974) and Kabat-Zinn (Kabat-Zinn, 1982) evolved the first evidence-based paradigms for the clinical use of meditation—the relaxation response and mindfulness-based stress reduction (MBSR)—they began studying the application of these methods in mental health (Benson et al., 1978; Kabat-Zinn et al., 1992). The results of the first pilot studies in anxiety were promising enough to prompt more research, and the development of clinical paradigms tailored for mental health (Linehan et al., 1991; Teasdale et al., 1995). These early paradigms used mindfulness in treatment-resistant conditions like borderline personality and recurrent depression. As studies of Linehan's dialectical behavior therapy (DBT) and Teasdale's mindfulness-based cognitive therapy (MBCT) showed reductions in self-injurious behavior and depression-relapse, mindfulness was applied to other conditions, and interest in it as an adjunct in mental health grew (Baer, 2003).

Meanwhile, our understanding of the neural mechanisms of mindfulness grew exponentially (Tang et al., 2015). In my first review (Loizzo, 2000), I proposed that meditation shares a common mechanism with psychotherapy, combining two elements: the reduction of stress, and the enrichment of learning. The most common conditions we treat in psychiatry have been linked to "wear and tear" on the brain, caused by overexposure to stress hormones and inflammatory cytokines (McEwan & Stellar, 1993). In contrast to the adaptive responses to normal challenges called "allostasis," the syndrome of "wear and tear" caused by chronic stress and trauma has been dubbed "allostatic load/overload." Meanwhile, others reported seemingly contradictory findings: under persistent positive stimulation, the brain underwent tissue growth, repair, and regeneration. This "use it or loose it" process we now know as neuroplasticity not only counterbalanced the wear and tear of stress, but was linked to findings that learning and neurogenesis were enhanced in "enriched environments" (Rosensweig & Bennet, 1996)

The implications of neuroplasticity did not escape the attention of pioneers like Kandel, who made it the basis for a new paradigm in psychiatry (Kandel, 1998). Yet the paradigm he proposed would not be complete without another line of research. Twenty years after the stress response was described, Benson introduced the idea of the relaxation response as its complement (Beary & Benson, 1974). Given the binary structure of the autonomic nervous system (ANS), and the role of sympathetic activation in stress, meditation was said to elicit the relaxation response, by increasing parasympathetic tone. Research on MBSR distinguished mindfulness as "a discipline of attention" from the relaxation response (Goleman & Schwartz, 1976). In contrast to relaxation alone, the effects of mindfulness were attributed to a hybrid mechanism like the one I proposed: the calming function of meditation improving allostasis by reducing the stress-response; and its attentional function enriching learning by stimulating use-dependent plasticity (Davidson, 2000).

Further studies supported the mechanistic role of neuroplasticity, linking mindfulness with EEG patterns and structural changes consistent with increased activation, myelination and neurogenesis (Lazar et al., 2000, 2005). One key study showed that Tibetan-trained experts were able to consciously induce EEG findings indicative of increased learning and plasticity—unprecedented trains of gamma activity and synchrony—at will (Lutz et al., 2004). More recent studies confirmed the link between meditation and neurogenesis (Luders et al., 2009; Holzel et al., 2011a) and also linked meditation to brain connectivity (Jang et al. 2010; Guard et al., 2014). Today meditation is seen as a missing link in conscious self-regulation, connecting mental training on the one hand, to the electrochemical processes of neuronal firing, epigenetic regulation of gene-transcription, and new neural connectivity on the other (Davidson et al., 2003; Kaliman et al., 2013).

While such studies have clarified how mindfulness enriches learning, a related set of findings have revealed the other side of its mechanism and effects: conscious ANS regulation. Decades of studies of conscious breath practices have all shown some modulation of the ANS (Morse et al., 1984; Harinath et al., 2004). Recently, our understanding of such shifts has been expanded by new work on the ANS (Porges, 2011). Porges explains how the myelinated "smart vagus" that evolved in mammals not only supports voluntary breathing but also helps modulate primitive vagal and sympathetic reflexes to support expanded use of higher cortical capacities for social engagement.

Another general model views meditation as an integrative practice. When attention and relaxation combine, they help shift the dissociative, reactive mode of neural processing that prevails under stress, trauma and insecure attachment to the integrative, responsive style of processing that emerges under conditions of social safety, positive stimulation, and secure attachment (Siegel, 2012). Integrative models and mindfulness converge in research on the most recently evolved brain region: the prefrontal cortex (PFC). An inventory of prefrontal functions reads like a wish list of human development: selective attention and working memory; planning and execution; emotional regulation; empathy and morality; problem-solving; and body-awareness. Given its intimate links with other brain regions—neocortical, limbic, subcortical, midbrain, and brainstem—the PFC is seen as the "conductor" of the neural symphony, and seat of conscious brain integration. Not surprisingly, it also plays the central role in current meditation research, as in Vago's model of mindfulness as enhancing an integrative network based in the PFC, fostering self-awareness, self-regulation, and self-transcendence (Vago et al., 2012, 2014).

Mindfulness and Psychotherapy: Vertical and Lateral Integration

For decades, researchers have reflected on the similarities between mindfulness and free-association (Delmonte, 1995; Loizzo, 2000; Germer, 2005). Apart from the surface resemblance between Freud's "evenly hovering attention" and descriptions of mindfulness as "unbiased awareness," these reflections raise two deeper mechanistic questions. What level of consciousness do mindfulness and free-association occupy along the spectrum from normal wakefulness to sleep or trance? And which mode of consciousness do they engage on the bimodal spectrum from abstract-analytic to embodied-sensorimotor.

EEG studies of transcendental meditation (TM) and mindfulness show gradually increasing neocortical alpha amplitude and coherence, suggesting an initial phase of deepening introspection and calm comparable to drowsiness (Fenwick, 1987; Cahn & Polich, 2006). However, meditators routinely stop the progression that normally leads to somnolence, and instead of generating slow theta or delta waves typical of stage 1 sleep show a rise of high frequency theta activity, consistent with increased attentiveness (Jevning et al., 1992; Gruzelier, 2009). A similar pattern of wakeful relaxation is thought to be cultivated by free association, which Freud conceived as "waking state hypnosis" (Reiser, 1984; Delmonte, 1995).

The question of where mindfulness falls on the spectrum of states of consciousness relates to the theme of vertical integration. While some dissociation between levels and states of consciousness is the default condition of the human mind-brain, it would appear that with the right methods and repeated practice, they can be reorganized into an integrated system. In fact, the level of consciousness at which insight and attention can be maintained is not fixed, but varies with the type of practice and the level of expertise. This is evident not just from studies that show self-regulation of deeper structures with expertise (Lutz et al., 2008; Luders et al., 2009, 2013), but also from studies of virtuosos who show markers of waking state consciousness in the dream and deep sleep states (Laberge, 1980; Mason et al., 1997), and of aroused consciousness in hypometabolic states resembling hibernation, estivation, and the diving state of aquatic mammals (Heller et al,, 1987).

Given the increasing evidence of lateral specialization among the cerebral hemispheres, as well as among key subcortical structures like the insula, cingulate, hippocampus, and amygdala, our second question is how meditation and psychotherapy alter hemispheric lateralization. Since Roger Sperry's studies of epileptics with surgically bisected hemispheres, evidence has mounted that the verbal-expressive left hemisphere preferentially supports analytic processing, optimistic thinking, positive affect, and approach behaviors, while the sensorimotor-receptive right supports synthetic processing, worst-case thinking, aversive affect, and avoidance. This is consistent with findings that vagal activation generally dominates left hemisphere processing while sympathetic activation tends to dominate on the right (Shannahoff-Khalsa, 2007). So the mix of moderate relaxation with heightened attention common to both meditation and psychotherapy suggests they may share a mechanism of altering hemispheric laterality (Delmonte 1995; Loizzo, 2009). This mechanism has been supported by numerous findings, and explained in two ways.

Delmonte suggested that a shift toward balanced dominance reduces the default dissociation between the hemispheres, offering verbal consciousness greater access to normally suppressed emotion and repressed trauma. This is consistent with findings that meditation increases the size of the corpus callosum (Luders et al., 2012); increases cortical integration (Guard et al., 2014); increases the activity and size of the right anterior cingulate cortex and the right insula (Lazar et al., 2005); decreases the activation and size of the right amygdala (Holzel et al., 2010); and increases activation in implicit learning structures like the caudate and putamen (Tang et al., 2009).

Davidson offers another explanation. Based on the left lateral shift in prefrontal activity in mindfulness, he attributes the enhanced emotional regulation in mindfulness to greater involvement of the left hemisphere (Davidson et al, 2003). This is consistent with the clinical evidence that mindfulness helps prevent depression relapse by enhancing metacognition (Teasdale et al., 1995), as well as with findings of increased attentional flexibility and resilience in meditators (Guard et al., 2014). It also overlaps with recent clinical models of common psychopathology—anxiety, depression, trauma, attention deficit, impulse control, and addictive disorders—as a syndrome of hypofrontality: a dysregulation of limbic reactivity and subcortical impulsivity based on developmental deficits or disuse of "top-down" prefrontal regulatory centers and pathways (Menon, 2011).

Both these explanations have validity, and reflect complementary mechanisms. Increased access to normally suppressed, dissociated, or repressed material opens the way to deeper insight, corrective experience, and transformation. Higher faculties of metacognitive insight, narrative reframing, and emotional regulation are equally necessary to constructively re-process the newly accessed material. This second general mechanism shared by meditation and psychotherapy clearly relates to the theme of lateral integration. As in vertical integration, it appears that the human mind and brain has a greater capacity for lateral integration than we thought, especially given rigorous methods and practice (Telles et al., 1993; Luders et al., 2012).

Mindful Body and Self-Awareness: Integrating the Neocortex

Of the five basic forms of mindfulness practice, the simplest—body mindfulness—begins by using breath as a focal point to reconnect conscious attention to the body. This practice offers an accessible, reproducible methodology for building attention and cultivating self-awareness. Since all mindfulness practice exercises awareness, it is no surprise that it has been found to heighten attention and expand working memory, increasing activation and grey matter in executive regions like the dorsolateral and anterior PFC (Lazar et al., 2005; Luders et al., 2009). Mindfulness has been shown to increase not just attention but metacognitive functions like attentional flexibility, fluid intelligence, resilience, global network efficiency, and network integration (Jha et al., 2007; Gard et al., 2014). Consistent with this expansion of metacognitive awareness, mindfulness has also been shown to enhance emotional regulation (Creswell et al., 2007), by greater activation of the orbitofrontal region of the PFC (Holzel at al., 2007, 2011b). Yet this does not come at the cost of a dissociation from sensitivity. In fact, mindfulness enhances bodily self-awareness, increasing the activation and size of the (right) insula, a deep neocortical region that serves as an interoceptive map or link to bodily sensations (Lazar et al., 2005; Farb et al., 2012), and increasing the activation and size of the right thalamus (Luders et al., 2009). Likewise, mindfulness and related practices have been found to enhance perceptual sensitivity, introspective accuracy, and the discrimination of emotions (MacLean et al., 2010; Fox et al., 2012).

Among the findings linking mindfulness with neocortical self-awareness, the most intriguing relate to the impact of mindfulness on the offline processing of the default mode network (DMN). The DMN maintains the internally generated loop of self-referential narrative and self-world imagery that fills the void when mind and brain are idling between tasks. This network functions differently in meditators than non-meditators, with the former showing less self-referential activity not just within practice sessions but also in everyday life (Brewer et al., 2014). Yet mindfulness practice does not lead to a detached self-awareness stuck in a pure, internal present. It opens self-awareness outward to the world, growing mirror regions and DMN regions that support facial recognition, the self-other empathy system, and cerebellar regions involved in planning and executing intentional action (Holzel et al., 2011b). These findings suggest that mindfulness increases self-awareness and neocortical integration by de-automatizing self-constructive processing, and bringing metacognitive awareness and flexibility to default habits of identity, social recognition, and intentionality. The evidence that mindfulness practice helps expand the capacity of the neocortex for integrated social engagement is also consistent with Porges' model of ANS modulation.

Therapeutically, basic mindfulness is not just a key element in mindfulness-based cognitive therapy (MBCT), but works like free-association to support dynamic psychotherapy, fostering the emergence of observing ego and insight as alternatives to self-limiting ego defenses. This neocortical mechanism may help explain why it strengthens recovery from depression (Teasdale et al., 1995), and why it has been taken up as a helpful adjunct in psychodynamic practice (Moleno, 1999).

Mindful Sensitivity, Kindness, and Self-Regulation: Integrating the Limbic System

The second basic form of mindfulness practice—mindful sensitivity—focuses on the raw feelings of pleasure, pain, and neutrality that color all experiences of body, mind, and world, and trigger subliminal reactivity to positive, negative, and neutral stimulation. This key practice trains the mind to anticipate and prevent sensory reactivity based on past conditioning. It also dovetails with the mindfulness-based practice of loving-kindness, which trains the mind to prevent reactive emotions like fear, rage, and shame, by anticipating and transforming them into proactive emotions like kindness, tolerance, and acceptance.

This level of practice relates to Vago's second rubric: self-regulation. The relevance of self-regulation to mindfulness stems from the vulnerability of the neocortex to dysregulation, based on the default self-protective structure of the human brain. The neocortex maintains its default social engagement mode—lead by the PFC—only under conditions of perceived safety. Once the brain detects potential harm, it typically shifts into stress-protective mode, under the influence of the amygdala. This shift not only triggers the general stress-response, with its sympathetic and HPAA components, but disables the "top-down" regulation of the PFC and "hijacks" the neocortex. In this mode, the brain falls into a functional syndrome of hypofrontality. The damage done is compounded when the stresses are chronic, and we end up in states of allostatic overload like depression, chronic fatigue syndrome, learned helplessness, or PTSD.

There are several mechanisms by which mindful sensitivity and kindness practice foster a deeper level of sensory and emotional self-regulation (Van den Hurk et al., 2010; Teper at al., 2013). Mindfulness has been shown to decrease levels of anxiety and perceived stress, a finding correlated with decreased activation and gray matter in the right amygdala (Holzel et al., 2010; Goldin et al., 2011). One mechanism for this enhanced self-regulation of "bottom-up" stress-reactivity is increased activation of the anterior cingulate cortex (ACC) by regions of the PFC known to moderate fear and stress perception, since the ACC is the hub for "top-down" control of the limbic system by cognitive-emotional integration (Posner at al., 2007; Tang et al., 2015). Along with heightened attention, Tang found a practice of mind/body self-regulation similar to mindfulness increased ACC activation as well as heart rate variability (HRV), a measure of smart vagal activation (Tang et al., 2007, 2009).

Another mechanism of self-regulation in mindful sensitivity reflects the increasing emotional context provided by the hippocampus. If the amygdala is the brain's emotional alarm bell, the hippocampus serves as its emotional moderator or damper. Given its function to form and retain explicit memories, the hippocampus maps present data points onto an inner universe of spatiotemporal, social emotional and narrative perspective. The reference setting of the hippocampus helps contextualize raw sensory input processed in the amygdala, reframing worst-case fears in light of a broader range of personal and interpersonal experience. Numerous studies of mindfulness have found increased activity and gray matter density in the hippocampus, and related this to the self-regulating effect of mindfulness on the limbic brain (Holzel et al., 2011b; Wells et al., 2013).

The second main practice for self-regulation of the emotional brain is loving kindness or compassion practice. While research on kindness practice is more recent, the last decade has seen a number of key findings that clarify its effectiveness and mechanisms. Barbara Fredrickson found that simple loving-kindness meditation—exercising and gradually expanding positive emotions towards self and others in a mindful state—enhanced a range of positive emotions, expanded well-being, and enriched social resources and relationships (Fredrickson et al., 2008). More recent studies have shed light on the mechanisms of compassion training. The normal brain typically responds to seeing distressed faces with activation of the frontopariental mirror neuron system and middle ACC, which triggers conditioned disgust activation in the anterior insula and fear reactivity in the amygdala. After brief mindful compassion training, novices' brains showed less connectivity of the PFC with the AI and amydgala, more activation of PFC regulatory regions (dlPFC, mOFC) and the superior ACC intentional hub, reflecting an executive readiness for prosocial responsiveness, and also showed significant activation of mesolimbic reward system structures (Klimecki et al., 2012; Weng et al., 2013). These effects of kindness-compassion practice reflect a self-regulatory shift in limbic functioning from a "bottom-up" social emotional stress-reactive mode to a "top-down" mode of positive affective self-regulation and proactive social engagement (Lieberg et al., 2011; Engen & Singer, 2015).

Clinically, the first intervention integrating mindful sensitivity and kindness practices was Linehan's DBT (Linehan et al., 1991). More recently, the study of inwardly directed kindness practice as "self-compassion" was proposed as integral to the effects of interventions like MBSR and MBCT, suggesting the broad therapeutic potential of self-regulatory forms of mindfulness practice (Neff, 2003; Kuyken et al., 2010). A second generation of interventions has developed around Tibetan methods, formulated as cognitive behavioral compassion training (CBCT) and compassion cultivation training (CCT) (Desbordes et al., 2012; Klimecki et al., 2014). The most developed of these has been the compassion-focused therapy formulated by Paul Gilbert based on MBCT (Gilbert, 2014). Initial studies show that it has real promise in a range of mental and physical health applications including depression, anxiety, psychosis, and smoking cessation (Leaviss & Uttley, 2015). Finally, the practice of mindful sensitivity and kindness has been artfully woven into object relational approaches to psychotherapy by psychoanalysts Mark Epstein and Jeffrey Rubin (Epstein, 1995; Rubin, 1996).

Mindful Mindset, Mentality, and Self-Transcendence: Integrating the Core Brain

This last set of practices—mindful mindset and mentality—is the least known. In mindful mindset, attention is focused on the primary process of mind, traditionally taken to mean the raw data of sense intuitions or mental impressions prior to any association with verbal concepts, symbolic images, or emotional memories. The benefits of such "upstream" access to preprocessed mind-body states has obvious relevance to the correction of conditioned associations involved in "bottom-up" reactivity to stress and trauma. The complement to this practice is mindful mentality. Based on direct access to preprocessed input *via* mindfulness of mindset, this practice brings unbiased awareness to the way that input is processed by conditioned associations to memory images, emotional responses, and verbal narratives. It allows a metacognitive assessment and correction of the mentality with which the input is processed, including correcting perceptual distortions, reactive emotions, and/or traumatic narratives. This set of practices presents a depth-psychological insight practice meant to support self-transcendence through the deconstruction and reconstruction of personality (Dahl et al., 2015).

The first potential mechanism for the practice of mindful mindset comes from findings that mindfulness increases activation and grey matter in core brain regions critical to sense perception and implicit learning: the caudate, putamen, and thalamus (Tang et al., 2012; Pickut et al., 2013). Further evidence supporting this mechanism is the finding that expert meditators appear to regulate sense perception and reactivity more by altering "bottom-up" processing in subcortical structures, while novices do so more by altering "top-down" processing (Lutz et al., 2008; Chiesa et al., 2013). The deeper structures altered by expertise include not just elements of the thalamus and basal ganglia, but also midbrain structures that support the motivation and reinforcement of behavior (Klimecki at al., 2014; Zeidan et al., 2015).

A second mechanism involves modulation of primary regulatory structures and processes within the pontine brainstem. A recent study shed light on the possible mechanism of the much discussed impact of mindfulness practice on well-being (Carmody & Baer, 2008). The study showed that increases in well-being from mindfulness were correlated with increases in gray matter concentration the dorsal pons (Singleton et al., 2014). The correlation appears to support the mechanistic link between the well-being generated by mindfulness and the pontine nuclei of the mood and arousal modulating neurotransmitters serotonin, norepinephrine, and acetylcholine. This mechanism is supported by the findings of a prior study on the closely related practice of Zazen, that greater prefrontal activation and increased serotonin are correlated with the improved mood in novice practitioners (Yu et al., 2011).

While the Singleton study offers a plausible mechanism of how mindful mindset and mentality could support the affective component of self-transcendence, it is likely that the cognitive component involves alterations in the medullary brainstem, where the two vagal complexes intersect with the main centers of cardiorespiratory regulation and regenerative states. Early studies found that bare awareness practices linked with advanced breath control could elicit profoundly hypometabolic states akin to lucid hibernation, supporting paradoxically high levels of cortical arousal (Benson et al., 1990; Heller et al., 1987). Recent studies have replicated these findings, and linked them to increased gray matter density in the medulla oblongata (Verstergaard-Poulsen et al., 2009; Amihai & Koshevnikov, 2014). This is consistent with Porges' theory that full integration of the brainstem social engagement system is supported by smart vagal modulation of primitive vagal freeze reactivity.

As for the clinical applications of these deeper practices, efforts have been made to integrate mindful mindset and related practices into trauma therapy (Van der Kolk, 2014; Seppala et al., 2014) and various analytic approaches, including those of Jung, Reich, and Kohut (Kahn, 1985; Moacanin, 1986; Jennings, 2007).

Conclusion: Mindfulness and the Future of Neuropsychiatry

For clinicians, the single most remarkable and significant conclusion of this review is that mindfulness practices seem to share not only many of their beneficial effects but also their primary brain mechanisms with psychotherapy. This, in addition to the rising tide of neural research on these practices and the promising findings of mindfulness interventions in many conditions, makes a strong case for all mental health professionals to take an interest in the growing field of contemplative psychotherapy. In this review, I have brought together converging breakthroughs in neuroscience and physiology, including key elements of the emerging paradigm for psychiatry in the twenty-first century: allostasis, neural plasticity, social neuroscience, affective neuroscience, and polyvagal theory. The ways in which different forms of mindfulness help moderate traumatic stress reactivity and support social engagement at all levels of the nervous system further illumines the therapeutic benefits of mindful brain integration, rekindling the original promise of psychoanalysis to help bring unconscious structures and processes into the light of higher consciousness.

References

Amihai I & Kozhevnikov M: Arousal vs. relaxation: a comparison of the neurophysiological and cognitive correlates of Vajrayana and Theravada meditative practices. *PLoS ONE* 9(7):e102990, 2014.

Baer RA: Mindfulness training as a clinical intervention: a conceptual and empirical review. Clin. Psychol. Sci. Practice 10, 125–143, 2003.

Beary J Benson H: A simple psychophysiologic technique which elicits the hypometabolic changes of the relaxation response. Psychosom Med 36:115-120, 1974.

Benson H Lehman J Malhotra M et al: Body temperature changes during the practice of gTummo heat yoga. Nature 295:234-236, 1982.

Benson H Malhotra M Goldman R et al: Three case reports of the metabolic and electroencephalographic changes during advanced Buddhist meditative techniques. Behav Med 16:90-95, 1990.

Benson H Frankel FH et al: Treatment of anxiety: a comparison of the usefulness of self-hypnosis and a meditational relaxation technique. An overview. Psychother Psychosom 30(3-4):229-42, 1978.

Brewer J Worhunsky P Gray J Tang Y et al: Meditation experience is associated with differences in default mode network activity and connectivity. *Proc Natl Acad. Sci* USA 108:20254-20259, 2011.

Cahn B R & Polich J: Meditation States and Traits: EEG, ERP, and Neuroimaging Studies. Psychol Bulletin Vol. 132, No. 2:180–211, 2006.

Carmody J Baer RA: Relationships between mindfulness practice and levels of mindfulness, medical and psychological symptoms and well-being in a mindfulness-based stress reduction program. J Behav Med 31:23–33, 2008.

Chiesa A Serretti A & Jakobsen JC: Mindfulness: top-down or bottom-up emotion regulation strategy? Clin Psychol Rev 33, 82–96, 2013.

Creswell JD, Way BM, Eisenberger NI, Lieberman MD: Neural correlates of dispositional mindfulness during affect labeling. Psychosom Med 69:560–565, 2007.

Dahl CJ Lutz A Davidson R: Reconstructing and deconstructing the self: cognitive mechanisms in meditation practice. Trends Cogn Sci Vol. 19, No. 9, 2015.

Davidson R: *The Emotional Life of Your Brain*. New York: Plume Books, 2013.

Davidson R Kabat-Zinn J Schumacher J Rosenkranz M et al: Alterations in brain and immune functions produced by mindfulness meditation. Psychosom Med 65(4):564-570, 2003.

Davidson R: Affective style, psychopathology and resilience: Brain mechanisms and plasticity. Am Psychologist 1196-1214, 2000.

DelMonte M: Meditation and the unconscious. *J Contemp Psychother* Vol. 25;3: 223-242, 1995.

Desbordes G Negi L Pace T Wallace B et al: Effects of Mindful Attention and Compassion Meditation Training on Amygdala Response to Emotional Stimuli in an Ordinary, Non-Meditative State. Front Hum Neurosci 6:292, 2012.

Engen HG & Singer T:Compassion-based emotion regulation up-regulates experienced positive affect and associated neural networks. *Soc Cogn Affect Neurosci* 10(9), 1291-1301, 2015.

Epstein M: *Thoughts Without a Thinker: Psychotherapy from a Buddhist Perspective*. New York Basic Books, 1995.

Farb NA Segal ZV & Anderson AK: Mindfulness meditation training alters cortical representations of interoceptive attention. Soc Cogn Affect Neurosci 8, 15–26, 2013.

Fenwick PB: Meditation and the EEG. In West MA, Ed. *The Psychology of meditation*. New York: Clarendon Press, 104–117, 1987.

Fox KCR et al: Meditation experience predicts introspective accuracy. PLoS ONE 7, e45370, 2012.

Fredrickson B Cohn MA Coffey KA Pek J et al: Open Hearts Build Lives: Positive Emotions, Induced Through Loving-Kindness Meditation, Build Consequential Personal Resources. J Pers Soc Psychol 95(5): 1045–1062, 2008.

Gard T et al: Fluid intelligence and brain functional organization in aging yoga and meditation practitioners. Front Aging Neurosci 6, 76, 2014.

Germer C: Mindfulness in Psychotherapy. In Germer, C. K., Siegel, R. D., & Fulton, P. R. (Eds.). *Mindfulness and psychotherapy*. New York: Guilford Press, 2005.

Gilbert P: The origins and nature of compassion focused therapy. Brit J Clin Psychol 53, 6–41, 2014.

Goldin P Ziv M Jazaieri H Hahn K et al: MBSR versus aerobic exercise in social anxiety: fMRI of emotion regulation of negative self-beliefs. Soc. Cogn. Affect. Neurosci. 8, 65–72, 2013.

Gruzelier J: A theory of alpha/theta neurofeedback, creative performance enhancement, long distance functional connectivity and psychological integration. Cogn Process. 10 Suppl 1:S101-9, 2009.

Goleman DJ & Schwartz GE: Meditation as an intervention in stress reactivity. J. Consult. Clin. Psychol. 44, 456–466, 1976.

Harinath K Malhotra AS Pal K et al: Effects of Hatha yoga and Omkar meditation on cardiorespiratory performance, psychologic profile, and melatonin secretion. J Altern Complement Med 10(2):261-8, 2004.

Heller C Elsner R Rao N: Voluntary hypometabolism in an Indian Yogi. J Therm Biol 2:171-173, 1987.

Holtzel BK Carmody J Vangel M Congleton C et al: Mindfulness practice leads to increases in regional brain gray matter density. Psychiatry Res. 191:36-43, 2011a.

Hölzel BK et al: How does mindfulness meditation work? Proposing mechanisms of action from a conceptual and neural perspective. Perspect. Psychol. Sci. 6, 537–559, 2011b.

Hölzel BK Carmody J Evans KC Hoge EA et al: Stress reduction correlates with structural changes in the amygdala. Soc Cogn Affect Neurosci 5(1), 11–17, 2010.

Holzel BK Ott U Hempel H Hackl A et al: Differential engagement of anterior cingulate and adjacent medial frontal cortex in adept meditators and non-meditators. Neurosci.Lett. 421:16–21, 2007.

Jang JH Jung WH Kang DH Byun MS et al: Increased default mode network connectivity associated with meditation. Neurosci Lett 487, 358–362, 2010.

Jennings P: East of Ego: The Intersection of Narcissistic Personality and Buddhist Practice. J Relig and Health 46; 1:3-18, 2007.

Jha AP Krompinger J & Baime MJ: Mindfulness training modifies subsystems of attention. Cogn. Affect. Behav. Neurosci. 7, 109–119, 2007.

Kabat-Zinn J Massion AO Kristeller J Peterson LG et al: Effectiveness of a meditation-based stress reduction program in the treatment of anxiety disorders. Am J Psychiat 149(7):936-43, 1992.

Kabat-Zinn J: An outpatient program based in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: theoretical considerations and preliminary results. Gen Hosp Psychiat 4:33—47, 1982.

Kahn M: Vipassana Meditation and the Psychobiology of Wilhelm Reich. J Humanistic Psych vol. 25 no. 3 117-128, 1985.

Klimecki O Leiberg S Lamm C Singer T: Functional Neuroplasticity and Associated Changes in Positive Affect After Compassion Training. Soc Cogn Affect Neurosci 9 (6): 873-879, 2014.

Kuyken W Watkins E Holden E White K et al: How does mindfulness-based cognitive therapy work? Behav Research and Ther, 48, 1105–1112, 2010.

Laberge S: Lucid dreaming: An exploratory study of consciousness during sleep. PhD thesis, Stanford University: University Microfilms No. 80-24, 691, 1980.

Lazar SW et al: Meditation experience is associated with increased cortical thickness. NeuroReport 16(17): 1893-7, 2005.

Lazar SW Bush G Gollub RL et al: Functional brain mapping of the relaxation response and meditation. Neuroreport 11(7):1581-5, 2000.

Leaviss J Uttley L: Psychotherapeutic benefits of compassion-focused therapy: an early systematic review. Psychol Med 45, 927–945, 2015.

Leiberg S Klimecki O Singer T: Short-Term Compassion Training Increases Prosocial Behavior in a Newly Developed Prosocial Game. PLoS ONE 6(3): e17798, 2011.

Linehan MM Armstrong HE Suarez A Allmon D et al: Cognitive-behavioral treatment of chronically parasuicidal borderline patients. Arch Gen Psychiat 48: 1060–64, 1991.

Loizzo J: Optimizing Learning and Quality of Life Throughout the Lifespan: A Global Framework for Research and Application. In In Bushell, W., Olivo, E. & Thiese, N. (Eds). *Longevity, Regeneration and Optimal Health: Integrating Eastern and Western Perspectives*. New York: Annals of the New York Academy of Sciences, 186-198, 2009.

Loizzo J: Meditation and Psychotherapy: Stress, Allostasis and Enriched Learning. In P. Muskin (Ed,), *Complementary and Alternative Medicine and Psychiatry*. Washington: American Psychiatric Association Press, 2000.

Luders EK et al: Global and regional alterations of hippocampal anatomy in long-term meditation practitioners. Hum. Brain Mapp. 34, 3369–3375, 2013.

Luders EK Phillips O Clark KL Kurth F et al: Bridging the hemispheres in meditation: Thicker collosal regions and enhanced fractional anisotropy (FA) in long-term practitioners. Neuroimage 61:181-187, 2012.

Luders EK Clark KL Narr A Toga AW: Enhanced Brain Connectivity in Long-term Meditation Practitioners. Neuroimage 57(4): 1308–1316, 2011.

Luders EK Toga AW Lepore N Gaser C: The underlying anatomical correlates of long-term meditation: larger hippocampal and frontal volumes of gray matter. Neuroimage 45(3):672-8, 2009.

Lutz A Brefcyznyski-Lewis J Johnstone T Davidson R: Voluntary regulation of the neural circuitry of emotion by compassion meditation: Effects of expertise. PLoS One 3: e1897, 2008.

Lutz A Grieschar L Rawlings N et al: Long-term meditators self-induce high amplitude gamma synchrony during mental practice. Proc National Acad Sci 101:16369-16373, 2004.

MacLean KA et al: Intensive meditation training improves perceptual discrimination and sustained attention. Psychol Sci, 21, 829–839, 2010.

Mason L Alexander C Travis F et al: Electrophysiological correlates of higher states of consciousness during sleep in long-term practitioners of the transcendental meditation program. Sleep 20:102-110, 1997.

McEwen BS Stellar E: Stress and the individual: mechanisms leading to disease. Arch. Int. Med. 153, 2093–3101, 1993.

Menon V: Large-scale brain networks and psychopathology: a unifying triple network model. Trends Cogn Sci. 15(10):483-506, 2011.

Moacanin, R: *Jung's Psychology and Tibetan Buddhism:Western and Eastern Paths to the Heart*. Boston: Wisdom, 1986.

Molino A Ed: *The Couch and the Tree: Dialogues in Psychoanalysis and Buddhism*. New York: North Point Press, 1999.

Neff KD: Self-compassion: An alternative conceptualization of a healthy attitude toward oneself. Self and Identity, 2, 85–101, 2003.

Pickut BA et al: Mindfulness based intervention in Parkinson's disease leads to structural brain changes on MRI: a randomized controlled longitudinal trial. Clin. Neurol. Neurosurg. 115, 2419–2425, 2013.

Porges S: *Polyvagal Theory: Neurophysiological Foundations of Emotions, Attachment, Communication and Self-Regulation*. New York: W.W. Norton & Co, 2011.

Posner MI Sheese B Rothbart M Tang YY: The anterior cingulate gyrus and the mechanism of self-regulation. Cogn. Affect. Behav. Neurosci. 7, 391–395, 2007.

Rieser M: *Mind, Brain, Body: Toward a Convergence of Psychoanalysis and Neurobiology*. New York: Basic Books, 1984.

Rosenzweig MR Bennett EL: Psychobiology of plasticity: effects of training and experience on brain and behavior. Behav Brain Res. 78(1):57-65, 1996.

Rubin J: *Psychotherapy and Buddhism: Toward an Integration*. New York: Springer, 1996.

Seppälä E Nitschke JB Tudorascu DL Hayes A et al: Breathing-Based Meditation Decreases Posttraumatic Stress Disorder Symptoms in U.S. Military Veterans: A Randomized Controlled Longitudinal Study. J Traumatic Stress 27; 4:379–500, 2014.

Shannahoff-Khalsa D: Selective unilateral autonomic activation: Implications for psychiatry. CNS Spectrum 12(8):625-634, 2007.

Siegel D: *Pocket Guide to Interpersonal Neurobiology: An Integrative Handbook of the Mind*. New York: W.W. Norton & Co, 2012.

Siegel D: *The Mindful Brain: Reflection and Attunement in the Cultivation of Wellbeing*. New York. W.W. Norton & Co, 2007.

Tang YY Hölzel BK Posner MI: The neuroscience of mindfulness meditation. Nature Rev Neurosci Vol. 16: 213, 2015.

Tang YY Rothbart MK Posner MI: Neural correlates of establishing, maintaining and switching brain states. Trends Cogn. Sci. 16, 330–337, 2012.

Tang YY Ma Y Fan Y et al: Central and autonomic nervous system interaction is altered by short-term meditation. Proc Natl Acad Sci USA, 106(22):8865-70, 2009.

Tang YY et al: Short-term meditation training improves attention and self-regulation. Proc. Natl Acad. Sci. USA 104, 17152–17156, 2007.

Teasdale J Segal Z Williams J: How does cognitive therapy prevent depressive relapse and why should attentional control (mindfulness) training help? Behav Res Ther, 33:25-39, 1995.

Telles R Raghavendra B Naveen K Manjunath N et al: Changes in autonomic variables following two meditative states described in yoga texts. Altern Complement Med 19(1):35-42, 2013.

Teper R Segal ZV Inzlicht M: Inside the mindful mind: how mindfulness enhances emotion regulation through improvements in executive control. Curr. Dir. Psychol. 22, 449–454, 2013.

Vago D: Mapping modalities of self-awareness in mindfulness practice: a potential mechanism for clarifying habits of mind. In “Advances in Meditation Research: Neuroscience and Clinical Applications.” S. Sequiera, Ed:28-42. New York: Annals of the New York Academy of Sciences, 2014.

Vago D Silbersweig D: Self-awareness, self-regulation, and self-transcendence (S-ART): a framework for understanding the neurobiological mechanisms of mindfulness. Front Hum Nuerosci 6:296, 2012.

Van den Hurk P Janssen B Giommi F et al: Mindfulness meditation associated with alterations in bottom-up processing: psychophysiological evidence for reduced reactivity. Int J Psychophysiol, Nov;78(2):151-7, 2010.

Van der Kolk B: *The Body Keeps the Score: Brain, Mind, and Body in the Healing of Trauma*. New York: W.W. Norton & Co, 2014.

Vestergaard-Poulsen P Van Beek M Skewes J et al:Long-term meditation is associated with increased gray matter density in the brain stem. Neuroreport 28;20(2):170-4, 2009.

Wells RE et al: Meditation's impact on default mode network and hippocampus in mild cognitive impairment: a pilot study. Neurosci. Lett. 556, 15–19, 2013.

Weng HY Fox AS Shackman AJ et al: Compassion training alters altruism and neural responses to suffering. Psychol Sci 24(7):1171-80, 2013.

West MA Ed: *The psychology of meditation*. New York: Oxford University Press, 1987.

Yu X Fumoto M Nakatani Y et al: Activation of the anterior prefrontal cortex and serotonergic system is associated with improvements in mood and EEG changes induced by Zen meditation practice in novices. Int J Psychophysiol 80(2):103-11, 2011.

Zeidan FN Emerson M Farris SR Ray JN et al: Mindfulness Meditation-Based Pain Relief Employs Different Neural Mechanisms Than Placebo and Sham Mindfulness Meditation-Induced Analgesia. J Neurosci, 18, 35(46):15307-15325, 2015.