REVIEW ARTICLE

How Does the Body Affect the Mind? Role of Cardiorespiratory Coherence in the Spectrum of Emotions

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ABSTRACT

The brain is considered to be the primary generator and regulator of emotions; however, afferent signals originating throughout the body are detected by the autonomic nervous system (ANS) and brainstem, and, in turn, can modulate emotional processes. During stress and negative emotional states, levels of cardiorespiratory coherence (CRC) decrease, and a shift occurs toward sympathetic dominance. In contrast, CRC levels increase during more positive emotional states, and a shift occurs toward parasympathetic dominance. The dynamic changes in CRC that accompany different emotions can provide insights into how the activity of the limbic system and afferent feedback manifest as emotions. The authors propose that the brainstem and CRC are involved in important feedback mechanisms that modulate emotions and higher cortical areas. That mechanism may be one of many mechanisms that underlie the physiological and neurological changes that are experienced during pranayama and meditation and may support the use of those techniques to treat various mood disorders and reduce stress. (*Adv Mind Body Med.* 2015;29(4):4-16.)

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Many years ago, James and Lange[1] independently proposed the idea that emotions occur as a result of physiological reactions. Their complex theory has been "oversimplified to the point of caricature,"[2] and, although some aspects have been disproven,[1] many tenets of the hypothesis have been difficult to disprove, and substantial evidence has accumulated in the theory's favor.[3] Currently, most studies on emotions focus on the brain and neurotransmitters and examine the generation and processing of emotions as a linear process,[2] with singular causality, when in fact emotions are the result of the processing of efferent and afferent feedback in loops between the brain and body.[3] The current, mainstream scientific consensus is that the widespread homeodynamic changes that occur during various emotional states are the result of top-down signaling from the brain, but, in fact, those changes involve dynamic feedback between the body and brain. Differentiating between emotion generation and emotion processing may help to further elucidate those processes.[4] Critchley[5] has shown that internal feedback from physiological changes influences emotions, but those effects have been largely overlooked.

The authors propose that cardiorespiratory coherence (CRC) modulates the autonomic nervous system (ANS) and brainstem, leading to inhibition of the amygdala and thalamus[6] via hyperpolarization.[7,8] That process leads to increased cognition and focus because the brain is not distracted by chaotic neuronal signaling and feedback from the body. The current article offers color-coded images of dynamic changes in physiology and neuronal activity during different emotional states to demonstrate the possible synchronizing mechanisms that involve the cardiorespiratory modulation of the brainstem, limbic system, and cortex.

The authors also suggest that the differential activation and inactivation of the limbic system and cortex during different emotions corresponds, in part, to the underlying physiological input that is channeled through various conductive tissues to the brainstem. That basic feedback mechanism needs to be taken into account when considering treatments for many medical conditions.

Cardiorespiratory rhythms and hemodynamic changes have been associated with corresponding changes in the brainstem; however, those events are not clearly linked to the ascending reticular activating system, serotonin, and other monoamine activity. Far less clear is the association of cardiorespiratory-coherence rhythms with the limbic system, amygdala, and cortex. Many studies have shown that cognitive changes occur during emotional states such as those present in states of anxiety and in meditation; however, those studies do not demonstrate a cohesive link between CRC, emotions, and homeodynamic changes.

The authors propose a model in which physiological changes modulate cortical activity via the brainstem and influence executive functions. Investigating that potential homeodynamic mechanism would allow the development of clinical interventions and treatments that can intercept the cascade of feedback events that lead, when repeated, to anxiety disorders, stress-related disorders, and emotional disorders. Based on recent data, stress-related disorders now include heart disease, high blood pressure, and gastrointestinal (GI) problems, among many others. A better understanding of the inhibitory and neurophysiologic, synchronizing input of synchronized cardiorespiratory oscillations could help medical practitioners to understand and treat many disorders better.

Emotions and associated physiological changes involve both feedforward and feedback signaling. Emotions are influenced by neurotransmitter activity. Therefore, it is widely accepted that emotions arise within the brain, which provides feedforward signaling, whereas the influence of physiological signaling originating throughout the body has been overlooked. The feedforward mechanisms have been well studied and are considered to be the main drivers of both emotions and the physiological changes associated with those emotions. Although that efferent neural signaling is vital to those processes, the authors propose that feedback from throughout the body, such as cardiorespiratory oscillatory activity, can also modulate them.

The modulatory effects of that afferent feedback can be seen in the physiological and neurological changes that occur during meditation and pranayama. Slow, deep breathing increases the CRC levels, which likely modulates the ANS and underlies the widespread neurological and physiological changes that occur during meditation and pranayama.[7,8] The authors propose that CRC during the mind-body response can lead to hyperpolarization and to decreases in the intrinsic excitability of cells. Those changes likely underlie the modulation of the ANS and neural activity that occurs during those practices[8] and can influence emotional states. The emotional and neurological changes that arise during pranayama and meditation illustrate the effects that feedback from the body can have on emotions, the ANS, and neurological activity.

In the current article, the authors discuss how meditation and other slow, deep-breathing techniques, which increase CRC, can be used to treat anxiety, stress, and emotional disorders, as well as increase well-being and positive affect.[9] The mechanisms underlying the positive health benefits of meditation and the physiological and neurological changes that occur during and after meditation are not well understood. The authors propose that increased levels of CRC modulate the ANS, the limbic system, and other areas of the brain and may be one of the mechanisms that underlie the mind-body response of meditation. Further study of that possible mechanism can help elucidate the underlying mechanisms of meditation and increase its use as a treatment for many disorders.

Inherent difficulties exist in monitoring cardiorespiratory, brainstem, and amygdala activity, as well as in finding direct evidence of the cause-and-effect mechanisms that occur as a result of physiological feedback. Research on feedforward mechanisms can establish more direct cause-and-effect relationships due to the origin of signaling from neural control centers. However, when examining feedback mechanisms, researchers must decipher how those control centers adjust their output due to modulation from feedback signals originating throughout the body, the existence of which makes direct cause-and-effect relationships difficult to establish.

In this article, the authors discuss relevant clinical studies to establish the possible modulatory effect of CRC on emotions, and they have proposed a hypothesis that may explain one of the many mechanisms at play during the homeodynamic processes that occur during various emotional states. Further studies are needed to elucidate that mechanism and to determine the possible direct effects of CRC on emotions so that researchers can obtain a more complete picture of the homeodynamic mechanisms involved in those processes.

INFLUENCES ON EMOTIONS

Autonomic Nervous System

Both sympathetic and parasympathetic efferents originate in the brainstem. Sympathetic neurons project from the brainstem through the spinal cord to sympathetic neurons in spinal segments T1–L2, whereas the parasympathetic nervous system innervates most peripheral organs via the vagus nerve from the brainstem.[5] Terminal sympathetic synapses are typically noradrenergic, while parasympathetic synapses are typically cholinergic. The hypothalamus, pons, and medulla are involved in homeostatic autonomic control. Brainstem areas, such as the locus coeruleus, are involved in sympathetic control, whereas the nucleus ambiguous is involved in parasympathetic control. The brainstem innervates the release of neurotransmitters to the hypothalamic-pituitary adrenal axis and limbic system,[10] suggesting that autonomic signals from the brainstem, such as CRC, may modulate emotions.

Another area of the brain involved in modulation of both the ANS and emotions is the periaqueductal gray (PAG) located in the midbrain. The PAG is involved in pain modulation, autonomic control of the cardiovascular system[11] and the expression of emotions.[12] The ascending activity from the vagus and other afferent signaling affects

the PAG matter on the lateral and ventrolateral axis differently during various emotional states, such as during states of anger and sadness, suggesting that the circuitry of emotions involves both the brain and peripheral input.[13]

Buhle et al[14] found that physical pain and negative-image viewing, which are conditions known to cause strong emotional responses, led to increased activity in the PAG, suggesting that the PAG is highly involved in affective and emotional responses. Two studies, one by Miranda-Paiva et al[15] and a second by Bartels and Zeki,[16] found that the PAG was also associated with maternal bonding and behavior and the related positive emotions. In their study, Bartels and Zeki[16] found that the PAG, reticular formation, locus coeruleus, and raphe nucleus were all activated during the experience of maternal love, whereas the amygdaloid region was deactivated. That study and one by Rizvi et al[17] found that the brainstem activity likely originated in the PAG, which has strong afferent and efferent connections to the amygdala and limbic system. Bartels and Zeki[16] also found that the PAG contains a dense population of vasopressin and oxytocin receptors.

In addition, another study found that oxytocin-receptor activity in the ventrocaudal PAG modulates and reduces anxiety-related behaviors in postpartum rats.[15] Huber et al[16] found that oxytocin and vasopressin modulate autonomic fear responses, likely via an inhibitory network. The research team found that oxytocin can directly modulate amygdala activity by binding with receptors in the central nucleus, thereby enhancing the activity of γ-aminobutyric acid (GABA),which leads to the inhibition of signaling from the amygdala to the hypothalamus and brainstem. The studies discussed above on the role of PAG demonstrate the role of the brainstem in emotions and in modulation of higher brain areas.

Cardiorespiratory System

Respiration is one of the many physiological processes that are affected by emotions.[17-19] In addition, respiratory feedback has been shown to influence the induction of emotions.[20] Distinct respiratory, cardiac, and other peripheral activities are associated with different emotions,[21] and those specific respiratory[22] and cardiorespiratory[21] patterns can be used to distinguish basic emotions. For example, arousal states are associated with more rapid breathing.[23] Those respiratory rhythms are generated in respiratory centers in the medulla and pons in the brainstem,[24] which have been shown to have both efferent and afferent connections with the limbic system,[19,25-27] further illustrating the communication and feedback loops between the respiratory and emotional centers of the brain.

The cardiovascular system has also been shown to modulate emotions and even emotional-appraisal processing. Gray et al[28] found that images of disgusted facial expressions were judged as more intense when presented at systole. They also found that activity within the prefrontal cortex (PFC) was correlated with emotionality ratings and increases in heart rate, whereas activity in the orbitofrontal cortex and PAG matter was correlated with both increases in heart rate and cardiac timing. Overall, they found that processing of emotional stimuli was altered by cardiac afferent information, such as baroreceptor activation, and that cardiovascular signaling can influence the evoked autonomic responses.[28]

Cardiorespiratory Coherence

Cardiac and respiratory rhythms are known to exhibit both synchronized and desynchronized dynamics. Healthy individuals experience higher ratios and higher levels of 4:1 CRC when compared with patients with diseases.[29] CRC refers to the results of various methods of assessing the phase synchronization between the heartbeat and respiration, including the use of synchograms,[30] algorithms,[31] and various data-analysis techniques.[32]

Some researchers have proposed that cardiorespiratory synchronization may be an artifact rather than a true interaction within the cardiorespiratory system, but Toledo et al[31] found that the phenomenon was real. The direct effects of emotional stimuli on CRC and the effects of CRC on emotions have not been extensively investigated. However, different emotions can be identified using CRC levels[33] and distinct cardiorespiratory activity.[21] In addition, high levels of CRC are associated with parasympathetic dominance and low levels with sympathetic dominance, so much so that CRC levels can actually be used to assess the state of the ANS.[34]

Sympathetic blockade leads to increases in the duration of synchronized epochs and the percentage of synchronization within all ratios, whereas parasympathetic blockade leads to decreases in those measures.[35] In addition, bilateral vagotomy eliminates coupling between the systolic blood pressure and respiration, suggesting that the coupling is mediated by the central nervous system (CNS).[36] In a study by Dudnik and Glazachev,[34] simulating emotional tension in participants caused significant desynchronization of the heart and respiratory rates that was likely due to sympathetic activation, and a study by Zhang et al[37] showed that stress during mental tasks decreased CRC.

Those studies have demonstrated the role of CRC as a possible indicator and modulator of ANS activity. However, although CRC can be used to assess sympathovagal activity, heart-rate variability remains an accurate and better established measure of that activity. Peupelmann et al[38] found that schizophrenic patients experienced decreased CRC levels, indicating decreased vagal modulation of the brainstem, and, possibly, a lack of inhibition and control over the brainstem. Berger et al[39] found that autonomic dysfunction was also present in healthy relatives of schizophrenic patients, therefore indicating a genetic predisposition for reduced CRC and vagal modulation of the brainstem. Those studies illustrate the interactions between the brainstem and CRC and their possible implications; however, the possible role of CRC feedback in modulating activity in the brainstem, brain, and the ANS has not been addressed and has not been well studied.

During states that are more sympathetically dominant, such as those seen during stress, levels of vagal activity are reduced and CRC levels are lower.[37,40] Patients with coronary

artery disease experience more 2:1 CRC, as compared with the 4:1 synchronizations of healthy patients.[29] In addition, patients with obstructive sleep apnea,[41] diabetes, and breast cancer experience lower CRC levels, with a loss of coordination ability in patients with metastasized breast cancer.[42] CRC levels can also be used for development of a prognosis after myocardial infarction,[43,44] with lower levels of CRC indicating an increased mortality rate.[43]

CRC AND NEUROPHYSIOLOGIC COHERENCE

Synchronization and coherence is likely an important organizing principle and may be important for health and optimal functioning of body systems.[45] Stapp has proposed a quantum-based theory in which consciousness exercises top-level control of neural excitation in the brain rather than of neural events occurring at the synaptic level. Each conscious event is experienced as a *feel* of an event, relating the psychological to the quantum. That view of consciousness may be supported by the properties of gamma synchrony and other neural synchronizations.

The principles of synaptic-level transmission likely do not apply to more complex neural activity that involves networks and dynamic coordination of large areas of the brain.[46] The properties of synaptic transmission do not apply to large-scale dynamics within the brain, and that fact may support more homeodynamic models of consciousness that involve neural synchrony and connectivity.

In addition, Hameroff and Penrose[47] have proposed that electroencephalogram (EEG) rhythms arise from microtubule vibrations within neurons. The recent discovery of warm-temperature conductive resonances in microtubules has provided the much-needed evidence to support that model[48] and suggests the involvement of massive global synchronization in consciousness.[49] Those models emphasize the importance of synchronization at the neuronal level in conscious experience, such as during the experience of feelings and emotions, as well as of quantum coherence at the microtubule level. The authors have examined oscillations and oscillatory coherence on a more global scale but recognize that higher-scale coherence may also be modulated and affected by processes on the quantum level as well.

Some researchers have proposed that negative emotions are felt as a result of chaotic and unsynchronized, neurophysiologic interactions, whereas positive emotions facilitate or emerge when efficient and synchronized physiological, cognitive, and emotional interactions exist.[50,51] That state of synchronization is referred to as a state of psychophysiological coherence.[50] Sustained states of positive emotions can lead to psychophysiological coherence, in which synchronization of the heart, respiratory, and brain rhythms occurs.[50] A study in which high-school students were trained to regulate their emotions better by using psychophysiological coherence found that the students had less test anxiety and improved test performance after training. In addition, students with high test anxiety exhibited increased heart rate variability (HRV) and heart-rhythm coherence, even during a resting condition.[52]

Many studies have examined static, functional connectivity, but more recent studies have begun to examine temporal, large-scale, functional organization. Changes in functional connectivity occur during various mental states, such as during learning,[53] sleep,[54] and meditation.[55] Some researchers have proposed that dynamic functional connectivity may actually be noise rather than neural activity, but a study by Hutchison et al[56] that simultaneously examined electrophysiological data and behavior, in addition to fMRI, showed that functional connectivity likely has neural origins and may be involved in changes in cognitive and vigilance states.

Positive emotions may also benefit psychological and physiological health.[57] Some studies have shown that positive emotions, such as amusement and contentment, broaden the scope of attention, whereas negative emotions, such as anger and anxiety, narrow thoughts and actions.[58] Positive emotions have been shown to enhance perception and cognition,[58-62] yet very few theories exist regarding how that well-documented phenomenon occurs.[60]

A study by Alabdulgader[63] has shown that emotional self-regulation techniques, together with heart-rhythm-coherence training, can be used to lower blood pressure in hypertensive patients. Positive emotions, such as appreciation, have been found to elicit more high-frequency HRV and parasympathetic dominance.[64] Onorati et al[65] found a strong correlation between respiration, high-frequency HRV, and positive emotions. Another study, on EEG-wavelet coherence, found that synchronization increased in the left frontal-temporal lobe during pleasant melodies, whereas desynchronization occurred in the temporal lobe and the occipital lobe during unpleasant melodies and melodies with no emotional responses, respectively.[66] An EEG study found that greater coherence in the beta, delta, theta, and gamma frequencies existed during induction of positive emotions, whereas desynchronization also occurred between the anterior and posterior areas of the cortex.[67]

Those studies have shown that positive emotions can correlate with increased synchrony throughout the body and brain. The authors propose that synchrony during positive emotions is the result of high CRC levels and parasympathetic dominance, whereas asynchrony during negative emotions is the result of desynchronized cardiorespiratory oscillations and sympathetic dominance. During positive emotions, an increased coupling between the limbic system, brainstem, and other areas of the brain likely occurs. Likewise, during negative emotions, a decrease in functional coupling and connectivity between the limbic system, brainstem, and other areas of the brain likely takes place.

For example, Song et al[68] found that a significant decrease in the white matter of the solitary tract, which connects the brainstem and amygdala, occurred in patients with a major depressive disorder. In addition, Anticevic et al[69] found that schizophrenic patients showed decreased connectivity between

the amygdala and orbitofrontal cortex, and Yoo et al[70] found that sleep deprivation led to inappropriate modulation of emotional responses to negative stimuli due to lack of connectivity between the amygdala and PFC.

However, results have not always been consistent. For example, Kirsch et al[71] found that oxytocin-mediated reductions in amygdala activity were accompanied by a decreased coupling of the brainstem and amygdala. In addition, Gross et al[72] found that some emotions, such as crying, were associated with a mixture of sympathetic and parasympathetic activation.[72]

Positive Emotions: Parasympathetic Dominance

HRV parameters, which are indicative of an autonomic state, can be used to estimate mood states[73,74] and to discriminate between psychiatric and healthy patients because levels of high frequency HRV are reduced in schizophrenic, bipolar, and posttraumatic stress disorder (PTSD) patients.[75] Happiness is associated with high-frequency HRV, whereas frustration is associated with low-frequency HRV.[76]

Stimulation of the vagus nerve, which is involved in parasympathetic control, has been shown to alter electrical activity in the brain and inhibit neural processes.[77] For example, one study[78] has shown that the amygdala-evoked responses of cortical neurons can be inhibited by vagal nerve stimulation (VNS), suggesting that negative emotions can be inhibited by a shift toward parasympathetic dominance. A study by Zagon and Kemeny[79] showed that low-intensity VNS can cause slow hyperpolarization of cortical neurons, which may suggest that the GABAergic cortical inhibition that occurs during meditation[83] may be due in part to a vagal shift toward parasympathetic dominance. In addition, Zagon and Kemeny[79] proposed that repeated low-intensity VNS would likely result in sustained inhibition.

Epileptic patients treated with VNS have experienced significant mood improvements. That result could be attributed, in part, to a reduction in seizures; however, patients who experienced little to no improvement in seizure frequency also have experienced mood improvements,[80,81] suggesting that stimulation of the vagus nerve and parasympathetic nervous system can lead to improvements in mood.

VNS has also been used to treat treatment-resistant depression[82-84] and has been shown to have long-term efficacy.[82,84] Studies on VNS in epileptic patients have shown a decreased blood flow to the amygdala, hippocampus, and cingulated gyri,[85] which suggests that VNS may treat depression by modulating limbic and cortical activity.[86] CRC may be involved in the modulation of the limbic and cortical activity, but further research is needed to examine the phenomenon.

Negative Emotions: Sympathetic Dominance

During negative emotions such as anger, anxiety, frustration, and worry, sympathetic dominance, a lack of coherence, and erratic and unsynchronized oscillations occur.[64,87] For example, studies on depression have found reduced levels of respiratory sinus arrhythmia (RSA), a form of cardiorespiratory synchronization, indicating reduced vagal modulation.[88,89] Similarly, one study found that nondepressed participants experienced increases in RSA and vagal rebound at the resolution of crying, whereas depressed participants did not.[90] Another study found that participants with anxiety disorders exhibited lower levels of metabolic-cardiorespiratory coupling,[91] whereas another study found a decreased HRV in participants experiencing anger and sadness,[65] which is indicative of decreased parasympathetic activation. Those studies suggest that negative emotions can lead to a shift toward sympathetic dominance.

High levels of circulating stress hormones impair working memory and retrieval.[92] Exaggerated amygdala responses are associated with stressed states, such as in anxiety,[93] PTSD,[94] and depression.[95] Anxiety has also been shown to impair cognition.[96] Neuroimaging studies on patients with mood disorders have shown an increased activation of limbic and other emotion-related areas of the brain and decreased activation in areas involved in emotional regulation and higher cognition, such as the frontal lobe. That finding suggests that mood disorders may involve a decreased inhibition of emotional areas of the brain by the frontal regions of the brain.[97] In addition, although amygdala activity varies depending on the mood state of patients with bipolar disorder, the consistently decreased activity of the PFC suggests that the emotional dysregulation and depression seen in mood disorders may be due to the frontal-limbic dysfunction.[98]

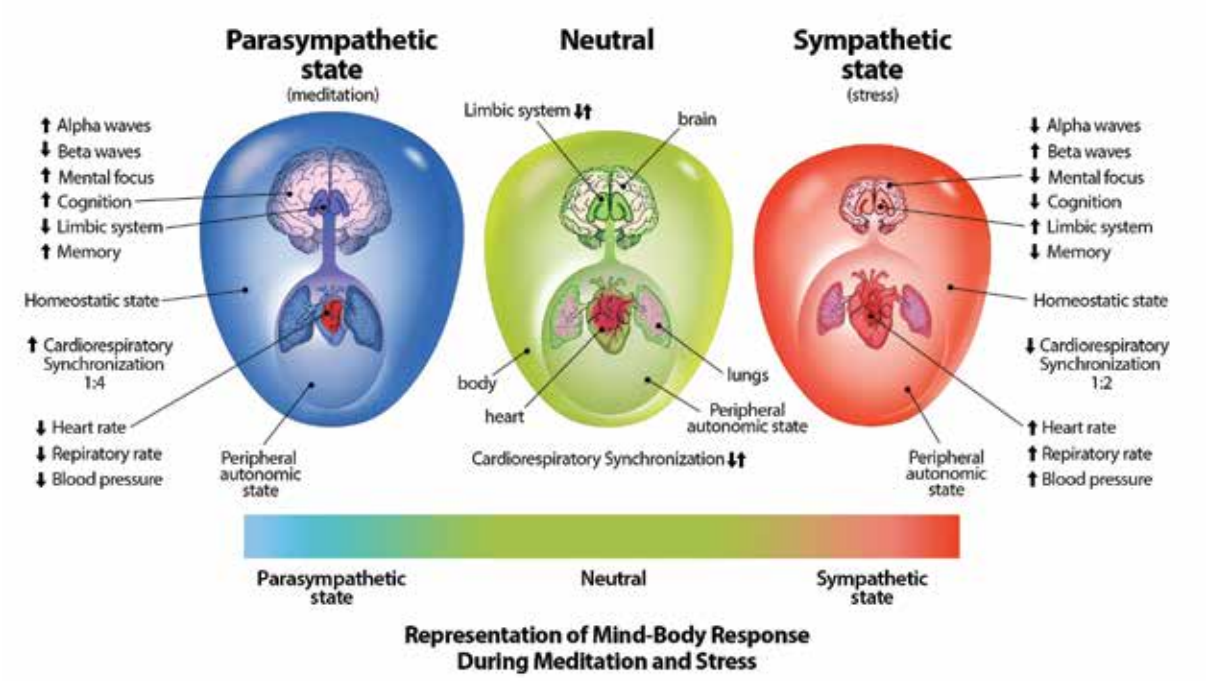
The authors propose that slow, deep breathing and meditation can lead to a shift toward parasympathetic dominance,[6] due in part to increased CRC levels. That increase in CRC may lead to increased synchronization and connectivity within the brain via inhibitory mechanisms and brainstem activity.

MEDITATION

The authors propose a spectrum of corresponding autonomic and emotional states, ranging from a parasympathetic state with high CRC levels during meditation and positive emotional states to a sympathetic state with low CRC levels during stressed and negative emotional states. Increased CRC levels have been consistently observed in many studies on meditation.[99-101] In one study, higher levels of 4:1 and 5:1 CRC were measured in participants practicing meditation as compared with resting controls as were an increase in the number of synchronous epochs and an increase in the total length of synchronizations.[100] In addition, another study showed that advanced practitioners had continuously high CRC levels, even during rapid breathing.[101]

CRC has many potential health benefits, and when coherence deteriorates, the condition may lead to autonomic dysautonomia.[102] In fact, CRC may have restorative effects.[101,103] However, synchronization can occur in different ratios of n:m (ie, heart rate to respiration rate). Therefore, in some studies the synchronization ratios need to be taken into account when examining data regarding increases and decreases in CRC. For

Figure 1. Representations of mind-body response during stress and meditation. The figure illustrates the spectrum of emotional states and the corresponding physiological states. In all states, the largest encompassing oval sphere represents the entire body and a homeostatic state, whereas the large oval inside it represents afferent signaling from the body. At the left end of the spectrum in the parasympathetic meditative state, the heart is smaller to depict a decreased heart rate and increased CRC. The heart and brain are depicted as connected to illustrate the increased synchronization and coherence that occurs in more calm states. The brain is large to show the increased cognitive abilities during the state and the oval representing the afferent signals from the body is smaller in size to depict less-chaotic and more-synchronized signaling. At the far right end of the spectrum in the stressed sympathetic state, the afferent signaling from the body in the interior oval is larger to depict how the brain is dominated and distracted by powerful and chaotic afferent signaling throughout the body. The heart is also larger to show the increased heart rate during the state and the decreased CRC. The brain is smaller to illustrate the decreased cognitive abilities during states of anxiety and stress. In addition, the brain and heart are depicted as separate because many neural and physiological oscillations are desynchronized during the state. Overall, a relaxed mind is associated with decreased excitation and CRC, whereas a stressed or anxious mental state, with highly activated emotional centers in the brain, is associated with more-desynchronized cardiorespiratory rhythms and high excitation throughout the body.



Abbreviation: CRC, cardiorespiratory coherence.

example, a previously mentioned study had found that patients with coronary-artery disease experienced more 2:1 CRC, but that type of CRC is indicative of poorer health than the higher 4:1 ratio seen in healthy patients.[29]

Some studies have shown that individuals can cultivate positive emotions through the practice of compassionate meditation and that their practice can alter the activation of networks associated with empathy and the mind.[104] Well-being and a positive affect are associated with left-prefrontal activation, modulation of activation in the amygdala, and fast recovery when faced with stressful events.[9] In addition, those patterns of well-being are associated with lower levels of basal cortisol and higher immune responses. Practice of meditation and similar techniques may shift practitioners toward a more positive affect and a state of well-being, accompanied by the associated neurological changes and health benefits.[9]

The authors propose that CRC may be one of the mechanisms that underlie those changes and that meditation and similar techniques could be used to increase well-being and treat stress and anxiety disorders. In comparison, stress leads to neurological and physiological changes, such as activation of the PFC, changes in its glucose metabolism, and increases in salivary cortisol[105] as well as numerous other effects.[106]

Studies on meditation have shown that practitioners show increased memory,[107] enhanced cognitive function and brain plasticity,[108] and sustained attention.[109] Even brief meditation training has been shown to improve working memory, visuospatial processing, and executive functioning.[110] A study on loving-kindness meditation has shown that it can induce increases in positive emotions, increase mindfulness, and decrease illness symptoms.[111] During dhyana meditation, changes in autonomic variables and breathing, including decreases in low-frequency and increases in high-frequency HRV, have suggested increased parasympathetic and decreased sympathetic activity.[112] Another study found that transcendental meditation (TM)

can modify the activity of the ascending, reticular activating system and influence autonomic centers in the brainstem, thus affecting cardiorespiratory activity.[113]

Increased alpha-phase synchrony has been shown during TM.[114] Palva and Palva's[115] study has suggested that alpha synchrony can contribute to cognitive functions, whereas Dubovik et al[116] found that decreases in alpha synchrony correlated with declines in cognitive function. Cover et al[117] found that such decreases correlated with neurological disorders such as multiple sclerosis. Another study found that parietal peak alpha power and alpha power lagged coherence (ie, volume conduction corrected coherence) but that both increased with heart coherence during autogenic meditation, when compared with baseline.[118]

Kim et al[118] found that the strong correlation of heart coherence with EEG alpha activity and increased synchronization between the heart and brain can help to restore physiological synchrony. That activity also suggested to those researchers the possibility that harmonic oscillatory activity existed between the 10-Hz alpha oscillations and 0.1-Hz cardiorespiratory oscillations.

Lutz et al[119] found that gamma synchrony was associated with cognitive processing, and long-term Buddhist practitioners showed increases in high-amplitude gamma synchrony during meditation. That finding suggested to the researchers that neural synchrony is a temporal integrative mechanism that underlies meditation and that meditation can lead to both short- and long-term neural changes. In addition, they proposed that the increase in gamma synchrony could reflect a change in moment-to-moment awareness and consciousness in those practitioners.

Transient coupling between low-frequency theta oscillations and high-frequency gamma oscillations has been shown to coordinate activity during cognitive processing,[120] and coupling between theta and gamma oscillations is a well-documented phenomenon.[120,125] Gamma synchrony has been associated with attention, learning, and conscious perception,[121] and theta and alpha oscillations have been associated with cognitive and memory processes.[122] Gamma oscillations tend to arise from coordinated excitation and inhibition, and those rhythms can be modulated by slower oscillations.[123]

EEG-neurofeedback training that raises the theta/alpha-wave ratio has been shown to reduce anxiety, depression, and PTSD as well as increase creativity.[124] Alpha and theta waves increase connectivity between the frontal lobe and other areas throughout the cortex and are likely involved in the increased focus, memory, and plasticity and the decreased anxiety and sympathetic activation experienced during meditation.[124] Studies on meditation have shown increased alpha-wave[125,126] and decreased beta-wave activity.[127]

In addition, the improved cognition and emotional regulation seen in meditators is likely due to the GABA-modulated cortical inhibition that occurs during meditation.[128] Decreased amygdala activity has also been found during meditation,[129] and in individuals trained in meditation, that decrease occurs even when they are in nonmeditative states.[130] One study found that after 8 weeks of mindfulness-based, stress-intervention training, participants had an increase in brainstem grey matter that correlated with enhanced psychological well-being.[131] That increase occurred in brainstem areas involved in mood and arousal, such as the pons, nucleus raphe pontis, and locus coeruleus. Last, chronic obstructive pulmonary disease has been associated with high levels of anxiety and depressive symptoms, and those symptoms are greatly reduced with rehabilitation programs that include various forms of respiratory therapy and exercise with oxygen supplementation.[132]

Although direct evidence is lacking on the effects of CRC on emotions and widespread synchronization, the many available studies provide a wealth of indirect evidence. For example, anxiety states, which are associated with rapid breathing, can be diminished by techniques using slow, deep breathing, such as meditation. That fact may demonstrate that feedback from CRC can modulate the ANS and emotions; however, direct studies are needed to confirm that possible mechanism.

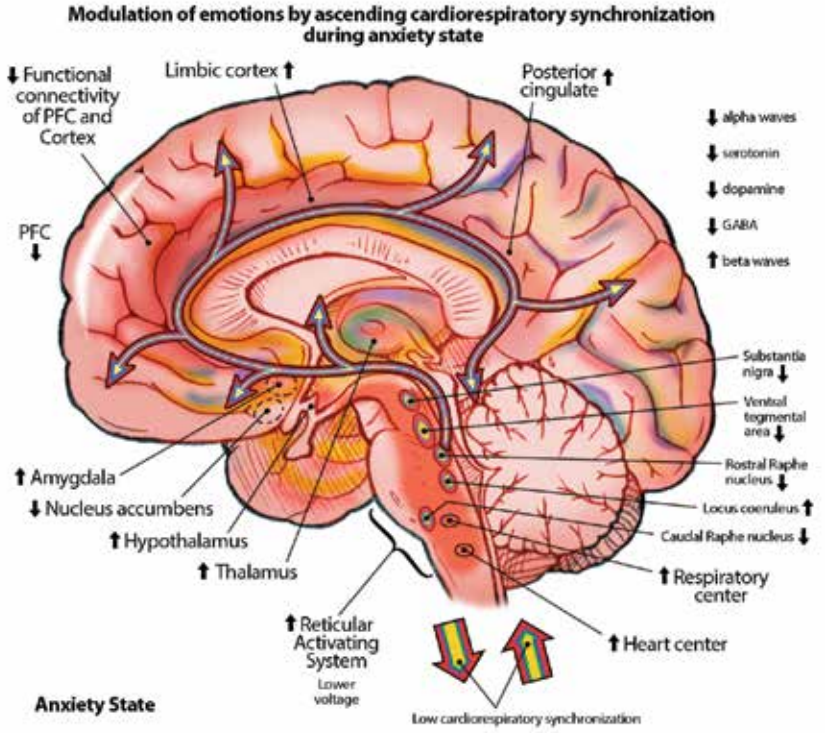
In a recently published paper, the authors discussed how CRC may modulate the ANS via changes in the cellular membrane,[8] and they propose that the cardiorespiratory system's modulatory effects on emotions may work via a similar mechanism. The authors emphasize that efferent signaling is also highly involved in those processes, but it is likely that the afferent signaling from slow, deep breathing and the subsequent increase in CRC levels are involved in the modulation of the ANS and the neuronal signaling that leads to the changes seen during various meditative and relaxation techniques.

NEURAL CORRELATES AND NEUROTRANSMITTERS

The brainstem contains nuclei that control respiration and cardiovascular physiology as well as nuclei that release neurotransmitters that modulate brain activity, yet the brainstem is not readily associated with modulating emotions. It has also been difficult to identify and distinguish the direct effects of cardiorespiratory signals on the brainstem and the subsequent effects on emotions. The modulating effect of emotions on the respiratory and cardiovascular systems is well-established,[19] but the effects of cardiorespiratory signals on emotions via afferent signaling from the brainstem remain poorly researched. However, cortical and limbic areas have been shown to communicate efferent and afferent directions to respiratory centers of the brainstem.[19,26,27]

The authors propose that CRC feedback to the brainstem modulates brainstem activity via neurotransmitter release, which modulates the activity of the limbic system and other emotional areas of the brain. In addition, slow, deep breathing and increased CRC may enhance changes to the global inhibitory membrane that can occur during inspiration.[133] That inhibitory mechanism may underlie the possible inhibition of emotional areas of the brain by CRC. Jerath et al[134] provides a more detailed review of that related mechanism.

Figure 2. Modulation of emotions by ascending CRC during the anxiety state. The figure illustrates the widespread activation of the emotion-related areas of the brain when low CRC levels exist (ie, the levels are not strong enough to cause inhibition). Decreases in the activity in the rostral raphe nucleus and caudal raphe nucleus occur that result in lower levels of serotonin and decreases in activity in the ventral tegmental area, substantia nigra, and nucleus accumbens. That decreased activity results in lower levels of dopamine. Increases in the activity in the locus coeruleus also result in higher levels of norepinephrine being released. Decreases also occur in the inhibitory neurotransmitter GABA. Alpha waves, which are associated with relaxed mental states, decrease, and beta waves, which are associated with anxiety, increase. Also, the functional connectivity of the PFC and other cortical areas decreases, and activity throughout the limbic system increases. The available evidence lends support to the hypothesis that low CRC levels are unable to inhibit the activity of the emotion-related areas of the brain; rather, an increased heart rate and respiration rate and increased desynchronization result in a feedback loop that leads to increased activation of the emotion-related areas.



Abbreviations: CRC, cardiorespiratory coherence; GABA, γ-aminobutyric acid; PFC, prefrontal cortex.

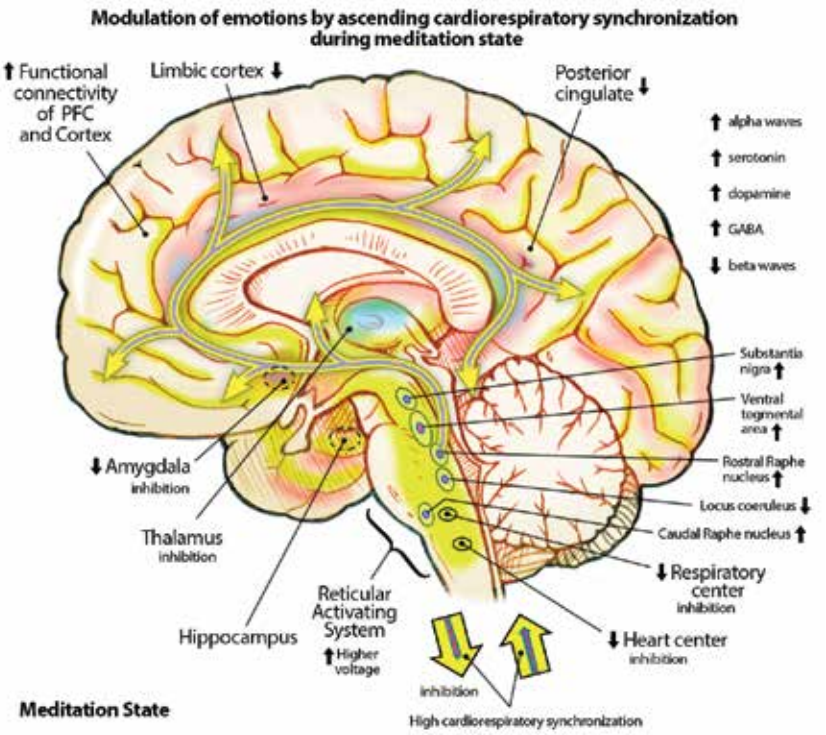
Discussing the involvement of specific neurotransmitters with various states of emotion requires first identifying the relevant brainstem nuclei and their associated neurotransmitters. The rostral and caudal raphe nuclei, in the midline of the brainstem, are the main components of the serotonergic system.[135] The ventral tegmental area[136] and the substantia nigra in the midbrain,[137] together with the nucleus accumbens in the basal forebrain,[138] are the main brainstem areas involved in the dopaminergic system. The nucleus basalis[139,140] is involved in the cholinergic system, whereas the pedunculopontine nucleus is involved in the cholinergic and GABAergic systems.[141]

The direct modulation of brain activity by respiration has not been well studied, but the association of specific neurotransmitters with emotional states has. The authors propose that varying CRC levels during different autonomic and emotional states may modulate brainstem and brain activity, although CRC would make up only a portion of the many mechanisms that influence brain activity and emotions. A study using EEG dipole tracing found that 350 to 400 ms after the onset of inspiration, respiration-related anxiety potentials (RAPs) were detected in limbic areas of the brain.[142] In addition, as respiration increased in the study, so did the RAPs. The study illustrates the direct modulating effect that respiration can have on limbic areas and emotion.

In addition, in another study,[143] aggressive behavior has been associated with decreases in serotonin, and decreases in serotonin leads to dysregulation and hyperfunction of the dopamine system.[146] Such behavior has also been linked to increases in acetylcholine and decreases in GABA.[144] That imbalance in the regulatory systems in the PFC, as well as the hypersensitivity of the amygdala and other limbic areas, results in aggressive acts resulting from provoked anger.[144]

Decreased levels of serotonin[145] and dopamine[146] have been associated with depression and with increased levels of acetylcholine in the hippocampus, whereas dysregulation of the cholinergic system has been shown to induce depression-like and anxiety-like symptoms.[147] Low levels of serotonin[148]

Figure 3. Modulation of emotions by ascending CRC during the meditative state. The figure illustrates the widespread inhibition of the emotion-related areas of the brain, due in part to high CRC levels during meditation. Increases in activity in the rostral raphe nucleus and caudal raphe nucleus occur, resulting in increases in serotonin and in activity in the ventral tegmental area, substantia nigra, and nucleus accubens. That increased activity results in increases in dopamine. Activity in the locus coeruleus decreases, resulting in decreased release of norepinephrine. Increases in the inhibitory neurotransmitter GABA also occur. Alpha waves, which are associated with relaxed mental states, increase, and beta waves, which are associated with anxiety, decrease. The functional connectivity of the PFC and other cortical areas increases and activity throughout the limbic system decreases. Evidence supports the hypothesis that high CRC levels can modulate the activity of the emotion-related areas of the brain via the ascending projections of the reticular activating system as well as the release of neurotransmitters from the many nuclei of the brainstem.



Abbreviations: CRC, cardiorespiratory coherence; GABA, γ-aminobutyric acid; PFC, prefrontal cortex.

and decreased levels of dopamine have been associated with stress and anxiety.[149] Dopamine likely plays a role in coping with stress,[150] and it has been found that a greater dopamine-storage capacity in the amygdala can contribute to a person's tendencies toward experiencing events as less stressful or less anxiety inducing.[151] Decreased levels of the inhibitory neurotransmitter GABA are also associated with stress and anxiety,[152] and stress has been shown to have short- and long-term effects on GABA receptors.[153] In addition, during transient sadness, widespread activation of the limbic system and paralimbic structures such as the cingulated cortex occurs, and activity in the thalamus and brainstem increases. In contrast, during transient happiness, a widespread decrease in activity occurs throughout the cortex.[154]

Happiness activates the ventral striatum,[155] which contains the nucleus accubens of the dopaminergic reward system.[156] Anger activates the ventral pallidum, a component of the limbic loop.[155] During meditation, feelings of contentment are associated with deactivation of the posterior cingulated cortex, whereas feelings of discontent and distraction are associated with activation of the posterior cingulate cortex.[157] Happiness is associated with increased levels of serotonin[158] and levels of serotonin in the amygdala and orbitofrontal cortex modulate positive emotions.[159] In addition, serotonin-reuptake inhibitors (SSRIs), which increase serotonin functioning by inhibiting the reuptake of serotonin in the brain, are widely used to treat depression.[160] In addition, dopaminergic signaling is involved in reward-and-pleasure pathways[161,162] in the brain.

TM has been shown to increase levels of serotonin and decrease levels of epinephrine and norepinephrine.[163] A study on SSRIs found that prolonged SSRI treatment enhanced serotonin's tonic inhibition of locus coeruleus (LC) norepinephrine neurons, suggesting that increases in serotonin from treatments other than SSRIs, such as meditation, may decrease norepinephrine neuronal activity as well.[164] In addition, respiration has been shown to modulate the membrane potentials of LC neurons, suggesting that respiration may affect the release of norepinephrine and modulate limbic-system activity.[165] Studies on the modulation

of brainstem activity by respiration have occurred,[166,167] but not in terms of affecting emotions. Meditation has also been shown to increase dopamine tone,[168] increase GABA cortical inhibition,[128] and lower levels of the stress hormone cortisol.[169,170]

CONCLUSIONS

At present, the pathophysiology of stress, anxiety, and various psychiatric disorders are considered to be limited to the brain and have implicated dysfunctions of various neurotransmitters and receptors. Current primary treatments consist of potent medications, which may have harsh side effects, as well as time-consuming and expensive cognitive therapies. Recently, clinical studies have revealed a vital link between low CRC levels and anxiety, depression, and other psychiatric disorders. Based on our review of CRC during anxiety, various other emotional states, psychiatric disorders, and different forms of meditation, ascending visceral impulses to the brainstem, may play a significant role in modulating mental states.

The current authors present a spectrum of associated autonomic and emotional states, ranging from parasympathetic states with high CRC levels and with positive emotions that are seen during meditation and sympathetic states with low CRC levels that are seen during stressed and negative emotional states. The current article illustrates the vital link between the mind and body during health and diseased states. Brain activity is subject to visceral and peripheral input via the brainstem, and, as a result, the brain and body act as 1 unit.

During the experience of emotions, modulation of the ANS involves widespread sympathetic and parasympathetic homeostatic changes. The authors propose that modulation of the limbic system and emotions by afferent signaling from the body via the brainstem is carried out, in part, by synchronized cardiorespiratory oscillations. Future research and treatment of anxiety, depression, and other mental disorders may benefit from applying an alternative approach.

The use of techniques such as pranayama, meditation, and present-moment stress-reduction programs as tools for the successful treatment of anxiety, depression, and other mental disorders has been supported by a wealth of studies; however, the underlying mechanisms by which these techniques work are not well understood. The authors propose that those deep breathing and relaxation techniques work by modulating visceral afferent signaling, such as cardiorespiratory oscillations, which subsequently modify the ANS, brainstem, limbic, and cortical areas of the brain. Future research on that mechanism, which addresses the pathophysiology of the entire body and brain, rather than one that uses an approach based solely on neurotransmitters, may help in the development of improved treatments for chronic stress, anxiety, and emotional disorders.

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