Neurocardiology through the Lens of the Polyvagal Theory

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Abstract

This chapter describes Polyvagal Theory as a theoretical framework to expand the scientific and clinical research in neurocardiology. The Polyvagal Theory describes an autonomic nervous system that regulates the heart, which is influenced by the central nervous system, sensitive to afferent influences, characterized by an adaptive reactivity dependent on the phylogeny of the neural circuits, and interactive with source nuclei in the brainstem regulating the striated muscles of the face and head. The theory emphasizes the evolutionary and developmental shifts in neural regulation of the heart in vertebrates. The theory is dependent on accumulated knowledge describing the phylogenetic transitions in the vertebrate autonomic nervous system. Its focus is on the phylogenetic shift between reptiles and mammals that resulted in specific changes to the vagal pathways regulating the heart. As the source nuclei of the primary vagal efferent pathways regulating the heart shifted from the dorsal nucleus of the vagus in reptiles to the nucleus ambiguus in mammals, a face–heart connection evolved with emergent properties of a social engagement system that would enable social interactions to regulate visceral state and visceral dysfunctions to be manifested in the neural regulation of the heart.

1. The brain-body connection in medicine

Knowledge and experience frame our perspective of how the brain and the autonomic nervous system interact. What we are taught influences how we form research questions and test hypotheses. As understanding of the neurophysiology of the autonomic nervous system expands, it changes the scope of inquiry. New knowledge slowly permeates medical education and even more slowly impacts how clinicians understand and treat conditions.

The conceptualization of the autonomic nervous system within medical education has not kept the pace of the neurophysiological research expanding our understanding of bidirectional connections between the brain and visceral organs. Medical education provides few opportunities to learn how neural circuits in the brain regulate peripheral organs and even fewer opportunities to learn how peripheral organs influence brain function. This limited knowledge results in many physicians not understanding the potential pathways that would promote health or result in dysfunction. When diagnoses are negative and there is no measurable functional or structural manifestation in the organ, a lack of understanding the role of the bidirectional neural communication between the brain and visceral organs may result in the physician assuming that patient's symptoms are not credible.

Medical specialties are organ focused, resulting in disciplines that study the organ and not the neural regulation of the organ. In addition, when there is a more general 'system' dysfunction in neural regulation, this strategy may result in the appearance of dysfunction in more than one organ (i.e., comorbidities). Frequently, the assessment of an organ, without a concrete metric of disruption of function, assumes that the disorder is not physiologically based and is solely psychological. This conclusion limits the support and treatment that the clinician can provide and places the patient at risk. Several disorders have been assumed to have

psychological components, since the neural pathways are not known and the intensity of symptoms is frequently linked to stressful situations.

A primary objective for 'integrating' disciplines, such as neurocardiology, is to objectively describe the relationship between the nervous system and visceral organs. However, for those who study the neural regulation of the heart and other visceral organs, there is a shared knowledge that brain structures and peripheral organs are interconnected through neural pathways that send signals from visceral organs to the brainstem and from the brainstem to the visceral organs. These bidirectional communication circuits provide dynamic regulatory mechanisms through which brain structures influence visceral organs and visceral organs inform and influence brain function. This premise is the basis of Polyvagal Theory and an important assumption in neurocardiology.

2. Historical perspectives on the brain-body connection

The contemporary conceptualization of bidirectional communication between visceral organs and the brain is rooted in the work of Walter Hess. In 1949 Hess was awarded the Nobel Prize in Physiology/Medicine for his paradigm shifting work on the central control of visceral organs. His Nobel lecture discussing brain control of visceral organs was entitled *The Central Control of the Activity of Internal Organs*[1]. The first paragraph of his Nobel Prize speech is both prescient and historical. It provides the context upon which development, application, and acceptance of neuro-autonomic disciplines, such as neurocardiology, have emerged. This context provides the contradictory values of encouraging a better understanding of the dynamics of neural regulation of an integrated nervous system, while being constrained by reductionistic experimental methods and limited paradigms.

> *A recognized fact, which goes back to the earliest times, is that every living organism is not the sum of a multitude of unitary processes, but is, by virtue of interrelationships and of higher and lower levels of control, an unbroken unity. When research, in the efforts of bringing understanding, as a rule examines isolated processes and studies them, these must of necessity be removed from their context. In general, viewed biologically, this experimental separation involves a sacrifice. In fact, quantitative findings of any material and energy changes preserve their full context only through their being seen and understood as parts of a natural order. This implies that the laws governing organic cohesion, the organization leading from the part to the whole, represent a biological uncertainty, indeed an uncertainty of the first order. It becomes all the more acute, the more rapidly the advances of specialization develop and threaten the ability to grasp, or even to appreciate it. While this state of affairs has just been referred to, our subject is defined by its general content. In particular it deals with the neural mechanisms by which the activity of the internal organs is adapted to constantly changing conditions, and by which they are adjusted to one another, in the sense of interrelated systems of functions. It only remains to be added that broadening of our knowledge in these respects is of benefit not only with regard to the human compulsion to understand, but also to the practical healing art. For man also, in health and sickness, is not just the sum of his organs, but is indeed a human organism.*[1]

Hess's view of an integrated nervous system involving the mutual and dynamic bidirectional interactions between the brain and visceral organs did not receive traction within

traditional medical education. In contrast, medical education confirmed Hess's view that advances in specialization resulting in medical subdisciplines threaten the ability to appreciate the organization from an organ to the integrated organism.

Few physicians are familiar with Hess's landmark research and his warning against partitioning the body into central and peripheral nervous systems. From Hess's perspective there is only one integrated nervous system. Instead of incorporating Hess's prescient view, medical education remained dependent on an earlier and more limited view of the autonomic nervous system proposed by Langley; a model proposed in 1921, which has remained the predominant model taught in medical schools[2]. If you doubt this, ask a cardiologist, a nephrologist, a hepatologist, a gastroenterologist, or even a more eclectic internist, if specific neural pathways could contribute to symptoms of dysfunction. If they are in agreement, ask them what 'neural' test would confirm this speculation. In addition, ask the specialist if anxiety, depression, or chronic stress could be a function of or the cause of an organ dysfunction. Also inquire about the possibility that medical treatments to peripheral organs could, via afferent feedback from the organ to the brain, contribute to the specific symptoms experienced. These inquiries will provide an understanding of the massive gaps in our knowledge involving the role of the nervous system in health and illness.

Langley was a distinguished professor of physiology at the University of Cambridge. In 1898 he proposed the term autonomic nervous system "to describe the sympathetic system and the allied nervous system of the cranial and sacral nerves, and for the local nervous system of the gut" (p. 270)[3]. Collectively, the autonomic function of the cranial and sacral nerves defined the parasympathetic nervous system and the nervous system of the gut became known as the enteric nervous system. In the first paragraph of his classic text, The Autonomic Nervous System Part I,

he clearly provided his definition of the autonomic nervous system[2]. He stated that "the autonomic nervous system consists of the nerve cells and nerve fibres, by means of which efferent impulses pass to tissues other than multi-nuclear striated muscle."

Langley's view of the autonomic nervous system consists of efferent pathways and target organs in the viscera, a top-down model excluding both the brain structures involved in regulation or the afferent pathways communicating peripheral organ status back to the brain. In fact, the Langley model does not include the requisite components of a 'system' capable of regulation through feedback. Such a system would require a central regulator connected to a target structure via both motor and sensory pathways. The Langley model disrupted the expanding view of an integrated 'whole body' nervous system proposed by Bernard[4] and described by Darwin[5] characterized by bidirectional communication between the brain and the visceral organs.

A naive treatment of autonomic responses without the consequential influence of afferent feedback is consistent with Langley's definition[2] of a limited autonomic nervous system excluding the influence of the sensory fibers that accompany most visceral motor fibers. Although the definition is often expanded to include both visceral afferents and central structures (e.g., medulla, hypothalamus), contemporary textbooks focus on the motor components, minimizing in their description the important role of afferent and central contributions to the regulation of the peripheral autonomic organs. This bias, by ignoring the importance of the afferent pathways, neglects the feedback and central regulatory features of a functional system. Moreover, it limits the study of the dynamic regulatory function of the autonomic nervous system, since the regulation of visceral state and the maintenance of homeostasis implicitly assume a feedback system with the necessary constituent components of motor, sensory, and

regulatory structures. Thus, from a systems perspective, the autonomic nervous system includes afferent pathways conveying information regarding the visceral organs and the brain areas that interpret the afferent feedback and exert control over the motor output back to the visceral organs.

Darwin[5] provided historical insight into the potential importance of the vagus in bidirectional communication between the brain and the heart. Although Darwin focused on facial expressions in defining emotions, he acknowledged the dynamic relationship between the vagus and the central nervous system activity that accompanied the spontaneous expression of emotions. He speculated that there were identifiable neural pathways that provided the necessary communication between specific brain structures and peripheral organs to promote the unique pattern of autonomic activity associated with emotions. For example:

> *...when the mind is strongly excited, we might expect that it would instantly affect in a direct manner the heart; and this is universally acknowledged ... when the heart is affected it reacts on the brain; and the state of the brain again reacts through the pneumogastric [vagus] nerve on the heart; so that under any excitement there will be much mutual action and reaction between these, the two most important organs of the body. (p.69)*

For Darwin, when an emotional state occurred, the beating of the heart changed instantly (i.e., via vagal efferents) and the change in cardiac activity influenced brain activity (i.e., via vagal afferents). He did not elucidate the neurophysiological mechanisms that translate the initial emotional expression to the heart. Our current knowledge of brainstem anatomy and the

neurophysiology of the vagus were not available to Darwin. At that time, it was not known that vagal fibers originate in several medullary nuclei and that the branches of the vagus exert control over the periphery through different feedback systems. However, Darwin's statement is important, because it emphasizes the afferent feedback from the heart to the brain, independent of the spinal cord and the sympathetic nervous system, and the regulatory role of the pneumogastric nerve (renamed the vagus at the end of the 19th century) in the expression of emotions.

Darwin attributed these ideas to Claude Bernard as an example of nervous system regulation of *le milieu interieur* ("the environment within"). Consistent with more contemporary psychophysiology and neurocardiology, Claude Bernard viewed the heart as a primary response system capable of reacting to all forms of sensory stimulation. He explicitly emphasized the potency of central nervous system pathways to the heart[6]. These pathways may be assumed to travel through the vagus. These ideas are expressed in the following observation by Claude Bernard:

> *In man the heart is not only the central organ of circulation of blood, it is a center influenced by all sensory influences. They may be transmitted from the periphery through the spinal cord, from the organs through the sympathetic nervous system, or from the central nervous system itself. In fact the sensory stimuli coming from the brain exhibit their strongest effects on the heart. (p. 118)*[6]

Bernard and Darwin, by appreciating the importance of afferent feedback in the neural regulation of the heart, may serve as historic founders of neurocardiology.

Langley was not alone in minimizing the potential bidirectional communication between visceral organs and the brain. Walter Cannon, another iconic physiologist, proposed that the autonomic responses associated with emotions were driven primarily by brain structures and transmitted through sympathetic-adrenal pathways to support fight-flight behaviors[7]. Cannon's view contradicted William James, who proposed that it was the afferent feedback from the body that framed the emotional experience[8]. Cannon's view was readily accepted and merged with the views of Hans Selye[9, 10] to dominate contemporary views of stress physiology. Perhaps James's lack of physiological sophistication and an inability to describe the neural pathways through which the afferent feedback traveled from the periphery to the brain contributed. The generalized stress responses described by Cannon and Selye emphasized the sympathetic nervous system and the adrenals. These views minimized the role of the vagus and did not acknowledge the primary role of afferent vagal pathways, as a surveillance system in physiological and emotional regulation, communicating organ status to brain structures.

As researchers attempt to communicate and translate findings and conceptualizations into clinical practice, they continue to be confronted with the products of a medical education that conceptualized the autonomic nervous system within the limitations of the Langley definition. This restricted model influenced physicians' general understanding and conceptualization of the communication between the brain and visceral organs. At best, physicians acknowledge the top-down communication from brain to organ. Although virtually all physicians have limited knowledge about the afferents monitoring visceral organs and informing the brain centers that regulate the organs.

The Langley model, in part, has been misunderstood, since its contribution represented important progress by providing an organizing principle to the efferent regulation of visceral

organs. It was not proposed as an alternative to the more integrative features of visceral regulation proposed 50 years earlier by Bernard. From a historical perspective, it is important to reconcile these discontinuities as the science and clinical practice become reintegrated into neuro-autonomic disciplines such as neurocardiology. It was in search of a more integrative model of the neural regulation of the autonomic nervous system that the Polyvagal Theory emerged[11, 12, 13, 14, 15, 16].

3. The Vagal Paradox: Origin of the Polyvagal Theory

Polyvagal Theory emerged from a paradox observed while studying heart rate patterns in human fetuses and newborns. In obstetrics and neonatology bradycardia is a clinical index of risk and assumed to be mediated by the vagus. With the same clinical populations beat-to-beat heart rate variability is a clinical index of resilience and also is assumed to be mediated by the vagus. If cardiac vagal tone is a positive indicator of health of a fetus or neonate when monitored with heart rate variability, then how could vagal tone be a negative indicator of health when it is manifested as bradycardia? Animal research demonstrated that both signals could be disrupted by severing the vagal pathways to the heart or via pharmacological blockade (i.e., atropine) interfering with the inhibitory action of the vagus on the sino-atrial node[11].

The resolution to the paradox came from the observation that through the evolution of the vertebrate autonomic nervous system, mammals evolved with two vagal efferent pathways. One has a respiratory rhythm, is uniquely mammalian, is myelinated, originates in an area of brainstem known as nucleus ambiguus, travels primarily to organs above the diaphragm, and interacts within the brainstem with structures regulating the striated muscles of the face and head. The other does not have a respiratory rhythm, is observed in virtually all vertebrates, is

unmyelinated, travels primarily to organs below the diaphragm, and originates in an area of the brainstem known as the dorsal nucleus of the vagus.

4. Respiratory Sinus Arrhythmia (RSA): An index of cardiac vagal tone

To explore the distinction between vagal mediated bradycardia and vagal mediated heart rate variability, we need to understand the neural mechanisms mediating both responses through the vagus. The mechanism producing massive bradycardia is well understood as a surge of vagal inhibition of the sino-atrial node and can be mimicked by electrical stimulation of the vagus directly or indirectly via brainstem areas. Validation experiments using similar protocols are unable to distinguish between the tonic background vagal activity and the vagal activity due to the acute stimulation. Nor are the stimulation studies able to selectively distinguish between myelinated and unmyelinated vagal pathways. Moreover, the manipulation of acute changes in vagal efferent activity does not provide insight into the mechanisms that produce tonic variations in heart rate variability.

In healthy mammals, the heart does not beat at a constant rate. Although intrinsic firing rate of the sino-atrial node, the heart's pacemaker, may be relatively fixed, this rate is modulated by the transitory inhibition of the pacemaker by vagal pathways. When the spontaneous respiration rate is manifested in the heart rate pattern it is called respiratory sinus arrhythmia (RSA).

References to RSA were made in the early 1900s. Wundt stated that "respiratory movements are … regularly accompanied by fluctuations of the pulse, whose rapidity increases in inspiration and decreases in expiration."[17] Hering reported the functional relation between the amplitude of RSA and cardiac vagal tone[18]. Hering reported that breathing provided a functional

test of the vagal control of the heart. Hering stated, "It is known with breathing that a demonstrable lowering of heart rate is indicative of the function of the vagi." Contemporary neurophysiology supports these early reports[19]. Since the neural mechanisms mediating RSA are well understood as the functional output of myelinated efferent vagal pathways, our research has focused on RSA and not on other metrics of heart rate variability, the origins of which have yet to be clearly defined.

5.1 Polyvagal Theory: Phylogenetic shifts in vertebrate autonomic nervous systems

By tracking the evolutionary changes in vertebrates, a phylogenetic pattern emerges in which two vagal pathways to the heart evolved in mammals. This pattern could be described as three evolutionary stages during which neural circuits evolved to regulate the heart. During the first stage vertebrates relied on an unmyelinated vagus with efferent pathways originating in an area of the brainstem resembling the dorsal vagal complex, containing the origin of efferent and the termination of afferent pathways. As vertebrates evolved, a spinal sympathetic nervous system developed. Finally, with the emergence of mammals there was a transition in how the autonomic nervous system was regulated. During this transition some of the cells of origin of the vagus migrated from the dorsal nucleus of the vagus to the nucleus ambiguus. During this evolutionary process, many of the vagal efferent fibers originating in the nucleus ambiguus became myelinated and integrated in the function of the brainstem regulation of special visceral efferent pathways, which regulated the striated muscles of the face and head. Interestingly, Langley hypothesized a phylogenetic shift in the vagal fibers consistent with this description in the Polyvagal Theory[2, 11]:

> *The hypothesis I would suggest as to the proximate cause of the existence of the two kinds of nerve fibres is that cells with non-medullated [unmyelinated] fibres were the first in phylogeny to migrate from the central nervous system, a later migration occurring when a further specialisation of the central nervous cells had occurred, and that the cells of this migration gave rise to medullated [myelinated] fibres. On this hypothesis, the two forms of embryonic cells have persisted to a varying degree in different vertebrates, each form giving rise to its own kind of axon [page 25].*[2]

In mammals, the unmyelinated vagal pathways originating in the dorsal nucleus of the vagus primarily regulate the organs below the diaphragm, though some of these unmyelinated vagal fibers terminate on the sino-atrial node. Polyvagal Theory hypothesizes that these unmyelinated vagal fibers primarily remain dormant until life threat and are probably potentiated during hypoxia and states in which the influence of the myelinated vagal input to the heart is depressed. This sequence is observable in human fetal heart rate, when bradycardia are more likely to occur when the tonic influence of the myelinated vagal pathways, manifested in RSA, is low[20].

In ancient vertebrates, an unmyelinated vagal pathway emerging from the brainstem was a critical component of the neural regulation of the entire viscera. This bidirectional system reduced metabolic output when resources were low, such as times of reduced oxygen. The nervous systems of primitive vertebrates did not need much oxygen to survive and could lower heart rate and metabolic demands when oxygen levels dropped. Thus, this circuit provided a conservation system that in mammals was adapted as a primitive defense system manifested as death feigning and trauma-driven responses of syncope and dissociation. Because this defense

system could be lethal in oxygen-demanding mammals, it functioned as the last option for survival. The phylogenetically older unmyelinated vagal motor pathways are shared with most vertebrates and, in mammals when not recruited as a defense system, function to support health, growth, and restoration via neurally regulation of subdiaphragmatic organs (i.e., internal organs below the diaphragm).

The myelinated vagal circuit with efferents originating in a brainstem area called the nucleus ambiguus is uniquely mammalian. The "newer" myelinated vagal motor pathways regulate the supradiaphragmatic organs (e.g., heart and lungs) and are integrated in the brainstem with structures that regulate the striated muscles of the face and head via special visceral efferent pathways resulting in a functional social engagement system. This newer vagal circuit slows heart rate and supports states of calmness.

5.2 Polyvagal Theory: The Emergence of the Social Engagement System –

The integration of the myelinated cardiac vagal pathways with the neural regulation of the face and head gave rise to the mammalian social engagement system. As illustrated in Figure 1, the outputs of the social engagement system consist of a somatomotor component and a visceromotor component. The somatomotor component involves special visceral efferent pathways that regulate the striated muscles of the face and head. The visceromotor component involves the myelinated supradiaphragmatic vagus that regulates the heart and bronchi. Functionally, the social engagement system emerges from a heart–face connection that coordinates the heart with the muscles of the face and head. The initial function of the system is to coordinate sucking-swallowing-breathing-vocalizing. Atypical coordination of this system early in life is an indicator of subsequent difficulties in social behavior and emotional regulation.

INSERT FIGURE 1 ABOUT HERE

Figure 1 The Social Engagement System

Figure 1 caption: The social engagement system consists of a somatomotor component (solid blocks) and a visceromotor component (dashed blocks). The somatomotor component involves special visceral efferent pathways that regulate the striated muscles of the face and head, while the visceromotor component involves the myelinated vagus that regulates the heart and bronchi.

When full engaged, two important biobehavioral features of this system are expressed. First, bodily state is regulated in an efficient manner to promote growth and restoration (e.g., visceral homeostasis). Functionally, this is accomplished through an increase in the influence of myelinated vagal motor pathways on the cardiac pacemaker to slow heart rate, inhibit the fight-or-flight mechanisms of the sympathetic nervous system, dampen the stress response system of the hypothalamic–pituitary–adrenal axis (responsible for cortisol release), and reduce inflammation by modulating immune reactions (e.g., cytokines)[14]. Second, the phylogenetically mammalian face–heart connection functions to convey physiological state via facial expression and prosody (intonation of voice) as well as regulate the middle ear muscles to regulate listening frequency response[14, 15, 16, 21, 22].

The brainstem source nuclei of the social engagement system are influenced by higher brain structures (i.e., top down influences) and by visceral afferents (i.e., bottom up influences). Direct corticobulbar pathways reflect the influence of frontal areas of the cortex (i.e., upper

motor neurons) on the medullary source nuclei of this system. Bottom up influences occur via feedback through the afferent vagus (e.g., tractus solitarius), conveying information from visceral organs to medullary areas (e.g., nucleus of the solitary tract) and influencing both the source nuclei of this system and the forebrain areas that are assumed to be involved in several psychiatric disorders[22, 23, 24]. In addition, the anatomical structures involved in the social engagement system have neurophysiological interactions with the HPA axis, the social neuropeptides (e.g., oxytocin and vasopressin), and the immune system[25, 26].

Afferents from the target organs of the social engagement system, including the muscles of the face and head, also provide potent afferent input to the source nuclei regulating both the visceral and somatic components of the social engagement system. The source nucleus of the facial nerve forms the border of nucleus ambiguus and afferents from the trigeminal nerve provide a primary sensory input to nucleus ambiguus. Thus, the ventral vagal complex, consisting of nucleus ambiguus and the nuclei of the trigeminal and facial nerves, is functionally related to the expression and experience of emotion. Activation of the somatomotor component (e.g., listening, ingestion, lifting eyelids) could trigger visceral changes that would support social engagement, while modulation of visceral state, depending on whether there is an increase or decrease in the influence of the myelinated vagal efferents on the sino-atrial node (i.e., increasing or decreasing the influence of the vagal brake), would either promote or impede social engagement behaviors[11, 14]. For example, stimulation of visceral states that would promote mobilization (i.e., fight or flight behaviors) would impede the ability to express social engagement behaviors.

The face–heart connection enabled mammals to detect whether a conspecific was in a calm physiological state and ‘safe’ to approach, or in a highly mobilized and reactive

physiological state during which engagement would be dangerous. The face–heart connection concurrently enables an individual to signal ‘safety’ through patterns of facial expression and vocal intonation, and potentially calm an agitated conspecific to form a social relationship. When the newer mammalian vagus is optimally functioning in social interactions (i.e., inhibiting the sympathetic excitation that promotes fight-or- flight behaviors), emotions are well regulated, vocal prosody is rich, and the autonomic state supports calm spontaneous social engagement behaviors. The face– heart system is bidirectional with the newer myelinated vagal circuit influencing social interactions and positive social interactions influencing vagal function to optimize health, dampen stress-related physiological states, and support growth and restoration. Social communication and the ability to co-regulate interactions, via reciprocal social engagement systems, lead to a sense of connectedness and is an important defining feature of the human experience.

5.3 Polyvagal Theory: Dissolution

The human nervous system, similar to that of other mammals, evolved not solely to survive in safe environments but also to promote survival in dangerous and life-threatening contexts. To accomplish this adaptive flexibility, the mammalian autonomic nervous system, in addition to the myelinated vagal pathway that is integrated into the Social Engagement System, retained two more primitive neural circuits to regulate defensive strategies (i.e., fight–flight and death-feigning behaviors). It is important to note that social behavior, social communication, and visceral homeostasis are incompatible with the neurophysiological states that support defense. Polyvagal response strategies to challenge are phylogenetically ordered with newest components of the ANS responding first. This model of autonomic reactivity is consistent with John

Hughlings Jackson's construct of dissolution in which he proposes that "the higher nervous arrangements inhibit (or control) the lower, and thus, when the higher are suddenly rendered functionless, the lower rise in activity".[27] In this hierarchy of adaptive responses, the newest social engagement circuit is used first; if that circuit fails to provide safety, the older circuits are recruited sequentially.

5.4 Polyvagal Theory: Neuroception

Polyvagal Theory proposes that the neural evaluation of risk does not require conscious awareness and functions through neural circuits that are shared with our phylogenetic vertebrate ancestors. Thus, the term neuroception was introduced to emphasize a neural process, distinct from perception, capable of distinguishing environmental (and visceral) features that are safe, dangerous, or life threatening[28, 29]. In safe environments, autonomic state is adaptively regulated to dampen sympathetic activation and to protect the oxygen-dependent central nervous system, especially the cortex, from the metabolically conservative reactions of the dorsal vagal complex (e.g., vasovagal syncope).

Neuroception is proposed as a 'reflexive' mechanism capable of instantaneously shifting physiological state. Neuroception is a plausible mechanism mediating both the expression and the disruption of positive social behavior, emotion regulation, and visceral homeostasis. Neuroception might be triggered by feature detectors involving areas of temporal cortex that communicate with the central nucleus of the amygdala and the periaqueductal gray, since limbic reactivity is modulated by temporal cortex responses to biological movements including voices, faces, and hand movements. Embedded in the construct of neuroception is the capacity of the nervous system to react to the 'intention' of these movements. Neuroception functionally

decodes and interprets the assumed goal of movements and sounds of inanimate and living objects. This process occurs without awareness. Although we are often unaware of the stimuli that trigger different neuroceptive responses, we are aware of our body's reactions. Thus, the neuroception of familiar individuals and individuals with appropriately prosodic voices and warm, expressive faces translates into a positive social interaction promoting a sense of safety.

5.5 Polyvagal Theory: Autonomic state is an intervening variable

The Polyvagal Theory proposes that physiological state is a fundamental part, and not a correlate, of emotion and mood. According to the theory, autonomic state functions as an intervening variable biasing our detection and evaluation of environmental cues. Depending on physiological state, the same cues will be reflexively evaluated as neutral, positive, or threatening. Functionally, a change in state will shift access to different structures in the brain and support either social communication or the defensive behaviors of fight/flight or shutdown. Contemporary research on the impact of vagal nerve stimulation on cognitive function and emotion regulation supports this model[30]. The theory emphasizes a bidirectional link between brain and viscera, which would explain how thoughts change physiology, and how physiological state influences thoughts. As individuals change their facial expressions, the intonation of their voices, the pattern in which they are breathing, and their posture, they are also changing their physiology primarily through circuits involving myelinated vagal pathways to the heart.

5.6 Polyvagal Theory: The role of visceral afferents in regulating the heart

The prevalent focus of research investigating the neural regulation of the heart has focused on efferent pathways emerging from brainstem nuclei and sympathetic ganglion.

Limited research has been conducted on the influence of visceral afferents in the neural regulation of the heart and how these influences are manifested in the neural regulation of the heart and other visceral organs. This is, in part, due to the efferent bias in medical education that has resulted in a limited conceptualization of the neural regulation of the heart. However, this bias is rapidly changing due to vagal nerve stimulation, a bottom up model that focuses on the vagus as an afferent nerve (approximately 80% of the vagal fibers are sensory). Interestingly, the side effects of vagal nerve stimulation are frequently due to the influence of vagal nerve stimulation on efferent pathways. These side effects are primarily noted on features of the social engagement system including changes in voice and difficulties swallowing[31]. However, in some cases the stimulation has been manifested in subdiaphragmatic organs resulting in diarrhea[32]. As vagal nerve stimulation becomes more commonly applied to medical disorders, there is an emerging awareness of the role of vagal afferent input on neurophysiological function (e.g., epilepsy), emotional state (e.g., depression), and cognition (e.g., learning and attention)[32, 33].

According to the Polyvagal Theory, the source nuclei of the myelinated vagus are regulated by complex neural circuits, involving both visceral afferents (i.e., bottom up) and higher brain structures (i.e., top down) that influence the brainstem source nuclei controlling both the myelinated vagus and the striated muscles of the face and head (i.e., the social engagement system). As the function of the visceral afferents is incorporated into an understanding of the autonomic nervous system, clinicians and researchers begin to recognize manifestations in the vagal control of the heart in patients with a variety of disorders of peripheral organs. Rather than interpreting the atypical neural regulation of the heart, which may reflect forms of heart and cardiovascular disease, co-morbidities become interpreted not as correlates but as manifestations of ‘system’ dysfunction consistent with the prescient views of Walter Hess.

Several chronic diseases manifested in specific subdiaphragmatic organs (e.g., kidney, pancreas, liver, gut, genitals, etc.) have identifiable features that have lead to treatments that target organs (e.g., medication, surgery). However, other disorders that impact on quality of life such as irritable bowel syndrome and fibromyalgia are defined by nonspecific symptoms. The literature links these nonspecific chronic disorders with atypical vagal regulation of the heart reflected in diminished heart rate variability[34, 35]. Consistent with these findings, heart rate variability has been proposed as a biomarker for these disorders.

Polyvagal Theory proposes an alternative interpretation of this covariation. Consistent with the integrated model of the autonomic nervous system described in the theory, atypical heart rate variability is not interpreted as a biomarker of any specific disease. Rather, depressed heart rate variability is proposed as a neurophysiological marker of a diffuse retuning of the autonomic nervous system following an adaptive complex autonomic reaction to threat. Compatible with this interpretation, there are strong links between the prevalence of a history of abuse, especially sexual abuse in women, and the manifestations of nonspecific clinical disorders such as irritable bowel syndrome and fibromyalgia. In addition, emotional stress intensifies symptoms and hinders positive treatment outcomes and trauma may trigger or aggravate symptoms[36, 37]. We propose that an initially adaptive neural response to threat, via visceral afferent feedback from the visceral organs to the brainstem, may result in a chronic reorganization of the autonomic regulation observed in vagal regulation of the heart (i.e., depressed heart rate variability) in conjunction with altered subdiaphragmatic organ function and afferent pain signaling.

6. Conclusion

Neurocardiology defines an emergent discipline that provides an opportunity to study the bi-directional communication between the brain and the heart. By viewing living organisms as a collection of dynamic, adaptive, interactive, and interdependent physiological systems, it becomes apparent that the autonomic nervous system cannot be treated as functionally distinct from the central nervous system. Consistent with the Polyvagal Theory, the heart is not "floating in a visceral sea," but is metaphorically anchored to central structures by efferent pathways and continuously signaling central regulatory structures via an abundance of afferent pathways. Thus, the treatment and assessment of cardiac function and the manifestation of other manifestations of autonomic dysfunction in the neural regulation of the heart should be based on bidirectional connections between autonomic and central brain structures. Such knowledge informs us about vulnerability to cardiac disease and dysfunction associated with triggering the autonomic nervous system into chronic states of defense as well as the resilience promoted by the functional management by the social engagement system.

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