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The Polyvagal Theory: phylogenetic contributions to social behavior

Stephen W. Porges

Brain-Body Center, Psychiatric Institute, Department of Psychiatry, University of Illinois at Chicago, 1601 W. Taylor Street, M/C 912, Chicago, IL 60612, USA

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Abstract

The scientific legacy of Paul MacLean provides important insights into the neural substrate of adaptive social behavior in mammals. Through his research and visionary conceptualizations, current investigators can legitimately study social behavior from a neurobiological perspective. His research and writings provided three important contributions. First, he emphasized the importance of evolution as an organizing principle that shaped both the structure of the nervous system and the adaptive social behavior. Second, by defining the limbic system, he legitimized the biological perspective in the study of emotion. Third, he recognized the important role of the vagal afferents in the regulation of higher brain structures. The paper will focus on the Polyvagal Theory. The Polyvagal Theory is a new conceptualization of the role of vagus and employs several features that MacLean emphasized including the importance of evolution, limbic structures and vagal afferents. The Polyvagal Theory builds on these early findings by MacLean and focuses on the link between phylogenetic changes in the autonomic nervous system and social behavior. By focusing on the phylogenetic changes in the structure of the vagus and the role that vagus plays in the neural regulation of visceral state, new insights regarding social behavior emerge. Moreover, by articulating the phylogenetically organized hierarchy of neural circuits, insights into benefits of social behavior become evident as do an understanding of the behavioral and physiological features associated with stress and psychiatric disorders.

Keywords: Vagus; Autism; Heart rate variability; Autonomic nervous system; Polyvagal; Social behavior

1. Introduction

As the scientific knowledge of neuroanatomy and neurophysiology expands, there is a growing interest in the role neural structures play in normal social behavior and in the expression of the atypical social behaviors that have been associated with several psychiatric disorders such as depression, autism and posttraumatic stress disorder. Recent advances in imaging methods have enabled researchers to study brain function and structure in the intact living individual. Now, neuronal function can be studied and the structural hypotheses derived from animal models and postmortem histology can be challenged and explained. The new methods of assaying brain structure and function, coupled with the breakthroughs in molecular genetics, are dominating the research in the neurobiology of social behavior and psychopathology. However, other research strategies, which provide an opportunity to dynamically monitor neural function with noninvasive technologies, are necessary for the development of an integrated neurobiological and neurobehavioral model of social behavior. Because autonomic function is intricately linked to observable motor behaviors, research investigating the neurophysiology of autonomic function is paramount among these strategies.

For decades, researchers studied autonomic function in clinical populations with the hope of gaining a new insight into the etiology of psychiatric disorders. Because noninvasive direct measurements of the nervous system and especially of the brain did not exist, early researchers intuitively monitored autonomic function as a noninvasive index of neural regulation of visceral state. As neuroscience advanced with more sensitive indicators of brain function, interest in the autonomic nervous system waned from a *neural* emphasis to a more global measurement of arousal and activation. Researchers lost the insight that the autonomic nervous system was not a separate neural system but is integrated into the function of other neural structures.

This paper focuses on how a specific component of the autonomic nervous system, the vagus, is involved in the expression of several of the behavioral, psychological and

E-mail address: sporges@uic.edu (S.W. Porges).

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physiological features associated with social behavior. The vagus will be presented not only as a cranial nerve meandering through the periphery but also as an important bidirectional conduit carrying specialized motor and sensory pathways involved in the regulation of visceral state and affect. Moreover, it will be emphasized that spontaneous social engagement behaviors become more understandable if the autonomic nervous system, and especially the vagus, is included in the integrated model.

2. The autonomic nervous system

The autonomic nervous system is the portion of the nervous system that controls visceral functions of the body. This system innervates smooth and cardiac muscles and glands and regulates visceral processes including cardiovascular activity, digestion, metabolism and thermoregulation. The autonomic nervous system functions primarily at a subconscious level and is traditionally partitioned into two divisions, the sympathetic and the parasympathetic, based on the region of the brain and spinal cord in which the autonomic nerves (i.e., preganglionic fibers) have their origin. The sympathetic system is defined by the autonomic fibers that exit thoracic and lumbar segments of the spinal cord. The parasympathetic system is defined by the autonomic fibers that exit either the brainstem via the cranial nerves or the sacral segments of the spinal cord.

Because most organs in the viscera receive both sympathetic and parasympathetic input, the regulation of the autonomic nervous system has been modeled as a balance system. Several researchers have proposed that imbalance in the neural regulation of the autonomic nervous system might be an indicator of behavioral or psychiatric disturbances. Researchers have proposed that dysfunctional mental states are associated with an excessive vagal outflow [13], an imbalance between sympathetic and parasympathetic branches of the autonomic nervous system [32,45], an excessive sympathetic outflow [9] and a deficient vagal outflow [37].

The defining features of the autonomic nervous system were initially limited to motor fibers regulating glands and smooth and cardiac muscles [23]. This arbitrary definition limited the autonomic nervous system to visceral efferent fibers and excluded the sensory fibers that accompany most visceral motor fibers. Although the definition is often expanded to include both peripheral and central structures (e.g., hypothalamus), contemporary textbooks continue to define the autonomic nervous system solely as a motor system. This bias ignores the importance of the afferent pathways. Moreover, it confuses the study of the dynamic regulatory function of the autonomic nervous system, because 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 components. Thus, from a functional perspective, the autonomic nervous system includes afferent pathways conveying information regarding the visceral organs and the brain areas (e.g., medulla and hypothalamus) that interpret the afferent feedback and exert control over the motor output back to the visceral organs.

3. The vagus as a functional system

The vagus, the 10th cranial nerve, is a major component of the autonomic nervous system. The vagus is more than a motor nerve from the brainstem to various target organs in the periphery. The vagus represents an integrated neural system that communicates in a bidirectional manner between the viscera and the brain. Although recent research appears to have discovered that stimulation of vagal afferents change brain function [14], this relation between affect and vagal afferent activity is not a recent idea. For example, Darwin [11] noted in *The Expression of Emotions in Man and Animals* the importance of the bidirectional neural communication between the heart and the brain via the "pneumogastric" nerve, now known as the vagus nerve.

> . . .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 and felt to be the case. Claude Bernard also repeatedly insists and this deserves especial notice, that when the heart is affected it reacts on the brain; and the state of the brain again reacts through the pneumo-gastric [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, emotional state represented a covariation between facial expression and autonomic tone. However, he did not elucidate the specific neurophysiological mechanisms. Our current knowledge of the neuroanatomy, embryology and phylogeny of the nervous system was not available to Darwin. At that time, it was not known that vagal fibers originated in several medullary nuclei, that branches of the vagus exerted control over the periphery through different feedback systems, that sensory information conveyed through the vagus regulated structures in the brain and that the function of the branches of the vagus followed a phylogenetic principle. Darwin's statement is important, because it emphasized two points: (1) afferent feedback from the heart to the brain through the vagus was independent of the spinal cord and the sympathetic nervous system and (2) the vagus played a regulatory role in the expression of emotions.

The Darwinian description of the vagus, emphasizing a bidirectional communication between the periphery and the central nervous system, assumes that the vagus is part of a feedback system. Implicit in this "vagal system" are the three defining components of a feedback system: motor pathways to change visceral state, sensory pathways to

monitor visceral state and brain structures to evaluate the sensory input and to regulate the motor output. However, when Langley [23] defined the autonomic nervous system as a purely visceral motor system that consisted of ''visceral efferent cells and fibers that pass to tissues other than the skeletal muscle,'' several important features emphasizing the feedback features of an integrated vagal system were omitted. This omission limited interest in conducting research investigating the relation between vagal activity and brain function and how vagal activity might be related to affect regulation.

Approximately 80% of the vagal fibers are afferent and provide important information regarding visceral state. The importance of the vagal afferents in the regulation of visceral state, mood and affect is recently being rediscovered through the current research demonstrating that stimulation of the vagal afferents regulate brain structures involved in epilepsy [4], depression [14] and even repetitive self-destructive behaviors often associated with autism [29].

From a systems perspective, a vagal system would naturally have output to peripheral target organs (e.g., heart and gut) through efferent pathways, input from visceral afferents and a central regulator involving source nuclei in the brainstem (i.e., dorsal motor nucleus of the vagus, nucleus ambiguus and nucleus of the solitary tract). Because the central regulator of the vagus in the brainstem is both an input and an output of other feedback systems, the vagal system becomes both a component of a more integrated neural feedback system and a portal to neural systems in other areas of the brain.

Motor pathways from the two source nuclei of vagus project to different structures in the periphery. The vagal motor fibers originating in the nucleus ambiguus regulate the striated muscles of the face and head and the cardiac and smooth muscles of the heart and bronchi. The vagal motor fibers originating in the dorsal motor nucleus regulate the subdiaphragmatic visceral organs including the digestive tract. Vagal sensory information travels from the periphery to the medullary nucleus tractus solitarius (the source nucleus of the afferent vagus), and neural pathways from the nucleus tractus solitarius project to areas in the forebrain and the brainstem. In addition, there are neural pathways that have direct projections from the cortex to the medullary source nuclei of the vagus (e.g., corticobulbar), and other less direct pathways originating in the cortex project to limbic structures and medullary nuclei to regulate both the striate muscles of the face and autonomic function. Thus, there is a strong neuroanatomical and neurophysiological justification to predict that stimulation of vagal afferents (e.g., vagal nerve stimulation used for the treatment of epilepsy and depression) would change activity of higher brain structures, and the change in output of these higher systems might influence the function of target organs such as the face, heart, gut or pancreas.

If we were to conceptualize the autonomic nervous system as a functional system, we would include both the afferent pathways conveying information regarding the visceral organs to the central nervous system and the specific brain structures that interpret the afferent feedback and exert control over the motor output to the visceral organs. This broader definition of the autonomic nervous system provides us with the scaffolding necessary to evaluate the role of the vagus in several of the behavioral and physiological features associated with psychiatric disorders.

4. Polyvagal Theory

Evolutionary forces have molded both human physiology and behavior. The mammalian nervous system is a product of evolution. Via evolutionary processes, the mammalian nervous system has emerged with specific neural and behavioral features that react to challenge in order to maintain visceral homeostasis. These reactions change physiological state and, in mammals, limit sensory awareness, motor behaviors and cognitive activity. To survive, mammals must determine friend from foe, evaluate whether the environment is safe and communicate with their social unit. These survival-related behaviors are associated with specific neurobehavioral states that limit the extent to which a mammal can be physically approached and whether the mammal can communicate or establish new coalitions. Thus, environmental context can influence neurobehavioral state, and neurobehavioral state can limit a mammal's ability to deal with the environmental challenge. Through stages of phylogeny, mammals, and especially primates, have evolved a functional neural organization that regulates visceral state to support social behavior. The Polyvagal Theory [33–36] emphasizes the phylogenetic origins of brain structures that regulate social and defensive behaviors, domains compromised in individuals with autism and several psychiatric disorders. The Polyvagal Theory proposes that the evolution of the mammalian autonomic nervous system provides the neurophysiological substrates for the emotional experiences and affective processes that are major components of social behavior. The theory proposes that physiological state limits the range of behavior and psychological experience. In this context, the evolution of the nervous system determines the range of emotional expression, quality of communication and ability to regulate bodily and behavioral state. The Polyvagal Theory links the evolution of the autonomic nervous system to affective experience, emotional expression, facial gestures, vocal communication and contingent social behavior. Thus, the theory provides a plausible explanation of several social, emotional and communication behaviors and disorders.

The Polyvagal Theory, based on the neurophysiological and neuroanatomical distinction between the two branches of the vagus, proposes that each branch supports a different adaptive behavioral strategy. The theory is based on an understanding of the adaptive behaviors supported by three

neural circuits, each representing a different phylogenetic stage of the vertebrate autonomic nervous system. The stages reflect the emergence of three distinct autonomic subsystems, which are phylogenetically ordered and behaviorally linked to social communication (e.g., facial expression, vocalization and listening), mobilization (e.g., fight–flight behaviors) and immobilization (e.g., feigning death, vasovagal syncope and behavioral shutdown). The phylogenetic order, in which these neural circuits appeared, represents a response hierarchy in mammals with the most recent neural circuit responding first (Table 1).

By investigating the phylogeny of the regulation of the vertebrate heart [28], four principles can be extracted. First, there is a phylogenetic shift in the regulation of the heart from endocrine communication to unmyelinated nerves and finally to myelinated nerves. Second, there is a development of opposing neural mechanisms of excitation and inhibition to provide rapid regulation of graded metabolic output. Third, with increased cortical development, the cortex exhibits greater control over the brainstem via direct (e.g., corticobulbar) and indirect (e.g., corticoreticular) neural pathways originating in motor cortex and terminating in the source nuclei of the motor pathways exiting the brainstem in specific cranial nerves regulating both striated muscles of the face and head (i.e., special visceral efferent pathways located in cranial nerves V, VII, IX, X and XI) and visceral structures (i.e., heart, bronchi and thymus) via myelinated vagal pathways. Fourth, the brainstem structures involved in the regulation of the muscles of the face and head are also involved in the regulation of autonomic state.

These phylogenetic principles provide a basis for speculations regarding the behavioral and physiological responses associated with psychiatric disorders. In general, phylogenetic development results in increased neural control of the heart via the myelinated mammalian vagal system, which can promote transitory mobilization and the expression of sympathetic tone without requiring sympathetic or adrenal activation. With this new vagal system, transitory incursions into the environment or withdrawals from a potential predator can be initiated without the severe biological cost of the metabolic excitation associated with sympathetic-adrenal activation. Paralleling this change in neural control of the heart is an enhanced neural control of the face, larynx and pharynx that enables complex facial gestures and vocalizations associated with social communication. This phylogenetic trajectory results in more complex neural structures being involved in the regulation of behavior, especially the social communication behaviors needed to engage others. Moreover, these phylogenetically more recent systems not only provide mechanisms for social communication but also are involved in regulating visceral organs to promote calm states. Thus, the Polyvagal Theory provides a neurobiological model to explain how positive social behavior, social support and positive affective states might support health and growth. In contrast to the health-related states associated with prosocial behavior, withdrawal of this new neural system would promote mobilization behaviors such as fight and flight as well as other physiological responses (e.g., increased sympathetic activity and activation of the HPA axis) that may be potentially damaging if maintained for prolonged periods. Thus, it is possible that individuals with specific psychiatric disorders, in which compromised social behavior is a diagnostic feature, are experiencing neurophysiological states that foster defensive and not social behaviors.

Table 1
The three phylogenetic stages of the neural control of the heart proposed by the Polyvagal Theory

Phylogenetic stage	Autonomic nervous system component	Behavioral function	Lower motor neurons
III	Myelinated vagus	Social communication, self-soothing and calming inhibit sympathetic-adrenal influences	Nucleus ambiguus
II	Sympathetic-adrenal	Mobilization (active avoidance)	Spinal cord
I	Unmyelinated vagus	Immobilization (death feigning and passive avoidance)	Dorsal motor nucleus of the vagus

The Polyvagal Theory provides an explicit neurobiological model of how difficulties in spontaneous social behavior are linked to both facial expressivity and regulation of visceral state and, alternatively, how social behavior may serve as a regulator of physiological activity. The theory proposes a possible mechanism to explain how these difficulties might form a core domain of several psychiatric profiles. Relevant to this focus on psychiatric disorders are the specific deficits associated with several diagnoses in both somatomotor (e.g., poor gaze, low facial affect, lack of prosody and difficulties in mastication) and visceromotor (difficulties in autonomic regulation resulting in cardiopulmonary and digestive problems).

Embryologically, components of several cranial nerves known as special visceral efferent pathways develop together to form the neural substrate of a Social Engagement System [35]. This system, as illustrated in Fig. 1, provides the neural structures involved in social and emotional behaviors. The Social Engagement System has a control component in the cortex (i.e., upper motor neurons) that regulates brainstem nuclei (i.e., lower motor neurons) to control eyelid opening (e.g., looking), facial muscles (e.g., emotional expression), middle ear muscles (e.g., extracting human voice from background noise), muscle of mastication (e.g., ingestion), laryngeal and pharyngeal muscles (e.g., vocalization and language) and head turning muscles (e.g., social gesture and orientation). Collectively, these muscles function as filters that limit social stimuli (e.g., observing facial features and listening to human voice) and determinants of engagement with the social environment. Interestingly, the neural pathway that raises the eyelids also tenses

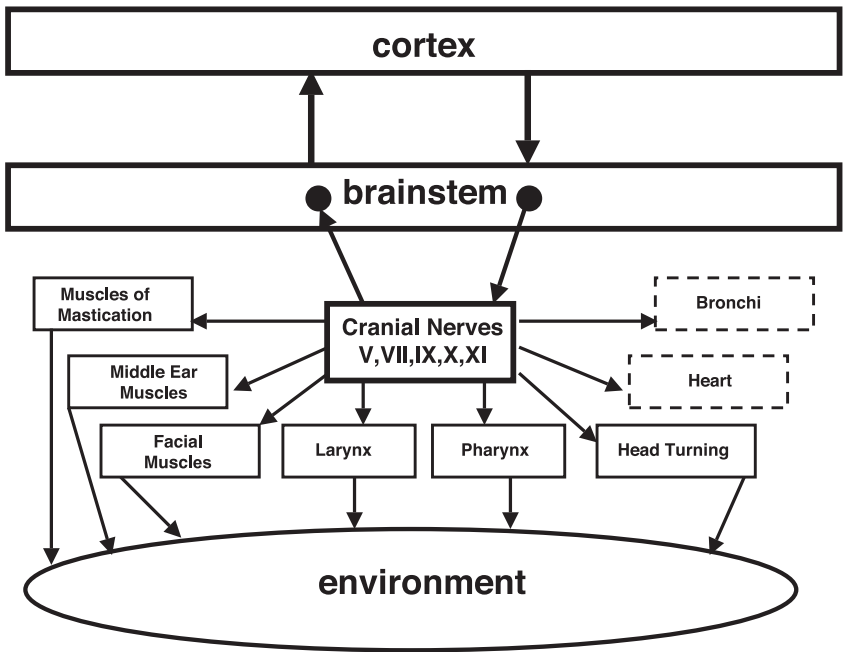

Fig. 1. The Social Engagement System: Social communication is determined by the cortical regulation of medullary nuclei via corticobulbar pathways. The Social Engagement System consists of a somatomotor component (i.e., special visceral efferent pathways that regulate the muscles of the head and face) and a visceromotor component (i.e., the myelinated vagus that regulates the heart and bronchi). Solid blocks indicate the somatomotor component. Dashed blocks indicate the visceromotor component.

the stapedius muscle in the middle ear, which facilitates hearing human voice. Thus, the neural mechanisms for making eye contact are shared with those needed to listen to human voice. As a cluster, difficulties behaviors associated with the Social Engagement System (e.g., gaze, extraction of human voice, facial expression, head gesture and prosody) are common features of individuals with autism.

The study of comparative anatomy, evolutionary biology and embryology provides important hints regarding the functional relation between the neural control of facial muscles and the emergent psychological experiences and behavior. The nerves that control the muscles of the face and head share several common features. Pathways from five cranial nerves control the muscles of the face and head. Collectively, these pathways are labeled as special visceral efferent [42]. The source nuclei (i.e., lower motor neurons) of these nerves, which are located in the brainstem, communicate directly with an inhibitory neural system that slows heart rate, lowers blood pressure and actively reduces arousal to promote calm states consistent with the metabolic demands of growth and restoration of our neurophysiological systems. Direct corticobulbar pathways reflect the influence of frontal areas of the cortex (i.e., upper motor neurons) on the regulation of this system. Moreover, afferent feedback through the vagus to medullary areas (e.g., nucleus of the solitary tract) influences forebrain areas that are assumed to be involved in several psychiatric disorders. In addition, the anatomical structures involved in the Social Engagement System have neurophysiological interactions with the HPA axis, the neuropeptides of oxytocin and vasopressin and the immune system (for overview, see Ref. [36]).

As vertebrates evolved from reptiles to mammals, the structures at the end of the mandible (i.e., jaw bone) that define components in the middle ear became detached [24,39,44]. For mammals, the sound in our environment impinges on the eardrum and is transduced from the eardrum to the inner ear via the small bones in the middle ear known as ossicles. The stapedius muscle (innervated via a branch of the facial nerve) and the tensor tympani (innervated via a branch of the trigeminal nerve), when innervated, stiffen the ossicular chain and dampen the amplitude of the low-frequency activity reaching the inner ear. The functional impact of these muscles on the perceived acoustic environment is to markedly attenuate low-frequency sounds and to facilitate the extraction of high-frequency sounds associated with human voice. For example, our acoustic environment is often dominated by loud low-frequency sounds that have the functional effect of masking the soft high-frequency sounds associated with human voice. In humans, the ossicular chain is regulated primarily by the stapedius muscle and tensing the stapedius prevents this masking effect [5]. In fact, individuals who can voluntarily contract middle ear muscles exhibit an attenuation of $\sim$30 dB at frequencies below 500 Hz, while there is no or minimal attenuation at frequencies above 1000 Hz [22].

The evolution of the mammalian middle ear enabled low-amplitude, relatively high-frequency airborne sounds (i.e., sounds in the frequency of human voice) to be heard, even

when the acoustic environment was dominated by low-frequency sounds. This phylogenetic innovation enables mammals to communicate in a frequency band that could not be detected by reptiles that were only able to hear lower frequencies due to their dependence on bone conduction to "hear." This ability to hear low-amplitude, high-frequency airborne sounds in an acoustic environment dominated by loud low-frequency sounds could only be accomplished when the middle ear muscles are tensed to create a rigidity along the ossicular chain. The tensing of these muscles prevent the low-frequency sounds from being transduced through the middle ear bones from the eardrum to the cochlear and masking the high-frequency sounds associated with human voice.

Studies have demonstrated that the neural regulation of middle ear muscles, a necessary mechanism to extract the soft sounds of human voice from the loud sounds of low-frequency background noise, is defective in individuals with language delays, learning disabilities and autistic spectrum disorders [40,41]. Middle ear infection (i.e., otitis media) may result in a total inability to elicit the "reflexive" contraction of the stapedius muscles [47]. Disorders that influence the neural function of the facial nerve (i.e., Bell palsy) not only influence the stapedius reflex [2] but also affect the patient's ability to discriminate speech [46]. Thus, the observed difficulties that many autistic individuals have in extracting human voice from background sounds may be dependent on the same neural system that regulates facial expression.

Thus, deficits in the Social Engagement System would compromise spontaneous social behavior, social awareness, affect expressivity, prosody and language development. Following the same logic, if interventions were designed to improve the neural regulation of the Social Engagement System, hypothetically, they also would enhance spontaneous social behavior, state and affect regulation, reduce stereotypical behaviors and improve language skills.

5. Predictions based on the Polyvagal Theory

To test predictions based on the Polyvagal Theory, it is necessary to conceptualize the vagus as a component of a dynamic neural feedback system. At a basic level, a vagal regulatory system will include negative feedback from the periphery that would travel via vagal afferent pathways to medullary source nuclei, which, based on the quality of the afferent signal, would regulate the outflow of the vagal efferent pathways directly to the target organs. This simple conceptualization describes a system that by monitoring visceral state would adjust efferent outflow and maintain physiological homeostasis. Although this system may represent a decerebrated brainstem preparation or perhaps a phylogenetically primitive vertebrate, it does not adequately describe the neural systems of mammals.

Through the process of vertebrate evolution, the primitive brainstem structures have become neurally intertwined with higher brain structures. In mammals, the brainstem provides a portal conveying sensory information that contributes to the regulation of the higher brain structures, and as with any feedback system, the higher brain structures have a regulatory influence on the brainstem. Aspects of this bidirectional communication may provide insight into how peripheral vagal activity might be related to the expression of normal social behavior or a contributor to the challenged social behavior associated with several psychiatric diagnoses. For example, measurements of this system may serve as assessments or stimulation of this system may form treatments.

The Polyvagal Theory describes the phylogenetic changes in the neural regulation of autonomic function to support adaptive behaviors. The theory proposes a hierarchy of autonomic states that are phylogenetically organized. Each of the states described in the theory is linked to a different neural feedback system in which the vagus is involved. The most recent phylogenetic system links the myelinated vagus to the structures of social engagement, the muscles of the face and head. The Polyvagal Theory describes this integrated system as the Social Engagement System.

Observations of the behaviors and physiological responses of autistic individuals suggest that they have great difficulties in recruiting the neural circuit that regulates the Social Engagement System. Rather, it appears that autism and perhaps other psychiatric disorders are associated with autonomic states that remove the individual from direct social contact by supporting the adaptive defensive strategies of mobilization (i.e., fight or flight behaviors) or immobilization (i.e., shutdown). Behaviorally, the retraction of the neural regulation of the Social Engagement System would be expressed in the regulation of the muscles of the face and head. The functional consequences would limit facial expression and head gesture, create difficulties in extracting human voice from background sounds result in a lack of prosody. Neurophysiologically, because the vagus is integrated into several feedback systems involving both peripheral and central structures, this retraction might be manifested on several levels. First, it may compromise the regulation of visceral organs such as the gut, heart and pancreas [43]. Second, because the vagus is involved in the regulation of cytokines and the HPA axis, there may be regulation disorders in those systems. Third, because the brainstem areas regulating the myelinated vagal system provide both output and input to feedback systems involving other brain structures, the vagal system may provide a portal to assess and to stimulate higher neural processes. Although there is a limited scientific literature evaluating the role of vagus in autism, the plausibility of these predictions will be evaluated against the current literature, which includes studies with other clinical populations and animal preparations.

5.1. Vagal regulation of heart rate and heart rate variability

Due to the tonic vagal influences on the sinoatrial node (i.e., the heart's pacemaker), resting heart rate is substan-

tially lower than the intrinsic rate of the cardiac pacemaker. When the vagal tone to the pacemaker is high, the vagus acts as a brake, slowing heart rate. When vagal tone to the pacemaker is low, there is little or no inhibition of the pacemaker and heart rate increases. Thus, a brake may be used as a construct to describe the functional modulation of heart rate by the myelinated vagal efferent pathways. Modulation of the vagal brake provides a neural mechanism to rapidly change visceral state by slowing (i.e., increasing vagal influences) or speeding (i.e., reducing vagal influences) heart rate. Functionally, the vagal brake, by modulating visceral state, enables the individual to rapidly engage and disengage with objects and other individuals and to promote self-soothing behaviors and calm behavioral states. These behaviors are obviously compromised in several psychiatric disorders including autism. Consistent with the assumptions of the Polyvagal Theory, the vagal brake is dependent upon the myelinated vagal inhibitory fibers that originate in the nucleus ambiguus.

Because vagal efferent pathways to the heart are cardioinhibitory, changes in vagal tone can influence the metrics used to monitor heart rate and heart rate variability. In general, greater cardiac vagal tone produces slower heart rate and regulates the transitory changes in heart rate in response to stimulation. The myelinated vagal efferents that synapse on the sinoatrial node have a respiratory rhythm. This rhythmic increase and decrease in cardioinhibitory activity through the vagus produces a heart rate rhythm known as respiratory sinus arrhythmia. The greater the cardioinhibitory influence through the vagus, the greater the rhythmic increases and decreases in this heart rate pattern. Thus, the amplitude of respiratory sinus arrhythmia provides a sensitive index of the influence the myelinated vagus has on the heart. The rapid changes in heart rate in response specific stimuli are primarily under vagal control. The characteristic heart rate pattern to stimulus changes of an immediate deceleration followed by either a continued deceleration or an acceleration is due primarily to dynamic increases or decreases in cardioinhibitory activity through the myelinated vagus.

The literature suggests that autism is associated with reliable differences in the amplitude of respiratory sinus arrhythmia and the transitory heart rate response pattern to various stimuli and task demands. An early publication [17] reported that normal children suppressed respiratory sinus arrhythmia more than autistic children. Similarly, a more recent publication [1] found that PDD-NOS children did not suppress respiratory sinus arrhythmia. Consistent with these findings, an early study of children diagnosed with schizophrenia [31] identified significant differences in respiration and in the covariation between respiration and heart rate. The schizophrenic children had significantly faster and shallower breathing patterns, a pattern consistent with reduced vagal efferent activity.

Studies report that autistic children have dampened transitory heart rate responses to a variety of stimulation. Autistic children have been reported to have unusually small deceleratory heart rate responses to auditory stimulation including socially relevant speech, nonsense phrases and pure tones [30,49]. Others report a total lack of heart rate reactivity [10].

These findings, describing compromised cardiac vagal regulation in autistic individuals, support predictions from the Polyvagal Theory. Consistent with the Polyvagal Theory, both visceromotor (i.e., vagal) and somatomotor (e.g., eye gaze and facial expression) components of the Social Engagement System are compromised in individuals with disorders such as autism.

5.2. Vagal nerve stimulation

Although not currently being used to treat autism, vagal nerve stimulation has been effective in treating epilepsy and depression. Vagal nerve stimulation is based on the assumption that stimulation of vagal afferents has a direct effect on the regulation of higher brain structures. In 1949, MacLean and Pribram were involved in early research that demonstrated that stimulation of the vagus influenced the pattern of EEG in anesthetized monkeys [25]. Maclean continued research in this area and conducted several studies demonstrating that vagal afferent stimulation resulted in activation in several brain structures [3,38]. In addition, MacLean demonstrated that stimulating the trigeminal nerve, another afferent related to the Polyvagal Theory, had an inhibitory effect on hippocampal seizures [48].

The source nucleus of the vagal afferents is the nucleus of the solitary tract. This medullary nucleus plays an important role in the regulation of behavioral state, respiration and blood pressure and in conveying information to higher brain structures. The nucleus of the solitary tract relays the incoming sensory information via three primary pathways: (1) feedback to regulate the periphery, (2) direct projections to the reticular formation in the medulla and (3) ascending projections to the forebrain primarily through the parabrachial nucleus and the locus coeruleus. The parabrachial nucleus and the locus coeruleus send direct connections to all levels of the forebrain (e.g., hypothalamus, amygdala and thalamic regions that control the insula and orbitofrontal and prefrontal cortices), areas that have implicated in neuropsychiatric disorders. Thus, vagal afferent stimulation has direct input to both the lower motor neurons in the brainstem and the upper motor neurons in the cortex that regulate the Social Engagement System. Recent reviews provide a detailed description of the neurophysiological basis for the intervention [14] and provide an explanation of the neural mechanisms involved in the treating depression with vagal nerve stimulation [26]. Missing from the current explanation is an acknowledgment of the communication between vagal afferents and source nuclei of the nerves that regulate striated muscles of the face and head (i.e., special visceral efferent pathways), which collectively form the motor part of the Social Engagement System. It is

this interaction that is emphasized in the Polyvagal Theory [36].

Extrapolating from the vagal nerve stimulation model, one might speculate that other forms of vagal stimulation might have beneficial effects. Behaviorally, one of the most potent strategies for vagal stimulation is to stimulate the peripheral baroreceptors that regulate blood pressure. Rocking and swinging in which the position of the head is changed relative to the position of the heart will stimulate the baroreceptors and engage this feedback loop. This suggests that the frequently observed rocking and swinging behaviors in autistic individuals may reflect a naturally occurring biobehavioral strategy to stimulate and regulate a vagal system that is not efficiently functioning. In support of this speculation, a study with normal adults [7] demonstrated that rhythmic oscillatory tilt result in a posttilt increase in cardiac vagal tone (i.e., an increase in the amplitude of respiratory sinus arrhythmia).

One publication reported that vagal nerve stimulation reduced autistic-like behaviors [29]. In this study, vagal stimulation was administered to six patients with hypothalamic hamartoma, a congenital brain malformation that is associated with medically refractory epilepsy and injurious autistic behavior. Four of the six patients had autistic behaviors that included poor communication, ritualisms, compulsions, no social skills and injury to self and others. The authors report that during vagal nerve stimulation all four had impressive improvements in behavior. In one subject, the behavioral improvements were immediately reversed when the vagal nerve stimulation was temporarily discontinued without worsening of seizure frequency. The authors report that another patient, who had no decrease in seizure frequency, had a remarkable improvement in behavior. Consistent with the Polyvagal Theory, it appears that afferent stimulation of the vagus increases the quality of the somatomotor component and possible the visceromotor component of the Social Engagement System.

5.3. The vagus and the immune system

The link between the vagal regulation of immune function and the Polyvagal Theory is not clear. However, it might be plausible to speculate that the neural mediation of the myelinated vagus may via direct influence on thymus and direct inhibition of the sympathetic nervous system trigger a physiological state that would promote immune function. Likewise, mobilization strategies resulting in a withdrawal of vagal tone to the heart, increased sympathetic tone and release of cortisol have been associated with suppressed immune function. More relevant to the expression of psychiatric disturbances is the finding that the afferent vagus mediates behavioral depression, but not fever, in response to peripheral immune signals following abdominal inflammation [21]. Consistent with this model, it has been reported that autism spectrum disorder patients with developmental regression express excessive innate immune responses [20].

5.4. Vagal regulation of the HPA axis

The vagus is involved in the regulation of the HPA axis. Vagal afferents exhibit an inhibitory influence on HPA axis and reduce cortisol secretion [6,27]. Studies [8,15] have demonstrated a covariation between increases in cortisol and decreases in cardiac vagal tone (i.e., the amplitude of respiratory sinus arrhythmia). Thus, there appears to be a coordinated response that functions to promote metabolic activity and mobilization behaviors by withdrawal of vagal tone through the myelinated vagus and increasing both sympathetic activity and activation of the HPA axis.

To test this possible coordination between the function of the myelinated vagus and the excitation or inhibition of the HPA axis, an experiment was conducted in my laboratory [12]. In this study, salivary cortisol and cardiac vagal tone were assessed from preschool children during two experimental tasks, one designed to elicit negative affect and the other designed to elicit positive affect. The experiment took ~30 min to complete. Heart rate and cardiac vagal tone were monitored continuously during the entire experiment, and salivary cortisol was sampled before and after the entire experiment. As predicted by the Polyvagal Theory, the pattern of cardiac vagal tone in response to the negative task was related to the direction of the cortisol reaction. Subjects who increased cortisol exhibited a decrease in cardiac vagal tone and subjects who decreased cortisol exhibited an increase in cardiac vagal tone. Thus, in healthy normal young children, there is a coordination in the reactivity of the HPA axis with the neural regulation of the heart. Moreover, this coordination might be expressed in two different strategies with different metabolic and behavioral consequences. Subjects, who increase cortisol and decrease the inhibitory influence of the vagus on the heart, appear to increase cardiac output to provide the physiological resources to increase mobilization behaviors. In contrast, the subjects, who decrease cortisol and increase the inhibitory influence of the vagus on the heart, appear to reduce cardiac output to maintain calm visceral states.

Two strategies have been developed to evaluate the regulation of the HPA axis. The first strategy is to study the naturally occurring diurnal rhythm of cortisol. The second is to suppress cortisol by administering dexamethasone. Poorly developing autistic children were more likely to have an abnormal diurnal rhythm and an abnormal response on the dexamethasone suppression test than less severe cases. [16]. The results suggest that the negative feedback mechanism of the HPA axis may be disturbed in autistic children, especially the poorly developing cases. Similarly, it has been reported [19] that most of the autistic patients failed to suppress cortisol with the dexamethasone test. Consistent with these reports, PDD-NOS children have been observed to have a diminished cortisol response in response to physical stress [18].

6. Clinical applications of the Polyvagal Theory

The Polyvagal Theory forces us to interpret compromised social behavior from a different perspective. The theory emphasizes that the range of social behavior is limited by physiological state. The theory emphasizes that mobilization and immobilization behaviors may be adaptive strategies for a challenged (e.g., frightened) individual. Thus, it may be possible that states of calmness may potentiate positive social behavior by stimulating and exercising the neural regulation of the Social Engagement System. This perspective or intervention paradigm focuses on how spontaneous positive social behavior is dependent upon physiological state, in contrast to the more commonly administered behavioral and biochemical (i.e., pharmacological) intervention strategies.

We developed a biologically based behavioral intervention that uses acoustic stimulation to improve social behavior and tested the approach with children diagnosed with autism. The intervention was based on several principles derived from the Polyvagal Theory. First, the area of the brainstem that regulates the heart (i.e., via the mammalian or myelinated vagus) also regulates the muscles of the head, including those of the face, middle ear, mouth, larynx and pharynx. Collectively, these muscles function as an integrated Social Engagement System that controls looking, listening, vocalizing and facial gesturing. If the neural regulation of this group of muscles is dysfunctional, the face will not work (e.g., lack of facial expressiveness, dropping eyelids, poor prosody and difficulty listening to human voice). Interestingly, these facial features reflect common behavioral symptoms that have been used to describe several psychopathologies (e.g., autism, depression, aggressive disorders and posttraumatic stress disorders) or emotional states during severe challenge (e.g., grief, rage, anger and loneliness) or medical illness (e.g., senility, AIDS and fever).

Second, the middle ear muscles play an important role in extracting human voice from our complex acoustic environment. When the neural tone to the middle ear muscles is low, the middle ear structures do not actively filter out the low-frequency sounds that dominate the acoustic environment of our modern industrial world and do not amplify the frequencies associated with human voice. This difficulty in listening to human voice might occur even in an individual who has normal hearing (i.e., normal function of the cochlea, the auditory nerve and the brain areas processing acoustic information).

Third, the neural regulation of the middle ear muscles is linked to the neural regulation of the other muscles of the face, which control facial expression and vocal intonation. Thus, stimulation improving neural regulation of the middle ear muscles should integrate and stimulate the neural regulation of facial expression, looking, listening and vocalizing.

The area of the brain that contains the ''lower'' motor neurons for the Social Engagement System is near the lower portion of the brainstem. During periods of appropriate social communication (e.g., facial expressivity and vocal intonation), the ''lower'' motor neurons are regulated by the ''upper'' motor neurons in the cortex. During periods characterized by fight–flight behaviors and fear-induced shutdown or immobilization, the theory proposes that cortical regulation of these ''lower'' motor neurons is displaced by phylogenetically more primitive systems. The more primitive systems are dependent upon subcortical structures that evolved to negotiate survival by managing metabolic resources to promote mobilization (i.e., fight–flight behaviors) or to conserve metabolic resources by immobilizing (e.g., freezing or death feigning). Thus, a critical feature of whether an individual appropriately communicates with the social environment or engages in a strategy of fight–flight or freezing behaviors is determined by the individual's perception of the environment. Does the individual perceive the environment as safe or dangerous? The theory states that there is a degrading of the function of the Social Engagement System when the individual perceives the environment as dangerous. Conversely, if the individual perceives the environment as safe, there is the neurophysiological possibility that the cortex could regulate the ''lower'' motor neurons of the Social Engagement System to promote communication and social behavior. Thus, the perception of safety is the primary requirement for our intervention.

The intervention was designed to recruit specifically the cortical regulation of the Social Engagement System to promote the voluntary prosocial behaviors that are lacking in autistic children. The model is an optimistic model, because it assumes that for many children with social behavior and communication difficulties, the Social Engagement System is neuroanatomically and neurophysiologically intact. The problem is conceptualized as a functional deficit. Thus, to obtain the desired behavior, the intervention must stimulate the cortical regulation of the brainstem system that regulates the muscles of the head. The theory predicts that once the cortical regulation of this brainstem system is engaged, social behavior and communication will spontaneously occur as the natural emergent properties of this biological system. Thus, the intervention is seen as ''stimulation'' and ''exercise'' of a corticobulbar neural system (i.e., nerves that connect the cortex to the brainstem) that regulates the muscles of the head.

The intervention is based on two primary principles: (1) cortical control of listening and the other components of the Social Engagement System via the corticobulbar pathways requires the environment to be perceived as safe and (2) exposure to acoustic stimulation within the frequency band of human voice is capable of stimulating and exercising the neural regulation of the middle ear muscles and other components of the Social Engagement System. Thus, the intervention attempts to engage the active cortical control of the middle ear muscles as a portal to the Social Engagement System. The intervention resulted in noticeable improve-

ments in social behavior and communication skills in most of the children diagnosed with autism. In addition, there were noticeable changes in parental interaction styles with the children, with the parents being less intrusive following the intervention. These improvements persisted when assessed during a 3-month follow-up.

7. Conclusions

This paper illustrates how the vagus is involved in the expression of several disparate symptoms associated with autism and other psychopathologies. Consistent with the Polyvagal Theory, the symptom clusters are associated with components of the vagal system. First, there are the behavioral characteristics linked to the neural regulation of the striated muscles of the face via special visceral efferent pathways (i.e., the somatomotor component of the Social Engagement System). Second, autism is associated with dysfunctional regulation of target organs (e.g., heart) regulated by vagal efferent pathways (i.e., the visceromotor component of the Social Engagement System). Third, the vagal afferents exert a powerful regulatory influence on several systems including the visceral and tactile pain thresholds, the HPA axis and the immune system that are dysfunctional in autism. Fourth, the nucleus of the solitary tract (the source nucleus of the afferent vagus) influences areas of the forebrain that have been speculated to be compromised in autism.

The Polyvagal Theory provides a theoretical platform to interpret social behavior within a neurophysiological context. The emphasis on phylogeny provides an organizing principle to understand the hierarchical sequence of adaptive responses. The Social Engagement System not only provides direct social contact with others but also modulates physiological state to support positive social behavior by exerting an inhibitory effect on the sympathetic nervous system and the HPA axis. From the Polyvagal Theory perspective, social behavior is an emergent property of the phylogenetic development of the autonomic nervous system. Consistent with this hierarchical model, perceived challenges to survival often result in a neural dissolution from the more recent systems of positive social behavior and social communication to the more primitive fight–flight and avoidance systems. The theory not only leads to the explanation of the pathophysiological states associated with various clinical disorders but also supports the introduction of a new paradigm that may have general applications for individuals with difficulties in social behavior.

MacLean's research and writings provide a preliminary platform to investigate the relation between the vagus and social behavior. The Polyvagal Theory is a new conceptualization employing several of the features that MacLean emphasized including the importance of evolution, limbic structures and vagal afferents. The Polyvagal Theory builds on these early findings and focuses on the link between phylogenetic changes in the autonomic nervous system and social behavior. By focusing on the phylogenetic changes in the structure of the vagus and the role that the vagus plays in the neural regulation of visceral state, new insights regarding social behavior emerge. Moreover, by articulating the phylogenetically organized hierarchy of neural circuits, insights into benefits of social behavior become evident as does an understanding of the behavioral and physiological features associated with stress and psychiatric disorders.

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